

# Final Report

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

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## List of acronyms

ACP	STD/AIDS control programme
Afi	Area for intervention
AHD	Advanced HIV disease
ALD	Abacavir-lamivudine-dolutegravir
ANRS	Agence Nationale de Recherche sur le Sida et les Hépatites Virales
APWG	Antiretroviral Procurement Working Group
ART	Antiretroviral treatment
ARV	Antiretroviral
BE	Bioequivalence
BMGF	Bill & Melinda Gates Foundation
CAB	Community advisory board
CAB-LA	Cabotegravir long-acting injectable
CDC	Centers for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
COHIVE	Coronavirus Outcomes in HIV Evaluation in Resource Limited Settings
CSO	Civil society organisation
CSSE	Community and civil society engagement
DSMB	Data and Safety Monitoring Board
DRV/r	Darunavir/ritonavir
DTG	Dolutegravir
EFV	Efavirenz
EFV400	Efavirenz 400mg
EGPAF	Elizabeth Glaser Paediatric AIDS Foundation
EQ	Evaluation question
EVA	External verification agent
FDA	Food and Drug Administration
FGD	Focus group discussion
GAP-f	Global Accelerator for Paediatric Formulations
Global Fund	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HIC	High-Income Country
HSS	Health systems strengthening
KEMSA	Kenya Medical Supplies Authority
KII	Key informant interview
KPI	Key performance indicator

LMIC	Low and middle-income country
LPV/r	Lopinavir/ritonavir
MoH	Ministry of Health
MPP	Medicines Patent Pool
NASCOP	National AIDS and STI Control Programme
NGO	Non-governmental organisation
NTD	Neural tube defect
OECD	Organisation for Economic Co-operation and Development
OECD-DAC	OECD Development Assistance Committee
PAC	Programme advisory committee
pALD	Pediatric abacavir-lamivudine-dolutegravir
pDTG	Pediatric dolutegravir
pDRV/r	Pediatric darunavir/ritonavir
PE	Procurement entity
pDTG	Paediatric DTG
PEPFAR	United States President's Emergency Plan for AIDS Relief
PNLS	Programme National de Lutte contre le Sida
PPPY	Per person per year
PQ	Prequalification
pTAF	Paediatric tenofovir alafenamide
RfP	Request for proposals
SPAAN	Securing Paediatric ARV Access Now
TAC	Treatment Action Campaign
TAF	Tenofovir alafenamide
TB	Tuberculosis
TDF	Tenofovir disoproxil fumarate
TLD	Tenofovir disoproxil, lamivudine, dolutegravir
ToC	Theory of change
TRIO	NAMSAL, DolPHIN-2 and ADVANCE
TWG	Technical working group
UK	United Kingdom
UNAIDS	Joint United Nations Programme on HIV/AIDS
US	United States
USAID	US Agency for International Development
WHO	World Health Organisation



# 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 the 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)<sup>1</sup>; 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.

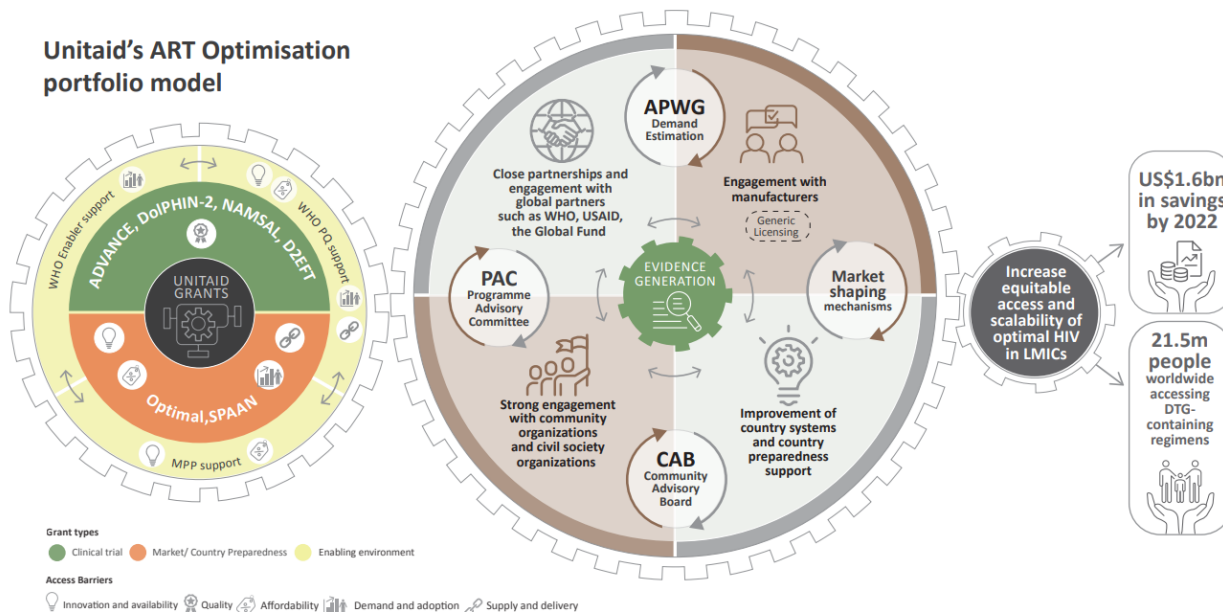


Figure 2: Unitaid’s model

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

<sup>1</sup> 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.

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

Table 1 Barriers to access – summary findings

		Geography							
Access barrier		Benin	Cameroon	Côte d’Ivoire	Kenya	Nigeria	South Africa	Uganda	Global
	Innovation and availability	Medium	High	High	N/A	High	Medium	High	High
	Quality	Medium	High	High	N/A	High	High	High	High
	Affordability	Medium	High	High	High	High	High	High	High
	Demand and adoption	Medium	High	High	High	High	Medium	Medium	High
	Supply and delivery	Medium	High	High	High	Medium	Medium	Medium	Medium

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). 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, Unitaïd 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. Unitaïd'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

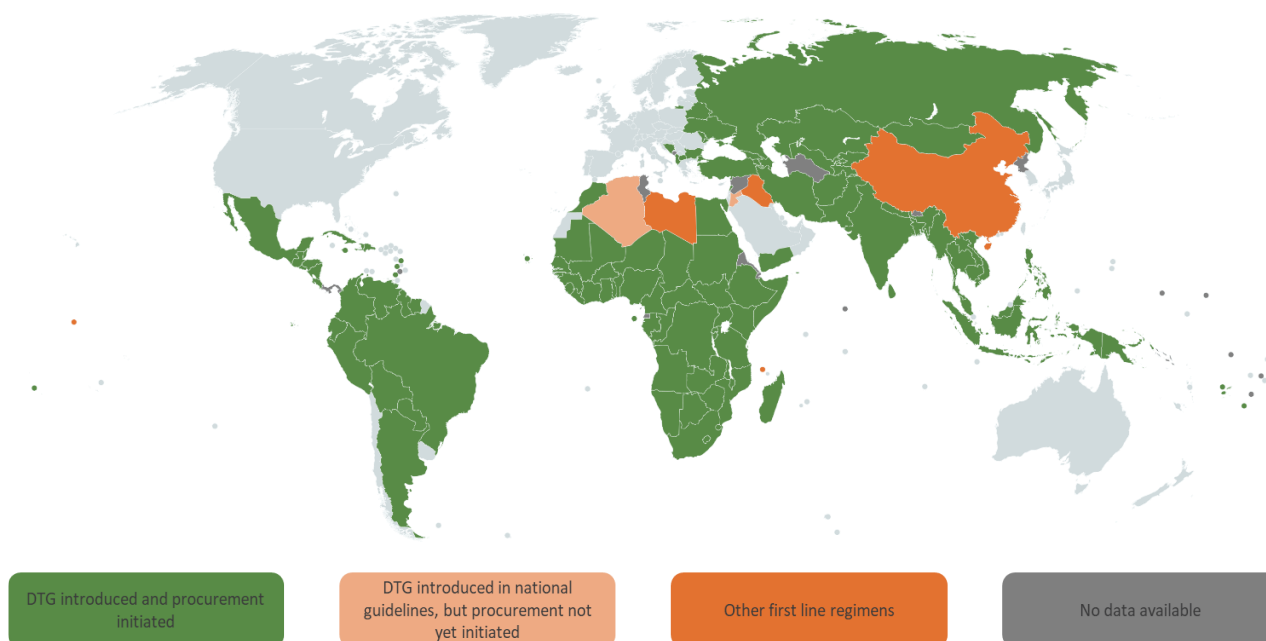


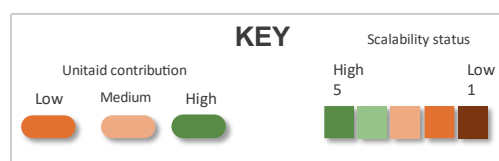
Figure 3. Status of DTG introduction in LMICs in 2022

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.

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 the Table 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).

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



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

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

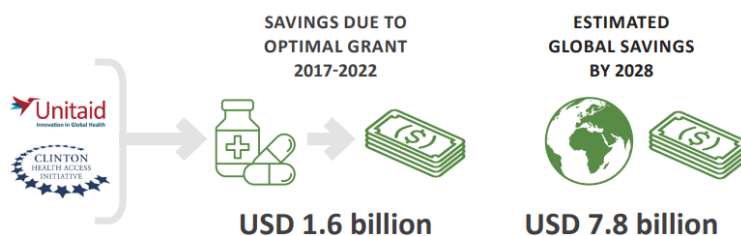


Figure 4 Savings generated by the Optimal grant

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).

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 and recommendations

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.

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 strategise 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.

# 1 Introduction

UNAIDS (Joint United Nations Programme on HIV/AIDS) published a report in 2015 showing that, if 90-90-90 targets were achieved by 2020, the HIV/AIDS epidemic would end by 2030.<sup>2</sup> However, to achieve those targets, HIV funding would need to increase considerably and low and middle-income countries' (LMICs) access to treatment would need to double in the span of five years. Recognising this urgency, global health partners swiftly collaborated to identify a selection of priority products to be implemented in LMICs. The expectation was that these products would enhance the utilisation of antiretroviral therapy (ART) in LMICs, leading to substantial improvements in both health outcomes and budget allocation. Yet, these products had not been tested in LMIC settings, so neither the World Health Organisation (WHO) guidelines nor LMICs recommended them widely.

In the same year, Unitaids' Executive Board endorsed the area for intervention (Afl) "improving antiretroviral therapy in low and middle-income countries," paving the way for Unitaids' investment in this space and for the establishment of the ART optimisation portfolio. This portfolio aimed to increase the access to, and adoption of, optimal first- and second-line treatment for adults and children in LMICs by: (1) providing critical evidence on the safety and efficacy of optimal HIV treatment products in diverse populations, and (2) using market shaping mechanisms to accelerate the market entry of these optimal HIV treatment products. This was undertaken to inform WHO HIV treatment guidelines, to reduce the cost of optimal regimens and to prepare the ground in LMICs for the adoption and uptake of these regimens through supply- and demand-side interventions.

The portfolio included six grants, which covered four Phase III clinical trials (ADVANCE, DolPHIN-2, NAMSAL and D<sup>2</sup>EFT) and two catalytic implementation initiatives (Securing Paediatric ARV Access Now—SPAAN—and Optimal). It also comprised three cross-cutting enabling grants: WHO HIV enabler, Medicines Patent Pool (MPP) and WHO prequalification (PQ). In addition, as part of the portfolio, an Optimal community advisory board (CAB) and a programme advisory committee (PAC) were established to help with awareness, demand creation and support portfolio implementation.

As the grants in the ART optimisation portfolio drew to a close, Unitaids wanted to step back and understand the contribution of its work to increasing access to optimal first- and second-line treatment for adults and children in LMICs, lowering access barriers, and supporting global and country scale-up. As a result, in September 2022, Unitaids commissioned Itad – a UK management consultancy specialising in monitoring, evaluation and learning – to conduct an evaluation of its ART optimisation portfolio implementation between 2016 and 2022 and to generate actionable recommendations to support Unitaids' future investments in ART optimisation in the new 2023–27 strategy cycle.<sup>3</sup>

## 1.1 Evaluation objectives

The overall purpose of this evaluation was to assess the relevance, coherence, efficiency, effectiveness, impact and sustainability of Unitaids' ART optimisation portfolio and to identify lessons learnt, good practices and actionable recommendations to inform Unitaids' next steps in ART optimisation space.

The evaluation required a light touch assessment of the individual performance of the six ART optimisation grantees and Unitaids' Secretariat. It also involved an overall assessment of Unitaids' portfolio contribution between 2016 and 2022 to closing critical gaps and accelerating the access to and scale-up of optimal HIV treatment in LMICs. Finally, it looked at the complementarity and

<sup>2</sup> [https://www.unaids.org/en/resources/documents/2015/UNAIDS\\_PCB37\\_15-18](https://www.unaids.org/en/resources/documents/2015/UNAIDS_PCB37_15-18).

<sup>3</sup> [https://unitaid.org/assets/Unitaid\\_Strategy\\_2023-2027.pdf](https://unitaid.org/assets/Unitaid_Strategy_2023-2027.pdf).<sup>3</sup> The United Nations set ambitious targets to end the HIV/AIDS epidemic. Called the 95-95-95 targets, these goals aim to ensure that 95% of people living with HIV know their status, 95% of people who know their status are receiving treatment and 95% of people on HIV treatment have a suppressed viral load by 2030.

synergy of the direct and enabling investments and in the context of other partners working in this field (for example, the United States Agency for International Development (USAID) and the United States President's Emergency Plan for AIDS Relief (PEPFAR)).

In summary, this evaluation aimed to provide information about the following:

- The **collective performance** of the portfolio against its strategic aims and objectives.
- The extent to which **Unitaid's model of combining evidence generation, community engagement, market shaping and partner engagement** mechanisms was effective.
- The ability of **clinical trials to adapt** effectively, according to emerging evidence.
- The role of **Unitaid's secretariat** in supporting the implementation of the ART optimisation portfolio.

## 1.2 Final report

This final evaluation report synthesises the overall findings, conclusions and recommendations of the ART optimisation portfolio evaluation. It details the extent to which the portfolio has contributed to the following:

- Accelerating the introduction of quality-assured, fit-for-purpose health products/innovations in LMICs.
- Improving equitable access to optimal HIV treatments, using market-shaping approaches.
- Facilitating demand, adoption and scale-up to generate impactful and sustainable gains across LMICs.

The report's findings and conclusions are structured according to the criteria of the OECD Development Assistance Committee (OECD-DAC): relevance, coherence, effectiveness, efficiency, scale-up/sustainability and impact. With each finding, we provide a graphic outlining the strength of supporting evidence, based on our strength of evidence framework (see Table 3). Finally, our recommendations follow the three strategic objectives in Unitaid's 2023–27 strategy.

Table 3. Strength of evidence framework

Rank	Justification	Evidence...
1 (good)	The finding is supported by multiple data sources of generally strong quality (good triangulation).	Is based on a good degree of triangulation (a) within interviews, (b) across stakeholders and types of stakeholders, and/or (c) across data sources. Considers the position, knowledge, analytical capacity, reflexivity and potential biases of primary informants (and also what we know about the broader context around ART optimisation).
2 (moderate)	The finding is supported by few data sources, of lesser quality (limited triangulation).	Suffers from shortcomings in triangulation and/or Is affected by minor concerns that the position, knowledge, analytical capacity, reflexivity and potential biases of primary informants lowers its reliability.
3 (poor)	The finding is supported by very limited evidence (single source) or by	Comes from a small number of sources with limited triangulation and/or Is affected by major concerns that the position, knowledge, analytical capacity, reflexivity and potential biases of primary informants lowers its reliability.

	incomplete or unreliable evidence.	
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Section 1 Introduces the evaluation. Section 2 defines the evaluation’s approach, methodology and limitations. Section 3 presents an overview of the relevance and coherence of the ART optimisation portfolio, while Section 4 outlines its results. Section 5, 6 and 7 provide – respectively – our findings regarding sustainability (including supporting global conditions for scale-up as well as country readiness), efficiency and impact. Finally, Section 8 specifies the evaluation’s main conclusions and recommendations for Unitaid.

## 2 Evaluation approach, methodology and limitations

### 2.1 Evaluation approach

As shown in Figure 5, the approach was designed around two main analytical workstreams: clinical trial grants (Workstream 1) and market-shaping and country-preparedness grants (Workstream 2), and supported by a light-touch review of the cross-cutting grants.

These workstreams were designed to identify the extent to which the grants did the *right things* (relevant activities and outputs) in the *right way* (engaging stakeholders and course correcting) to achieve the *right results* (outcomes). The workstreams also identified how the grants contributed to Unitaid’s goal of improving access to optimal HIV treatment in LMICs and to the achievement of the UNAIDS 95-95-95 fast-track targets for HIV elimination.<sup>4</sup>

Across both workstreams, we collected data on the important cross-cutting issues of community engagement, demand generation, partner engagement and equity—and on what has or has not worked.

The overall approach was theory-based, utilisation-focused and underpinned by equitable, inclusive and environmentally sustainable principles (see Box 1).

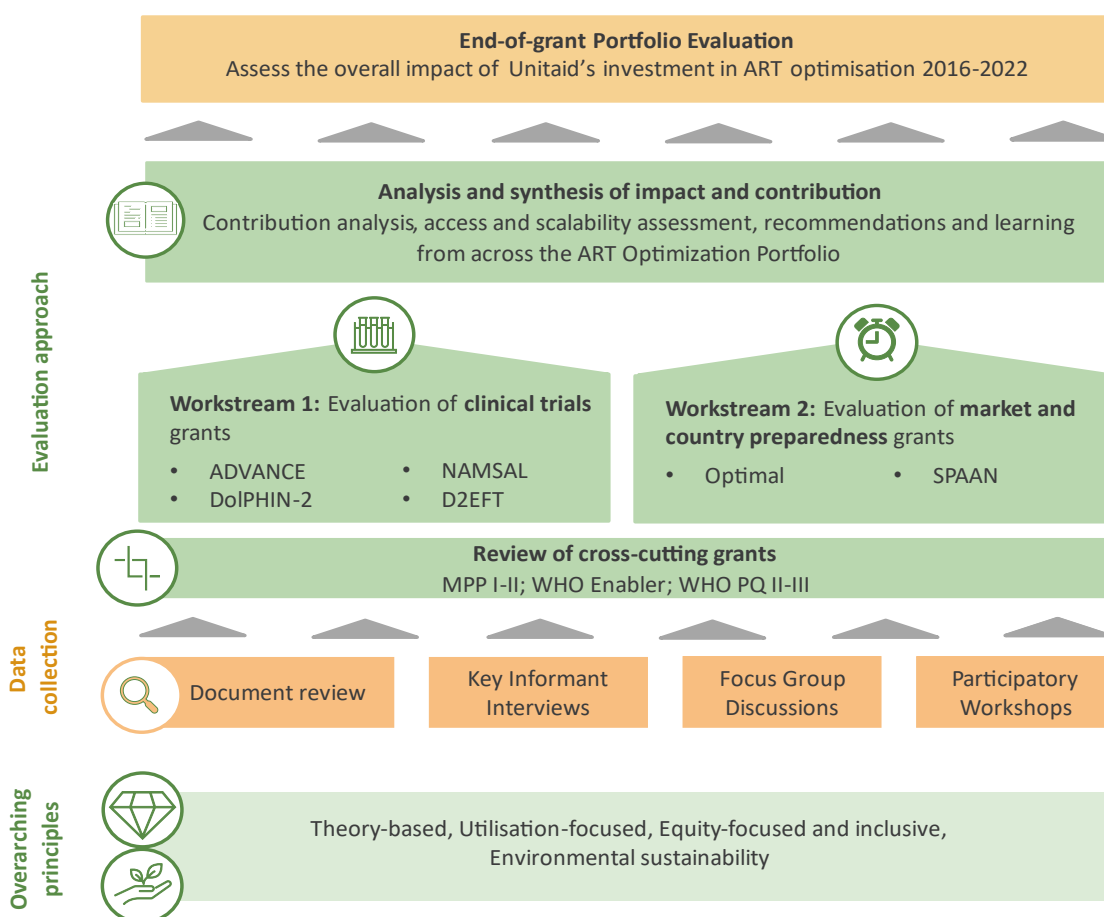


Figure 5. Approach diagram

<sup>4</sup> The United Nations set ambitious targets to end the HIV/AIDS epidemic. Called the 95-95-95 targets, these goals aim to ensure that 95% of people living with HIV know their status, 95% of people who know their status are receiving treatment and 95% of people on HIV treatment have a suppressed viral load by 2030.

### Box 1. Overarching approach

- **Theory-based:** We tested the assumptions and explanations underlying processes. This in turn helped us conceptualise and document the long-term change that the ART portfolio intended to support.
- **Utilisation-focused:** The evaluation was implemented to foster a strong sense of engagement with and ownership of the evaluation process and outputs among the primary intended users within Unitaid.
- **Equity-focused and inclusive:** Evaluation questions addressed these issues and sought to understand whether the portfolio adhered to these principles throughout implementation.
- **Environmentally sustainable:** We reduced the project's carbon footprint by having a core team working remotely, having the in-country data collection performed by locally based consultants and by having workshops and presentations conducted entirely online.

## 2.2 Design and methodology

Our evaluation design was centred on the OECD-DAC evaluation criteria. As a result, the evaluation aimed to understand the relevance, coherence, efficiency, effectiveness, impact and sustainability of the ART optimisation portfolio, focusing on 17 main evaluation questions (EQs) related to both the OECD-DAC criteria and Unitaid’s learning interests (see Annex C for the evaluation matrix).

The methodology drew on contribution analysis principles. Contribution analysis is a flexible evaluative approach. It allows for the assessment of the relative contributions of different factors and actors to the outcomes of interest. Underpinning this contribution analysis is the idea that no one factor causes change. This approach is particularly useful in complex settings such as the improvement of HIV treatment outcomes.

As the ART optimisation portfolio did not have an explicit theory describing how to achieve its aims, during the inception phase we developed a Theory of Change (ToC) to guide the analysis and findings of this evaluation (see Annex F).

### 2.2.1 Data sources

We collected data in person in 7 countries (Benin, Cameroon, Cote d'Ivoire, Kenya, Nigeria, South Africa, and Uganda) and remotely in 2 countries (Malawi and Zimbabwe). In addition, we conducted remote focus group discussions (FGDs) and key informant interviews (KIIs) with global stakeholders.

Each of the 7 teams that carried out in-person data collection produced a country report. These reports were structured using the evaluation matrix and summarised learnings from each country. The final evaluation report was informed by a number of data sources (Figure 6).



Figure 6. Data sources of the Unitaid’s ART optimisation portfolio evaluation

We triangulated KIIs and FGDs with grantees,

Unitaid, global partners, manufacturers and APWG members with country reports and a document review. This allowed for informed analysis on the degree to which the ART optimisation portfolio model and its grantees contributed to change in HIV treatment, as well as on the factors that shaped change and on the role played by Unitaid.

### 2.2.2 Analysis and synthesis

Data from all sources were thematically coded in MAXQDA, using a coding tree based on the evaluation matrix. The analysis from the country reports was triangulated and synthesised into this report's findings.

Triangulation in our analysis took place at three levels (where possible) and informed the strength of evidence for the findings, as follows:

- different data collection methods
- different stakeholder groups
- different team members

In total, we coded 4,832 excerpts of data, which we gathered from 26 global KIIs, seven country reports and more than 300 documents reviewed. See Annex D for more details on how the excerpts were distributed across a selection of key codes for an indication of the strength of evidence behind the findings.

## 2.3 Limitations

The limitations of this evaluation include:

**Limited resources allocated to in-country consultants.** The Itad team comprised six in-country consultants who assisted in data collection, analysis and reporting. Collectively, they were responsible for conducting most of the in-country interviews for this evaluation. However, due to resource limitations, they were not able to engage much in the writing of this final report.

**The contribution of Unitaid was less known to some in-country stakeholders.** Unitaid does not have country offices and operates through partnerships to fast-track access and reduce the costs of more effective medicines, technologies and systems. We found that some stakeholders at the country level were not aware of Unitaid's contribution to the roll-out of optimal HIV treatment. For example, all stakeholders interviewed in Benin were unaware of the Optimal grant or that Unitaid supported the Clinton Health Access Initiative (CHAI). In addition, as the Bill & Melinda Gates Foundation (BMGF) also supported CHAI, it was difficult to separate Unitaid's contribution from BMGF's in this sense. This was also true of contributions from Unitaid and other funders in other cases.

### 3 Relevance and coherence of the ART optimisation portfolio

This section reports on the relevance and coherence of Unitaid’s ART optimisation portfolio. It firstly provides the background to the portfolio (3.1) and describes its funded grants and governance arrangements. This is followed by our findings on the relevance of the portfolio to people living with HIV, including Unitaid’s approaches to market shaping and community engagement (3.2). Finally, we assess the coherence of the ART optimisation portfolio with the work done by global and national partners (3.3).

#### Summary points

- Through a relevant design – capable of tackling supply and demand side barriers in LMICs – Unitaid’s ART optimisation portfolio addressed the urgent need for new evidence, market intervention and support for national governments to help improve access to optimal ART for people living with HIV, including women and children.
- Strong community and civil society engagement, including through community advisory boards (CAB) and the programme advisory committee (PAC), helped to ensure the ongoing relevance of the portfolio and individual grants to people living with HIV.
- The portfolio was coherent with the work of scale-up partners in the HIV treatment space, in particular by working through the PAC and APWG, as well as in partnership with national governments and implementers within national health systems in LMICs.
- Unitaid added value in unique catalytic and enabling roles by combining market shaping, country preparedness and community engagement activities in one comprehensive model (Unitaid was particularly successful in achieving this combination, when compared with other donors and partners).

#### Key lessons learnt

- Time and resources invested in the engagement of global scale-up partners, manufacturers and researchers – including through tailored platforms such as the PAC – facilitates more effective collaboration and synergies.
- At a country level, broad-based engagement (pivoting around country governments) is critical to the effective implementation of Unitaid’s comprehensive model and approach.
- Engagement with community and civil society representatives is important during both the design and implementation stages, and at the strategic (upstream) and country (downstream) levels, to support portfolio and grant relevance and acceptability.
- Effective community engagement involves systematically building this into grant activities from the start, utilising diverse sensitisation materials, drawing on existing groups, and elevating community representatives to the strategy level through the use of CABs.

### 3.1 Background to the portfolio

#### 3.1.1 Public health context

In 2015, UNAIDS published a report showing that achieving the 90-90-90 fast-track targets<sup>5</sup> by 2020 would end the HIV/AIDS epidemic by 2030. This report stated that reaching these goals would largely depend on achieving targeted coverage rates. For this to be possible, UNAIDS suggested that

<sup>5</sup> A concept introduced by the United Nation’s programme on HIV/AIDS in 2013. The idea was that by 2020, 90% of people who are HIV infected would be diagnosed, 90% of people who are diagnosed would be on antiretroviral treatment and 90% of those who receive antiretrovirals would be virally suppressed.



there was a need to double the number of people accessing treatment in LMICs within five years.<sup>6</sup> In this context, global partners<sup>7</sup> agreed on a shortlist of priority products, which could contribute to the effort of increasing the number of people on ART in LMICs, resulting in substantial health and budgetary benefits around the world.

The products list included lower dose efavirenz 400mg (EFV400); darunavir/ritonavir (DRV/r); tenofovir alafenamide (TAF); and dolutegravir (DTG). Each of the products had shown superior or non-inferior efficacy compared to the existing standard of care. In some cases, they also demonstrated improved durability and tolerability and fewer adverse events.

Nonetheless, the practicality of many of the new treatment options had not been tested extensively in LMIC settings and were, therefore, not widely included in WHO and country guidelines.


Thus, for these more optimal products to be introduced in LMICs, sufficient efficacy and safety evidence had to be generated for key populations in resource-limited settings (for example, pregnant women and tuberculosis (TB) co-infected people and children). Furthermore, the market conditions on both the supply and demand sides needed to be improved, specifically around incentivising generic manufacturing and novel combinations, improving the time-to-market on the supply side, reducing the cost of goods sold and the final ex-works prices, and creating an enabling environment for product uptake.

### 3.1.2 Portfolio design

In 2014, Unitaid held its first HIV market forum, co-hosted with WHO. It brought together a diverse group of stakeholders and experts and created an opportunity for them to discuss the challenges and gaps in accessing optimal treatments and to identify potential market interventions to strengthen the response to HIV in LMICs. This served as a starting point for the design of the Unitaid ART optimisation portfolio.<sup>8</sup>

The design of the portfolio was informed by the need to improve access to optimal ART in LMICs, building on Unitaid's previous work. This area for intervention focused on promoting the earliest possible adoption of first- and second-line formulations using the evidence needed for the adoption of new ART. This evidence was generated by specific clinical trials for priority regimens. A portion of the portfolio focused on preparing the market to accelerate the adoption and scale-up of newer regimens (considering formulations, prices and demand) in cases where they were to be introduced into country treatment guidelines.<sup>9</sup> This work would be supported and coordinated alongside two main global partners: the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and PEPFAR.

The ART optimisation portfolio included six main grants (ADVANCE, DoLPHIN-2, NAMSAL, D<sup>2</sup>EFT, Optimal and SPAAN) and three cross-cutting grants (WHO HIV enabler, MPP and WHO PQ). The four Phase III clinical trials supported by Unitaid aimed to generate the evidence required for the inclusion of new optimal formulations and products into WHO and national treatment guidelines. This was expected to contribute to global-level policy changes in ART optimisation. These trials were



Year	People on ART	CLHIV on ART
2015	17.1 million	39%
2021	28.7 million	52%

Figure 7. Increase of people living with HIV and % children living with HIV on ARTs, 2015–21

Source: CHAI market reports 2016–22

<sup>6</sup> UNAIDS, fast-track: ending the AIDS epidemic by 2030, 2014 -

[https://www.unaids.org/sites/default/files/media\\_asset/JC2686\\_WAD2014report\\_en.pdf](https://www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf).

<sup>7</sup> In meetings such as the conferences on drug optimisation (CADO-1, CADO-2 and CADO-3); the paediatric conference on ARV drug optimisation (PADO-1 and PADO-2); and the paediatric HIV treatment initiative (PHTI).

<sup>8</sup> KIIIs 35, 36, 37, 46, 50.

<sup>9</sup> 2015 Strategic Narrative for HIV and Areas for Intervention.

established with safety, efficacy and equity in mind and, as noted above, they targeted vulnerable and underserved population groups, including TB co-infected individuals and pregnant women.

The Optimal and SPAAN grants were established to be catalytic implementation initiatives. These investments would contribute to the acceleration of product development and support countries in preparing for the introduction of new HIV products, and to catalysing demand and uptake of new optimal formulations. Through these six projects, Unitaid invested more than US\$93m across 24 countries between 2016 and 2022, with the aim of increasing the proportion of people living with HIV who were on sustained, optimal treatments.

In addition to these grants, the ART optimisation portfolio contributed to three cross-cutting investments which encouraged an enabling environment for HIV treatment. WHO HIV Enabler promoted the scale-up of optimal HIV treatments by: providing direct technical support to countries; supplying guideline development in response to evidence generated through clinical trials and projects within the Unitaid portfolio; and convening technical experts and civil society to inform key policy decisions related to new products and tracking scale-up. MPP aimed to expand the production and supply of generic medicines through negotiating voluntary licences with the originators and supporting the creation of product development partnerships. WHO PQ department aimed to apply a unified set of acceptable quality, safety and efficacy standards to health products in LMICs (including ART) by performing robust quality checks and thus certifying the quality of products to be introduced to the LMIC market.

Table 4, on the following page, provides further details on each of the six main grants.<sup>10</sup>

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<sup>10</sup> Unitaid ART Portfolio Evaluation Inception Report and how clinical trials inform WHO guidelines.

Table 4. Overview of grants

Grant name	Timescale	Lead grantee	Consortium members	Countries	Budget (US\$)	Access Barriers	Product	Manufacturer
ADVANCE	October 2016– April 2023 (~6.5 years)	Wits RHI	University of Cape Town, University of Liverpool; HIV iBase and AfroCAB; Treatment Action Campaign; Southern African HIV Clinicians Society;	South Africa	19.8m	Innovation & availability and quality	DTG, TAF	ViiV
	Description: generate evidence to support adoption in LMICs of optimal ART regimens (DTG and TAF), which are cheaper, more tolerable and have a higher barrier to resistance than existing first-line regimens.							
D <sup>2</sup> EFT	January 2017– December 2022 (6 years)	University of New South Wales (UNSW, Kirby Institute).		Brazil, Colombia, Guinea, India, Indonesia, Malaysia, Mali, Mexico, Nigeria, South Africa, Thailand and Zimbabwe.	10.3m	Innovation & availability and quality	DTG, DRV/r	ViiV Janssen
	Description: generate evidence to support adoption and scale-up of DTG-based regimens in second-line HIV treatment, in resource-limited settings.							
DoIPHIN-2	November 2016– July 2023 (~6.5 years)	University of Liverpool	Liverpool School of Tropical Medicine; TSC/IDSMB; Infectious Disease Institute; Radboud University and University of Cape Town	Uganda and South Africa	10.8m	Innovation & availability and quality	DTG in late pregnancy	-
	Description: Generate evidence to support adoption of DTG-based regimens among late-presenting pregnant women in LMICs and to reduce the incidence of mother-to-child transmission of HIV.							
NAMSAL	June 2016– December 2021 (5.5 years)	Institut Bouisson Bertrand	Agence Nationale de Recherche sur le Sida et les Hépatites Virales	Cameroon	3.1m	Innovation & availability and quality	DTG, lamivudine (3TC), TDF versus EFV400	ViiV

			(ANRS) (Paris, France: trial sponsor and co-funder); Central Hospital of Yaoundé; IAME; INSERM; IRD; SESSTIM and TransVIHMI					
Description: generate evidence to support adoption and scale-up of DTG-based regimens in first-line treatment for HIV, in resource-limited settings and in HIV genotypes common to West Africa.								
Optimal	September 2016– August 2023 (~7 years)	Clinton Health Access Initiative (CHAI)	Delivery partners: AfroCAB and Ministries of Health (MoHs) Sub-agreement with EGPAF from November 2020 – December 2022 to support the roll-out of pDTG in Cote d'Ivoire, Eswatini, Lesotho and Mozambique	Benin, Cambodia, Cameroon, Kenya, Malawi, Nigeria, Senegal, South Africa, Togo, Uganda and Zimbabwe.	45.2m <sup>11</sup>	Innovation & availability, affordability, demand & adoption, and supply & delivery	DTG, pDTG), DRV/r, pALD, LPV/r 4-in-1, LPV/r 2-in-1, pDRV/r, pTAF	-
Description: Reduce morbidity and mortality of people living with HIV and increase cost-efficiencies in health systems by accelerating access to affordable, optimal products for HIV treatment in adults and children.								
SPAAN <sup>12</sup>	August 2019– November 2020	Elizabeth Glaser Pediatric AIDS Foundation (EGPAF)	Delivery partners: TWGs and PENTA/CIPHER	Côte d'Ivoire, Eswatini, Lesotho, Mozambique and Zimbabwe.	3.2m	Quality, demand & adoption, and supply & delivery	LPV/r, pDTG	-
Description: increase the number of HIV-positive children initiated on new, improved paediatric antiretroviral (ARV) formulations.								

<sup>11</sup> Budget for the ARV-related activities under the grant; the grant also included an AHD component, but that is excluded here, as it is not the focus of this evaluation.

<sup>12</sup> SPAAN resulted from a no-cost extension & reprogramming of an existing EGPAF grant focused on HIV point-of-care early infant diagnosis.

### 3.1.3 Portfolio governance and partnerships

Based in Geneva, Unitaid's secretariat staff manages the organisation's relationship with global and country partners and its day-to-day operations. The secretariat is also responsible for implementing decisions and policies approved by the Unitaid Executive Board. In this report, we use the terms 'Unitaid secretariat' and 'ART optimisation team' interchangeably.

Unitaid's constitution document states that, to meet its objectives, Unitaid will rely on contractual and collaborative partners. Currently, the organisation relies on more than 40 partner organisations to give technical guidance and implement grants in the field.<sup>13</sup>

#### Box 2. Unitaid partner classification

Unitaid classifies partners into the following five categories:

- Technical partners, who implement new techniques and bring innovations to the field.
- Companies in the private sector, who use market forces to make medical innovations more accessible.
- Funding partners, who help lower the cost of medicines and diagnostics through systems such as co-payments.
- Implementing partners, who work to bring health innovations to those who need them the most.
- Civil society organisations (CSOs), who help raise awareness about medical issues.

As part of the ART optimisation portfolio, Unitaid invested in several mechanisms to ensure that its partnerships contributed to increasing access to optimal HIV treatment, as follows:

**The Antiretroviral Procurement Working Group (APWG):** The APWG is a partner coordination platform that supports the ARV market in LMICs via monitoring and facilitating ARV supply and demand, coordinated procurement and reduced fragmentation. It received funding from Unitaid for its secretariat, as well as strategic and technical support from CHAI through the Optimal grant. It was established in 2011 and was formerly known as the paediatric APWG. It evolved in 2016 to include ARVs for adolescents and adults in line with the ART optimisation portfolio. The APWG, currently co-chaired by USAID, Global Fund and iPlus Solutions, serves as a forum for sharing market intelligence, troubleshooting issues and seeking advice from peer organisations. On the supply side, the APWG engages with manufacturers to discuss key product supply forecasts.<sup>14</sup>

**The programme advisory committee (PAC):** The PAC, convened by Unitaid and USAID and chaired by WHO and Global Fund, facilitated engagement and coordination across partners with the participation of all Unitaid-funded grant implementers. PAC meetings were hosted annually and members represented over 40 ART optimisation experts comprising global and country partners, including PEPFAR, the United States (US) National Institutes of Health, community and civil society representatives, researchers/academics and grant implementers.

**The community advisory board (CAB):** The CAB was established in 2016 as part of the Unitaid ART optimisation portfolio (specifically, the Optimal grant) to help with user awareness and demand creation. The Optimal CAB, which was a CHAI/AfroCAB partnership, aimed to strengthen community engagement in product adoption, ensuring smooth transition and roll-out of new products, fostering demand and understanding of ARV commodities and ensuring the voices of people living with HIV were at the centre of decision making. The Optimal CAB also played a role in supporting advocacy for equitable access to DTG-based regimens (see 4.1.5).

<sup>13</sup> <https://unitaid.org/how-we-work/partners/#en>.

<sup>14</sup> 10 years of successes and challenges at the antiretroviral procurement group.

### 3.1.4 Theory of Change for the ART optimisation portfolio

The evaluation constructed a ToC for the portfolio. The ToC is a visual representation of the work undertaken by Unitaid's ART optimisation portfolio between 2016 and 2022; it helped guide the evaluation process. At the proposal stage, Itad developed a draft zero ToC for the ART optimisation portfolio and subsequently hosted a workshop to discuss and refine the model with the ART optimisation team. The refined ToC is available in [Annex F](#).

## 3.2 Addressing need: people living with HIV, vulnerable and underserved groups and communities

1

**Finding 1: The goal of Unitaid's ART optimisation portfolio, which focused on removing access barriers to optimal HIV treatments in LMICs, was highly relevant to the needs of targeted beneficiaries.**

**At the time of creation of the ART optimisation portfolio, UNAIDS and WHO warned the global health community that, without the scale-up of optimal HIV treatment in LMICs, the 90-90-90 targets would not be met.** People living with HIV in LMICs had poor treatment outcomes compared to those in high-income countries (HICs). This was largely because of the suboptimal treatment offerings, which had led to poor adherence, side effects and a loss to follow-up. In 2016, for example, South Africa had the highest population of people living with HIV in the world (7.4m people), yet only 3.4m people were accessing ART, and most of these were on regimens that had low barriers to resistance (resulting in transitions to more expensive and toxic second-line regimens). Some first-line regimens had toxicity issues in a significant number of people, further affecting adherence. In LMICs, such as Kenya, with the introduction of the WHO's Test and Start policy (starting all people living with HIV on treatment regardless of their CD4 cell count), the number of people living with HIV increased significantly: from 719,810 people in March 2015 to 1,040,540 people in December 2017.<sup>15</sup> This increase meant that more people had to be prescribed more tolerable and optimal formulations to increase viral suppression.

1

**Finding 2: The comprehensive design of the ART optimisation portfolio, which combined multiple and complementary interventions on the supply and demand sides, was highly relevant to tackling the barriers that make it difficult for people living with HIV in LMICs to access the optimal HIV treatments available in HICs.**

**The comprehensive design of the ART Optimisation portfolio was relevant to tackling the major barriers to the scale-up of optimal treatments in LMICs. Specifically, the design elements which combined investments in critical evidence generation via clinical trial grants and boosted supply and demand through market shaping, country preparedness and global enabling-environment interventions were especially relevant.** The major barriers to scale-up included a lack of evidence on efficacy and safety for key population groups (including mothers, people co-infected with TB or hepatitis, and children); a lack of adapted formulations and fixed-dose combination tablets; poor market visibility, leading to high prices and slow market entry; and supply instability. Specific examples are outlined below.

- The **DOLPHIN-2** clinical trial, which was conducted in South Africa and Uganda, was designed to yield high-quality evidence on the efficacy and safety of DTG (see Box 3) to allow definitive recommendations and operational guidance to be established for its use by pregnant women, and to reduce vertical transmission in this high-risk scenario.
- The **NAMSAL** clinical trial, which was conducted in Cameroon, was designed to demonstrate the non-inferiority of DTG-based first-line regimens when compared with

<sup>15</sup> NASCOP, 2019.

the standard of care (EFV in combination with tenofovir disoproxil fumarate (TDF) / Lamivudine or emtricitabine (XTC)). This trial also aimed to enable the transitioning of people living with HIV on national HIV treatment programmes to DTG-based first-line regimens. It focused on the diversity of people living with HIV and their needs, including people with TB in Africa.

- The **D<sup>2</sup>EFT** clinical trial, which was conducted in multiple LMICs (Brazil, Colombia, Guinea, India, Indonesia, Malaysia, Mali, Mexico, Nigeria, South Africa, Thailand and Zimbabwe), was centred around population diversity with the goal of providing robust and generalisable data on DTG+DRV/r. The data would inform international and national regimen guidelines on optimised, second-line ART regimens in order to deliver life-saving combination antiretroviral therapy for millions of people in LMICs.
- The **ADVANCE** clinical trial, which was conducted in South Africa, targeted participants from specific vulnerable and underserved populations to address LMIC evidence gaps and to contribute to the scale-up of DTG/TAF-improved regimens in first-line treatment.

### Box 3. Relevance of DTG to addressing need

In 2016, DTG was recognised as a highly effective and important advancement in ARV medication. DTG-based regimens had already been in use in HICs, such as the US and Canada, since 2014. They were also adopted in some LMICs, such as Botswana, and were being considered for broader use in others. DTG is more effective, easier to take, and has fewer side effects than the alternative drugs that were being used in most LMICs.

DTG also has a high genetic barrier to developing drug resistance, which is important, given the rising trend of resistance to EFV- and nevirapine-based regimens (in 2019, 12 out of 18 countries surveyed by WHO reported pre-treatment drug resistance levels exceeding the recommended threshold of 10%). If resistance to HIV medicine builds, a person must be switched to second- or third-line treatments, which can cost up to ten times more.

Given that DTG is better tolerated and has a higher resistance barrier, it offers resource-constrained governments and programmes a less risky product to administer, particularly in environments where monitoring does not take place as often as necessary.

Together, the ADVANCE, DolPHIN-2 and NAMSAL trials included approximately 2,000 people living with HIV in sub-Saharan Africa (randomised to either DTG- or EFV-based regimens, with TDF or TAF). These trials represented three of the largest independent cohorts worldwide in which DTG and other new ARVs were being analysed in populations most affected by HIV. However, there was no equivalent source of information with the same level of detail and reliability available for evaluating the safety of DTG and the evolution of its side effects.<sup>16</sup>

The **Optimal** and **SPAAN** grants were then designed to respond to different aspects of need for people living with HIV in LMICs by focusing on supporting relevant country-preparedness and market-shaping activities to help accelerate the introduction and scale-up of improved HIV regimens. For the Optimal grant, CHAI worked in coordination with global and national partners, and with manufacturers and regulatory authorities to promote healthy markets and to improve country access to affordable, high-quality HIV treatments (see Box 4).

<sup>16</sup> TRIO Extension executive summary.

#### Box 4. Relevance of Unitaid's market-shaping approach

Since 2016, the market-shaping approach of Unitaid and CHAI (under the Optimal grant) has combined the following complementary activities:

- **Accelerating product development**, including support for product development partnerships for generic versions of optimal HIV treatments, as well as engagement with regulatory authorities to accelerate review timelines—for example, by developing innovative review mechanisms for pDTG.
- **Accelerating time-to-market**, including through catalytic procurement of DTG 50mg in Kenya, Nigeria and Uganda; catalytic procurement of DRV/r 400/50 mg in Zambia and Nigeria; catalytic procurement of DTG 10mg (pDTG) in Benin, Kenya, Malawi, Nigeria, Uganda, and Zimbabwe; and the development of incentive programmes—for example, for pDTG and pDRV/r. Catalytic procurement aims to rapidly introduce commodities and mobilise investment from major procurers, stimulate enhanced monitoring, and accelerate development of the market for quality-assured products (that is, rapid product access and uptake).<sup>17</sup>
- **Contributing to affordability** by negotiating lower prices on the supplier side—for example, through ceiling price agreements and securing price parity or better, as was the case for tenofovir disoproxil, lamivudine, dolutegravir (TLD).
- **Increasing country demand** for optimal ARV products, including through the Optimal CAB and technical support provided to governments.
- **Supporting adoption, roll-out and uptake** in focal countries, including through collaboration with governments to update national guidelines, quantification and forecasting; development of tools such as the HIV new product introduction toolkit, training curriculum, facility and counselling job aids; and other resources.
- **Operations research**, including initiatives focused on people living with HIV/caregiver satisfaction, side effects, viral load suppression, multi-month dispensing, and adherence to pDTG in Nigeria, Uganda, Benin, Eswatini, Lesotho and Mozambique.

**This combined market-shaping approach was both innovative and highly relevant to improving equitable access for both adults and children**, helping to address critical commercial barriers to adult and paediatric product entry, alongside systems strengthening activities to support the scalability of DTG- and pDTG-based treatments in LMICs. Further findings on the **results** of the market-shaping work and the **key lessons learnt** are included in Box 8.

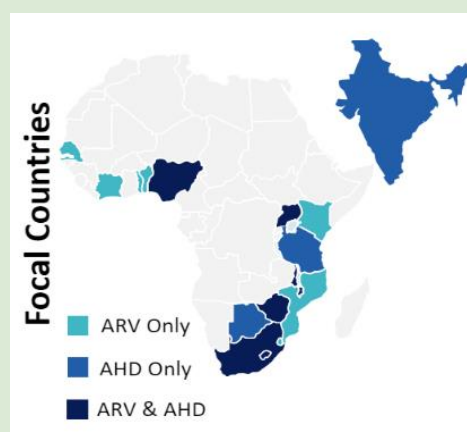


Figure 8. The Unitaid market shaping approach

**The portfolio approach (working alongside scale-up, technical and community partners through mechanisms such as the PAC and CAB) helped to increase the relevance of each of the individual grants funded.** The clinical trials (ADVANCE, D2EFT, NAMSAL and DolPHIN-2) and the market-shaping and country-preparedness grants (Optimal and SPAAN) were mutually supportive: the trials generated evidence, which helped to create demand for quality optimal products, and the Optimal and SPAAN grants helped to shape the market for those products by increasing supply, driving affordability, and helping to ensure that countries were prepared to adopt and roll out new treatments. The portfolio's cross-cutting enabling grants addressed further aspects of need, but at a global level. For example, the MPP supported the expansion of the supply and production of generic medicines in LMICs. The grant focused on supporting the negotiations of voluntary licences with originators and issuing sub-licenses to generic manufacturers, thus expanding access.

<sup>17</sup> <https://unitaid.org/assets/Landscape-of-innovative-tools-and-delivery-strategies-2022.pdf>.



*“This was the first time that a really good drug moves from the north to the south very, very quickly. All questions that needed to be answered were answered in one portfolio. The research grants were going on to answer all outstanding questions like TB co-infection.” Key Informant Interview (KII 51)*

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**Finding 3: The portfolio design addressed relevant critical issues related to gender and social inclusion to help promote equitable access to optimal HIV treatments.**

**The portfolio specifically targeted vulnerable and underserved groups of people living with HIV in one of the poorest regions in the world.** The portfolio invested in interventions across 24 countries, the majority of which were located in sub-Saharan Africa.<sup>18</sup> The investment targeted six of the top ten countries that are most affected by HIV.<sup>19</sup> The ART optimisation portfolio’s clinical trials involved targeted vulnerable and underserved populations, such as adolescents and pregnant women (ADVANCE and DolPHIN-2). More specifically, it contributed to addressing evidence gaps in TB co-infections and in the use of DTG during pregnancy and vertical transmission.

*“There was a huge equity component, and the big driver of this portfolio was ensuring access of these products and that they are best available products. Some of the gaps included gaps in evidence and gaps in data for a global guidance and WHO was very clearly saying, to be able to recommend these products, we need to have data from specific resource-limited settings, but also we need data in pregnancy.” (KIIs 35 and 37)*

**Two further examples of Unitaid’s ART optimisation portfolio addressing relevant equity barriers include the investment in the NAMSAL, DolPHIN-2 and ADVANCE trials (together known as TRIO), and the strong focus on children and adolescents.** To strengthen the scientific community and women living with HIV’s understanding of the weight gain and clinical obesity risks associated with DTG and TAF/TDF use, Unitaid granted costed extensions for TRIO. TRIO supported 192 weeks of monitoring and enabled the pooling and analysis of safety data on weight gain. This was particularly relevant for equity, since the trials were showing that the risks were highest for some black women.<sup>20</sup> By creating linkages across investigators, countries and partners, TRIO’s design maximised the ART portfolio’s ability to generate evidence and analysis around DTG and respond to emerging issues. It has also provided a model for future clinical trial research collaboration.

When establishing the portfolio, children’s access to HIV treatment was a challenge that the global health community needed to overcome. In 2018, UNAIDS data showed that just over half of the children (aged 0–14) living with HIV in its focus countries received ART and that viral load suppression in that population was below 70%.<sup>21</sup> This suggested that the available paediatric ARV formulations were either not very effective or were not being administered correctly (or both). In 2019, Unitaid invested in the SPAAN project to focus exclusively on increasing the number of children living with HIV who were initiated on improved paediatric ARV formulations in five LMICs: Côte d’Ivoire, Eswatini, Lesotho, Mozambique and Zimbabwe. The project was initially scheduled to end in 2020, but dispersible pDTG was not available before 2022 and generic approval was only expected at the end of that year. Therefore, in order not to miss the opportunity to leverage the learning from SPAAN and ensure that implementing countries continued to be covered, SPAAN was

<sup>18</sup> Benin, Cameroon, Côte d’Ivoire, Eswatini, Kenya, Lesotho, Malawi, Mali, Mozambique, Nigeria, Senegal, South Africa, Togo, Uganda and Zimbabwe.

<sup>19</sup> <https://www.statista.com/statistics/270209/countries-with-the-highest-global-hiv-prevalence/#:~:text=The%20countries%20with%20the%20highest,significantly%20decreased%20their%20HIV%20prevalence.>

<sup>20</sup> TRIO Proposal, 2020.

<sup>21</sup> EGPAF, Unitaid and SPAAN report update – project overview document.

integrated into the Optimal grant (building on existing paediatric work under Optimal). This expanded Unitaid's paediatric work to 2023 and supported the roll-out of pDTG in more countries. These renewed efforts comprised supporting four out of the five SPAAN/Elizabeth Glaser Paediatric AIDS Foundation (EGPAF) countries in developing more stable and effective paediatric ART delivery models (Côte d'Ivoire, Eswatini, Lesotho, Mozambique), overcoming supply and demand challenges, and generating data on paediatric cohorts to address DTG concerns.

1

**Finding 4: Community representatives were consulted throughout the creation and duration of the ART optimisation portfolio. This helped to ensure that the portfolio was relevant to the needs of people living with HIV.**

**People living with HIV's voices were heard during the process of designing the ART Optimisation portfolio and they helped to shape its research.** A community engagement strategic pillar was embedded into the portfolio from its inception, in 2016. Unitaid ran consultations with community organisations and CSOs to discuss and validate the objectives of the new Afl, which was under development and gather insights on their relevance.<sup>22</sup> At the grant level, Unitaid's RfP had a requirement for bidders to include both a budget and activities for engaging communities meaningfully during grant implementation. The ADVANCE trial proposal, for example, had a very strong community component from the outset as the grantee had "been working in that way for years." The trial was planned in close collaboration with Treatment Action Campaign (TAC), a prominent community/HIV activist organisation in South Africa with support from HIV i-Base. The clinical trial grantees unanimously emphasised the importance of community engagement in shaping the relevance of their research.

*"As a researcher, they don't know what is suitable for people on the ground. They should engage people who are already in the community and are close to them and know what the community needs to engage them in a meaningful way."*  
ADVANCE FGD

**Research grantees engaged with community representatives to different degrees and at different levels throughout the project cycle, supporting further innovation and adaptation.** For example, DolPHIN-2 employed a peer mother to be the interface between the research team and the participants in the trial. ADVANCE engaged communities from inception and submitted a proposal with communities as an important part of the project. In addition, global stakeholders reported that this community engagement supported adaptations during the implementation of clinical trials' research activities.

*"I think it helps push us to ensure that, when thinking about innovation, even in shaping research and development, you need to bring in community leaders to ensure that the end-user perspective is captured early on in the product life cycle."*  
(KII 45)

The participation of community representatives in both the PAC and the CAB was an integral part of the ART Optimisation portfolio's design, and facilitated mutual understanding of the programme and intervention needs, as well as empowering the community. Most stakeholders suggested that this was a strong element of Unitaid's model, and agreed that these mechanisms allowed people living with HIV's views and knowledge to inform portfolio implementation and the global disease response (including in response to unforeseen changes in context and product data). The CAB and PAC approaches also contributed to the portfolio remaining relevant to the target population throughout

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<sup>22</sup> KII 36.

its lifetime. It supported informing communities on the most recent information and data available and ensured consideration of the need for health and treatment literacy to translating complex data into information for communities to create demand. Stakeholders felt that Unitaaid maintained strong communication through the CAB and that people living with HIV's were empowered by including their voices in decision-making on the global stage.

*“Having that component of community engagement is adding much more value to the interventions because people can sit at high-level meetings and come up with all these wonderful interventions that they want to introduce or they want to try out. But if you don't involve the community, it really doesn't work.” (KII 49)*

Further information on the CAB and Unitaaid's community engagement approach, its added value and the key lessons learned is provided in Box 5 below.

**Box 5. Community and civil society engagement in the ART optimisation portfolio: “Nothing for us, without us.”**

**Unitaid's approach to community and civil society engagement (CSSE) and the ART optimisation portfolio**

Unitaid's approach highlights the crucial role that communities and CSOs can play in facilitating demand creation and the adoption of new health products. For Unitaaid, partnering with communities and civil society is key to ensuring the successful scale-up of its interventions. One of four strategic commitments set out in Unitaaid's 2017–2021 strategy was, therefore, “we succeed in partnership”. Since then, the 2023–2027 strategy has been developed, with strategic objective three aiming to foster “inclusive and demand-driven partnerships for innovation.” The main goals are to maximise the engagement of affected communities and responsiveness to their needs, as well as to maximise alignment and synergies with governments, in-country stakeholders, affected communities and CSOs.

In 2017, Unitaaid's working definition of CSOs included not only international non-governmental organisations (NGOs) but also local community-based organisations comprised of people living with HIV and national networks working on HIV and co-infections.<sup>23</sup> These definitions have now evolved and, importantly, the current working definition of CSSE differentiates between the engagement of CSOs and community representatives (Figure 9). In this case-study (and report), the ART optimisation portfolio's achievements and lessons are analysed using Unitaaid's most up-to-date working definition of CSSE.

**Table 5. Community organisation/s per clinical trial**

Community organisation	Grant
TAC and HIV i-Base, Southern African HIV Clinicians Society	<b>ADVANCE</b>
REDS Association	<b>NAMSAL</b>
AfroCAB Treatment Access Partnership	<b>Optimal</b>
HIV i-Base, and Ugandan DoIPHIN-2 CAB	<b>DoIPHIN-2</b>
D <sup>2</sup> EFT CAB	<b>D2EFT</b>
N/A	<b>SPAAN</b>

<sup>23</sup> Strategy 2017–2021, Unitaaid, 2017.

In line with (but also pre-empting and informing) Unitaid’s 2023-2027 strategic objectives, the ART optimisation portfolio emphasised CCSE as a key driver of scalability from the outset. All grants funded as part of the ART optimisation portfolio were required to include CCSE activities aligned with each grant’s objectives and to track the progress of these activities in the project log frame. To ensure this was feasible, from the RfP through to each project’s development and implementation, the ART optimisation team provided guidance and technical support to grantees on how to design, integrate and monitor their CCSE component. The activities included in each grant proposal varied across the portfolio.

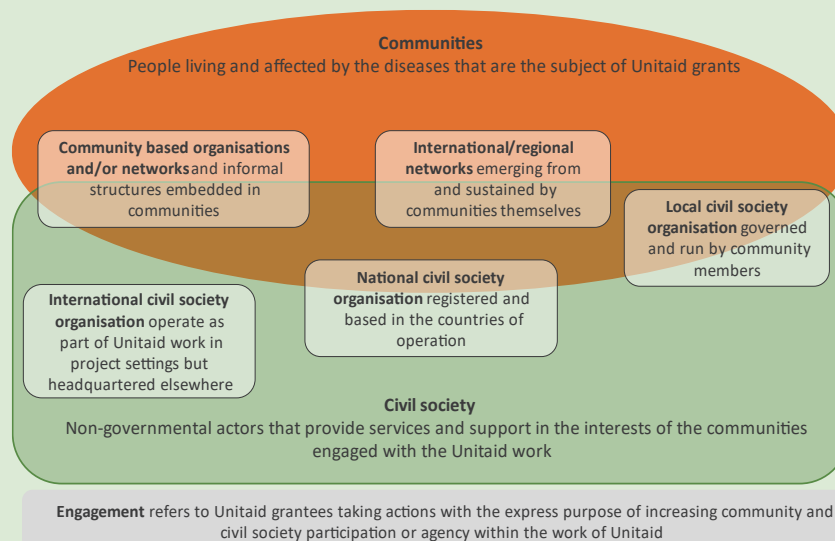


Figure 9. Unitaid’s working definition of CCSE

Through its grantees, the portfolio then engaged with existing community organisations, CSOs and with networks of people living with HIV (see Table 5 **Error! Reference source not found.**). These groups played a critical role in driving the demand for new optimal products both at global and country levels. They advocated for the scale-up of optimal treatments with government, provided significant inputs into trial research and roll-out strategies, and disseminated information to increase treatment literacy and awareness and ensure that people living with HIV were fully informed of both the benefits of new products and their potential risks. also fostered engagement among community members through CAB and PAC mechanisms.

- The **Optimal CAB** was established to foster the engagement of members of communities and civil society groups to co-develop product adoption and roll-out strategies and to improve understanding of new treatment and regimens and generate demand. The Optimal CAB supplied strategic direction and leadership in strengthening community engagement in portfolio implementation (including during Covid-19). It produced demand generation; enhanced treatment and health literacy; ensured the voices of people living with HIV were at the centre of decisions made during the implementation of Unitaid’s ART optimisation portfolio and in WHO guideline development; nurtured coherence among the portfolio grants; and supported and complemented the activities of the global HIV treatment community.
- During **PAC** meetings, community and civil society representatives elevated their perspectives, understanding and needs to the strategic planning level. As a consequence of PAC meetings, people living with HIV expertise and the issues facing them informed Unitaid, USAID and Global Fund’s work in the HIV optimisation space. PAC meetings contributed to a more effective global disease response, supporting speedy action in cases where challenging unforeseen circumstances (Covid-19) or emerging trial data impacted the HIV treatment space. In PAC meetings, community representatives were also exposed to the most up-to-date scientific information regarding HIV treatment optimisation. They had the opportunity to ask clarification questions and have their concerns heard early on in the process.

### What did the community and civil society partners do?

During the implementation of the portfolio, project partners including AfroCAB, HIV i-Base, TAC and community networks worked with clinical trial and market shaping partners. With research grantees these groups worked to ensure that clinical trial research tools and consent procedures were appropriate and that there was acceptability of the tested products and research results dissemination. Through the market-shaping and country-preparedness grants, community organisations aimed to generate and increase

demand for optimal HIV treatments by promoting treatment literacy, information sharing, awareness raising, materials development, community acceptance and advocacy, and demand capacity strengthening. More specifically, the community and civil society groups involved in this portfolio engaged in the following:

- **Built treatment literacy and demand for new products by creating publicity for new drugs and by communicating up-to-date research information clearly and concisely to communities living with HIV.** Community organisations and treatment networks (AfroCAB, HIV i-Base and TAC), in partnership with CSOs and CHAI through the Optimal CAB, worked to build community literacy, awareness and demand around new, optimal treatments and to address misconceptions and resistance to uptake. In Malawi, for example, media engagement played a significant role as AfroCAB representatives relied heavily on local and national radio stations to disseminate information and to build demand for DTG and pDTG.
- **Developed context-appropriate and language-sensitive treatment literacy tools, which became key to the demand for, and uptake of, new treatment regimens.** For example, in South Africa, TAC and HIV i-Base developed the Modern ART campaign, which aimed to increase treatment literacy through the dissemination of up-to-date treatment information and advocacy messaging in booklets, street murals, a mobile app and social media channels (such as Facebook, Instagram, Twitter and YouTube). In addition, the Modern ART app supported people living with HIV in managing their new treatment. In Côte d’Ivoire – under the leadership of the Programme National de Lutte contre le Sida (PNLS) and in collaboration with the Ivorian Paediatric Society – the Optimal grant supported the update of treatment literacy materials, such as fact sheets on key national guidelines for the management of HIV in children and adolescents. These materials were made publicly available through the New Product Introduction Toolkit and also by coordinating with partners such as PEPFAR for them to adopt these materials rather than duplicate effort.
- **Advocated at both global and country levels for the inclusion of more tolerable, optimal products (in this case, DTG-based regimens) in WHO and country guidelines.** For example, following emerging safety signals for early pregnancy (see 4.1.5, finding 2), women living with HIV from several focal countries advocated at the country and global levels for changing WHO and country guidelines around the use of DTG/TLD by women of reproductive age. In Kenya, the mobilisation of community representatives and lobbying resulted in a petition being drafted to the National AIDS and STI Control Programme (NASCOP) and the Ministry of Health (MoH), asking for a revision of the cautionary measures barring women from accessing DTG, which were based on medical advice.

*“We take the voices representing the communities of people living with HIV across the country and bring it back to the policymakers and MoH.” (KII 120)*

- **Monitored the roll-out of the new regimens at the facility and district levels, and informed governments of any changes in treatment outcomes.** In Malawi, for example, AfroCAB (through the Optimal CAB) filled a key gap in community engagement and monitored the roll-out of DTG and pDTG. AfroCAB also ensured supply to health facilities through on-going communications with the MoH on uptake and stock-outs and, as a result, were seen by the government as key strategic partners in HIV response. In Côte d’Ivoire, AfroCAB contributed to strengthening community action on treatment literacy in the most disadvantaged areas (such as rural and remote areas), thus contributing to reaching underprivileged populations.
- **Provided training and mentorship to community representatives, CSOs, people living with HIV and their carers on adherence and the side effects of the new optimal treatments.** Community representatives who participated in Optimal CAB and PAC meetings shared their knowledge with CSOs, health workers and people living with HIV in LMICs.
- **Provided key inputs to guide ART optimisation portfolio implementation.** Community organisation representatives gained the skills necessary to represent communities and ensure the voices of people living with HIV were heard by projects in relation to implementation and strategic decision-making during Optimal CAB and PAC meetings.

- **Shared learning and best practices in engaging with communities, global-level organisations and government representatives; influenced them to pursue a similar approach.** For example, in Kenya, NASCOP – influenced by the Optimal grant – has now updated the National Transition and Treatment Optimisation Workplan to ensure that community engagement is one of eight key performance areas in optimising treatment.<sup>24</sup> Moreover, in Uganda, Unitaids’ community engagement approach was replicated during Global Fund’s country coordination mechanism engagements.<sup>25</sup> Influence on global partners is further covered in 7.2.
- **Helped to address concerns about research and the perception of people being used, or experimented on, for research.** Community organisations in partnership with project teams sensitised the broader community through journalist training and murals around the cities. They were also available for open conversations throughout the research implementation in Cameroon and South Africa (NAMSAL and ADVANCE/ HIV-i-Base Modern ART campaign).
- **Adapted their approach to engaging with communities and CSOs during the pandemic.** Community engagement organisations had to adapt their approach during the Covid-19 pandemic and started engaging with members of the community using virtual platforms for information dissemination. They relied on radio messaging, WhatsApp groups, information hotlines, the online provision of training, the use of YouTube and other social media networks to ensure that activities continued.
- **Helped to bridge gaps in the Covid-19 response.** For example, in South Africa, TAC and HIV i-Base campaigns incorporated messaging around Covid-19 and vaccine literacy.

#### Added value of CCSE

This evaluation found that the community engagement model implemented by Unitaids was instrumental in the successful roll-out of optimal new regimens in LMICs. The cascade effect of passing on knowledge to the community on a regular basis influenced the way in which the population began to demand DTG at health facilities. Further findings on the results of Unitaids’ CCSE work can be found in 5.3, 6.1 and 7.2.

Stakeholders suggested that without this approach, the same results would not have been achieved. One stakeholder experienced in community engagement compared the case of DTG with a newly available, optimal treatment for malaria. Whereas people would demand DTG following Unitaids’ comprehensive community engagement model, for malaria, the medicines would remain on the shelf without being used at scale due to a lack of knowledge among both health professionals and the population.<sup>26</sup>

Further illustrating this, where the community was not as engaged from the outset of Unitaids’ grants, and/or initial funding allocations for community engagement were limited, some grantees encountered challenges with the community and wider public’s acceptance of new treatments. Lessons from the NAMSAL trial’s difficulty in gaining initial buy-in from the media and communities in Cameroon highlight the need for early engagement with broader society around research objectives. Following an initial, relatively light-touch approach to community engagement working with peer support groups, the community engagement budget for the NAMSAL grant was increased following the cancellation of a (pharmakinetics) sub-study, and in response to negative press and the risk of a boycott of the trial.<sup>27</sup> The project team then developed a civil society engagement plan to organise discussions with local groups and trained journalists to raise the awareness of the local population regarding HIV care and clinical trial issues:<sup>28</sup>

*It must be said that, at the beginning, the conception of journalists in relation to research was ‘there are people who will be used as guinea pigs.’ Through NAMSAL, this language has changed. I think that this is an important element for Cameroon and for research in general in our country. (NAMSAL FGD)*

<sup>24</sup> KII 89, KII 90.

<sup>25</sup> KII 111.

<sup>26</sup> KII 51.

<sup>27</sup> NAMSAL FGD; NAMSAL 2017 reprogramming request.

<sup>28</sup> NAMSAL 2017 annual report.

Furthermore, following the Covid-19 outbreak, some populations were not adhering to the optimal treatments, which clinical trial implementers said was due to social determinants.<sup>29</sup> Whilst the implementation partners in the ADVANCE clinical trial recognised the significance of engaging with the community from the outset, a lesson from their trial was that more effort could have been expended in educating the community in treatment literacy. D<sup>2</sup>EFT and NAMSAL learnt that engagements with the community should not be limited to community groups, or to people directly affected by the research, since broader support from society can help raise acceptance of results by the community.<sup>30</sup>

*But we can do better with people living with HIV, who can participate in the design.  
(NAMSAL FGD)*

### Key lessons learnt

The portfolio's CCSE activities have demonstrated that community organisations and their representatives have unique capabilities, which, when effectively leveraged, can support the introduction of new optimal products and their uptake. **Key lessons learnt** are that this involves:

- Systematically building community engagement into grant activities.
- Engaging the community early (from the design stage).
- Utilising diverse sensitisation materials.
- Providing sufficient resources and flexibility to support effective engagement.
- Drawing on (and helping to bring together) existing groups and representative structures.
- Elevating community representation to the level of strategic discussions (globally and nationally) – for example, through the use of CABs and the inclusion of the community within other governance structures, such as the PAC.
- Partnering and closely collaborating with established technical partners and national governments.

Further details on these lessons are shared below.

1. **Unitaid's early push to implement community engagement activities was instrumental in embedding and expanding the successful approach.** Unitaid believed that the organisation would not be able to achieve equity unless communities were involved in both the strategy and delivery of programmes. Thus, for example, for the first time CHAI designed such a large market-shaping project that also included major community involvement and received critical funding and support. Nonetheless, there is scope to go deeper and earlier. Some grantees reported that despite including community engagement in their project proposals, community stakeholders were not involved at the design stage. Grantees identified this as a missed opportunity.
2. **Unitaid's community engagement model effectively combined traditional and innovative downstream community engagement activities with the strategic involvement of community members.** For example, involving community organisations in the planning for the roll-out of the new treatments, discussions regarding guideline development, clinical trial design, implementation and dissemination of results, and advocacy. Other organisations have used strategies such as developing information, education and communication materials or training community and civil society representatives to increase community knowledge and treatment literacy. However, for Unitaid's approach to be successful and recognised as an added value by other global partners (for example, Global Fund and USAID) and by the wider community working to improve HIV treatment, the combination of the traditional demand generation and community literacy activities with the creation of a CAB was fundamental. This combination allowed for the sharing of experiences and the participation of the community in the PAC to ensure that strategic decisions were made according to the most pressing needs of people living with HIV.

<sup>29</sup> ADVANCE FGD.

<sup>30</sup> KIIs 35, 37; D<sup>2</sup>EFT; NAMSAL FGD notes.

- 3. Investments in forums, such as the PAC and Optimal CAB, was central to the approach working constructively.** These two forums enabled the portfolio to remain relevant to people living with HIV and coherent with other donor investments over time. The PAC and Optimal CAB also ensured that up-to-date information about HIV treatment was made accessible to communities much faster than would normally have been the case, and also contributed to the empowerment of these communities and increased their capacity to advocate for the inclusion of optimal HIV treatment products at national and global levels. Indeed, in some instances, community members had access to knowledge that even doctors did not have. Through such empowering, the PAC and Optimal CAB served as important links between grassroots and global advocacy.
- 4. Meaningful engagement of communities required commitment from both donors and grantees.** Unitaid's strong focus on implementing interventions with community engagement as a guiding design and implementation principle determined the overall successes of CSSE in this portfolio. Without the commitment of Unitaid's Board and portfolio team, miscommunications and the grantees' limited expertise in engaging community organisations meaningfully could have hindered the effectiveness of such an approach. This would have resulted in less positive outcomes. In addition, this evaluation found that it is important to establish foundations for equal partnerships between grantees and the community organisations responsible for implementing community-level activities. A two-way learning path should be fostered so that power dynamics are better managed and so that both the grantees and community organisations are able to truly learn throughout the implementation process. Finally, transparent communications and mutual trust is fundamental to ensuring that the collaboration works.
- 5. Leveraging existing community structures as a channel for implementation contributed to efficiency and sustainability.** Unitaid-funded community organisation representatives worked in partnership with existing community-based organisations and treatment activists to develop community engagement tools, increase treatment literacy and awareness and build community health capacity.<sup>31</sup> Working with established organisations, which have demonstrated a genuine commitment to the programme's goals, supported efficiency and helped increase the potential for intervention sustainability. For example, the engagement of community representatives who already worked at the facility-level increased the chances of them championing HIV optimisation principles and use of DTG beyond the lifetime of Unitaid's programme.
- 6. Creating strategies and opportunities for sharing learning contributed to the efficiency, effectiveness and scale-up of community engagement.** The evaluation found that community engagement interventions benefit from on-going learning opportunities during implementation. Coordination of community engagement across investments (CAB) and knowledge dissemination moments mainly during conferences (IAS) produced positive results and improved the capacities of community organisations across countries. It is also important to ensure the outputs and learnings from research projects and trials are made accessible to non-scientific audiences, and that spaces to ask questions are created to foster learning and capacity building. Lastly, by documenting tools, lessons, and results in articles, blogs, and other learning materials, the lessons can be scaled up beyond the founding organisation.
- 7. There was value in investing in broader-ranging community engagement activities as part of clinical trial research.** The importance of community leadership and end-user perspectives in shaping clinical trial research and the development of new products, training and protocols was recognised by most stakeholders. However, community engagement should not be limited to representatives during the design of consent forms, as standard practice requires. The engagement of these stakeholders should include the creation of forums to discuss other areas, such as drug

<sup>31</sup> Such as the National Empowerment Network of People living with HIV/AIDS in Kenya and the Kenya Red Cross Society; KII 52.



introduction and quality aspects of the trials. In addition, trials should invest in encouraging broader community involvement to ensure the successful interpretation and acceptance of results.

- 8. Sufficient and flexible funding was required to allow for effective community engagement.** Flexibility in the funding disbursements and processes, such as milestones and log frames, are essential in engaging community organisations. This enables adaptation and ensures a rapid response to urgent needs and unplanned crises. In some trials the funding was not sufficient; therefore, community organisations felt that their engagement activities were not implemented effectively.
- 9. Knowledge production and dissemination was key to fostering the sustainability and scale-up of community-engagement best practices.** Investments in the creation and dissemination of treatment-literacy materials and other resources (such as the New Product Introduction Toolkit under the Optimal grant) ensures that learning and best practice from the community engagement strategies are shared with other partners, governments, and the broader global community who are working to reduce HIV incidence and improve the lives of people living with HIV.
- 10. Strengthening the capacities of community-based organisations, including their ability to manage large amounts of funding, has the potential to generate long-term gains for the country in which they are based.** For example, the Optimal grant supported the enhanced engagement of AfroCAB and enabled the organisation to expand its reach. However, donors such as Unitaid are needed to invest in further strengthening these organisations' capacities. One way this can be achieved is to invest in training and systems that can enable community organisations to directly receive and manage larger amounts of funding in the future. The assumption is that if their processes are improved, community organisations will be able to attract funding from other sources. This funding would enable them to continue their work in propagating advocacy and literacy beyond Unitaid's investment. It would also ensure continued scale-up benefits for the communities in which they are based.

### 3.3 Coherence and added value

1

**Finding 1: Unitaid worked closely and synergistically with global scale-up and international partners during the implementation of the ART optimisation portfolio (including through the PAC) ensuring strong alignment with other interventions.**

**Unitaid worked closely with other international organisations in the HIV landscape to ensure alignment across priorities for meeting global targets, including jointly accelerating the introduction of optimal treatments in LMICs.** Partners included the US government – PEPFAR, the Centers for Disease Control and Prevention (CDC) and USAID –, WHO, Global Fund, BMGF and other private foundations, US national research institutes, bilateral donor programmes, and other international funders supporting innovation in ART optimisation,<sup>32</sup> as well as civil society actors and representatives of people living with HIV communities. From the outset, Unitaid's ART optimisation portfolio relied on the support and expertise of these partners to help in the design of the portfolio and to agree mandates.

**In 2016, Unitaid and USAID specifically created the ART Optimisation PAC to enhance coordination efforts around improving treatment access.** By connecting industry scale-up partners, policymakers and researchers, the PAC and APWG (Box 9) provided platforms for increased global collaboration around ART optimisation. By convening international donors, implementing partners, community representatives, manufacturers and academics, the PAC, which was co-chaired by the WHO (evidence) and the Global Fund (service delivery), provided important technical advice, informing

<sup>32</sup> KIIIs 35, 36, 37, 38, 45, 47, 54, 55, 58.

decision making and the joint organisation of activities in three areas: 1) ensuring accelerated and sustained access to optimal regimens, 2) clinical trials and research, and 3) second-line novel product development and formulations. PAC efforts have supported the alignment of global ART simplification efforts, highlighted potential gaps or areas of duplication, fostered the dissemination of emerging evidence and created a space for the cross-learning of attendees (Box ).<sup>33</sup>

#### Box 6. Contribution of the PAC to global coordination

Unitaid is recognised as a strong leader in bringing together partners and acting as an incubator for new markets. The PAC—co-chaired by the two main partners: WHO and Global Fund—provides a strong example of this approach. Unitaid and USAID established the PAC following their joint funding of the ADVANCE clinical trial grant, having identified the need to bring together bodies working on evidence and product scale-up and to share evidence with global forums and avoid duplication.

**The PAC played a vital role in the coordination of organisations working on improving access to affordable, optimal HIV care.** For example, the PAC facilitated answering specific research and implementation questions raised by WHO. Once connected through the PAC, clinical trial studies freely exchanged information and tools to address research gaps and opportunities (and avoid duplication) and help solidify relationships.<sup>34</sup> Open and consistent communications within the PAC then allowed Unitaid to update WHO on the status of new HIV products, promoting faster review prior to products being moved to the APWG for further roll-out.<sup>35</sup> Finally, Unitaid took advantage of the PAC (as well as existing partnerships) to push learning and to promote holistic approaches on specific issues, for example, the introduction of care packages for AHD and creating mechanisms and ways to channel investment into that area.<sup>36</sup>

**The PAC (alongside the APWG) also played an important role in attracting manufacturers to new product markets in LMICs – in turn tackling affordability barriers, and increasing the availability of optimal HIV treatments.**<sup>37</sup> While the clinical trial data were developed, grantees continued to engage with industry partners through the PAC. Manufacturers, in turn, gained confidence in the clinical trials through regular meetings and quarterly in-person connections to discuss the development of the products, thus reducing the time-to-market. The involvement and collaboration of key global partners—such as PEPFAR, WHO and Global Fund, fostered by the PAC (and the APWG)—enabled stronger negotiations with manufacturers to lower prices. Manufacturers also reported valuing Unitaid’s support for advocacy and the engagement of community and implementing partners, which they felt helped to accelerate the roll-out of new treatments.<sup>38</sup>

**The presence of community representatives at the PAC meetings was an important driver of portfolio success.** In the PAC meetings, community members had the opportunity to elevate their communities’ perspectives and demands to the level of strategic planning.<sup>39</sup> Establishing a forum such as the PAC, where different groups could come together and talk with community input, was helpful in the implementation process, and helped resolve issues as they arose.<sup>40</sup> Community members also reported that these meetings were essential to keeping them informed of the latest developments from the clinical trials and that it allowed them to play a bridging role between the global developments on HIV treatment and people living with HIV.<sup>41</sup>

**The PAC annual conventions provided a valuable platform for Unitaid grantees to share progress and learning from their work with WHO and other global partners.** Held between 2017 and 2019, these allowed for the gathering of over fifty ARV optimisation experts, country and industry representatives,

<sup>33</sup> 2019 ART Optimisation PAC Report DISTRIBUTED 2020.02.24.

<sup>34</sup> KII 35, 37; DolPHIN-2 FGD; Unitaid FGD; D<sup>2</sup>EFT 2017 annual report; ADVANCE 2017 GBA; ADVANCE 2017 Jul Monthly Update; Dolphin 2019 GBO.

<sup>35</sup> KII 22, 36.

<sup>36</sup> KII 35, 37, 49, 56, 57.

<sup>37</sup> KII 22, 35, 37.

<sup>38</sup> KII 54, 57, 62.

<sup>39</sup> KII 39, 50, 51.

<sup>40</sup> KII 39, 49, 50.

<sup>41</sup> For example, KII 49.

donors, community representatives and implementing partners, and the sharing of previous experiences around, for example, working with procurement actors to inform manufacturers' pipelines.<sup>42</sup>

**Specific examples (not exhaustive) of how the PAC supported the ART optimisation portfolio and its grantees include the following:**

Ensuring accelerated and sustained access to optimal regimens

- Provided advice to CHAI in assessing and addressing regulatory issues (for example, for DTG in India).
- Supported CHAI's continued briefing of key stakeholders to determine agreements on strategies to lower DTG prices at its launch and to incentivise investment in manufacturing capacity.
- Supported i-Base, AfroCAB and CHAI's efforts in the coordination of global and country-specific community engagement efforts, including supporting local partners where community engagement was lacking.

Clinical trials and research

- Provided recommendations around planning for future clinical trial studies, emerging safety signals and the need to complement clinical trial learning with other types of data and research.
- Supported grantees in conducting implementation science studies to maximise the learning from DTG pilots. Also recommended the extension of trials to ensure they could address both immediate and emerging research gaps.

Second-line novel product development and formulations

- Provided recommendations for revisiting the potential to combine DTG and DRV/r to further reduce the dose and pill size for second-line fixed-dose combinations when more information becomes available in the coming months.

**There was a desire among some partners to continue the PAC model and to apply it to new areas.**

The stakeholders that we interviewed at the global level confirmed that the PAC promoted good coordination among the donors across ART product research, production and roll-out (including the preparation of global guidance).<sup>43</sup> Because of this, stakeholders raised questions about why the PAC was disbanded despite its effectiveness. There is concern that slower pathways, without the PAC platform, could delay the progress on other drugs, such as long-acting injectables for pre-exposure prophylaxis (PrEP).

**The evaluation found that there was strong internal coherence, coordination and evidence-sharing between clinical trial research partners, and with the Optimal grant.**

Examples include the collaboration between the Universities of Liverpool and Cape Town, resulting in sub-studies and publications, and the data from NAMSAL being analysed in parallel with the ADVANCE trial, which was presented at the Conference on Retroviruses and Opportunistic Infections (CROI) 2022 and at the TRIO satellite session at the International AIDS Society Conference 2022.<sup>44</sup> Similarly, while the clinical trial data were developed, scientists from CHAI (operating under Optimal) synthesised and translated emerging evidence from the clinical trials to pass it on to MoHs in focus countries (for example, on neural tube defects—NTDs).<sup>45</sup>

**1**

**Finding 2: Unitaid's emphasis on close partnership working with national governments ensured a strong fit between the ART optimisation portfolio and HIV programmes and the national health systems within targeted countries.**

<sup>42</sup> How clinical trials inform WHO guidelines.

<sup>43</sup> KIIs 39, 56, 57, 58.

<sup>44</sup> ADVANCE FGD.

<sup>45</sup> KIIs 56, 57.

**Early country engagement was important in identifying the needs/gaps, informing and aligning the focus of the investments and securing early buy-in from national governments.** During the project planning, Unitaid, CHAI and EGPAF representatives from the country teams held discussions with multiple national government authorities and other stakeholders to discuss specific gaps that could be addressed through the portfolio’s market-shaping and country-preparedness activities (including support to the early introduction of DTG). This comprised funding needs, government systems integration and quantification needs. For example, when the catalytic introduction of DTG was being planned, this was discussed with countries and was perceived as a success for Unitaid:

*“It meant that Unitaid was having these direct discussions with countries, which we don’t always get to do because we are only about only 95 people.... grantees normally have the relationships with partners”. (KII 35 and 37)*

**Downstream, the portfolio was strongly aligned with the needs of national governments, including through the Optimal and SPAAN grants, providing support for the health systems strengthening (HSS) necessary to enable the roll-out of optimal HIV treatments in LMICs.**

During implementation, grantees continued their engagement with national governments through a wide variety of mechanisms and systems-level support, including the following:

- Presentation of clinical and operational findings and knowledge-sharing with health ministries to inform decision-making.
- Drafting national action plans based on financial and clinical modelling.
- Supported national guidelines updates in advance of new product availability.
- Quantification and forecasting exercises.
- Technical assistance support for treatment sensitisation and literacy, including development of materials.
- Supporting pharmacovigilance systems.
- Tool development to support the rapid roll-out of treatments.
- Product uptake monitoring and mentorship/supervision support.
- Integration of CAB and community networks into national processes.

Clinical trial grantees collaborated with, and conducted training for, national government stakeholders to encourage evidence-based policymaking, demand for new treatments and the adoption of public health recommendations.<sup>46</sup> Similarly, AfroCAB worked with policymakers to advocate for optimal treatments for people living with HIV, including for updated national guidelines and increased national budgets. Through SPAAN, in Côte d'Ivoire EGPAF worked in close collaboration with a wide range of country agencies (including the MoH and implementing partners such as Baylor, ICAP, Médecins Sans Frontières, and Chemonics) as well as technical agencies (such as the CDC, USAID, UNICEF and WHO).<sup>47</sup> Through the Optimal grant, CHAI promoted strong coordination with governments around decision-making processes and capacity building, alongside a range of other local and international partners<sup>48</sup> who are involved in the delivery of national HIV programmes.<sup>49</sup> CHAI recognised the need for joint planning meetings between MoHs and other

<sup>46</sup> KIIs 26–33, 35, 37; ADVANCE FGD; DoIPHIN-2 FGD; NAMSAL FGD; South Africa Country Report; Uganda Country Report.

<sup>47</sup> Annex 1\_EGPAF-POC-EID\_NCE Project Plan vF.

<sup>48</sup> Partners involved in supporting national MoHs included not only technical bodies (such as WHO) and large funders of HIV programmes (such as Global Fund and PEPFAR), but also a wide range of international, national and local NGOs, community-based organisations and CSOs.

<sup>49</sup> KIIs 26, 33, 44, 51; 2019\_HIV-Disease-narrative.

partners to achieve scalability. This involved a clear and phased approach for the roll-out of new treatments outlining the roles and contributions of each stakeholder and the future integration of ART optimisation activities within national health systems.

Our evaluation found that Unitaid's ART optimisation investments supported national government HIV programmes and relevant HSS activities in at least four key areas: (1) access to essential medicines; (2) health information systems; (3) health workforce development; and (4) leadership and governance. CHAI works in close collaboration and at the request of partner governments, allowing trust built from long-standing relationships to support accelerated product introduction and improving sustainability of interventions.

**Close engagement with MoHs through TWGs and other national bodies helped to ensure no duplication.**<sup>50</sup> For example, the Optimal grant built on existing supply chains, working closely with PEPFAR and Global Fund, rather than setting up parallel supply chains. The rationale was that once demand was generated and demonstrated, these scale-up partners would provide funding to support large-scale procurement. Finally, close partnerships enabled the portfolio to share information on the challenges in early adopter countries as well as across countries.<sup>51</sup>

*“CHAI was very strategic in the way they engaged partners and MoH. They were able to galvanise all parties to a single purpose of getting in the life-changing products and ensuring they reach the intended beneficiaries”. (KII 114)*

1

**Finding 3: Unitaid's catalytic and comprehensive approach (including novel market shaping, country preparedness and community engagement activities) has added unique value when compared with the work of other donors and partners.**

**Unitaid was described as a critical and sometimes unique donor in ART through the catalytic and enabling roles played by its investments and its coordination work with partners.** For example, Unitaid was perceived to have added significant value in paediatric treatments, including the promotion of long-acting options and new market modalities during strategic discussions with partners<sup>52</sup> and through its focus on accelerating affordability and widespread access to DTG/TLD in LMICs through the critical, catalytic market-shaping approach.<sup>53</sup>

*“Those programmes supported by Unitaid that have catalytic funding are much more streamlined and faster (than other global donors), which ultimately help[s] the APWG and all the members”. (KII 22)*

In Kenya, it was reported that it would have been exceedingly difficult to find alternative funding to drive novel product introduction without Unitaid. In addition, the Kenya Medical Supplies Authority (KEMSA) noted that, although other donors do offer to fund HIV treatments, Unitaid provided all of the additional ancillary support (including flexible technical assistance to improve health systems) which is not often provided by other donors. Finally, ASCOP and Kenya's MoH highlighted that, although other partners and donors provide support for optimal HIV treatments, Unitaid and its grants have a higher level of responsiveness and understanding regarding technical needs.

**The stakeholders who participated in this evaluation agreed that Unitaid's community engagement approach was unique.** Historically, community engagement activities have been implemented by organisations such as Unitaid; however, they were focused on influencing the

<sup>50</sup> ADVANCE and Optimal FGDs.

<sup>51</sup> KIIs 35, 37, 44, 51.

<sup>52</sup> Optimal FGD.

<sup>53</sup> Optimal project overview 2022.

demand for new treatments through improving treatment literacy outcomes. Other organisations have used strategies such as developing information education and communication (IEC) materials or training community and civil society representatives to increase community knowledge and treatment literacy. However, for the ART Optimisation portfolio, the voices of community organisations were placed at the centre of the decision making and directly influenced the revision of the WHO's HIV treatment guidelines and the portfolio's community engagement strategy.

## 4 Results of the ART optimisation portfolio

This section reports on the effectiveness of Unitaid’s ART optimisation portfolio. It provides an assessment of Unitaid’s contribution to lowering key barriers for people living with HIV in accessing optimal treatments in LMICs by 2022 (4.1).

### Summary points

- The ART optimisation portfolio contributed to lowering all barriers to people living with HIV accessing optimal treatments in LMICs, to different degrees. Its comprehensive design:
  - demonstrated the quality and safety of DTG-based regimens through innovative clinical trials (accelerating approval and availability);
  - led to a reduction in prices through successful market shaping activities. For example, the DTG catalytic procurement initiative supported the breakthrough TLD ceiling price agreement, enabling the rapid global shift to TLD;
  - increased demand and accelerated national adoption through partner engagement, capacity building and community advocacy; and
  - helped ensure availability by supporting demand visibility (through the APWG) and the strengthening of supply chain systems.
- The portfolio’s close work with manufacturers, on technical assistance and advocacy work, accelerated the manufacturing of generic drugs and their time to market in LMICs.
- The community engagement efforts were particularly innovative and significantly contributed to demand generation, acceptability, and adherence to new optimal regimens. Significant support was provided in these areas by the Optimal grant, including through the Optimal CAB, as well as by the PAC.

### Key lessons learnt

- Funding multiple trials simultaneously can pave the way for accelerated global and national policy revisions.
- Further targeted research is required to help improve access to products for specific underserved populations (including younger children and older people), to support national guideline revisions and monitor safety risks such as weight gain.
- Lower volume paediatric and 2nd/3rd line products are likely to need further market support (for example, catalytic or pooled procurement) to ensure supply, as well as ongoing product introduction activities.
- Broad community engagement from the outset of clinical trials is important to ensure demand and meaningful outcomes.
- Country-preparedness activities had some impact on improving supply and delivery systems, but addressing all barriers to reaching those in need in a reliable and timely manner requires longer-term support for governments.

### 4.1 Reducing barriers to access

Table 6 outlines Unitaid’s access barriers and the desired outcomes.

Table 6. Access barriers and desired outcomes of Unitaid’s ART optimisation portfolio

Access barriers	Desired outcome
Innovation & Availability	Better HIV treatment products (new, adapted and superior) are commercially available for rapid introduction in LMICs.
Quality	HIV treatment products are quality-assured (stringent regulatory authority and WHO PQ).

Affordability	Optimal HIV treatment products are available at the lowest price, sustainable for suppliers, and are not unreasonable for governments, donors or people living with HIV, with a view to increasing access for the under-served.
Demand & Adoption	National country programmes introduce and adopt the most cost-effective HIV treatment products within their local context. Proven delivery models for HIV treatment in LMICs exist.
Supply & Delivery	Supply chain systems, including quantification, procurement, storage and distribution, function effectively to ensure that optimal HIV treatment products reach those in need in a reliable and timely manner. An adequate and sustainable supply exists to meet global needs.

It should be noted that, in this chapter, we focus on describing Unitaid's contribution to intended outcomes. The following chapter on scalability provides a before-and-after assessment of the status of the scale-up of optimal treatments.

#### 4.1.1 Overview

1

**Finding 1: Unitaid has contributed significantly to the reduction in access barriers relating to innovation, quality, affordability, demand and adoption.**

Although some barriers persist, the work undertaken by the portfolio has made a significant contribution to the reduction in the barriers to access in LMICs (Table 6). The Unitaid ART optimisation portfolio investment led to better regimens, with fewer side effects, and to new products being given to people living with HIV in LMICs with unprecedented speed. In support of this, Unitaid's LMIC clinical trials played a significant role in generating new evidence to ensure that optimal HIV treatment products were safe and effective for vulnerable and underserved African populations, and that they could be rapidly introduced in LMICs. The clinical trials also increased country ownership and awareness of the results, further establishing the importance of conducting clinical trials in LMICs. Simultaneously funding multiple trials enabled broad WHO guideline revisions and rapid quality approval. Innovative market interventions through the portfolio, including incentive mechanisms and development programs, supported accelerated generic development of DTG and affordable pricing. Community engagement, capacity building and technical support for MoHs contributed to the increased demand for and adoption of cost-effective optimal HIV treatment products. The ART optimisation portfolio contributed to the reduction of supply and delivery barriers. However, the level of contribution was variable by country.

**Overview of remaining gaps:** In summary, additional or ongoing work to strengthen supply chain systems, working with Unitaid's partners, will be crucial to ensuring better product access and sustained supplies going forward. Other outstanding barriers to be addressed include access for specific underserved populations (requiring further targeted research and monitoring of safety concerns), rapid quality and regulatory approval of pipeline drugs (such as pDRV/r), and issues in communication and training among healthcare workers.



Below, we explore the contribution of Unitaid to each of these barriers in more detail and provide a rating of Unitaid's contribution (as per the key below):



#### 4.1.2 Innovation and availability

Better HIV treatment products (new, adapted and superior) are **commercially available for rapid introduction** in LMICs.



**1**

**Finding 1: Through funding innovative LMIC-based clinical trials, Unitaid demonstrated the quality and safety of DTG-based regimens in African population groups, thus expediting manufacturer production and accelerating the introduction of better HIV treatment products in LMICs.**

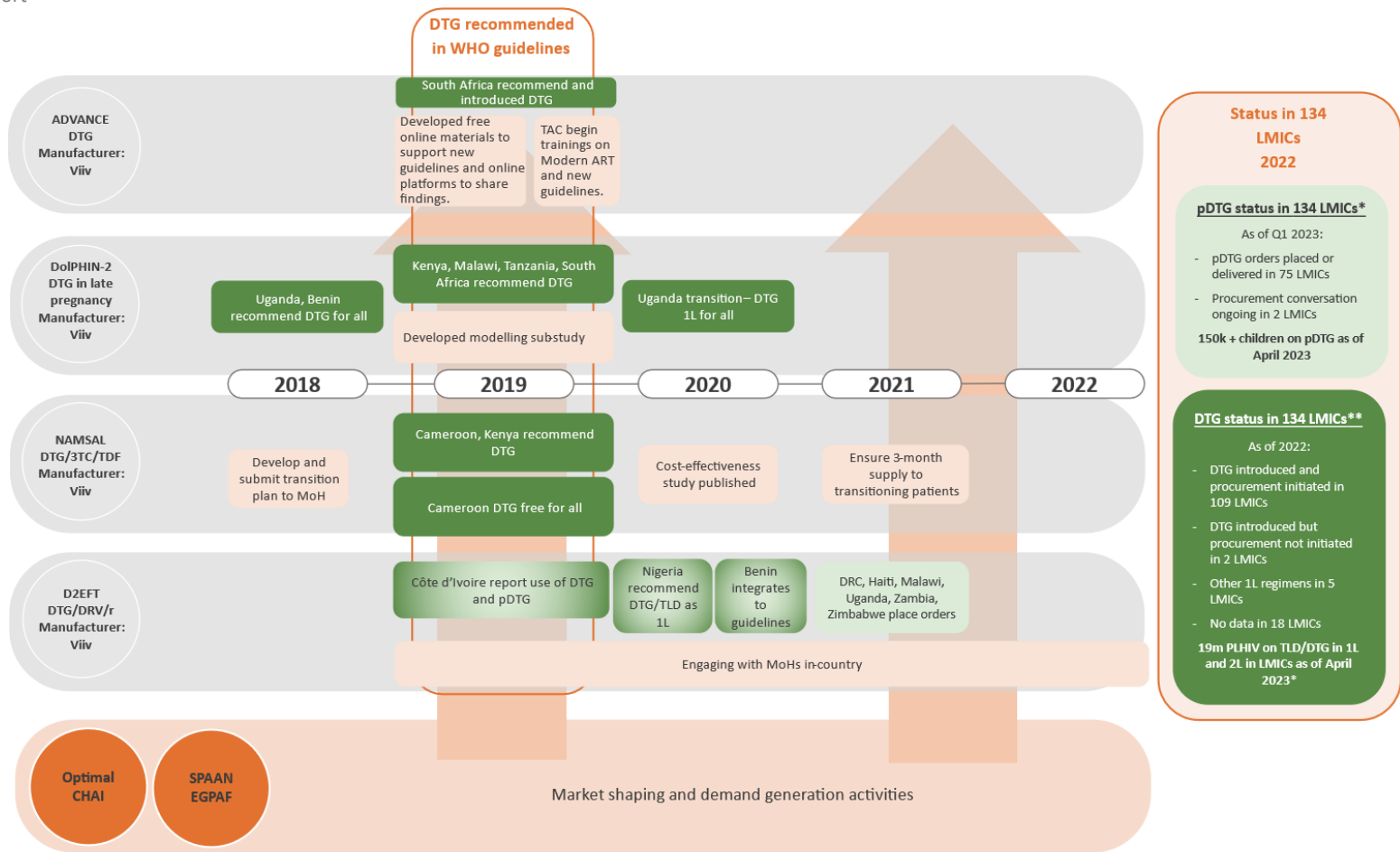
**New evidence generated by the clinical trial grants played a critical role in changing the standard of HIV care in LMICs and in increasing the availability of better HIV treatment products.** The identification of emerging drug formulations requiring additional evidence on safety and efficacy was a crucial step in this process. For example, Unitaid's involvement was crucial in enabling the originator, ViiV Healthcare, and NAMSAL to complete the purchase of a molecule for genetic resistance testing. The trials showed that the treatment products were the best available options (if not yet the absolute ideal) for viral load suppression, including for pregnant women and children, by identifying side effects and events that were not previously documented. This made it easier to include new drugs in country treatment guidelines (see Figure 10) and increased community acceptability, further highlighting the importance of rigorous testing in LMICs themselves. The investment in generating evidence on innovative drug formulations, coupled with market-shaping approaches and partnerships, triggered manufacturers' engagement, thus ensuring the commercial availability of products.

Figure 10 details a timeline of product introduction across the ART optimisation portfolio, including the specific contributions of the clinical trial grants. The horizontal grey bars denote the different clinical trials. Within these grey lines, the boxes denote:

- Market shaping activities done under each grant (peach box).
- Milestones in the introduction in each of the grant focus countries:<sup>54</sup>
  - DTG (dark green)
  - pDTG (light green)
  - both (faded colour)

This in turn contributed to the global take-up of DTG and pDTG in LMICs (final column), further supported by the Optimal grant, work of the PAC and APWG, and community advocacy.

<sup>54</sup> These milestones included in the diagram do not necessarily denote milestones achieved by the particular trials (for example, for DolPHIN-2, DTG use in late pregnancy was not recommended by Tanzania in 2018), but instead show the progression of the countries of focus toward DTG use more generally.



\*Source: 2023 HIV Mid-Year Market Memo, CHAI  
 \*\* Source: <https://cfs.hivci.org/index.html>

Figure 10. Timeline of optimal product introduction 2018-2022, per clinical trial grant

**Active communication and awareness of LMIC trial results, including the early sharing of data with global partners, manufacturers and national governments, shortened the time between innovation, evidence generation, the commercial availability of DTG products, and their translation into national HIV programmes and practices.**<sup>55</sup> The effective communication of the interim clinical trial data to manufacturers, and the acceptability of each study regimen helped to accelerate the supply of new treatments. This was estimated to be three years faster in Cameroon thanks to NAMSAL.

*NAMSAL has shown a first line with dolutegravir and an improved alternative first line with EFA 400... the impact is that countries that had decided to eliminate EFA 600 have started to think: 'Well, there is EFA 400, it may work just as well and it is a good alternative for certain patients who cannot tolerate dolutegravir'... They used our presence in national conferences to sensitise other countries about the effectiveness of the EFA 400. (NAMSAL FGD)*

*"With DTG there was a fast availability to the market. This was available quickly, usually takes up to two years, this was available to the consumers in six months."* (KII 56 and 57)

The DolPHIN-2 project accelerated the timeline for the introduction of DTG, including through supporting the MoH's policy changes in South Africa and Uganda and demonstrating the potential for future generic production.<sup>56</sup> Under the Optimal grant, clinical trial data sharing and partnerships between CHAI, generic manufacturers and regulatory bodies led to quality generic products being formulated and made available to countries more rapidly.

**2**

**Finding 2: Manufacturers felt that the portfolio's close work with them on technical assistance and advocacy work also supported the manufacturing of generic drugs and accelerated the time-to-market.**

**The Optimal grant's technical support for product development (including through product development partnerships) played a pivotal role in upstream innovation and research and development, and alongside associated advocacy work, further aided the commercialisation of products.**<sup>57</sup> This included negotiating with manufacturers and assessing their production capacity and capability to ensure a reliable supply. Following a rigorous and externally reviewed selection process, regular product development meetings helped further reduce the time-to-market for optimal HIV products. For example, through the pDTG incentive program, for the first time ever, close collaboration and engagement between CHAI, the generic manufacturers (Viatris and Macleods) and the innovator (ViiV) enabled the generic HIV medication to be filed with the US Food and Drug Administration (FDA) while the product was still under review (Box 7). CHAI reported that pDTG was approved 12 times faster than the average for generic paediatric ARVs since PEPFAR was established. Additionally, the Optimal grant was able to assist in reducing production costs and provided estimated costing support to aid in the commercialisation process. For example, CHAI's process chemistry work identified cost reduction opportunities for DRV, resulting in an optimised chemistry protocol that contributed to reducing the price of DRV/r from \$340 per person per year (PPPY) to \$210 PPPY. This work targeted the bisfuran synthesis process – which accounts for 60% of DRV's cost – and identified efficiencies that reduced its price. CHAI completed DRV technology transfers to more than three manufacturers to support research investments beyond the Optimal project. The impact of Optimal's work was not limited to a single country, as manufacturers were

<sup>55</sup> KII 39, 49, FGD DolPHIN-2.

<sup>56</sup> KIIs 26–33, 36, 49, 39; FGD DolPHIN-2.

<sup>57</sup> 2019\_HIV-Disease-narrative.

able to utilise the experience gained from working with CHAI to influence their overall product production and supply, including to countries where Optimal did not operate.<sup>58</sup>

**Overall, therefore, the contribution of Unitaid’s ART optimisation portfolio to the increased availability of optimal HIV treatment products in LMICs is considered ‘high.’** Further details on the scale-up of the optimal HIV treatment products supported by Unitaid’s portfolio are provided in Section 5.1.

**Remaining gaps:** It was suggested that further implementation research is needed to support availability of better HIV treatment products for the paediatric population:<sup>59</sup> for example, testing innovations in diagnostics and treatments for AHD.<sup>60</sup> Research on the management of weight gain caused by DTG (including use of weight-loss medications among people living with HIV) should also be accelerated to address concerns related to the use of this now commonly-used ART drug. To ensure that any adverse effects of ART drugs can be continuously monitored and addressed promptly, grantees suggested institutionalising HIV-related pharmacovigilance into routine care at all ART sites and national HIV programmes. Dissemination of uptake monitoring tools developed through the portfolio was also suggested.<sup>61</sup>

### 4.1.3 Quality

HIV treatment products are **quality assured** (for example, by stringent regulatory authority and WHO PQ).



1

**Finding 1: By funding multiple clinical trials which filled the identified evidence gaps and by directly engaging WHO through the PAC and Enabler grant, the portfolio created pathways to WHO guideline revisions and to the rapid approval of HIV treatment products in LMICs.**

**WHO guidelines were changed based on Unitaid’s clinical study evidence, which used multiple trials to consider previously excluded sub-populations, thus facilitating rapid global and national approval.** The portfolio’s market-shaping work also supported national regulators in streamlining their review and registration processes to introduce high-quality regimens (as further described in Section 5.2.1). This included engaging pharmaceutical companies to jointly collaborate with regulators to establish regulatory pathways, and novel ones where precedent was lacking. For example, following the research into the safety and efficacy of the lower dose of EFV400 – which was tested in the NAMSAL trial –, this is now the first alternative recommended in WHO HIV treatment guidelines.<sup>62</sup> The novel filing strategy that was developed through the Optimal grant had a significant impact on its availability, achieved through Unitaid’s investment (see also Section 6.1). Additionally, the results of the NAMSAL trial guided the MoH in Cameroon in updating their national treatment guidelines in 2020, aligning with WHO recommendations. Manufacturers stated that support from Unitaid helped them better navigate the regulatory pathways.

**The PAC co-chair being a member of the WHO facilitated engagement and informal communications with the WHO, alongside the Enabler grant, regarding evidence gaps and emerging findings.** See evidence on Box 7.

<sup>58</sup> KIIs 56, 57, 59, 60; EVA Optimal ARV Grant Final Report.

<sup>59</sup> FGD Optimal.

<sup>60</sup> KII 45.

<sup>61</sup> ADVANCE FGD; DOLPHIN2 FGD; NAMSAL FGD.

<sup>62</sup> FGD NAMSAL, ADVANCE, KII 47, 26-33, 38.

### Box 7. Contribution of the PAC to revision of WHO HIV treatment guidelines

The process of updating WHO guidelines involved initial discussions with WHO itself to ensure that Unitaid-funded clinical trials were designed to address critical research questions and evidence gaps. Regular touchpoints between the Unitaid teams and their WHO counterparts, including through the PAC, were then maintained throughout implementation. PAC meetings provided a valuable platform for Unitaid’s grantees to share progress, data and the outcomes of their work with WHO and other partners. Facilitating this, the co-chair of the PAC was the Coordinator of HIV Treatment and Care in the Department of Global HIV, Hepatitis and STI Programmes at WHO.

This on-going communication with WHO supported the guideline changes based on Unitaid’s clinical study evidence. For example, in early 2019, data from the clinical trials (NAMSAL interim results and evidence from other trials) were presented to WHO. After undergoing a systematic review of available evidence, this data was then shared with the WHO guidelines review committee. This influenced the updated recommendations for the first- and second-line ARV regimens in July 2019. The updated recommendations favoured a DTG-based regimen as the preferred option and an EFV400-based regimen as an alternative.

The systematic review requested by WHO and published in 2020 further informed the comprehensive guidelines on HIV prevention, testing, treatment, service delivery and monitoring in 2021. These guideline revisions facilitated the wider adoption of improved HIV treatments in LMICs, including West Africa, providing people with HIV access to more effective and affordable, with fewer side effects and less prone to drug resistance, regimens.<sup>63</sup>

Because of these results, Unitaid’s contribution to facilitating regulatory approvals/market authorisation for HIV treatments is considered ‘high.’

**Remaining gaps:** Improving access to certain drugs, such as DRV/r as the preferred second-line option among people living with HIV failing on DTG. These have yet to be listed as preferred in WHO guidelines and are thus not prioritised in national guidelines (and country procurement plans). Additionally, there is a need for further research on the use of these drugs in key groups such as younger children and pregnant women.

#### 4.1.4 Affordability

Optimal HIV treatment products are available at the **lowest price**, are sustainable for suppliers and are not unreasonable for governments, donors and people living with HIV, with a view to increasing access for the under-served.



1

**Finding 1: Product partnerships, ceiling price agreements and demand forecasts – which were facilitated by the portfolio and the APWG – succeeded in reducing the cost of optimal treatment products for HIV, making it easier for national governments to switch to recommended regimens.**

**Partnerships with manufacturers made optimal treatment products more affordable than former treatments.**<sup>64</sup> This included support for generic licensing and production, which was essential for reducing treatment costs, scaling-up treatment access in LMICs, and sustainability. The ADVANCE clinical trial expedited access to results data for generic manufacturers, while CHAI facilitated the entry of generic companies (for example, by supporting generic manufacturers’ dossier submissions

<sup>63</sup> NAMSAL-WHO guidelines contributions\_23-Sep-2022.

<sup>64</sup> KII 26-33.

to the US FDA—as described in Section 5.2.1, finding 3), leading to accelerated supply of generic products and to lower prices.<sup>65</sup>

*That wasn't the whole point of our programmes, the price thing, but dolutegravir is a drug that is easy to make and that doesn't cost much to make generically.  
(NAMSAL FGD)*

**Pricing agreements and increased demand helped to secure price reductions for optimal HIV treatment products for adults, including TLD.** A ceiling pricing agreement made the first affordable, generic, single-pill HIV treatment regimen containing DTG available in LMICs. The agreement, driven by BMGF and CHAI, and supported by various organisations – including governments, UNAIDS, Unitaid, UK Department for International Development, PEPFAR, USAID and Global Fund – aimed to provide DTG-based treatments at approximately US\$75 PPPY, below the existing standard of care, to public-sector purchasers in LMICs. The generic fixed-dose combination of TLD was developed by Mylan and Aurobindo under licensing agreements from ViiV Healthcare, the original developer of DTG. Accelerating the availability of the new fixed-dose combination in over 90 LMICs, the agreement was estimated to save public-sector purchasers over US\$1bn over six years.<sup>66</sup>

**Unitaid contributed to securing lower prices for paediatric treatment.** CHAI's partnerships with national governments and manufacturers generated savings and allowed for increased investment in additional procurement volumes (for example: for pDTG). Through an incentive grant and support for accelerated product development, as part of a comprehensive package of access conditions overseen by Unitaid, CHAI negotiated lower pricing for pDTG 10mg, which resulted in a reduction of the annual cost of care from US\$480 to US\$120 PPPY. As a result of the reduced product prices, PEPFAR and Global Fund were able to invest in increased drug volumes to support more people living with HIV on treatment.<sup>67</sup>

Further details on the contribution of Unitaid's pricing and financial incentive mechanisms in securing lower costs and in accelerating product development, including their added value, is provided in Box 8 and Section 5.2.1.

**The APWG's annual demand forecasts from industry buyers further contributed to price reduction and increased availability of optimal treatment products by increasing commercial viability for manufacturers.**<sup>68</sup> The reliable supply and affordable pricing of commodities within a sensitive market depend on the aggregated demand across partners, including a willingness to agree on minimum batch procurements. This insight stems from consolidated acquisitions driven by expected demand across nations, rather than relying on a volume incentive mechanism. As further described in Section 5.2.2, knowing the expected volumes of a product can help manufacturers optimise production planning, reduce inventory costs, avoid stock-outs and help negotiate better pricing. For example, generic manufacturers reduced their production costs by promoting multi-month packs and by using APWG annual forecasts and procurement volume commitments to better negotiate with raw material suppliers. While individual members of the APWG may have conducted these activities regardless of Unitaid's involvement, Unitaid funding provided the catalyst for members to work on this together and effectively coordinate around accelerating access.

<sup>65</sup> ADVANCE FGD.

<sup>66</sup> [https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2017/september/20170921\\_TLD](https://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2017/september/20170921_TLD).

<sup>67</sup> Uganda country report, Itad.

<sup>68</sup> KIIs 22, 23, 26–33, 56, 57; ADVANCE FGD; D<sup>2</sup>EFT 2019 Annual Report.

Based upon the success of the pursued market-shaping approaches, the degree to which Unitaid's ART optimisation investments contributed to making optimal HIV treatment products available at lower prices – and therefore affordable for governments and other potential donors – is considered 'high.'

### Box 8. Contribution and added value of market-shaping mechanisms

#### Relevance/rationale

Part of the market-shaping approach employed by CHAI and Unitaid under the Optimal grant to accelerate product development and to catalyse the market for optimal HIV treatment products was the development of incentive and pricing mechanisms. These mechanisms were developed with the understanding that, when the market size for a product is small, in addition to some products being more technically complex to make, manufacturers are often reluctant to invest in the development and commercialisation of such products (and/or supply them at an affordable price) as the financial risk is too great. To address this, for each product, and in consultation with Unitaid, CHAI developed a flexible product commercialisation plan, to outline the current product development pathway, identify the need for a market intervention (for instance, a financial incentive) and support adaptation as the product market changes. The incentive mechanisms outlined below were designed as competitive mechanisms to identify manufacturers offering best value for money and were implemented with oversight and support from the Unitaid secretariat.

#### Contribution

The incentive mechanisms employed to catalyse the availability of different products included the following:

- **DRV/r:** financial incentive and pricing agreement with **Hetero Labs** to manufacture DRV/r as an affordable second-line HIV treatment. Prior to the CHAI agreement and financial incentive, in 2019, Hetero had attained Global Fund/ERP category two 'no objection' and subsequent WHO PQ for the product. However, the market price was not affordable for LMICs. After their initial price offering of US\$36/pack, an agreement was reached at US\$17.50/pack (US\$210 PPPY), which was below the price of LPV/r (the existing standard of care). This price agreement was made in exchange for a subsidy as part of an integrated package of market-shaping activities provided through the Optimal grant (also including catalytic procurement – see Box 4 – to accelerate product introduction and scale-up in countries). We found that, while the Unitaid financial incentive/subsidy did not affect initial product development, it was solely responsible for the final price agreement and commercialisation.
- **pDRV/r:** financial incentive mechanism with **Laurus Labs** to accelerate development, commercialisation and registration of the paediatric formulation of DRV/r (second- and third-line treatments). The incentives from CHAI provided fixed payments according to completion of agreed-upon development milestones, such as bioequivalence studies. A bioequivalence (BE) study and pre-investigational new drugs (PRE-IND) activities were funded.<sup>69</sup> In this case, if the incentive had not been provided, the product would most likely not have been developed. The incentive mechanism for pDRV/r has the potential to impact over 100,000 children living with HIV across many countries.
- **pDTG:** a pricing agreement and financial incentive were provided for the development of this paediatric version of DTG, which set a historic precedent for the time it took to gain regulatory approval. As noted above, the price was negotiated at US\$4.50 per 90 pack, or at an annual cost of US\$36/child (a 75% reduction from the standard of care), for all public procurers and for use in over 123 countries. This is perceived as a great success in the field of paediatric HIV. Both

<sup>69</sup> Through bioequivalence studies, generic manufacturers demonstrate that their products satisfy the same standards as those applicable to the innovator product and provide assurance that it is clinically interchangeable (that is, bioequivalent or therapeutically equivalent) with the innovator product. Pre-Investigational New Drug (PRE-IND) activities are primarily designed to foster communications between manufacturers, drug sponsors, and the FDA as they begin the process of bringing a new drug to market.

manufacturers unsuccessful in their bids for the incentive stated that they will proceed with pDTG development.

- **pTAF and pALD:** market failures have delayed the development of certain essential paediatric products despite consensus by the Paediatric Antiretroviral Drug Optimization group on their necessity and prioritization. These challenges have affected several key paediatric priority products, including Abacavir-lamivudine-dolutegravir (pALD) and pTAF. For these paediatric HIV treatments, CHAI determined that no direct financial incentive was required, but developed a market accelerator programme to overcome development bottlenecks:
  - **pALD:** In collaboration with **ViiV Healthcare**, CHAI implemented a market accelerator partnership with generic manufacturers (**Viatis** and **Aurobindo**) to speed-up the development, regulatory filing and commercialisation of pALD. CHAI negotiated contracts with each supplier and provided technical support to reach critical development milestones (including PRE-IND meetings). Viatis and Aurobindo completed product development milestones, including analytical method validation, process optimisation, manufacturing of exhibit batches and BE studies. Both manufacturers subsequently submitted US FDA dossier filings, which are currently under review for tentative approval under the PEPFAR program (see Section 4.1.2).
  - **pTAF:** To accelerate development of paediatric TAF, CHAI established a partnership with **Gilead** through development of a memorandum of understanding and completion of a project charter. CHAI established a partnership with Gilead for the development of paediatric TAF (pTAF) and executed contracts with two generic suppliers. The Optimal project continues to play a critical role in ensuring that progress against global priorities is realised.
- **TLD:** The ceiling price agreement and volume guarantee through the product coalition (see above) was the first time that any first-line treatment product came to the market below the price of the current standard of care. This enabled the rapid global shift to TLD.

### Added value

Milestone-based incentive mechanisms are an attractive option for ‘de-risking’ manufacturers’ investments, while at the same time attaching the incentive to developmental milestones. Large manufacturers may have other priorities and de-risking an option helps them prioritise. Incentives post product development can also help offset costs that would otherwise lead to higher product prices. Conversely, financial incentives may not always be needed: for example, in cases where a new/sub-population formulation is based on an existing one already under manufacture, or where the new product is already WHO pre-qualified (that is, they are ready for commercialisation), or where the manufacturer is a large company with a considerable footprint (for instance, it has an existing infrastructure and network which it can rely upon for commercialisation and introduction). In such instances, the size of the market incentive should be carefully considered, and/or funds may be better spent on other catalytic activities (for example, to fund BE studies, pre-IND activities, catalytic procurement or process chemistry improvements).

Overall, we found that the use of the accelerator programme, pricing agreements and the financial incentive for pDRV/r were appropriate given the small market (especially for paediatric products), especially since manufacturers were unlikely to have invested in the development of products with such low volume and revenue potential. According to the external verification agent (EVA) report on the Optimal grant, both successful applicants to the pDTG incentive mechanism stated that they would have developed the product without the incentive. However, coming to the market would have taken longer without the technical transfer from ViiV Healthcare and the unique regulatory strategy that CHAI pioneered.

### Alternative approaches

Some manufacturers and scale-up partners noted that there are alternative market-shaping approaches and that these could have added to the effectiveness of Unitaid’s implementation. The main alternative approaches include active pharmaceutical ingredient stockpiling and volume guarantees (used for TLD), where the manufacturer covers the cost of development but the company remains incentivised (the



financial risk is lowered) because there is a guaranteed volume of procurement waiting for them upon product development. However, volume guarantees are not without risk because products are typically not yet pre-qualified or included in WHO treatment guidelines.

Whilst volume guarantees could have been considered as a complementary approach (once generics were available), CHAI avoided them by combining other activities to accelerate the introduction of optimal HIV treatment products, including the following:

- Catalytic procurement (six countries)
- Generated demand from people living with HIV (the Optimal CAB)

CHAI supported forecasting and quantification exercises and developed national forecasts and supply plans. The market-shaping approach employed by CHAI, being an integrated package, was relevant when compared with other, more expensive incentive mechanisms, such as volume guarantees. This integrated approach included a careful combination of supply- and demand-side activities, including the development of product commercialisation plans, market intelligence, demand creation and direct host country government support for the overall ecosystem. In the absence of any of these critical pieces, the market-shaping work would have likely failed in accelerating the introduction of optimal HIV treatment products.

Going forward, Unitaid grantees should continue to consider market-shaping needs along the entire value chain (including clinical trials, market acceleration, product introduction and scenario planning for future market dynamics/developments). BE and additional clinical trial studies could be considered as highly cost-effective mechanisms for accelerating the time-to-market. We also concur with the recommendation of the EVA: “Incentives should preferably be awarded to more than one company to avoid creation of a monopoly and to ensure supply security—provided that the market is capable of sustaining more than one supplier.”

**Remaining gaps:** With the Optimal grant coming to an end, there may be critical market development activities that are still required to help ensure supplier sustainability. This is especially the case for pDRV/r, since Laurus Labs is a smaller manufacturer and paediatrics involve lower volumes (further details in Section 5.2.1, finding 5, under scalability).<sup>70</sup>

#### 4.1.5 Demand and adoption

National country programmes **introduce and adopt** the most cost-effective HIV treatment products within their local context. Proven delivery models for HIV treatment in LMICs exist.



2

**Finding 1: Community engagement activities, healthcare worker training and technical support to MoHs (and other national authorities) combined to effectively tackle demand-side barriers, supporting the adoption of cost-effective HIV treatment products within national programmes.**

**Ongoing community engagement was both successful and critical in tackling demand-side barriers related to the acceptance of clinical trial results, other evidence and new optimal treatments.** The portfolio’s community engagement activities, including treatment literacy and information and communication campaigns, contributed to countering negative perceptions about the new optimal treatments and helped to boost demand. Firstly, the community engagement process that was established to promote different clinical trials and products helped to mitigate the risk that target

<sup>70</sup> KIIs 43, 45, 54, 55; NAMSAL FGD.

populations would not participate, as well as helping with the interpretation and acceptance of results.

*“Community engagement gives increased credibility to the trials with the community (i.e. trust)”. D2EFT FGD*

Successful examples of this diverse work include drama group performances in waiting rooms (DolPHIN-2), the dissemination of videos on YouTube, graffiti murals, development of a mobile application and accompanying materials in South Africa (ADVANCE), and the translation and dissemination of leaflets on the results of the studies and impact on people living with HIV (DolPHIN-2). The creation of forums to discuss drug introduction was also an important quality aspect of the trials.

*“By working closely with peers of the participants and community members, this built trust by having the face of the portfolio be familiar and allowed for more honest conversations around issues of equity and other ‘sticky’ issues”. DolPHIN-2 FGD*

Fostering close relationships with the participants enrolled on the clinical trials also meant that they were more invested in the trials - this care relationship between the operational and medical staff was responsive to people’s needs and was collaborative.<sup>71</sup>

*“The support of the people who are in the projects during and after the project is fundamental”. NAMSAL FGD*

Alongside the trials, AfroCAB – supported by the Optimal grant, and in collaboration with CHAI – played a decisive role in the adoption of optimal treatments in countries, including through raising community awareness and advocating to the government for the approval of new treatments. Demonstrating adaptability, two examples stand out: during Covid-19, community members were trained via Zoom and, in response to the neural tube defects safety signal in 2018, a forum for women living with HIV was rapidly mobilised to discuss the impact of the emerging concerning evidence around use of DTG by women of reproductive age.

Finally, Unitaid, grantees, community representatives and global stakeholders all believed the Optimal CAB contributed enormously to the effectiveness of the ART optimisation portfolio:

*CAB helped to personalise the interventions... and sensitise peers to the advantages of new medicines [over] the previous medicines they were accustomed [to] for years. (Unitaid FGD)*

Stakeholders believed that this range of community engagement work played a crucial role in increasing treatment literacy among people living with HIV in LMICs.<sup>72</sup>

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<sup>72</sup> South Africa Country Report; Uganda Country Report.

*“The drugs are pointless if there is not community engagement. It is essential to involve the community because you will have people to take it, and if they don’t know how to do it, they will do it wrong.” (KII 50)*

Further details on Unitaid’s community engagement activities, as well as **key lessons learnt**, are included in Box 5.

**Training and training resources for healthcare workers also contributed to strengthening demand by tackling capacity barriers as well as supporting advocacy efforts.** For example, through ADVANCE funding in South Africa, healthcare workers received training on new guidelines, including the delivery of DTG and AHD management courses. Optimal and SPAAN’s work with healthcare workers and communities, through training and knowledge dissemination and communications, was critical to building confidence and generating demand.

*“CHAI was important to promote the understanding of available drugs... The training was critical during the catalytic phase (and PEPFAR came and did the accelerating phase). They focused on 15 facilities sites, developing the materials, which were then printed and distributed at a large scale by the Ministry of Health.” (KII 130)*

Training and resources, including journalist training as a part of NAMSAL and the New Product Introduction Toolkit,<sup>73</sup> were translated into simple materials, graphics and videos that were adopted by MoHs (for example, Uganda) and partner organisations (for example, PEPFAR).

**The country-preparedness work of CHAI and other grantees provided support for MoHs across the product introduction pathway, further tackling capacity barriers and helping to strengthen the capabilities and demand required at national government level for rapid adoption of new HIV treatments.** The availability of clinical trial data from LMICs boosted stakeholder confidence and increased partner and country demand for the drugs. In Cameroon and Uganda, government engagement during clinical trials led to the introduction and adoption of tested drugs, partly through generating a sense of ownership. This included working with national governments (and global partners and the community) to help develop country guidelines and revise standard operating procedures—for example: in Benin, Cameroon, Kenya, Malawi, Nigeria, South Africa, Uganda and Zimbabwe to help finalise the transition from TLE to TLD. In Uganda, the CHAI team supported the MoH in convening key advisory committees to review policy changes that aligned with optimal product adoption. Additionally, CHAI provided support in strengthening safety monitoring through the development of guidelines for pharmacovigilance. These efforts aimed to ensure that the best possible HIV treatment options were available to all Ugandans and that they were used safely and effectively.<sup>74</sup> In Kenya, CHAI’s support accelerated the adoption of new regimens and guidelines, with over 500,000 people living with HIV receiving DTG by 2020:

*“It [new treatments] can be in guidelines, it can even be available, but you need to ensure that people have access to it and ask for it at health facilities.” (KII 88)*

Further details of these capacity building efforts are provided in Section 5.3.2 under country scalability.

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<sup>73</sup> <https://www.newhivdrugs.org/resource-library/tags/cab>.

<sup>74</sup> KII 21, 23, 26-33, and 52, Kenya and Uganda country report.

1

**Finding 2: Following a reported potential association between neural tube defects in babies and mothers exposed to DTG during the periconception period, mobilisation and advocacy campaigns from community groups, partially funded by the Optimal grant, helped to protect informed choice and the ongoing adoption of this cost-effective HIV treatment within country programmes.**

In 2018, the use of DTG as a first-line regimen for women of reproductive age was discouraged due to safety signals on potential neural tube defects (NTDs) in babies born to mothers exposed to DTG during the periconception period. This included safety communications and recommendations from the Southern African HIV Clinicians Society, South African Health Products Regulatory Authority (SAHPRA) and WHO. By the time WHO issued its warning, Kenya had already started administering DTG to women living with HIV. The country subsequently withdrew the use of DTG for women of reproductive age (15-49). Communities of women living with HIV in Kenya were highly concerned that they had not been consulted on this decision, which would fundamentally affect their right to choose their treatment options (regardless of their age) and their ability to make decisions regarding their reproductive lives. In response to this, intensive mobilisation and advocacy campaigns were launched by community groups supported by the Optimal grant, including AfroCAB. Alongside lobbying international partners, in Kenya this resulted in a petition drafted to NASCOP and the MoH, asking for a revision of the cautionary measures barring women from accessing DTG based on more recent medical opinion. Subsequently, in 2019, WHO lifted the caution on the use of DTG for women of childbearing age (focusing instead on informed consent) after additional research found that the risk of NTDs was lower than previously suspected. NASCOP subsequently issued an updated circular in Kenya.

Based upon this evidence, the contribution of Unitaid’s ART optimisation portfolio to tackling demand-side barriers and accelerating the adoption and introduction of cost-effective HIV treatment products is also considered ‘high.’

**Remaining gaps:** Continued expansion of optimal treatments is necessary in some countries - this was noted in Cameroon, Cote d’Ivoire, Kenya, Nigeria, Uganda and Zimbabwe – and demand creation efforts should be inclusive of all stakeholders and all geographies. In South Africa, poor communication and lack of training were reported to have led to scepticism and reduction in uptake among some healthcare workers and clinicians.<sup>75</sup> Specifically, the more recent introduction of adult DRV/r has shown that introducing second-line regimens is more complicated than introducing first-line regimens. Adoption of pDRV/r at scale within national HIV programmes (and maximizing Unitaid’s investment in the development of such products), requires ongoing product-introduction activities at a country level. These include, for example, incorporating pDRV/r into national guidelines, developing country-specific transition and sequencing plans, implementing clinical mentorship and supervision for healthcare workers, working with community members to generate demand and conducting operational research in early adopter countries to generate evidence and best practices for broader pDRV/r roll-out.

#### 4.1.6 Supply and delivery

Supply-chain systems, including quantification, procurement, storage and distribution, function effectively to ensure that optimal HIV treatment products reach those in need in a reliable and timely manner. Adequate and sustainable supply exists to meet global needs.



<sup>75</sup> 2019\_ HIV disease narrative; 2021 Annual Report; Kenya Country Report.

2

**Finding 1: At the global level, the APWG successfully supported demand visibility for optimal HIV treatment products enabling adequate and stable supply planning. Country preparedness activities had some impact on improving supply and delivery systems, but not all barriers to reaching those in need have been addressed.**

**The APWG successfully aligned supply with demand, reducing lead times and stock-outs by coordinating procurement between major purchasers and improving visibility for manufacturers.**

As introduced above, CHAI (with Unitaid funding) worked with partners and industry through the APWG to support demand aggregation and procurement coordination, in turn securing affordability and an adequate supply of optimal HIV treatment products to meet global needs. These efforts in supply planning resulted in generic DTG introduction in dozens of LMICs less than ten months after receiving tentative US FDA approval.<sup>76</sup> The Optimal grant's catalytic procurement of DTG was also successful in accelerating roll-out of HIV treatment products to those in need. For example, catalytic funding was used to facilitate pDTG roll-out in Zimbabwe, a critical approach in countries that lacked child-friendly regimens.<sup>77</sup>

**The Optimal grant provided effective support for supply-planning at a country level with national MoHs. However, this support was limited, relative to the scale of the challenge.**

One strong example is in Kenya, where technical assistance is provided to NASCOP for forecasting and quantification exercises. This includes the continued use and adaptation of a CHAI-developed ART allocation tool to manage national orders from health facilities and address order errors down to the dispensing level to help close gaps in the order cycle. In Uganda, support was provided through participation in routine national quantification and supply-chain-planning meetings to optimise supply chains and coordinate sub-national partners through data calls for stock availability, ordering, reporting and redistribution. As noted in Section 5.3.2, this support helped improve national quantification, procurement, storage and distribution systems, in turn contributing to ensure that the supplies of new optimal HIV treatments reached those in need (although not always in the most reliable and timely manner). In other countries, for example in Cameroon, there remain significant barriers to effective supply and delivery—the national supply chain in Cameroon lacks adequate quantification of treatment doses, stock availability and formulations for paediatric dosage to improve therapeutic compliance among people living with HIV.

Based upon this evidence, the contribution of Unitaid's ART optimisation investments to tackling supply and delivery barriers and ensuring that optimal HIV treatment products reach those in need is considered 'medium.'

**Remaining gaps:** There remains significant need for government support (including as part of wider health system strengthening initiatives from partners) to address issues of national supply-chain weaknesses in African countries and help ensure that optimal HIV treatments reach those in need in a timely manner. This includes help with improving stock quantification, storage and distribution, supply to clinical facilities and technical support/advocacy for building in-country manufacturing capacity. By developing this capacity, countries will reduce dependence on foreign suppliers and increase access.<sup>78</sup> Additionally, there is a need for further investment (for example, catalytic procurement) to overcome barriers to paediatric and third-line procurement (since volumes are small and there are not many children, as was reported, for example, to be the case for Darunavir in Uganda).

<sup>76</sup> ARV supply and demand, CHAI report.

<sup>77</sup> KIIs 130, 131.

<sup>78</sup> KIIs 26–33; ADVANCE FGD.

## 5 Sustainability of the ART optimisation portfolio

This section reports on the Unitaid ART optimisation portfolio's contribution to sustainability. It first looks at the extent to which targeted products have been scaled-up across the project countries and beyond (5.1). This is followed by an assessment of global (5.2) and country (5.3) scale-up conditions in 2016 and 2022, using Unitaid's scalability factors framework. It is important to note that strengthening scalability factors is not the sole responsibility of Unitaid and its grantees: Unitaid works alongside other global partners and country stakeholders to achieve this goal.

### Summary points

- Unitaid's ART optimisation portfolio was successful in supporting the transition and scale-up of optimal treatments, including DTG and pDTG. Trial drugs were recommended in WHO and national guidelines, prices lowered and optimal treatments rolled out across target LMICs. By 2022, DTG was recommended as the first-line treatment for HIV for adults in the national guidelines of 111 LMICs. 75 countries adopted DTG for children.
- The ART optimisation portfolio also strengthened a wide range of global and country-level scalability conditions which will enhance the sustainable impact of the portfolio:
  - The PAC and APWG helped to: increase collaboration and alignment among scale-up partners; aggregate demand and enable more competitive pricing; accelerate supply; facilitate the sharing of rigorous evidence on the safety and efficacy of optimal treatments (leading to updated guidance, approvals and integration within policy/planning); and share implementation tools.
  - Country readiness factors which saw the highest level of success include garnering political support for scale-up, coordination amongst partners, recommendation of optimal products within national health policies, capacity building of health workers and strengthening the advocacy capacity of civil society organisations (CSOs).
- At the global level, further work is needed on synthesizing and sharing lessons learnt on implementation and facilitating successful scale-up (within a range of health systems). Amongst country-level factors, increased allocation of domestic resources showed a more mixed level of success alongside the need to strengthen grassroots CSOs in addition to national advocates.

### Key lessons learnt

- Strategic engagement with global and national partners during all stages of Unitaid's model is critical to the successful scale-up of optimal treatments. This includes early and ongoing engagement with national governments, working within existing government and donor partnership structures.
- The low volume of products for underserved populations and establishing a sustainable market for these products are significant challenges. Manufacturers suggested a comprehensive approach involving financial incentives and/or longer-term contracts as part of a sustainable supply plan.
- Guaranteeing future national government ownership of scale-up is a critical challenge, once Unitaid grants have ended, in terms of ensuring governments meet domestic resourcing commitments and ongoing capacity-strengthening needs (for example, within supply and distribution systems, clinician training, support and monitoring of implementation tools). This could be expedited through the development of robust handover plans, working with grantees and partners.
- Putting in place the conditions for sustainable advocacy from community and civil society organisations is important for holding governments and partners accountable. This includes formally integrating community support structures within future HIV treatment planning and funding cycles and further developing capacity at the grassroots level to advocate for optimal HIV treatments, including amongst the most marginalised.

## 5.1 Evidence of transition and scale-up

1

**Finding 1: Overall, the portfolio was successful in supporting transition to, and scale-up of, optimal treatments. Trial drugs were recommended in WHO and national guidelines and prices were lowered in target countries.**

The clinical trials successfully demonstrated the non-inferiority of DTG-based therapies in comparison to EFV-based therapies, as well as evidence of successful transition both globally and in national programmes.<sup>79</sup> DTG-based therapies and lower-cost, lower-toxicity EFV-based therapies (EFV400 instead of EFV600mg) are now preferred. In 2019, WHO guidelines recommended DTG-based regimens as the preferred first-line option and EFV400-based regimens as the alternative option, and 82 LMICs were reported to be transitioning to DTG-based HIV treatment regimens.<sup>80</sup> By 2022, adult DTG was recommended as the first-line treatment for HIV (including for pregnant women) in the national guidelines of 111 LMICs, and 109 of these countries had initiated procurement (Figure 11).<sup>81</sup>

The rapid introduction and roll-out of pDTG is crucial for implementing WHO guidelines.<sup>82</sup> By 2022, 75 countries adopted pDTG as the preferred treatment initiation option for children (Figure 12).<sup>83</sup>

Unitaid's clinical trials and its market-shaping and country-preparedness grants achieved successful transition through early, close and long-term engagement with global scale-up partners, manufacturers, civil society and country health departments, as well as by supporting capacity building activities.<sup>84</sup> Unitaid's wide-ranging contributions to global and country scalability are explored in the following sections.

<sup>79</sup> ADVANCE 2021 annual report; DolPHIN-2 2022 semi-annual report; D<sup>2</sup>EFT 2021 annual report; NAMSAL project presentation, 16 September 2022: Enabling Access to a Robust and Well Tolerated New Generation First Line Antiretroviral Treatment in Low Income Countries.

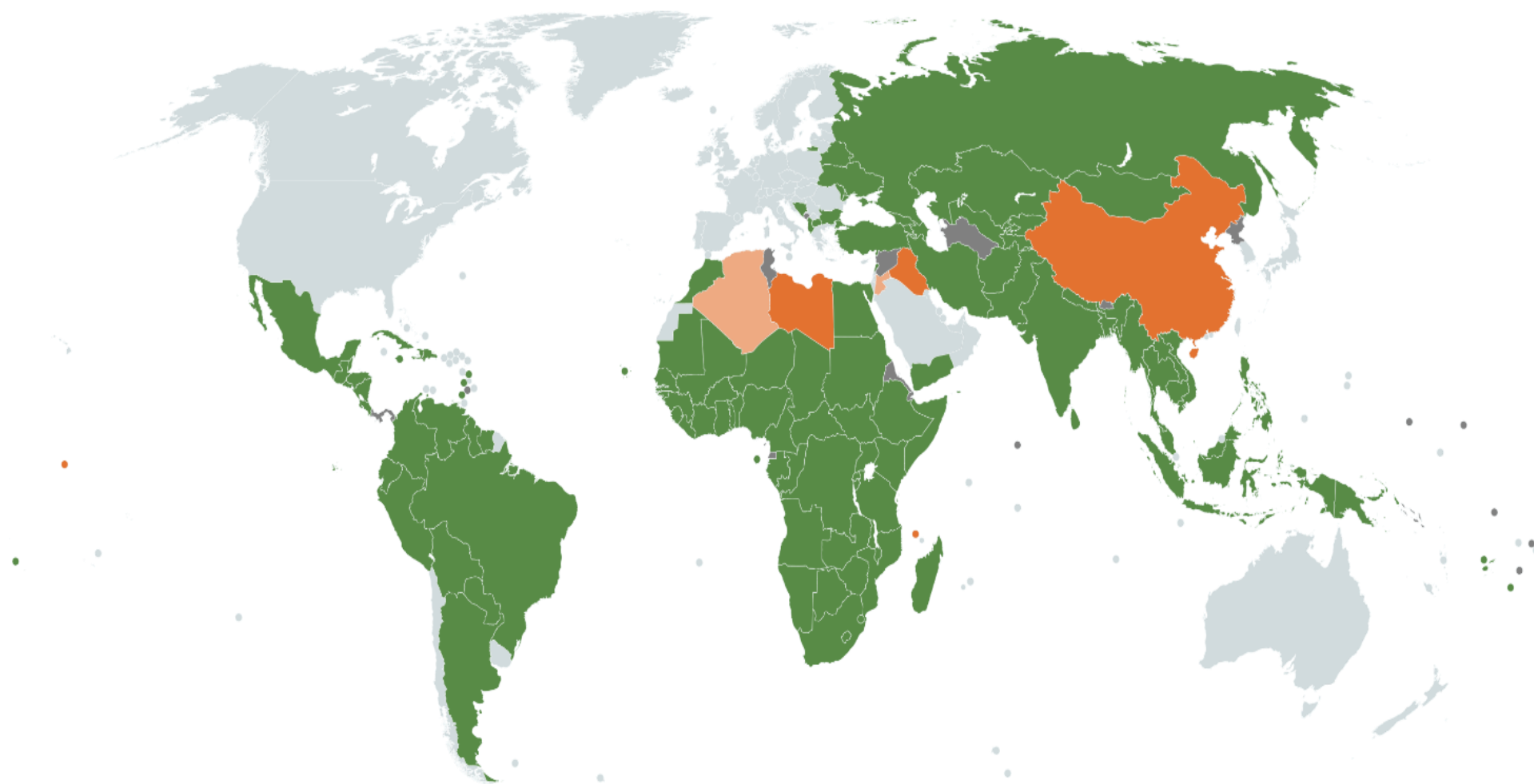
<sup>80</sup> <https://www.who.int/news/item/22-07-2019-who-recommends-dolutegravir-as-preferred-hiv-treatment-option-in-all-populations>.

<sup>81</sup> Source: <https://cfs.hivci.org/index.html>.

<sup>82</sup> [https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/2022gapfdtgguidance\\_english.pdf?sfvrsn=c12f257d\\_10&download=true](https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/2022gapfdtgguidance_english.pdf?sfvrsn=c12f257d_10&download=true).

<sup>83</sup> <https://unitaid.org/assets/Better-health-solutions.pdf>; [https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/2022\\_global\\_summary\\_web\\_policy\\_uptake\\_25nov2022.pdf?sfvrsn=ef1226ca\\_8/](https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/2022_global_summary_web_policy_uptake_25nov2022.pdf?sfvrsn=ef1226ca_8/) from: Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and Global HIV, Hepatitis and STIs Programmes (HHS), WHO, 2022.

<sup>84</sup> KIs 26, 33, 35, 37, 51 and 44.



DTG introduced and procurement initiated

DTG introduced in national guidelines, but procurement not yet initiated

Other first line regimens

No data available

**Figure 11. Status of DTG introduction in LMICs in 2022**  
Source: Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and Global HIV, Hepatitis and STIs programmes (HHS), WHO, 2022.



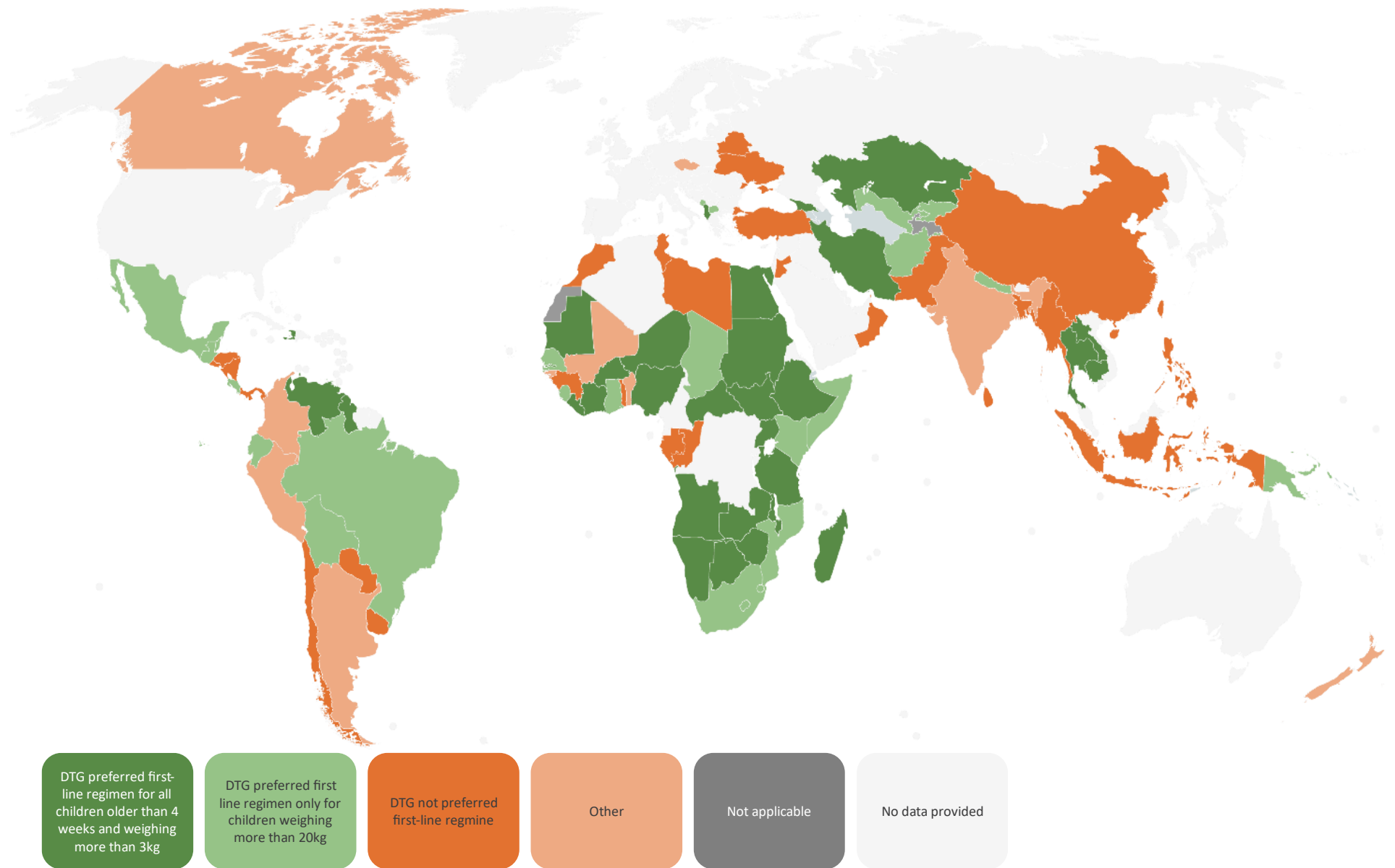


Figure 12. Status of pDTG adoption globally in 2022

Source: Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and Global HIV, Hepatitis and STIs programmes (HHS), WHO, 2022.

## 5.2 Supporting global conditions for scale-up

**1 Finding 1: At the global level, Unitaid contributed to strengthening the conditions for sustainable access to HIV treatments across a broad range of important factors.**

Most progress and contributions were seen in: (1) increasing a rigorous evidence base, (2) making products available at an affordable price (and in adequate quantities) in LMICs, (3) making products a strategic priority for scale-up among major partners (and integrating them within regular budgeting and planning cycles), and (4) disseminating rigorous results.

Table 7 provides a summary of the progress made against each barrier in 2016–22 and Unitaid’s contribution to this progress.

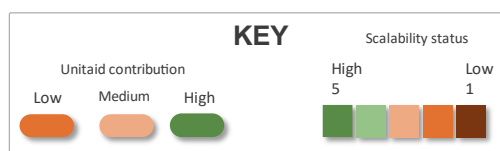


Table 7. Overview and heatmap of global scalability factors

Global scalability factor	2016	2022	Unitaid contribution
<b>Sustainable access conditions</b>			
A <b>rigorous evidence base</b> supports the safety, feasibility, effectiveness and cost-effectiveness of optimal regimens at the global level (critical to enable normative guidance).	2	4	
Optimal regimens are recommended in <b>policy and normative guidance</b> , for example, in WHO guidance.	3	4	
Efficient and safe optimal HIV treatments meet appropriate <b>quality standards</b> , such as WHO PQ status or approval from a recognised global regulatory authority, and/or <b>product registration and market authorisation</b> at the global and country levels.	2	3	
The product/intervention is available at an <b>affordable price</b> for LMICs (to public-sector purchasers)	3	5	
The product/intervention is supplied in <b>adequate quantities and in a timely manner</b> in relevant LMICs (including diversification of the <b>supply base</b> to ensure supply security and to promote competitive pricing where demand is sufficient).	2	3	
Improved <b>procurement</b> and appropriate <b>delivery</b> mechanisms, increasing the timely and sufficient availability of high-quality/affordable products in LMICs.	3	4	
<b>Alignment and coordination with global donors and partners</b>			
The product/intervention is made a <b>strategic priority for scale-up</b> among major global donors and implementing partners (as evidenced by inclusion in global policy/strategy documents, donor-specific plans, coordinated fund allocation, etc.).	3	5	
Quality, field-tested <b>tools/resources are available</b> to support scale-up of the product/intervention, adapted for various contexts and health systems.	3	4	
Newly approved optimal HIV treatments are included as part of regular global donor, government and relevant international implementing partner <b>planning and budgeting cycles</b> to secure adequate resources for scale-up at both the global and country levels.	2	4	
<b>Generation and dissemination of knowledge and evidence</b>			
The portfolio effectively and widely <b>disseminates evidence of rigorous results</b> (including the results from the four clinical trials) to key stakeholders to support the scale-up of optimal HIV treatments across the globe.	0	4	

**Lessons learnt on implementation** feasibility and on what is needed to facilitate successful scale-up within a range of health systems are synthesised and shared with global and national stakeholders.

0

3



## 5.2.1 Sustainable access conditions

Increase in a **rigorous evidence base**, which supports the safety, feasibility, effectiveness and cost-effectiveness of optimal regimens at the global level (critical to enable normative guidance).



1

**Finding 1: Unitaid conducted simultaneous clinical trials to evaluate the safety and efficacy of new formulations on the clinical outcomes in target populations. Global evidence coordination platforms were established to ensure early engagement with industry stakeholders.**

In 2016, DTG was recommended by WHO as part of an alternative adult first-line regimen, with restrictions pending further research.<sup>85</sup> DTG-based regimens would not be a preferred regimen in LMICs until clinical trials provided more data on safety, feasibility and effectiveness in key population groups (including pregnant mothers and people suffering from TB). The generation of new clinical trial evidence through the ART optimisation portfolio, with scientific accuracy and effective messaging for stakeholders, was crucial to the scale-up of new regimens in LMICs and had global significance.

For example, the ADVANCE clinical trial shared emerging evidence directly with manufacturers. Sharing the data in real time, with no red flags, allowed manufacturers to submit to regulators before the trials were complete and accelerated generic approval. The D<sup>2</sup>EFT trial shared the emerging results with WHO, strategically releasing 24-week results to influence treatment guidelines (ahead of the 48-week results which are standard for testing efficacy).<sup>86</sup> The generation of rigorous evidence was further supported by the PAC, which ensured that partners stayed updated.<sup>87, 88</sup> Because of this work, the 2022 position of this factor is rated as 'high,' and **Unitaid's contribution to a rigorous evidence base is rated as 'strong.'**

**Remaining gaps:** Both the D<sup>2</sup>EFT clinical trial and the extended monitoring of weight gain through TRIO were ongoing at the time of the evaluation (TRIO is now completed). There is scope to further inform WHO (and country level) guidelines.

Optimal regimens being recommended in **policy and normative guidance**, for example WHO guidance.



2

**Finding 2: The clinical trials' results were shared at WHO meetings – including from NAMSAL, ADVANCE and DoIPHIN-2 –, leading to updated public health recommendations for optimal treatment (DTG and EFV) in policy and normative guidance.**

<sup>85</sup> World Health Organisation (2016). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach, 2nd ed. World Health Organisation. <https://apps.who.int/iris/handle/10665/208825>.

<sup>86</sup> D<sup>2</sup>EFT FGD.

<sup>87</sup> KII 35, 37; ADVANCE FGD.

<sup>88</sup> KIIs 26–33, 35, 37, 58; ADVANCE FGD; D<sup>2</sup>EFT FGD; DoIPHIN-2 FGD; NAMSAL FGD; D<sup>2</sup>EFT 2019 annual report.

In 2017, WHO recommended transitioning to DTG-based first-line regimens in settings where pre-treatment non-nucleoside reverse transcriptase inhibitor drug resistance exceeded the recommended 10% threshold, such as in East and Southern Africa.<sup>89</sup> In 2018, WHO released interim guidelines recommending a cautious approach to DTG use in women due to reported potential risks during pregnancy, including NTDs when used in the preconception period.<sup>90</sup> DTG usage was restricted to women who were using effective contraception or already in the second or third trimester of pregnancy.

However, in 2019, WHO updated its guidance to recommend use of DTG for women regardless of contraceptive use or pregnancy status. The 2019 guidelines referred to data from the ADVANCE and NAMSAL trials, which expanded the evidence base for DTG and EFV, including on the benefits and risks of NTDs for pregnant women. As described in Section 4.1.2, the ADVANCE and NAMSAL study teams worked directly with WHO to change the guidelines and the DolPHIN-2 study provided further data to support the changes. Unitaid's clinical trials also informed the 2021 WHO HIV treatment guidelines, with updated guidance on the use of DTG, based on the latest evidence and emerging safety concerns (see Section 6.2). Now, DTG is the preferred treatment option for all populations (except for neonates), with LPV/r as an alternative for  $\leq 20\text{kg}$ .

Unitaid's contribution to global guideline changes is, therefore, also rated as 'strong.'<sup>91</sup> It should be noted that, alongside clinical trial evidence, WHO guidelines also considered mathematical models of the benefits and harms associated with the two drugs (DTG and EFV), the values and preferences of people living with HIV, and factors (such as cost) related to the implementation of HIV programmes in different countries.<sup>92</sup>

Efficient and safe optimal HIV treatments meeting appropriate **quality standards**, such as WHO PQ status or approval from a recognised global regulatory authority and/or **product registration and market authorisation** at the global and country levels.



2

**Finding 3: The portfolio supported product regulatory planning and approval, helping to overcome time-consuming regulatory processes and accelerating the shift to less expensive generic products.**

The regulatory landscape for HIV treatments in 2016 was well developed, with strict guidelines and regulatory processes in place to ensure the safety and efficacy of HIV medications. Several new ARV medications had been introduced in the years leading up to 2016 and were being considered for use in LMICs. However, the process of registering and authorising a new drug for use can take several years. In addition, country policymakers tended to wait for FDA approval before including new products in guidelines and implementing them. Key informants considered regulatory input as the slowest and biggest barrier to scalability (along with shipping issues due to Covid-19 and the inexperience of some generic manufacturers):

*“Prior to this intervention, regulatory input was the slowest/biggest barrier.” (KII 58)*

Manufacturer inexperience and unpredictability with regulators was mitigated by the proactivity of the CHAI and EGPAF teams respectively implementing the Optimal and SPAAN grants. CHAI

<sup>89</sup> WHO. Update of recommendations on first-and second-line antiretroviral regimens. World Health Organisation: Geneva, Switzerland; 2019.

<sup>90</sup> Labhardt ND, et al. Adoption of new HIV treatment guidelines and drug substitutions within first line as a measure of quality of care in rural Lesotho: health centres and hospitals compared. *Tropical Med Int Health*. 2012;17(10):1245–54.

<sup>91</sup> KIIs 19, 22; ADVANCE FGD; DolPHIN-2 FGD; NAMSAL FGD.

<sup>92</sup> SPAAN 2020 GBO.

supported expediting FDA authorisation for pDTG and engaged regulators directly to strategise a people-friendly policy (Section 4.1.2). This shortened the regulatory process (from the typical 3 years to a matter of months). The portfolio's work with national regulators was significant in clearing extensive backlogs, streamlining their review and registration processes and enabling them to focus on bringing in higher quality regimens (for example, in South Africa). Through the clinical trial research, grantees were also able to work with the regulatory agencies to prioritise drugs that addressed significant unmet medical needs and that had demonstrated a strong safety and efficacy profile.

Through support to manufacturers and regulators, Unitaid helped accelerate the approvals needed to make efficient and safe optimal HIV treatments available in LMICs, although with room for improvement for the benefit of future treatments. Unitaid's contribution to regulatory approval is therefore rated as 'medium.'

**Remaining gaps:** The country regulatory process for registration of optimal regimens remains slow and complex, requiring continued attention from Unitaid and its partners to help expedite the approval and authorisation of new optimal treatments.<sup>93</sup>

Products/interventions being made available at an **affordable price** for LMICs (to public-sector purchasers).



2

#### **Finding 4: Unitaid grantees' interventions facilitated generic development and introduction of DTG at an affordable price in LMICs.**

The ART market in 2016 was well established and characterised by a high level of collaboration between pharmaceutical companies, governments and non-profit organisations to ensure that people living with HIV had access to the most effective treatments available. The 2016 ARV market was also seeing increased competition from generic versions of existing drugs, which were becoming more widely available due to patent expirations. In this context, an important aspect of DTG introduction is that DTG is required only in small dosages and this makes it ideal for combination with other ARVs in a single tablet,<sup>94</sup> as well as profitable for generic manufacturers. As noted in Section 4, however, there were other demand-side barriers to the introduction of DTG in LMICs.

Unitaid-funded clinical trial evidence enabled DTG-based products to become (from being an alternative) the in-demand and preferred first-line regimen. Generic formulations became available and this drove prices down. Product partnerships and negotiated pricing deals further helped drive down prices and increase access to affordable HIV treatment in LMICs (see Section 4.1.4). For example, prior to the generic introduction of DTG, Kenya paid US\$50–60 for a 30-day supply pack, whereas the generic version cost approximately US\$4 per pack. With Unitaid's support through MPP licensing agreement, the first generic version of DTG was launched in 92 LMICs by an Indian pharmaceutical company in early 2018, with the pricing agreement and volume guarantee capping the public sector price at US\$75 PPPY. Supported by Unitaid and CHAI, Kenya, Nigeria and Uganda became the first LMICs to debut generic DTG. After a year of advocacy, CHAI, the originator supplier, the generic supplier and treatment advocates succeeded in ensuring that the pricing deal would be honoured in a further 39 LMICs, as MPP licensing allowed supply to countries without patents. The

<sup>93</sup> KIs 26–33, 46, 51, 58; South Africa Country Report; D<sup>2</sup>EFT project plan.

<sup>94</sup> [Policy-Brief-Dolutegravir-in-Southern-Eastern-Africa.pdf \(healthgap.org\)](#).

announcement of this development was made publicly by CHAI during the Middle East and North Africa community advisory board meeting (Morocco, October 2018).<sup>95</sup>

Today, TLD costs less than its target price of US\$75 (below US\$50 PPPY, using carton-less 180-count packs).<sup>96</sup> A 75% price reduction to US\$36 PPPY was also negotiated for pDTG 10mg,<sup>97</sup> the cost of which has continued to decline and is currently at \$34.40 PPPY. In addition, lower prices have resulted from economies of scale, market competition and the lower cost of goods. Unitaid's contribution to optimal treatment price reduction is therefore rated as 'strong.'

Product/interventions have been supplied in **adequate quantities** and in a **timely manner** in relevant LMICs (including diversification of the **supply base** to ensure supply security and to promote competitive pricing where demand is sufficient).



1

**Finding 5: Unitaid grantees and partners worked with manufacturers and MoHs to ensure the stable and timely supply of products by providing aggregated partner demand forecasts and shortening manufacturer product commercialisation timelines.**

In 2016 some LMICs, such as Kenya, had already begun to adopt DTG. The APWG, however, facilitated sharing clinical trial data and forecasts of the total product procurement demand from partners with manufacturers to determine minimum batch requirements, which secured product supply for a much greater number of LMICs. For example, in 2020, members of the APWG procured ARVs for 102 countries, including ARVs for approximately 400,000 children living with HIV, with 60% of orders placed with sufficient advance to ensure enough time for manufacturers to produce the drugs and for the supply chain to deliver them, which prevented stockouts, treatment interruptions and potential negative health consequences for people living with HIV. In 2020, 93% of the paediatric ARVs ordered were considered optimal by WHO, an improvement from 71% in 2011.<sup>98</sup> The APWG committee also helped alleviate potential issues around supply security by monitoring production and stock-outs, mitigating the impact on delivery systems during the first years of Covid-19.

As described in Section 4.1.4, Unitaid (through the Optimal grant and CHAI) financially incentivised manufacturers to develop generic products, reducing the time-to-market by 2-3 years (and in anticipation of WHO 2019 guideline changes), and then worked with manufacturers to ensure a stable supply of these products. The establishment of diversified generic manufacturing helped ensure a sustainable global supply of DTG. In Uganda, the catalytic procurement of DTG products (50mg and 10mg) meant that the Optimal grant was the first to bring these commodities to the country (with PEPFAR and implementing partners taking the lead on the procurement of products for scale-up across the entire country).

The current position with regards to the supply of optimal treatments in adequate quantities and in a timely manner in LMICs is rated as '3' (see the key to scalability status in Table 8). Unitaid's contribution to the supply of optimal treatments is also rated as 'strong.'

**Remaining gaps:** As noted in Section 4.1.4, there are potential hurdles to overcome regarding the supply security of small volume paediatric products (and transitioning the remaining population to DTG). To help ensure a sustainable market, manufacturers have requested more security that their products will remain at profitable volumes for a minimum of two years after their investment. A comprehensive approach, including financial incentives and longer-term

<sup>95</sup> <https://medicinespatentpool.org/licence-post/dolutegravir-adult-dtg>.

<sup>96</sup> Optimal VFM Summary (May 2023).

<sup>97</sup> Optimal 2021 GBO.

<sup>98</sup> APWG 10-year summary document: ARV supply and demand — 10 years of successes and challenges at the Antiretroviral Procurement Working Group, CHAI.

contracts – as part of the development/implementation of a sustained supply plan with manufacturers – could help facilitate post-grant supply of optimal treatments to people living with HIV.

Improved **procurement** and appropriate **delivery** mechanisms, increasing the timely and sufficient availability of high-quality/affordable products in LMICs.



3

### **Finding 6: The partnership with procurement partners (including USAID), NGOs and manufacturers helped to improve procurement and accelerate the roll-out of drugs such as DTG.**

By 2016, ARV drugs were typically procured by governments, international organisations and NGOs through a variety of mechanisms, including direct purchasing from manufacturers, bulk purchasing agreements and donor-funded procurement programmes. Delivery mechanisms for ARV drugs can vary by country, but most commonly distribution takes place through public health facilities, where ARV drugs are dispensed to people living with HIV (the strengthening of national health systems is covered in the following section on country scalability factors).

Optimal/SPAAN supported the inclusion of new products in regularly scheduled procurement timelines and assisted in identifying scale-up partners to conduct procurement for government. For example, the catalytic procurement of DTG was successful in Nigeria due to effective engagement with partners and the government (in Nigeria, PEPFAR and Global Fund committed to funding and procuring DTG). Uganda has successfully introduced DTG across all regions (with PEPFAR and Global Fund resources). CHAI/Unitaid also offered webinars to assist countries in including products in their procurement pipelines and determine their optimal formularies. Unitaid's portfolio interventions helped increase (to some degree) the timely and sufficient availability of high-quality/affordable products in LMICs. Unitaid's contribution to improving procurement mechanisms is therefore rated as 'medium.'

**Remaining gaps:** To help accelerate the introduction of new products while reducing wastage of old products, procurement partners (including national governments) could better monitor the pipeline of new ARTs and plan further in advance for the phase-out of old products and phase-in of new products. The goal would be to overcome challenges at the level of delivery mechanisms, including (1) a lack of national protocols on how healthcare providers should respond to potential weight gain (as noted by DolPHIN-2 grant implementers in its focus countries), and (2) the need to transition remaining children and adults to DTG (as noted in Benin).

## 5.2.2 Alignment and coordination with global donors and partners

Products/interventions being made a **strategic priority for scale-up** among major global donors and implementing partners (as evidenced by inclusion in global policy/strategy documents, donor-specific plans, coordinated fund allocation, etc.).



1

### **Finding 7: Unitaid and its grantees strengthened existing collaboration between diverse partners such as PEPFAR, Global Fund and other APWG members around prioritising optimal HIV treatments for scale-up.**

In 2016, global partners were already collaborating directly and DTG was widely predicted to both provide better ARV options for LMICs and reduce the cost of global ART. The transition to DTG-based

regimens in the procurement of ART by PEPFAR and Global Fund started in 2017–2018, following WHO recommendation on using DTG-based regimens (with restrictions). Subsequently, PEPFAR and Global Fund began to revise their ART procurement policies to align with WHO guidelines. However, clear clinical trial evidence from Unitaid further contributed to making optimal HIV products a strategic priority for scale-up among major global donors and implementing partners, alongside the APWG’s broad membership and role in the market coordination of supply and demand (Box 9). Unitaid’s contribution to donor alignment in adopting and investing in new optimal products is therefore rated as ‘strong.’<sup>99</sup>

### Box 9. Contribution of the APWG to global partner coordination

The APWG serves as a global monitor and facilitator of ARV procurement. It does not directly place orders with manufacturers; instead, it consolidates information from member procurement entities (PEs). Established in 2011, the APWG initially focused on paediatric ARV procurement. In 2016, the group expanded its scope to include ARVs for adolescents and adults to coordinate procurement allocation and to prevent ARV stock-outs, globally<sup>100</sup>. In 2019, the scope again expanded to include commodities for managing AHD<sup>101</sup>. Unitaid provides operational and strategic support to the APWG.

To drive market coordination, APWG member PEs hold quarterly reviews to identify potential issues that could affect ARV market. During these meetings, PEs share market intelligence, troubleshoot issues and seek advice from other organisations. Major market updates are shared with HIV stakeholders on monthly calls. The APWG also engages with manufacturers on the supply side and publishes a quarterly forecast of 18-month member PE demands.

For example, PEPFAR and Global Fund’s involvement in the APWG (and the PAC) enabled a more comprehensive 18-month demand forecast, supporting increased market visibility and greater purchasing power during price negotiations with manufacturers. By combining diverse partners and a procurement consortium, APWG members have collectively supported a coordinated global procurement approach, resulting in APWG member PEs procuring ARVs on behalf of 102 countries by 2020. PEPFAR and Global Fund were also involved in policy and guideline discussions and worked on the innovative pricing agreement to accelerate access to generics (Section 4.1.4). The APWG also served as a broader platform for the global coordination of ARV drugs, including tracking repurposed drugs to ensure there were no stock-outs during the Covid-19 crisis.

*“This is where Unitaid and the APWG have been helpful, attracting the market... leading to affordability and price reductions, and that leading to greater availability.” (KII 22)*

The small secretariat is composed of members from organisations who support the APWG in addition to their regular jobs. The secretariat’s belief in the APWG’s mission and willingness to dedicate time to the group have been essential to its continued activity for over a decade. In terms of gaps, the APWG does not have complete visibility of the ARV market, since not all global PEs and country procurement organisations are members. This is a recognised gap (although the APWG works with large independent buyers to ensure consistent messaging and shared intelligence).

Quality, field-tested **tools/resources are available** to support the scale-up of products/interventions, adapted for various contexts and health systems.



<sup>99</sup> KIIs 26–33, 35, 37, 45, 50, 56, 57; D<sup>2</sup>EFT FGD; NAMSAL FGD; Optimal FGD.



## 1

**Finding 8: Detailed planning resources, regional pharmacovigilance network, healthcare worker tools, training materials and treatment literacy guidance were developed to close gaps and help implement new products.**

In 2016, several tools and resources were already available to support LMICs in introducing new HIV treatment products, including WHO HIV treatment guidelines. MPP, Global Fund and PEPFAR also provided funding, data and analyses, licensing agreements and recommendations for the use of new ARV drugs and regimens to help LMICs make informed decisions and improve access to affordable HIV medicines.

There is complexity in dealing with HIV-related drug transitions, however, including the management of drug-induced toxicities, risk communication and responses to side effects. Since DTG was a relatively new drug, information about user-experiences and the management of side effects – as well as communication of DTG risks – was critical to optimising wider roll-out.<sup>102</sup> In response to this, the portfolio helped develop a number of high-quality tools and resources to support the scale-up of optimal product intervention, informed by user perspectives from various contexts:

- The HIV New Product Introduction Toolkit<sup>103</sup> and accompanying HIV New Project Introduction Guide<sup>104</sup> (developed by CHAI under Optimal) provides global access to product introduction resources and tools and was referenced in the 2019 WHO guidelines. The toolkit aims to support MoHs and implementing partners to accelerate new product introduction by compiling information, tools and resources which cover adoption, forecast, procurement, facility phase-in, supply planning and monitoring. It was introduced in 2017 as a response to WHO guidelines, the recommendations of multiple new ARVs and Unitaids' objectives for the Optimal grant to accelerate scale-up.<sup>105</sup>
- The portfolio developed (1) an impact calculator (CHAI under Optimal) to help countries make informed policy decisions, and (2) electronic healthcare worker training materials (Optimal) and treatment literacy guidance – customised to local community contexts (multiple grants) – to support the implementation of new products. Literacy guidance was adopted as part of national guidance in some countries. Further details on country-level resources are provided in Section 5.3.2.
- The DolPHIN-2 project expanded its regional pharmacovigilance network to Uganda, Kenya and South Africa to enhance the safe scaling-up of new products.
- In Uganda, CHAI (through the Optimal grant) used the ARV Order Quality Management Tool, which was integrated within the national aggregator reviews, the quality parameters of orders and the reports for ARV product replenishments by facilities.<sup>106</sup> This could have been employed in other countries.

Stakeholders emphasised the importance of community leadership and end-user perspectives in shaping the development of new products, training and protocols. The Toolkit and community engagement resources were translated into simple materials, graphics and videos which were adopted by MoHs (for example, in Uganda) and partner organisations (for example, PEPFAR). Stakeholders believed that this played a crucial role in increasing treatment literacy in LMICs.

<sup>102</sup> <https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06851-9>.

<sup>103</sup> <https://www.newhivdrugs.org/>.

<sup>104</sup> <https://clintonhealth.app.box.com/s/lkshjlcxrss8l37g7onpf4jj5te1dcxc>.

<sup>105</sup> <https://unitaid.org/news-blog/chai-launches-toolkit-aid-introduction-new-hiv-products/#en>.

<sup>106</sup> EVA CHAI Optimal ARV Grant FINAL Report 10 April.

Because of this work, Unitaid’s contribution to the availability of field-tested tools/resources is rated as ‘strong.’

**Remaining gaps:** Looking ahead, it would be useful to collect more information and monitor the uptake of tools/resources by different countries. For example, a range of stakeholders reported that the Covid-19 pandemic affected the prioritisation of tool uptake in certain countries. It is important to ensure that ongoing support to utilise tools is available and that updates to tools and resources are made as required.<sup>107</sup>

Newly approved optimal HIV treatments being included as part of regular global donor, government and relevant international implementing partner **planning and budgeting cycle** to secure adequate resources for scale-up at both the global and country levels.



2

**Finding 9: Acceptance of research results and ongoing relationships with global partners and government stakeholders have promoted inclusion in national policy, planning, training and procurement cycles.**

In 2016, DTG was still largely considered an alternative treatment. Key informants understood that donors such as PEPFAR and Global Fund aligned their planning and budgeting decisions strongly with the available evidence (rather than advocacy efforts alone). Therefore, Unitaid and its grant implementers worked with Global Fund and PEPFAR from the beginning to ensure readiness to procure and introduce new drugs and combination therapies, with the evidence from clinical trials playing an important role in driving donor alignment and investment. This evidence was also connected with national guidelines to support country readiness, planning and budgeting—with the adoption of clinical trial results estimated to be faster as they were being held in LMICs. Integration within country planning and budgeting (and outstanding gaps in this area) are covered in more detail under country scalability (5.3.1). Other stakeholders contributed to the transition and inclusion of new optimal regimens within planning and budget cycles at the global and country levels, and thus Unitaid’s contribution to securing adequate resources is rated as ‘moderate.’

### 5.2.3 Generation and dissemination of knowledge and evidence

The portfolio effectively and widely **disseminates evidence of rigorous results** (including the results from the four clinical trials) to key stakeholders to support the scale-up of optimal HIV treatments across the globe.



**Lessons learnt on implementation** feasibility and on what is needed to facilitate successful scale-up within a range of health systems are synthesised and shared with global and national stakeholders.



2

**Finding 10: Clinical trial evidence informing revised WHO guidelines, as well as the sharing of implementation guidance with global and national stakeholders, was crucial in driving the adoption of and investment in new products.**

The baseline for the generation and dissemination of knowledge and evidence for the portfolio is considered to be ‘zero.’ As noted throughout this chapter, the clinical trials and Optimal/SPAAN shared evidence widely with global and national stakeholders, including through PAC meetings,

<sup>107</sup> KIIs 35, 37, 45; ADVANCE FGD; DoIPHIN-2 FGD; Optimal FGD; 2018 Annual Report ADVANCE South Africa.

meetings with manufacturers, conferences, academic publications and WHO guideline revision forums. Once the disseminated evidence informed WHO guidelines, grantees supported countries to interpret the evidence and implement policy. For example, the Cameroon MoH utilised international guidelines – which included clinical trial evidence and grantee-generated cost-effectiveness studies (generating a compelling investment case) – to include a new product in their national guidelines. Overall, the portfolio effectively and widely disseminated evidence of rigorous results from the four clinical trials to key stakeholders to support the scale-up of optimal HIV treatments across the globe. Therefore, **Unitaid’s contribution to disseminating rigorous evidence is rated as ‘strong.’**

**Remaining gaps:** Retrospective lessons learnt on implementation feasibility and what is needed to facilitate successful scale-up (within a range of health systems) have not yet been synthesised and shared with global and national stakeholders. This is identified as an area of remaining work to facilitate successful scale-up within a range of health systems and to share these lessons with global and national stakeholders.<sup>108</sup>

### 5.3 Supporting country readiness for scale-up

1

#### Finding 1: Unitaid made strong contributions to progress across almost all country-level scalability factors, supporting the sustainable scale-up of optimal HIV treatments.

Areas of the greatest progress included encouraging the political endorsement of new products, capacity building of health systems to support scale-up and strengthening civil society advocacy organisations. Areas where progress remains needed include securing financial commitments from national governments to support scale-up and strengthening grass roots community organisations.

Table 8 below provides the average score of country-level scalability in 2016–22, as well as Unitaid’s contribution to the change.

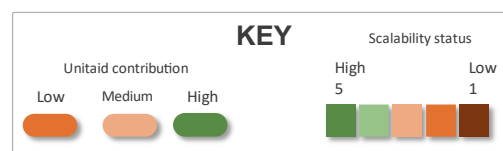




Table 8. Country-level average scalability factor change 2016–22 and Unitaid’s contribution.

Country-level scalability factor	2016	2022	Unitaid’s contribution
<b>Secure political and financial support</b>			
Critical decision makers demonstrate <b>political support</b> for national scale-up of optimal HIV treatments.	2	4	
<b>Major donors actively collaborate and allocate funding</b> to enable national scale-up in a coordinated manner.	4	5	
National governments signal support for scale-up by <b>allocating resources</b> (for example, national budget line for products/interventions).	3	4	
<b>Ensure programmatic and operational readiness</b>			
The product/intervention is <b>recommended in national and sub-national health policies</b> .	2	4	
National health systems have <b>adequately trained staff, supplies and other resources</b> to enable quality and equitable scale-up of the product/intervention.	2	4	

<sup>108</sup> KII 19; ADVANCE FGD; D<sup>2</sup>EFT FGD; DoIPHIN-2 FGD; NAMSAL 2022 final report.

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	

### 5.3.1 Secure political and financial support

Critical decision makers demonstrate **political support** for national scale-up of optimal HIV treatments.



2

**Finding 2: Key discussions and engagements between CHAI and national government authorities helped increase political support from critical decision makers for the national scale-up of optimal HIV treatment products.**

Although there were expressions of political support for optimal HIV treatments prior to the Unitaid investment, these were not always evidence-based. There were also indications of low awareness in some countries about optimal treatment products, and/or key decision makers were reluctant to endorse and implement new treatments because of fears about the cost implications or safety (hence the baseline score of ‘2’ – see Table 2 8 above – across countries in 2016).

Since then, the significant improvement in this factor (now rated as a ‘4’) are reported to have been driven by CHAI’s lobbying work through the Optimal grant, which included critical meetings with national government authorities, Global Fund and PEPFAR in Unitaid implementation countries. This engagement started from the outset (the design of clinical trials and market shaping) and continued during grant implementation (to establish sustainability frameworks and identify scale-up partners to take on the work once proof of concept had been established). Key examples of this include high-level engagement with the MoH and NASCOP in Kenya, with the MoH and the Agence Nationale de Recherche sur le Sida et les Hépatites Virales (ANRS) in Cameroon and with the National Department of Health in South Africa. Because of this, **Unitaid’s contribution to securing political support for the national scale-up of optimal HIV products is deemed ‘strong.’**

**Remaining gaps:** Country stakeholders noted that political support from critical decision makers has yet to fully translate into domestic financial commitments for scale-up (see finding 4 below). To bridge remaining gaps, ongoing technical guidance—for example on supply chain systems strengthening—may be helpful for maintaining momentum and commitments from critical decision makers. Additionally, continued community advocacy will be important to ensure that governments fulfil their commitments to scale-up.

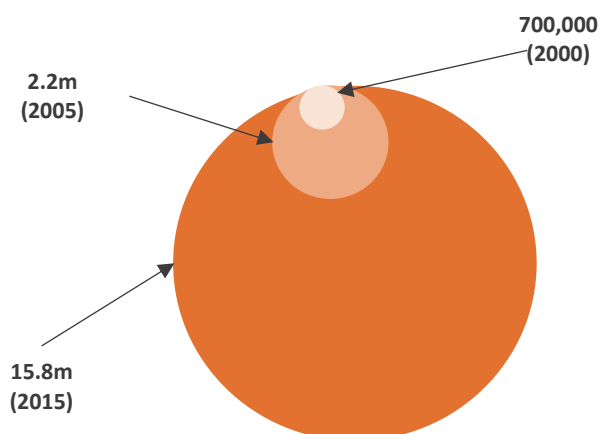
**Major donors actively collaborate and allocate funding** to enable national scale-up in a coordinated manner.



1

**Finding 3: The results of Unitaid’s clinical trials provided evidence that major donors were able to actively collaborate around and subsequently allocate funding, strengthening ongoing coordination efforts to scale-up optimal HIV treatments.**

Across Unitaid project countries, major donors were already actively collaborating around the national scale-up of HIV treatment products through the Treatment 2015 Initiative<sup>109</sup> (building on previous successes in increasing the accessibility of ARVs such as Option B+ – see Figure 13).



**Figure 13. Number of people receiving ART 2000–2015**

*Source: Global AIDS Response Progress Reporting (UNAIDS/UNICEF/WHO and UNAIDS/WHO estimates, and Global Health Sector Response to HIV, 2000-2015)*

In 2016, major donor joint-funding was also being coordinated in most countries. For example, in Kenya, PEPFAR, Global Fund, the World Bank and UNAIDS collaborated on a 2012 national survey to inform the scale-up of ARVs in the country.<sup>110</sup> Outside of the portfolio’s focus countries, in Tanzania, the government used Global Fund resources to procure first-line ARVs and PEPFAR funding focused on strengthening regional and district health systems, training healthcare and public-health management personnel and providing support for innovation and quality improvement.<sup>111</sup> The position in 2016 was therefore already ‘high’ (with a score of ‘4’). Unitaid investments were nonetheless influential in further shifting donor support to optimal products (Figure 14), especially as results from the clinical trials became available.

<sup>109</sup> “The 2013 WHO HIV treatment guidelines greatly expanded the number of people eligible for antiretroviral therapy. To meet this challenge, UNAIDS in July 2013 joined with the World Health Organisation (WHO), the US President’s Emergency Plan For AIDS Relief (PEPFAR), the Global Fund to Fight AIDS, Tuberculosis and Malaria and other partners to launch the Treatment 2015 initiative. Treatment 2015 aims to ensure that the world reaches its 2015 HIV treatment target of 15m as a critical stepping-stone towards universal access to antiretroviral therapy.”

[https://www.unaids.org/sites/default/files/media\\_asset/20131219\\_AccessARTAfricaStatusReportProgressTowards2015Targets\\_en\\_0.pdf](https://www.unaids.org/sites/default/files/media_asset/20131219_AccessARTAfricaStatusReportProgressTowards2015Targets_en_0.pdf).

<sup>110</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4786176/>.

<sup>111</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3445041/>.

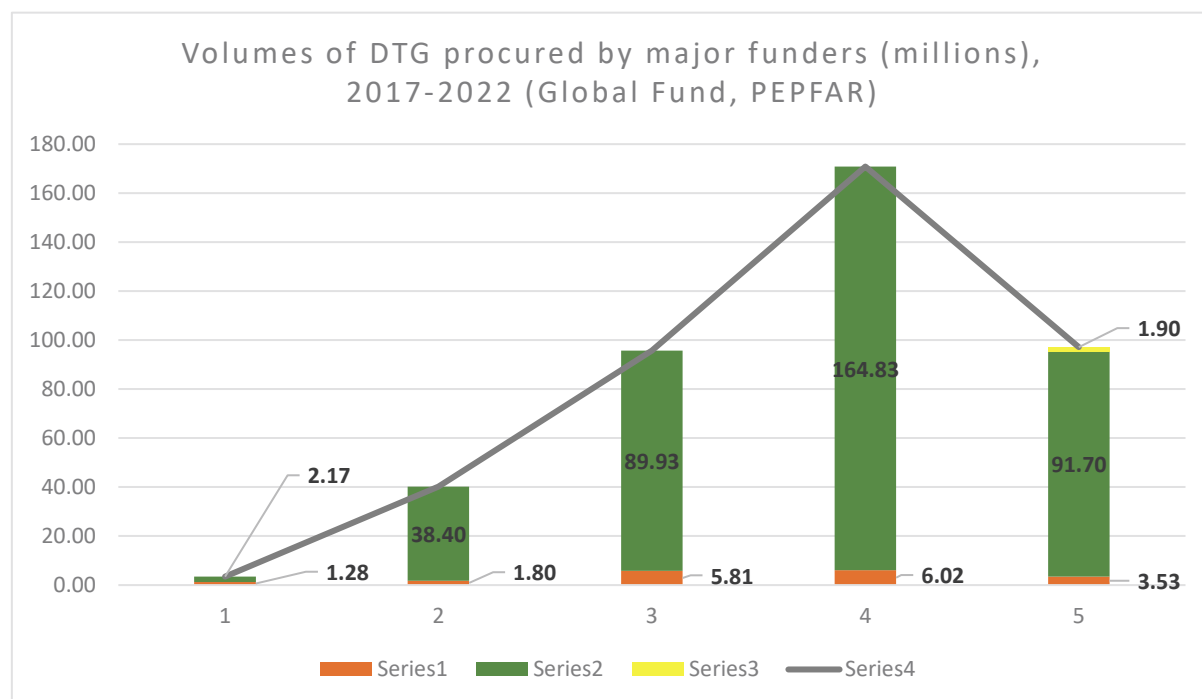


Figure 14. Chart showing volumes of DTG procured by major funders (millions), 2017-2022  
 Source: CHAI procurement database (2023)

For example, PEPFAR funded DTG 10mg in Côte d’Ivoire.<sup>112</sup> Additionally, D<sup>2</sup>EFT and Optimal’s work to introduce DRV/r in Nigeria supported price reductions, availability and scale-up by proving impact and lasting effects during discussions and by adopting a catalytic approach with other donors (such as PEPFAR, which supported the programme). Following scale-up in two states, Nigeria is planning a nationwide scale-up of DRV/r, starting in 2024. The APWG and PAC facilitated some of these discussions and coordination meetings and ensured the continued allocation of funding beyond the catalytic backing provided under the Optimal grant. CHAI sat as a partner on national coordination meetings and engaged in joint planning and procurement discussions and activities (collaborating actively with major donors). For example, in Uganda, CHAI’s work to sustain national stakeholder collaborative meetings led to the commitment of PEPFAR, CDC and USAID funds through their respective implementing partners (including within government structures at national, regional, district and health facility levels).<sup>113</sup> Unitaid’s contribution to this factor is therefore considered ‘moderate.’

National governments signal support for scale-up by **allocating resources** (for example, national budget lines for products/interventions).



**1**

**Finding 4: Evidence from the clinical trials and collaboration with Optimal also contributed to national governments signalling support for scale-up, by allocating increased domestic funding for optimal ART products/interventions.**

<sup>112</sup> KII 84.

<sup>113</sup> Uganda country report.

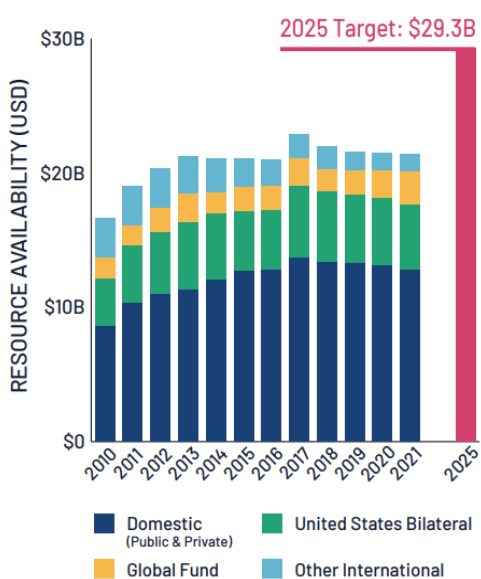


Figure 15. Resource availability for HIV in LMICs, 2010-2021 and 2025 target  
Source: CHAI HIV Market Report 2022

Prior to 2016, most evaluated countries experienced challenges in the national allocation of resources to HIV response (hence the average baseline score of ‘3’) and were partly reliant on major donors for resources. Whilst this challenge has to some extent continued to the present day (Figure 15), some national governments demonstrated support for scale-up by increasing their national budget allocations (including for DTG) over the period of the portfolio’s implementation.

For example, Kenya’s commitment to the national HIV programme increased three-fold, from US\$36m in 2016 (20% Government of Kenya/80% donor contributions) to US\$60m (a 30% Government of Kenya contribution).<sup>114</sup> In 2022, the Government of Benin contributed around 40% of the budget to the national HIV programme (up from 30% in 2016).<sup>115</sup>

Across Unitaids project countries, national government authorities were actively engaged in collaborative discussions around national and sub-national budgets and the allocation of funds for optimal HIV treatment

products, which supported these increases. This was alongside systems strengthening efforts, standard operating procedures development and training on the part of the Unitaids Optimisation portfolio. However, Unitaids was not the only contributing actor in this area, given the important role of scale-up partners such as PEPFAR and Global Fund.

**Unitaid’s contribution to national government resource allocation is therefore assessed as ‘moderate.’**

Some governments committed funds but struggled to achieve the same level of commitment as those named above. For example, Uganda’s health expenditure funding for HIV stagnated at approximately 18% of the total health sector budget<sup>116</sup> (and the scale-up plan was heavily funded by PEPFAR). In Côte d’Ivoire, despite the commitments made to allocate 15% of national budget to health, only 5% is currently allocated. For HIV, the resources made available by the government are mainly for salaries and operating costs, and this represents a danger in the event of the withdrawal of external aid. Additionally, in South Africa, while the change in regimen has freed up funds, allocations to the National Department of

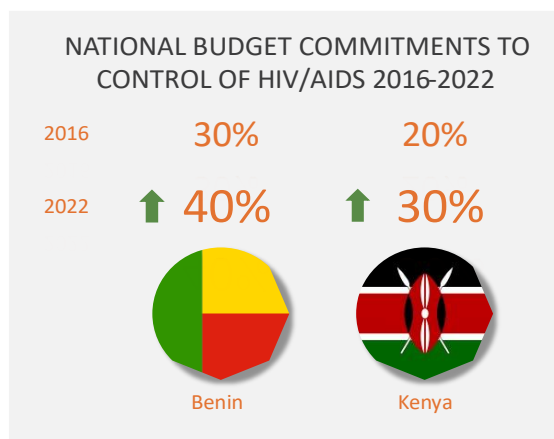


Figure 16. Sample of national budget commitments and percentage increases, 2016–2022

<sup>114</sup> Kenya Country Report.

<sup>115</sup> Benin Country Report.

<sup>116</sup> Ministry of Health. Health Sector HIV/AIDS Strategic Plan (2018/19 – 2022/23).

Health have decreased over the last five years.<sup>117</sup> In Nigeria, there is only a minimal budget line allocated to optimal treatments.<sup>118</sup>

**Remaining gaps:** Going forward, continued pressure from civil society is required to ensure that governments maintain and increase their funding commitments (see also finding 6 on the contribution of supply chain systems to resource allocation).

### 5.3.2 Ensure programmatic and operational readiness

Products/interventions are **recommended in national and sub-national health policies.**



**1**

**Finding 5: Optimal HIV treatment products/interventions were approved and recommended in national and sub-national health policies over the lifetime of the portfolio, with strong contributions from Unitaid.**

As noted earlier, by 2022, 111 countries had adopted DTG as their preferred first-line option for adults and adolescents. This is an increase from 60 countries in 2020.<sup>119</sup> Country programs started transitioning to pDTG tablets in mid-2021 to ensure that children living with HIV received optimal treatment. Between 2020 and 2022, there was a 71% increase in countries recommending the product as the preferred treatment for infants and children, with 75 out of 110 reporting countries including it in their guidelines (in 2020, only 35 countries, 32%, reported the adoption of pDTG).<sup>120</sup> Of these, 27 countries adopted pDTG for children over 20kg, while the rest now recommend it for all children older than four weeks and weighing more than 3kg.<sup>121</sup>

Evidence from CHAI's pilot studies ADVANCE, D<sup>2</sup>EFT, NAMSAL and DoIPHIN-2 were incorporated into the national guidelines and translated into training and tools. In Kenya and Uganda, the Optimal grant provided leadership and governance support to their health ministries through CHAI membership in TWGs and involvement in changes to national guidance. In South Africa, the grant supported the national regulator in streamlining their review and registration processes, enabling them to focus on bringing in the high-quality regimens recommended by new national guidelines. SPAAN also contributed to the revision and adoption of treatment protocols and updated national training tools. In addition, Unitaid's community engagement activities and support for community advocacy played an important role in guideline changes. For example, in South Africa, the Optimal CAB organised people living with HIV meetings to discuss the implications of the newly released evidence for treatment options. It also increased product adoption, brought community voices to national discussions on product roll-out and was critical in triggering change in both WHO and national guidelines (especially for women of reproductive age).<sup>122</sup>

**Unitaid's contribution is therefore rated as 'strong' because of the active grantee support for guideline development** and the release of clinical trial evidence. Nonetheless, the challenges in accelerating national government approval for new treatments and navigating country

<sup>117</sup> South Africa Country Report.

<sup>118</sup> Nigeria Country Report.

<sup>119</sup> ART Optimisation Portfolio, Trials closure/Optimal NCE proposition, 28 September 2022.

<sup>120</sup> [https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/2022\\_global\\_summary\\_web\\_policy\\_uptake\\_25nov2022.pdf?sfvrsn=ef1226ca\\_8/](https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/2022_global_summary_web_policy_uptake_25nov2022.pdf?sfvrsn=ef1226ca_8/) Source: Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and Global HIV, Hepatitis and STIs Programmes (HHS), WHO, 2022.

<sup>121</sup> ART Optimisation Portfolio, Trials closure/Optimal NCE proposition, 28 September 2022.

<sup>122</sup> Harris EL, Blumer K, Perez Casas C, Ferris D, Amole C, Doherty M, Auton M. Accelerating access and scale-up of optimised antiretroviral therapy in low-income and middle-income countries: results of a coordinated end-to-end approach. *AIDS*. 2021 Dec 15;35(Suppl. 2): S165-S171.



bureaucracies should not be underestimated. Some clinical trial grants faced delays in obtaining regulatory approval for the introduction of the drugs under study, which subsequently delayed shipping to trial sites.<sup>123</sup> In addition, national ART guidelines changed during the course of trials without sufficient warning, resulting in out-of-date training for community and health workers.<sup>124</sup> Difficulties in working with regulatory bodies produced delays in transition and roll-out in South Africa. Due to a long backlog, ensuring that optimal treatments were prioritised proved onerous.<sup>125</sup>

*Learning the systems was complicated. (DoIPHIN-2 FGD)*

**Remaining gaps:** Further work required to support guideline development includes evidence-generation on safety and efficacy for specific underserved populations, including younger children (for example, in Cameroon), older people (Cameroon, Kenya), people living with HIV on second-line and third-line treatments, and people suffering from AHD. In addition, further work is needed to align guidelines across the public and private sectors and ensure clinician uptake (South Africa).

National health systems have **adequate, trained staff, supplies and other resources** to enable quality and the equitable scale-up of products/interventions.



2

**Finding 6: Together, the Optimal, SPAAN and clinical trial grants made strong contributions to national health systems having adequate and trained staff, stronger supply chains and other resources to enable quality and the equitable scale-up of optimal HIV treatment products.**

The low score ('2') assigned in 2016 reflects gaps in staff training (especially regarding optimal treatments), distribution and harmonisation (countries were not yet effectively consolidating demand for batch procurement) across countries. In South Africa, for example (despite it having well-trained staff and good supplies in general), there was a shortage of staff trained on new regimens—a difficult challenge to overcome when there are budget deficits due to a country's economic instability.<sup>126</sup> Uganda and Zimbabwe also reported similar challenges, recognising that—due to worker attrition and retention problems—governments and partners need to continuously invest in healthcare worker capacity.<sup>127</sup>

Since then, beyond incorporation into national guidelines, the evidence generated from clinical trials has been incorporated into training material for national MoH staff, clinical staff, the SMS dissemination of clinical tips (see Section 4.1.5) and technical support for supply chain planning.

Based on findings from four of the countries that we focused on, the Optimal grant in particular provided technical support for systems strengthening as a sustainability strategy and as part of transition planning with national authorities in Kenya, Nigeria, South Africa and Uganda. This included working with governments and global partners to develop capacity in decision-making processes<sup>128</sup> as well as the development of new resources and tools (such as the ARV Dispensing Tool, which has since been mainstreamed). CHAI's work on access in Kenya, Cameroon, Uganda and Nigeria included the streamlining and co-development of roll-out plans for optimal HIV treatments

<sup>123</sup> DoIPHIN-2 2017 GBA.

<sup>124</sup> ADVANCE 2019 Sept update.

<sup>125</sup> Optimal FGD.

<sup>126</sup> South Africa Country Report.

<sup>127</sup> KII 131; Uganda Country Report.

<sup>128</sup> KIIs 26, 33, 35, 37, 51 and 44.

to support the approval and procurement of drugs. Based on the systems strengthening approach adopted for the transition and scale-up of DTG, the Government of Nigeria reported that it had high expectations of sustainability. Additionally, CHAI provided relevant healthcare worker training and sensitisation and toolkits for administering optimal products across countries, including Kenya, Malawi, South Africa, Uganda and Zimbabwe. Specific examples of this work are:

- In Kenya, the Optimal grant introduced activities to help KEMSA, the entity in charge of medicine distribution, to strengthen the overall supply chain, including planning for new IT infrastructure and the development of a forecasting tool to better predict supply needs. Optimal also assisted KEMSA in undertaking mid-year forecasting and quantification exercises to review their assumptions and targets for people living with HIV. Prior to Unitaids' support, the MoH reported that they did not have sufficient capacity in place: "CHAI really helped us from a technical standpoint." In addition, Optimal assisted NASCOP at the MoH in Kenya with the training of healthcare workers, the development of a paediatric toolkit and other documents, and with other technical oversight. This support also helped avoid the risk of weakening the health system by introducing new treatments too rapidly.<sup>129</sup>
- Optimal's technical assistance work was key in supporting Uganda's MoH in developing and reviewing policies that would be used to guide strategic planning at a national level. With CHAI's support, actors within the STD/AIDS Control Programme (ACP) and the Quantification and Procurement Planning Unit were able to lobby for regimen integration into national guidelines, plan for specific programme areas (for example, AHD) and map commodity needs, thereby also supporting health information systems.
- Similarly, the SPAAN grant contributed to HSS in Côte d'Ivoire. Activities included strengthening the ARV supply chain, providing approximately 47 training sessions to over 200 health workers at site levels, supporting the implementation of differentiated models of care for children and giving technical assistance to the government for new ART policy adoption. All of these interventions helped with the successful roll-out and scale-up of optimal ART.

Based upon this work, Unitaids' contribution to strengthening national health systems is rated as 'strong.'

**Remaining gaps:** To ensure that these efforts support the equitable scale-up of optimal HIV treatment products over the longer term, further training and awareness-raising is required with clinicians regarding new regimens, including engagement with the private sector (South Africa). Specifically, some healthcare providers require training to understand how herbal medicines may affect the effectiveness of DTG.<sup>130</sup> Distribution systems continue to need urgent improvements in countries such as Kenya (although the CHAI Optimal grant helped put an improvement plan in place and assisted with the systems automation) and Uganda. It was also suggested (in Cameroon and South Africa) that parallel work to strengthen the supply chain - including capacities to ensure timely ordering by health facilities, timely delivery by district pharmacies and adequate monitoring of product availability - would assist with accelerating government allocation of resources (finding 4). However, it should be noted that comprehensive health systems strengthening is beyond the scope and control of Unitaids.

### 5.3.3 Create community-driven demand

<sup>129</sup> KII 118.

<sup>130</sup> Optimal FGD; DolPHIN-2 FGD; Nigeria Country Report.

**Civil society groups have been strengthened** to actively demand equitable access to products/interventions.



**1**

**Finding 7: Community groups and networks have been strengthened, including through the Optimal grant and the CAB, to actively demand equitable access to optimal HIV treatment products.**

The position against this factor prior to Unitaids' ART optimisation investment in 2016 varied by country, with an average score of '2' ('low') rising to '4' ('high') in 2022. In some countries, community engagement in the HIV space was already well established prior to Unitaids' investment—as in South Africa with the South African National AIDS Council, which brings together government, civil society and the private sector to create a collective response. Other countries, however, had much less CSO presence working in this area in 2016. In countries such as Cameroon, Cote d'Ivoire, Kenya and Nigeria, the civil society response was characterised by fragmentation and a lack of genuine representation.

As described in Sections 3.1.2, 3.2, 4.1.5, 5.3.3 and 6.1, CHAI, through the Optimal grant, worked closely with the Optimal CAB (and community based networks and organisations such as AfroCAB, HIV i-Base and TAC) to strengthen their capacity to hold strategic engagements with governments, influence policy reviews, advocate for the inclusion of optimal HIV treatment products in national guidelines and use treatment literacy materials to help raise awareness of their benefits and side effects. In 2020, in Cote d'Ivoire, EGPAF, through the SPAAN grant: (1) involved the network of people living with HIV; CSOs in the guideline review process for pDTG, the quantification workshop and other key technical meetings; (2) shared information with local NGOs and updated the mentor mother package in Mozambique; and (3) worked with CSO leaders to develop training materials and healthcare worker and caregiver tools in Zimbabwe.<sup>131</sup>

Consequently, in countries such as Kenya and Nigeria, the communities and civil society 'space' increased and is more active than in 2016. Also, funding from the Optimal grant built the capacity of AfroCAB, allowing it to sit in more policy spaces in Kenya (including MoH and PEPFAR meetings) and to check more guidelines (and community awareness of these guidelines) in more countries across Africa. In South Africa, even though many CSOs sat in the National AIDS Council, the community engagement work of the Unitaids portfolio was said to have helped to enhance cohesion between TAC and other community actors working in the HIV space:

*"In a way, it solidified the relationship between the different civil society organisations, which led to us getting quite a lot of requests from organisations that we never thought we'd like to work with." (KII 49)*

Participants in Optimal CAB meetings reported increased capacity to advocate for the inclusion of optimal HIV treatment products, both at the national and global levels.<sup>132</sup> Several Optimal CAB members participated in international conferences to share their experiences and advocate for better HIV treatment on the global stage. Key examples include Optimal CAB members' participation in the 2018 AIDS conference in Amsterdam to demand that DTG/TLD be offered to women of childbearing potential and CHAI and AfroCAB sharing the successes of community engagement at the 2022 AIDS conference:

<sup>131</sup> Optimal 2020 Annual Report.

<sup>132</sup> KIIs 49, 51, 120.

*“One example is that one of the members of the CAB in the very first meeting in Senegal in 2016 wasn’t able to pronounce “dolutegravir”, and it was her aim by the next meeting that she would be able to pronounce the drug so that she’d be able to speak about it confidently back in Kenya. In the next annual meeting, she was already starting to speak on public stages about optimal HIV treatment, building demand, ensuring that people were ready and able to ask for the best available treatments in their respective countries.” (KII 35)*

This leverage and support for existing structures, alongside building the capacity of advocacy groups, should support sustainability. **Unitaid’s contribution to strengthening community representative organisations is therefore rated as ‘strong.’**

**Remaining gaps:** The need for countries to formally integrate these community support structures within future HIV treatment planning and funding cycles to help support sustainability beyond Unitaid funding.

**Grassroots organisations/community networks have been strengthened** to actively demand equitable access to products/interventions.



2

### **Finding 8: Unitaid funding helped strengthen grass roots organisations/communities to actively demand equitable access to optimal treatment products.**

Under the ART optimisation portfolio, community engagement played a strong role in combating misinformation and ensuring the more rapid roll-out of optimal ART. Grassroots organisations and community networks were critical to the engagement of people living with HIV within countries and to the ability of grantees to work within the local context (for example, through helping simplify the language used). These grassroots organisations/community networks were also strengthened to actively demand equitable access to optimal HIV treatment products, including through training from clinical trial grants and the engagement work of the CAB. Three of the trials (ADVANCE, Dolphin-2 and NAMSAL) undertook regular treatment literacy activities and exceeded their targets by reaching over 10,000 community members.

AfroCAB also actively engaged civil society groups and supported their activities to influence the rapid uptake and policy reviews. Over time, community engagement through grassroots organisations improved. For example, in July 2018, 40 women living with HIV from 18 different countries were engaged in dialogue to demand equitable access to optimal HIV treatments at an AfroCAB meeting in Rwanda with support from CHAI and funding from Unitaid (further detail on the context is provided in Section 4.1.5). Subsequently, these women living with HIV released a joint position statement demanding choice and access to TLD. The convening also served as a model for community consultations across a number of focal countries (including Zimbabwe, Kenya and Malawi).<sup>133</sup> Other examples include Malawian and Ugandan regulators consulting with community HIV groups. Few other organisations were reported to be working in this space and building community capacity in the same way.

Thus, Unitaid’s contribution to strengthening grassroots organisations/communities is rated as ‘strong’, but the current scalability status is rated as ‘3’. There is room for improvement, especially in comparison with the progress made on strengthening community representation at a country level.

<sup>133</sup> Harris EL, Blumer K, Perez Casas C, Ferris D, Amole C, Doherty M, Auton M. Accelerating access and scale-up of optimised antiretroviral therapy in low-income and middle-income countries: results of a coordinated end-to-end approach. *AIDS*. 2021 Dec 15;35(Suppl. 2): S165-S171.

For example, in Uganda the majority of demand-creation work was undertaken at the national level to transform the advocacy capacity of CSO and people living with HIV networks, engage with the government and generate health-literacy materials. At the regional and district levels, this meant that some grassroots organisations were left out of capacity development activities. There are, therefore, gaps at the grassroots level and further capacity-building is required in Cameroon, Cote d'Ivoire, Kenya and Nigeria.

**Remaining gaps:** Given the large scale and diversity of Unitaid's focus LMICs, understandably, there are gaps in grassroots representation and capacity to demand optimal products at a sub-national level. Specific priorities include increasing the engagement and capacity of grassroots organisations from the most marginalised local communities (for example, in rural areas) and ensuring that grassroots-community voices are represented and listened to within national discussions and decision-making. Moving forward, Unitaid will also need to make clear strategic decisions around how and at what level to engage the community organisations already supported to further strengthen sustainability and help deliver on the new strategy.

## 6 Efficiency of the ART optimisation portfolio

This section reports on aspects of the Unitaid ART optimisation portfolio's efficiency: it explores the Unitaid Secretariat's management and coordination role (6.1); it looks at how effectively risks have been identified and managed over the course of implementation, including during Covid-19 (6.2); and it provides findings on the extent to which the portfolio was perceived as cost-efficient and cost-effective (6.3). It should be noted that the team did not conduct a formal value-for-money assessment for the evaluation.

### Summary points

- Despite delays caused by Covid-19 and emerging safety signals, grant extensions, strong risk management and a collaborative and adaptive approach to grant management from Unitaid allowed the portfolio to be implemented successfully.
- The portfolio is perceived to have been cost-efficient. Individual grants, as well as components such as community engagement, are seen to have delivered good value for money.
- Unitaid's secretariat role was broadly effective. However, its systems and processes, including funding decisions, could have been more efficient and the role of Unitaid was not always clear and visible in country.

### Key lessons learnt

- Flexibility and allowing grantees to adapt is critical to delivering target outputs.
- It is important for grant-reporting requirements to consider differences in the types of investments (for example, clinical trial versus other grants).
- Improved communication to partners regarding Unitaid's role, the work it funds and its portfolio's successes could help foster stronger buy in (to scale-up, for example).
- A better-phased and balanced approach to procuring and rolling-out new regimens could enhance value for money.

### 6.1 Unitaid Secretariat

1

**Finding 1: Unitaid's ART optimisation team 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.** During project design, CHAI reported that early and consistent collaboration, including sharing timelines up front and meeting in person with the Unitaid project team, was critical to formulating a plan that met with Unitaid's expectations and accelerating timelines.<sup>134</sup> The ART optimisation portfolio team's reflection was that, going forward, they would like to collaborate even further during the grant design stage.<sup>135</sup>

**Grantees considered that the Unitaid secretariat added value by providing thought-leadership and strategic direction, including for community engagement.**<sup>136</sup> For example, early in the process, stakeholders<sup>137</sup> reported that communications between grantees and community organisations suffered from a lack of a shared understanding of success. Unitaid's secretariat played an important role in clarifying expectations between community organisations and grantees and in reiterating to

<sup>134</sup> 2017 Annual Report.

<sup>135</sup> Unitaid FGD notes.

<sup>136</sup> ADVANCE FGD; D<sup>2</sup>EFT FGD; DoIPHIN-2 FGD; NAMSAL FGD.

<sup>137</sup> KIIs 35, 37, 51.

grantees the importance of implementing this mechanism, which fostered an environment for supportive relationships.<sup>138</sup>

**Facilities to share the lessons learnt improved over time, supporting effective working in-country and adaptation.** Initially, Unitaid did not have sufficient mechanisms in place to ensure that lessons were synthesised and communicated across the portfolio; however, there were improvements over time.<sup>139</sup> The PAC was actively used as a learning mechanism, where Unitaid shared the lessons learnt from the portfolio, including around new regimen introduction.<sup>140</sup> Unitaid also annually convened portfolio representatives in Geneva for a two-day meeting and several cross-pollination meetings with grantees to discuss their priorities and experiences. These meetings were an opportunity for grantees to learn and share with each other on common areas such as community engagement, national guidelines and safety signals (see 6.2).<sup>141</sup> The lessons learnt contributed to the various adaptations across grantees. In addition, CHAI, through the Optimal grant, used expert groups, the CAB, focal points/key stakeholders and publications and newsletters to share lessons across countries and encourage collaboration, including, in particular, in the area of community engagement.<sup>142</sup>

1

**Finding 2: Grantees identified important areas where the secretariat could improve efficiency, including around decision making related to reprogramming and extensions, reporting requirements and communications.**

**Grantees praised Unitaid for its flexibility in supporting reprogramming and adaptations. However, grantees also reported that these processes can be lengthy and cause some delays during implementation (for example, in relation to the clinical trials).** This was seen by grantees and Unitaid as one of the biggest blocks, capable of curbing the organisation's potential to respond to emerging needs and what works in a timely manner.<sup>143</sup> Conversely, another interviewee noted that Unitaid's processes and systems, overall, are more efficient, agile and responsive than those of other donors.<sup>144</sup> One possible solution to reconcile this tension, as noted by one stakeholder, would be to provide long-term grant cycles, thus supporting greater predictability for grantees and long-term outcomes, as offered by some other global partners.<sup>145</sup>

**Stakeholders classified Unitaid's biannual reporting as onerous.**<sup>146</sup> Grantees felt that Unitaid's report format is repetitive and not sufficiently tailored to reporting the progress of clinical trials (although, there was recognition that improvements have been made over time).<sup>147</sup> This was also considered problematic when reporting against progress on community engagement due to the need to mobilise several community organisations that were not used to that level of reporting.<sup>148</sup>

**Unitaid's communications were identified as an area for improvement by partners.**<sup>149</sup> For example, end-of-grant communication to PAC members could better share the clinical trials' results and forward-looking updates. Unitaid itself recognises the need to better capture and catalogue the results of its work:

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<sup>138</sup> KIIs 35, 37, 49, 51.

<sup>139</sup> KIIs 22, 35, 37, 49, 56, 57.

<sup>140</sup> KII 22, 35, 37.

<sup>141</sup> KII 18, 19, 21, 35, 37.

<sup>142</sup> KII 18, 19, 21, 122.

<sup>143</sup> KIIs 35, 37; Grantees FGD notes; Unitaid FGD notes; D<sup>2</sup>EFT 2017 Annual Report.

<sup>144</sup> KIIs 38, 43, 58; Unitaid FGD.

<sup>145</sup> KII 45.

<sup>146</sup> KII 50; South Africa KIIs; Grantees FGD notes.

<sup>147</sup> Grantees FGD notes.

<sup>148</sup> KII 50.

<sup>149</sup> KIIs 46, 58.

*What we didn't do was develop a mechanism where we captured, successively, the successes and the achievements of the portfolio. (Unitaid, FGD)*

Overall, manufacturers were positive about their experience working with Unitaid and CHAI, although a minority also suggested room for improvement in communications. It was reported that relying solely on grantees for communication led to unclear messaging around the organisation of meetings and thus to missed opportunities for partners to attend. One manufacturer felt that there should have been more consistent and clear communication with them through the conduit of CHAI. In general, partners expressed a desire for regular and clear communication and for Unitaid to work more closely with them to share progress as part of a “true partnership.”

2

**Finding 3: Unitaid’s mandate is less known at the national level and several stakeholders suggested strengthening the organisation’s profile and information in countries.**

**Unitaid’s contribution to improving access to optimal HIV treatment in focus countries, including its funding contribution, was not always known or clear to stakeholders.**<sup>150</sup> In Benin, despite government stakeholders and community engagement representatives knowing that CHAI was implementing a project to introduce DTG-based regimens in the country, none seemed to know that the name of the project was Optimal nor that the funding came from Unitaid.<sup>151</sup> Due to this lack of Unitaid visibility within the country (and the fact that CHAI also received funding from other donors), the evaluation team found it difficult to directly link achieved results to the Unitaid grant.

**Stakeholders (in particular, community representatives)<sup>152</sup> felt that Unitaid’s in-country presence, especially at strategic government meetings, was weak.** Unitaid does not have country offices and operates through partners that are best placed to translate health innovations into practice. Unitaid teams visit countries<sup>153</sup> as part of programme MEL and some strategic visits provide an opportunity for dialogue between Unitaid and implementing partners and between Unitaid and country governments. However, for the ART optimisation portfolio, the planned frequency of these visits was unclear, as was whether all grants were entitled to the same number of visits.

**This is, potentially, a missed opportunity: 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.** This could lead to better results around sustainability, for example, and to other strategic benefits such as the scale-up of fundraising opportunities.<sup>154</sup> Governments considered that improved information on Unitaid programmes and funding would support better planning at a country level. Some country partners recommended that Unitaid provide more information and transparency on programme workplans, including, for example, what interventions are eligible for funding (Benin). Stakeholders from the Government of Kenya suggested that it would be helpful to know the size of the resource envelope available for planning purposes. This would include, for example, knowing the percentage of health workers that require training that Unitaid can support, or what specific programme areas the support is available for (for example, paediatrics), as well as opportunities for government partners to attend annual programme reviews.

## 6.2 Risk management and adaptation

2

**Finding 1: The experienced clinical trialists selected by Unitaid understood that implementation risks inherent to innovation require careful planning and monitoring,**

<sup>150</sup> KIIs 35, 37, 51.

<sup>151</sup> Benin Country Report.

<sup>152</sup> For example KIIs 49, 51, 120.

<sup>153</sup> For example, the ART Optimisation team visited all Optimal project’s focal countries.

<sup>154</sup> KII 49.



**and they demonstrated significant capacity for risk management and adaptation during implementation.**

**Multiple strategies were employed across the portfolio’s clinical trial grants to mitigate risk.** These included selecting experienced trialists, maintaining risk registers,<sup>155</sup> ensuring thorough consent forms<sup>156</sup> and starting sub-studies to monitor emerging risks.<sup>157</sup> The recruitment and retention of participants at some sites was a particular danger faced by the clinical trials, driven primarily by social issues and the mobility of study populations causing some minor delays at the beginning.<sup>158</sup> Trialists actively assessed people living with HIV moving off the trial for TB treatment and increased recruitment and activities as key strategies to mitigate this peril.<sup>159</sup>

**Grants anticipated a need for contingency funding to adapt to and actively investigate interim findings relating to safety risks and treatment outcomes, including side effects.**<sup>160</sup> For example, the ADVANCE study identified weight gain at 48-week outcomes from DTG, which were not detected earlier, during the development phase, and applied for additional funding to extend the study to 192 weeks to gather additional data and insights and adapt its safety monitoring to include the HBA1C haemoglobin test.<sup>161</sup> Unitaid and other grantees worked fast to understand such safety signals. Evidence was collected from several projects—including DolPHIN-2, ADVANCE and NAMSAL—to reveal the short-term and long-term effects of weight gain on people on DTG-based treatments (see Sections 3.2, 4.1.2, 5.2.1).<sup>162</sup>

**Clinical trialists remained engaged with relevant emerging global evidence and took precautions until evidence on participant risk was clear.** For example, although experienced trialists reviewed the neural tube defects (NTDs) evidence for DTG as weak, they took precautions to garner more evidence. Informed consent forms were introduced during the trials, including information about potential risks and the availability of other options. Participants were switched off DTG randomisation and moved to standard care if they declined consent.<sup>163</sup>

**1**

**Finding 2: Unitaid provided the necessary support and flexibility to allow grants – including clinical trials – to course-correct during the Covid-19 pandemic, and grantees responded with innovative solutions.**

**At the portfolio level, Unitaid pivoted, responding to challenges such as safety and supply risks and the changing government priorities during the Covid-19 pandemic.** Unitaid (with WHO support) developed and monitored a risk-management and risk-mitigation strategy at the portfolio level. Unitaid itself reported that this was key to enabling safety during the implementation of clinical trials (for staff and participants) and considered this to be a useful model that could be applied to other health emergencies. With Unitaid’s support, all clinical trials pivoted to look at the intersection with Covid-19 infections – through the Coronavirus Outcomes in HIV Evaluation in Resource Limited Settings (COHIVE) study – and generated further evidence on this, demonstrating the portfolio’s ability to adapt to changing contexts and synergise with other public health activities. Furthermore, across focal countries, funds disbursed by Unitaid facilitated the identification of risk-mitigation gaps in country-planning in response to Covid-19, as well as protocols and actions to help fill those gaps. These included direct support for facilities, caregivers and other delivery arms to help

<sup>155</sup> DolPHIN-2 2-17 Annual Report.

<sup>156</sup> 2016 Oct-Project Optimise Monthly Update; ADVANCE 2020 Annual Report; DolPHIN-2 Annual Report.

<sup>157</sup> NAMSAL 2019 Disbursement Memo; ADVANCE 2020 Annual Report; DolPHIN-2 Annual Report.

<sup>158</sup> D<sup>2</sup>EFT 2017 Annual Report; D<sup>2</sup>EFT 2020 GBO; D<sup>2</sup>EFT 2021 Annual Report.

<sup>159</sup> ADVANCE 2016 Project Plan; D<sup>2</sup>EFT 2016 Project Plan; D<sup>2</sup>EFT 2017 Annual Report.

<sup>160</sup> ADVANCE FGD; ADVANCE 2020 Annual Report; D<sup>2</sup>EFT 2018 Annual Report.

<sup>161</sup> ADVANCE FGD; ADVANCE 2020 Annual Report.

<sup>162</sup> ADVANCE FGD; ADVANCE 2020 Annual Report; D<sup>2</sup>EFT 2021 GBO.

<sup>163</sup> 2021 Annual Report.

reach people living with HIV, community-level engagement and the addressing of commodity needs and supply chain processes.<sup>164</sup>

**Covid-19 caused significant disruption to the implementation of Unitaid’s portfolio, but grantees responded well, effectively adapting to challenges such as lockdown.**<sup>165</sup> Covid-19 impacted clinical trial participant recruitment and completion, the ability to conduct planned fieldwork for qualitative studies and engagement with the public. To mitigate this, grantees responded by delaying recruitment, procurement and fieldwork activities and/or by identifying innovative approaches to remote research and engagement. For example, grantees shifted to electronic communication, such as WhatsApp video calls, for community engagement meetings. Socioeconomic studies were conducted over the phone (and these were also used as an opportunity to increase Covid-19 literacy among participants). The ADVANCE study adapted quickly to ensure the continued adherence of trial participants, including through the use of mobility clinic vans during Covid-19 lockdowns. These vans were adapted to serve as mobile primary healthcare clinics, seeing people living with HIV in their homes if they were isolating. They were also used for the COVER and COHIVE projects.<sup>166</sup> To protect participants and study staff from Covid-19 transmission, studies implemented spaced visits and remote monitoring and began collecting adverse-event data. Covid-19 also affected drug procurement, requiring earlier planning and the purchase of personal protective equipment for staff.<sup>167</sup>

**Finally, projects took advantage of new opportunities in response to necessary Covid-19 adaptations.** For example, Covid-19 delays in the D<sup>2</sup>EFT trials, which were initially designed to focus on TLD as a second-line therapy for people failing with first-line ARTs, required the need for specific changes. Following consultation with WHO and other key stakeholders, the D<sup>2</sup>EFT study shifted to the evaluation of a simplified DTG-based regimen.<sup>168</sup> From this, new evidence emerged suggesting that use of DTG with pre-determined nucleosides could be an additional useful approach to second-line therapies. DTG with pre-determined nucleosides is now available at an exceptionally low cost in LMICs, allowing for substantial reductions in the cost and complexity of care. In addition, Optimal’s extension following the pandemic allowed for a range of additional outputs, including ensuring the continuity of HIV treatment programmes through the Covid-19 response, but also accelerating access to optimal paediatric products and optimising second-line HIV treatments.

### 6.3 Cost efficiency and effectiveness

2

**Finding 1: The available evidence suggests that elements of the portfolio and its overall performance were cost-efficient and cost-effective.**

**Unitaid took specific actions to improve the efficiency and cost-effectiveness of the portfolio.**

Grantees consistently reported that Unitaid’s flexibility – allowing grantees to adapt within the budget – was critical to achieving the target outputs, for example, when clinical trials and market-shaping work required reprogramming due to the shifting HIV landscape (see Section 6.2).<sup>169</sup> Despite delays due to Covid-19 and associated challenges (for example, lockdowns and alternative health priorities for governments), costed and no-cost extensions allowed implementation to be completed satisfactorily.<sup>170</sup> The consolidation of Optimal and SPAAN activities also supported efficiency (through combining them under one grant) as well as cost-effectiveness, with the PAC remarking

<sup>164</sup> KII 118; Kenya Country Report; Nigeria Country Report.

<sup>165</sup> KIIs 36, 39, 45, 118; D<sup>2</sup>EFT FGD; South Africa Country Report; Nigeria Country Report; Kenya Country Report; CCSE for ART Opt. Evaluation October 2022.

<sup>166</sup> ADVANCE FGD; ADVANCE December 2017 update.

<sup>167</sup> KII 49; NAMSAL 2019 Disbursement memo; D<sup>2</sup>EFT 2021 GBO; DoIPHIN-2 2020 Annual Report.

<sup>168</sup> KIIs 35–39; D<sup>2</sup>EFT FGD; South Africa Country Report; Kenya Country Report; TRIO Extension\_ Executive summary 2020; 2021 Annual report.

<sup>169</sup> KIIs 36, 39, 45, 118; FGDs 9, 13; Kenya Country Report; Nigeria Country Report; South Africa Country Report.

<sup>170</sup> KIIs 26–33, 36, 39, 45; FGDs 9, 13; South Africa Country Report; 2019 Project Plan Amendment.

that this helped to focus paediatric optimisation efforts building on the achievements of both projects. It was also noted that the strategic alignment between CHAI and EGPAF was optimised through geographic mapping.<sup>171</sup> Additionally, community engagement (a cost-effective approach) was increasingly used by EGPAF, once embedded under Optimal.

**Individual grants were perceived to be cost-effective.** Illustrating this, for example, the DOLPHIN-2 study, with 250 women recruited from Uganda and South Africa, was perceived to be a low-cost grant which nonetheless generated evidence adopted globally by WHO and informed the revision of guidelines in over 90 countries.<sup>172</sup> An example of opportunistic performance by the grantees – generating additional learning from their data and increasing cost-effectiveness – was the pregnancy and weight gain sub-studies added as part of D<sup>2</sup>EFT (in response to the emerging safety signals) alongside the addition of a third arm (testing DTG+2N). For only a minor investment, this generated significant additional outcomes without the need for a new study.<sup>173</sup>

**The portfolio's community engagement work was perceived by stakeholders to be highly cost-effective.**<sup>174</sup> Community engagement activities were allocated a moderate budget relative to the total value of the Unitaid ART optimisation portfolio. Yet (as described in 5.3.3), they made a significant contribution to its success. According to some stakeholders, community engagement should be allocated a greater budget. Community-based organisations such as AfroCAB said that going forward they would prefer to receive direct funding from Unitaid (especially now that their capacity has increased), as this would enhance their flexibility and responsiveness to community needs and thus provide overall value for money.

3

**Finding 2: Some perceived that the value for money of the portfolio's market-shaping work could be enhanced, including through staggered country roll-outs for procurements and delivery.**

Longer-term cost-savings are generated from moving people living with HIV onto more optimal treatments and from the associated viral load suppression and lower treatment and care costs. However, some stakeholders argued that it is important to have a realistic transition plan when adopting a new treatment protocol. A smoother transition should be promoted, rather than one that is too rapid<sup>175</sup>. This would involve, for example, a staggered roll-out of product delivery to allow agencies to clear existing treatments (destruction of existing ART stocks was reported in Kenya and Nigeria), and to assist manufacturers with maximising production and registering with regulatory agencies. This could help enhance the efficiency of the procurement process and overall value for money<sup>176</sup>.

<sup>171</sup> 2020 CE Executive Summary.

<sup>172</sup> Uganda Country Report.

<sup>173</sup> D<sup>2</sup>EFT FG.

<sup>174</sup> KII 52.

<sup>175</sup> KIIs 35, 37, 45 and Optimal FDG.

<sup>176</sup> KIIs 56 and 57.

## 7 Impact of the ART optimisation portfolio

This section reports on Unitaid’s ART optimisation portfolio impact. It contains findings on the extent to which the portfolio has contributed to global targets and equity impact (7.1) as well as on any other strategic benefits and positive externalities that resulted from the work of the portfolio (7.2).

### Summary points

- Given Unitaid’s important role in accelerating access to optimal HIV treatments for the vulnerable and underserved, with increased tolerability and efficacy for viral suppression compared with previous treatments, the estimated contribution of the portfolio to global HIV targets is ‘high.’ CHAI estimates that 25m adults will have transitioned to DTG-based regimens by 2028. As a result of TLD roll-out, 1.1m lives will be saved by 2027.
- By delivering reduced cost of optimal ARTs for LMICs and longer-term health savings in target countries, the Optimal grant estimates that this will generate over US\$1.6bn in savings through 2022 and a US\$7.8bn saving by 2028.
- The ART optimisation portfolio was instrumental in shaping policy and triggering change in the treatment guidelines for women living with HIV.
- Unitaid’s impact has been facilitated by supportive policy environments and strong relationships with global and country partners active in scaling up HIV treatments.
- There has been a range of wider strategic benefits from the portfolio, including Unitaid and its partners learning from and adopting the community engagement model.

### Key lessons learnt

- Further action is required to reduce deaths from HIV, including accelerating the roll-out and uptake of paediatric formulations for children.
- Countries with weaker enabling environments for scale-up may need additional support for government strategy, systems and ownership of optimal ART to help enhance impact.

### 7.1 Global targets and equity

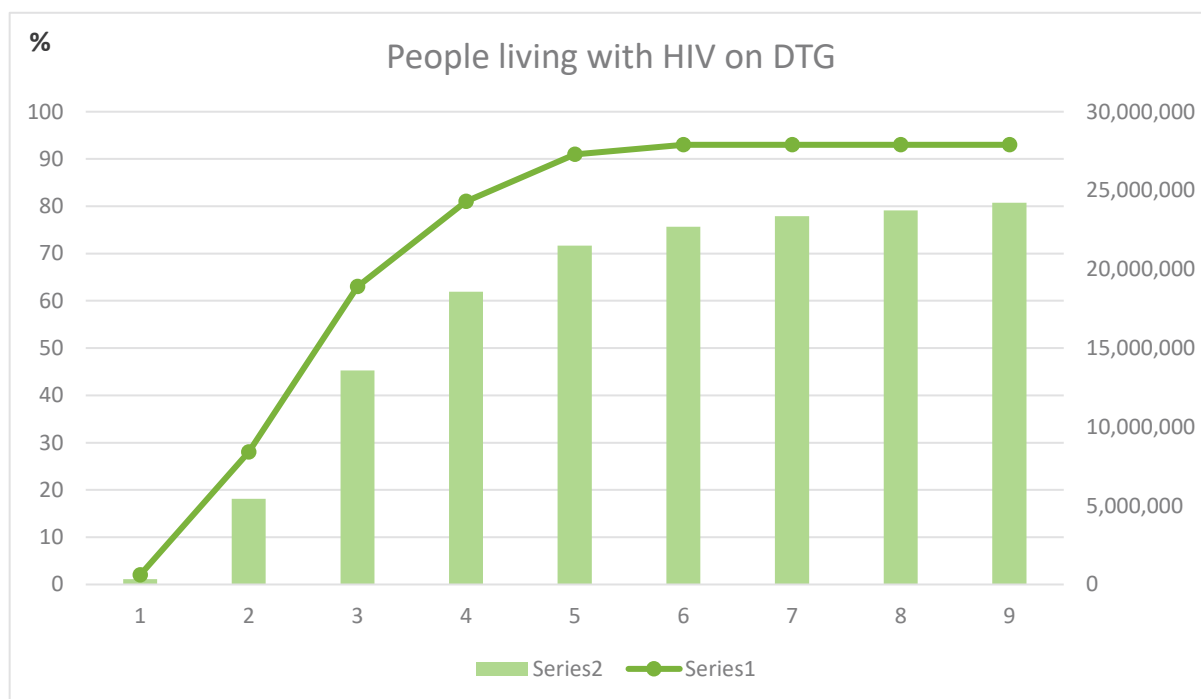
1

**Finding 1: In line with global HIV targets, focus countries have seen a significant decline in HIV infections and deaths from HIV and an increase in viral suppression alongside significant progress towards people living with HIV accessing optimal ART treatments.**

**Unitaid’s work to improve the access to, and roll-out of, DTG has led to a significant increase in the number of people living with HIV accessing optimal ART treatments in LMICs.** In 2019, 28% of adults accessing first-line ARTs 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 (Figure 17). CHAI forecasts that 25m adults will be adhering to DTG-containing regimens by 2028.<sup>177</sup>

**Focal countries for the ART optimisation portfolio made particular progress.** In Uganda, by 2022, of the estimated 1.42m people living with HIV and the 96% on ARTs (in comparison with 69% in 2016), over 95% were on DTG-based regimens, and 83% of eligible children transitioned to DTG 10mg. In Malawi, the country achieved 95% coverage for both TLD and pDTG by 2022. Several LMICs,

<sup>177</sup> Optimal VFM Summary (May 2023).



**Figure 17. Number of people living with HIV on DTG and % of people living with HIV on DTG**  
 Source: CHAI HIV Market Reports 2019-2022; CHAI Mid-year Memo 2023(2018-22 actuals, 2023-26 projected)

including Kenya, Nigeria and Tanzania, transitioned more than 1m.<sup>178</sup> Of the 5.5m people now on ART in South Africa, approximately 60% transitioned to DTG as a first-line treatment (as of June 2022)—a figure rising to 70% by March 2023.<sup>179</sup>

*“99% of progress on TLD can be attributed to Unitaid.” (KII 89)*

In parallel, between 2016 and 2022, focal countries experienced general improvements in mortality from HIV and new infections. In Kenya, the number of new infections halved, from 71,034 per annum. HIV-related mortality declined by approximately one-third (alongside a smaller reduction from 5.9% to 4.8% in Kenyans who are HIV-positive).<sup>180</sup> In 2016, South Africa had an estimated 430,000 new infections per year. By 2022, even though the number of people living with HIV had increased to 8.1m, there were only 210,000 new infections. Between 2016 and 2021, the number of deaths due to HIV/AIDS in Benin decreased by 29.41%, from 2,302 to 1,625. There were also fewer new infections during the period (2,852 in 2016; 1,683 in 2021).

**Box 10. Contribution of the ART optimisation portfolio to equity impact**

**The ART optimisation portfolio invested in the poorest and most vulnerable and underserved.** The portfolio focused on ensuring that children (Figure 18) and pregnant women had access to better HIV treatment. It invested in clinical trials to generate evidence in vulnerable and underserved populations and in resource-limited settings (including women in late pregnancy), and it supported the acceleration of children’s transition to new optimal regimens as part of the SPAAN grant (later embedded into the Optimal grant).

**Unitaid’s investments under the ART optimisation portfolio led to considerable changes in treatment for women living with HIV.** As previously discussed in the relevance section, the DolPHIN-2 trial filled the

<sup>178</sup> 2020 CHAI HIV Market Report 1.

<sup>179</sup> National Department of Health, South Africa.

<sup>180</sup> Kenya Country Report.

evidence gap on HIV treatment during pregnancy as it investigated the safety and effectiveness of DTG in late pregnancy. The results of the trial informed the revision of WHO guidelines, changed the way ethics committees around the world look at pregnancy ethics, and impacted on the changes in guidelines across more than 90 countries.<sup>181</sup>

**Unitaid financed market-shaping interventions to accelerate approval, lower global commodity costs and generate demand for rapid uptake for vulnerable and underserved children.** Unitaid’s incentive programme, supported CHAI, achieved the fastest ever regulatory approval of a generic product by the FDA (5.2.1). CHAI also negotiated, with both ViiV Healthcare and generic manufacturers, the 75% price reduction from the standard of care in pDTG 10mg.<sup>182</sup> This led to the accelerated roll-out of the drug in project countries and other LMICs. Recent data produced by CHAI state that 75+ countries have placed orders for pDTG 10mg, contributing to the widespread introduction of DTG for children <20 kg. Over 87,000 children living with HIV can now access pDTG in CHAI and EGPAF focal countries, contributing to over 150,000 children globally.<sup>183</sup>

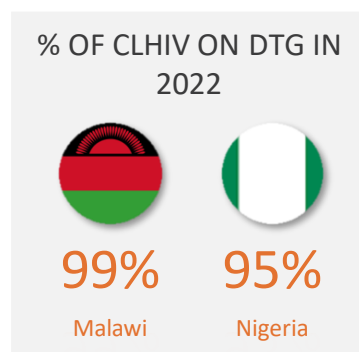
*“Within the field of paediatric HIV, I think it’s been the biggest driver of improvement for kids that we’ve seen in the last five years.” (KII 58)*

**Stakeholders at both the global and country levels drew a specific connection between the rapid roll-out of DTG in LMICs, facilitated by Unitaid, and increased virological suppression.** Whilst some of these improvements will be related to general increases in the uptake of ART, virological suppression is critical in reducing both HIV infections and deaths.

*“Looking at the statistics around the roll-out of dolutegravir in general for adults... I think that the shift towards that product has really occurred. On the paediatric side, we are seeing virological suppression of up to 90% from what used to be something like 30% in the span of very few years because of the roll-out of DTG.” (KII 45)*

*“By introducing TLD and DTG50 they have reduced the suppression rate to 96% for adults and 90% for children. The turning point was introducing paediatrics for children. Prior to that, treatments were drug resistant and were unpalatable to children.” (KII 85)*

In Kenya, by 2021, 95% of people on ART were virally suppressed. Uganda was also on course to achieve the 95% target for viral suppression. In Cote d’Ivoire, the suppression rate was reported to have increased from 49% in 2019 to 61% by 2021. In Benin, viral suppression increased from 54% in 2016 to 66% in 2021. In Nigeria, 89% of people placed on ART were virally suppressed by 2021, compared with fewer than 50% in 2018. Stakeholders, including the Government of Nigeria’s representatives and partners, stated that the shift to DTG resulted in increased adherence to HIV medication (including the paediatric dose) as well as an increase in suppression rates.



**Figure 18. Notable achievements in paediatric scale-up**  
Source: Optimal Project Overview\_ Oct 17 2022\_final

<sup>181</sup> DoIPHIN-2 FGD; Uganda Country Report.  
<sup>182</sup> Optimal Project Overview\_ Oct 17 2022\_final.  
<sup>183</sup> HIV Mid-year Market Memo – June 2023.

CHAI estimates that 1.1m lives will be saved through TLD roll-out 2018-2027<sup>184</sup> (0.6–0.7m in focal countries<sup>185</sup>). CHAI developed these estimates utilising the assumptions and findings from a recent modelling study by Phillips et al. (2019).<sup>186</sup> The authors found that 0.98 deaths are averted per 100 patient-years on DTG-based regimens such as TLD, compared with EFV-based regimens such as tenofovir disoproxil fumarate/lamivudine/efavirenz (TLE).<sup>187</sup> The difference in averted deaths is mostly due to people living with HIV being less likely to develop treatment resistance on DTG-based regimens. This can be compared with the estimated 16.2m AIDS-related deaths averted since 2001 through the scale-up of ART.

2

**Finding 2: Transitioning people living with HIV to more optimal HIV treatments in LMICs, accelerated by Unitaids portfolio, will generate significant health gains and cumulative cost savings, supporting good value for money over the long term.**

Through aggregating demand and promoting rapid uptake, Unitaids market-shaping work has contributed to lower drug prices (see 4.1.4) and important economic savings for LMICs. The estimated savings<sup>188</sup> that will result from the scale-up of less expensive and more optimal adult regimens, both during the Optimal grant period and over the five years post-grant (2017–28), is expected to be between US\$2bn and US\$2.1bn in the CHAI focal countries.

Globally, the Optimal project reports that it has achieved major impact, including generating over US\$1.6bn in savings through 2022, and a projected US\$7.8bn saving by 2028.<sup>189</sup>

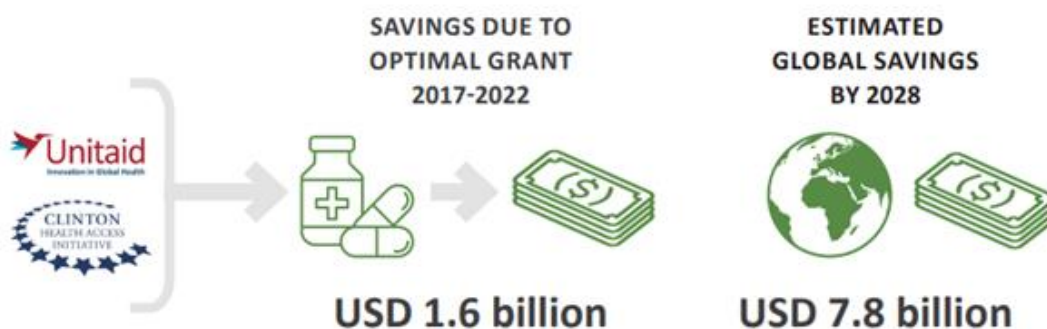


Figure 19. Savings generated by the Optimal grant

This is further illustrated by the case of Uganda, where the increase in the numbers prescribed ART improved virological suppression, reduced in vertical transmission rates and, overall, significantly impacted the lives of people living with HIV. Accordingly, Unitaids intervention was seen to be cost-effective:

<sup>184</sup> Optimal Project Overview\_ Oct 17 2022\_final.

<sup>185</sup> 2020 CE executive summary.

<sup>186</sup> 2021 CHAI HIV Market Report.

<sup>187</sup> Dugdale CM, Ciaranello AL, Bekker LG, Stern ME, Myer L, Wood R, Sax PE, Abrams EJ, Freedberg KA, Walensky RP. Risks and Benefits of Dolutegravir- and Efavirenz-Based Strategies for South African Women With HIV of Child-Bearing Potential: A Modelling Study. *Ann Intern Med.* 2019 May 7;170(9):614-625. doi: 10.7326/M18-3358. Epub 2019 Apr 2. PMID: 30934067; PMCID: PMC6736740.

<sup>188</sup> CHAI bases this modelling on the cost of the products, cost savings, pricing assumptions, patient volumes, demographics, viral suppression rates, and death rates. The counterfactual pricing assumption is that the cost of existing adult treatments would be 100% higher than the cost of TLD secured through the pricing agreement and subsequent reductions, whilst it is forecasted that 22m adults will have transitioned or be adhering to TLD by 2028. We did not independently verify the assumptions involved and present the results here at face value.

<sup>189</sup> 2020 CE Executive Summary; 2022 Semi-Annual Flash Report and Follow-Up; Optimal Project Overview\_ Oct 17 2022\_final; Optimal VM Summary (May 2023).

*“The Paediatric DTG 10mg was a cost-saver, and much cheaper than LPV/r syrup and pellets. This also aligned with the government’s aim of efficient use of scarce resources to ensure better treatment outcomes. When people living with HIV are doing well with none or very few opportunistic infections, this implies less expenses for government on drugs and increased productivity.” (KII 51)*

1

**Finding 3: Stakeholders consider that the main additional benefits for countries with a Unitaïd programme were the accelerated adoption of optimal treatments, alongside other contributing factors.**

**Stakeholders often spoke of the catalytic impact of Unitaïd’s funding in accelerating access to optimal HIV treatments.** Whilst countries often adopt WHO policy guidance as a foundation for their health policies and programmes, especially in resource-limited settings, adoption is not always immediate or universal due to political, economic, social, cultural, or regional factors. Differences in interpretation and implementation can also affect the quality and effectiveness of health interventions and policies. Within this context, the ART optimisation portfolio accelerated the roll-out of better HIV treatments (reported in some countries to be by as much as 3 years):

*“The adoption of new products where Unitaïd operated went much faster than non-Unitaid countries... and actually reached scale-up.” (KII 22)*

*“The programme from Unitaïd actually played a very big role in making sure that TLD is rolled out in South Africa because... it would have maybe taken an even longer time... the release of the guidelines took even longer than what was anticipated.” (KII 49)*

In Nigeria, the grants were seen as a catalyst that changed the landscape of ARV and commodity availability in-country (leading to an improved quality of care, HIV indices and cost savings):

*“Children and adults are happier as they are virally suppressed and do not spend much money on drugs anymore on other diseases.” (KII 94)*

In Côte d'Ivoire, catalysing the introduction of optimal ARV treatments (including DTG for children) and delivering end-to-end support for the expansion and scale-up of the treatment had significantly improved paediatric HIV care. In Kenya, CHAI suggested that “it would have taken years” to adopt optimal treatments without Unitaïd’s intervention. The manufacturer incentive programme accelerated the production of a generic version of DTG and the development of paediatric DTG. Holding clinical trials directly in LMICs also accelerated the adoption of results (estimated as three years faster in Cameroon). As noted by CHAI, these impacts were achieved against the backdrop of wider cuts to global HIV funding during the Covid-19 crisis.<sup>190</sup>

**Through generating specific evidence to influence guidelines and support the future scale-up of optimal ART regimens in LMICs, the clinical trial data will continue to shape public health approaches and improve the lives of people living with HIV beyond the lifetime of the portfolio:**

*Findings will help influence future directions for Unitaïd and other funders, on delivering effective second-line treatment and what are the difficulties and*

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<sup>190</sup> 2020 CHAI HIV Market Report 1.



*incentives. This will potentially impact and determine markets well beyond the life of this trial. Other strategic trials like this are still determining treatment roll-outs 5–10 years post and are still updating WHO treatment guidelines. (D<sup>2</sup>EFT FGD)*

**However, Unitaid’s grants do not operate in isolation and it should be acknowledged that wider contextual factors contributed to the high impact of the ART optimisation portfolio.** Moves towards universal access to ARVs (Test and Treat) had already resulted in the rapid scale-up of ART and significant increases in people living with HIV accessing treatment (albeit often on sub-optimal regimens). This both necessitated and helped increase the impact of Unitaid’s intervention. Supportive policy environments and scale-up partners were also important for enabling the progress towards fast-track targets, as is acknowledged by Unitaid:

*“The impact of the grant or the impact of the whole project can largely be attributed to that partnership working between the normative agencies, the international grant organisation, and the grant implementers coming together at one table”. KII 51*

1

**Finding 3: Despite such progress, globally, deaths from HIV are still too high given the optimal treatments now available. Continued action is required to meet global targets.**

**Despite the progress outlined above, including on virological suppression, the number of deaths from HIV remains high globally, especially relative to the scale-up of ARTs.** Over the past decade, the number of people dying from HIV-related causes has halved.<sup>191</sup> In 2019, HIV-related deaths fell below 700,000 (a decrease from 1m deaths in 2012). However, in 2021, new HIV infections declined only marginally and AIDS-related deaths, at 650,000, declined by only 6%. This is despite HIV now being a manageable chronic condition with first-line optimal treatments available for under US\$50 PPPY in LMICs. According to CHAI’s market intelligence, to achieve the fast-track 95-95-95 targets by 2025, significant additional efforts are required to accelerate equitable access to HIV care.<sup>192</sup>

**Priority areas include a focus on AHD and the continued scale-up of ARTs for children and young people.**

*While improving access to ART is a critical step in reducing HIV-related deaths, country programmes must also improve access to commodities for the management of advanced HIV disease. (2020 CHAI HIV Market Report 1)*

In response to this, an AHD component was added onto the Optimal grant in 2018 and Unitaid launched an AHD RfP at the end of 2022.<sup>193</sup> The other main priority identified for future Unitaid support (particularly in countries where this was not pursued, or was pursued with less intensity, as in South Africa and Cameroon) was continued improvement in access to, and uptake of, paediatric treatments for children. According to the most recent figures (2021), just over half of children living with HIV (under 15 years of age) are accessing ARTs (up from 43.7% in 2016).<sup>194</sup> The most recent CHAI HIV market report states:

<sup>191</sup> UNAIDS/WHO estimates.

<sup>192</sup> 2022-CHAI-HIV-Market-Report-12.8.22.

<sup>193</sup> <https://unitaid.org/call-for-proposal/preventing-deaths-among-adults-and-children-by-simplifying-advanced-hiv-disease-management/#en>.

<sup>194</sup> Global AIDS Monitoring and UNAIDS 2022 Estimates.

*Paediatric HIV outcomes continue to unacceptably fall behind those of adults. Persistent global disparities exist between children and adults on ART (52% compared to 76% respectively) and achieving viral suppression (40% compared to 67%). The Covid-19 pandemic put this population further off-track. In 2021, children living with HIV accounted for 98,000 AIDS-related deaths and 160,000 new HIV infections. (2022 CHAI HIV Market Report, 12 August 2022)*

## 7.2 Strategic benefits and positive externalities

2

**Finding 1: Successful components of the ART optimisation portfolio, including the PAC and community engagement model, have influenced other Unitaid portfolios, as well as global partners.**

**Unitaid reported that both the PAC model and the portfolio’s approach to community engagement, including the CAB, have been replicated across other Unitaid portfolios and influenced the approaches of their partners.** Because of the success of the approach, more emphasis is now placed on community engagement at an organisational level. Unitaid’s investment in demand creation through community engagement and the Optimal CAB was also reported to have influenced other actors investing in HIV programming to pursue similar approaches, including BMGF, CHAI, EGPAF and several other partners, such as WHO, who see the value of engaging communities from inception through to implementation.<sup>195</sup> In Malawi, there are ongoing discussions for Global Fund to finance community engagement activities as part of their ongoing HIV response in the country.<sup>196</sup> D<sup>2</sup>EFT relied less on community engagement and said that this would be included in their future trials based upon the lessons learnt from Unitaid’s funding. ADVANCE partners will be likely to replicate the same community engagement model going forward.

*“Many others are adopting the model because I think everybody has seen the value in engaging communities right from the first start and making them part of the implementation”. KII 51*

**The ART optimisation portfolio has acted as a catalyst, influencing the focus of some global partners on HIV treatment priorities that receive less attention.** By bringing AHD into the Optimal grant (also aligned with the mission to invest in the poorest and underserved communities), Unitaid encouraged Global Fund to bring AHD into the APWG, including expanding the scope of that group and discussing AHD and the package of care.<sup>197</sup> Unitaid’s successful efforts in advancing paediatric HIV treatments can now be leveraged for other areas and products to realise the full potential of these technologies for children. WHO has launched, with key partners, the Global Accelerator for Paediatric Formulations (GAP-f) to deliver a faster, more efficient and more focused approach to paediatric formulation development. This will accelerate the availability of optimised treatment options for a range of infectious diseases, including HIV, TB and viral hepatitis.<sup>198</sup>

**CAB members have participated more widely in international conferences to share their experiences, resources and tools, and to expand advocacy for optimal treatments beyond Unitaid grants.** For example, in June 2022, AfroCAB and CHAI convened a community forum to advance alignment on urgent advocacy efforts for cabotegravir long-acting injectable (CAB-LA), a long-acting prevention and treatment option. This meeting culminated in the development of a community-forum statement on the urgency to accelerate access at scale to CAB-LA for people living with HIV,

<sup>195</sup> Optimal FGD; KII 51.

<sup>196</sup> KII 118.

<sup>197</sup> KIIs 35, 37.

<sup>198</sup> 2021\_Accelerating optimised ART...results of a coordinated approach.

and in an advocacy group that would focus on demand-generation and engagement with policymakers. Further details on Optimal CAB advocacy efforts are included in Box 5.

## 8 Conclusions and recommendations

This section summarises the key learnings from the ART optimisation portfolio evaluation, with a focus on success factors (8.1), including the effectiveness of the portfolio’s overall model. It then provides conclusions and recommendations for Unitaid to take forward (8.2). Section 8.2 provides 12 recommendations, based on the lessons from the evaluation. These recommendations have been drafted under Unitaid’s 2023–27 strategic objectives.

### Summary points

- Unitaid’s comprehensive model was innovative and pivotal to the portfolio’s success.
- Also critical to the success of the portfolio was the secretariat’s development and leverage of strong and ongoing relationships with global partners, country governments, grantees and implementing partners.
- The portfolio’s community engagement activities have demonstrated that community organisations and their representatives have unique capabilities that, when effectively leveraged, can support the introduction of new optimal products and their uptake.
- Portfolio grants, including trial grants in particular, adapted well to risks and challenges, facilitating the successful delivery of portfolio outputs and outcomes.
- Key constraining factors included difficulties navigating government and regulatory systems.

### Key lessons learnt

- The comprehensive model of intervention is required to effectively tackle barriers to accessing optimal HIV treatments. Where a less comprehensive model of intervention was pursued at country level, gaps were identified in the relevance, effectiveness and equity of Unitaid’s approach.

### 8.1 Factors affecting success

1

**Finding 1: The key success factor influencing the achievement of portfolio objectives was the comprehensive design of the ART optimisation portfolio.**

The comprehensive design of Unitaid’s portfolio model contributed to its effectiveness through its use of simultaneous and sometimes collaborative grants, addressing the full range of access barriers that Unitaid needed to tackle to achieve the overall portfolio objectives. Multiple stakeholders confirmed that Unitaid accelerated the adoption and transition to optimal treatments. Unitaid did this by simultaneously funding clinical trials and market-shaping and country-readiness activities (including community engagement), which one stakeholder characterised as “mass introduction” in a country.<sup>199</sup>

The generation of new evidence on effective and tolerable regimens through clinical trials, alongside necessary country-preparedness support (for example, drug quantification), meant that governments were better prepared for the introduction of drugs once they had been approved and secured from the market at an affordable price (market shaping)—which then encouraged countries to expedite roll-out.<sup>200</sup> For example, governments were able to see – through both the external review by the Data and Safety Monitoring Board (DSMB) of the ADVANCE trial and the success of the drugs/trials in other African countries – that transition was not only possible but optimal.<sup>201</sup> In

<sup>199</sup> KIIs 38, 51, 52; Unitaid FGD; ADVANCE 2021 Annual Report.

<sup>200</sup> ADVANCE FGD; 2021\_Accelerating optimised ART...results of a coordinated appr; Uganda Country Report.

<sup>201</sup> Optimal FGD; December 2018 ADVANCE newsletter.

Kenya, the Optimal grant’s multi-pronged approach gave the market and Government of Kenya confidence to move faster on roll-out (for example, DTG50):

*“They [CHAI] were able to say ‘we can roll this out in X countries and facilitate trainings of health workers,’ which gives the government confidence to roll out the treatment to the entire country.” (KII 85)*

In turn, populations were ready to benefit from the increased accessibility and affordability of optimal treatments given that **demand had been boosted** by community advocacy and sensitisation activities.<sup>202</sup> Global partners found that undertaking market-shaping activities alongside community engagement was “E,”<sup>203</sup> and was a “game changer in the way we do business.”<sup>204</sup> The findings from Côte d’Ivoire also demonstrated the advantages of this holistic approach, resulting in several positive outcomes, including access to a new treatment which is both effective in suppressing the viral load and well-tolerated by people living with HIV, and the development of an adapted treatment formulation for children. Additionally, the investment led to an improvement in drug quantification and availability within the health system, and to an increase in demand.

**Conversely, where a less comprehensive model of intervention was pursued (that is, where less attention was paid to tackling specific demand or supply-side barriers, or where partnerships—for example with the state—were less strong), the effectiveness and impact of the intervention was weaker overall.** In South Africa, although it was concluded that both supply-side and demand-side interventions were largely effective, there nonetheless was a gap in clinicians’ uptake of optimal treatments in both the public and private sectors due to a reported lack of understanding. In Cameroon (ranked 153 out of 189 countries in the 2020 Human Development Index), shortcomings were identified in demand-creation within communities, including for the most vulnerable and underserved, in the following areas: civil society strengthening, the quantification of drug needs, reinforcements to the national supply chain and the state disbursement of drugs (as well as coverage of people living with HIV in conflict affected zones). This suggests the need for stronger partnerships in working with the Government of Cameroon in the future.

A summary of all key factors influencing the effectiveness of Unitaid’s portfolio is provided in Box 11.

#### **Box 11. Success factors influencing the success of the ART optimisation portfolio**

- The comprehensive design of the ART optimisation portfolio (see above).
- Broad-based, multi-level and ongoing stakeholder engagement. Inclusive and demand-driven innovation partnerships were integral to the ART optimisation portfolio model and a key factor in its success. The portfolio engaged with a range of stakeholders throughout the lifetime of the investment: global partners, manufacturers, national governments and community partnerships were all critical to effectively delivering portfolio objectives. Unitaid’s strong partnership work, for example, helped to secure buy-in and investments in the portfolio’s objectives, built confidence in clinical trial results, strengthened the capacity for scale-up and overall ensured a positive, enabling context for the adoption and roll-out of treatments. In Nigeria, for example, engagement with government drove political will and ownership; collaboration with global partners encouraged buy-in and scale-up; engagements with CSOs drove demand creation and increased uptake; and capacity building and the engagement of professional groups, such as healthcare workers, promoted institutional systems strengthening and sustainability. More details on Unitaid’s successful partnership work are provided in Section 3.3.

<sup>202</sup> KII 51.

<sup>203</sup> KII 51.

<sup>204</sup> KII 40.

- At a country level, ongoing effective collaboration and coordination with country governments. This was critical to generating government buy-in to the new optimal treatments and laid the foundations for their rapid introduction (through country-preparedness activities). The close collaboration between CHAI and national governments through the Optimal grant was a particular key success factor of the portfolio in Kenya. As a result, government ownership and confidence in the clinical trials' study results increased, funding was leveraged (in the case of ADVANCE<sup>205</sup>) and knowledge and experience of DTG-based regimens was increased, facilitating faster adoption into national guidelines and the scale-up of new treatments.<sup>206</sup> Conversely, in Cameroon – where we found that Unitaids' intervention delivered more a moderate impact – this was attributed to a need for greater support at the government level to help establish a scale-up agenda for ART optimisation (including an adequate strategic plan, the mobilisation of technical and financial assistance and a national coordination body with the authority and leadership to support ongoing scale-up), illustrating the importance of partnerships with national governments.
- Unitaids' community engagement approach, which contributed significantly to increasing demand, acceptability and the uptake of optimal HIV treatments (Box 5. Community and civil society engagement in the ART optimisation portfolio: "Nothing for us, without us."). The majority of global and country stakeholders interviewed for the evaluation agreed that Unitaids' community engagement and advocacy approach, which was employed to drive higher levels of demand and the uptake of new regimens at national levels, was one of the keys to the success of the portfolio:<sup>207</sup>

*"Generating demand, particularly for products that are new, posed a lot of questions and doubts. I think it's critical to have community leaders to take up on that. Certainly, on the messaging around DTG use in pregnancy, I think that was tremendously needed. Unitaids invested heavily on that and it was really important". (KII 45)*

Some clinical trials were unable to work as closely with community actors as was required for successful implementation, and this created risks the study outcomes. Deeper or more tailored community engagement from the outset would have helped mitigate these risks.

- The **adaptability of portfolio grants** (including trial grants in particular), which facilitated the successful delivery of outputs and outcomes in response to risks and challenges. This was further supported by funding a portfolio of clinical trials together, which enabled and encouraged evidence- and knowledge-sharing and learning across trials.<sup>208</sup> Further details on these adaptations is provided in Section 6.2.
- **Constraining factors included difficulties navigating country government and regulatory systems, as well as some logistical constraints.** Clinical trial grants faced difficulties in navigating **country governance systems**, including understanding complex regulatory systems (5.3.2) and slow bureaucracy. For example, miscommunication between community advocacy organisations and the Department of Health in South Africa hampered kit availability in a TAC-led testing event in Soweto, as well as the availability of trainers and training materials at dissemination and training events.<sup>209</sup> However, for the most part, grant implementers were still able to deliver their outputs, albeit on a delayed timeline, through adaptations.

## 8.2 Conclusions and recommendations

Through effectively addressing a range of relevant access barriers simultaneously, Unitaids has **accelerated access to optimal HIV treatments for vulnerable and underserved adults and children**

<sup>205</sup> ADVANCE 2018 Annual Report.

<sup>206</sup> KIIs 35, 37, 51; Cameroon Country Report; South Africa Country Report; Uganda Country Report; Zimbabwe Country Report; 2022 Semi-Annual Flash Report and Follow-Up; Optimal 2017 Annual report.

<sup>207</sup> KIIs 35, 37, 45, 46, 49, 54, 55, 120; South Africa Country Report.

<sup>208</sup> NAMSAL FGD; 2019 NAMSAL PPA.

<sup>209</sup> 2017 Sep-Optimise Monthly Update.

**in LMICs** (including DTG and DTG-based regimens), supported **global and country scalability** and delivered **high impact** (including on viral suppression amongst people living with HIV and lives saved). By 2022, DTG was recommended as the first-line treatment for adults with HIV in the national guidelines of 111 LMICs and 75 countries adopted DTG for children. CHAI estimates that 25m adults will have transitioned to DTG-containing regimens by 2028, resulting in more than US\$1.6bn in savings through 2022 and a US\$7.8bn saving by 2028, as well as in 1.1m lives saved by 2027.

This impact has been facilitated by Unitaids' **comprehensive intervention model** (balancing relevant supply-side and demand-side interventions), combined with **strong and coherent partnership work, extensive community engagement, adaptability**, and more widely **supportive partners and policy environments** (see Figure 20/Figure 19). The market-shaping and country-preparedness work conducted under Optimal and SPAAN were critical to ART optimisation, helping to address commercial barriers to product entry in LMICs while also supporting the adoption, roll-out and take-up of better HIV treatments in-country as clinical trial grants were filling important gaps in clinical research with vulnerable and underserved groups. Importantly, market-shaping also led to reduced prices for optimal treatment products and to the greater **cost-effectiveness** of the portfolio.

There is scope for more **efficiency** to help increase the value for money of Unitaids' interventions in the market, including ensuring the use of existing treatments during a phased period of transition to optimal treatments, which will prevent excessive waste. Other areas to increase portfolio management efficiency were identified by grantees and partners, particularly in relation to monitoring and reporting requirements. Unitaids recognises the value of documenting and **communicating lessons** and portfolio successes, and the need to do this more frequently and systematically with partners across future portfolios. Global and country partners would appreciate more opportunities to learn from, and be informed about, the results of Unitaids' work.

A **key lesson** is that more comprehensive models of intervention appear to have had the greatest influence on scalability, and thus hold the potential to offer greater **value for money** over the long term. In some countries, more intensive work was needed on the demand side with clinicians (as in South Africa) or in-country governance and supply chains (this was evident across a number of countries, Cameroon in particular). The identified **areas for improvement** include working on sustainable handover plans with country governments, helping to ensure sustainable markets for low-volume products for the most underserved groups and further support for strengthening the capacity of grassroots community representation.

## Unitaid's ART Optimisation portfolio model

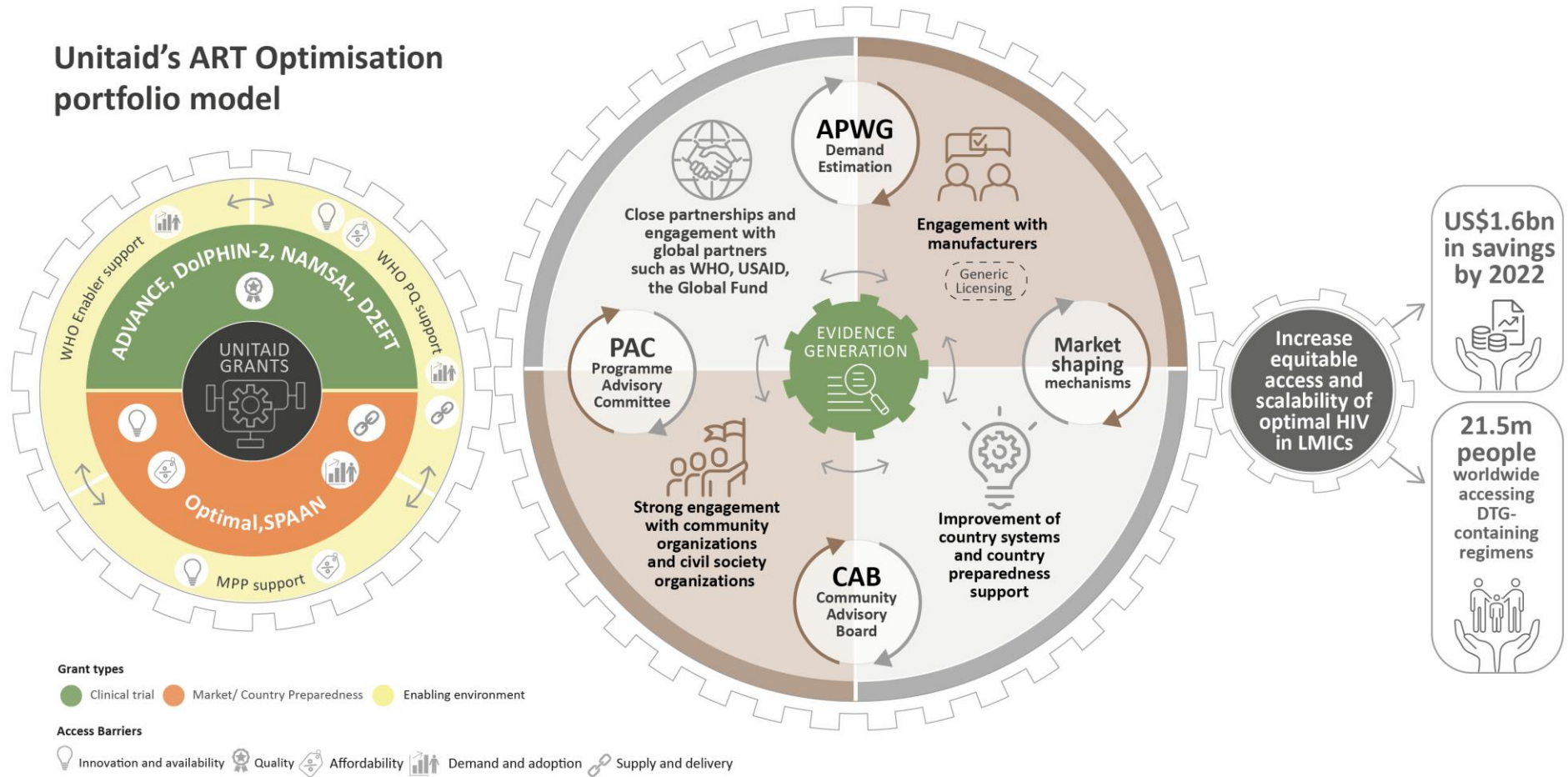


Figure 190. Unitaid's model



Based on these conclusions and evaluation findings, 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.** The outcomes for some groups living with HIV in LMICs, including children, are still unacceptably poor and are lagging when compared with the majority of people living with HIV. Where barriers to the access and uptake of optimal treatments— such as evidence gaps to inform guidelines and low-volume demand— remain for underserved groups, Unitaid and other global partners should develop tailored, long-term strategies for removing these barriers, including incentivising the market and supporting product introduction.<sup>210</sup>
- 2. The PAC, or a similar strategic body, should be reconvened to strategise and coordinate scale-up partners around addressing remaining gaps in access to optimal HIV treatments in LMICs.** Based on the effectiveness of the PAC (and the APWG), a long-term strategy for addressing access barriers should include leveraging or re-establishing a coordination mechanism that connects key global partners to collectively improve the pathways to progress in areas such as the regulatory process and evidence gaps in WHO treatment guidelines.
- 3. Prioritise delivering fully-comprehensive intervention models within target countries.** Complementary supply- and demand-side interventions tackling the fullest range of access barriers delivered the greatest impact and value for money. Enhanced efforts are required across some countries on strengthening supply chains, distribution and frontline delivery, working with Unitaid’s international and domestic partners. Some stakeholders suggested that Unitaid should work more closely with global partners and national governments to help strengthen predictability in the procurement cycle (including enabling local manufacturing capacity). Further work is needed to monitor and ensure the adoption of quality-assured HIV treatment products at a subnational level (including developing protocols on managing potential weight gain). This highlights the importance of tackling multiple barriers simultaneously. To support such comprehensive intervention models within the context of a finite budget Unitaid should consider focusing its resources on a set of priority LMICs (and priority underserved groups), whilst sharing evidence of what works and helping to embed good practices across other countries (see recommendation 5). Other options include reviewing whether Unitaid or its close partners are better placed to deliver specific ‘spokes’ of the model, securing buy-in and scaling financial commitments up or down accordingly.
- 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.** Global partners, country governments, communities, manufacturers and scientists would benefit from hearing more about the benefits of the ART optimisation model of working. If this is shared across multiple media platforms and in multiple languages, this would help embed good practices in delivery and may galvanise country and partner ownership/further investment in optimal treatments, as well as the application of the comprehensive intervention model to other diseases. For example, the creation of a direct communication mechanism with governments would allow for the direct

<sup>210</sup> KII 51; Community; DolPHIN-2 FGD; Kenya Country Report.

reporting of success stories as they happen, and it would help support the ongoing commitment to scale-up and sustainability.

5. **Integrate impact evaluation methodologies and a value for money assessment within future evaluations.** There is interest within Unitaid to further demonstrate the impact and added value of its work (for example, in relation to market incentives) and to help make informed decisions on the allocation of its limited resources. A greater emphasis on assessing impact (for example, using counterfactual approaches such as comparing progress in Unitaid and non-Unitaid supported LMICs, or between Unitaid-supported and non-supported products), as well as on conducting value for money assessment as part of future evaluation work, would help Unitaid better understand the additionality and cost-effectiveness of its investments.

## 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.** An important global scalability factor is the synthesis of the lessons learnt on implementation and what facilitates successful scale-up (within a range of health systems) and the sharing of this with global and national stakeholders. This would help to extend Unitaid's reach and impact beyond its focus countries. Unitaid has the potential to do more in this area. For example, the clinical trial implementers learnt the value of integrating community engagement throughout the research cycle, but there was a gap in reproducing such approaches across trials and other grants. ADVANCE grantees suggested that case studies could be written to encourage the wider community to engage more and apply similar approaches.<sup>211</sup> A need was also found for the ongoing (light-touch) monitoring of who is using Unitaid's tools and resources and for offering support for their use.
7. **Strengthen scalability plans within target countries, working closely with national governments and partners, to help ensure sustainability of country-readiness activities after Unitaid's investment.** Notwithstanding Unitaid's catalytic role, further work is needed to sustain capacity-building efforts with government, community and clinical stakeholders to strengthen national funding contributions for optimal ARTs and to ensure ownership of their roll-out. Unitaid requires grantees to produce transition plans for specific research, products and countries. CHAI will be continuing to monitor (and update as necessary) country transition plans for the Optimal grant in 2023. It would be helpful if this exercise included comprehensive scalability planning (building on Unitaid's scalability factors framework), in partnership with country stakeholders and aligned with national HIV programmes. This should include a focus on resolving remaining barriers to equitable scale-up (for example, in supply chain systems, predictability of supply and adverse treatment-effect monitoring) and assigning roles and responsibilities. Countries with weaker enabling environments for product introduction and scale-up will need additional support for government strategy, systems and ownership, and the development of these plans.
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).** This should include the connection of national civil society representatives with relevant grassroots organisations and community groups to help ensure that advocacy efforts are strong, broad-based, equitable and sustainable.

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<sup>211</sup> ADVANCE FGD; D<sup>2</sup>EFT FGD.

9. **Consider adapting Unitaid’s grant mechanisms to fund LMIC community organisations directly, and/or help build CSO capacity to manage larger grant funding.** Now that Unitaid’s CSSE approach is proven and more mature, greater flexibility and efficiencies could be achieved by funding community organisations directly. Some stakeholders also considered this is a missed opportunity for reducing inequity and helping to build the capacity of organisations in LMICs through the process of receiving grants and leading implementation. Unitaid should consider adapting its commissioning processes (call for proposals; grant application), as well as considering technical assistance to further strengthen the capacities of community-based organisations to manage their own funding.

### Pillar 3: Foster inclusive and demand-driven partnerships for innovation

10. **Leverage the experience and capacity of the established community network (members and CSOs) to support Pillar 3 of Unitaid’s new strategy, including future work on HIV and other diseases.** Unitaid has built a cadre of community activists experienced in the advocacy of optimal treatments. It has also demonstrated that a combination of downstream (community-level) and upstream (strategic-level) community-engagement activities is the most successful and impactful way of working. The portfolio’s network could be reconvened/repurposed to gather intelligence, support design and implementation, and share learning at an organisational level, not only for HIV (single portfolio) but across the range of diseases (multiple portfolios) that Unitaid focuses on.
11. **Strengthen Unitaid’s visibility in-country, including through more frequent and predictable country visits and other engagement mechanisms.** More visibility for Unitaid and the secretariat at the country level would help strengthen relationships with in-country partners and governments, improve the clarity of programmes and roles (including what is eligible for funding), and potentially to help further galvanise scalability efforts. This could include a combination of country visits and/or virtual presentations/workshops/programme debriefs with government and in-country partners, potentially on a bi-annual basis.
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.** Grantees flagged that Unitaid’s reporting is burdensome and that there are delays in implementation when funds are re-disbursed (for example, following the pandemic). The grantees suggested that more tailored monitoring and evaluation approaches are needed (depending on the type of grantee), as well as more efficient funding processes, which can respond more rapidly to changing contexts and (in the case of trials) to new emerging evidence.<sup>212</sup> In this sense, Unitaid has begun to implement some improvements, including simplifying the log frame for new grants.

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<sup>212</sup> D<sup>2</sup>EFT FGD notes; Unitaid FGD notes.

# Annexes

## Annex A. Terms of reference



### Terms of reference

#### Antiretroviral Therapy (ART) Optimisation Portfolio-Level End-of-Grant Evaluation

<b>Disease:</b>	<b>HIV</b>
<b>Areas for Intervention:</b>	Improving Adult Antiretroviral Therapy in Low and Middle-Income Countries (ART optimisation) – June 2015

#### ➤ Purpose of the Terms of Reference

These Terms of Reference (TOR) serve as an overall framework for the services to be provided under this project, in accordance with RfP 2022.12. This RfP is relaunched (retender process) as the previous tender did not lead to a positive outcome.

#### ➤ Desired timeframe

Requested start date: 01 September 2022 Expected completion date: April 2023

### Background

In June 2015, the Unitaid Executive Board endorsed the Area for Intervention (Afi) “Improving antiretroviral therapy in low and middle-income countries”<sup>213</sup> (ART optimisation), paving the way for Unitaid’s investment in this space. At the time of endorsement of the Afi, 11.7m people were estimated to be receiving antiretroviral therapy in low and middle-income countries (36% of all people living with HIV in these countries).<sup>214</sup> At the same time, UNAIDS modelling showed that achieving the fast-track targets for 2020 – 90% of people living with HIV diagnosed by 2020, 90% of people diagnosed with HIV on treatment, and 90% of those on treatment achieving viral suppression – would enable an end to the global HIV/AIDS epidemic by 2030.<sup>3</sup> In the absence of a fast response, the epidemic would continue to grow with serious public health ramifications as well as financial consequences due to an increasing demand for antiretroviral therapy and expanding costs for HIV prevention and treatment.

Achieving target coverage rates implied a need to more than double the number of people on antiretroviral therapy in low and middle-income countries (LMICs) in less than 5 years. At the time, it was assessed that this would only be possible with timely interventions to overcome current challenges and barriers to access. Available regimens at the time, despite significant improvements, still presented key limitations around tolerability and durability (low barriers to resistance), with implications both for treatment adherence and the need to revert to more costly second-line treatment when a first-line regimen fails. In addition, these optimal regimens remained costly for resource-limited settings. Newer and better antiretrovirals, with potential for fewer side-effects, less prone to resistance and at lower cost, became available in high-income markets but could not be considered for use at scale in LMICs. Challenges included: lack of evidence on efficacy and safety for key populations in resource-limited settings (including women of child-bearing potential, people

<sup>213</sup> UNITAID/EB22/2015/8 – Areas for Intervention.

<sup>214</sup> WHO, Global Update on the Health Sector Response to HIV, 2014. 3 UNAIDS, Fast-Track: Ending the AIDS Epidemic by 2030, 2014.

coinfected with tuberculosis (TB) or hepatitis and children) as well as implementation evidence in these settings; lack of adapted formulations and combination tablets; poor market visibility leading to high prices; supply instability and slow generic entry.

Further challenges to access included:

- *Slow generic entry*: Under traditional timelines, generic product development and approval can be delayed for up to 9 years following originator product approval in high-income markets.
- *Lack of evidence*: The inclusion of these products in WHO guidance was hampered by the lack of evidence on their use in vulnerable and underserved populations in resource-limited settings (for example, women of child-bearing potential, people with co-infections). WHO, through a vast consultative process had highlighted the most promising emerging and pipeline antiretrovirals and the data that was still missing for most affected populations. However, drug manufacturers have limited financial incentive to invest in such research, as their trials normally target approval for high-income markets.
- *High prices*: Without demand and incentives for competition to take place, prices of newer antiretrovirals remained high (for example, DTG in the US was over US\$14,000 PPPY at the time) and further contributed to delays in access and scale-up. This cycle was perpetuated as generic manufacturers typically delay investing in commercialisation of these products in LMIC markets until there is clarity on future demand.
- *Lack of adapted formulations*: Development of appropriate formulations and the combination of different products from different companies into a single pill, typically led by generic manufacturers, was delayed in absence of market visibility and incentives, thus further delaying access to optimal regimens. In addition, there was a risk of supply instability of new recommended products and lack of proper planning for transition in LMICs leading to price spikes and potential shortages.

Unitaid identified a clear need to intervene, both on the supply side (engaging with manufacturers) and on the demand side (enabling countries' adoption and transition), to make better products for HIV treatment for adults and children available broadly in LMICs. Six grants were awarded between 2016 and 2019 that focused on ART optimisation and are in scope for this evaluation.

- **ADVANCE<sup>215</sup>** (*clinical trial*), implemented by Ezintsha Wits RHI
- **DolPHIN-2** (*clinical trial*), implemented by the University of Liverpool
- **NAMSAL** (*clinical trial*), implemented by Institut Bouisson Bertrand
- **D<sup>2</sup>EFT** (*clinical trial*), implemented by the University of New South Wales
- **Optimal** (*market and country preparedness*), implemented by the Clinton Health Access Initiative
- **SPAAN** (*country preparedness*), implemented by the Elizabeth Glazer Paediatric AIDS Foundation (and subsequently incorporated into the Optimal grant)

Through these six projects, Unitaid invested more than US\$124m across 24 countries to contribute to UNAIDS Fast-Track targets to increase the proportion of people living with HIV on sustained

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<sup>215</sup> After meeting their primary objectives of increasing the evidence base for optimal antiretrovirals (ARVs) in first-line treatment for HIV and having the resulting evidence inform WHO's updated recommendation on preferred regimens in the HIV Treatment Guidelines 2019, as well as in national guidelines, the ADVANCE, DolPHIN-2 and NAMSAL clinical trials (also known as TRIO) began pooling data in 2020, with an aim to answer important safety questions around the use of DTG, including around weight gain.

treatment.<sup>216</sup> Together these projects aimed to increase access to optimal first- and second-line treatment in adults and children in LMICs by: (i) providing critical evidence on the efficacy of optimal HIV treatment products when used in populations in LMICs to inform WHO treatment guidelines, (ii) reducing the cost of optimal regimens, (iii) preparing the ground in LMICs for adoption and uptake of optimal regimens through supply- and demand-side interventions. **Error! Reference source not found.** lists key information about each grant, including grant implementation timeframe, budget, desired outcome, access barriers addressed, target countries, external evaluation activities already completed, and any reprogramming/extensions.

In addition, Unitaid included optimal HIV treatment in several cross-cutting investments, described below.

- **WHO HIV enabler – ART optimisation and ART Paediatrics workstreams**, to enable scale-up of optimal HIV treatment products for adults and children through direct technical support to Unitaid ART optimisation investments and more broadly through use of its global convening power to develop guidelines, generate estimates of the burden of disease, track national scale-up of optimal HIV treatment, and support prequalification of medicines and diagnostics. An internal Unitaid assessment of WHO Enabler grant (including HIV sub-grant) was conducted in July 2020.
- **Medicines Patent Pool (MPP)**, to expand production and supply of generic medicines for HIV by negotiating voluntary licenses for DTG-based and other optimal HIV treatment regimens, seeking broader geographical scope than current licensing policies, and establishing a well-managed sub-licensing system for speedy, robust, and quality generic competition. An end of grant evaluation for MPPII (2016 – 2020) grant was conducted in 2021.
- **WHO Prequalification (PQ)**, to apply a unified set of standards that are of acceptable quality, safety and efficacy to ensure that good quality health products are available particularly in LMICs through their prequalification programme. An external evaluation of PQ was conducted in (2016) and an impact assessment was completed in 2018.

The full range and timeframe of Unitaid’s HIV treatment optimisation direct and indirect portfolio is shown in **Error! Reference source not found.** and the principal areas of work of each of the implementers in the portfolio are depicted in .

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<sup>216</sup> [https://www.unaids.org/sites/default/files/media\\_asset/201506\\_JC2743\\_Understanding\\_FastTrack\\_en.pdf](https://www.unaids.org/sites/default/files/media_asset/201506_JC2743_Understanding_FastTrack_en.pdf).

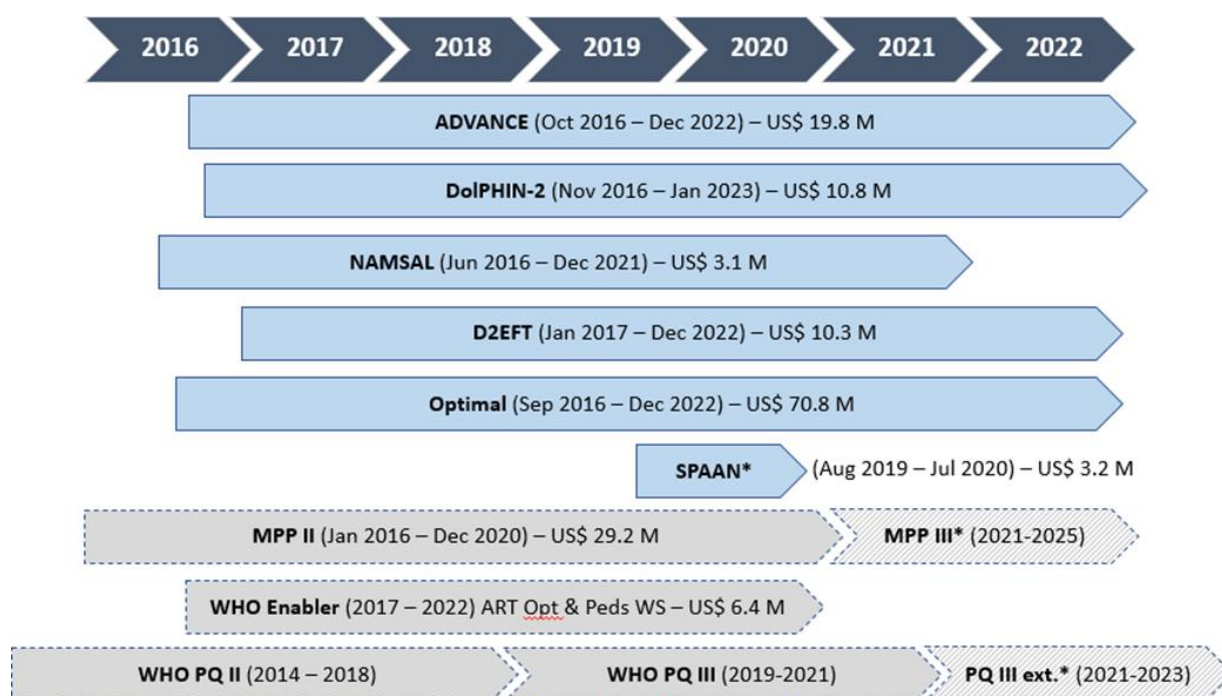
Element	ADVANCE	DoIPHIN-2	NAMSAL	D <sup>2</sup> EFT	Optimal	SPAAN <sup>217</sup>
<b>Implementation timeframe</b>	October 2016 – December 2022 (~6 years)	November 2016 – January 2023 (~6 years)	June 2016 – December 2021 (5.5 years)	January 2017 – December 2022 (6 years)	September 2016 – December 2022 (~ 6 years)	August 2019 – July 2020 (1 year)
<b>Budget</b>	US\$19.8m	US\$10.8m	US\$3.1m	US\$10.3m	US\$70.8m	US\$3.2m
<b>Desired outcome</b>	Generate evidence to support adoption of optimal ART regimens (DTG, TAF) in LMICs that are cheaper, more tolerable and with a higher barrier to resistance than existing first-line regimens	Generate evidence to support adoption of DTG-based regimens among late-presenting pregnant women in LMICs and to reduce the incidence of mother-to-child transmission of HIV	Generate evidence to support adoption and scale-up of DTG-based regimens in first-line treatment for HIV in resource-limited settings and in HIV genotypes common to West Africa	Generate evidence to support adoption and scale-up of DTG-based regimens in second-line HIV treatment in resource-limited settings	Reduce morbidity and mortality of people living with HIV and increase cost-efficiencies in health systems by accelerating access to affordable, optimal products for HIV treatment in adults and children	Increase the number of HIV-positive children initiated on new, improved paediatric ARV formulations
<b>Access barriers</b>	Innovation & availability Quality	Innovation & availability Quality	Innovation & availability Quality	Innovation & availability Quality	Innovation & availability Affordability Demand & adoption Supply & delivery	Quality Demand & adoption Supply & delivery
<b>Target countries</b>	<b>South Africa</b>	<b>South Africa, Uganda</b>	<b>Cameroon</b>	Brazil, Colombia, Guinea, India, Indonesia, Malaysia, Mali, Mexico, <b>Nigeria, South Africa, Thailand, Zimbabwe</b>	Benin, Cambodia, <b>Cameroon</b> , Kenya, Malawi, <b>Nigeria</b> , Senegal, <b>South Africa</b> , Togo, <b>Uganda, Zimbabwe</b>	Côte d'Ivoire, Eswatini, Lesotho, Mozambique and <b>Zimbabwe</b> <sup>218</sup>

<sup>217</sup> In LMICs for adoption and uptake of optimal regimens through supply- and demand-side interventions. Table 7 lists key information about each grant, including grant implementation timeframe, budget, desired outcome, access barriers addressed, target countries, external evaluation activities already completed, and any reprogramming/extensions.

<sup>218</sup> Côte d'Ivoire, Eswatini, Lesotho, Mozambique added as project countries to Optimal grant (ART) with integration of SPAAN work into Optimal.

Element	ADVANCE	DoIPHIN-2	NAMSAL	D <sup>2</sup> EFT	Optimal	SPAAN <sup>217</sup>
<b>External evaluation activities to date</b>	None	None	None	None	EVA assessment carried out in 2019	None
<b>Grant reprogramming or extension to date</b>	<ul style="list-style-type: none"> <li>July 2019 - switch of activities with USAID</li> <li>Dec 2020 – NCE: extension to Mar 2020</li> <li>Aug 2020 – TRIO Amendment &amp; extension to Aug 2022</li> <li>May 2022 – Reprogramming &amp; no- costed extension to Dec 2022</li> </ul>	<ul style="list-style-type: none"> <li>Oct 2019 - Addition of Infant Study &amp; Impact modelling &amp; Support for a pregnancy PK network</li> <li>Aug 2020 – TRIO Amendment &amp; extension to July 2022</li> <li>Apr 2022 – no-costed extension to Jan 2023</li> </ul>	<ul style="list-style-type: none"> <li>May 2017- Removal of PK study &amp; Approval of Civil Society engagement plan</li> <li>Apr 2018 – Addition of virologic resistance sub-study &amp; Long term DTG evaluation sub-study</li> <li>Aug 2020 – TRIO Amendment &amp; extension to Dec 2021</li> </ul>	<ul style="list-style-type: none"> <li>Apr 2019 - Addition of a 3rd arm &amp; Extension to Dec 2021</li> <li>Sep 2021 – Costed Extension to Dec 2022</li> </ul>	<ul style="list-style-type: none"> <li>Dec 2018 - addition of AHD &amp; extension to Dec 2020</li> <li>Sept 2020 – Costed Extension to Dec 2022</li> </ul>	<ul style="list-style-type: none"> <li>Sept 2020 - SPAAN activities integrated into Optimal grant extension (to Dec 2022)</li> </ul>





\* SPAAN activities integrated into Optimal grant from August 2020 onwards. MPP III is not directly relevant to this portfolio. PQ III costing extension is currently in progress.

Project overview	Lead grantee
<p>Gather critical evidence for use of new priority regimens in resource-limited settings</p> <ul style="list-style-type: none"> <li>Clinical trials and support studies</li> </ul>	
<p>Commercialization of adapted formulations and combinations, and lower global costs</p> <ul style="list-style-type: none"> <li>Upstream market-shaping interventions</li> </ul>	
<p>Driving rapid uptake of priority new products in high-burden countries</p> <ul style="list-style-type: none"> <li>Generating demand and supporting adoption</li> </ul>	
<p>Overarching support</p>	

## Investment goal and desired outcomes

Accelerating access to and scale-up of optimal ARV treatment in LMICs, including DTG-based regimens, is a key part of Unitaid's effort to support global targets to end the HIV epidemic by 2030.

In line with Unitaid's strategy to catalyse equitable access to better health products, Unitaid's investments in ART optimisation aimed to (i) provide evidence on new ARVs for first- and second-line therapy in LMICs to inform WHO and national treatment guidelines, (ii) ensure market and country preparedness for the priority regimens (from both supply and demand side), and (iii) support rapid introduction of optimal regimens in countries and develop the conditions for scale-up. All Unitaid-funded interventions in ART optimisation target one or more barriers to equitable access: innovation and availability, quality, affordability, demand and adoption, and supply and delivery.

The rapid uptake of DTG-based regimens including TLD, is expected to generate significant financial savings for health systems and result in additional lives saved since DTG is less expensive, clinically superior, has fewer side effects, and offers a reduced risk of viral resistance compared to previously available treatments, namely the TLE fixed-dose combination. Overall, Unitaid's DTG portfolio is expected to have significant public health impact and result in economic savings. This impact is expected as a result of Unitaid-funded projects such as MPP and Optimal, the work of other organisations such as WHO, scale-up partners including PEPFAR and Global Fund, and national governments.

Similarly, over the long-term, a subset of the grants is expected to offer a pathway for the scale-up of a second-line regimen (DTG and DRV/r; or TLD in second line) and result in additional lives saved, since both intervention regimens are easier to take (a one-pill, once-daily regimen), have fewer side effects, and are more durable to drug resistance than the current standard-of-care. It is expected that this will improve overall adherence and reduce drop-out rates to second-line treatment. Both regimens are also expected to generate significant financial efficiencies by reducing the need for third-line treatment, as well as for drug resistance testing for second-line treatment.

## Objectives of the consultancy

Under these Terms of Reference, the Evaluators will provide Unitaid with:

1. An assessment of the relevance, coherence, efficiency, effectiveness, impact, sustainability and lessons learnt for the six ART optimisation projects (ADVANCE, DoPHIN-2, NAMSAL, D<sup>2</sup>EFT, Optimal and SPAAN) as captured by the outcome, outputs and activities performed. **The grant evaluation is an assessment of both Unitaid and the grantees' performance.**
2. An assessment of the overall impact of Unitaid's investment in ART optimisation between 2016 and 2022, with a view towards the complementarity and synergy of the above six investments, including with WHO HIV Enabler, MPP and WHO PQ investments, and other stakeholders in this field (USAID, PEPFAR), and their contribution to closing critical gaps and accelerating access to better treatment for HIV in project countries and beyond.

## Work to be performed

Preliminary evaluation questions are outlined in Annex 2, based on the Unitaid evaluation framework,<sup>219</sup> strategic Key Performance Indicators (KPIs)<sup>220</sup> (Annex 3)<sup>221</sup> and scalability framework (Annex 4),<sup>222</sup> which underpin all internal and external evaluations. The evaluation framework criteria are aligned with the OECD-DAC's standard evaluation criteria. Please check Unitaid's Evaluation

<sup>219</sup> For more information on Unitaid's Evaluation Framework please refer to [https://unitaid.org/assets/Unitaid-evaluation-framework\\_guidance\\_Nov-2020.pdf](https://unitaid.org/assets/Unitaid-evaluation-framework_guidance_Nov-2020.pdf).

<sup>220</sup> Unitaid is developing a new strategy 2023 – 2027 and a new set of KPIs.

<sup>221</sup> For more information on Unitaid's Results Framework please refer to <https://unitaid.org/assets/Unitaid-Results-Framework.pdf> and [https://unitaid.org/assets/Unitaid-evaluation-framework\\_guidance\\_Nov-2020.pdf](https://unitaid.org/assets/Unitaid-evaluation-framework_guidance_Nov-2020.pdf).

<sup>222</sup> For more guidance on Unitaid's Scalability Framework, please refer to Scalability framework guidance: <https://unitaid.org/assets/Unitaid-Scalability-Framework.pdf>.

website (<https://unitaid.org/evaluations/#en>) for more details on our evaluation framework and examples of evaluation reports.

Specifically, the Evaluators are expected to undertake work in the following areas:

1. Based on existing documents and jointly with Unitaid, formulate a retrospective overarching theory of change for Unitaid's investments in ART optimisation for the period 2016-2022 to guide the evaluation.
2. Using the Unitaid access barriers and relevant KPIs as a framework<sup>223</sup> (see Annexes 2 and 3), compile and synthesise evidence to determine the status of access and scale-up of optimal HIV treatment (for adults and children) in LMICs in 2022 and assess the extent of Unitaid's contribution to progress achieved. This may include informant interviews to capture the status of ART optimisation in LMICs at the outset of the investment (2016).
3. Conduct an independent assessment of the extent to which each grant did the right things (activities, outputs), in the right way (engaging stakeholders, adapting course as needed) and at the right time to achieve the right results, as per the Unitaid evaluation framework. Unitaid is also interested in understanding the "so what" of results achieved – with a focus on whether the results are sustainable (following grant closure) and the difference the grants made in accelerating/enabling equitable access to improved HIV treatment for adults and children.
4. Assess the extent to which Unitaid investments accelerated access to optimal HIV treatment in LMICs (for adults and children) and the potential scalability of these products, through both its direct and cross-cutting investments<sup>224</sup> – using Unitaid's scalability framework (Annex 4). The assessment should highlight:
  - a. to what degree the Unitaid-supported ART optimisation initiatives contributed to laying the ground for scale-up of optimal HIV treatment (this should include an assessment of the status of scale-up conditions in 2016 and in 2022);
  - b. the extent to which targeted products and approaches have been scaled up across project countries and beyond;
    - a. factors that may have contributed towards, or limited, scalability and transition.
5. In addition, some specific questions to this investment that we would like the evaluators to examine are (including those listed in Annex 2): (i) the effectiveness of the Community Advisory Board model and other community engagement activities undertaken in the different projects for building awareness of and generating demand for optimal products, as well as the extent to which these activities strengthened the capacity of community members to advocate for better treatment products (and any other positive externalities); (ii) the effectiveness of the ART optimisation programme advisory committee and the role it played in facilitating the collaboration among the different grant implementers in the portfolio and with other partners working in this space (for example, WHO, USAID OPTIMIZE), as well as in securing key outcomes of the portfolio (that is, to what degree did it aid these, what would have happened in its absence, etc.); (iii) the appropriateness and effectiveness of market-shaping mechanisms employed under the portfolio (for example, incentive mechanisms in Optimal grant) to accelerate the development of generic priority formulations.
6. Assess grant performance against relevant Strategic KPIs – *Note: While the grants under review fall under Unitaid's strategy 2017 – 2021<sup>225</sup> and respective KPIs, Unitaid is currently*

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<sup>223</sup> Unitaid is developing a new strategy 2023 – 2027 and a new set of KPIs.

<sup>224</sup> By 'direct investments' we mean the six ART optimisation grants (ADVANCE, DoIPHIN-2, NAMSAL, D2EFT, Optimal and SPAAN), while the 'cross-cutting investments' refer to MPP, WHO Enabler and WHO PQ.

<sup>225</sup> The strategy has been extended to cover 2022.

*developing its next strategy 2023 – 2027<sup>226</sup> with a new set of KPIs. Evaluators will be expected to assess grant performance on key metrics that underpin both strategies and capture the rationale for grant investments such as equity, progress against securing equitable access conditions/overcoming access barriers for optimal HIV treatment products, progress on scalability, and scale-up status. As an example, the current set of Unitaid’s KPIs have been provided in Annex 3 as indicative with the proviso that new ones may be added on to / replace the current set of KPIs.*

7. Conduct a Validation Workshop with key stakeholders to corroborate progress against access barriers to optimal HIV treatment for adults and children between 2016 and 2022, assess scalability of optimal HIV treatment products, and identify lessons learnt and recommendations.
8. Lead a brownbag / thematic discussion on the ART optimal portfolio with the Unitaid secretariat and share findings, conclusions and lessons learnt.
9. Suggest comprehensive, actionable recommendations based on key findings and conclusions so that Unitaid can integrate lessons learnt. We expect the Evaluators to spend the required level of effort for this crucial piece of the evaluation report.

### **Evaluation methodology, place of work, and management**

**Methods:** The evaluation methodology will involve a combination of document reviews and qualitative interviews (KIs interviews, focus group discussions/workshops) with the relevant stakeholders (noting that data collection techniques may need adjustment to account for the respective COVID-19 context and any restrictions). For the document review, evaluators will undertake a review of the grants using grant documents such as: Project Plan, Logframe, Annual Reports, evaluation/EVA reports and any other grant-related material. Suggested participants for KIs and focus group discussions are provided in Section 6. **It is expected that the Evaluators would go beyond KIs and take it a step further to analyse and triangulate interviews with evidence and data analysis, especially when there are divergent views, for the evaluators to draw conclusions based on the strength of evidence.** Evaluators are expected to develop and apply rubrics to assess strength of evidence, strength of effect, and level of contribution to inform analysis and reporting of findings.

**Place of work:** The Evaluators will work remotely and may be required to conduct site visits and interviews in ~7 project countries from the following priority list: Benin, Côte d’Ivoire, Cameroon, Kenya, Nigeria, South Africa, and Uganda (countries to be finalised jointly as part of inception and depending on evolving global COVID-19 situation).<sup>227</sup> Progress in a selection of the remaining countries with ongoing ART optimisation activities (to be agreed as part of inception) will be assessed through a desk review plus remotely conducted interviews (as appropriate). The Evaluators, in consultation with Unitaid and grantees, will identify potential stakeholders to interview. In line with Unitaid’s effort in reducing its carbon footprint related to the procurement activities, it is required that the Evaluators have either a regional/local presence in the project countries (especially those targeted for travel) or have access to local counterparts that can assist the Evaluators in understanding the HIV treatment landscape of the country and help identify and interview stakeholders.

**Management and communication:** The Evaluators will be expected to participate in a virtual inception/kick-off<sup>228</sup> meeting and to prepare a presentation of the final findings, as well as hold a virtual Validation Workshop with stakeholders after Draft 2 of the report. In addition, the Evaluators

<sup>226</sup> The new strategy will be endorsed in June 2022 and will be implemented from 2023 onwards.

<sup>227</sup> Note - country visits will focus primarily on the grant specific evaluations, while the portfolio level work is anticipated to be based on document review and KIs and build upon the grant-specific evaluation findings.

<sup>228</sup> Note: the kick-offs will include on-boarding meetings and the entire evaluation team is expected to participate.

will be expected to provide regular (weekly/bi-monthly) status updates to the Unitaid focal point for the evaluation. External evaluations are a critical element to Unitaid's grant management. Hence, **Unitaid will take an active part in the process and dedicate a significant amount of time in reviewing and iterating on the various draft reports with the external evaluators**, while honouring the independence of the evaluators, so that we have a final evaluation report that meets our expectations.

### **Target respondents**

Target respondents would include (but are not limited to) the following:

- The lead grantees for each grant under evaluation and implementing partners;
- In-country partners / stakeholders such as key decision makers at the country level, officials (high and mid-level) at relevant Ministries, community groups and CSOs, in-country PEPFAR/USAID representatives, Global Fund's country coordination mechanism, Global Fund Principal Recipient (PR) and sub-recipients;
- Wider global stakeholders indirectly involved with the respective grants such as WHO Technical Working Groups;
- Relevant manufacturers engaged under the grants – ViiV, Viatrix (Mylan), Macleods, Laurus Labs, Hetero and others as relevant.
- Potential donors and scale-up partners – Global Fund (secretariat, relevant Fund Portfolio Managers, Sourcing Team, HIV Team), President's Emergency Plan for AIDS Relief (PEPFAR OGAC, CDC, USAID),
- Relevant staff at the Unitaid secretariat (project team, senior management).

The Evaluators are asked to dedicate a bigger proportion of KIIs to external stakeholders and partners as opposed to grantees or Unitaid secretariat, and to use focus group discussions (in lieu of individual interviews) where relevant, with various stakeholders. It is estimated that around 90-120 people will be interviewed for this evaluation, of which more than half will be stakeholders beyond Unitaid and grantees.

Unitaid secretariat interviews will be done in 2-3 group discussions with the Project Team: the Senior Management Team, including the Executive Director. Before the interview with the senior management and/or Executive director which is likely to happen after Draft 1 of the report, it is expected that the Evaluator will prepare a briefing note/PowerPoint slides and develop interview questions with the Project Team beforehand.

### **Qualification and skills**

The successful bidders will propose a multi-disciplinary team of 3-4 experienced evaluators, including the team leader. The team leader must have at least 10 years of experience leading evaluations of a similar scope and complexity and ideally a strong understanding of market dynamics and interventions to increase access treatment in low and middle-income countries. Core team members should have at least 5 years of individual experience in their respective areas of technical expertise.

The proposed evaluation team should meet the following requirements:

- Expert knowledge of the HIV field and the challenges related to HIV treatment in LMICs;
- Experience in conducting evaluations of grants in the field of HIV treatment and product development/market access;
- Experience in conducting evaluations of clinical trials / human subject research;

- Experience in evaluating community/civil society engagement and demand creation interventions;
- Demonstrated knowledge of the challenges and options around ensuring access to innovative health products in LMICs;
- At least one team member with expertise in HIV treatment;
- At least one team member with expertise in human subject research;
- At least one team member with expertise in collection and analysis of qualitative data;
- Have either a regional/local presence in the project countries (especially those targeted for in-country data collection) or access to local counterparts;
- Expert knowledge of the global health landscape and the dynamics of introducing and scaling up interventions for complex health issues in resource-limited settings, such as HIV treatment, at national and global levels;
- Include an appropriate representation with regard to sex, a broad mix of backgrounds, skills and perspectives, and national and international experience, including in resource-limited settings; and
- Proficiency in English and at least one team member proficient in French (ability to conduct interviews and interact with in-country stakeholders in French, if necessary).
- **The proposed team members who have been agreed on and accepted by Unitaid following the RfP evaluation process (including from the outcome of negotiation prior to award recommendation) shall be available throughout the contract period and shall not be changed after the award of contract, unless requested or agreed to by Unitaid.**

## Deliverables

The evaluation will run over ~7 months, with deliverables to be submitted on the following indicative dates:

Deliverable	Illustrative Timeline <sup>229</sup>
1. An inception report outlining the process for the evaluation, including tailored evaluation questions and sub-questions, methodology, draft tools, a work plan and list of interviewees, as well as a draft theory of change for Unitaid’s investments in ART optimisation	2nd half of September 2022
2. Final evaluation design, methods and tools, and portfolio theory of change	Mid-October 2022
3. Data collection: <ul style="list-style-type: none"> <li>- Document reviews</li> <li>- Country visits/data collection</li> </ul>	Document Reviews Sept – Nov 2022  Data collection Oct – Dec 2022

<sup>229</sup> The proposed timeline should account for a minimum of 2 weeks for Unitaid to provide feedback on each draft deliverable.

<p>4. First draft evaluation report submitted and presented for review and comment by Unitaid. This first draft report would include an (i) Introduction; (ii) Methodology; (iii) Overarching Theory of Change for the ART Portfolio; (iv) a Table synthesising status of access and scale-up of optimal HIV treatment (for adults and children) in LMICs in 2022 (compared to baseline in 2016) and assessing the extent of Unitaid’s contribution to progress achieved using Unitaid access barriers and relevant KPIs as a framework. <i>Where relevant, Unitaid will provide templates</i>; (v) Preliminary findings: comprehensive portfolio analysis, with separate sections for the two sets of grants (Clinical Trials and Market/Country Preparedness), evaluation of grant outcomes by relevant access conditions, Scalability and transition at portfolio level, (vi) conclusions, and (vii) recommendations. Evaluators may be expected to present findings to Unitaid based on the first draft report.</p>	Mid-January 2023
<p>5. Second draft evaluation report, including Executive Summary, with a Table on key findings and recommendations. This second draft will address feedback from Unitaid, which will likely require additional data collection, analysis, interviews and triangulation of data. The evaluators will concurrently share the second draft report with the grantees for a factual check and address their feedback in the final report.</p>	End February 2023
<p>6. (Potentially two) Workshops with Unitaid: A first standalone workshop with Senior Management (SMT) after the first draft report, with feedback incorporated into the second draft report;<sup>230</sup> a second validation / presentation to grantees and external stakeholders to validate findings and solicit feedback after the second draft report, with comments incorporated into the final report where relevant. Draft 2 of the report is to be shared with the participants at least one week before the grantees’ / external stakeholders’ workshop.</p>	<p>SMT: Mid – End Jan 2023</p> <p>Grantees / Stakeholders — early March 2023</p>
<p>7. Final Deliverables: (1) Final evaluation report (as per structure mentioned above) incorporating all feedback received; and (2) a PowerPoint slide deck summarizing the evaluation findings (3) a Brownbag with the Unitaid secretariat based on the final slide deck.</p> <p>**There might be some minor additional feedback from Unitaid on the final draft.</p>	End March – mid April 2023

*Note:* The final evaluation report will be available to the public on the Unitaid website ([www.unitaid.org](http://www.unitaid.org)). Unitaid reserves the right to redact sensitive or confidential information prior to publication of the final evaluation report.

## Budget

All bidders are expected to submit their proposed budget. It is required that firms have either a regional/local presence in the project countries or have access to local counterparts that can assist the Evaluators to minimise the need for international travel, in line with Unitaid’s effort in reducing carbon footprints related to the procurement activities. Where relevant, given the ongoing uncertainty regarding international, regional and local travel and holding in-person meetings due to COVID-19, firms are expected to include cost estimates for two scenarios, one in which restrictions on travel and in-person meetings remain largely in place, and one in which such activities (or a subset of the activities, for example, local travel) are possible. Breakdown of cost component for travels must be clearly provided in the Financial Proposal template.

## Payment terms and schedule

<sup>230</sup> The workshop with Unitaid’s senior management could take place after the first draft report. To be discussed with the contractor.

For professional fees, payment will be made following satisfactory completion of the terms of reference and of corresponding detailed invoices, along with a Financial Statement (using the template to be provided by Unitaid) detailing the actual level of effort incurred and breakdown of travel expenses, if any.

For travel costs (if possible and requested by Unitaid), payment will be made in accordance with WHO rates and upon submission of invoices indicating actual travel costs with proof of payment. Evaluators are responsible to organise all logistics of travel, including hotel booking and local transportation.

Basis for Payment	Payment Percentage
1. Upon satisfactory completion of Inception Report and acceptance by Unitaid	20% of Professional Fee
2. Upon satisfactory completion of First draft report and acceptance by Unitaid	25% of Professional Fee
3. Upon satisfactory completion of Second draft report and acceptance by Unitaid	25% of Professional Fee
4. Upon satisfactory completion of Final evaluation report and Validation Workshop and acceptance by Unitaid	30% of Professional Fee



## Annex B. List of stakeholders interviewed

Category	Individual	Organisation	Position
Grantees	Professor Saye Khoo	University of Liverpool	Director, PI
	Helen Reynolds	University of Liverpool	Programme Manager
	Justin Chiong	University of Liverpool	Programme Manager
	Catriona Waitt	IDI	Co-Investigator, IDI Uganda
	Prof. Francois Venter	Ezintsha/ Wits RHI	Director, PI
	Angela Tembo	Ezintsha/ Wits RHI	Project Manager
	Dr Simiso Sokhela	Ezintsha/ Wits RHI	Head, Clinical Research
	Matthew Law	UNSW	Programme Head
	Simone Jacoby	UNSW	Programme Manager
	Daren Draganic	UNSW	Director of Operations
	Anthony Kelleher	UNSW	TBD
	Gail Matthews	UNSW	TBD
	Prof Eric Delaporte	IBB/ IRD	Programme Head, PI
	Tamara Tovar-Sanchez	IBB/ IRD	Clinical Trial Project Manager
	Charles Kouanfack	ANRS Cameroon	Co-PI
	Carolyn Amole	CHAI	Sr Director - HIV Access Program
	Benvy Caldwell	CHAI	Sr Manager – HIV Access Program
	Ateen Paliwal	CHAI	Director - Global Markets Team
Procurement Working Group	Rebecca Bailey	EGPAF/SPAAN	Director, Catalytic Implementation
	Wesley Kreft	I+ Solutions (Global Fund Procurement Agent)	Director Global Supply Chain
	Christine Malati	USAID/PEPFAR	Pharmaceutical Adviser, Supply Chain Technical Branch
	Messai Belayneh	USAID	Pharmaceutical & Supply Chain Advisor
	Cathal Meere	Global Fund	Pharma Sourcing Manager
Unitaid	Ademola Osigbesan	Unitaid	Technical Manager, Strategic Sourcing and Supply
	Pamela Nawaggi	Unitaid	Technical Officer, Strategy
	Oana-Magdalena Baban	Unitaid	Programme Officer (PO)
	Serra Asangbeh	Unitaid	Programme Officer
	Denitza Andjelic	Unitaid	Monitoring & Evaluation Manager
	Ganesh Ramachandran	Unitaid	Grant Finance Manager
	Jemmy Dopas	Unitaid	Grant Finance Manager
	Mirchaye Negussie-Shepard	Unitaid	Grant Finance Officer
	Danielle Ferris	Unitaid	Programme Manager, Community and Civil Society Engagement

Category	Individual	Organisation	Position
	Carmen Perez Casas	Unitaid	Senior Technical Manager, Strategy
	Katherine Blumer	Unitaid	Programme Manager (PM)
Global partners	Hilary Wolf	CDC	Medical Officer
	Martin Auton	Global Fund	Senior Manager, Principal Recipient Services, Sourcing & Supply Chain Department / Co-Chair of Programme Advisory Committee
	Lin (Roger) Li	Global Fund	Senior Manager, Strategic Sourcing Team
	Siobhan Crawley	Global Fund	Head HIV
	Martina Penazzato	WHO	Medical Officer, Paediatric HIV, GAP-f
	Meg Doherty	WHO	Director, Department of Global HIV, Hepatitis and STI Programmes / Co-Chair of Programme Advisory Committee
	Marco Vitoria	WHO	Medical Officer
Community	Luckyboy Mkhondwane	Treatment Action Campaign	Treatment Literacy Training Coordinator
	Polly Clayden	HIV i-Base	Editor/ Director
	Kenly Sikwese	AfroCAB	Coordinator
	Imelda Mahaka	Pangaea Zimbabwe AIDS Trust	Executive Director
Manufacturers	Rohini Karde,	Macleods	Business development
	Shailesh Pednekar	Macleods	Business development
	Srinivas Sivareddypeta	Viartis (Mylan)	Sr Manager, Strategic Projects
	Prashant Sisodia	Viartis (Mylan)	Vice President
	Helen McDowell	ViiV	Head of Government Affairs and Global Public Health
	Bhaves Shah	Hetero	Vice President - International Marketing;
	Rahul Lande	Hetero	Vice President - International Marketing;
	Mr Umesh K	Aurobindo	Vice President – International Business
	Pavan Elisetty	Laurus Labs	Sr Vice President – Global Business Operations

Country	Individual	Organisation	Position
Benin	Prof. GANGBO Flore	National AIDS Control Program/ PSLs	National Coordinator for HIV
	Dr Moussa Bachabi	National AIDS Control Program/ PSLs	Deputy National Coordinator for HIV
	Dr AFANGNIHOUN Aldric	National AIDS Control Program/ PSLs	In charge of Treatment, Care and Support
	M. ADIFFON Arsene	ONG RACINES	Executive Director
	M. NASSARA Valentin	RÉBAP Bénin	Board Chairman (CEO)
Cameroon	Marie Varloteaux	Site ANRS Cameroon	ETI and Journalist training
	Justin Olinga	Site ANRS Cameroon	Trial Manager, Representative of clinical team from study sites
	Thèrese Abong	MINSANTE	Procurement/Medicines/Pharmacy
	Calice Talom	REDS	Civil society/community representative
	Tamara Tovar-Sanchez	IBB/IRD	Clinical trial project manager
	Alejandra Castro	IBB	Project Manager
Cote d' Ivoire	Diby Brou Charles J	EGPAF	Country Director
	Hié Carole	EGPAF	TA paediatric and adolescent care
	Ehui Eboi	PNLS	ACP executive coordinator
	Kouamé Komenan Eric	AIRP	Pharmacovigilance chief of department
	Codo Carine	NPSP	Director of Programs and Specific Supports
	Kouassi Agnés	Plateforme des réseaux et faitières de lutte contre le VIH/TB/Palu	In charge of monitoring and evaluation services and focal person at paediatric and adolescent HIV TWG
	Adingra Nadia	Afro CAB representative	In charge of community advisory board (CAB) activities for the Optimal project
	Prao Aka Kouamé	CDC PEPFAR	Focal person in charge of paediatric and nutritional services
Kenya	Dr Ngugi, Wangari Evelyn	CDC	
	Dr Imbuki, Evans	MoH - NASCOP,	Program Manager- Supply chain and Pharmacovigilance
	Kabuchi, John	KEMSA	Medical Commodities Program Director; Procurement Manager
	Wambui, Jacque	AfroCAB Treatment Access Partnerships;	Global Treatment and AHD CAB Facilitator
	Macharia, Gerald	CHAI	Vice President – East & Southern Africa and Country Director, Kenya
	Karambi, Davis	CHAI	Program Director – Access Programs Kenya
Nigeria	Folu Lufadeju	CHAI	Snr Deputy Country Director & Snr Director Access Program
	Nere Otubu	CHAI	Program Manager

Country	Individual	Organisation	Position
	Uzoma Atu	NASCP	Assistant Director Logistics
	Matthew Attah	GHSC-PSM	Director plan and source
	Adenike Adelanwa	USAID	Manager Pharmaceutical commodities
	Patrick Okoh	FHI-360 (Global Fund Principal Recipient)	Head of Downstream Logistics – Senior Technical Officer
	Buki Ayinde	Positive Response for Treatment Access, Adherence and Support	Team Lead
	Abiola Ajani	Network of people living with HIV/AIDS in Nigeria (NEPWHAN)	Zonal Coordinator
	Dr Nnakelu Eriobu	Institute of Human Virology, Nigeria	Principal Investigator
South Africa	Dr Boitumelo Semete	SAHPRA	Chief Executive Officer
	Yogan Pillay	CHAI	Country Director, South Africa, and Senior Global Director for Universal Coverage
	Dr Zukiswa Pinini	National Department of Health	Chief Director: National HIV/AIDS, STIs Programme
	Juliet Houghton	Southern African HIV Clinicians Society	Director
	Dr Richard KAPLAN	Desmond Tutu HIV Foundation	Principal Investigator
Uganda	Andrew Musoke	CHAI	Country Director
	Vennie Nabitaka	CHAI	Program Manager
	Dr Cordelia Katureebe	Uganda MoH	National ART Coordinator
	Dr Eleanor Magongo	Uganda MoH	National Paediatric ART Coordinator
	Dr Esther Nazziwa	CDC	Treatment Team Lead
	Dr Mohammed Lamorde	IDI	Co-investigator
Malawi	Dyson Telela and Andrews Gunda	CHAI	Program Manager HIV/AIDS (Country Director)
	Deidre Kaitana	CAB	CAB Member
	Andrews Gunda	CHAI	Country Director
Zimbabwe	Alexio Mangwiro, Carolyn Amole, Nicole Kawaza	CHAI	Country Director
	Imelda Mahaka	PZAT	Country Director and Optimal CAB member
	Talent Maphosa	CDC	Public Health Specialist
	Solomon Mukungunugwa	USAID	Project Management Specialist - HIV Clinical Services
	Dr Thato Chidarikire	National Department of Health	Chief Director: National HIV/AIDS, STIs Programme

## Annex C. Evaluation matrix

OECD-DAC criteria	Evaluation questions	Sub-questions
<p><b>Relevance:</b> Is Unitaid’s ART optimisation portfolio doing the right things?</p>	<p><b>EQ1:</b> To what extent did the objectives and design of Unitaid’s ART optimisation investments respond to the needs of targeted beneficiaries (people living with HIV, community and CSOs, government/national health systems, scale-up partners/ market)?</p> <p><b>EQ2:</b> Were approaches to optimal HIV treatment implementation appropriately adapted/course-corrected to respond to any changes in the HIV treatment context (for example, at the policy level – globally or within a national context, emerging and competing technologies/products/approaches)?</p>	<p><b>Sub-EQ 1.1:</b> To what extent have Unitaid’s ART Optimisation investments identified and addressed issues related to gender, social inclusion, and equity in line with Unitaid’s overall mission to reach the most disadvantaged populations in developing countries using innovative global market-based approaches?</p> <p><b>Sub-EQ 1.2:</b> To what extent did the ART Optimisation portfolio apply market shaping approaches, where necessary, to improve equitable access? Were the selected market shaping approaches the most appropriate ones, vs other potential approaches?</p>
<p><b>Coherence:</b> How well does the ART portfolio fit?</p>	<p><b>EQ3:</b> To what degree have Unitaid’s investments in ART optimisation fit with other interventions within targeted countries, sectors, or institutions (for example, creating synergies between relevant interventions and consistent with other initiatives within the same public health space)?</p> <p><b>EQ4:</b> Has the ART optimisation portfolio contributed to fostering inclusive and demand-driven innovation partnerships?</p>	<p><b>Sub-EQ 3.1:</b> How well does the intervention align with priorities/ needs identified by partners/ the global disease response?</p> <p><b>Sub-EQ 3.2:</b> To what extent have Unitaid’s investments in ART optimisation added value (and not duplicated efforts or established parallel systems)?</p> <p><b>Sub-EQ 4.1:</b> Has ART optimisation, including through the PAC, facilitated greater collaboration among (i) global partners working in the space (for example, WHO, USAID OPTIMIZE); and ii) grant implementers - and with what results (for example, contributions to outcomes, accelerating scale-up)?</p> <p><b>Sub-EQ 4.2:</b> How effectively have implementers engaged with and supported communities and CSOs (including <b>vulnerable groups</b>), and with what results (for example, to help increase demand, political support and financial commitments for optimal HIV treatment products)? What was the specific contribution of the CAB to these processes?</p>
<p><b>Efficiency:</b> How well are the portfolio</p>	<p><b>EQ5:</b> How timely, cost-efficient and cost-effective was implementation?</p>	<p><b>Sub-EQ 5.1:</b> What factors have been considered to ensure that value for money has been achieved from an efficiency standpoint?</p>

OECD-DAC criteria	Evaluation questions	Sub-questions
resources being used?		<b>Sub-EQ 5.2:</b> How well did grant implementers collaborate with national authorities in project planning, implementation and assessment to promote integration into existing health systems?
<p><b>Effectiveness:</b> Is the ART optimisation portfolio achieving its objectives?</p>	<p><b>EQ6:</b> To what extent did Unitaid’s ART optimisation investments achieve their objectives and expected outcomes (in terms of catalysing the market, and accelerating the introduction of optimal HIV treatments), by addressing targeted <b>access barriers</b>, within the specified timeframe and budget?</p> <p><b>EQ7:</b> What were the main factors influencing the achievement or non-achievement of the intended outputs or overall outcomes?</p>	<p><b>Sub-EQs 6.1-6: Access barriers</b></p> <p><b>Sub-EQ 6. 1 Innovation and availability:</b> To what extent have Unitaid’s ART optimisation investments contributed to increased availability of better HIV treatment products that are commercially available for rapid introduction in LMICs?</p> <p><b>Sub-EQ 6. 2 Quality:</b> How successful were Unitaid’s ART optimisation investments in bringing quality-assured HIV treatment products for adoption in LMICs?</p> <p><b>Sub-EQ 6. 3 Affordability:</b> To what degree have Unitaid’s ART optimisation investments contributed to making optimal HIV treatment products available at lower prices that are affordable for governments (and other potential donors)?</p> <p><b>Sub-EQ 6. 4 Demand and adoption:</b> What progress did the Unitaid’s ART optimisation investments in facilitating increased demand and uptake for scale-up of cost-effective HIV treatment products within target countries (and beyond)?</p> <p><b>Sub-EQ 6. 5 Supply and delivery:</b> To what extent did Unitaid’s ART optimisation investments improve supply and delivery systems to ensure that optimal HIV treatment products reach those in need in a reliable and timely manner?</p> <p><b>Sub-EQ 6. 6</b> How have Unitaid’s ART optimisation investments catalysed the development and testing of simplified, effective delivery models for optimal HIV treatment in LMIC settings? To what extent do these systems reach underserved/ <b>vulnerable populations</b>?</p> <p><b>Sub-EQ 7.1:</b> How and to what extent has i) Unitaid’s secretariat; ii) the PAC; and iii) the CAB played an effective role in contributing to accelerating access to optimal HIV treatment products?</p> <p><b>Sub-EQ 7.2:</b> To what extent were market shaping approaches effective? What were the strengths and weaknesses?</p>
<p><b>Sustainability:</b> Will the benefits of the</p>	<p><b>EQ10:</b> How have Unitaid’s ART optimisation investments contributed to an <b>enabling global environment</b> for scale-up – including i) generating evidence; ii) normative guidance; iii) affordable pricing; iv) tools to support</p>	<p><b>Sub-EQs 10.1-8:</b></p>

OECD-DAC criteria	Evaluation questions	Sub-questions
<p>ART portfolio last?</p>	<p>country adoption and uptake and advocacy, and v) strong partnerships among global actors? [NB some conditions covered under Access Barriers 6.1-6.6]</p> <p><b>EQ11:</b> To what extent have Unitaids’ ART optimisation investments contributed to establishing <b>country readiness</b> for scale-up – including securing ongoing i) political and ii) financial commitments by national governments and iii) other partners, iv) supportive policies and v) enhanced health system capacity for delivery, and partnering with vi) communities and vii) civil society (including <i>vulnerable groups</i>) to mobilise ongoing community demand and engagement? [NB some conditions covered under Access Barriers 6.1-6.6]</p> <p><b>EQ12:</b> To what extent have core elements of ART optimisation grant funded interventions been <b>transitioned</b> to ensure that the benefits of the intervention will continue beyond the life of the investment?</p> <p><b>EQ13:</b> To what extent have ART optimisation products and approaches been <b>scaled up</b> across project countries and beyond? (that is, integrated into relevant national programs and health systems to support sustainable, equitable scale-up)?</p> <p><b>EQ14:</b> What have been the main <b>factors</b> facilitating or limiting transition and/or scale-up?</p>	<p><b>Sub-EQ 10.1:</b> To what extent has the ART optimisation portfolio contributed to the <b>increase of a rigorous evidence base</b> that supports the safety, feasibility, effectiveness and cost-effectiveness of optimal regimens at global level (critical to enable normative guidance)?</p> <p><b>Sub-EQ 10.2:</b> Has the work of the ART optimisation portfolio contributed to optimal regimens being <b>recommended in policy and normative guidance</b>, like for example WHO guidance?</p> <p><b>Sub-EQ 10.3:</b> Has Unitaids’ ART optimisation portfolio work contributed to efficient and safe optimal HIV treatments meeting appropriate <b>quality standards</b>, such as WHO Prequalification status or approval from a recognised global regulatory authority? AND/OR How has the portfolio supported <b>product registration and market authorisation</b> of new optimal HIV treatment at the global and country levels?</p> <p>Sub-EQ 10.4: Is the <b>product/intervention available at an affordable price</b> for LMICs (to public-sector purchasers)?</p> <p>Sub-EQ 10.5: Is the product/intervention <b>supplied in adequate quantities in a timely manner</b> in relevant LMICs? (including diversification of the supply base to ensure supply security and promote competitive pricing, where demand is sufficient)</p> <p><b>Sub-EQ 10.6:</b> How has the work of the ART optimisation portfolio contributed to improving <b>procurement and appropriate delivery mechanisms</b> and <b>increasing the timely and sufficient availability of high-quality/ affordable products in LMICs</b>?</p> <p><b>Sub-EQ 10.7:</b> Is there <b>agreement among major global donors, implementing partners and government that the product/intervention is a strategic priority for scale-up</b> (as evidenced by inclusion in global policy/strategy documents, donor specific plans, etc.)</p> <p><b>Sub-EQ 10.8:</b> Are quality, field-tested <b>tools/resources available to support scale-up of the product/intervention, adapted for various contexts</b> and health systems?</p> <p><b>Sub-EQ 10.9:</b> Has the work of the Unitaids ART optimisation portfolio contributed to <b>newly approved optimal HIV treatments being included as part of regular global donor, governments and relevant international implementing partner planning and budgeting cycle</b> to secure adequate resources for scale-up both <b>at the global and country levels</b>?</p>

OECD-DAC criteria	Evaluation questions	Sub-questions
		<p><b>Sub-EQ 10.10:</b> How effectively has the portfolio widely <b>disseminated evidence of rigorous results</b> (including the results from the four clinical trials) to key stakeholders support the scale-up of optimal HIV treatments across the globe?</p> <p><b>Sub-EQ 10.11:</b> Have <b>lessons learnt on implementation</b> feasibility, and what is needed to facilitate successful scale-up within a range of health systems, been synthesised and shared with global and national stakeholders?</p> <p><b>Sub-EQ 10.12:</b> Is <b>evidence from Unitaid-funded projects and other sources being used to generate compelling investment cases</b> to support donors and governments to prioritise scale-up and increase investment in the product/intervention?</p> <p><b>Sub-EQ 10.13:</b> What gaps (if any) remain or what additional work needs to be undertaken to ensure continued scale-up and sustainability?</p> <p><b>Sub-EQs 11.1–6:</b></p> <p><b>Sub-EQs 11.1:</b> To what extent have critical decision makers in Unitaid’s implementation countries been meaningfully engaged and demonstrate political support for national scale-up of optimal HIV treatment?</p> <p><b>Sub-EQs 11.2:</b> To what extent have major donors at country level actively collaborated and allocated funding to enable national scale-up in a coordinated manner?</p> <p><b>Sub-EQs 11.3:</b> To what extent have national governments demonstrated/signalled support for scale-up by allocating resources (for example, national budget line for products/interventions)? What % of funding comes from national budgets/scale-up donors?</p> <p><b>Sub-EQs 11.4:</b> Is the product/intervention recommended in national and sub-national health policies?</p> <p><b>Sub-EQs 11.5:</b> Do national health systems have adequate, trained staff, supplies and other resources to enable quality, equitable scale-up of the product/intervention?</p> <p><b>Sub-EQs 11.6:</b> To what extent have civil society groups been meaningfully engaged and strengthened to actively demand equitable access to the product/intervention?</p> <p><b>Sub-EQs 11.7:</b> To what extent have grassroots organisations/communities been meaningfully engaged and strengthened to actively demand equitable access to the product/intervention?</p>



OECD-DAC criteria	Evaluation questions	Sub-questions
		<p><b>Sub-EQ 11.8:</b> What gaps (if any) remain or what additional work needs to be undertaken to ensure continued scale-up and sustainability?</p> <p><b>Sub-EQ 14.1:</b> How and to what extent has i) the PAC; and ii) the CAB played an effective role in contributing to scalability?</p>
<p><b>Impact:</b> What difference does the ART optimisation portfolio make?</p>	<p><b>EQ15:</b> To what extent have Unitaid’s ART optimisation investments generated, or are expected to generate:</p> <ul style="list-style-type: none"> <li>i. Equity impact (including through market shaping activities)</li> <li>ii. Strategic benefits and positive externalities (incl. generation and dissemination of evidence and lessons learnt on equitable access)</li> </ul>	<p><b>Sub-EQ 15.1:</b> To what extent has the ART optimisation portfolio improved access to optimal HIV treatments for vulnerable/underserved populations in LMICs?</p> <p><b>Sub-EQ 15.2:</b> How well have the investments disseminated knowledge, evidence, and lessons learnt on equitable access related to ART optimisation? To what extent has this contributed to broader awareness and increased support from other stakeholders for ART optimisation?</p> <p><b>Sub-EQ 15.3:</b> Have there been any wider positive externalities and unexpected benefits from the ART optimisation portfolio implementation?</p>
<p><b>Learning and risk mitigation</b></p>	<p><b>EQ16:</b> What have been the lessons learnt?</p> <p><b>EQ17:</b> How have lessons been incorporated in the lifetime of the grant or across other interventions?</p> <p><b>EQ18:</b> How effectively have strategic, implementation and sustainability/ scalability risks been identified and managed over the course of implementation?</p>	<p><b>Sub-EQ 16.1:</b> What have been the specific lessons learnt with regards to the appropriateness and effectiveness of (i) community engagement/ demand generation; and (ii) market shaping activities?</p> <p><b>Sub-EQ 16.2:</b> What has been learnt about Unitaid’s <b>ART optimisation portfolio model</b><sup>231</sup> overall (in terms of relevance, effectiveness and equity impact for targeted beneficiaries)?</p> <p><b>Sub-EQ 17.1:</b> What was learnt about how to support adaptive design and management of clinical trials, market shaping and market preparedness grants?</p> <p><b>Sub-EQ 17.2:</b> What mechanisms have Unitaid used to share learnings among grantees and with the wider sector?</p> <p><b>Sub-EQ 18.1:</b> What were the processes that grantees and implementing partners used for risk mitigation? What worked well and less well?</p>

<sup>231</sup> Brief exploration of the Unitaid Model through the lens of the ART Optimisation portfolio (that is, clinical trials + product introduction/country preparedness work + enabling grants + community engagement + partner engagement).

## Annex D. Coded segments

Code System	Frequency
Total number of excerpts	4832
1. Relevance of Unitaids' ART optimisation Portfolio to interna	9
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.1. Development of the portfolio	221
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.2 Addressing the needs/gaps	180
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.2 Addressing the needs/gaps > 1.2.1 Access to optimal HIV treatment 2016	156
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.2 Addressing the needs/gaps > 1.2.2 Access to optimal HIV treatment 2021-22	92
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.3. Relevance to the vulnerable and under-served	133
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.4. Relevance of Unitaids' Market Shaping approach	53
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.5 Adaptation of the portfolio model over time	53
1. Relevance of Unitaids' ART optimisation Portfolio to interna > 1.5 Adaptation of the portfolio model over time > 1.5.1 Adaptation of clinical trials	106
2. Coherence of Unitaids' ART optimisation investments	17
2. Coherence of Unitaids' ART optimisation investments > 2.1 Coherence of Unitaids' ART Optimisation investments at global	165
2. Coherence of Unitaids' ART optimisation investments > 2.2 Coherence of Unitaids' ART Optimisation investments at country level	66
3. Efficiency of resource utilisation	58
3. Efficiency of resource utilisation > 3.1 Grant implementers collaboration with national authorities	109
4. Effectiveness of Unitaids' ART optimisation Portfolio model	26
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.1 Clinical trials grants effectiveness	5
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.1 Clinical trials grants effectiveness > 4.1.2 Innovation and availability	58
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.1 Clinical trials grants effectiveness > 4.1.3 Quality	23
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.1 Clinical trials grants effectiveness > 4.1.4 Affordability	47
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.1 Clinical trials grants effectiveness > 4.1.5 Demand and adoption	73
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.1 Clinical trials grants effectiveness > 4.1.6 Supply and delivery	46
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.2 Clinical trials grants factors influencing the achievement	47
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.3 Clinical trials grants factors that hindered the achievement	45
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.4 Country preparedness and market shaping grants effectiveness	48

Code System	Frequency
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.4 Country preparedness and market shaping grants effectiveness > 4.4.1 Innovation and availability	54
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.4 Country preparedness and market shaping grants effectiveness > 4.4.2 Quality	24
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.4 Country preparedness and market shaping grants effectiveness > 4.4.3 Affordability	45
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.4 Country preparedness and market shaping grants effectiveness > 4.4.4 Demand and adoption	58
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.4 Country preparedness and market shaping grants effectiveness > 4.4.5 Supply and delivery	36
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.5 Country preparedness and market shaping grants factors influencing	55
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.6 Country preparedness and market shaping grants factors that	20
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.7 Effectiveness of Cross-cutting grants	89
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.8 Effectiveness of Unitaids' secretariat's role	115
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.9 Effectiveness of Programme Advisory Committee (PAC)	140
4. Effectiveness of Unitaids' ART optimisation Portfolio model > 4.10 Effectiveness of the community engagement activities and C	238
5. Sustainability of the Portfolio benefits	7
5. Sustainability of the Portfolio benefits > 5.1 Factors facilitating/limiting transition	82
5. Sustainability of the Portfolio benefits > 5.2 Global enabling environment for scale-up	22
5. Sustainability of the Portfolio benefits > 5.2 Global enabling environment for scale-up > 5.2.1. Dissemination and generation of evidence to support scale-up	239
5. Sustainability of the Portfolio benefits > 5.2 Global enabling environment for scale-up > 5.2.2 Products that are recommended in policy and normative guidance	118
5. Sustainability of the Portfolio benefits > 5.2 Global enabling environment for scale-up > 5.2.3 Products are available at affordable pricing in LMICs	71
5. Sustainability of the Portfolio benefits > 5.2 Global enabling environment for scale-up > 5.2.4 Products are supplied and delivered timely and in adequate	46
5. Sustainability of the Portfolio benefits > 5.2 Global enabling environment for scale-up > 5.2.5 Tools/ approaches that support country adoption and uptake	74
5. Sustainability of the Portfolio benefits > 5.2 Global enabling environment for scale-up > 5.2.6 Strong partnerships among global actors	120
5. Sustainability of the Portfolio benefits > 5.3 Establishing country readiness for scale-up	14
5. Sustainability of the Portfolio benefits > 5.3 Establishing country readiness for scale-up > 5.3.1 Securing political and financial support and buy-in, dome	78
5. Sustainability of the Portfolio benefits > 5.3 Establishing country readiness for scale-up > 5.3.2 Supportive policies, integration into national programs,	96
5. Sustainability of the Portfolio benefits > 5.3 Establishing country readiness for scale-up > 5.3.3 Community driven-demand such as support to civil society	140
6. Impact of the portfolio	61
6. Impact of the portfolio > 6.1 Equity impact	161
6. Impact of the portfolio > 6.2 Strategic benefits and positive externalities	70

Code System	Frequency
7. Risk mitigation	53
8. Lessons learnt	46
8. Lessons learnt > 8.1 Lessons incorporated by clinical trials, country preparedness	56
8. Lessons learnt > 8.2 Lessons incorporated – from and across other interventions	50
8. Lessons learnt > 8.3 Sharing learning	146
9. Recommendations for Unitaid	108
10. Countries	18
10. Countries > 10.1 South Africa	145
10. Countries > 10.2 Kenya	22
10. Countries > 10.3 Uganda	22
10. Countries > 10.4 Nigeria	23
10. Countries > 10.5 Benin	1
10. Countries > 10.6 Cote d'Ivoire	1
10. Countries > 10.7 Cameroon	1
10. Countries > 10.8 Malawi	11
10. Countries > 10.9 Zimbabwe	20

## Annex E. Strength of evidence framework

Strength of evidence relates to the internal validity of evaluation findings. This is underpinned by three broad considerations:

1. The extent of triangulation across stakeholders and/or data sources: Triangulation can be pursued on several levels:
  - Within interviews, by asking for examples. If a stakeholder claims to have observed an outcome, confidence that this is true is increased if they are able to give specific examples.
  - Across stakeholders and types of stakeholders. Confidence that an outcome has occurred is stronger if more people, across different groups, claim to have observed it. Where possible, this might include seeking out and comparing insights from the ART optimisation portfolio staff or grantees with other stakeholders, who have less of a stake in the portfolio being perceived as successful, and who, due to their position, have independent insights that provide corroboration and contextual information.
  - Across data sources: Triangulating insights from primary data collected through interviews with monitoring, evaluation and learning data collected by the portfolio, and where possible with documents that also give insights into portfolio outcomes.
  - Collection of additional evidence: Where and when needed, the team will collect additional evidence to seek further clarification and support triangulation.
2. **A consideration of the position, knowledge, analytical capacity, reflexivity, and potential biases of primary informants:** Stakeholders should not be solely considered in terms of homogenous categories, but as individuals positioned in unique ways in relation to the portfolio, with different levels of knowledge, capacity and incentives that may lead to bias. Weighing the strength of evidence requires a consideration of these issues, rather than simply considering the number of respondents who confirmed a particular outcome or theory. For example:
  - Different people can be expected to know different things about an expected outcome or change process. In some cases, only a small number of people are likely to know about an outcome, portfolio contribution, and how / why change happened. Weighing the strength of evidence requires the evaluators to judge whether those who can be expected to know about the issue have confirmed that things happened in a certain way.
  - Different respondents have different levels of capacity (and interest) in scrutinizing how and why something happened – particularly when this requires them to consider why they have (or have not) changed their attitudes or behaviours – and this affects the weight that should be given to their responses.
  - Different stakeholders will have different incentives which may lead to biased responses; most obviously an incentive to ‘tell the evaluator what they want to hear’ in order to paint the project in a positive light and potentially secure future funding.
  - The position of a respondent in relation to the portfolio gives them a particular perspective which needs to be considered, overlapping with all of the above considerations. An external sectoral stakeholder may be able to provide important independent insights about broader issues but may not know much about the specific individuals or teams who took part in the portfolio implementation (and therefore their opinions should be weighed accordingly). For example, a senior portfolio manager might have good insights into outcomes but may be unwilling to speak

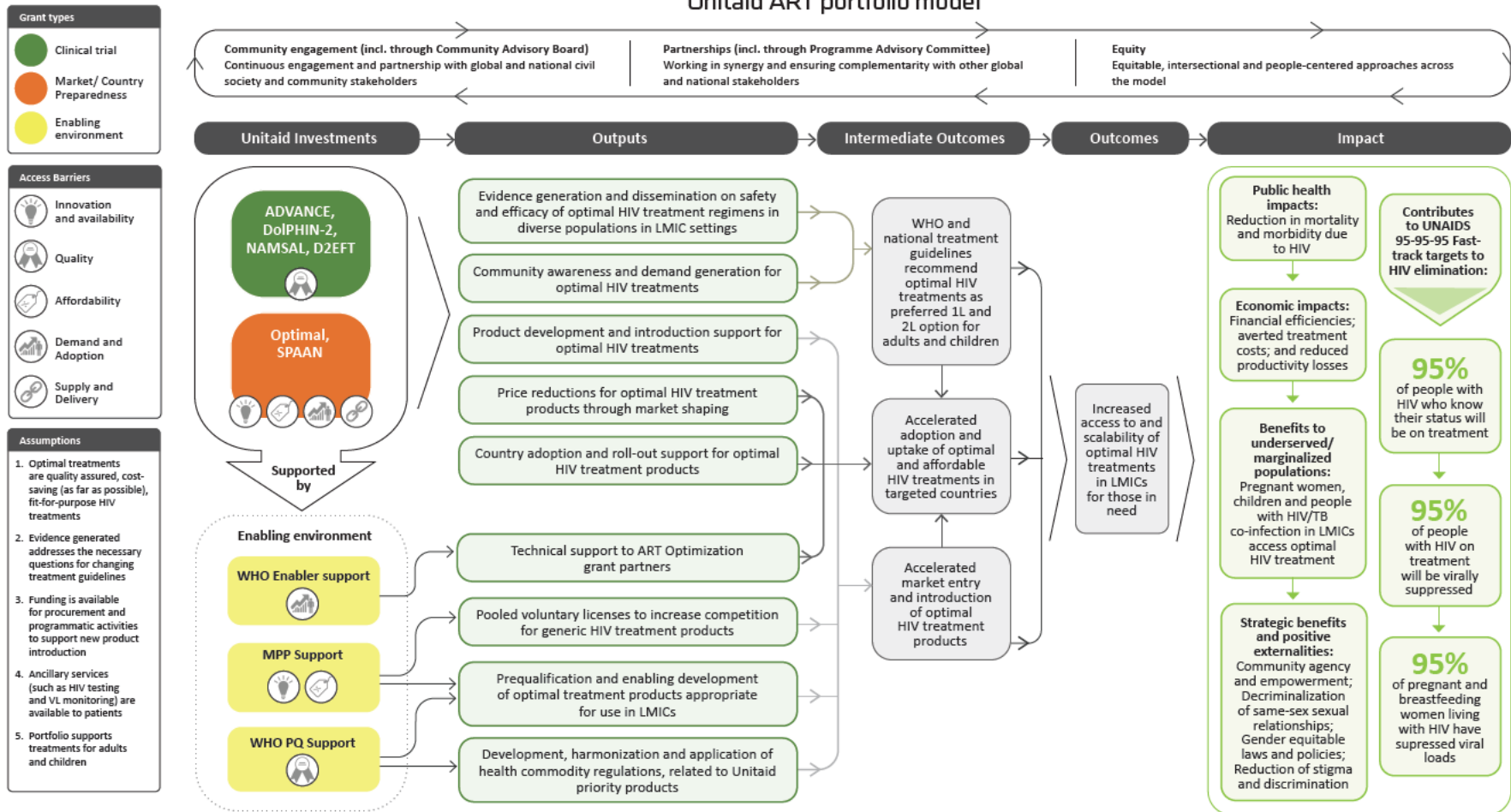
openly about the realities of incentives and power structures within their organisation, and although they may not have participated directly in the portfolio implementation, they still have a stake in its success which implies the need to mitigate possible bias.

Itad considers these issues both during the sampling process (when making decisions about who to interview), and during the interview write up and analysis (taking note of issues in order to feed these considerations into the write up).

3. **A consideration of the broader context:** It might be important to consider broader political economy and contextual factors that enable and constrain change in the settings and sectors under examination, and which provide opportunities and risks to the portfolio. This helps ensure that explanations of change are grounded in an understanding of the context and are not over-reliant on the explanations of stakeholders. This can also help identify other (non-portfolio) explanations of change, in order to help guard against over-attributing changes in ART optimisation only to Unitaid's portfolio.

We will use these three considerations to develop a qualitative approach to assessing the strength of evidence in this evaluation – see Table 2 to ensure the evaluative judgements are made systematically and are comparable across the evaluation. This framework will be agreed with Unitaid and finalised during inception.

## Annex F. Theory of Change





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