



Evaluation of Unitaid's Antiretroviral Therapy (ART) Optimisation Portfolio

Authors: Fernanda Pinheiro Sequeira, Joana Pereira, Jonathan France, Lindsey Hehman, Stacie Gobin and Yasmine Bettine

Executive summary

Introduction

Through its Antiretroviral Therapy (ART) optimisation portfolio of grants, Unitaid aimed to increase access to better HIV treatments for adults and children living in low- and middle-income countries (LMICs), and to directly contribute to meeting global HIV targets. This was to be achieved by providing robust clinical trial evidence on the efficacy of optimal HIV treatment products (within specific population groups), reducing the cost of optimal regimens, and catalysing the adoption and uptake of optimal treatments in LMICs in collaboration with government and community partners.

In 2022, Unitaid commissioned Itad to conduct an evaluation of the ART optimisation portfolio's implementation (2016-22) and generate actionable recommendations. The evaluation used a theory-based and mixed methods approach. It encompassed evaluations of the four ART optimisation clinical trials, and two cross-cutting grants. The team conducted an extensive document review, multiple key informant interviews (KIIs) and focus group discussions (FDGs), as well as nine country-level deep dives. These included interviews with Unitaid's programme staff, grantees, civil society and community representatives, global scale-up and technical partners (for example, Global Fund, PEPFAR and WHO), manufacturers and government officials. The team drew on programme and grant data and documentation, as well as on other literature, such as WHO guidelines and the HIV plans of country governments.



Figure 1. Data sources of Unitaid's ART optimisation portfolio evaluation

This Executive Summary provides the key findings from the evaluation, structured around the relevance, effectiveness, sustainability, efficiency and impact of the ART optimisation portfolio, as well as recommendations for the 2023-2027 Unitaid strategy and its delivery.

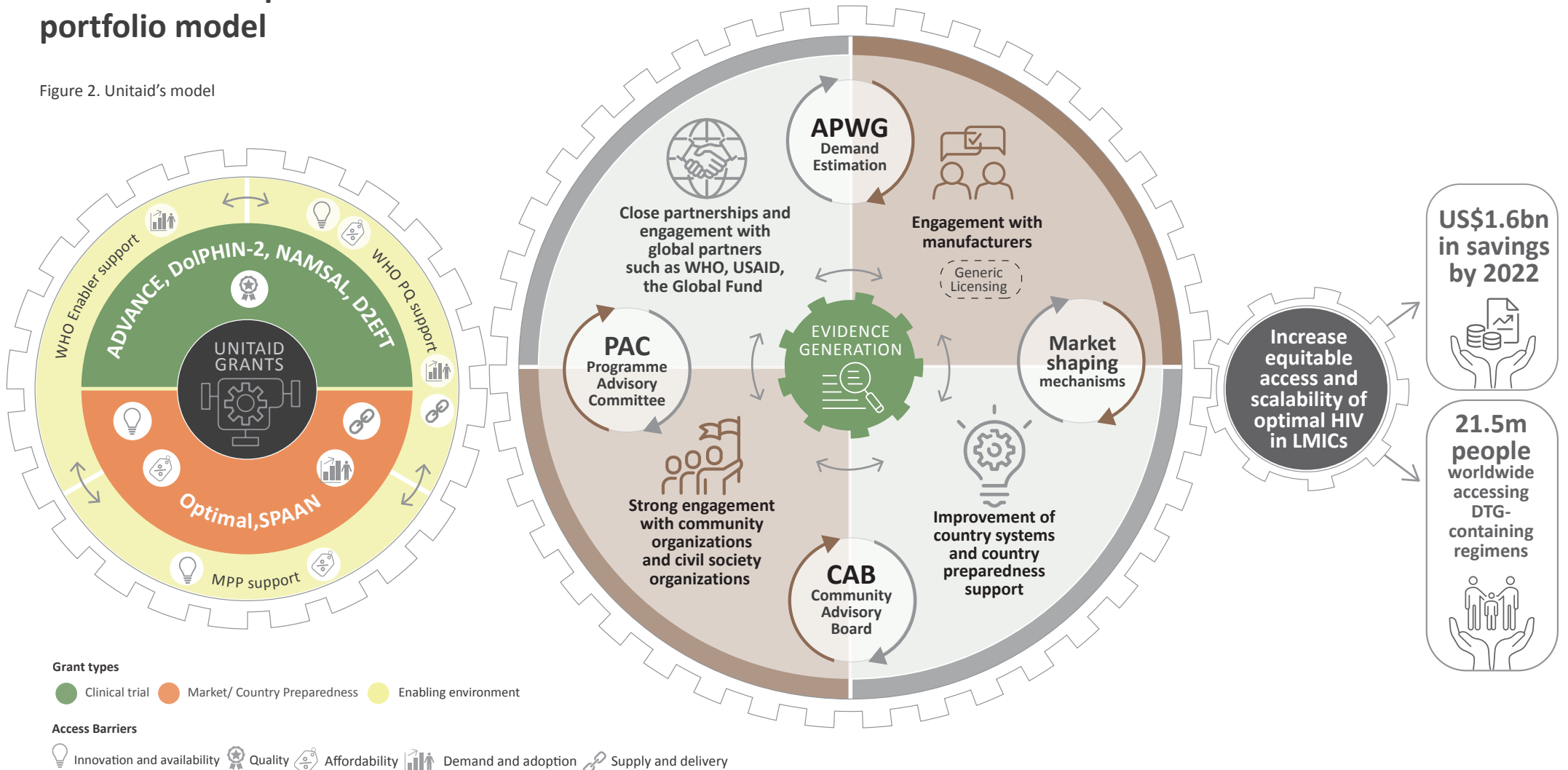
Portfolio relevance and coherence

Unitaid adopted a comprehensive approach to tackling a range of urgent supply and demand-side barriers to accessing optimal ARTs in LMICs. This included: generating evidence on the safety and efficacy of new treatments (including for women, children and other

vulnerable and underserved groups living with HIV)¹; market interventions to reduce prices and accelerate regulatory approval; and targeted support for national governments, health workers and communities to introduce the new treatments in-country.

Unitaid's ART Optimisation portfolio model

Figure 2. Unitaid's model



¹ For the purpose of this evaluation we use the following definitions: - Vulnerable populations: women and girls, and children. - Underserved populations: younger children and older people in some settings, people living with HIV on second-line and third-line treatments, and people suffering from AHD.



The ART optimisation portfolio was closely aligned with the efforts of other **partners working to expand the adoption and scale-up of better HIV treatments globally** (WHO, Global Fund, PEPFAR, etc). This alignment was achieved through the establishment of a Programme Advisory Committee (PAC) and participation in the Antiretroviral Procurement Working Group (APWG), which extended its scope to include adult antiretroviral medications (ARVs). Through annual meetings, the PAC, led by Unitaid and USAID and chaired by WHO and Global Fund, promoted collaboration among over 40 ART optimisation experts (including PEPFAR, US National Institutes of Health, and researchers) and community representatives worldwide. This committee played a crucial role in coordinating organisations committed to enhancing access to affordable, high-quality HIV care in low- and middle-income countries (LMICs), ensuring that the voices of community representatives were brought to the forefront of decision-making. Unitaid's participation in the APWG contributed to price reduction and increased availability of optimal treatment products by increasing demand visibility, commercial viability for manufacturers, and enabling adequate and stable supply planning.

Unitaid's grantees also intentionally worked closely with national governments, technical working groups (TWGs), country partners and national health systems in LMICs to support scale-up and sustainability. Unitaid added value to these partnerships through its unique catalytic and enabling roles, and by combining market shaping, country-preparedness and community-engagement activities in one comprehensive model.



Strong focus on community and civil society engagement, including through Community Advisory Boards (CABs) and the PAC, ensured the ongoing relevance of the portfolio and individual grants to the needs of people living with HIV. The presence of community representatives at PAC meetings and the creation of community driven activities (e.g. CABs) were important factors that contributed to the portfolio's success. Unitaid's portfolio approach and support of community and civil society engagement highlighted the crucial role that communities and civil society organisations can play in facilitating demand creation and the adoption of new health products.
















































Key lessons learnt

- ✓ Invest sufficient time and resources in the engagement of scale-up and technical partners, manufacturers, researchers, national ministries of health, and community actors, from the early stage of portfolio design through to grant implementation.
- ✓ For effective community engagement, utilise diverse approaches and sensitisation materials, leverage existing community and civil society groups, and create opportunities for community representatives to engage in strategic decision-making and feedback, including through tailored platforms such as the PAC and CABs.

Portfolio effectiveness: tackling barriers to access

The ART optimisation portfolio contributed to tackling all the barriers to people living with HIV accessing optimal treatments in LMICs, as identified by Unitaid during design. The portfolio’s contribution was ‘high’ with regards to most barriers (see Table 1, which summarises Unitaid’s contribution to the different barriers, by country and overall).

Table 1. Barriers to access – summary findings

Access barrier	GEOGRAPHY							
	Benin	Cameroon	Cote d’Ivoire	Keyna	Nigeria	South Africa	Uganda	Average score
 Innovation and availability								
 Quality								
 Affordability								
 Demand and adoption								
 Supply and delivery								

KEY

Unitaid contribution

 N/A

 Low

 Medium

 High

Through the comprehensive design of the portfolio, Unitaid successfully:



Demonstrated the quality and safety of Dolutegravir-based (DTG) regimens through innovative **clinical trials** (accelerating approval and availability);



Contributed to a **reduction in prices** through successful market-shaping activities; ;



Helped **improve the availability of treatments** by supporting demand visibility and aggregation (through the APWG) and strengthening supply chain systems; and



Increased demand and accelerated national adoption of optimal treatments through **government and partner engagement, health sector capacity building and community advocacy.**

By funding multiple clinical trials which filled identified evidence gaps and by directly engaging WHO, Unitaid facilitated the revision of WHO's HIV treatment guidelines and the rapid approval of HIV treatment products in LMICs. Product partnerships (including support for generic licensing and production), aggregated demand forecasts, catalytic procurement and other incentive and pricing mechanisms, contributed to reducing the cost of optimal HIV treatment products, making it easier for national governments to switch to recommended regimens. Unitaid's community engagement efforts made an important contribution to demand generation – including through boosting the acceptability of, and adherence to, new optimal regimens – by combining upstream and downstream community representation and engagement. Significant support was provided in these areas by the Optimal grant, including through the Optimal CAB as well as by the PAC, the APWG and other CABs set up through clinical trials. Manufacturers confirmed that the portfolio's close work with them through technical assistance and advocacy helped to accelerate the manufacturing of generic drugs and their time-to-market in LMICs.



Key lessons learnt

- ✓ Funding multiple trials that tackle different evidence gaps simultaneously helps accelerate the global and national policy revisions required to introduce new treatments in LMICs.
- ✓ Additional targeted research and ongoing monitoring of optimal treatments may be required for specific vulnerable and underserved populations, to alleviate any safety concerns and further inform guidelines.
- ✓ Funding simultaneous country-preparedness activities (for example, community-led demand generation activities, supporting governments with addressing supply, logistical and regulatory barriers) is critical to ensuring the smooth introduction of new treatments.
- ✓ Addressing all barriers to reaching those in need of better treatments in a reliable and timely manner requires long-term support for country governments (as part of wider health-system strengthening efforts).
- ✓ To tackle market barriers, manufacturers of lower volume paediatric and second- and third-line products may require additional support (for example, catalytic or pooled procurement) as well as ongoing product-introduction activities in country, beyond the period of grant funding.

Portfolio sustainability: scale-up of optimal treatments

Unitaid's ART optimisation portfolio was successful in supporting the transition to, and scale-up of, optimal HIV treatments, including DTG and paediatric DTG (pDTG). Trial drugs were recommended in WHO and national guidelines, prices were lowered, and optimal treatments were rolled-out across target LMICs. By 2022, DTG was recommended as the first-line HIV treatment for adults in the national guidelines of 111 LMICs (Figure 3). In addition, 75 countries had adopted pDTG.

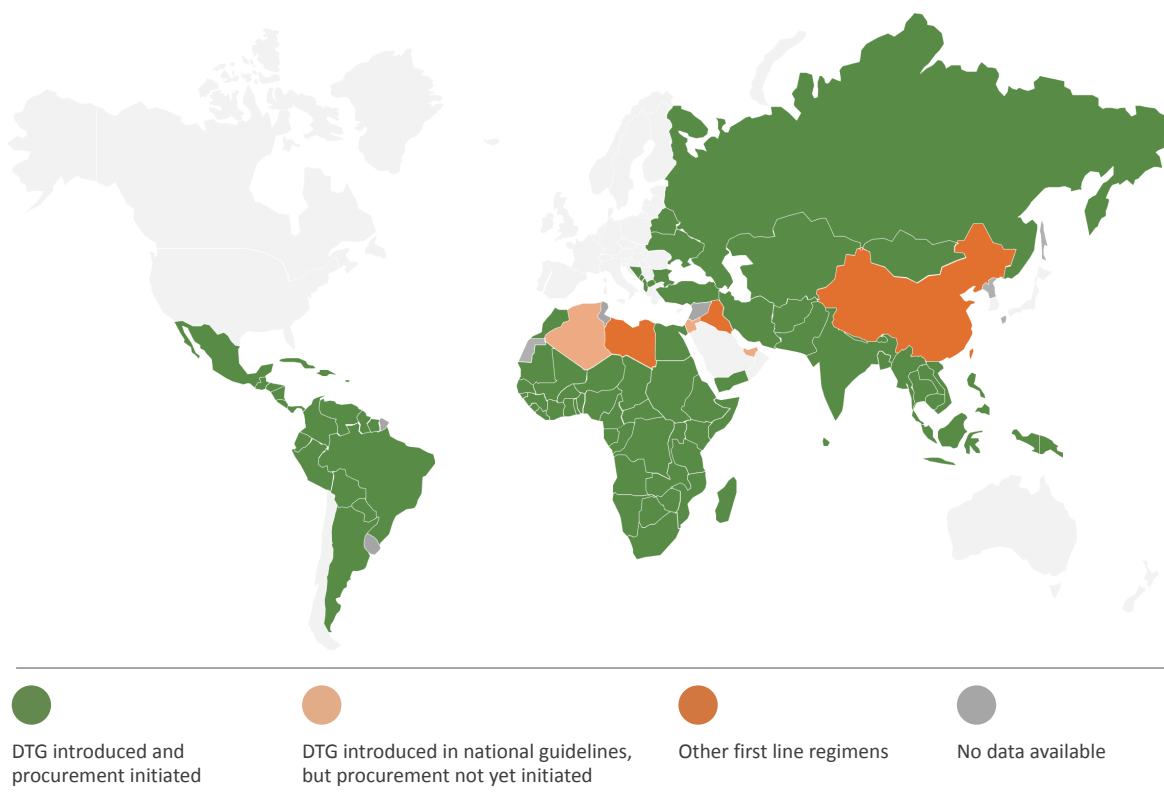


Figure 3. Status of DTG introduction in LMICs in 2022

The portfolio strengthened a wide range of global scalability and country-level readiness for scale-up conditions, which enhanced the sustainable impact of the portfolio. Within the global enabling environment, the PAC and APWG provided platforms for increased collaboration and alignment of scale-up partners working to improve access to better HIV treatments, aggregated demand and enabled more affordable pricing, accelerated the supply of optimal treatments, and facilitated the sharing of rigorous evidence on safety and efficacy (leading to updated WHO guidance, approvals and integration within national policy/planning).

Country readiness factors (listed in Table 2 below) which saw the greatest progress and strongest contributions from Unitaid included: generating national political support for scale-up; improved coordination among national partners; recommendation of optimal products within national health policies; capacity building of health workers; and strengthened advocacy capacity for community and civil society organisations (CSOs).

KEY	Unitaid contribution			Scalability status						
	Low	Medium	High	High	5	4	3	2	1	Low
Country-level scalability factor				2016	2022	Unitaid's contribution				
Secure political and financial support										
Critical decision makers demonstrate political support for national scale-up of optimal HIV treatments.				2	4					
Major donors actively collaborate and allocate funding to enable national scale-up in a coordinated manner.				4	5					
National governments signal support for scale-up by allocating resources (for example, national budget line for products/interventions).				3	4					
Ensure programmatic and operational readiness										
The product/intervention is recommended in national and subnational health policies .				2	5					
National health systems have adequately trained staff, supplies and other resources to enable quality and equitable scale-up of the product/intervention.				2	4					
Create community-driven demand										
Civil society groups have been strengthened to actively demand equitable access to the product/intervention.				2	4					
Grassroots organisations/communities have been strengthened to actively demand equitable access to the product/intervention.				2	3					

Table 2. Country-level average scalability factor change (2016–22) and Unitaid’s contribution

Amongst *country-level factors*, leveraging greater domestic resources and strengthening grassroots CSOs/national advocates, showed a mixed level of success. In terms of *global-level factors*, it was found that further work is needed on synthesising and sharing the lessons learnt on implementation, including how to facilitate the successful scale-up of optimal treatments (within a range of health systems).

Key lessons learnt

- ✓ Early and ongoing engagement with national governments, working within existing ministry and donor partnership structures, is critical to the successful scale-up of optimal treatments in LMICs.
- ✓ Guaranteeing future national ownership of scale-up emerged as a key challenge, for example, in ensuring that governments meet their domestic resourcing commitments, and in addressing ongoing capacity-strengthening needs. This requires the development of robust handover/scalability plans, and alignment with broader partner efforts to strengthen HIV policies and health systems in-country.
- ✓ Putting in place the conditions for sustainable advocacy from civil society was highlighted as a further solution—and one where Unitaid can make a difference—to ensuring that governments and partners meet their scale-up commitments.
- ✓ Establishing a sustainable market for some low-volume products for vulnerable and underserved populations is a challenge that requires sustained supply plans with manufacturers, including potentially longer-term incentives.

Portfolio efficiency

Unitaid's Secretariat was broadly efficient and effective. It maintained strong leadership and collaboration with grantees throughout the design of the portfolio and its implementation, including sharing lessons learnt to aid adaptation. Grantees reported consistent collaboration with Unitaid in the form of regular calls, country visits and in-person meetings, and felt that the Unitaid secretariat added value by providing thought-leadership and strategic direction.

Despite the delays caused by Covid-19 and other challenges, Unitaid's collaborative and adaptive approach to grant management, as well as strong risk management, allowed the portfolio to be implemented on track. Unitaid provided the necessary support and flexibility to allow grants (including clinical trials) to course-correct and respond to challenges such as safety and supply risks – and changing government priorities – during the Covid-19 pandemic, and grantees responded with innovative solutions.

Grantees praised Unitaid for its flexibility in supporting reprogramming and adaptations but also reported that these processes can be lengthy and cause some delays during implementation (for example, in relation to the clinical trials). Systems and processes, including expediting funding decisions and monitoring requirements, could have been more efficient.

Partners such as representatives from national governments or non-governmental organisations, thought that the role of Unitaid was not always clear and visible in-country. This surfaced as a potentially missed opportunity, as several stakeholders agreed that a stronger presence in-country would contribute to the consolidation of key relationships and the elevation of Unitaid's profile in-country and globally.

The evaluation did not conduct a full value-for-money analysis, but the available evidence suggests that, overall, the portfolio has been cost-effective. Individual grants, as well as components such as community engagement, delivered good value for money considering their costs, results and impact. However, two significant points surfaced from the data analysis. Firstly, two countries reported that the rapid acceleration of DTG adoption led to the waste of some existing ARVs—not optimal from a value-for-money perspective despite the clear benefits for public health outcomes. Finally, suggestions were made to highlight that the value for money of community engagement activities could potentially be enhanced through direct funding for community organisations.



Key lessons learnt

- ✓ Unitaid's flexibility in allowing grantees to adapt was critical to the efficient delivery of outputs.
- ✓ Grant monitoring and reporting requirements should take into account differences in the types of investments.
- ✓ Improved communication to partners regarding Unitaid's role, the work it funds and its portfolio successes could support Unitaid's influencing role and foster stronger buy-in (to scale-up optimal treatments, for example).
- ✓ The phasing of procurement and roll-out of new regimens should aim to minimize the wastage of legacy stock to help improve value for money (whilst noting that, longer-term, the clinical benefits of new products can outweigh potential financial losses).

Portfolio impact

The evaluation found that Unitaid played a pivotal role in contributing to significantly expediting access to high-quality HIV treatments for marginalized and underserved populations in LMICs, leading to improved tolerability and efficacy for viral suppression, as well as advancing progress towards global HIV targets. For example, in 2019, 28% of adults accessing first-line ART in LMICs were estimated to be on DTG-based regimens, with this number increasing to 91% by 2022. This is equivalent to more than 21.5m people worldwide accessing DTG-containing regimens. The Clinton Health Access Initiative (CHAI) estimates that 25m adults will have transitioned to DTG-containing regimens by 2028, and that as a result of this transition 1.1m lives will be saved by 2027. In terms of equity impact, the ART optimisation portfolio was instrumental in shaping policy and triggering change in treatment guidelines for women living with HIV.

In addition, the portfolio helped deliver reduced treatment costs for optimal ART in LMICs. It also generated longer-term and more significant savings in the targeted countries through improved health outcomes. According to CHAI estimates, the Optimal grant generated over US\$1.6bn in savings by 2022, with forecasted savings of US\$7.8bn by 2028 (see Figure 4).

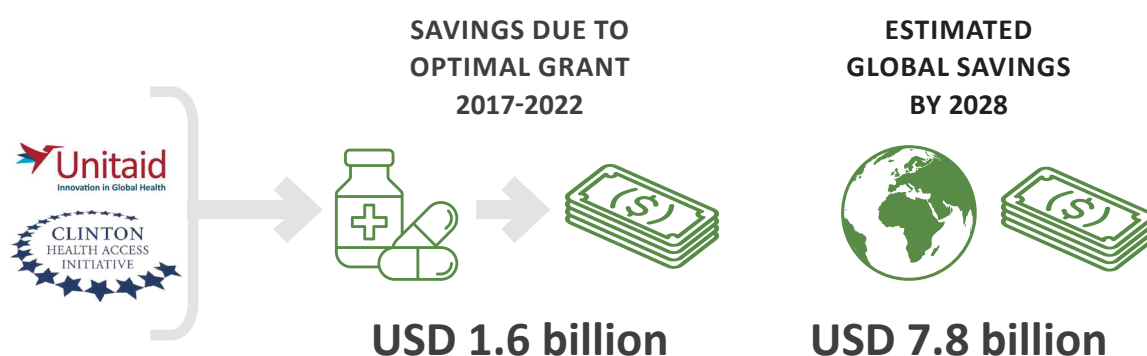


Figure 4. Savings generated by the Optimal grant






Unitaid's impact was facilitated by supportive policy environments and strong relationships with global and country partners who were active in scaling-up HIV treatments. The evaluation also found a range of wider strategic benefits from the portfolio, including Unitaid and its partners learning from and adopting the successful community engagement model.



Key lessons learnt

- ✓ Further targeted action is required to reduce deaths from HIV among particular underserved groups, including through the ongoing roll-out of paediatric formulations for children, and the introduction of optimal diagnostics and treatments for people living with HIV with advanced HIV disease (AHD) – whom Unitaid is currently targeting – and support for their uptake.

Conclusions

-  Through effectively targeting a range of relevant barriers simultaneously, Unitaid has **accelerated access** to optimal HIV treatments (including DTG and DTG-based regimens) for vulnerable and underserved groups in LMICs (including women and children). Unitaid has also: supported **global and country scalability**, delivered **high impact** (including on viral suppression and lives saved amongst people living with HIV) and provided **good value for money**.
-  Unitaid's **comprehensive model** was innovative and pivotal to the portfolio's success. The market-shaping and country-preparedness work (conducted under Optimal and SPAAN) were critical to the availability and introduction of new treatments in LMICs, whilst the clinical trial grants (simultaneously) filled important gaps in rigorous research focusing on vulnerable and underserved groups, further facilitating new product development and regulatory approval.
-  Major success factors included: the Unitaid secretariat's development and leverage of **strong and ongoing relationships** with global partners, country governments, grantees and industry; the **adaptability** of the grants and the portfolio and management at Unitaid and grantee level; and Unitaid's **community engagement** activities. On the other hand, key constraining factors comprised challenges in navigating government and regulatory systems, including traditional procurement and supply-planning cycles and systems.
-  An overarching **key lesson learnt** is that the comprehensive model of intervention is required to effectively tackle the range of barriers that exist to improving access to optimal HIV treatments in LMICs: shortcomings in tackling any one barrier (for example, in country governance, or supply chains) will weaken the overall impact and sustainability of a portfolio, however effective it might be in other areas.
-  The major **identified areas for improvement** include working on sustainable handover plans with country governments, ensuring more sustainable markets for low-volume products for the most underserved groups, further support for capacity-strengthening of grassroots community representation and aspects of portfolio-management efficiency, and better communication/visibility of Unitaid's important contributions to ART optimisation in-country.

Recommendations

Based on the evaluation's findings and conclusions, we provide the following **actionable recommendations** for Unitaid's consideration, organised around the three pillars of its new strategy:

Pillar 1

Accelerate the introduction and adoption of key health products



1. Develop long-term strategies for removing access barriers to specific underserved groups, including children living with HIV, people on second and third-line treatments and people suffering from AHD.
2. The PAC, or a similar strategic body, should be reconvened to strategize and coordinate scale-up partners around addressing remaining gaps in access to optimal HIV treatments in LMICs.
3. Prioritise delivering fully-comprehensive intervention models within target countries.
4. Improve the communication of news and successes from Unitaid investments, tailoring them to different audiences, to generate further buy-in and help drive impact.
5. Integrate impact evaluation methodologies and a Value for Money assessment within future evaluations.

Pillar 2

Create systemic conditions for sustainable, equitable access



6. Strengthen the collection and dissemination of evidence on successful implementation models to support replicability and scalability across LMICs.
7. Strengthen scalability plans within target countries, working closely with national governments and their partners, to help ensure the sustainability of country readiness activities following Unitaid's investment.
8. Scalability plans should ensure support for the integration of community representation within regular HIV treatment planning and funding cycles (and strengthen connections with grassroots community groups).
9. Consider adapting Unitaid's grant mechanisms to fund LMIC community organisations directly, and/or help build CSO capacity to manage larger grant funding.

Pillar 3

Foster inclusive and demand-driven partnerships for innovation



10. Leverage the experience and capacity of the established community network (community members and CSOs) to support Pillar 3 of Unitaid's 2023-2027 strategy, including future work on HIV and other diseases.
11. Strengthen Unitaid's visibility in-country, including through more frequent and predictable country visits, virtual engagements, programme debriefs and/or virtual presentations/workshops/programme debriefs with government and in-country partners.
12. Improve the operational efficiency of the secretariat and project team in some key areas, including better differentiating reporting requirements by type of grantee, and streamlining processes for reprogramming and funding.