



Unitaid investments in Hepatitis C – portfolio evaluation and end of grant evaluations of the FIND HEAD-Start and Coalition PLUS grants

Unitaid

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Final Report

Important notice

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ACRONYMS

Acronym	Full description
Afi	Area for Intervention
cAg RDT	Core Antigen Rapid Diagnostic Test
CDC	Centers for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
CL	Compulsory Licence
DAA	Direct acting antiviral
DAC	Development Assistance Committee
DBS	Dried Blood Spot
DCV	Daclatasvir
DNDi	Drugs for Neglected Diseases Initiative
FIND	Foundation for Innovative New Diagnostics
HCV	Hepatitis C Virus
HCVST	HCV self-test
HRS	Harm Reduction Sites
KII	Key informant interview
KPI	Key Performance Indicator
LMIC	Low and middle income country
LTFU	Lost-to-follow-up
MoH	Ministry of Health
MPP	Medicines Patent Pool
MSF	Médecins Sans Frontières
OECD	Organisation for Economic Co-operation and Development
POC	Point-of-care
PQ	Prequalification
PLHIV	People Living with HIV
PWID	People who inject drugs
RDT	Rapid Diagnostic Test
R&D	Research and Development
RfP	Request for Proposal
SOF	Sofosbuvir
TB	Tuberculosis
ToC	Theory of Change
ToRs	Terms of Reference
VL	Voluntary Licence
WHA	World Hepatitis Alliance
WHO	World Health Organisation

REPORT STRUCTURE

Cambridge Economic Policy Associates (CEPA) was appointed by Unitaid to conduct a portfolio-level evaluation of its investments in the Hepatitis C Virus (HCV) alongside end-of-grant evaluations of two of the grants to FIND and Coalition PLUS. This report presents evaluation findings, conclusions and recommendations, structured in three parts:

- Part A is the portfolio evaluation
- Part B is the end-of-grant evaluation of the FIND HEAD-Start grant
- Part C is the end-of-grant evaluation of the Coalition PLUS grant

All parts can be read as stand-alone evaluations, however Part A on the portfolio evaluation also provides the overall evaluation background, objectives and methodology (Section 1), which is relevant introductory information for the end-of-grant evaluations included in Parts B and C. Further, detailed information on both the FIND HEAD-Start and Coalition PLUS grants are included in the grant evaluations (i.e. Parts B and C), with more summarised and portfolio-wide details and evidence-base included in Part A. As such, should readers be interested in some of the details with regards to FIND and Coalition PLUS' work, please refer to Parts B and C respectively. Each part has a concluding section, with Part A on the portfolio evaluation also presenting CEPA's overall recommendations to Unitaid.

The main report is supported by the following appendices: Appendix A presents the bibliography; Appendix B lists the interviewees we have consulted for the evaluation; Appendix C presents the guides we used for our stakeholder interviews; Appendix D explicates the results of our impact modelling; Appendix E presents the global and country-level Scalability Matrices; Appendix F summarises our evaluation against the OECD DAC Criteria; Appendix G presents progress against Unitaid's KPIs ; Appendix H provides the definitions of Unitaid's global conditions for scale-up; Appendix I lists the participants at a workshop held to discuss preliminary findings; and Appendix J documents the Terms of Reference (TOR) upon which this report is based.

EXECUTIVE SUMMARY

Executive summaries are provided below for the portfolio-level evaluation as well as each of the two end-of-grant evaluations.

Unitaid HCV portfolio evaluation

Cambridge Economic Policy Associates (CEPA) was appointed by Unitaid to conduct a portfolio-level evaluation of Unitaid's investments in the Hepatitis C Virus (HCV), alongside end-of-grant evaluations of the grants to Foundation for Innovative Diagnostics (FIND) and Coalition PLUS.

Background

In 2021, the World Health Organization (WHO) estimated that there were 58 million people living with chronic HCV, and in 2019, 290,000 people died from HCV-infection related causes¹. Low and Middle Income Countries (LMICs) have faced significant barriers to access HCV diagnosis and treatment, with, prior to 2014, treatment being complex with limited efficacy and a range of potential side effects. However, with the advent of Direct Acting Antivirals (DAAs), HCV treatment has become faster, less complex and more effective, curing over 90% of HCV infections within 12 weeks. This presented an unprecedented opportunity for HCV elimination, as a result of which Unitaid identified HCV diagnosis and treatment as an area of work in 2013. By helping to remove key access barriers, Unitaid aimed to catalyse the market for HCV diagnosis and treatment, and create conditions and tools to enable and facilitate scale-up by countries and partners going forward. Unitaid awarded three grants focused on HCV with funding of over US\$45 million, including the following:

- Coalition PLUS, HIV/HCV Drug Affordability Project (2015-21, US\$10.1 million);
- FIND, Hepatitis C Elimination through Access to Diagnostics (2016-20, US\$27.4 million); and
- Médecins Sans Frontières (MSF), Ensuring access to HCV treatment revolution for HCV/HIV co-infected patients in low and middle-income countries (2015-18, US\$8 million).

In addition, Unitaid included HCV-related support in three of cross-cutting investments to the Medicines Patent Pool (MPP), the WHO Prequalification Programme (WHO PQ) and the WHO Enabler grant².

The overall evaluation objectives were to assess: (i) the extent to which Unitaid has established an environment to catalyse the HCV diagnostic and treatment markets; and (ii) the extent to which Unitaid investments have contributed to creating conditions and tools for scale-up and the potential for scale-up going forward. The evaluation framework was structured along four pillars: (i) relevance and implementation; (ii) effectiveness (including the Unitaid access barriers); (iii) scalability and transition; and (iv) impact of the HCV portfolio. The methodology employed a theory-of-change based approach and was based on a mixed-methods comprising desk-based document review; stakeholder interviews; country case studies; impact modelling; and quantitative data analysis. The evaluation also conducted a workshop on preliminary findings with a select group of stakeholders in the HCV space.

Evaluation findings are presented below by each of the four pillars in the framework, followed by overall conclusions and recommendations for Unitaid.

Relevance and implementation

Unitaid's HCV portfolio has been highly relevant, appropriate and aligned with Unitaid's mandate as well as global and country needs, to enable an effective response to HCV given the existing market challenges.

Through a portfolio approach, Unitaid has provided a comprehensive response to HCV by addressing a range of access barriers across the commodity value chain for HCV – from limited awareness on HCV and lack of global guidelines and country policies, to addressing the availability and quality of HCV diagnostics and affordability of HCV treatments. The portfolio represents a good example of coherence in terms of funding grants which aimed to address

¹ WHO (2021) Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021. Accountability for the global health sector strategies 2016-2021: actions for impact, available at: <https://www.who.int/publications/i/item/9789240027077>

² Unitaid has other grants on intellectual property rights that also encompass HCV, but were not included in this evaluation.

multiple access barriers whilst also being complementary, with good synergies and coordination in support of overall objectives. Some of the grants sought to target a similar issue from different standpoints (e.g., affordability through licensing by MPP and advocacy by Coalition PLUS), and through this approach the grants have worked effectively in supporting each other (in some cases achieving progress much faster than would have been the case, such as with the advancement of HCV self-testing).

From an equity perspective, whilst the initial portfolio focused on HIV/HCV co-infection, this emphasis was appropriately diluted overtime although with an overall strong focus on key and vulnerable populations. In particular, through the country work, the grants demonstrated the feasibility of activities to address the needs of key and vulnerable populations who have a higher prevalence of HCV, with a particular focus on people who inject drugs (PWID). Our assessment is that the HCV portfolio is one of the most effective disease portfolios within Unitaid in terms of its degree of emphasis on vulnerable and marginalised population groups, such as PWIDs and prisoners.

Several grants faced challenges in implementation, in part due to operational capacity issues with the partners selected, which resulted in several grant reprogrammings and related burden and delays for both Unitaid and grantees. There were multiple timelines extension and budget re-sizings, which were ultimately necessary to enable both grants to achieve their intended outcomes, but viewed as time-consuming for both Unitaid and the grantees.

Effectiveness – progress against access barriers³

Table i.1 presents the evaluation’s overall assessment of the progress made by the HCV portfolio of grants against Unitaid’s access barriers. Progress and key achievements are described in detail below.

Table i.1: Portfolio-level progress against Unitaid’s access barriers

Access barrier	Level of progress
Innovation and availability	Significant
Quality	Good
Affordability - treatments	Good
Affordability - diagnostics	Limited
Demand and adoption	Good
Supply and delivery	Significant

Innovation and availability – significant progress

Pre-2015, there was a lack of quality-assured, cost-effective and simple to use diagnostics, with no prequalified RDTs and no point of care (POC) diagnostics for HCV testing, as a result of which testing was limited and not accessible to the majority of the people in need in most LMICs. Through the FIND grant, the HCV portfolio addressed the diagnostics gap by focussing on R&D of new and innovative HCV tools, increasing the pipeline of HCV diagnostics across the diagnostic pathway, with a specific focus on developing diagnostics that would facilitate decentralized testing and thereby bring diagnosis closer to HCV patients. A number of HCV diagnostic tools have been supported, some of which have already come onto the market, whilst others are in the pipeline. In particular, the evaluation highlights three main achievements:

- FIND demonstrated the feasibility of cAg testing in RDT format and has developed a prototype product which has the potential to decentralise confirmatory testing to point of care and simplify the diagnostic algorithm thereby enabling greater reach of HCV testing. This product has been characterised as a “*gamechanger*” given its significance in terms of enabling: (i) the decentralisation of HCV confirmation to primary health care settings, especially to reach settings targeting high-risk groups; and (ii) the simplification of the diagnostic algorithm from a two-step to a one-step approach, particularly for high-risk groups.

³ Level of progress (i.e. the extent of achievements) has been assessed on a scale of Significant – Good – Limited.

- FIND worked closely with two manufacturers who already had prototypes for HCV self-testing (HCVST) to conduct the studies needed both to show usability and acceptability, based on which WHO is in the process of issuing guidelines on HCV self-testing, thereby unlocking the market for HCV self-testing as well as supporting two HCVST products to come onto the markets in the future.
- FIND supported the development of an HCV test for a near-POC platform - Molbio Truenat - that can be decentralized to the primary health care level at a slightly lower cost than the GeneXpert platform, and has significant potential to become the first true competitor to the GeneXpert platform in the long-run.

Work under the FIND grant has also helped increase the diversity of manufacturers involved in HCV diagnostics, with multiple manufacturers for multiple products thereby fostering competition and potentially lowering prices in the medium-term. The progress made in increasing the HCV diagnostic pipeline has also been possible through the contribution of the WHO Enabler and WHO PQ grants, which highlight the benefits of the portfolio approach and complementarity across grants

Quality – good progress

Prior to 2015 there was a lack of pre-qualified HCV diagnostics and treatments. Unitaid’s investment across the portfolio have led to an increase in the number of HCV diagnostics and treatments receiving pre-qualified status, enabling countries to have better visibility of the quality and performance of the HCV diagnostics and treatment they procure. However, progress against this access barrier was assessed as “good” given that there are still a number of HCV diagnostics which are yet to receive WHO-PQ.

- In terms of **diagnostics**, the number of diagnostics with WHO prequalification grew from one in 2015 to 12 at the end of 2020, with five tests undergoing dossier review and the number of overall manufacturers of HCV PQ products having increased from two in 2016 to ten in 2020. In addition, the FIND grant also worked with manufacturers to stimulate their interest in applying for WHO PQ and CE-mark and has supported data collection for a number of the products developed to facilitate dossier preparation and submission to WHO PQ, which has increased the number of applications.
- In terms of **treatments**, the number of HCV DAAs prequalified has increased from one in 2016 to 20 in 2020.

In the absence of Unitaid’s grant to WHO PQ, stakeholders noted that progress on getting HCV diagnostics and treatment prequalified would have been slower, as generally manufacturers did not prioritise WHO-PQ or CE-mark for their HCV products.

Affordability – good progress for treatments, limited progress for diagnostics

During the initial years of Unitaid’s investments in HCV, DAAs were already available globally. For sofosbuvir (SOF), Gilead first issued a VL in 2014, which enabled 91 LMICs to be supplied by generic manufacturers; however, key middle-income countries (MICs) with significant prevalence of HCV were originally excluded, which meant that countries had to pay tens of thousands of dollars for a full course of treatment.

DAAs have become increasingly more affordable in LMIC countries, in part as a result of Unitaid’s HCV portfolio of grants, which have sought to target affordability from very different standpoints, including:

- MPP through its licensing agreement has enabled a larger territory and faster price declines than would have been possible without the agreement; Unitaid and MPP played a key role by negotiating and obtaining the licensing of daclatasvir (DCV) in 2015, initially covering 112 LMICs where more than 65% of the estimated population of people living with HCV lived. As a result, nearly 1 million treatments have been sold across 34 LMIC countries, while the weighted average price of DCV has fallen from US\$106 in 2016 to below US\$20 in 2020 for countries benefitting from the MPP license.
- Coalition PLUS and its partners have played an important role in facilitating more affordable treatments through advocacy for compulsory licences (CL) and voluntary licences (VL) for DAAs; the issuing of the compulsory licence (CL) in Malaysia being a key example that resulted in far more affordable SOF being available in the

country, which also had indirect implications for other countries. Across all Coalition PLUS countries, prices of key DAAs have fallen significantly over the period the grants have been operating, although in some contexts they continue to be unaffordable for meaningful rollout to take place.

- The MSF grant has also been noted as being a key contributor to facilitating affordability, particularly through announcements of price through its Access Campaign, support to generic manufacturers in being included on innovator VL and for filing patent oppositions in key MICs that have facilitated more affordable access.

Progress against this access barrier was assessed as “good” given that Voluntary Licenses for some HCV treatments were already in place before the Unitaid HCV portfolio and given that one the Malaysia CL for SOF, which was a key achievement of the portfolio, has now expired.

In terms of the affordability of HCV diagnostics, Unitaid’s investments through the FIND and MSF grants demonstrated that patients could be diagnosed and treated using simplified models of care which would lower the overall cost of the diagnostic and treatment pathway. This included removing the need for genotype testing by using pan-genotypic regimens, as well as the reduced need for continuous viral load monitoring during treatment. However, the overall cost of diagnosing HCV patients still remains relatively high and viewed as unaffordable in many countries. Although the FIND grant negotiated some entry prices for HCV diagnostics, prices are not yet low enough and more efforts are needed to make prices of diagnostics affordable in LMICs, particularly for confirmatory tests. Progress against this access barrier was assessed as “limited” primarily given that feedback from country stakeholders indicated that the cost of currently available HCV diagnostics continues to be relatively high. However, views were not unanimous and global stakeholders considered that good progress has been made towards this condition.

Demand and adoption – good progress

Prior to 2015, there was limited roll-out of HCV programmes in countries, which was driven by numerous factors including: limited awareness of HCV as a public health problem in many countries, a limited understanding of HCV prevalence, and in turn a relatively low commitment from governments to establish/ scale-up HCV programmes. There was also limited normative guidance on HCV globally and nationally, as well as limited knowledge of HCV across both key populations (KPs) and the general population.

To address the demand and adoption barrier, the Unitaid HCV portfolio of grants has been relatively unique in its approach of building awareness amongst both policymakers and communities, with the Coalition PLUS grant playing a particularly important role in this regard. Key achievements include:

- Increased awareness among policymakers and communities has been essential for increasing government commitment to HCV, including for marginalised populations, and the Coalition PLUS grant has been critical for ensuring that these commitments have turned into policy developments. In terms of implementation, Unitaid’s HCV portfolio has been important for demonstrating how HCV testing and treatment could be done across a number of countries, particularly for KPs.
- Raising the profile of HCV globally, with Unitaid being one of the few global organisations supporting HCV and through its wide portfolio of investments that operate at the global and multi-country level. This has not only increased the visibility of HCV as a public health problem, but also helped put “*HCV on the map*” in terms of global awareness of the disease and the unique opportunity the world has to eliminate the disease with innovative diagnostics and treatments.
- Made important contributions to evidence generation and normative guidance (through the WHO Enabler grant and the FIND and MSF grants), with previous and forthcoming guidelines updates drawing on Unitaid-funded projects. Importantly, the inclusion of project evidence in WHO guidelines will help to inform testing and treatment strategies for other non-project countries.
- Generating awareness of HCV among KPs, enabling these groups to demand better access to HCV services. In particular, Coalition PLUS and its in-country partners undertook a range of education campaigns, workshops and grassroots activities to generate demand and awareness among key groups, such as PWID.

Although Unitaid's investments have made important contributions for putting in place conditions and tools to facilitate wider demand and adoption, going forward it is expected that the scale up of HCV testing and treatment will remain limited. In the absence of significant investments from larger international donors, domestic financing will need to be in place to ensure HCV programmes are scaled-up.

Supply and delivery – significant progress

The FIND and MSF grants demonstrated the feasibility of decentralised, integrated and simplified models of care in LMICs, generating evidence that high testing and cure rates can be achieved even in resource-limited settings. The grants piloted various models, including:

- Decentralisation: demonstrated the use of RDTs for HCV screening; demonstrated the use of GeneXpert for confirmatory testing at the point of care; demonstrated the feasibility of HCV screening, testing and treatment in non-traditional settings such as ARTs centres, Harm Reduction Sites (HRS), community clinics.
- Simplification: demonstrated feasibility of simplifying algorithms by reducing the number of patient visits and by delivering treatment by training medical doctors and health care workers as opposed to specialised hepatologists; demonstrating the feasibility of simplified care models by removing the need for genotyping; task-shifting and removing the need for specialised hepatologists and removing the need for monitoring.
- Integration: demonstrating the integration of HCV testing with testing for other diseases such as HIV and TB.

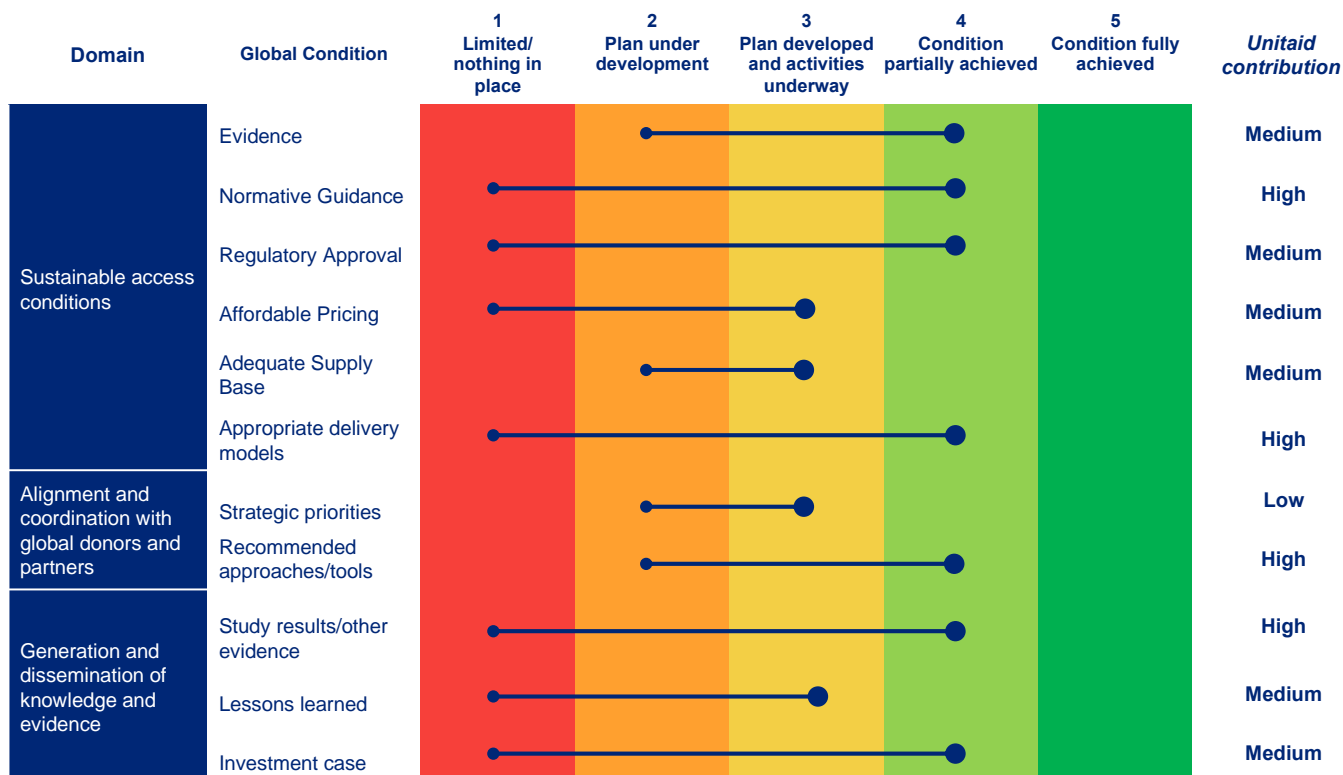
The evidence generated by the FIND and MSF pilot projects has been used and is being used as part of the systematic reviews to support updates to WHO guidelines, thereby informing testing strategies that WHO recommends to countries (including beyond project countries).

Scalability⁴

Through its HCV portfolio, Unitaid has helped put in place some of the conditions and tools for scale-up at the global level, and to some extent at the country level – although further progress is needed to catalyse the HCV market fully to enable large scale scale-up. As part of the evaluation, we have undertaken an assessment of the global conditions for scale-up based on Unitaid's Scalability Framework, which includes 13 conditions organised within three domains: (i) create sustainable access conditions; (ii) align and coordinate with global partners and donors; and (iii) generate and disseminate knowledge and evidence. Figure i.2 provides an overview of progress across the most relevant global conditions. As shown in the figure, Unitaid's investments have made important contributions across the three domains, particularly in the areas of normative guidance and appropriate delivery models, recommended approaches and tools, and study results and other evidence.

Figure i.2: HCV portfolio progress across the key global conditions for scale-up, as per Unitaid's Scalability Framework

⁴ Aspects relating to transition are discussed in the detailed report.



At the country level, the Unitaid’s Scalability Matrix includes 11 conditions to establish country readiness for scale-up. The extent to which Unitaid projects have created these country readiness conditions is variable across the project countries, with good progress having been made on advancing political commitment and community-driven demand, but more limited progress on domestic funding allocations.

Impact

Overall, the impact of the portfolio is significant and comprises many components from new and innovative diagnostics (which will enable more people to be reached) to more affordable DAAs (which will enable patients with HCV to be cured). It is therefore important to highlight that the quantitative impact figures presented in this report only cover a subset of the full public health and economic impact achieved through the portfolio of grants, and should be viewed as ‘case studies’ of the impact of the HCV portfolio, rather than portraying its full impact.

To-date, in terms of measurable impact, the HCV portfolio led directly to avert ~ 4,000 deaths mostly due to the MPP licence for Daclatasvir and, to a lesser extent, the in-country studies conducted by FIND. The scale-up of cAg RDT globally, the scale-up of Molbio Truenat in India and the reduction of genotyping alone could lead to an additional 6,100 deaths averted by 2025 and additional 23,000 deaths averted between 2026 and 2030. These numbers are reflective of the pilot stage of the projects and relevant assumptions with regards to scale-up, as per Unitaid’s role in the global architecture. Furthermore, the HCV portfolio has already achieved significant economic impacts, in particular due to the substantial costs savings that the MPP grant has achieved through the lowering of DCV prices (leading to ~US\$100 million saved by 2020).

Importantly, although not all achievements of the HCV portfolio can be quantified, overall the combination of new HCV diagnostics on the market and the availability of more affordable DAAs, combined with more effective delivery and care models and greater awareness and demand from communities, will have a multiplier effect on impact that will be achieved in the HCV space going forward.

Conclusions and recommendations

To conclude, Unitaid’s work in HCV over the period 2015-21 has been extremely relevant and coherent, and of much added value given limited funding for HCV both globally and in countries. Unitaid has played a significant role in raising the profile and visibility of HCV. Unitaid’s HCV investments have helped to “kick-start” the overall market for

HCV, with a number of transformational achievements across key access barriers. Some of the biggest achievements are with regards to significantly progressing the development of a range of decentralised tools for screening and testing of HCV, which combined with more affordable treatments in LMICs and simplified and decentralised testing, treatment and care models offer countries the means to support their elimination efforts. Furthermore, through its HCV investments, Unitaid has helped put in place some of the conditions for scale-up at the global level, and to some extent at the country level – although further progress is needed to catalyse the HCV market fully to enable large scale scale-up. Financing for HCV remains the critical issue given both the absence of key global donors as well as the limited domestic budgets being allocated to HCV, and it is important that Unitaid and partners continue to build the momentum created through its portfolio of grants to further leverage existing gains. Continuing advocacy and awareness raising efforts with policymakers, specifically to ensure that HCV is “picked-up” in national UHC packages and that governments are aware of the benefits of HCV testing and treatment, for example through further demonstration projects in-countries, will be key to ensure adequate prioritisation and funding allocation of national budgets to HCV programmes.

Key recommendations for consideration include the following:

- **Recognising the multiple funding opportunities for Unitaid, our evaluation strongly recommends to continue funding investments in support of alleviating access barriers and scaling-up HCV programmes in countries in the next Unitaid strategic period 2022-25** – key areas include improving affordability of the care cascade, supporting commitment and implementation/ operationalisation of HCV programmes by country governments (e.g. through investment cases, working with multilateral and regional development banks that provide broader health funding to countries), taking forward work on cAg RDT and HCVST, and continuing emphasis on key populations (especially on marginalised and vulnerable groups such as PWID).
- **Emphasise integration of HCV diagnostics where feasible as well as a broad health systems approach to the HCV cascade of care** (i.e. no verticalization) as a means to also ultimately support affordability and scale-up. While integration is a complex area, at a minimum, Unitaid HCV projects in the future should observe the integration priority in their work.
- Whilst beyond the Unitaid mandate, there are critical issues with regards to **mobilising domestic financing** and having **quality data on HCV burden**, amongst others, that are key to ensuring the impact of Unitaid investments and successful scale-up. **Unitaid should continue with efforts to working with other global partners and countries in this regard.**
- **Consider improvements to the Unitaid model and processes** in terms of (i) developing approaches/ mechanisms to monitor and evaluate portfolio-wide performance and results (i.e. beyond a focus on grant evaluations); (ii) ensuring a more effective balance between upfront project preparation and the need for reprogramming to avoid excessive transaction costs (especially in the initial years of any grant); and (iii) better aligned key processes (such as with regards to M&E, reprogramming, etc.) by ensuring more consideration is given to grant context and value of grants. This means potentially differentiating Unitaid processes by the type or value of grant (i.e. more or detailed processes for larger value grants or more complex grants or high risk grants) with relatively simpler and nimbler approaches for low value grants.

End-of-grant evaluation – FIND HEAD Start grant

The FIND HEAD-Start (Hepatitis C Elimination through Access to Diagnostics) grant was approved by Unitaid in October 2016. The goal of the grant was to contribute to the WHO targets on HCV for 2030: 90% reduction in incidence, 65% reduction in mortality, 80% of patients receiving treatment. The outcome of the grant was the increased availability and adoption of new and existing HCV diagnostic technologies that are quality assured, and a decrease in the cost of the overall package of HCV diagnosis and treatment. The grant had four main outputs, but in terms of relevance and resource allocation, there was a heavy emphasis on Outputs 1 and 2:

- Output 1: Expand the number of technologies available for HCV screening, confirmation, and test of cure that are ready for purchase or use in countries
- Output 2: Prepare the market for the introduction, use and placement of new technologies for HCV screening, confirmation and test of cure, through demonstration studies in Georgia, Malaysia, India (Punjab, New Delhi and Manipur) and Myanmar.
- Output 3: Increase affordability of HCV diagnostics and testing pathway
- Output 4: Generate evidence to support global, regional and national policy change, implementation guidelines and scale-up prepared, disseminated, and shared with key stakeholders

The evaluation framework was structured along four pillars of: (i) relevance and implementation; (ii) effectiveness (including the Unitaid access barriers); (iii) scalability and transition; and (iv) impact, based on a mixed-methods comprising desk-based document review; stakeholder interviews; country case studies; impact modelling; and quantitative data analysis.

The following are key findings from the end-of grant evaluation of the FIND HEAD Start grant.

Relevance and implementation

The focus of the FIND HEAD-Start grant on both R&D (Output 1) and demonstration studies (Output 2) was extremely relevant given that in 2015 the “diagnostic bottleneck” was a key challenge for HCV. The FIND HEAD-Start grant was also appropriately focussed, with the right balance of undertaking clinical and operational studies to inform both research gaps identified in the 2017 WHO HCV testing guidelines as well as the needs of countries in implementing the simplified diagnostic algorithm included in these WHO guidelines. While the initial emphasis of the grant on HCV-HIV co-infected patients was diluted over the years, the grant appropriately maintained an emphasis on high-risk and vulnerable populations. However, despite the appropriate focus of the grant, the FIND HCV team is not considered to have been the best-placed partner to undertake in-country demonstration projects. Whilst FIND’s strength was on research and product development with manufacturers, the FIND HCV team, particularly at the start of the grant, had more limited experience in undertaking demonstration work in countries. As a result, the FIND HCV team took longer to get its country operational capacity up to speed, which led to delays in implementation and slower progress.

Grant reprogrammings were important to streamline the focus of the grant and strengthen linkages across the grant outputs, but required significant time inputs and approval processes and led to substantial delays in timelines and implementation. The reprogrammings focussed on streamlining the activities by prioritising those with the greatest strategic significance, removed three countries where work was not considered feasible to conclude within the timeframes of the grants, extended timelines to account for delay of the COVID-19 pandemic and reduced the budget accordingly. Overall, these reprogrammings were useful in content but challenging in relation to the overall timelines of the grant.

Good synergies were harnessed in FIND’s global-level work, with FIND working closely with the WHO Enabler grant and WHO PQ grant. Synergies at country level were more variable, with FIND and Coalition Plus working together in some countries/ states but not all. Collaboration with national authorities in the country projects was generally strong, thanks to the upfront time FIND invested in building a working relationship with government stakeholders.

Effectiveness – progress against access barriers⁵

Innovation and availability (key access barrier) – significant progress; moderate strength of effect

The FIND HEAD-Start grant has made a significant contribution to the range of products being developed for HCV screening and diagnosis. In particular, the FIND grant contributed to increasing the suite of diagnostic tools in the pipeline, with a specific focus on diagnostics that would facilitate decentralised testing, bringing diagnosis closer to the people who needed it. Table i.2 provides key details of the HCV diagnostics supported by FIND and their significance for the HCV market.

Table i.2: FIND grant achievements in Innovation and Availability

Diagnostic	Achievement	Benefit and implication
cAg RDT	<ul style="list-style-type: none"> Demonstrated the feasibility of cAg testing in RDT format Developed a cAg RDT prototype product which is being taken forward for manufacturing 	<ul style="list-style-type: none"> Characterised as a “gamechanger” Enables (i) decentralisation of HCV confirmation to primary healthcare settings; (ii) simplification of the diagnostic algorithm from a two-step to a one-step approach
HCV self-testing	<ul style="list-style-type: none"> Helped to bring two HCVSTs into the pipeline 	<ul style="list-style-type: none"> HCVST increases decentralisation of HCV screening by bringing the diagnostic directly to the user thereby reaching people that would otherwise not be reached
Near HCV (Molbio) POC test	<ul style="list-style-type: none"> Supported the development of an HCV test for a near-POC platform - Molbio Truenat 	<ul style="list-style-type: none"> Supports decentralisation of HCV confirmatory testing at the primary health care level Significant potential to become the first true competitor to the GeneXpert platform in the long-term
Near HCV (GeneXpert Fingerstick) POC test	<ul style="list-style-type: none"> Supported the development of the Xpert HCV viral load Fingerstick test 	<ul style="list-style-type: none"> Enables near-POC testing using multi-disease GeneXpert platform, supporting integration Simpler to conduct and has higher acceptability particularly amongst PWID
RDTs	<ul style="list-style-type: none"> Generated data and evidence on the performance of a range of HCV RDTs already on the market 	<ul style="list-style-type: none"> Improved the visibility of the quality of available RDTs Stimulated the market of pre-qualified RDTs, as two additional companies have now applied to WHO PQ
Dried Blood Spot	<ul style="list-style-type: none"> Supported the development of DBS protocols for HCV assays 	<ul style="list-style-type: none"> Extends reach of HCV testing to rural populations / test to be run on existing platforms in countries

The FIND grant accelerated the development of HCV diagnostic products by providing incentives to diagnostic manufacturers to invest in HCV; FIND’s work was critical to signal to manufacturers that there is interest for a range of HCV tests and the investments accelerated the development of select HCV diagnostic products.

Quality (key access barrier) – good progress; high strength of effect

Through its work on R&D, the FIND grant has increased the number of HCV diagnostics which have received or applied for quality approvals such as WHO PQ and CE-mark by supporting data collection to facilitate manufacturer’s application to quality-assurance mechanisms. The data collected through FIND’s clinical, feasibility and performance studies of the various diagnostic tools supported by FIND has been used by manufacturers to support the dossier submission of five products through the WHO PQ and CE processes, with another five products planning submission in due course.

Affordability – limited progress; low strength of effect

⁵ The three key access barriers that the FIND grant sought to address were: Innovation and Availability; Quality; and Supply and Delivery; whilst Affordability and Demand and Adoption were addressed more indirectly. Against each access barrier, we provide an assessment of the strength of effect (i.e. the magnitude/ value of the progress given the market context as well extent of attribution to the grant) on a scale of High – Moderate – Low, with overall progress as per the portfolio evaluation.

The FIND HEAD-Start grant has contributed to improved affordability primarily by simplifying the diagnostic pathway. The simplified algorithms introduced in some of FIND's in-country projects enabled a decrease in the price of the diagnostic pathway through the elimination of unnecessary steps, thereby making the diagnostic algorithm more affordable for the government. Furthermore, although FIND, together with other partners, was part of price negotiations with manufacturers to reduce the price of some HCV diagnostics, this was not a core area of the grant and more needs to be done to lower the cost of HCV tests, particularly confirmatory tests, to make them more affordable for countries.

Demand and adoption – good progress; moderate strength of effect

FIND has contributed to improving demand and adoption by generating evidence at the global and country level which will inform revision of WHO guidelines as well as national guidelines. In particular:

- FIND's demonstration projects in countries generated evidence that will be used in the process of updating the WHO guidelines on HCV testing, specifically HCVST.
- The research work and evidence generated by FIND's work in countries is also being used to update national guidelines and protocols on HCV testing, such as in Malaysia, Punjab and Georgia.
- The FIND grant supported the development and publication of an advocacy tool to increase HCV diagnostic literacy especially amongst HCV affected communities.
- FIND disseminated lessons learnt and best practices from its projects globally and in countries to support increased dialogue and focus on HCV diagnostics, although the reach of the dissemination events, beyond HCV-specific events, has been a challenge.

Supply and delivery (key access barrier) – significant progress; moderate strength of effect

Through the in-country projects, the FIND grant has demonstrated the feasibility of decentralized, simplified and integrated approaches that will improve delivery of HCV care in countries. In particular:

- Decentralisation and integration of HCV testing and treatment is feasible in public primary health care facilities and non-traditional settings, such as ART centres, HRS and community health facilities.
- Decentralisation of HCV testing and treatment also reduced LTFU and improved retention across the care cascade by reducing turnaround time between screening and confirmation and enabling more HCV patients to be started on treatment.
- The FIND projects also demonstrated the simplification of the HCV algorithm by reducing the number visits along the testing and treatment pathway without the need for specialised doctors.
- Integration of HCV testing with HIV and TB testing has demonstrated the operational feasibility to increase HCV testing using existing multi-disease platforms without compromising testing targets of other diseases.

Transition and scalability

The extent to which the FIND projects have transitioned, and will continue following project closure, varies by country. Of the project countries and states, three (Punjab, Malaysia and Georgia) out of six have allocated funding for HCV programmes to continue going forward. There is some evidence that improved testing models are being expanded nationally/state-wide, but the lack of domestic and donors financing is a barrier to national scale-up.

FIND's diagnostics R&D work has been transformational in nature and helped unlock a very challenging HCV diagnostics market. The diagnostic pipeline has been much strengthened through the FIND work, and indeed there is a large diagnostic gap in the market to enable scale-up to happen. For example, our impact modelling estimates

that within the five years of grant closure, the introduction of cAg RDT could help to diagnose an additional ~91,000 and help to treat an additional ~74,000 people.⁶

Impact

The evaluation modelled the impact of selected technologies supported by FIND, as such the estimated impact presented only covers a subset of the grant's full public health and economic impact. In particular, the cAg RDT technology has the potential to lead to substantial increases in people being successfully diagnosed and treated, with potentially ~501,267 patients being successfully treated by 2030. As such, cAg RDT would offer one important tool towards reaching the WHO HCV elimination targets. The Molbio Truenat HCV test can lead to an additional 180,000 people being diagnosed in India alone by 2025, by leveraging on the recent expansion of Molbio platforms due to COVID-19. FIND's in-country demonstration studies to date have contributed to 9,563 patients being cured with an additional 3,792 expected to be cured within the next year. Within the next five years, this will lead to 640 averted deaths, 39,924 averted DALYs and around US\$19 million in disease management costs savings.

Conclusion

The FIND grant aimed to increase the availability and adoption of new and existing HCV diagnostic technologies. FIND's work has been critical and transformational in this regard, specially noting the state of the diagnostics market at the start of the grant and where FIND's work has helped progress it today. In this sense, the work of FIND has been catalytic and helped kick-start the diagnostics market for HCV, and while some progress has been made with regards to mobilising the interest of the range of stakeholders involved – country governments, affected communities, manufacturers, etc. – more progress and financial commitment is needed to support larger scale scale-up.

⁶ These figures capture the impact of the reduction in loss-to-follow-up due to decentralisation of confirmatory testing as well as increases in patients covered due to the reduced cost of testing. The estimates can be considered to be conservative as they do not account for potential shifts in testing policies and guidelines that could significantly lead to further scale-up of HCV testing.

End-of-grant evaluation – Coalition PLUS HIV/HCV Drug Affordability Project

The Coalition PLUS HIV/HCV Drug Affordability Project was first approved by Unitaid in July 2015. The overall goal of the project was to contribute to universal access to HCV care in low and middle income countries (up to 2018) and to contribute to 2030 targets for HCV mortality reduction (from 2019 onwards). The outcomes of the project were improved government commitments, national protocols, budgets, and/or policies for HCV treatment access in target countries for hepatitis and HIV co-infected patients (up to 2018) and increased adoption of proactive and affordable HCV care policies aiming at elimination (2019-2020). The grant was largely implemented at the country level working across seven countries – Brazil, Colombia, India, Malaysia, Morocco Thailand and Indonesia (the latter two only up to 2018); Coalition PLUS also undertook a number of international advocacy-related activities to support its country programmes as well as input into international policy dialogue.

The evaluation framework was structured along four pillars of: (i) relevance and implementation; (ii) effectiveness (including the Unitaid access barriers); (iii) scalability and transition; and (iv) impact, based on a mixed-methods comprising desk-based document review; stakeholder interviews; country case studies; impact modelling; and quantitative data analysis.

The following are key findings from the end-of grant evaluation of the Coalition PLUS grant.

Relevance and implementation

Although not a “typical” Unitaid grant given its advocacy focus, the Coalition PLUS grant has been noted as highly relevant in terms of both addressing country needs and Unitaid’s mandate on market dynamics. Despite advocacy not being a key area of intervention for Unitaid, the evaluation found that the grant was much needed in the context of the market dynamics for HCV where low demand and affordability have been key challenges. Indeed, some stakeholders have commented that the value of Unitaid’s market focused investments in HCV would not have been adequate in the absence of the advocacy through the Coalition PLUS grant.

In terms of country level work, the focus of the countries covered within the Coalition PLUS grant has mainly been upper-middle income countries (UMIC). This differs from Unitaid’s typical focus across its portfolio, which is on countries at lower income levels. But given the issuance of VLs from Gilead and BMS for their DAAs, significant barriers to affordable treatments were reduced in LICs ahead of the grant being initiated, so the focus of the grant on UMICs was more appropriate. Within countries, Coalition PLUS selected highly relevant local partners, with many being well respected and highly regarded in their respective country contexts. The mixture of supporting organisations with direct relationships with government and those with close contacts with HCV communities has meant that in-country organisations have been able to consider both perspectives in their advocacy work. At the country level, Coalition PLUS has demonstrated its effectiveness in engaging and integrating its work with that of national authorities and implementing partners. National stakeholders noted that local Coalition PLUS partners have played an important role in taking forward HCV programmes, including the development of national testing and treatment guidelines and training national healthcare workers on approaches for testing and treating patients.

The Coalition PLUS grant is arguably one of the most effective grants for considering the views and issues facing marginalised groups in Unitaid’s portfolio. The equity focus of this grants on vulnerable and marginalised populations has drawn on Coalition PLUS’ extensive experience and network of CSOs that have long advocated for the rights of marginalised groups in the context of HIV, and through this grant has been able to learn lessons on what has worked in these contexts while tailoring the focus for the key populations in HCV.

One key area where the Coalition PLUS grant has experienced challenges throughout the grant has been on the timeliness of achieving results. External factors have mostly influenced this, including changes of governments and key staff within ministries, but the long start-up period for the grant was also a contributory factor. There have been numerous reprogrammings and extensions to the grant over its lifetime, which have taken considerable time and effort from Unitaid and Coalition PLUS staff. This mix of reprogrammings and extensions have mostly been appropriate, and reflect the changing nature of the environments in which the grant has operated in and the fact that advocacy takes time and efforts. But even with course correction and extensions, the level of ambition within the grant has often been above what was feasible in given timeframes.

Effectiveness – progress against access barriers⁷

The Coalition PLUS HIV/HCV Drug Affordability Project aimed to address two of the five access barriers: affordability and demand and adoption.

Affordability – good progress; moderate strength of effect

Coalition PLUS and its partners have been important in facilitating more affordable treatments. As part of its support to project countries, Coalition PLUS partnered with key civil society organisations (CSOs) to advocate for more affordable treatments in countries. In many countries, this involved a multi-pronged approach of working with CSOs focused on different areas. Malaysia is a key example of the advocacy work of Coalition PLUS in facilitating more affordable prices. In 2017, Malaysia took a major step towards obtaining more affordable DAAs when it issued a compulsory licence (CL), the first country in the world to issue a CL for HCV treatments, which enabled the country to be able to access generic treatments. Up to the end of 2020, Malaysia was able to access SOF for as little as US\$80. For other countries, particularly Brazil and Colombia, prices have fallen significantly, with advocacy by local partners noted as being key contributors to this. Across all Coalition PLUS countries supported by Unitaid's investments, prices of key DAAs have fallen over the period that the grants have been operating, although in some contexts they continue to be unaffordable for meaningful rollout to take place.

Demand and adoption – good progress; moderate strength of effect

The main achievement of Coalition PLUS' interventions across countries has been the role it has had in giving communities a voice at the national and global level. At the outset of the Coalition PLUS grant, despite countries having national plans and policies in place to address HCV, awareness and commitment to HCV was low, the rollout of testing and treatment was very limited and programmes were only being implemented on a small scale. At the national and state policy level, Coalition PLUS country partners have played an important role in supporting updates to national elimination policies and guidelines. Key examples of this include:

- In Malaysia, Coalition PLUS partners MTAAG+ and MAC have undertaken important outreach activities for PLHCV to ensure they are well-linked to national health services, acting as a key link that may have otherwise not been in place in the absence of Unitaid's funding
- In India, Coalition PLUS partners DNP+ and CoNE have been instrumental in enabling key populations, especially PWID, in accessing testing, treatment and care under the NVHCP. This support has been critical for PWID who are more likely not to seek health services and more likely to be lost to follow-up.
- In Morocco, advocacy by ALCS, Coalition PLUS's partner contributed to convincing the MoH to include PWID in the government list of key populations, which has resulted in PWID now being able to access free healthcare, including HCV services, through the government health insurance scheme RAMED.
- In Brazil, members of local partner network organisation FOASP have integrated HCV into their routine HIV awareness raising activities with KPs and communities and assist in referral to health care facilities.
- In Colombia, advocacy by local partner IFARMA convinced the government that HCV is a public health issue, that the MoH should also centrally procure DAAs for populations covered by the subsidised health insurance regime targeting the informal sector to achieve lower prices.

Despite some progress, wider rollout of HCV services has not been fully implemented across any of the countries. Progress between countries has varied considerably, with implementation of services being further along in Malaysia and India. But even for these countries, stakeholders noted that considerable momentum is needed to

⁷ Against each access barrier, we provide an assessment of the strength of effect (i.e. the magnitude/ value of the progress given the market context as well extent of attribution to the grant) on a scale of High – Moderate – Low, with overall progress as per the portfolio evaluation.

ensure these countries are truly on the path towards HCV elimination. Overall, progress remains fragile in many instances, and has been severely hampered by the COVID-19 pandemic.

Transition and scalability

The critical challenges to the scalability of national HCV responses are partly related to high prices of treatment, which means that governments cannot afford to expand treatment services to the scale required to address the WHO 2030 elimination targets. The evaluation noted that although good progress has been made towards increasing the affordability of HCV treatments, governments are still not prioritizing HCV due to a number of factors beyond high treatment costs, such as lack of political will. Rollout of HCV testing and treatment across almost all Coalition PLUS countries needs to be scaled up significantly in order for countries to move towards elimination, and this will require political commitment from governments to do so given the absence of large-scale external funding.

Impact

There are clear examples of how the Coalition PLUS grant has been able to achieve impact, particularly through its role in facilitating more affordable treatment as well as direct support for ensuring that people with HCV are able to access testing and treatment services. For economic impacts, the main impact of the Coalition PLUS grant is likely to have been the cost savings brought about by the lower cost of DAAs, particularly in Malaysia. Given the upstream nature of the Coalition PLUS grant, it is not possible to quantify and attribute the public health and economic impact (in terms of deaths averted and economic savings) of the grant in the countries it has supported. The Coalition PLUS grant has also had an equity enhancing impact in terms of offering communities and CSOs in-country a voice to advocate for improved access to testing and treatment of HCV, which is likely to have a long-term effect in the countries where the grant has operated.

Conclusion

Overall, the Coalition PLUS grant has been vital for giving communities and CSOs a voice for advocating for improved access to HCV treatment in the countries that have been supported. The support Coalition PLUS and grantees have given to these countries has been essential for ensuring that national programmes have considered the needs of key and marginalised populations, particularly PWID and prisoners, where the work of in-country partners through its pilot programmes as well as direct engagements with government has ensured these groups are represented in government elimination plans.

PART A: PORTFOLIO EVALUATION

1. INTRODUCTION

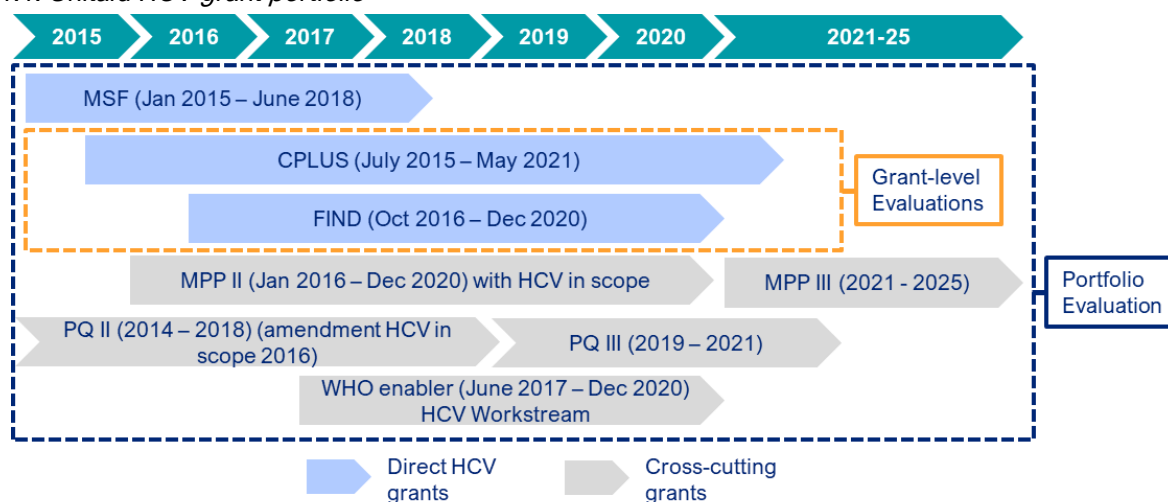
This section provides a background and summary of the Unitaid HCV portfolio (Section 1.1), evaluation objectives (Section 1.2), and evaluation framework and methodology (Section 1.3).

1.1. BACKGROUND AND SUMMARY OF HCV PORTFOLIO

In 2021, the World Health Organization (WHO) estimated that there were 58 million people living with chronic HCV, and in 2019, 290,000 people died from HCV-infection related causes.⁸ Low and Middle Income Countries (LMICs) have faced significant barriers to access HCV diagnosis and treatment. Diagnosis was complex and expensive, in part because it required the identification of a patient’s HCV genotype. Treatment was also expensive initially, had low efficacy, and posed several side-effects. However, since 2014, with the advent of Direct Acting Antivirals (DAAs), HCV treatment has become faster, more affordable and more effective, with few side-effects. Additionally, the development of a pan-genotypic regimen in 2015 has obviated the need for genotyping, greatly simplifying the diagnostic process and treatment decision-making. However, despite the removal of key technological barriers, access to HCV treatment remains limited. Generic DAAs remain unavailable in some LMICs, key populations are not adequately reached, and populations remain unaware of HCV transmission, diagnosis and treatment.

In light of the opportunities for elimination brought about by DAAs, coupled with the high levels of HIV/HCV co-infection, Unitaid identified HCV as an area of work in 2013 – considering the removal of technological barriers as an unprecedented opportunity to contribute to the elimination of HCV by addressing barriers to access. By removing these access barriers, Unitaid aimed to catalyse the market for HCV diagnosis and treatment, creating the tools and conditions to enable and facilitate scale-up by other actors. Figure 1.1 presents the Unitaid HCV portfolio.

Figure 1.1: Unitaid HCV grant portfolio



In particular, Unitaid awarded three direct project grants in 2015 and 2016 which were focused solely on HCV and represent funding of over US\$45 million for interventions across 14 countries.

1. **Coalition PLUS, HIV/HCV Drug Affordability Project: 2015-21 (US\$10.1 million):** The project seeks to increase the uptake of affordable HCV programmes, with a view to progress countries to consider elimination. The project also operates internationally to advocate for greater investment and prioritisation of HCV elimination. Countries covered include India, Malaysia, Colombia, Brazil and Morocco, in addition to Indonesia and Thailand where implementation was supported from mid-July 2015 to end 2018.
2. **FIND, Hepatitis C Elimination through Access to Diagnostics (HEAD Start): 2016-20 (US\$27.4 million):** The project supports the development of new, simpler HCV diagnostic products on a global scale. It has also operated at the country level through implementing pilot programmes that provide evidence for reducing the complexity

⁸ WHO (2021) Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021. Accountability for the global health sector strategies 2016-2021: actions for impact, available at: <https://www.who.int/publications/i/item/9789240027077>

and cost of HCV diagnosis and treatment, and has carried out activities in Georgia, India, Myanmar and Malaysia as part of this. In particular, the project aims to develop simpler, cost-effective screening and testing algorithms (including for HIV/HCV co-infected persons) in the target countries.

3. **Médecins Sans Frontières (MSF), Ensuring access to HCV treatment revolution for HCV/HIV co-infected patients in low and middle-income countries: 2015-18 (US\$8 million):** The MSF project operated in seven LMICs across Africa and Asia, and aimed to demonstrate the feasibility of HCV treatment in resource limited settings, develop HCV care models that are simple and affordable, generate evidence on their effectiveness and cost-effectiveness and conduct advocacy to promote uptake at national and global levels.

In addition, Unitaid has the following cross-cutting investments that support a range of activities in the HCV space (alongside other diseases):

4. **Medicines Patent Pool (MPP): (since 2010, total of US\$94.6 million):** The MPP aims to facilitate rapid access to medicines for HIV in LMICs. In 2015, MPP extended its mandate to include TB and HCV. MPP aimed to expand production and supply of quality generic HCV medicines, by negotiating voluntary licences (VLs), broadening the geographical scope of existing VLs, and establishing a sub-licensing system to encourage competition in the market for generic HCV medicines. Unitaid approved a third grant for the MPP in November 2020, pledging a further US\$34.3 million to enable its work in negotiating VLs and expanding production for HIV, TB and HCV.⁹
5. **WHO Prequalification (PQ): (since 2006, total of US\$157 million):** The WHO PQ scheme aims to establish global technical specifications, including for HCV, and evaluate the quality of diagnostics and medicines, including HCV diagnostics and medicines.
6. **WHO Enabler: 2017-20 (US\$2.4 million)¹⁰:** The WHO Enabler grant provides technical support to Unitaid HCV investments, and uses its global convening power to encourage the development of HCV guidelines, develop estimates of the disease burden, documentation of national scale-up for HCV programmes, provide technical support to countries, and support prequalification.

Other grants working on intellectual property rights also work, among others, on HCV, but were not included in this evaluation.

1.2. EVALUATION SCOPE AND OBJECTIVES

Figure 1.2 sets out the overall evaluation scope and objectives.

⁹ Unitaid (2020), Unitaid reaffirms its support to the Medicines Patent Pool, a key player for equitable access to life-saving medicines. Available at: <https://unitaid.org/news-blog/unitaid-reaffirms-its-support-to-the-medicines-patent-pool-a-key-player-for-equitable-access-to-life-saving-medicines/#en>.

¹⁰ This amount, which includes Programme Support Costs, is that of the HCV workstream of the WHO Enabler grant. Unitaid are in the process of negotiating an extension to the WHO Enabler to December 2021.

Figure 1.2: Evaluation scope and objectives

Main evaluation questions:	
(i) To what extent has Unitaid established an environment to catalyse the HCV diagnostic and treatment markets? (ii) Have Unitaid investments contributed to creating conditions for scale-up, and what is the potential for scale-up?	
Grant level evaluation	Portfolio level evaluation
<ul style="list-style-type: none"> Assessment of the relevance, coherence, implementation, effectiveness, sustainability, scalability, impact and lessons learnt of two grants: <ul style="list-style-type: none"> FIND (2016-2020) Coalition PLUS (2015-2021) 	<ul style="list-style-type: none"> Assessment of the effectiveness and catalytic impact of Unitaid's HCV investments Analysis of how the portfolio contributed to enabling conditions for scale-up High-level review of alignment of portfolio to global needs, Unitaid Strategy and coherence between grants

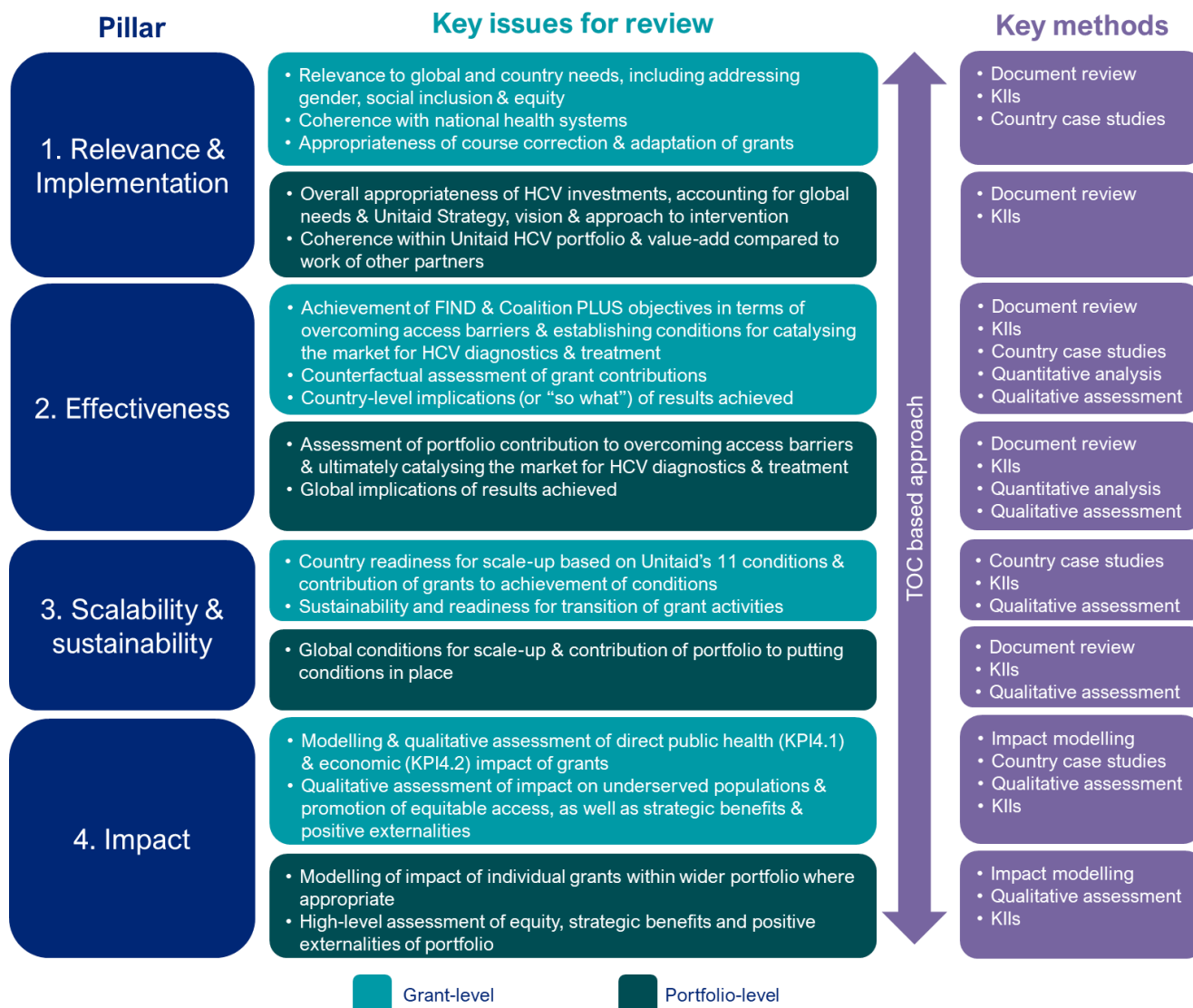
The scope of work involves a consideration of the Organisation for Economic Co-operation and Development (OECD) Development Assistance Committee (DAC) evaluation criteria with regards to a review of each of the two grants, alongside a consideration of performance against Unitaid's Key Performance Indicators (KPIs) and Scalability Framework. More details are included in the evaluation Terms of Reference included as Appendix H.

1.3. EVALUATION FRAMEWORK AND METHODOLOGY

Evaluation framework

Figure 1.3 sets out the evaluation framework which is based on the evaluation objectives. The framework is structured as four pillars (relevance and implementation, effectiveness, scalability and transition, and impact), highlighting key review aspects for the portfolio-level review and the two grant-level evaluations. The overall methodology follows a theory-of-change based approach (see Section 2), alongside a mixed methods approach.

Figure 1.3: Evaluation framework



Methods and limitations

This is a mixed-methods review comprising the following methods:

- **Desk-based document review** encompassing project plans, logframes, annual reports, grant brief analyses, evaluation reports and presentations for the grant reviews, and Unitaaid strategic narratives, landscape reports, WHO guidelines and reports and selected relevant academic and grey literature for the portfolio review. Appendix A includes the bibliography.
- **Stakeholder interviews** with FIND and Coalition PLUS staff, representatives from the lead grantees of the portfolio, manufacturers, potential donors, staff at the Unitaaid Secretariat, wider global stakeholders such as US Centre for Disease Control (US CDC), WHO, Clinton Health Access Initiative (CHAI), as well as country-level stakeholders as part of the country case studies. These interviews were conducted remotely due to COVID-19 travel restrictions and were supported by tailored interview guides. Appendices B and C provides the consultee list and interview guides.
- **Country case studies**, including three deep-dive studies for Georgia, India and Malaysia (India and Malaysia were chosen due to the presence of both FIND and Coalition PLUS projects being implemented in-country; Georgia was chosen to ensure geographical diversity). This involved a desk review of country level documents and data, stakeholder interviews, quantitative analysis of the data and achievements of the grants, and a scalability matrix to assess the extent to which the grants have contributed to establishing the conditions and tools for scale-up for HCV diagnosis and treatment in each country. In addition, we conducted four high-level case studies for

Brazil, Colombia, Myanmar and Morocco. This involved a review of grant documentation, with a specific focus on results, and stakeholder consultations.

- **Impact modelling**, implementing a “bottom-up aggregate approach” to capture the public health and economic impact across the HCV portfolio. This included: (i) for the FIND grant, the impact of potential new technologies (cAg RDT and Molbio Truenat HCV test) and the impact from in-country FIND studies under Output 2; (ii) for the MSF and WHO Enabler grants, the potential impact the grants had in speeding up the acceptance of sofosbuvir/daclatasvir (SOF/DCV) as a pan-genotypic treatment, and the WHO recommendation to move away from genotyping; and (iii) for the MPP grant, the benefits from voluntary licencing on generic competition and subsequent price reductions.¹¹ The first three workstreams were addressed with Excel-based impact models. We have only quantified and reported impact estimates when we consider the input assumptions and underlying data sufficient to model robust results, due to data limitations in the HCV space. A detailed approach to the impact modelling is presented in Appendix D.
- **Quantitative data analysis** of the extent to which market barriers have been overcome. This includes an analysis of: (i) price reductions achieved; (ii) timeframe and number of quality assured products; and (iii) number of newly developed HCV products.
- **Workshop on preliminary findings** with select stakeholders, including the grantees as well as other key stakeholders in the HCV space, to discuss preliminary findings with regard to the progress made against the access barriers and scalability of HCV programmes at the global level. Appendix I provides the list of participants in the workshop.

There are several potential key limitations of the above-noted evaluation methods, presented in Table 1.1 alongside our proposed mitigating measures that have been adopted.

Table 1.1: Key limitations and mitigating measures

Limitations	Mitigating measures
Challenges with attribution of impact, recognising the role of multiple factors.	Theory of change based approach which outlines impact pathways, stakeholder consultations.
Data limitations impacting modelling including lack of: (i) historic data on diagnostic and treatments by country; (ii) full costs of diagnosis and treatment of HCV, including health system costs; (iii) data across the diagnosis cascade such as loss-to-follow-up by stage; and (iv) projections on the diagnostic and treatment markets by products. ¹²	Triangulation of data sources, sensitivity testing and scenario development, qualitative assessment
Consultation limitations including respondent bias, staff turnover and possible political sensitivities.	Triangulation across data sources, expert interview techniques and rating by strength of evidence
Limited insight from the remote country assessments due to COVID-19, given the more limited scope of key respondent enquiry	Use of in-country associates where possible, pre-testing of interview guides.

Assessment frameworks

Several assessment frameworks have been employed in this evaluation:





Robustness framework

Findings have been assessed for robustness based on both the quantity (i.e. triangulation) and quality of evidence, as per the scale outlined in Table 1.2 below.

¹¹ A data review, and resulting justification for our approach to impact modelling is presented in our Inception Report.

¹² Impact modelling related limitations are discussed in more detail in Appendix D.

Table 1.2: Robustness rating for findings

Rating	Strength of evidence
Strong 	<ul style="list-style-type: none"> The finding is supported by data and/or documentation which is categorised as being of good quality by the evaluators; and The finding is supported by majority of consultations, with relevant consultee base for specific issues at hand.
Moderate 	<ul style="list-style-type: none"> The finding is supported by majority of the data and /or documentation with a mix of good and poor quality; and/or The finding is supported by majority of the consultation responses.
Limited 	<ul style="list-style-type: none"> The finding is supported by some data and/or documentation which is categorised as being of poor quality; or The finding is supported by some consultations as well as a few sources being used for comparison (i.e. documentation).
Poor 	<ul style="list-style-type: none"> The finding is supported by various data and/or documents of poor quality; or The finding is supported by some/few reports only and not by any of the data and/or documents being used for comparison; or The finding is supported only by a few consultations or contradictory consultations.

Assessment framework for the access barriers

We have employed two further scales to assess progress and achievements on the Unitaid-defined access barriers:

- Level of progress (i.e. the extent of achievements) on a scale of Significant – Good – Limited; and
- Strength of effect (i.e. the magnitude/ value of the progress given the market context as well extent of attribution to the grant) on a scale of High – Moderate – Low.

This is slightly different to the various scales employed by Unitaid for their Scalability Matrix, given what we view useful in terms of assessing the access barriers. It is also different from Unitaid’s scale used in their KPI framework.

Assessment framework for scalability

There are three further scales employed here:

- Importance of condition to the assessment of scalability as a whole – along a scale of High – Medium – Low – Not relevant
- Status rating – on a scale of one (limited/nothing in place) to 5 (condition fully achieved)
- Strength of contribution – using the following scale – High – Medium – Low – None

2. PORTFOLIO-LEVEL THEORY OF CHANGE

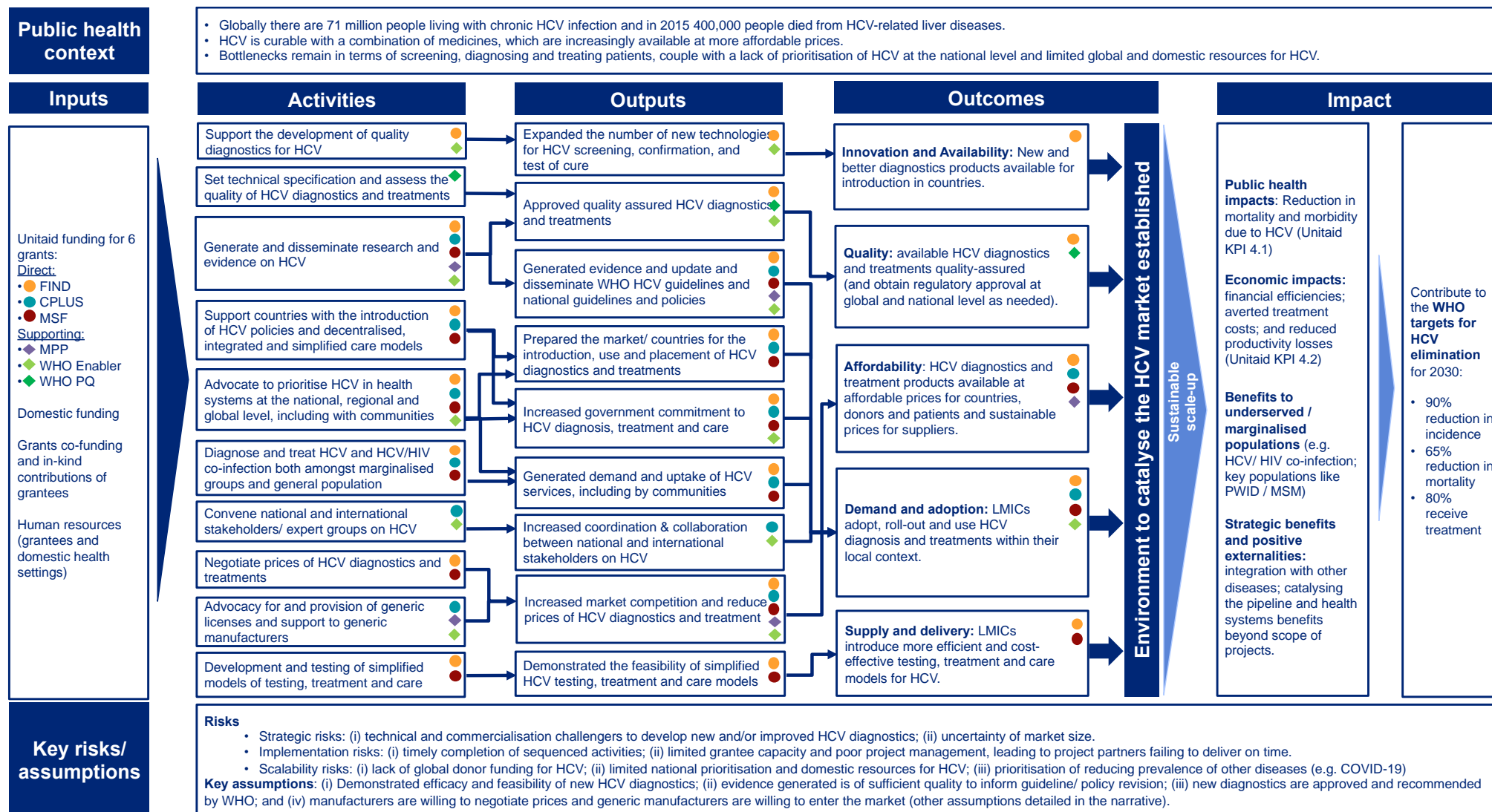
The evaluation adopts a Theory of Change (ToC) based approach, which means that it is grounded on a theory of what the different grant activities of Unitaid's investments in HCV were seeking to achieve, considering the pathways to impact. Specifically, the ToC elaborates the conceptual pathways along the results chain through which the HCV grants have aimed to address the access barriers, whilst noting the key assumptions and risks. Thus, the main objective of the ToC is to serve as a base for understanding the contribution of Unitaid's investments in HCV to supporting the 2030 goal of HCV elimination by analysing what Unitaid set out to achieve through its investments and what has actually happened in practice. As such, there is also a clear linkage between the ToC and our evaluation framework.¹³

The ToC was developed in the Inception Phase of the evaluation, retrospective of Unitaid's investments in the HCV portfolio between 2015 and 2020. It was developed based on the review of grant documents, especially project plans and logframes, and initial consultations with Unitaid and grantees, and was updated based on feedback received by Unitaid.

The ToC maps the main inputs, activities and outputs of Unitaid HCV portfolio grants and the pathways leading to the desired outcomes, i.e. the access barriers which the projects have sought to address to overcome these above-mentioned challenges. By overcoming these access barriers, Unitaid's overall objective was to establish an environment to catalyse the market for HCV diagnostics and treatments. This was envisaged as a precursor to the sustainable scale-up by countries and partners, which would lead to the impact articulated through Unitaid's KPIs and the vision of the HCV portfolio is to contribute to the WHO's 2030 elimination targets. Figure 2.1 depicts the ToC.

¹³ Our evaluation framework is detailed in the Inception Report.

Figure 2.1: Theory of Change of Unitaid HCV portfolio 2015-2020 (dark blue line arrows indicate processes directly influenced by Unitaid while light blue block arrows indicate areas where Unitaid has a less direct influence, given these are further down the results chain and impacted by multiple factors beyond Unitaid grants)



The ToC illustrates the pathways through which the inputs, activities and outputs have sought to address each outcome barrier. Some grants have had a direct role in addressing the access barriers, with other grants playing a supportive role, as follows:

- **Innovation and availability:** by supporting the development of quality diagnostics for HCV the FIND grant sought to expand the number of new technologies for HCV screening, confirmation and test of cure with the aim of having new/improved diagnostics available for introduction in countries, with the WHO Enabler grant providing support in terms of guiding research development and protocol review.
- **Quality:** the WHO PQ grant set quality standards and evaluated regulatory submissions with the aim of having HCV diagnostics and treatments which are quality-assured by producing evidence related to the feasibility, performance and impact of HCV diagnostics; the FIND grant sought to generate evidence and data to enable submission for regulatory approvals, update WHO guidelines and national policies on HCV; and the WHO Enabler grant played a supportive role in facilitating high-quality research to inform product approval and use.
- **Affordability:** by providing generic licences and support to generic manufacturers and advocating for affordable diagnostics and treatments, four grants (FIND, Coalition PLUS, MSF, MPP) have sought to reduce prices and increase generic market competition with the aim of having HCV diagnostics and treatment that are affordable for countries, donors and patients and sustainable prices for suppliers, with a supportive role played by the WHO Enabler grant.
- **Demand and adoption:** a range of grants have sought to prepare countries for the introduction, use and placement of HCV diagnostics and treatments by:
 - advocating to prioritise HCV diagnosis, treatment and care in health systems, including through decentralization, integration and simplification, and at the community level to increase government commitment to HCV in three grants (FIND, Coalition PLUS, MSF and WHO Enabler);
 - diagnosing and treating HCV and HCV/HIV co-infected patients to generate demand and uptake of HCV services in three grants (FIND, Coalition PLUS and MSF); and
 - bringing together national and international stakeholders on HCV to increase coordination and collaboration on HCV in two grants (Coalition PLUS and WHO Enabler).
- **Supply and delivery:** by demonstrating more efficient and cost-effective HCV testing and treatment models for HCV, two grants (FIND and MSF) have sought to support countries with the introduction of decentralised, integrated and simplified HCV policies and care models.

Although the grants in the HCV portfolio are separate/ standalone, they have undertaken complementary activities and are highly interconnected at the portfolio level, as visible by the various arrows connecting the results chain. The ToC thereby lays out the intended results for all HCV grants enabling us to assess performance at each step and to provide an assessment of the overall contribution of the Unitaid HCV portfolio.

We have also identified a number of risks (e.g. strategic, implementation and scalability risks) and cross-cutting assumptions underpinning the ToC (i.e. the conditions that need to be in place for the grants to deliver the expected results, but which are outside the control of the grant). Table 2.1 below focuses on project specific assumptions, which are in addition to the standard assumptions such as political stability in country and political willingness.

Table 2.1: HCV portfolio cross-cutting assumptions

Access barrier	Assumption
Innovation and availability	<ul style="list-style-type: none"> ● Clinical trials demonstrate efficacy and feasibility of new HCV diagnostics (FIND) ● Sufficient interest and engagement from manufacturers to bring new diagnostics to market (FIND)
Quality	<ul style="list-style-type: none"> ● Manufacturer interest in taking forward their product for prequalification (FIND/WHO PQ) ● New diagnostics are approved and recommended by WHO (WHO PQ)

Access barrier	Assumption
Affordability	<ul style="list-style-type: none"> • Manufacturers willingness to negotiate prices and issue licences (FIND/Coalition PLUS/MSF) • Generic companies are willing to enter the market once IP barriers have been removed (MPP)
Demand and adoption	<ul style="list-style-type: none"> • Willingness to expand fiscal space/ funding for HCV (FIND/ Coalition PLUS/ MSF) • Willingness of manufacturers to apply for registration in countries (FIND/MSF/ MPP) • Willingness of countries to adopt the new diagnostics (FIND/Coalition PLUS/MSF) • Site readiness and patient willingness to participate in the projects/studies (FIND/ MSF/Coalition PLUS) • Evidence generated is of sufficient quality to inform guideline/ policy revision (FIND/Coalition PLUS/MSF/ WHO Enabler)
Supply and delivery	<ul style="list-style-type: none"> • HCV testing and treatment delivery systems demonstrate efficiency and cost-effectiveness (FIND/ MSF)

3. PORTFOLIO REVIEW

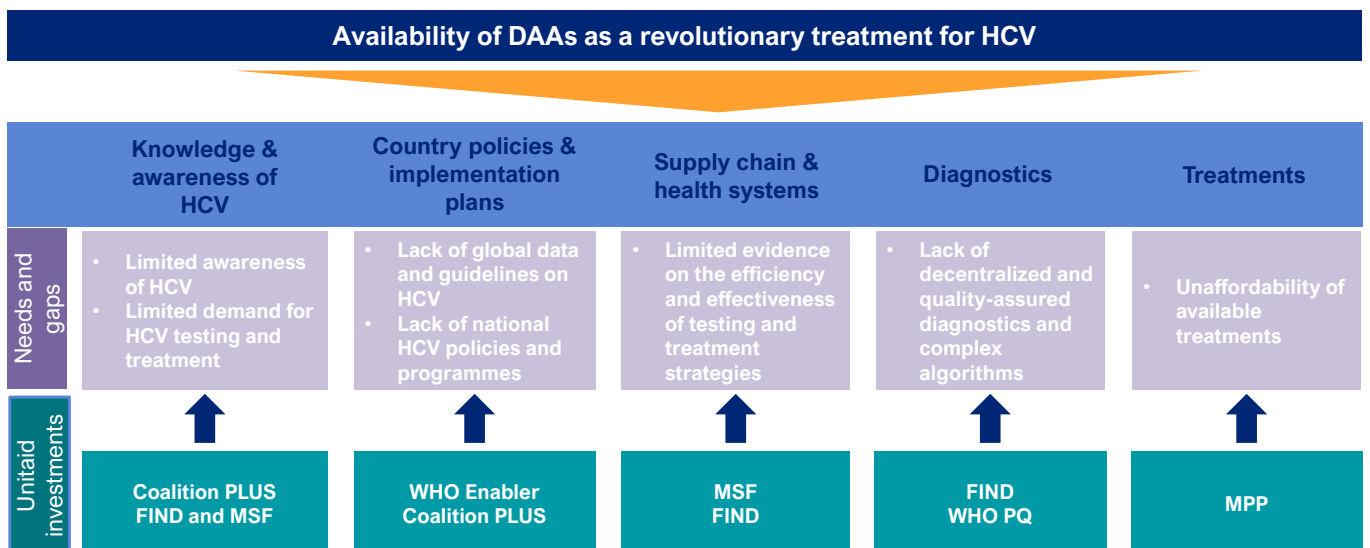
This section presents CEPA’s review of the Unitaid HCV portfolio, structured as per the four pillars of the evaluation on relevance and implementation (Section 3.1), effectiveness (Section 3.2), scalability and transition (Section 3.3) and impact (Section 3.4).

3.1. RELEVANCE & IMPLEMENTATION

Key findings	Strength of evidence
<p>Unitaid’s HCV portfolio has been highly relevant, appropriate and aligned with its mandate as well as global and country needs, to enable an effective response to HCV given the existing market challenges.</p> <p>The HCV portfolio represents a good example of coherence in terms of “joint-up” and complementary grants, with good synergies and coordination across grantees in support of overall objectives.</p> <p>The initial focus on HIV/HCV co-infection was appropriately diluted overtime, but importantly, the grants maintained an emphasis on key and vulnerable populations.</p> <p>The portfolio faced significant implementation challenges, in part due to operational capacity issues with the partners selected, which resulted in several grant reprogrammings and related burden and delays.</p>	

Unitaid’s HCV portfolio has been highly relevant, appropriate and aligned with its mandate as well as global and country needs, to enable an effective response to HCV given the existing market challenges. In 2015, the availability of DAAs that could cure HCV offered an opportunity to support the global and country response to HCV; however, despite the availability of DAAs, these revolutionary treatments were out of reach for the majority of LMICs. In its Strategic Narrative on Hepatitis C in the Context of Co-infection with HIV, Unitaid noted that “*these new treatments are not reaching people due to their high costs and because services to diagnose and treat HCV are limited or non-existent in many countries*”.¹⁴ In this context, Unitaid has developed a highly appropriate portfolio of investments in HCV that have been well targeted to support the range of market barriers across the product value chain for HCV, as demonstrated in Figure 3.1.

Figure 3.1: Unitaid’s HCV portfolio in relation to key gaps



¹⁴ Unitaid (2015), Strategic Narrative – Hepatitis C in the context of co-infection with HIV, Executive Board Meeting.

The portfolio is very much aligned with Unitaids' mandate to support the three diseases and related co-infections as well as target access barriers. The value add of the Unitaids HCV portfolio is further highlighted by the limited engagement of other donors and organisations in HCV.

The HCV portfolio represents a good example of coherence in terms of “joint-up” and complementary grants, with good synergies and coordination across grantees in support of overall objectives. A review of the Unitaids HCV portfolio indicates a holistic/ joint-up approach in terms of the suite of grants targeting the range of access barriers, with significant complementarities and minimal duplication. For example, the Coalition PLUS grant uses an advocacy-based approach to tackle affordability issues, while the MPP has a more direct approach through licensing of patents. Together, the two investments seek to target a similar issue from very different standpoints and thereby impact. The WHO Enabler grant is also a useful investment to support grantees across the portfolio.

Further, the grants have worked effectively in supporting each other, in particular:

- At the global level, there has been close collaboration between the WHO Enabler grant, the WHO PQ grant and the FIND grant through quarterly meetings and clear communication channels. This collaboration enabled FIND to work closely with the Global Hepatitis Programme at WHO on the data requirements for WHO guidelines on HCV self-testing (HCVST) and with WHO PQ on the technical specifications for HCVST, resulting in the Guidelines Development Group meeting on HCVST and an upcoming recommendation on HCVST, an output which would have been slower to be achieved in the absence of the collaboration and synergies across the three grants. The FIND grant also worked closely with: (i) the Global Hepatitis Programme through the WHO Enabler grant to ensure alignment of data needs for WHO guidelines systematic reviews; and (ii) with the WHO PQ on data requirements for the dossier submissions of relevant diagnostics.
- At the country-level, there have been some examples of successful collaboration between the FIND and Coalition PLUS grants, including alignment to government on their advocacy efforts; for example, in New Delhi, India, FIND supported diagnostic literacy workshops for representatives of communities which empowered them and provided them with the knowledge and tools to support advocacy efforts both for policy dialogue on HCV and demand generation for HCV services which were being supported by Coalition PLUS. In Malaysia, FIND collaborated with MAC and the Malaysia MoH to implement a national screening programme as part of World Hepatitis Day 2019, and with the Positive Malaysian Treatment Access and Advocacy Group (MTAAG+) to deliver an HCV diagnostics advocacy workshop in 2019. However, coordination was more limited in other cases such as in Manipur where both FIND and Coalition PLUS worked but did not initially collaborate due to issues related to selection of implementing partners and limited communication.

The initial focus on HIV/HCV co-infection was appropriately diluted overtime, but importantly, the grants maintained an emphasis on key and vulnerable populations. Unitaids' HCV portfolio of grants was the first broadening of scope for the organisation beyond the three diseases (HIV, TB and malaria). The inclusion of the HCV portfolio was initially justified on the basis of the prevalence of HCV co-infection with HIV and the fact that DAAs offered an opportunity to help HIV/HCV co-infected patients who are more vulnerable given their faster progression to the more serious stages of HCV infection.¹⁵ However, the MSF grant found lower-than-expected HIV/HCV co-infection rates and also raised ethical questions about not supporting the treatment of mono-infected HCV and the future risk of re-infection through mono-infected partners, thereby “*highlighting the limitations of focussing on co-infection as a way to catalyse HCV care in the broader population*”.¹⁶ Further, any market shaping impact would be limited by only focussing on the smaller population of HIV/HCV co-infected patients. As a result, gradually, all of the direct HCV grants in the portfolio were re-purposed to have a broader scope (although we understand this was a challenging process given Unitaids' mandate). All grants continued to undertake some work on HIV/HCV co-infection¹⁷, and importantly expanded to emphasise a range of key and vulnerable populations who have a higher prevalence of HCV, including people who inject drugs (PWID), gay men and other men who have sex with men

¹⁵ Ibid.

¹⁶ Dalberg (2019), Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs. Evaluation for Unitaids; Final Report.

¹⁷ For example, the FIND grant worked on evaluating the performance of HCV rapid diagnostic tests (RDTs) on samples of HIV/HCV co-infected patients and was originally planned to support the development of combo diagnostics for HIV and HCV.

(MSM), prison inmates, and supported them with awareness raising on HCV and demand generation for HCV testing and treatment. Indeed, the Unitaid HCV portfolio is one of the most effective portfolios within Unitaid in terms of focusing on key populations and vulnerable groups, especially through its work with PWIDs, who are one of the most marginalised populations.

The portfolio faced significant implementation challenges, in part due to operational capacity issues with the partners selected, which resulted in several grant reprogrammings and related burden and delays.

Stakeholders noted a number of issues with regards to the implementing capacity of the selected grantees:

- Coalition PLUS had to build its capacity at the start of the project, starting from essentially recruiting all full-time and some part-time staff dedicated to the HIV/HCV Drug Affordability Project from the ground-up. This took nearly the full first year of the grant to complete (alongside some initial country scoping activities for Malaysia and Thailand, the first two countries where activities were implemented). This implied significant delays in the early stages of the grant and close involvement by Unitaid, resulting in high transaction costs for both Unitaid and Coalition PLUS.¹⁸
- Whilst FIND has very strong technical expertise in research and development (R&D) and supporting product development (Output 1 of the grant), the FIND HCV team had limited in-country operational capacity at the start of the grant nor established government relationships (for Output 2 of the grant). This required a lot of upfront work by the FIND HCV team, resulting in slower initial progress at the start of the grant and delayed timelines. As a result, during the second grant reprogramming in 2018, the scope of Output 2 was reduced, countries were dropped and overall grant budget reduced in order to enable targets to be achieved within the timeframe.
- The MSF grant also faced a number of delays on account of learnings from being the first grant to work on HCV response in countries. Delays resulted from: (i) manufacturer challenges with in-country registration of DAAs; (ii) repurposing of the grant's focus to Asia due to lower-than-expected rates of HIV/HCV co-infection in MSF clinics in Africa; and (iii) longer-than-expected timelines for approval of research. These delays also contributed to a large underspend in the grant (from US\$15m to US\$8.2m).

The reprogramming undertaken for both the FIND and Coalition PLUS grants with timelines extension and budget resizing are described in detail in the FIND and Coalition PLUS end-of-grant evaluations in Part B and C respectively, and were ultimately necessary to enable both grants to achieve their intended outcomes. Furthermore, the WHO Enabler grant was a useful approach employed within the portfolio, given the capacity issues across the grantees as well as the nascence of HCV work more generally.

Furthermore, Output 1 of the FIND grant (the R&D component) was more upstream than usual for Unitaid investments and was an area in which Unitaid had limited expertise and experience on how to manage investment decisions related to product development. As a result, Unitaid and FIND agreed to introduce “go/no go decisions” at key development points to define what diagnostic product should move forward and which ones should not. Although in principle this approach was adequate, the lack of clarity around the type and level of detail of information that was required to inform a go/no go decision resulted in submission and review delays due to lengthy approval processes.

In general, grantees have highlighted the challenge with Unitaid's lengthy and burdensome reprogramming processes and requirements. While this evaluation has not reviewed these processes in detail, there has been a clear message from grantees on the need to reform these processes going forward for smoother grant implementation.

3.2. EFFECTIVENESS

We review effectiveness of the Unitaid HCV portfolio through the progress achieved on the access barriers. Figure 3.2 provides an overview of the key questions for review, and relevant grants considered within the HCV portfolio.

¹⁸ For additional details regarding the early stages of the grant, see CEPA (2017), Mid-term evaluation of the HIV-HCV Drug Affordability Project.

Figure 3.2: Key questions by access barrier¹⁹

Access barrier	Innovation & availability	Quality	Affordability	Demand & Adoption	Supply & Delivery
Evaluation question	1. To what extent have Unitaid's HCV investments contributed to the development & increased availability of HCV diagnostics?	2. To what extent did Unitaid's investments ensure high-quality diagnostics & treatments were developed?	3. To what extent were Unitaid's investments in HCV critical for ensuring diagnostics & treatments were affordable to LMICs & other funders?	4. How did Unitaid's HCV investments facilitate the uptake and rollout of cost-effective HCV diagnostics & treatments within focus countries & globally?	5. To what extent did Unitaid's HCV investments contribute to improvements in supply & delivery systems diagnostics & treatments, and have these been rolled-out?
Focus grants	FIND	FIND	FIND & Coalition PLUS	FIND & Coalition PLUS	FIND
Supporting grants in portfolio	WHO Enabler	WHO PQ WHO Enabler	MSF MPP	MSF WHO Enabler	MSF

Table 3.1 presents the evaluation's overall assessment of the progress made by the HCV portfolio of grants against Unitaid's access barriers.

Table 3.1: Portfolio-level progress against Unitaid's access barriers

Access barrier	Level of progress
Innovation and availability	Significant
Quality	Good
Affordability - treatments	Good
Affordability - diagnostics	Limited
Demand and adoption	Good
Supply and delivery	Significant

For each access barriers, we first describe the pre-grants status, and then set out the key areas of progress and achievements. A summary table is provided upfront for each access barrier, highlighting the key areas of contribution, progress made, strength of effect and strength of evidence.

3.2.1. Innovation and availability

Access barrier	Key areas of contribution	Progress made	Strength of effect	Strength of evidence
Innovation and availability	<ul style="list-style-type: none"> The core Antigen (cAg) RDT prototype test has been developed and offers the potential to: (i) decentralise HCV confirmation; (ii) simplify the diagnostic algorithm from a two-step to a one-step approach, particularly for high-risk groups. HCVST was taken forward, which also has transformative potential to bring screening directly to the end user. 	<p>Significant progress: FIND's R&D has increased the pipeline of HCV diagnostics across the diagnostic pathway with a specific focus on tools to enable decentralized testing which have transformational potential.</p>	<p>Moderate: some tools already on the markets with others in the pipeline, and expected to come onto the market within the next 1-3 years.</p>	

¹⁹ In line with the ToC developed, we understand that the WHO Enabler grant is intended to play a facilitating role in enabling access barriers to be achieved, as opposed to a direct role. As such, we do not assess the role of the WHO Enabler on its own in addressing most the access barriers, but instead how it has supported other Unitaid grants in achieving results. The key exception to this is on demand and adoption, where the WHO Enabler has had a more direct role through its guidelines development.

- Other products supported are important to increase the availability of tools, including additional RDTs; one additional point of care (POC) platform; one additional test for near-POC platform and Dry Blood Spot (DBS) cards.

Pre-grant status: Availability of diagnostics

At the start of the portfolio in 2015, the tools available for the diagnosis of HCV in LMICs were based on the use of RNA tests only suitable for centralised platforms in high-resource national laboratories or tertiary care institutions meaning that there were not available to the majority of the population. There was a lack of quality-assured, cost-effective and simple to use diagnostics, with no prequalified RDTs and no POC diagnostics for HCV testing, as a result of which testing was limited and not accessible in most LMICs.

The FIND grant addressed the diagnostics gap by focussing on R&D of new and innovative HCV tools, increasing the pipeline of HCV diagnostics across the diagnostic pathway, with a specific focus on developing diagnostics that would facilitate decentralized testing and thereby bring diagnosis closer to HCV patients. The Innovation and Availability section of the FIND grant (see Table 5.2 in Section 5.2 of Part B) provides in-depth details on the activities, achievements and implications of all of FIND's R&D work. In particular the FIND investment has allowed the development of both new and innovative tools which hold transformational potential, including:

- *FIND demonstrated the feasibility of cAg testing in RDT format and has developed a prototype product which has the potential to decentralise confirmatory testing to point of care and simplify the diagnostic algorithm thereby enabling greater reach of HCV testing.* This product has been characterised as a “gamechanger” by a number of stakeholders, who agreed about the significance of this achievement for the HCV diagnostic market in terms of enabling: (i) the decentralisation of HCV confirmation to primary health care settings and specially to reach settings targeting high-risk groups; (ii) the simplification of the diagnostic algorithm from a two-step to a one-step approach, particularly for high-risk groups. Decentralisation of confirmatory testing and simplification of the diagnostic algorithm could also allow for the implementation of “test and treat” programmes to be provided at point of care (for non-complicated cases), thereby reducing loss-to-follow-up and providing time and cost savings to patients. Although the product is yet to enter the market (expected within 2-4 years), and dependant on a number of steps being achieved, the feasibility of developing a cAg RDT has been shown which is a significant achievement with much potential for the decentralisation of HCV confirmation and testing and thereby increased access.²⁰
- *FIND has helped to unlock the market for HCV self-testing as a screening tool and has helped to bring two HCVSTs into the pipeline.* FIND supported the studies to demonstrate the acceptability, usability and performance of self-testing across various population groups, based on which WHO is in the process of issuing guidelines on HCV self-testing, thereby opening up the market for HCV self-testing. HCVST is a key tool as it increases even further the level of decentralisation of HCV screening by bringing the diagnostic directly to the user. As such, it can play an important role in terms of increasing testing rates, especially amongst high-risk groups. FIND worked closely with two manufacturers who already had prototypes for HCVST to conduct the studies needed both to show usability and acceptability, as well as the clinical studies to support application to WHO-PQ and CE.

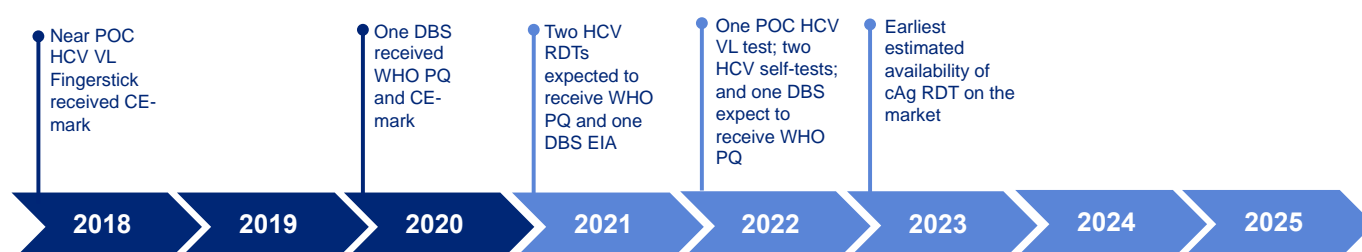
²⁰ The Original Project Plan states that Output 1 of the FIND grant is “focussed on bringing new HCV POC products to the market”, although stakeholder consultations for this evaluation indicate difference of opinion as to whether grant progress needs to be assessed in terms of market entry or not. Nevertheless, stakeholders noted that there has been significant progress in this access barrier and recognised the challenges of bringing complex new and innovative diagnostics to the market and that it is not often feasible to assign precise timelines for products entering to the market due to many steps and linkages involved in product development, optimisation and commercialisation.

FIND also supported the development of HCV diagnostics which will play a key role in terms of expanding the range of available tools for countries, increasing the diagnostic pipeline with the potential to increase competition and improve affordability in the future. In particular:

- *FIND supported the development of an HCV test for a near-POC platform - Molbio Truenat - that can be decentralized to the primary health care level at a slightly lower cost than the GeneXpert platform, thereby having the potential to increase competition in this market segment*, which is currently dominated by the GeneXpert platform as a monopoly. The Molbio platform can decentralise HCV confirmatory testing at the primary health care level given that it is portable, battery-operated and the HCV test cartridges are stable at room temperature with a 12-month shelf-life. Furthermore, sample preparation is very simple and automated with minimal intervention, with the potential of task-shifting the running of the HCV test to non-skilled personnel. Although the Molbio HCV test still requires the upfront investment in the machine and recurring cost of cartridges, it is at a slightly lower cost than GeneXpert and with the potential to lower prices further in the case of pooled procurement/ volume guarantees, with significant potential to become the first true competitor to the GeneXpert platform in the long-term.
- *FIND generated data and evidence on the performance of a range of HCV RDTs already on the market, improving the visibility with regards to the quality of these RDTs*. FIND's study also had an additional effect of stimulating the market of pre-qualified RDTs, as two additional companies have now applied to WHO PQ. If both products receive WHO PQ, there will be an additional two affordable quality-assured RDTs for HCV, thereby increasing competition and the menu of HCV RDTs which countries can procure from, which is critical to enable countries to accelerate case-finding efforts in support of WHO's elimination targets.
- *FIND supported the clinical studies of the Xpert HCV viral load Fingerstick test which enables near-POC testing using multi-disease GeneXpert platforms reducing turnaround time for confirmatory testing and loss-to-follow-up (LTFU)*. The Fingerstick test is simpler to conduct thereby allowing for greater decentralisation, and has higher acceptability particularly amongst high-risk groups such as PWID. Furthermore, developing an HCV viral load test for an existing platform with a large footprint such as GeneXpert also provides the potential for greater integration. However, GeneXpert is still expensive and requires upfront investment in the platform as well as the significant cost of the cartridges and the annual maintenance coverage, meaning that it is will not be extensively rolled out in LMICs in the absence of donor funding.
- *FIND supported the development of Dried Blood Spot (DBS) protocols for HCV assays which offers a number of benefits to increase testing rates as it:* (i) allows to reach rural populations; (ii) allows the test to be run on existing platforms in countries, therefore offering the potential to increase machine throughput (and potentially negotiate lower prices); and (ii) allows the test to be run at a similar price of the molecular test with a very minor cost-addition, given that DBS cards cost around US\$1/card. However, turnaround time is slightly longer than centralised testing due to sample transportation and strong linkages to care need to be in place to avoid a large number of lost-to-follow-up.


In terms of value add, the FIND grant was critical to provide incentives and mitigate risks of entering the HCV diagnostic market for manufacturers. Through all these investments the FIND grant has also **increased the diversity of manufacturers involved in HCV diagnostics**, with multiple manufacturers working on a number of products thereby fostering competition and potentially lowering prices in the medium-term. By increasing the number of tools in the pipeline which will be available to countries in the short-to-medium term (see Figure 3.3), the grant is enabling countries to have a range of diagnostics available to support HCV testing in support of their elimination efforts.

Figure 3.3: Estimated availability of diagnostic products supported by FIND



The progress made in increasing the HCV diagnostic pipeline has been possible thanks to the contribution of the WHO Enabler and WHO PQ grants, which highlight the benefits of the portfolio approach and complementarity across grants. Both the WHO Enabler and the WHO PQ grants have supported FIND's R&D work and the close collaboration between the grants has enabled the faster progression of some key achievements. In particular, FIND worked closely with the WHO Global Hepatitis Programme and WHO PQ on the development of guidelines for HCVST: WHO PQ published technical service specification for HCVST and the Global Hepatitis Programme convened a Guidelines Development Group meeting based on the data collected by the FIND's grant work on HCVST. The more rapid advancement of this process (as compared to standard timelines) can be attributed to the collaboration and synergies across the three partners. As a result, it is expected that WHO will issue guidelines on HCVST in mid-2021, unlocking the market and the potential of this screening tool. FIND also worked closely with WHO Global Hepatitis Programme on ensuring that the FIND R&D work and demonstration work in country would help support the research needs of WHO (e.g. decentralised POC HCV testing). FIND also liaised with WHO PQ on the structure of its studies (e.g. for DBS) so as to ensure that the data generated would be aligned with the WHO PQ process requirements for manufacturers.

3.2.2. Quality

Access barrier	Key areas of contribution	Progress made	Strength of effect	Strength of evidence
Quality	<ul style="list-style-type: none"> Unitaid's investments have led to an increase in the number of HCV diagnostics and treatments receiving pre-qualified status enabling countries to have better visibility of the quality and performance of the HCV diagnostics and treatments they procure. Manufacturers are more aware of the value of WHO PQ and more willing to apply 	<p>Good progress: there has been a significant increase in the number of HCV diagnostics and treatments pre-qualified, with a number of diagnostics still in the pipeline</p>	<p>High: funding to WHO PQ enabled faster progression of rate at which HCV diagnostics and treatment could be pre-qualified</p>	

Pre-grant status: Quality assurance of diagnostics and treatments

Prior to 2015 there was lack of pre-qualified HCV diagnostics and treatment given the costly nature of the treatments which had just come onto the market and the absence of national HCV programmes to support testing and treatment. Furthermore, in the absence of significant global health donors for the procurement of HCV diagnostics and treatment, manufacturers were not prioritising WHO PQ or CE applications. In fact, WHO PQ or CE-mark are not required for in-country registration, so there was little incentive for manufacturers to apply to these regulatory bodies given the costly and extensive review processes requiring significant clinical data submissions.

Unitaid's investment across the portfolio have led to an increase in the number of HCV diagnostics and treatments receiving pre-qualified status, enabling countries to have better visibility of the quality and performance of the HCV diagnostics and treatment they procure. In 2016, the scope of the WHO PQ grant funded by Unitaid was expanded to cover HCV diagnostics and treatments²¹. Unitaid's financial support to WHO PQ is substantial (approx. total 50% funding) which has allowed for an increase in the manpower and expansion of the scope of its work. In 2017, Unitaid's WHO PQ grant extension noted that the PQ teams "*plans to expand the scope of its Technical Guidance Series and Technical Specification Series documents in order to cover the entire range of*

²¹ Mckinsey (2019), Impact assessment of the WHO Prequalification and Systems supporting activities.

IVDs currently eligible for prequalification assessment; for example, to also cover HCV rapid tests, HCV viral load²². As a result, there has been an increase in the focus of the pre-qualification of HCV diagnostics and treatments, which has led to an increase in the number of products pre-qualified.

In terms of **diagnostics**, the number of diagnostics with WHO prequalification grew from 1 in 2015 to 12 at the end of 2020, with 5 test undergoing dossier review and the number of overall manufacturers of HCV PQ products having increased from 2 in 2016 to 10. Table 3.2 illustrates the number of pre-qualified HCV diagnostics and treatments in 2015 and 2020.

Table 3.2: Number of pre-qualified HCV diagnostics in 2015 and 2020

HCV Diagnostic	Type of diagnostic	2015	2020 (cumulative)	Year of first prequalification
RDT	Screening/ antibody test	0	4	2016
EIA	Screening/ antibody test	1	4	2015
NAT	Confirmation/ viral load test	0	4	2017

Source: WHO PQ as of October 2020 – RDT: rapid diagnostic test; EIA: enzyme immunoassay; NAT: nucleic acid testing. Note: see Table 5.3 in Section 5.2 in Part B for details on which diagnostics were supported by the FIND grant.

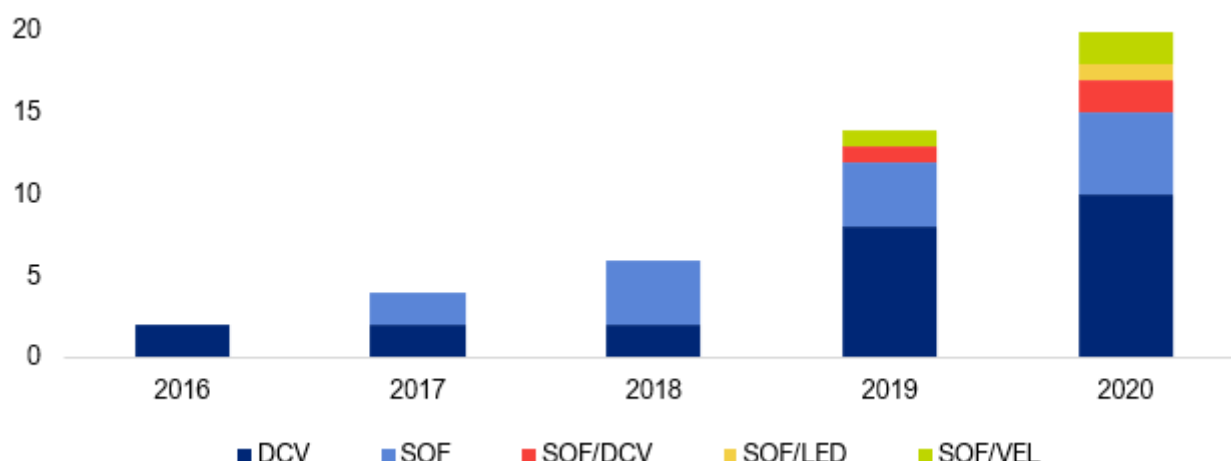
In addition, as part of its investments under Output 1 of the grant, FIND has worked with manufacturers to stimulate their interest in applying for WHO PQ and CE-mark and has supported data collection for a number of the products developed under Output 1 to facilitate dossier preparation and submission to WHO PQ, which has increased the number of applications. In total, data collected through the FIND grant has been used to support dossier submission of five diagnostics, including the Cepheid Fingerstick, two DBS products and two RDTs, and three additional products that are planning submission in 2021/22 (two HCV self-tests and one HCV POC platform (Molbio)). Even though WHO PQ is not required for in-country registration, stakeholders noted that WHO PQ focus on HCV has been important to provide countries, especially those with weaker regulatory agencies and processes, a standard of quality they can rely on. As one stakeholder noted “for governments it is critical, especially those who do not have well-resourced SRA, as they know they can rely on PQ products and that makes a huge impact on procurement at country level by taking away that worry about the quality of the product”. Despite this positive progression, the extent to which diagnostic products are registered in country is difficult to ascertain given that each country follows their own processes and do not publish this information in structured way. As a result, it has not been possible for the evaluation to assess the extent to which these diagnostics are registered and used in country.

In terms of **treatment**, the number of HCV DAAs prequalified has increased from one in 2016 to 20 in 2020. Figure 3.4 below shows how WHO prequalified DAAs have changed over time with the implementation of Unitaids’ investments. In 2018 the first generic Sofosbuvir was pre-qualified which is a key component of the pan-genotypic regimens and transform HCV treatment. The first daclatasvir active pharmaceutical ingredient (API) was also pre-qualified which is an important achievement as it means that there are now WHO pre-qualified APIs for a full pan-genotypic regimen.²³

²² Unitaids (2017), WHO-Unitaid PQ cost extension project plan.

²³ Unitaids (2019), Grant Brief Analysis, WHO prequalification of medicines and diagnostics (Cost Extension) from 1 July 2017 to 31 December 2018.

Figure 3.4: WHO prequalified DAAs 2016-20 (cumulative)



Source: WHO PQ as of January 2021

In the absence of Unitaids’s grant to WHO PQ, stakeholders noted that progress on getting HCV diagnostics and treatment prequalified would have been slower, as generally manufacturers did not prioritise WHO-PQ or CE-mark for their HCV products. Furthermore, FIND also played a key role in demonstrating to manufacturers the value of pre-qualification for their products and stimulating their interest in dossier submission for a number of diagnostics.

3.2.3. Affordability

Access barrier	Key areas of contribution	Progress made	Strength of effect	Strength of evidence
Treatment	<ul style="list-style-type: none"> • MPP voluntary licences (VLs), particularly for DCV, have enabled a wide range of countries to access more affordable treatment. • Coalition PLUS in-country advocacy work has enabled some countries, particularly Malaysia, to significantly reduce the price of DAAs in the public sector. • MSF has enabled countries to access more affordable prices both directly through its global access price negotiations, as well as indirectly through its price signalling to other organisations, patent oppositions and facilitating supply from generic manufacturers. 	<p>Good progress: Prices for key DAAs have fallen in many LMICs, enabling countries to have better access to treatments for HCV. That said, some MICs continue to face high prices, and many countries are not accessing low prices.</p>	<p>Moderate: Unitaids’s investments have been important for enabling more affordable medicines in LMICs, allowing countries, including non-project countries, to access treatments faster, and in some cases would not have had more affordable treatment without the grants. But key VLs were also in place prior to Unitaids investments.</p>	
Diagnostics	<ul style="list-style-type: none"> • MSF and FIND demonstration studies 	<p>Limited progress: DAAs and</p>	<p>Low: some important contributions through</p>	

helped show that genotype testing was no longer needed with pan-genotypic treatment and that algorithms could be simplified.

- **Price reductions of HCV diagnostics have not been substantial** and currently available HCV diagnostics are generally not affordable for LMICs.

implementation studies have shown that less steps are needed in diagnostic algorithms, but overall cost of diagnosing HCV patients still remains high and viewed unaffordable in many countries.

demonstration studies, but in essence HCV diagnostic prices remain too high, particularly confirmatory test.

Treatment

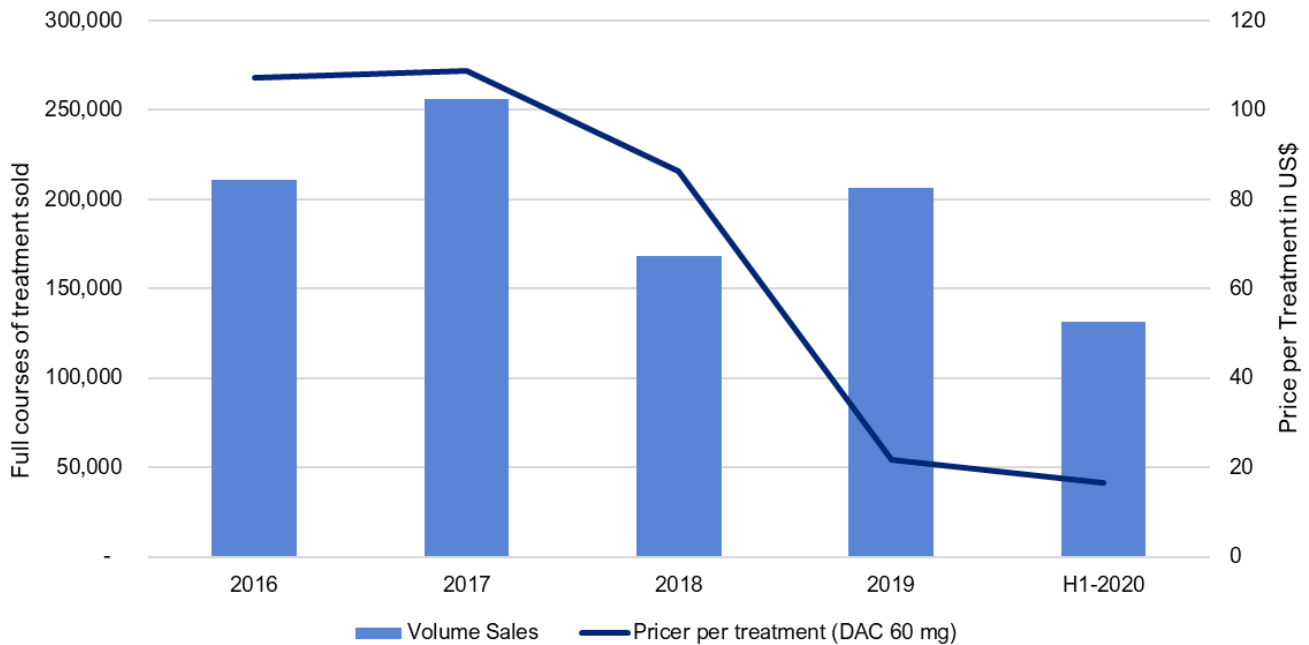
Pre-grant status: Affordability of treatment

During the initial years of Unitaid's investments in HCV, DAAs were already available globally. For example, innovator SOF first received FDA approval in October 2013 in combination with ribavirin, while DCV received approval in the EU in August 2014. Following these initial SRA approvals, innovator companies also issued VLs for their products. For SOF, Gilead first issued a VL in 2014, which enabled 91 LMICs to be supplied by generic manufacturers, and included both SOF single dose and SOF/LED as a combination therapy, while the licence was expanded to SOF/VEL in 2015. Despite the widespread covered of the VLs, key middle-income countries (MICs) were originally excluded, which meant that countries had to pay tens of thousands of dollars for a full course of treatment.

DAAs have become increasingly more affordable in LMIC countries, in part as a result of Unitaid's support through MPP with considerable value-add through its licensing agreement. In addition to the key developments around the time of commencement of the Unitaid portfolio (as noted in the box above), Unitaid and MPP played a key role in negotiating and obtaining the licensing of DCV in 2015, initially covering 112 LMICs where more than 65% of the estimated population of people living with HCV lived. As a result of the MPP licence, 87 countries were able to benefit from both SOF and DCV, paving the way for potentially affordable pan-genotypic treatment.²⁴ For DCV, an additional 34 countries outside of the agreement can be supplied by the sub-licensees included within the MPP agreement, since BMS has stated it has no intention of applying for patents in these countries, suggesting that the scope of countries that can access more affordable treatment could be higher. As of June 2020, 10 sub-licensee agreements had been made for DCV, with five manufacturers applying for WHO PQ and three receiving approval, with the increased competition being a key driver of improved affordability. In addition, one generic manufacturer obtained WHO PQ for SOF/DCV in fixed-dose combination (FDC) in 2019, which will enable countries to treat patients with a more convenient formulation (one tablet per day). As a result of the competition generated as part of the sub-licensing agreements, nearly 1 million treatments have been sold across 34 LMIC countries, while the weighted average price of DCV has fallen from US\$106 in 2016 to below US\$20 in 2020, as shown in Figure 3.5 below.

²⁴ Based on countries being included in both Gilead and BMS VLs.

Figure 3.5: Weighted average price of 12-week MPP-licensed DCV 2016-20 (US\$)



Source: MPP

The MPP licensing agreement has enabled a larger territory and faster price declines than would have been possible without the agreement. For example:

- Based on expert insights, it is believed that some 22 countries included in the MPP DCV licence would not have been included in a bilateral VL issued by the company itself. Kazakhstan is an example of a country that was included in the VL but would have likely not been included in an agreement in case issued by the company itself. Facing high prices in the absence of the VL, it is extremely unlikely that Kazakhstan would have ordered the same volume levels of HCV treatments as it currently does under the MPP VL.
- For India, the main beneficiary country of the MPP licence to date accounting for 77% of the procured treatments, CEPA’s previous analysis²⁵ of the impact of MPP’s licence agreements has suggested that the country was able to benefit from affordable treatment at least one year faster than it would have done otherwise, enabling more people to be treated faster.

While having limited procurement to date, MPP has also entered into licensing agreements with innovator producers of glecaprevir/pibrentasvir (G/P) (2018) and ravidasvir (2017). G/P could offer additional competition to the SOF/DCV and other pan-genotypic treatments in future, while ravidasvir will offer countries a more affordable alternative to DCV in some contexts once approved. Ravidasvir is currently in clinical trials in Malaysia and Thailand, which is assessing pan-genotypic treatment of ravidasvir and SOF. Initial findings from trials suggest treatment is highly effective in treating people with cirrhotic HCV, and once approved for use will be available at US\$294 or less for treatment.

Despite the widespread cover of the VLs, key middle-income countries (MICs) were originally not included. In such contexts, Coalition PLUS and its partners have been important in facilitating more affordable treatments, with the issuing of the compulsory licence (CL) in Malaysia being a key example that resulted in far more affordable SOF being available in the country, which also had indirect implications for other countries. As part of its work, Coalition PLUS partnered with key CSOs to advocate for more affordable treatments in countries. In the context of Malaysia, where Gilead had previously been granted a patent for SOF, the cost to the government of procuring such treatment meant that during the initial years of the grant, treatment with DAAs in public health facilities were almost non-existent. However, the country took a major step towards obtaining more affordable DAAs in September 2017 when it issued a compulsory licence (CL), the first country in the world to issue a CL for HCV treatments. Up to the end of 2020, Malaysia was able to access SOF for as little as US\$80. Having access to

²⁵ CEPA (2020), Revising MPP’s impact methodology.

treatments at this price was noted by stakeholders as overcoming the “*key blockage to unlocking the HCV programme*”. Country stakeholders noted that Malaysia benefits from strong CSOs which has been important for the continued emphasis on affordability; and that without the collaboration of Coalition PLUS grantees and other in-country partners, the issuance of the CL would have been much slower (with the support by all organisations speeding up the issuance by 2-3 years). Following the issuance of the CL in Malaysia, the country was included in the SOF VL, along with Thailand, Belarus and Ukraine, highlighting the indirect effect that this had. Despite the success in Malaysia of reducing the price of DAAs, these results may not be sustained in future without continued efforts to advocate for further competition in the country, including potential through the reissuance of the CL. When the CL was first issued in September 2017, this was only to apply for a three-year time period, and as a result needed to be renewed in September 2020. However, due to the unstable political environment, competing interests in the country and the COVID-19 pandemic, the CL lapsed, meaning that the country could only obtain SOF going forward from sublicensees of the innovator VL. In Thailand, where only one company covered under the VL is currently registered, the cost of full treatment for SOF/DCV is estimated to be US\$750 by project stakeholders. While Malaysia may still benefit from prices of SOF/DCV under the VL, these will be significantly higher than the US\$80 cost they obtained for SOF when the CL was issued. This shows that despite the initial successes, big risks remain to the Malaysia programme going forward that could hinder its wider rollout.

Across all Coalition PLUS countries, prices of key DAAs have fallen significantly over the period the grants have been operating, although in some contexts they continue to be unaffordable for meaningful rollout to take place. In some markets, prices have fallen significantly, particularly in India (US\$284 in 2016 to US\$16 in 2020 for full treatment cost of SOF) and Malaysia (US\$12,000 in 2015 to US\$79 for full treatment cost of SOF), with the former having access to generic competition in its domestic market (partly thanks to the work of the MSF grant in working closely with generics manufacturers in India²⁶), while the latter, as mentioned previously, has been able to facilitate competition through the issuance of the CL and being included in the VL for SOF. For other countries, particularly Brazil and Colombia, prices have fallen significantly, with advocacy by local partners noted as being key contributors to this. For example, in Colombia the move to centralise DAA procurement was long advocated for by local partner IFARMA through meetings with government and published articles. Similar advocacy in Brazil also contributed to centralised procurement, as well as capacity strengthening within the Ministry of Health (MoH) by local partner FOASP. But prices in both countries remain comparatively high, which is limiting the extent to which these countries can roll out wider HCV programmes.

The MSF grant has also been noted as being a key contributor to facilitating affordability, particularly through announcements of price through its Access Campaign, support to generic manufacturers in being included on innovator VL and for filing patent oppositions in key MICs that have facilitated more affordable access. However, in many contexts prices remained unaffordable. The MSF evaluation noted that the grant helped to facilitate more affordable prices through its disclosure of a US\$120 SOF/DCV price it was able to receive to support its programmes. This price was also used as a benchmark for other international organisations such as UNDP. Aside from this, MSF has been noted for playing an important role in patent opposition rulings in China and India, two countries with among the largest estimated number of PLHCV in the world. For example, in China, MSF’s patent opposition filings for velpatasvir (VEL) was used as part of the public hearing against Gilead for sofosbuvir, which eventually resulted in the State Intellectual Property Office cancelling the sofosbuvir patent, suggesting that these patent oppositions have had some contributory effect on enabling the production and use of affordable DAAs in the country with the largest HCV burden in the world, as well as allowing exports to take place to other countries.

Despite progress made, affordability of DAAs continues to be one of many reasons why HCV treatments are not widely available. For example, while the MSF price was noted as providing an important signal for others in their price negotiations, it is unclear the extent to which all countries have been able to benefit from similar price agreements, with the MSF evaluation noting that many LMICs still were paying US\$600-US\$800 for pan-genotypic treatment. In addition, the MPP licensing agreement for DCV has predominantly resulted in procurement in India, where there is a high level of domestic DAA competition that has helped drive down prices. In other countries, the lack of registration of multiple manufacturers has been noted as a key challenge for ensuring that countries benefit

²⁶ More details available in the MSF; Dalberg (2019), Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs. Evaluation for Unitaaid; Final Report.

from truly affordable prices. For example, according to WHO's recent report on access to HCV medicines, just one generic manufacturer had been approved in 10 countries and had filings in 31 additional countries for DCV; while for SOF one generic manufacturer had been approved in 33 countries and filed in 20 more, while an additional manufacturer had filed in 11 countries. This means that competition in countries where these manufacturers are registered is very limited, and there are a large number of countries without generic manufacturers registered. In order to be interested in registering, manufacturers are likely to need to see increased demand from countries in terms of wider scale rollout of their HCV programmes, which in many contexts has been relatively limited (see Section 3.2.4 of this Part A for further details).

Diagnosics

Pre-grant status: Affordability of diagnostics

During the initial years of Unitaid's investments, DAAs were just coming to the market, and in many cases had yet to be utilised in resource-limited settings. While these medicines had been shown to be highly effective in treating HCV compared to previous treatments, there was limited evidence that these treatments could be provided and administered at the primary health care (PHC) level. Previously, HCV positive patients were treated in tertiary level facilities that often required specialist hepatologists to not only administer the treatment, but also monitor patients continuously over time to ensure that treatments were effective. This ongoing monitoring of viral load added significantly to the cost of treatment, and was a key reason why undertaking the full diagnostics work was so expensive in many contexts. For example, in 2013 it was estimated that full diagnosis of HCV could cost anything between US\$300 and US\$1,380, with ongoing viral load monitoring estimated to cost between US\$80-US\$320. Pan genotypic treatment also meant that patients no longer needed a genotype test, which back in 2013 was estimated to cost between US\$20 and US\$500, depending on the type of test undertaken.

Unitaid's investments demonstrated that patients could be diagnosed and treated using simplified models of care which would lower the overall cost of the diagnostic and treatment pathway. This included removing the need for genotype testing, as well as the reduced need for continuous viral load monitoring during treatment.

As discussed further in Section 3.2.5 of Part A, the MSF grant in particular helped demonstrate the efficacy of DAAs against genotypes 5 and 6, which demonstrated that with pan-genotypic treatment countries did not need to undertake genotype testing, thus reducing the overall cost of testing HCV patients. In addition to the removal of genotype testing, the MSF grant showed that less monitoring was required when treating patients with DAAs, thus further enabling countries to provide a more affordable diagnostic algorithm that just included screening, confirmation, liver staging and test of cure. The FIND grant also demonstrated that a decrease in the price of the diagnostic pathway was possible by introducing simplified algorithms which included removing key steps such as genotyping and treatment monitoring, as well as reducing algorithm from a three-step to a two-step in Malaysia or using reflex testing to reduce the number of patient visits, thereby making the overall diagnostic algorithm more affordable. The full cost of HCV diagnosis has fallen, primarily due to the removal of genotyping and viral load monitoring in the diagnostic algorithm.

Although the FIND grant negotiated some entry prices for HCV diagnostics, more efforts are needed to make prices of diagnostics affordable in LMICs, particularly with regards to confirmatory tests. Through its work with diagnostic manufacturers FIND has negotiated some entry price for HCV diagnostic tests. For example, the Fingerstick HCV test for the GeneXpert platform was negotiated at US\$14.90 per cartridge by FIND and other partners, and is the same price as the cartridges for other diseases tested on the GeneXpert platform.²⁷ Similarly, FIND and partners also negotiated with Roche for the inclusion of Hepatitis C and B in its Global Access Programme²⁸ as well as a price of less than US\$10/test for its HCV test for use on its newer molecular platforms, which are however not extensively available in LMICs. However, many stakeholders have noted that these prices are still too high for most LMICs to be able to afford to procure widely, especially given the absence of donor funding for HCV

²⁷ FIND, GeneXpert negotiated prices. Available at: <https://www.finddx.org/pricing/genexpert/>.

²⁸ Roche (2019), Roche expands the Global Access Program beyond HIV to also include diagnostic tests for Tuberculosis, Hepatitis, and Human Papillomavirus. Available at: <https://www.roche.com/media/releases/med-cor-2019-07-22b.htm>

procurement.²⁹ Ideally stakeholders noted that sub-US\$10/test for confirmatory tests are desirable in order for them to be extensively procured in LMICs. Stakeholders also indicated that more needs to be done in terms of price reductions of HCV confirmatory tests and that integration of HCV testing by (i) using existing GeneXpert platforms in countries, and (ii) integrating HCV testing with testing for other diseases on multi-disease platforms, offers the potential to improve affordability for countries. The FIND grants have shown the feasibility of integration of HCV testing in Georgia (integration on GeneXpert platforms used for TB) and Myanmar (integration with centralised laboratory platforms used for HIV). However, there is still limited evidence on the cost-effectiveness and savings that could be achieved through these approaches.

3.2.4. Demand and adoption

Access barrier	Key areas of contribution	Progress made	Strength of effect	Strength of evidence
Demand and adoption	<ul style="list-style-type: none"> Raising awareness among communities and policymakers, and turning this into policy developments and national guidelines Demonstration projects undertaken by the Unitaids grants have helped shape national programmes and generate demand at the policy as well as community level for more inclusive and simplified HCV services Overall portfolio raised profile of HCV, with Unitaids being one of the few funders in this area Grants have contributed extensively to global HCV normative guidance 	<p>Good progress: Unitaids has supported the initial creation of demand for HCV testing and treatment, but globally HCV programmes continue to be relatively small scale in most countries</p>	<p>Moderate: Unitaids' role as a funder of multiple activities to support demand and adoption highlighted as a key strength of the portfolio by multiple stakeholders, but roll-out in project countries is still limited and it is unclear whether progress has been sufficient to date to enable full scale-up.</p>	

Pre-grant status: Demand and adoption

Despite the availability of new and innovative DAAs at the start of Unitaids' HCV investments, the widespread rollout of HCV services was very low. This was driven by very limited awareness of HCV as a public health problem in many countries, a limited understanding of HCV prevalence, and in turn a relatively low commitment from governments to scale-up HCV programmes. In most LMICs, knowledge of HCV was limited among both the general population and among key populations. There was also limited normative guidance on HCV globally and nationally.

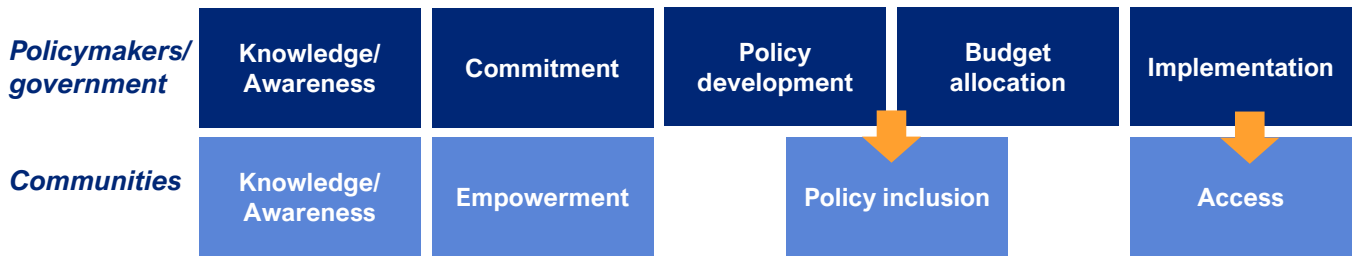
The Unitaids HCV portfolio has played a multi-faceted role with regards to increasing the demand and adoption of HCV programmes and services in countries. The achievements and contribution can be looked at in terms of both the country and global levels, as set out below, followed by a discussion on overall progress and implications.

²⁹ Opinions expressed during the Preliminary Findings Workshops indicate that stakeholders generally view progress on the affordability of diagnostics as more advanced compared to our assessment; whilst there may be good progress being made at the global level, our findings from the country case studies indicate that current prices of HCV diagnostics remain unaffordable for many governments in LMICs and more needs to be done to improve their affordability.

Country level

Country activities have varied depending on context, but overall have targeted HCV policy development and community awareness and access. Within this, different aspects have been in focus, again context specific and based on developments over time, as depicted in Figure 3.6 below.

Figure 3.6: Focus areas in support of demand and adoption



The extent to which Unitaïd’s investments have contributed to these different aspects is discussed below.

With both policymakers and communities, the Unitaïd HCV portfolio has been relatively unique in its approach of building awareness of both these groups, with the Coalition PLUS grant playing a particularly important role in this regard.

Key examples of how the portfolio has contributed to raising awareness among policymakers and communities include (with further details of activities included in Section 6.2 of Part C of this report):

- Ongoing engagements with MoH and other government departments to demonstrate that HCV is a public health issue in countries that needs to be considered.
- National education campaigns among key populations (including both FIND and Coalition PLUS) to raise awareness of status, dissemination of materials to key populations on the risks of HCV and how they can get tested and national media campaigns.
- Community participation alongside MoH in-country level workshops.
- Integration of HCV awareness raising in CSO healthcare facilities in multiple countries.

Across all countries where Unitaïd’s investments have operated, stakeholders noted that awareness of HCV was significantly higher than when these investments were first initiated, and country-level grantees have been integral in this awareness raising.

The increased awareness among policymakers and communities has been essential for increasing government commitment to HCV, including for marginalised populations, and Unitaïd’s investments have been important for ensuring that these commitments have turned into policy developments.

There have been important contributions, particularly from Coalition PLUS, but also FIND and MSF³⁰, both for wider policy development and also for demonstrating the importance of ensuring marginalised HCV patients can be reached with testing and treatment services. Key examples include:

- In Malaysia, MAC was noted as being a key stakeholder that contributed to the 2019 National Strategic Plan, as well as being a key member of the steering committee that developed the recent 2020 Clinical Practice Guidelines, which partly as a result of MAC’s advocacy, recommend screening of high-risk populations and outreach testing. In addition, the FIND demonstration study of decentralised testing using RDTs for screening at 25 primary healthcare facilities (PHCs) has been widely credited as a key factor behind the country’s decision to

³⁰ As part of its support to countries, MSF utilised its technical knowledge and experience of implementing care models to advise national governments on their guideline development across multiple countries, including Kenya, Cambodia, Mozambique and in Manipur, and was noted for providing important on-the-ground experience. See Dalberg (2019), Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs. Evaluation for Unitaïd; Final Report.

expand the testing approach more widely in the country, and findings from FIND's work was incorporated into Malaysia national guideline updates.

- In Manipur in India, CoNE advocated for and developed state-level HCV Standard Operating Procedures (SOP) which are more detailed and extensive than the National Viral Hepatitis Control Programme (NVHCP) guidelines and include specific testing strategies for key populations, which have been approved by the State Government and are awaiting to become a law.
- In Colombia, IFARMA lobbied for and contributed to the development of an integrated HIV and HCV strategic plan and of HCV testing and treatment guidelines.
- In Brazil, FOAESP contributed to the public consultations on the updating of national HCV screening and treatment guidelines.
- In Georgia, consultees were unanimous in their view that FIND played a critical role in decentralising of testing at harm reduction sites (HRS) through its pilot activities. As discussed further in Section 5.5 of Part B of the report, FIND's demonstration study helped facilitate the government's decision to initiate treatment decentralisation at HRS, and that this would not have happened without Unitaids support.

While the progress made on national policy development has been important, as noted previously, budgetary commitments from countries have been relatively limited, even in the case of Malaysia where, though increases in the HCV budget have taken place, may not be significant to fully attain its HCV elimination goals³¹.

In terms of implementation, Unitaids' HCV portfolio has been important for demonstrating how HCV testing and treatment could be done across a number of countries, particularly for KPs. However, actual rollout in most countries continues to be limited, as described in the country case studies of the FIND and Coalition PLUS grants (see Section 5.5 of Part B and Section 6.5 of Part C).

Coalition PLUS together with its partners, played an important role in supporting the demand and adoption of HCV models of care, including decentralised and simplified approaches, through a combination of advocacy and demonstration projects for marginalised populations such as PWID and prison inmates. In particular, advocacy has been critical to ensure that evidence-based models and approaches are adopted and implemented in practice. Key demonstration projects across countries noted as being particularly important include:

- In Malaysia, local partner MTAAG+ initiated a pilot programme that focused on improving HCV services in prison settings, and partners in-country noted these programmes as being important for demonstrating the prevalence of HCV in such settings and that continued testing of these groups was needed. In addition to this, MAC, the other local Coalition PLUS partner, initiated a project to ensure prisoners living with HCV could access services once they are released, which is being adopted by the MoH. More widely, MAC has created training materials for doctors on avoiding discrimination of marginalised groups (including PWID, transgender and prisoners), which has been noted as having a noticeable impact on discrimination for those accessing public health services. In addition, in 2019 the FIND decentralised model of testing was rolled out to all PHCs with a resident primary healthcare physician. This amounts to 146 PHCs, replacing the previously more centralised approach to screening. While this was seen as a positive step, consultees noted that Malaysia's current diagnostic algorithm still faces challenges, with confirmatory testing taking up to 4 weeks, and that LTFU remains for these patients.³²
- In India, the FIND HEAD-Start grant conducted decentralised and simplified pilot studies in New Delhi, Punjab and Manipur. These pilots demonstrated the feasibility of the decentralised approach and how they could be integrated into other health services. For example, in Punjab the study was able to demonstrate how PLHIV could access HCV testing and treatment at ART centres, which has resulted in the wider adoption of this model in the state. However, wider roll-out in New Delhi and Manipur has been more limited, which in New Delhi has partly

³¹ For example, data from the Coalition Plus logframe indicates that India and Malaysia increased their HCV budgets in 2019, and Morocco in 2020. In Malaysia, the budget increased from 3.7m MYR to 7mMYR for the purchase of DAAs. See Coalition PLUS (2019), HIV/HCV Drug Affordability Project: 2019 Annual Report.

³² To overcome this, stakeholders noted that POC testing for confirmation would be highly beneficial to reduce this, either in the form of a cAg RDT or near-POC solutions such as those offered by GeneXpert.

been due to the COVID-19 pandemic, while in Manipur wider rollout has hampered by a number of factors including COVID-19, operational and financial barriers for the use of GeneXpert and general lack of awareness amongst PWID, who are the main target group. In Manipur, Coalition PLUS local partner CoNE launched screening campaigns in local Drug Treatment Centres (DTCs), an opioid substitution therapy (OST) centre, enabling PWID to access HCV services that they otherwise would likely not have accessed, given the limited awareness of HCV in these communities. CoNE also successfully demonstrated the decentralised testing of prison inmates, through a pilot project to screen inmates in Manipur's central jail. Following the successful pilot, it also advocated for the active screening of inmates in prisons and stakeholders reported that the state government had committed to active screening in Manipur's prisons.³³ This community-led HCV outreach programme for the screening and awareness raising of prison inmates was the first of its kind in the entire south Asia and was included in a 2019 WHO policy brief on HCV community interventions in prisons³⁴ and has been replicated in other countries. With regards to simplification, CoNE in Manipur has also supported the simplification of the diagnostic algorithm at the state level; through its advocacy with the state government, ultrasound test is now no longer mandatory for patients who have an APRI score lower than 2. This means that non-complicated cases can access treatment faster as they do not need to wait for an appointment for an ultrasound test.

- In Georgia, the FIND grant was largely focused on PWID who are most vulnerable and affected by HCV population. The vulnerability of PWID is exacerbated by existing legislation criminalizing drug use, which drive PWIDs underground. Many consultees from government agencies and CSOs highlighted that the FIND grant managed to demonstrate the feasibility of engagement of low-threshold Harm Reduction Sites (HRS) in HCV decentralized testing and treatment.
- The WHO Enabler grant has also contributed to generating evidence on service delivery models through demonstration project. In particular, WHO Global Hepatitis Programme helped to design and supported the implementation of two demonstration projects in Egypt^{35,36} and Punjab (Pakistan) based on a model of simplified service delivery. In Egypt the project demonstrated that mass testing and treatment is feasible covering 90% of the population and reduced new infections and transmission, demonstrating proof of principle in moving towards elimination; the project is now being scaled-up and replicated nationally thanks to the commitment and financing from the national government to achieve elimination. Based on the experience of Egypt, the project was replicated in the Pakistani state of Punjab, where again it demonstrated that testing and treatment is feasible; the Punjab study has been taken onboard by the Government of Pakistan who have now committed to rolling out the same approach nationally and allocated funding to do it. Furthermore, other countries, such as Rwanda and Mongolia are now looking at these models in support of their own elimination efforts. As part of this work to demonstrate models to achieve elimination, the WHO Enabler grant is also working on guidance for countries on validating elimination.

Across the portfolio, partners have been important for ensuring that countries address the needs of KPs, which may not have been given so much focus in the absence of Unitaids support. That said, challenges with ensuring KPs are able to access services remain.

The COVID-19 pandemic has had a profound impact on the rollout of HCV programmes, as well as other disease programmes, in many countries, with national lockdowns meaning that HCV testing and treatment rollout was either stopped or significantly reduced. The economic implications of COVID-19 could also have significant implications for the rollout of HCV programmes going forward. While Unitaids grantees have provided specific support for countries during the pandemic, many activities that were intended to support programme rollout

³³ Although prisoners were already included as target populations in the NVHCP guidelines, in practice in Manipur they were not being actively tested.

³⁴ WHO (2019) Access to hepatitis C testing and treatment for people who inject drugs and people in prisons – a global perspective, Policy Brief, available at <https://www.who.int/hepatitis/publications/idu-prison-access-hepatitis-c/en/>

³⁵ Shiha G. Solian R., Mikhail NNH., and Easterbrook P. (2019) An educate, test and treat model towards elimination of hepatitis C infection in Egypt: Feasibility and effectiveness in 73 villages in *Journal of Hepatology*, vol 72, 658-669

³⁶ Shiha G. Solian R., Mikhail NNH., and Easterbrook P. (2021) Reduced incidence of hepatitis C in 9 villages in rural Egypt: progress towards national elimination goals, in *Journal of Hepatology*, 2021 vol 74, 303-311.

were cancelled. The pandemic's impact on fiscal budgets is also likely to delay or limit national HCV rollout going forward, with consultees noting the extent to this happening dependent on the in-country advocacy efforts being maintained. More information on advocacy efforts going forward is presented in Section 6.3 of Part C.

Global level

Unitaid has played a significant role in raising the profile of HCV globally, being one of the few global organisations supporting HCV and through its wide portfolio of investments that operate at the global and multi-country level. Unitaid's involvement in HCV, in the absence of larger global donors, is fully aligned with its mandate of being a "first mover" in health commodity markets. Stakeholders were unanimous in their view that Unitaid's involvement in the HCV space had really "*put HCV on the map*" in terms of global awareness of the disease and the unique opportunity the world has to eradicate the disease with innovative treatments, as well as raise awareness of the key challenges that have been in place to achieve this through its direct and indirect interventions.

Through the WHO Enabler and direct project grants, the Unitaid HCV portfolio has made important contributions to evidence generation and normative guidance, as well as providing technical assistance to countries and sharing lessons and good practices. The WHO Enabler grant in part supported the 2018 guidelines revision as well as forthcoming updates, by drawing on Unitaid-funded projects. This has included: i) updates to the testing guidelines with the removal of the need for genotyping given the evidence that SOF plus DCV – the most widely available treatments – is pangenotypic; ii) informing upcoming recommendations on HCVST; iii) informing future recommendations on service delivery models, including decentralisation and POC testing. For genotyping and HCVST, the Unitaid investments were highlighted as being integral contributions in these areas, while for decentralisation and POC the findings from the FIND country projects are part of the broader systematic review. In particular:

- For genotyping, MSF was recognised for providing critical evidence for the 2018 WHO guidelines on the effectiveness of SOF/DCV as treatment for genotypes 5 and 6, which had previously been less-researched. This evidence removed the need for genotype testing, which could cost up to US\$250 per patient, a significant amount in LMICs.
- On HCVST the FIND grant has been highlighted across several stakeholders as being critical for demonstrating the feasibility and acceptability of HCVST, and without the support from this grant it is unlikely such evidence would have been generated. Based on the studies undertaken by FIND, WHO is expected to make a recommendation on the use of HCVST in mid-2021. Drawing on the experiences from HIVST, this is anticipated to be an important early step towards facilitating wider uptake of HCVST in the future.
- In addition to the above areas, through the WHO Enabler grant, the Global Hepatitis Programme is in the process of updating its guidelines for the testing and treatment of HCV in 2021/2022. These guidelines are expected to include updates on simplified models of care (including decentralised testing and task shifting), as well as the use of POC testing for HCV. The MSF grant is expected to contribute to both these aspects from the studies that were conducted under the Unitaid grant. Similarly, the findings from the FIND demonstration projects in countries will also inform the systematic review on POC testing for HCV service delivery and decentralised models of care. Whilst this is an important contribution to the guideline development process particularly in terms of providing country evidence, the FIND studies were observational studies in nature, and stakeholders have noted this may not be as clinically robust as other types of studies such as randomised controlled trials (RCTs).

The WHO Enabler grant has also provided important support to the Global Hepatitis Programme which enabled it to function at a critical point in time. In 2015 and 2016 there were so many needs in HCV given the rapidly changing landscape as well as WHO's commitment to the elimination agenda: the Global Hepatitis Programme was very lean in terms of technical staff and financial resources, with very limited bilateral funding support received by WHO for HCV. The Global Hepatitis Programme was tasked with producing guidelines for HCV testing in 2017 and HCV treatment and care in 2018 as well as a range of other technical publications and the WHO Enabler grant supported all those processes. Furthermore, the Enabler grant allowed for the Global Hepatitis Programme to work and advance the agenda on other key issues including:

- Work on HCV financing, including the work on the Universal Health Care (UHC) price tag, which showed that the cost of HCV elimination is possible and countries should add HCV to the UHC package of care.³⁷ Without the Unitaid funding, this would have not happened and HCV would not have been included in UHC (with other research now showing that HCV is understood to be an essential health service for UHC³⁸). The inclusion of HCV in a UHC approach is particularly significant given the lack of donor funding for countries and the need to rely on domestic financing.
- Convened meetings of partners working in the HCV space to discuss good practices and lessons learned in HCV programming, which is informing a WHO publication on 17 areas critical to have successful HCV programming in countries, structured around planning, implementing and evaluating countries HCV response.³⁹ This will be used as a key dissemination tool both for countries and other actors within and external to the HCV space.
- Work on paediatric treatments for HCV, including evidence generation and modelling on the use of SOF/DCV as a paediatric treatment to inform future guidelines revisions.

Unitaid's investments have also been critical for generating awareness of HCV among KPs, enabling these groups to demand better access to HCV services. This has been a key feature of several of Unitaid's investments. In particular, Coalition PLUS and its in-country partners undertook a range of education campaigns, workshops and grassroot activities to generate demand and awareness among key groups such as PWID, as discussed above. These activities significantly rose the profile of HCV as a public health problem in countries, and combined with other advocacy-based interventions helped CSOs and the communities themselves to advocate for more inclusive HCV testing and treatment programmes within countries.

Overall progress and implications

Unitaid's investments have made important contributions for putting in place conditions and tools to facilitate wider demand and adoption. However, actual rollout of HCV testing and treatment will be the key barrier to address going forward. In the absence of significant investments from larger international donors, domestic will need to be in place to ensure HCV programmes are scaled-up and advocacy is important to tool to support the allocation of domestic financing. Stakeholders were almost unanimous in their view that financing for HCV remained the key outstanding challenge facing wider uptake and adoption of HCV elimination programmes. While key international organisations such as the Global Fund have started to support countries test and treat HCV as part of their HIV co-infection funding requests, the investments have been limited to a handful of countries and very small scale and will remain limited going forward. Stakeholders also noted that it is unlikely that significant funding will be available from other international donors going forward. This means that domestic financing will need to be relied upon to fund future programmes in HCV, which has been very limited to date. As shown to date in countries such as Egypt, this may only take place on a significant scale once HCV becomes a major public health crisis. In terms of testing, some stakeholders highlighted that from their own experiences, governments are not currently incentivised to provide widespread, low-cost public testing. This is because, even when the diagnostic infrastructure is in place in the public sector, in some countries, patients pay significant amounts out-of-pocket to get tested. By offering UHC in HCV, countries will lose this source of funding while also have to fund significant amounts for testing and treating patients. This suggests that more work, including continuous advocacy, is needed to change the incentive structures countries face when providing health services, which many feel will require international organisations to work in

³⁷ Tordrup et al. (2019), Additional resource needs for viral hepatitis elimination through universal health coverage: projections in 67 low-income and middle-income countries, 2016-30.

³⁸ Blanchet et al. (2020), Protecting essential health services in low-income and middle-income countries and humanitarian settings while responding to the COVID-19 pandemic.

³⁹ The 17 areas of good practice include: (i) Planning the response: political will and leadership; strong partnerships and champions; community mobilisation and engagement; defining the epidemic/ use of modelling to inform strategies; comprehensive and costed national plans; mapping of testing infrastructure for diagnostics network optimisation; opportunities for diagnostics integration; economic analysis in viral hepatitis; financing options and national health insurance; (ii) driving the response: access strategies for drugs and diagnostics; registration strategies for drugs and diagnostics; forecasting and quantification for supply management; optimising procurement for drugs and diagnostics; simplified service delivery; integration with harm reduction amongst PWID; training the workforce; and (iii) Evaluating the response: data monitoring systems. WHO (forthcoming) Good Practices and Lessons Learned in the Global Viral Hepatitis Response.

partnership with governments so that they can understand and realise the positive benefits widespread HCV testing and treatment can bring.

3.2.5. Supply and delivery

Access barrier	Key areas of contribution	Level of progress	Strength of effect	Strength of evidence
Supply and delivery	<ul style="list-style-type: none"> FIND demonstrated the feasibility of decentralised, integrated and simplified models of care in LMICs which reduce LTFU and improve retention in the care cascade. MSF demonstrated that simplified models of care offer efficient and cost-effective testing and treatment strategies in LMICs. The evidence generated by the FIND and MSF projects has been used/ is being used to update WHO guidelines on HCV testing and treatment. 	<p>Significant progress: the feasibility of a number of models has been demonstrated.</p>	<p>Moderate: although these models have helped to inform updates to WHO guidelines, the extent to which there are being integrated into national programmes is dependent on a number of factors.</p>	

Pre-grant status: Supply and delivery

Prior to the start of the portfolio, countries who did have HCV programmes in place were relying on centralised testing approaches and there was limited evidence on optimal testing and treatment strategies. Diagnostic algorithms were complex with many doctor visits, especially with hepatologist, and whilst pan-genotypic DAAs reduced the need for genotyping and monitoring during treatment, countries were still implementing these as part of standard of care.

The FIND and MSF grants demonstrated the feasibility of decentralised, integrated and simplified models of care in LMICs, generating evidence that high testing and cure rates can be achieved even in resource limited settings. Both the FIND and the MSF grants piloted models of care across a number of countries and demonstrated the feasibility of simplified testing approaches in ensuring retention across the care cascade and treatment outcomes, whilst also being more cost-effective. Furthermore, the FIND grant demonstrated that HCV diagnosis and treatment is possible in public health sector programmes/settings, such as in public hospitals in New Delhi and in state ARV clinics in Punjab. FIND's achievements and their significance are presented in Table 3.3.

Table 3.3: FIND achievements on supply and delivery

Model of care	Achievement	Significance/ implication
Decentralisation of testing using RDTs and near POC viral load tests	Demonstrated the use of RDTs for HCV screening	<ul style="list-style-type: none"> Halved the time between screening and treatment initiation from eight weeks to four weeks Allowed individuals to be screened without having to travel to a tertiary level hospital.
	Demonstrated the use of GeneXpert for HCV confirmatory testing in various settings	<ul style="list-style-type: none"> Turnaround times between confirmatory testing and treatment initiation were significantly reduced (same day for Georgia; 3

Model of care	Achievement	Significance/ implication
		<p>days for Myanmar), leading to lower LTFU and good retention across the care cascade.</p> <ul style="list-style-type: none"> • GeneXpert continues to be expensive and not fully decentralizable in all settings.
Decentralised care models integrated in non-traditional settings	Demonstrated feasibility of HCV screening, testing and treatment in non-traditional settings (such as ART centres, HRS, community clinics)	<ul style="list-style-type: none"> • Offering “one-stop-shop” approaches for key populations at high risk of HCV infection increases retention in the care cascade; • Reduced stigma and discrimination for high-risk groups compared to hospital settings.
Simplification of testing and treatment algorithm	<p>Demonstrated feasibility of simplifying algorithm by reducing the number of patient visits</p> <p>Demonstrated feasibility of delivering by trained non-specialist doctors as opposed to specialised hepatologists</p>	<ul style="list-style-type: none"> • It is possible to reduce the number of visits whilst maintaining high standards of care; • Non-complicated cases can successfully be treated and managed by trained non-specialist doctors, such as general practitioners, with referral protocols in place for complicated cases.
Integration of HCV testing with other diseases	Demonstrated the feasibility of integrating HCV testing with testing for other diseases such as HIV and TB	<ul style="list-style-type: none"> • Increased the utilisation of existing testing platforms, whilst enabling cost-sharing; • Spare capacity on existing machines can enable expansion of testing services for HCV.

The MSF grant also demonstrated that simplified models of care offer efficient and cost-effective testing and treatment, in particular, “*evidence gathered from these [MSF] treatment sites demonstrated that cure rates of 85-95% (similar to treatment outcomes to High Income Countries) can be achieved with far fewer clinic visits and without the need for specialised hepatologists*”⁴⁰. In particular the MSF projects demonstrated the feasibility of simplified care models by:

- **Removing the need for genotyping:** The MSF grant tested the efficacy of SOF/DCV against genotypes 5 and 6 and demonstrated that it achieved the same treatment outcomes as other genotypes thereby highlighting the fact that countries did not need to undertake genotype testing and that the diagnostic algorithm could be simplified by removing this step.
- **Removing the need for specialised hepatologist** by task-shifting treatment, monitoring and other exams such as fibro-scans to nurses.
- **Reducing the need for treatment monitoring:** MSF projects showed that less monitoring was required when treating patients with DAAs and eliminated the need for treatment monitoring at 4 weeks as well as clinical monitoring at the end of the treatment, thus further enabling countries to provide a more affordable diagnostic algorithm that just included screening, confirmation, pre-treatment assessments/ liver staging and test of cure.




MSF findings noted that whilst a more streamlined diagnostic algorithm with fewer patient visits was feasible for the general population (as it demonstrated in Cambodia), for high-risk groups such as PWID it would be preferable to include more visits such as counselling and follow-up monitoring due to the risk of non-adherence and to the high rates of LTFU. The MSF project also demonstrated the efficiency of the SOF/DCV regimen and cost-effectiveness of this simplified model of care, which has been published in peer reviewed journals and shared widely. In particular: (i) MSF research from their Cambodia simplified algorithm showed that the simplified model of care was cost-saving compared to no-treatment, emphasising the importance of simplifying the diagnostic algorithm to improve access to care in LMICs. The research showed that the total cost of treatment per patient under the full model of care was

⁴⁰ Dalberg (2019), Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs. Evaluation for Unitaidd; Final Report.

US\$925 versus US\$376 for the simplified model of care;⁴¹ and (ii) MSF research from the use of SOF/DCV on a large cohort of patients using the simplified model of care showed high rates of treatment effectiveness and safety across patient sub-groups and during progressive simplification.⁴² However, the extent to which these models have been rolled out is relatively limited, meaning countries are not yet fully benefiting from these simplified lower cost testing pathways.

The evidence generated by the FIND and MSF pilot projects has been used and is being used to update WHO guidelines, as described in Section 3.2.4 above on demand and adoption, thereby informing testing strategies that WHO recommends to countries, including beyond project countries. The MSF grant provided key evidence on the less-researched genotype 5 and 6 by demonstrating the effectiveness of SOF/DCV on these two genotypes making the treatment pan-genotypic. This finding was incorporated in the 2018 WHO Guidelines for the care and treatment of persons with HCV and is particularly important given that SOF/DCV is the only pan-genotypic regimen which is affordable and available in the majority of LMIC. The findings on models of care simplification are also being used in WHO’s forthcoming systematic review on HCV service delivery models including task-shifting and simplification, which will inform the revision of WHO guidelines on testing, treatment and care. Similarly, the findings from the FIND projects will also inform the systematic review on POC testing and decentralised models of care to be published in 2021 with updated WHO guidelines expected in 2021/2022.

3.3. SCALABILITY AND TRANSITION

Key findings	Strength of evidence
For the FIND and Coalition PLUS projects, there is some evidence that project activities will continue after the Unitaid grants are concluded, but this varies considerably by grantee and country.	
In terms of global conditions for scale-up, Unitaid’s portfolio has been critical for putting in place some of the key conditions/tools including on normative guidance and appropriate delivery models, but the lack of domestic and donor funding is likely to be the major barrier inhibiting global scale-up going forward, and there is limited evidence at present that this is going to change.	
For country scale-up, there is evidence that Unitaid has contributed to creating some country conditions and tools for scale-up, and a few countries are beginning to scale-up parts of their HCV programmes, but overall the rollout of HCV elimination programmes at the country level remain low.	

3.3.1. Transition⁴³

For the FIND and Coalition PLUS projects, there is some evidence that project activities will continue after the Unitaid grants are concluded, but this varies considerably by grantee and country. For example:

- For the **FIND grant**, there have been numerous examples of FIND’s pilot/demonstration projects being adopted through government directives/ordinances and SOPs, which is resulting in activities being embedded in national strategies and programmes. However, across many countries the high cost of diagnostic technologies as well as COVID-19 have caused delays and/or challenges to transition. FIND also has access to funding from the Dutch government to continue some of its work in HCV diagnostics R&D, whilst the development costs for the cAg RDT going forward will be borne by the commercialisation partner.

⁴¹ Walker JG, Mafirakureva N, Iwamoto M, et al. (2020), Cost and cost-effectiveness of a simplified treatment model with direct-acting antivirals for chronic hepatitis C in Cambodia.

⁴² Zhang M, et al. (2020), High sustained viral response rate in patients with hepatitis C using generic sofosbuvir and daclatasvir in Phnom Penh, Cambodia, in Journal of Viral Hepatitis.

⁴³ CEPA have contacted MSF to provide insights on how the activities previously funded by Unitaid have been transitioned, but have been unable to schedule a consultation with them.

- **Coalition PLUS** is planning to continue supporting its members' work on HCV as part of their own projects on HIV, and Coalition PLUS will continue to provide technical support for advocacy activities to its members and partners on HCV. Some members and partners have also applied for other funding and/or drawing on private sources. However, activities are likely to be scaled down after the finalisation of the Unitaid grant, given funding will be more limited.

More details are provided in Section 5.4 of Part B and Section 6.4 of Part C.

3.3.2. Global conditions for scale-up⁴⁴

Scalability is one of Unitaid's strategic objectives and refers to creating the conditions for scale-up to happen post-projects. It is noted that Unitaid investments are aimed at catalysing the market and do not fund scale-up of the interventions per se.

As part of the evaluation, we have undertaken an assessment of the global conditions for scale-up based on Unitaid's Scalability Framework⁴⁵. As part of this assessment, we have analysed the status of each of the 13 global conditions for scale-up included in the framework to help inform the extent to which progress has been made towards meeting these conditions.

The 13 global conditions are structured across three domains and include:

1. **Create sustainable access conditions**, which includes: i) Evidence; ii) Normative guidance; iii) Regulatory approval; iv) Affordable pricing; v) Adequate supply base; and vi) Appropriate delivery models.
2. **Align and coordinate with global partners and donors**, which includes: vii) Strategic priorities/needs; viii) Recommended approaches/tools; ix) Planning/budgeting cycles; and x) Procurement.⁴⁶
3. **Generate and disseminate knowledge and evidence**, which includes: xi) Study results/other evidence; xii) Project progress/lessons learned; and xiii) Investment case/global advocacy.

For each domain we present tables to map out our assessment of where each condition was at the start of the portfolio and where condition is at the end of the portfolio, with arrows representing progress, and a final column indicating our assessment of the level of Unitaid's contribution to improving each of the conditions.

In terms of understanding the level of progress of each condition, it is noted that it was not the expectation that Unitaid's HCV portfolio alone would ensure that all conditions are met within the lifetime of the grants. However, the assessment of progress toward each condition provides an indication on the sense/ direction in which the conditions have been put in place and scale-up can happen in the post-portfolio period.

Each global condition was discussed during a stakeholder workshop, which is reflected in the findings below.

Create sustainable access conditions

Unitaid's investments have made important contributions to all the conditions related to creating sustainable access, particularly around normative guidance and appropriate delivery models, as shown in Figure 3.7.

⁴⁴ Further details of Unitaid's Scalability Framework can be found at: <https://unitaid.org/assets/Unitaid-Scalability-Framework.pdf>

⁴⁵ Whilst Unitaid's Scalability Framework is new, Unitaid is not introducing scalability as a new concept and all grants are aware of Unitaid's focus on scalability.

⁴⁶ It is important to note that two global conditions, planning and budgeting cycles and procurement, were not the focus of the portfolio and therefore are not presented in this analysis

Figure 3.7: Global scalability scores for 2015 and 2020 related to creating sustainable access conditions (status ratings are scored between one (limited/nothing in place) to 5 (condition fully achieved) and Unitaid contribution to each condition (high-medium-low)

Condition	Ltd./ nothing in place	Plan under dev	Plan dev & activities underway	Partially achieved	Fully achieved	Level of Unitaid contribution
Evidence		◆	→	◆		Medium
Normative guidance	◆		→	◆		High
Regulatory approval	◆		→	◆		Medium
Affordable pricing	◆		→	◆		Medium
Adequate supply base		◆	→	◆		Medium
Appropriate delivery models	◆		→	◆		High

Source: CEPA analysis based on Unitaid Scalability Framework.

- Normative guidance and appropriate delivery models:** As shown in Figure 3.7, significant progress and contribution from the HCV portfolio has been made in developing normative guidance on HCV and in demonstrating appropriate delivery models. As outlined in Section 3.2.4 of Part A of the report, Unitaid’s investments, particularly the WHO Enabler as well as the MSF and FIND grants, have been key in generating the evidence to support updates WHO HCV guidelines, as well as demonstrating the feasibility and effectiveness of various models of HCV care (decentralisation, simplification and integration).
- Evidence:** FIND and MSF grants generated substantial and critical evidence, both on models of care as well as on the feasibility and effectiveness of diagnostic tools; further work is needed to generate evidence on other tools (e.g. cAg RDT) as well as demonstrating how available models and products could work in different contexts.
- Regulatory approval:** Unitaid’s support to WHO PQ, FIND’s support to diagnostic manufacturers and MSF’s support to generic DAA manufacturers have been important for ensuring products receive regulatory approval, which has led to an increase in the number of both diagnostics and treatments which are quality assured at the global level, with some in the pipeline.
- Affordability⁴⁷:** The MPP, Coalition PLUS and MSF grants have enabled price reductions through licensing agreements and advocacy work at the country and global levels; however, as discussed in Section 3.2.3, challenges remain in ensuring global affordable pricing. Diagnostic affordability also remains a key challenge in many contexts, especially for confirmatory tests, though depending on future product developments could be overcome through new products and increased competition.

⁴⁷ Global-level stakeholders’ opinions from the Preliminary Findings Workshop suggest that this condition is viewed as being partially achieved. Although we recognise the challenge in achieving price reductions for both treatments and diagnostics, our assessment is that this condition is still underway given the strong country stakeholder feedback we have received in this evaluation that prices of DAAs continue to be unaffordable for many countries and that more progress is needed on the affordability of HCV diagnostics.

- **Adequate supply base**⁴⁸: FIND has played a critical role in supporting the development of new products which are currently in the pipeline and on the market, though as noted in Section 3.2.1 of Part A, more work is needed to get some of these products to market over the coming years.

Align and coordinate with global partners and donors

There has been progress in aligning strategic needs and priorities across global partners and demonstrating approaches/tools, but more efforts are needed given limited donor interest, as shown in Figure 3.8.

Figure 3.8: Global scalability scores for 2015 and 2020 related to aligning and coordinating global donors and partners (status ratings are scored between one (limited/nothing in place) to 5 (condition fully achieved) and Unitaid contribution to each condition (high-medium-low)

Condition	Ltd./ nothing in place	Plan under dev	Plan dev & activities underway	Partially achieved	Fully achieved	Level of Unitaid contribution
Strategic priorities/ needs		◆	→	◆		Low
Recommended approaches/ tools		◆	→		◆	High
Planning/ budgeting cycles	◆	→	◆			Low
Procurement	◆	→	◆			Low

Source: CEPA analysis based on Unitaid Scalability Framework. Note: the planning and budgeting cycles and the procurement conditions were not a focus of Unitaid’s portfolio of HCV grants and only some limited work has been done to advance these conditions at the country-level rather than at the global level, hence they are not discussed here.

Strategic needs and priorities⁴⁹: Unitaid’s portfolio of HCV grants has raised the profile and visibility of HCV in alignment with WHO’s Global Hepatitis Strategy,⁵⁰ and the grants have helped to fill some of the key research gaps in HCV as identified by WHO (such as the FIND and MSF grants through evidence generation), however the lack of donor interest/ priorities for HCV is a limiting factor to progress on this condition. In particular, we note that there are opportunities to engage with multilateral and regional development banks, who could work closely with national governments to provide financing for HCV programmes as part of a UHC approach.

Recommended approaches/ tools: as discussed above the grants, particularly FIND, MSF and WHO Enabler grants, have demonstrated the feasibility and effectiveness of approaches and tools for countries to utilise in their delivery, although such approaches/ tools need to be more integrated into national health systems going forward, as shown through the demonstration projects done in Egypt and Punjab (Pakistan) by the WHO Enabler grant.

Generate and disseminate knowledge and evidence

Unitaid has been an important contributor to disseminating evidence and knowledge across its investments, although continued dissemination is needed particularly at the global level and with non-project countries. As

⁴⁸ Stakeholder views from the Preliminary Findings Workshops generally noted that this condition was more partially achieved as opposed to our rating of activities underway, which we have kept given that a number of HCV diagnostics are still undergoing WHO PQ and/or are still in the pipeline and not yet on the market.

⁴⁹ Stakeholders’ opinions from the Preliminary Findings Workshop suggest that this condition is viewed as being partially achieved as opposed to our assessment of activities underway; although we recognise that progress has been made in increasing the profile and visibility of HCV, our assessment is that this condition is still underway as more efforts are needed to align more donors in the HCV space, as noted above.

⁵⁰ This was developed in the early years of the Unitaid HCV portfolio. The Unitaid portfolio did not make a direct contribution to its development.

outlined in Figure 3.9 below, considerable progress has been made in addressing the conditions in this domain. In particular:

- **Study results/ other evidence:** as discussed, the grants have generated significant evidence and study results have been published and presented including in peer-reviewed journals and publications, as well as through webinars and grey literature, with more studies expected to be published in 2021. The grantees have also participated in major HCV and liver-related conference and global and regional meetings.
- **Project progress/lessons learnt:**⁵¹ grants have shared progress and lessons learned from country level activities regularly through stakeholder meetings and dissemination workshops. Although global dissemination commenced and is happening with these lessons being picked up by other non-project countries, the COVID-19 pandemic in 2020 has to some extent hampered broader dissemination efforts at the global level. Furthermore, continued efforts to share evidence is needed especially in non-project countries, as these are likely to want to see models piloted in their own country before national adoption and roll-out.
- **Investment case:** Whilst the HCV portfolio did not fund the production of the 2020 global investment case for HCV, Unitaids investments are listed as contributing towards the evidence supporting the investment case for HCV.⁵²

Figure 3.9: Global scalability scores for 2015 and 2020 related to generating and disseminating evidence (status ratings are scored between one (limited/nothing in place) to 5 (condition fully achieved) and Unitaids contribution to each condition (high-medium-low)

Condition	Ltd./ nothing in place	Plan under dev	Plan dev & activities underway	Partially achieved	Fully achieved	Level of Unitaids contribution
Study results/ other evidence	♦	→			♦	High
Project progress/ lessons learnt	♦	→		♦		Medium
Investment case	♦	→			♦	Medium

Source: CEPA analysis based on Unitaids Scalability Framework.

Overall, progress has been made on establishing global conditions and tools for scale-up, but more work is needed to ensure these conditions are built on going forward to enable scale-up to happen. As per the above findings by domain, good progress has been made across the board, with important contributions by Unitaids. The biggest challenge, however, is the lack of domestic and/ or donor funding for country HCV programmes, which is the key limiting factor for scale-up. This challenge is partly linked to affordability challenges, particularly diagnostics but also treatments, given that many countries continue to face relatively high prices despite the issuances of VLs (see Sections 3.2.3 of Part A and Section 6.3 of Part C for further details).

⁵¹ Stakeholders' opinions from the Preliminary Findings Workshop suggest that this condition is viewed as being partially achieved; however, in our view, although dissemination has started, there is space for more to be done to ensure broader dissemination of lessons learnt and project findings, not just at the global level, but specifically with non-project countries.

⁵² The investment cases funded by Unitaids, such as those carried out as part of the Coalition PLUS project, were done on a country-specific basis.

3.3.3. Country conditions for scale-up

Similar to the assessment of the global conditions for scale-up, as part of this review, we have also assessed the country conditions for scale-up using the Unitaid Scalability Framework, which encompasses three key readiness domains and component conditions:

1. **Secure political and financial support**, which includes: i) Political engagement and buy-in; ii) Donor funding; iii) Domestic funding; and iv) national advocacy.
2. **Ensure programmatic and operational readiness** which includes: v) Supportive policies; vi) Integration into national programmes; vii) Effective supply chain systems; viii) Adequate health systems capacity; and ix) Timely registration of products.
3. **Create community driven demand**, which includes: x) Civil society demand; and xi) Grassroots advocacy.

This assessment has been conducted for the three deep-dive country case studies of Georgia, India and Malaysia, although we provide some high-level comments for the less detailed country case studies as well (Brazil, Colombia, Morocco and Myanmar). These have been done at the portfolio level, in the sense that we have considered the combined impact of both the Coalition PLUS and FIND grants when reviewing progress. Appendix E provides the detailed frameworks for Georgia, India and Malaysia. For India it is important to note that whilst the framework was completed at the aggregate level for New Delhi, Manipur and Punjab, there are significant state-specific variations. Figure 3.10 provides an overview of progress against the conditions with key points from the matrices are summarised below.

Figure 3.10: Summary of progress towards country conditions for scale up from baseline (2015) to end of grant evaluation (2020) for Georgia, India and Malaysia

	Baseline (2015)			End of grant evaluation (2020)		
	Political & financial support (4)	Programmatic & operational readiness (5)	Community driven demand (2)	Political & financial support (4)	Programmatic & operational readiness (5)	Community driven demand (2)
Georgia	●●●	●●●●●	●●	●●●●	●●●●●	●●
India				●	●●	●●
Malaysia		●		●●●	●●	●●
<i>Average scalability assessment</i>	1	2	0.3	2.3	3	2

Source: CEPA case studies for Georgia, India and Malaysia. Note for India, the table reflects the aggregate level, whilst the details are provided in the discussion below.

The blue dots represent the status for each country for the 11 conditions for scale up according to Unitaid's Scalability Framework,⁵³ estimated based on the assessment of country readiness at the time of the baseline (corresponding with pre-grant situations in 2015 or 2016) and at the time of the end-of-grant evaluation in early 2021. The status at the end of grant evaluation is based on the scalability rating given by the evaluators for each of the 11 conditions, with a rating of fully achieved or partially achieved corresponding to a dot. The average scalability represents the average number of dots per condition category.

Our findings by domain are as follows:

- **Securing political and financial support – good progress on the political side, less so on financing⁵⁴:** Coalition PLUS focus on advocacy with policymakers has helped to raise the profile of HCV at the country level, with FIND also working closely with government stakeholders to ensure political engagement and buy-in on HCV.

⁵³ Unitaid (2020), Unitaid's Scalability Framework – Guidance for Implementers, draft, October 8 2020.

⁵⁴ We note that whilst Unitaid's work in these countries was not focussed at increasing financing from international donors and that Unitaid's intervention to increase domestic financing were limited to funding advocacy in countries.

Indeed, our assessment has been that there is significant political commitment to HCV in Georgia and Punjab as evidenced by the strong championing of HCV at the policy level as well as financial allocations to support HCV programming; good commitment in Malaysia and weaker levels of commitment in New Delhi and Manipur. Furthermore, national/state advocacy efforts are in place in all three countries, although their level of stakeholder engagement varies. However, in terms of financial support, the condition for scale-up has not yet been widely created, except for Georgia where external financial support from both Gilead (in kind DAAs) and other partners (US CDC and Global Fund) was in place before the Unitaid grants. In India and Malaysia, there is no donor funding allocation for HCV, with domestic financing being main source of funding for the national programmes and is expected to continue as such going forward. While there are some budget allocations and treatment targets for both India and Malaysia, these are nowhere near the required level for a full-scale HCV programme.

- **Ensure programmatic and operational readiness⁵⁵ – good progress on policy-making, less so on operationalisation:** All three countries have supportive policies in place for HCV with contributions from Unitaid in terms of advocacy and contribution to policy development in India (both for the national action plan as well as for state specific policies such as the SOPs in Manipur) and in Malaysia (where the MAC’s advocacy contributed to the 2019 National Strategic Plan and the recent 2020 Clinical Practice Guidelines). However, the extent of their implementation/ operationalisation varies substantially with more progress in Georgia and Punjab and some progress in Malaysia through the CL-related work. The FIND grant has demonstrated the feasibility of various decentralised, integrated and simplified models of HCV care, but the extent to which they have been/ are being integrated into national programmes varies across countries (from greater adoption in Georgia, Malaysia and Punjab⁵⁶ to less integration in New Delhi and Manipur). Capacity in the health systems has been increased, notably through capacity building and training of non-specialist doctors and health care providers to deliver HCV treatment and care and laboratory technicians to undertake HCV testing, particularly in India, Georgia and Malaysia (in PHC settings) where capacity has been strengthened, and to some extent in Myanmar. In general, this readiness domain is even further back for Brazil, Colombia and Morocco, where there are some policies, but limited operationalisation.
- **Create community-driven demand – more substantial progress:** Thanks to the work of both grants this condition has been put in place across all three countries with communities and grassroots organizations engaged and strengthened to support advocacy efforts, awareness raising and community mobilisation. However for this condition to support scale-up continued funding is needed for these community organizations.

As such, the assessment highlights considerable progress with regards to community mobilisation and related demand creation, although less so in terms of national policies, and in particular their implementation. The reason for this varies by country, and while limited funding is a common challenge across countries, in some cases it is more because of competing priorities for government budgets and need for further awareness (e.g. India), while in others it is on account of affordability issues with DAAs (e.g. Malaysia, Myanmar some of the Latin American countries), and still others on account of low political commitment (e.g. Morocco). Further, the COVID-19 pandemic will have significant implications on domestic financing for HCV. While not a focus of Unitaid, and also not emphasised in this scalability framework, lack of quality data on HCV burden is also a big challenge impacting awareness and political commitment.

Between 2012 and 2018, the number of countries globally with national strategic plans for HCV increased from less than 20 to 124.⁵⁷ While having a national strategic plan is an important step, in practice many stakeholders and evidence on the rollout of HCV programmes suggest far more work is needed to ensure countries meet WHO’s 2030 HCV elimination targets. For example, a recent assessment of 66 countries with the highest burden of HCV suggested

⁵⁵ Unitaid interventions were not focussed on supporting the ‘effective supply chain system’ nor the ‘product registration in countries’, so these conditions are not relevant for the assessment.

⁵⁶ Factors supporting this greater adoption include high levels of commitment from national/state government and champions in place, as well as availability of domestic financing to support roll-out. COVID-19 has also impacted adoption for example in New Delhi and Manipur where momentum on HCV has been halted and efforts re-directed to addressing COVID-19.



⁵⁷ WHO (2019), Access to hepatitis C testing and treatment for people who inject drugs and people in prisons – a global perspective.

that just eight of 66 had policies in place that would put them on track to achieve HCV elimination by 2030, and the vast majority of these were high-income countries.⁵⁸ Domestic funding allocations will be critical to ensure countries are able to finance their HCV programmes (as shown for example through the WHO Enabler grant demonstration project in Egypt) and this requires continued advocacy and awareness raising of HCV as well as greater dissemination of project results amongst policy makers (particularly for non-project countries) to ensure there is awareness of the positive benefits widespread HCV testing and treatment can bring. This will need to take place alongside the increased availability of more quality assured and affordable diagnostics and treatments.

3.4. IMPACT

This section provides an overview of the estimated public health and economic impacts of grants in the HCV portfolio against Unitaids’ KPI’s 4.1 and 4.2. The HCV portfolio included a large number of activities and achievements, whose impact is not possible to fully quantify and capture through an impact model alone. It is therefore important to highlight the following points:

- The quantitative impact figures presented here **only cover a subset of the full public health and economic impact achieved through the portfolio of grants**, and should be viewed as ‘case studies’ of the impact of the portfolio, rather than portraying the full impact. Furthermore, the figures presented are conservative; for example, they do not include any impacts from a shift in testing policy and guidelines in-countries (beyond an expansion due to cost reduction).⁵⁹
- As noted throughout the evaluation, the HCV portfolio grants have interacted synergistically, tackling multiple issues in HCV, **resulting in a ‘multiplier impact’ of the work of the portfolio as a whole**. Importantly, there have been a number of key achievements which have been presented qualitatively in this evaluation and their impact should not be underestimated.

Key findings	Strength of evidence
<p>The direct impact of the Unitaids HCV portfolio on deaths averted and additional patients cured has been limited to-date in part due to lack of investment into scale-up of diagnostic technologies, but more substantial health impacts are expected in the future once further diagnostic technology is scaled-up.</p> <p>To-date, the HCV portfolio led directly to avert ~ 4000 deaths mostly due to the MPP licence for Daclatasvir and, to a lesser extent, the in-country studies conducted by FIND. More substantial health impact is expected going forward through the scale-up of new technologies (cAg RDT and Molbio Truenat), the simplification of diagnostic pathways and the fact that impact of treating additional patients is only fully realised over time (when the condition of HCV positive patients would worsen in the absence of treatment). The scale-up of cAg RDT globally, the scale-up of Molbio Truenat in India and the reduction of genotyping alone could lead to an additional 6,100 deaths averted by 2025 and additional 23,000 deaths averted between 2026 and 2030.</p>	
<p>The HCV portfolio has already achieved significant economic impacts, in particular due to the substantial costs savings that the MPP grant has achieved through the lowering of DCV prices (leading to ~US\$100 million saved by 2020). There are also significant potential cost savings from the simplification of the testing algorithm, with the reduction in genotyping alone estimated to lead to cost savings of around US\$ 25 million [9m – 51 m] by 2025.</p> <p>The biggest economic impact can be achieved by reducing the disease management costs in the future reducing the burden to the health systems and out-of-pocket</p>	

⁵⁸ Palayew et al. (2020), Do the most heavily burdened countries have the right policies to eliminate viral hepatitis B and C?

⁵⁹ The modelling took this more conservative approach focusing on the areas with more robust data that are linked directly to the technology (e.g., loss-to-follow-up; cost reduction). In contrast, changes in testing policy are also highly depending on other country-specific factors (e.g., political willingness, financing etc.) and, thus, there is large uncertainty on how the new technology would influence countries testing policies.

payers. Across the additional treatments by FIND, MPP and through reducing genotyping, reductions in disease management costs of ~ US\$ 137 million [61m – 242m] could be possible by 2025, increasing further to ~ US\$ 316 million [47m – 802m] between 2026- 2030.

With regards to qualitative impacts, the Unitaid HCV portfolio has been noted as having a particularly positive equity impact in terms of its support to marginalised populations across its direct grants. There is also a number of examples of the portfolio providing key strategic benefits and positive externalities, including: i) raising the profile of HCV at the global and country level; ii) enabling grantees to broaden their work in HCV; and iii) reducing prices of DAAs for other organisations and countries not included in the portfolio.



The different grants in the Unitaid HCV portfolio cover a very wide range of activities with different impact pathways and large variation in the level to which the Unitaid grant contributed to the impact. Additionally, the comprehensiveness and quality of the HCV diagnostic and treatment data has been limited. As such, this review adopted a “bottom-up approach” to capture the public health impact across those activities within the Unitaid HCV portfolio that could be reliably modelled. For areas with sufficient data, a separate impact model was developed which captured the additional benefits of the supported intervention. There is considerable uncertainty in the impact estimates due to the poor data availability in HCV, in particular on diagnosis and treatment estimates as well as on the expected scale-up of the technologies - cAg RDT and Molbio Truenat. A conservative, central and best scenario have been developed for each of the models to capture key uncertainties in particular around: (i) scale-up speed and magnitude; (ii) loss-to-follow-up for testing step; (iii) sensitivity of testing; (iv) commodity costs; (v) year of market entry. A detailed description of the model designs as well as input assumptions is outlined in Appendix D of the main report. More detailed impact estimates for FIND are outlined in the grant specific evaluation in Section 5.4 of Part B of this report.

Table 3.4 below provides a summary of the public health and economic impacts by grant against Unitaid’s KPIs. The figures for the FIND grant are still subject to final verification. The estimates provided state only additional impact achieved through the supported intervention and, thus, ensure that gains that would have also been made regardless of the Unitaid project are taken into consideration. As outlined at the start of this section, data limitations have meant that not all interventions in the HCV portfolio could be robustly modelled. The quantitative estimates presented in Table 3.4 should therefore be interpreted as providing only one part of the full public health and economic impact achieved through the HCV portfolio. While still subject to final review, the current impact modelling and qualitative evidence suggests the following findings:

- **The direct impact of the Unitaid HCV portfolio on deaths averted and additional patients cured has been limited to-date due to lack of investment into scale-up of diagnostic technologies, but more substantial health impacts are expected in the future once further diagnostic technologies are scaled-up.** To-date, the HCV portfolio directly averted ~ 4000 deaths, mostly due to the MPP licence for DCV and, to a lesser extent, the in-country studies conducted by FIND. More substantial health impact is expected going forward through the scale-up of new technologies (cAg RDT and Molbio Truenat), the simplification of diagnostic pathways and the fact that impact of treating additionally patients is only fully realised over time (when the condition of HCV positive patients would worsen in the absence of treatment). The scale-up of cAg RDT globally, the scale-up of Molbio Truenat in India and the reduction of genotyping alone could lead to an additional 6,100 deaths averted by 2025 and additional 23,000 deaths averted between 2026 and 2030.
- **The HCV portfolio has already achieved significant economic impacts,** in particular due to the substantial costs savings that the MPP grant has achieved through the lowering of DCV prices (leading to ~US\$100 million saved by 2020). There are also significant potential cost savings from the simplification of the testing algorithm, with the reduction in genotyping advocated through the MSF and updated guidelines of WHO alone is estimated to lead to cost savings of around US\$ 25 million [9m – 51 m] by 2025. The biggest economic impact can be achieved by reducing the disease management costs in the future, lowering the burden to the health systems and out-of-pocket payers. Across the additional treatments by FIND, MPP and through reducing genotyping, reductions in disease management costs of ~ US\$ 137 million [61m – 242m] could be possible by 2025, increasing further to ~ US\$ 316 million [47m – 802m] between 2026- 2030.

- Various studies have shown that investing in HCV diagnosis and treatment is cost-effective in the medium-to-long term in particular due to the substantial disease management costs that are being averted by curing HCV. While absence of quality costing data for HCV interventions (especially costs beyond commodities) makes it not possible to calculate a robust return on investment of Unitaid's HCV portfolio, **the available evidence suggests that the portfolio delivers positive returns in the medium to long-term due to the substantial cost savings realised through the MPP grant, costs savings through testing algorithm simplification and future averted disease management costs.**

Table 3.4: Public health and economic impacts by grant in Unitaid's HCV portfolio

KPI	Indicator	FIND		MPP	Coalition PLUS	MSF & WHO Enabler
		<i>Improved diagnostic tools⁶⁰</i>	<i>Improved diagnostic approaches⁶¹</i>			<i>Simplification of testing algorithm⁶²</i>
Public health impacts (KPI 4.1)	Deaths averted	2021-25: ~ 3,600 [600 - 8,900] 2026-30: ~ 17,700 [3,100 - 49,600]	2018-2025: ~ 640	2015-2026: ~ 4,000 (of which ~ 3,400 by 2020)	<i>Coalition PLUS grantees have directly linked patients to healthcare services, enabling them to benefit from treatment and as a result, contribute to improved health of these individuals. Coalition PLUS's support for removing affordability barriers have also ensured countries such as Malaysia were able to increase DAA treatment that might otherwise not have happened.</i>	2019-2025: ~ 2,500 [930 - 4,810] 2026-2030: ~ 5,200 [1890 - 10,200]
	Total DALYs averted	2021-25: ~ 240,000 [40,000 - 600,000] 2026-30: ~ 1.1m [0.2m - 3.1 m]	2018-2025: ~ 39,900	Not reported		2019-2025: ~ 160,000 [59,000 - 305,000] 2026-2030: ~ 153,000 [55,589 - 312,135]
	Additional patients cured	2021-25: ~ 222,000 [32,000 - 595,000] 2026-30: ~ 443,000 [100,000 - 1.2 m]	2018-2025: ~ 13,300	2015-2026: ~ 12,600		2019-2025: ~ 66,000 [24,000 - 135,000]
Economic impacts (KPI 4.2)	Averted disease management costs	2021-25: ~ US\$37m [3m - 87m] 2026-30: ~ US\$262m [33m - 692m]	2018-2025: ~ US\$18.9m	2015-2026: ~ US\$19m	<i>Coalition PLUS's role in issuing the CL in Malaysia is also likely to have contributed to cost savings in the country, with expenditure on treatments falling from US\$3.7 million in 2013 to US\$2 million in 2019, despite increasing the number of patients treated from less than 300 to more than 3,100.</i>	2019-2025: ~ US\$ 62m [20m - 117m] 2026-2030: US\$ 54m [14m - 110m]
	Cost savings from price reductions	<i>Cost savings from the lower cAg RDT price are considered to be used for treatment costs</i>	<i>FIND supported cost reductions in countries through testing pathway simplifications</i>	2015-2026: US\$105 million (with an additional US\$13 million in cost savings used to pay for the additional treatments)		2019-2025: ~ US\$ 25m [9m - 51 m]

⁶⁰ Includes impacts for cAg RDT globally and impacts from Molbio Truenat HCV testing in India and as such only provides a partial impact of FIND's work on diagnostic tools.

⁶¹ Includes direct impacts from FIND studies conducted during the project or shortly after project end (e.g., in cases where study participants are still expected to receive treatment). Additional impacts from FIND donations are listed in section 5.4 of Part B of the report. The estimates do not include any additional impact from FIND of expanding the use of testing pathway decentralisation and simplification and as such the provided figures only provide a partial impact of FIND's work on diagnostic approaches.

⁶² The MSF grant, which has supported updates to WHO guidelines through the WHO Enabler grant, led to cost savings and reduction in loss-to-follow-ups by encouraging simplification of HCV testing algorithm. The estimate presented only include the benefits of the reduction in genotyping (by reducing costs and loss-to-follow-up) and as such only represent partial benefits of the simplification of HCV testing algorithms.

In addition to the impact modelling, key qualitative impacts highlighted during the review include:

- **Equity impact:** Unitaid’s direct investments have been noted for the critical role they have had in addressing the needs of marginalised populations, particularly PWID, prisoners and MSM, which are key populations groups frequently overlooked in a number of LMICs (see Section 6.4 in Part C of this report for further details), and has been noted as one of Unitaid’s more effective portfolio’s in addressing the needs of marginalised populations, driven considerably by the work of Coalition PLUS as well as FIND’s in-country pilot activities and some of MSF’s pilot projects.
- **Strategic benefits and positive externalities:** Key strategic benefits and positive externalities outlined across the portfolio include:
 - The importance of Unitaid’s investments in **raising the profile of HCV** both with global partners such as WHO, MSF, and in countries. As mentioned by one stakeholder, Unitaid “*brought that visibility to the HCV space that wasn’t there before; also because no other big donor is operating in this space*”. In fact, stakeholders noted that the Unitaid’s HCV portfolio included some of the very first grants from international organisations to support work in HCV in LMICs, which helped to bring visibility to the HCV space.
 - **The portfolio has also enabled grantees to significantly expand their support for HCV beyond the grants.** For example, Unitaid’s support for Coalition PLUS has enabled the organisation to establish its presence in the HCV space, enabling it and its members to advocate globally for more inclusive and widespread HCV programmes. Contributions the Coalition PLUS grant has also helped build community networks and CSO capacity across different countries, enabling them to advocate for improved HCV testing and treatment at both national and global levels. In some contexts such as Malaysia, the Coalition PLUS grant was also noted as being an important contributor to local CSOs being included as part of key in-country mechanisms such as the Global Fund CCM, where partners have and stated they will continue to advocate for greater HCV funding and integration with other disease responses as part of this. For the MSF grant, the support Unitaid provided was also noted as being important for catalysing MSF’s wider work in this space, with HCV programming within MSF being launched in 13 countries following the initiation of the grant.⁶³
 - **There is also evidence that price reductions achieved in the portfolio has had a spill-over effect into other areas.** For example, in the context of the MSF grant, the access pricing achieved may have had positive externalities in terms of prices obtained by other international organisations such as the Global Fund and UNDP. In addition, as noted in Section 6.2 of Part C, the issuances of the CL in Malaysia had positive impacts in terms of enabling other MICs to be included in the VL for SOF.

⁶³ Dalberg (2019), Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs. Evaluation for Unitaid; Final Report.

4. CONCLUSIONS AND RECOMMENDATIONS

Unitaid's portfolio in HCV has been extremely relevant and coherent, and of considerable value-add given limited funding for HCV both globally and in countries. The advent of DAAs in 2015 provided Unitaid with a unique opportunity to harness its role in supporting market interventions to enable commodity access in LMICs, tackling a range of critical gaps along the product value chain including: (i) lack of knowledge and awareness on HCV; (ii) limited country policies and lack of global guidelines; (iii) limited evidence on efficiency and effectiveness of HCV testing and treatment strategies; (iv) lack of available and quality assured diagnostic tools; and (v) unaffordability of available treatment in LMICs. The HCV portfolio represents a good example of coherence in terms of "joint-up" and complementary grants, with good synergies and coordination across grantees in support of overall objectives. With limited funding and action on HCV both globally and in countries, Unitaid's foray into HCV has been of much value-add; indeed, Unitaid has played a significant role in raising the profile and visibility of HCV. This portfolio is also one of the strongest examples within Unitaid of focusing on marginalised and vulnerable populations.

Unitaid's HCV investments have helped to "kick-start" the overall market for HCV, with a number of transformational achievements across key access barriers. While DAAs were available at the start of Unitaid investments, they were not accessible, and the Unitaid supported grants have helped mobilise the market in a number of critical ways. Some of the biggest achievements are with regards to significantly progressing the availability of a range decentralised tools for screening and testing of HCV, which combined with more affordable treatments in LMICs and simplified and decentralised testing, treatment and care models offer countries the means to support their elimination efforts. Key contributions by access barrier include:

- **Innovation and availability:** Through the FIND grant, developed a new "game-changing" tool (cAg RDT) and took forward innovative products (HCVST), as well as additional HCV diagnostics (Molbio HCV test, Fingerstick HCV test, HCV RDTs, DBS), which are now further along the pipeline than they would otherwise have been, with the significance that once they enter the market, they have the potential to enable implementation of decentralised and simplified testing of HCV across various settings and different population groups.
- **Quality:** Through the WHO PQ grant, increased the number of HCV diagnostics and treatments which are quality-assured, thereby enabling countries to have better assurance of the HCV diagnostics and treatment they procure. The FIND grant also worked with manufacturers to stimulate them to apply for WHO PQ and facilitated dossier submission by using data generated by the grant.
- **Affordability:** MPP voluntary licence for DCV has enabled many LMICs to access more affordable treatment; Coalition PLUS in-country advocacy work enabled some countries, particularly Malaysia, to significantly reduce the price of DAAs in the public sector; MSF enabled countries to access more affordable prices both directly through its global access price negotiations as well indirectly through price transparency and patent oppositions. In terms of diagnostics, MSF and FIND demonstrated the feasibility of simplified cost-saving algorithms, although the overall cost of diagnosing HCV patients remains relatively high.
- **Demand and adoption:** WHO Enabler grant supported the development of normative guidance on HCV, incorporating data and evidence from the FIND and MSF grants; Coalition PLUS supported HCV policy development, including on decentralisation and simplification, and community awareness in project countries with a number of countries having national programmes and guidelines in place; Coalition PLUS and FIND have supported community empowerment and mobilisation to enable communities to demand and access HCV services.
- **Supply and delivery:** FIND and MSF demonstrated the feasibility of decentralised, integrated and simplified models of HCV testing and treatment, which can achieve high rates of cure in LMICs in a cost-effective and efficient manner.

Furthermore, through its HCV investments, Unitaid has helped put in place some of the conditions and tools for scale-up at the global level, and to some extent at the country level, which are critically important to support the path to elimination by 2030. At the global level, Unitaid's investments have made important contributions to the conditions for creating sustainable access as well as disseminating evidence and knowledge, and some progress has been made on aligning strategic priorities and needs through the development of WHO's

elimination strategies. However, major challenges remain with regards to financing for HCV and the extent to which testing and treatment is being procured in countries. At the country level, the extent to which Unitaid has created the conditions for scale-up is variable, with good progress having been made on advancing political commitment and community-driven demand. Although supportive policies are in place across a number of countries, the extent to which these policies are being implemented and HCV care cascade integrated into public health programmes is still limited. As such, globally and in countries, there are a number of remaining challenges before full scale-up can be achieved, including: (i) a number of the diagnostics developed and taken forward by FIND need to come onto the market and will then need to be registered and piloted in countries before they can be deployed and used; (ii) there is a need for price negotiations with manufacturers and price transparency of HCV diagnostics globally; (iii) country programmes need to ensure greater commitment from policymakers and prioritisation of HCV; and (iv) general awareness on HCV continues to be low in many countries and more efforts are needed to ensure communities are aware and empowered to seek HCV testing, treatment and care services.

Financing for HCV remains the critical issue given both the absence of key global donors as well as the limited domestic budgets being allocated to HCV. Whilst some countries have increased budget allocation to support national HCV programmes (e.g. India), the availability of sufficient finances to enable scale-up to happen remains challenge for the majority of countries. This is particularly true for countries where treatment prices continue to be unaffordable, thus hampering the ability and willingness of governments to support screening and treatment using domestic resources. Furthermore, Unitaid’s investments have not been able to catalyse HCV funding from other global health donors, and there continues to be little appetite from major funders such as the Global Fund. Continuing advocacy and awareness raising efforts with policymakers, specifically to ensure that HCV is “picked-up” in national UHC packages and that governments are aware of the benefits of HCV testing and treatment, will be key to ensure adequate prioritisation and funding allocation of national budgets to HCV programmes. This is particularly important given that COVID-19 has diverted priorities and funding across the majority of LMICs.

To conclude, significant progress has been made through the Unitaid HCV portfolio of investments, and it is important that Unitaid continue to build this momentum for HCV to further leverage existing gains. Integration of HCV with other diseases and through a primary health care approach will be critical to support countries in their elimination efforts. Specifically, integration of HCV testing on existing multi-disease platforms offers the potential to avoid vertical programming for HCV at the health system level, whilst also potentially reducing costs. There is also a need for improved data on HCV incidence and prevalence, both globally and in-countries, which is important to highlight the magnitude of the issue as well as to enable better targeting of interventions and monitoring of progress. Whilst these issues are broader than Unitaid’s mandate they are critical to enable scale-up globally and nationally.

Drawing on our overall evaluation findings and conclusions we make the following recommendations:

Recommendations with regards to Unitaid HCV portfolio

1. Recognising the multiple funding opportunities for Unitaid, our evaluation strongly recommends to continue funding investments in support of alleviating access barriers and scaling-up HCV programmes in countries in the next Unitaid strategic period 2022-25. A review of the current access conditions and impact of the portfolio suggests the following key areas:
 - a. Improving the affordability of the care cascade including both diagnostics as well as where treatments are unaffordable.
 - b. Supporting the ongoing commitment and implementation/ operationalisation of HCV programmes by country governments – this may include continuing/ greater advocacy efforts with policymakers, including through building the investment case and highlighting the economic benefits of investing in country HCV programmes. It may also include working closely with donors such as the World Bank and regional development banks that provide general health funding to countries.
 - c. Taking forward the transformational breakthrough achieved on cAg RDT in terms of seeing through the arrangements with the commercialisation partner (including pricing) as well as consideration of any implementation support required for countries.
 - d. Taking forward the progress made with HCVST in terms of availability of products in the market and their use in practice.

- e. Continuing the emphasis on key populations, especially on marginalised and vulnerable groups such as PWIDs; this will be particularly important for donors such as Unitaid to support given limited potential for domestic government funding in countries where PWIDs have high HCV prevalence but continue to be stigmatised, marginalised and even criminalised.

Unitaid should ensure continued coherence and coordination between any future HCV investments including with the work of other partners, with greater allocation of responsibility for coordination to Unitaid who has a portfolio perspective. Unitaid should also put greater effort towards dissemination of portfolio evidence-base and achievements to non-project countries and globally.

2. Emphasise integration of HCV diagnostics where feasible as well as a broad health systems approach to the HCV cascade of care (i.e. no verticalization) as a means to also ultimately support affordability and scale-up. While integration is a complex area, at a minimum, Unitaid HCV projects in the future should observe the integration priority in their work.
3. Whilst beyond the Unitaid mandate, there are critical issues with regards to mobilising domestic financing and having quality data on HCV burden, amongst others, that are key to ensuring the impact of Unitaid investments and successful scale-up. Unitaid should continue with efforts to working with other global partners and country efforts in this regard.

Recommendations with regards to Unitaid model and processes

These are based on learnings from this evaluation and include the following:

4. Useful to introduce mechanisms in the next Unitaid Strategy that consider impact at the level of the portfolio e.g. developing a TOC from the outset, defining parameters on the success of the portfolio and not just individual grants, etc. We understand that some measures in this regard have begun to be implemented by Unitaid in recent years.
5. Consider a more effective balance between upfront project preparation and the need for reprogramming, especially in the initial years of any grant. There should be greater attention by Unitaid to ensure clarity of expectations from the outset with regards to grant targets, objectives and outcomes, even if these need to be revised during grant implementation.
6. Key Unitaid operational processes such as with regards to reprogramming, grant M&E, etc. should be better aligned with grant context and the value of grants. This means potentially differentiating Unitaid processes by the type or value of grant (i.e. more or detailed processes for larger value grants or more complex grants or high risk grants) with relatively simpler and nimbler approaches for low value grants.

These operational recommendations 4-6 should be considered as part of the next Unitaid Strategy development process.

PART B: GRANT EVALUATION – FIND HEAD START

5. FIND HEAD-START GRANT


The FIND HEAD-Start (Hepatitis C Elimination through Access to Diagnostics) grant was approved by Unitaid in October 2016. The goal of the grant was to contribute to the WHO targets on HCV for 2030: 90% reduction in incidence, 65% reduction in mortality, 80% of patients receiving treatment. The outcome of the grant was the increased availability and adoption of new and existing HCV diagnostic technologies that are quality assured, and a decrease in the cost of the overall package of HCV diagnosis and treatment. The grant had four main outputs, but in terms of relevance and resource allocation, there was a heavy emphasis on Outputs 1 and 2:

- Output 1: Expand the number of technologies available for HCV screening, confirmation, and test of cure that are ready for purchase or use in countries
- Output 2: Prepare the market for the introduction, use and placement of new technologies for HCV screening, confirmation and test of cure
- Output 3: Increase affordability of HCV diagnostics and testing pathway
- Output 4: Generate evidence to support global, regional and national policy change, implementation guidelines and scale-up prepared, disseminated, and shared with key stakeholders

Through these four outputs, the FIND HEAD-Start grant aimed to address all five access barriers defined by Unitaid, but only to overcome the innovation and availability, the quality, and the affordability access barriers⁶⁴.

Sections 5.1-5.4 present findings across the four pillars of the evaluation framework (relevance and implementation, effectiveness, impact, scalability and transition); Section 5.5 presents summary findings from the three focus country case studies of Georgia, India and Malaysia, and the non-focus case study of Myanmar; and Section 5.6 concludes. For introductory information on this grant evaluation in terms of the evaluation background, scope and objectives as well as framework and methodology please refer to Section 1 included in Part A of this report.

5.1. RELEVANCE AND IMPLEMENTATION

Key findings	Strength of evidence
The focus of the FIND grant on “unlocking the diagnostic bottleneck” was extremely relevant and much needed.	
The emphasis of the project on high-risk and vulnerable populations was of much value given their high burden and limited access.	
FIND’s work at the global level and in terms of product development was more in line with its comparative advantage as an organisation, with its work in country demonstration projects being more challenging given limited field presence and expertise.	
Grant reprogrammings were of value in terms of content but inefficient in terms of process.	

The focus of the FIND HEAD-Start grant on both R&D (Output 1) and demonstration studies (Output 2) was extremely relevant given that in 2015 the “diagnostic bottleneck” was a key challenge for HCV. When the grant was conceptualised in 2015/16, screening for HCV was costly and there were no quality-assured RDTs on the market, whilst confirmatory testing was not only expensive, but limited to centralised laboratories and available only in few major cities across LMICs. Furthermore, HCV diagnosis was based on complex diagnostic algorithms and HCV treatment and care was only provided in specialised tertiary hospitals in LMICs. As a result, people remained undiagnosed and not able to access the revolutionary DAA treatments. Given this context, the FIND grant appropriately focussed on two core areas: (i) R&D to expand the number of diagnostics to screen and test HCV

⁶⁴ As noted in the 2019 Project Amendment “The current amendment does not affect the goal of the FIND HEAD Start grant. The access barriers identified under outcome have been streamlined from 5 to 3 access barriers during the rest of programme implementation: Innovation; Quality; and Affordability”. However, as per the discussion with the Unitaid project team, the three key access barriers that the FIND grant sought to address were: innovation and availability; quality; and, supply and delivery.

(through work under Output 1); and (ii) demonstration studies to show the operational feasibility and effectiveness of implementing decentralised, integrated and simplified models of HCV testing, treatment and care in LMICs.

The FIND HEAD-Start grant was also appropriately focussed with the right balance of undertaking clinical and operational studies to inform both research gaps identified in the 2017 WHO HCV testing guidelines as well as the needs of countries in implementing the simplified diagnostic algorithm included in these WHO guidelines. Despite the WHO 2017 HCV testing guidelines outlining a simplified HCV diagnostic algorithm – screening, confirmatory testing, pre-treatment assessment, and test of cure – countries still lacked clear strategies and approaches on how to roll-out and implement screening and confirmatory testing for HCV in practice. Thus the FIND grant:

- Undertook research and development activities and clinical studies under Output 1 to inform the key research gaps identified by WHO in terms of additional data on HCV self-testing, POC viral load testing, DBS, Combo testing, and use of cAg RDT as alternative measure to VL; and,
- Undertook demonstration studies under Output 2 to generate evidence on HCV screening/confirmatory approaches using different testing approaches (decentralisation through POC testing and hub-and-spoke models, simplification of diagnostic algorithm, integration with multi-disease testing) and service delivery models (community- or health-facility -based) across a range of epidemic settings and populations in LMICs.⁶⁵ Although initially the FIND grant had selected seven countries in order to implement demonstration in countries at various stages of their HCV programme development⁶⁶, the number of countries were revised down to four during the reprogrammings (details on why are included in the findings below), which unfortunately limited the potential for evidence-generation on approaches and service delivery models across various settings and stages of national HCV programmes.

Despite the appropriate strategic intent of the grant, the FIND HCV team is not considered to have been the best-placed partner to undertake in-country demonstration projects, particularly at the start of the grant. Stakeholders noted that FIND's strength was on research and product development with manufacturers (Output 1). In particular, manufacturers praised FIND's technical expertise on product development and product optimisation/validation, the support and collaborative approach on clinical protocol development, the access to FIND's HCV clinical sites and FIND's knowledge about data required for CE and WHO PQ submissions. However, stakeholders noted that FIND HCV team was not the best choice of partner to undertake the demonstration work in countries: the FIND HCV team, particularly at the start of the project, did not have sufficient field presence, had limited experience with country project implementation and was not sufficiently embedded in countries (except for India⁶⁷), nor did it have strong pre-existing relationship with governments (although worked hard towards this end, as per the last findings in this section). As a result, the FIND HCV team took longer to get its country operational capacity up to speed, which led to delays in implementation and slower progress.

While the initial emphasis of the grant on HCV-HIV co-infected patients was diluted over the years, the grant appropriately maintained a focus on high-risk and vulnerable populations. Initially, the focus of the grant was on HIV-HCV co-infected patients as per the requirements of the Unitaid Board. Although this focus was gradually diluted (rightly so, in that this was perpetuating a silo-ed approach which is not aligned with the prevalence of the disease), the HEAD-Start grant maintained a strong focus on demonstrating HCV testing approaches and service delivery models amongst high-risk populations including: (i) PWID in Georgia, Myanmar and the Indian states of Manipur and Punjab; and (ii) high-risk groups such as MSM and PLHIV in Malaysia and PLHIV in Punjab. Furthermore, in India the grant supported HCV diagnostic literacy amongst key communities such as PWID, MSM and transgender (TGs). The diagnostic R&D work under Output 1 also included the development of technologies to address needs of high-risk and vulnerable populations. In particular: HCVST is viewed as a key tool to reach high-risk and vulnerable populations such as MSM; the evaluation of 13 HCV RDTs assessed their performance on HIV-HCV co-infected samples; the

⁶⁵ FIND (2019) Project Plan, Second Amendment.

⁶⁶ Non-existent HCV programme in Cameroon; nascent HCV programmes in Thailand, Viet Nam, India, Malaysia; new programme in Myanmar; and expanding programme in Georgia.

⁶⁷ FIND has a had a country presence in India since 2007.

development of the Xpert HCV viral load Fingerstick greatly benefits PWID given the greater challenge in drawing their blood; and the DBS sampling validation work is particularly important to help reach remote and rural populations, who would otherwise not have access to HCV confirmatory testing. This focus on high-risk and vulnerable populations is of much added value given these are the groups with the largest HCV prevalence across countries and also have traditionally been marginalized in terms of accessing health services and funding.

Good synergies were harnessed in FIND’s global-level work. In particular, we note that at the global level, the FIND HEAD-Start grant worked closely with the WHO Enabler grant and WHO PQ grant on evidence generation and WHO guidelines development. Through the Enabler and PQ grant, the WHO Global Hepatitis Programme and WHO PQ collaborated closely with FIND on the needs of WHO with regards to evidence generation. This has been particularly key for some products such as HCV self-testing, whereby the close collaboration has led to WHO calling for a Guidelines Development Meeting on HCVST in February 2021, with the aim of issuing a recommendation on HCVST in mid-2021. FIND worked with WHO PQ with regard to the technical service requirements for HCVST and the data for the recommendation is fully based on the clinical studies data of HCVST done by the FIND grant under Output 1. Coalition PLUS also collaborated with FIND on the HCVST work and the synergies with Coalition PLUS helped to identify the communities to be an active part in the clinical studies and research. The FIND country work under Output 2 will also help to inform the next revision of the WHO guidelines on HCV testing and treatment, but the input is expected to be more limited than for HCVST, due to the fact some of the studies were not designed in a sufficiently robust way to include the findings in WHO’s systematic reviews (see section 5.2 on Demand and Adoption for more details on this).

Synergies at country level were more variable. At the country level, the FIND and Coalition PLUS grants overlapped in India and Malaysia and synergies have been built, with some exceptions. In Malaysia, FIND collaborated with MAC to conduct a national screening campaign as part of World Hepatitis Day 2019, and with MTAAG+ to deliver a HCV Diagnostics Advocacy Workshop. In India, there was good collaboration in Delhi, where both FIND and Coalition PLUS partnered with DNP+ and were able to establish linkages between community empowerment and mobilization and treatment. In Manipur, there was no collaboration between the FIND and Coalition PLUS projects due to the lack of clarity and coordination between the two partners on the ground. However, it is not clear if this resulted in missed opportunities for synergies.

The original project timeline of three years implementation, plus a six-month preparation period, was not adequate given both the nature of the grant as well as Unitaid processes, and has resulted in inefficiencies in the implementation of the grant. Specifically, we note the following key issues:

- The fact that original grant had not been thought out in detail led to three major reprogrammings (and consequent project amendments) and one minor re-programming over the course of the grant, which resulted in significant delays due to the ‘activity freeze’ during the reprogrammings. There is an important lesson here for Unitaid in terms of both requiring a sufficient level of project preparation before project commencement, as well as how to optimally manage the re-programming process during the grant.
- For the global level R&D work, the original aim was to bring some HCV diagnostic products to the market during the lifetime of the grant⁶⁸; however, the many reprogrammings which included changes on the range of HCV technologies that would be the focus of the R&D work, coupled with the initial delays of the grant, reduced the overall timeline available for R&D. The inclusion of go/no decision by Unitaid was an important step to define what diagnostic product should move forward and which ones should not, but also fueled further delays due to the multiple iterations/ revisions by the grantee and extensive approval processes at Unitaid.
- For the country-level work, timelines were too short due to: (i) longer planning processes due to FIND HCV team limited experience with country project implementation, particularly at the start of the grant; (ii) relationship-

⁶⁸ The Original Project Plan states that Output 1 of the FIND grant is “focussed on bringing new HCV POC products to the market”, although stakeholder consultations for this evaluation indicate difference of opinion as to whether grant progress needs to be assessed in terms of market entry or not. Nevertheless, stakeholders noted that there has been significant progress in this access barrier and recognised the challenges of bringing complex new and innovative diagnostics to the market and that it is not often feasible to assign precise timelines for products entering to the market due to many steps and linkages involved in product development, optimisation and commercialisation.

building with the governments in countries to ensure collaboration and project buy-in, which is critical for potential scale-up but took a lot longer than anticipated; and (iii) lack of HCV service delivery experience in the majority of the countries/states. Country-level work was also significantly disrupted by COVID-19, which resulted in the need for a no-cost extension until December 2020 to mitigate risks of activities not being completed.

Grant reprogrammings were important to streamline the focus of the grant and strengthen linkages across the grant outputs, but required significant time inputs and approval processes and led to substantial delays in timelines and implementation. Stakeholders noted that the grant approved in 2016 had not been fully thought out in detail and there were still gaps in terms of how the grant was to achieve its objectives. Thus, the first re-programming in 2017 was particularly important to streamline resources and strengthening the linkages between Output 1 and Output 2, whilst providing clarity on the range of activities to be conducted. The first reprogramming also expanded the focus of Output 1 (including through the doubling of its budget) to support a larger number of HCV diagnostic technologies at various stages of product development, including a cAg RDT and HCV self-tests. One country was also removed (Thailand). The second re-programming in 2018 was mainly a result to the delays with the country work and “*concerns regarding the feasibility of obtaining concrete results from the operational research studies before the conclusion of the Unitaid grant period in mid-2020*”.⁶⁹ The reprogramming focussed on streamlining the activities under Output 2 by prioritising those with the greatest strategic significance and the best chance of achieving targets within the remaining timelines. As a result, Cameroon and Vietnam were removed as pilot project countries and the budget was reduced significantly from US\$38.3m to US\$30.1m. There was also a minor re-programming in 2019 to amend activities related to Combo testing and HCVST: Combo testing was refocussed on clinical performance in the field, and the focus on HCVST was strengthened given its priority from a WHO guidelines perspective. The overall grant budget was also reduced to US\$27.4m (with budget reallocated across activities). Finally, the third re-programming in 2020 was a no-cost extension to extend the project timelines until December 2020 and enable country projects to be fully completed and transitioned given delays from lockdowns as a result of the COVID-19 pandemic. Overall, as noted, these reprogrammings were useful in content but challenging in relation to the overall timelines of the grant.






Collaboration with national authorities in the country projects was generally strong, thanks to the upfront time FIND invested in building a working relationship with government stakeholders. FIND did not have country presence in the project countries (except for India) and had to build a relationship with the MoH almost from scratch in most countries. In Malaysia and Georgia, FIND engaged closely with the Ministries of Health and the national HCV programmes, using existing health care sites (hospitals in Malaysia and harm reduction clinics in Georgia), which enabled the projects to be robustly implemented and have resulted in successful transition and scale-up in both countries. In India, given its federal structure, FIND collaborated closely with state-level viral hepatitis control programmes and State Nodal Officers for HCV; however, collaboration with the National Viral Hepatitis Control Programme was more limited. In Myanmar, FIND invested significant time in bringing together the stakeholder from the HCV and HIV vertical programmes to demonstrate the potential integration of HCV testing using existing viral load platforms in central laboratories.

5.2. EFFECTIVENESS

This section provides an assessment of the FIND’s grant contribution to the Unitaid defined access barriers, including key achievements and their significance in catalysing the HCV market. Table 5.1 provides a summary of our assessments including level of progress (i.e. the extent of achievements as significant/ good/ limited), strength of effect (i.e. the magnitude/ value of the progress given the market context as well extent of attribution to the grant, considered along a scale of high, moderate and low) and key areas of contribution as well as the strength of evidence of the finding. This is followed by a detailed consideration of each of the five access barriers in turn.

⁶⁹ FIND (2019), Project Plan, Second Amendment.

Table 5.1: Summary of findings on the FIND grant's contribution to Unitaid's access barriers

Access barrier	Key areas of contribution	Level of progress	Strength of effect	Strength of evidence
Innovation and availability (key access barrier)	<ul style="list-style-type: none"> Supported the R&D processes thereby accelerated progress of diagnostics, in particular: for cAg RDT, HCVST and the Molbio HCV test Provided incentives to minimise risks given uncertainty around size and reach of HCV diagnostic market 	Significant progress: FIND's R&D has increased the pipeline of HCV diagnostics with a range of products for screening, centralised and decentralised testing	Moderate: some tools already on the markets, with others in the pipeline, and expected to come onto the market within the next 1-3 years	
Quality (key access barrier)	<ul style="list-style-type: none"> Enabled select manufacturers to have clinical data needed for preparation of dossiers to WHO PQ and CE Highlighted the value of WHO PQ and stimulated interest of diagnostic manufacturers to apply to WHO PQ and CE 	Good progress: a number of HCV diagnostics have applied for WHO PQ and CE-mark which will increase the range of pre-qualified products on the market	High: FIND has supported manufacturers in application submission as well as in stimulating their interest in applying to WHO PQ	
Affordability	<ul style="list-style-type: none"> Simplification of diagnostic algorithms introduced in some of FIND's projects enabled decreases in the cost of countries' diagnostic pathways through the elimination of unnecessary tests/ steps 	Limited progress: shown the potential to reduce the diagnostic pathway cost through simplification, but limited progress made on reducing the price of existing HCV diagnostics, particularly confirmatory tests.	Low: demonstrated affordability through simplification of algorithms, but uptake is an issue	
Demand and adoption	<p>Evidence generated by the demonstration studies is being used to:</p> <ul style="list-style-type: none"> inform WHO HCV Testing Guidelines revisions, specifically on the role of decentralised approaches by some of the countries to update their national/state policies to adopt these models in their national HCV programmes 	Good progress: generated evidence which is being used to update both WHO guidelines and national guidelines	Moderate: evidence generated will help inform some WHO guidelines revisions on decentralisation and PoC testing, as well as national guidelines (for select countries)	
Supply and delivery (key access barrier)	<p>Demonstrated a number of key aspects that would improve diagnostics delivery:</p> <ul style="list-style-type: none"> Decentralisation of HCV testing and treatment in non-traditional settings such as ART centres, HRS, community-based centres is feasible and reduced LTFU and retention across the HCV care cascade 	Significant progress: the in-country studies have demonstrated the feasibility and effectiveness of implementing decentralised, simplified and integrated models of care	Moderate: the extent to which they will be sustained and scaled-up is still unclear for many countries and dependant on many factors	

Access barrier	Key areas of contribution	Level of progress	Strength of effect	Strength of evidence
	<ul style="list-style-type: none"> • Simplification of the HCV algorithm increases retention by reducing the number visits along the testing and treatment pathway without the need for specialised doctors • Integration of HCV testing with HIV and TB testing is operationally feasible to increase HCV testing using existing multi-disease platforms 			

Innovation and availability – key access barrier

The FIND HEAD-Start grant has made a significant contribution to the range of products being developed for HCV screening and diagnosis.

In terms of unlocking the market for HCV, in 2015, DAAs offered the opportunity to successfully treat the majority of patients with active HCV infections. But countries needed to first “find” the people who required treatment: prior to 2015, testing for HCV in LMICs was limited to central laboratories, implying that most patients were unable to access testing in a timely and affordable manner. In particular, there were:

- Limited availability of quality-assured RDTs and no HCV self-testing RDTs to screen for HCV;
- No confirmatory RDTs that could be fully decentralised; and,
- Limited point-of-care (POC) HCV viral load diagnostics available in LMIC countries.

The FIND grant has contributed to increasing the suite of diagnostic tools in the pipeline in each of these three areas, with a specific focus on diagnostics that would facilitate decentralised testing, bringing diagnosis closer to the people who needed it. A summary of FIND’s contribution is depicted in Figure 5.1.

Figure 5.1: FIND HEAD-Start contribution to increasing the availability of diagnostics along the diagnostic pathway



Table 5.2 details the progress of FIND’s R&D investments in the development of new tools and outlines the gaps pre-grant, activities undertaken by the grant alongside a consideration of the counterfactual (with the latter being largely based on stakeholder perspectives), benefits of the diagnostics (i.e. a consideration of the “so what”), and the next steps/ implications for scale-up going forward.

Table 5.2: FIND HEAD-Start investments in R&D

Diagnostic pathway	Pre-grant status	FIND activities and counterfactual	Benefits	Next steps
Screening - RDTs	<p>In 2016/17, there were a number of RDTs for HCV screening on the market, but only two were PQ'ed (SDBioline and OraSure), and one of these affordable (SDBioline).</p> <p>Many countries, especially LMICs were procuring non-PQ RDTs, with no visibility with regards to quality and performance of these RDTs, especially amongst HIV-HCV co-infected patients.</p>	<ul style="list-style-type: none"> Evaluated the performance of a range of RDTs, which also enabled companies to apply for WHO PQ Data was published in a peer-reviewed article, providing countries with an indication of the performance of a significant number of RDTs on the market <p>Counterfactual: RDT market would still lack clarity on the performance of a range of RDTs and RDT manufacturer would not have been incentivised to apply for PQ.</p>	<p>The study had an additional effect of stimulating the market of PQ'ed RDTs, as two additional companies have applied for WHO PQ using the data generated by the FIND study.</p> <p>If both products receive WHO PQ, there will be an additional two affordable quality-assured RDTs for HCV, thereby increasing competition and the menu of HCV RDTs which countries can procure from.</p>	<p>Countries will be able to reference the study to have an understanding of the performance of the RDTs they plan to procure,</p>
Screening - HCVST	<p>HCVST was identified as core gap in the 2017 WHO HCV guidelines, given the absence of data on acceptability as well as on performance of existing prototypes.</p> <p>There was also limited manufacturer interest, given the absence of WHO guidelines on the use of self-testing and therefore no clear market for manufacturers.</p>	<ul style="list-style-type: none"> FIND worked together with two manufacturers who already had HCV self-test prototypes to conduct studies to demonstrate the acceptability, usability and performance of self-testing across various population groups in 10 countries. FIND worked in close collaboration with the WHO Global Hepatitis Programme and WHO PQ with regard to the technical service requirements and HCVST guidelines development <p>Counterfactual: In the absence of FIND's investment there would have been no data for the WHO guidelines revisions and manufacturers would not have prioritised the development of their HCVST prototypes</p>	<p>FIND's investment has been the main contributor to unlocking the market for this HCV screening tool.</p> <p>HCVST increases even further the level of decentralisation by bringing the diagnostic directly to the user. As such, it can play an important role in terms of increasing testing rates. In particular, it has the potential to increase testing rates especially amongst high risk groups, as one of the main advantages is that it addresses the fear of stigma, discrimination or even prosecution for some high-risk groups (e.g. for MSM).</p>	<p>Based on the FIND HCVST data, WHO has called for a Guidelines Development Group (GDG) meeting in February 2021 to provide a recommendation and issue guidance on HCV self-testing, thereby opening up the market for HCV self-testing.</p> <p>Implementation gaps:</p> <ul style="list-style-type: none"> <i>At the users' level:</i> key issues around the marketing of HCVST given the limited awareness around HCV and the fact that it is asymptomatic for long periods of time. <i>At the policy level,</i> demonstration studies needed to support the adoption and inclusion of HCVST national guidelines.

Diagnostic pathway	Pre-grant status	FIND activities and counterfactual	Benefits	Next steps
Confirmation test – cAg RDT	No confirmatory cAg diagnostic in RDT format available on the market. Limited understanding of the feasibility of cAg in RDT format.	<ul style="list-style-type: none"> • FIND working with academic institutions and research development companies and demonstrated the technical feasibility of developing a cAg in RDT format with an acceptable level of sensitivity. • Engaged a manufacturer that will take the product forward to commercialisation. <p>Counterfactual: in the absence of the FIND grant there would be no cAg RDT at prototype stage, which is now being taken forward by a commercialisation partner.</p>	<p>This product has been characterised as a “<i>gamechanger</i>” by a number of stakeholders given its significance in terms of:</p> <ul style="list-style-type: none"> • Allowing the decentralisation of HCV confirmation test to Level 0 health care facilities, including community settings, with the potential to allow for the implementation of “test and treat” programmes to be provided at point of care (for non-complicated cases). • Simplification of the diagnostic algorithm from a two-step to a one-step approach, particularly for high-risk groups (with cAg RDT being performed on high-risk groups without the need for prior screening). 	<p>The introduction of cAg would also require implementation support such as task shifting and access to HCV care at the primary health care level. These would need to be part of a comprehensive country policies that include cAg RDT testing.</p> <p>The timeline for market entry of the cAg RDT is still long, and dependant on a number of steps being achieved, (including signing of commercialisation agreement, clinical studies, manufacturing, PQ process, demonstration projects and country roll-out)</p>
Confirmation test – decentralised Molbio	<p>Only one near-POC platform available in the market (GeneXpert) and some in the pipeline.</p> <p>Cost and format of GeneXpert (i.e. still requires some level of infrastructure such as electricity) continue to be challenging.</p>	<ul style="list-style-type: none"> • FIND supported the development of an HCV test for the Molbio Truenat POC platform. • Supported the validation studies and clinical trials that will enable Molbio to apply for CE-mark and WHO PQ. <p>Counterfactual: In the absence of FIND’s investment, stakeholders have noted that the Molbio HCV test would:</p> <ol style="list-style-type: none"> a. still have been at early stage of development and it would not have been a priority for the company; b. not have prioritised the clinical trials to generate data for WHO PQ and CE-mark; and, c. not be thinking about the global market, but just the Indian market. 	<p>The Molbio platform can decentralise HCV confirmatory testing at the PHC level given that it is portable, battery-operated and the HCV test cartridges are stable at room temperature with a 12-month shelf-life. Furthermore, sample preparation is very simple and automated with minimal intervention, with the potential of task-shifting the running of the HCV test to non-skilled personnel.</p> <p>The Molbio platform still requires the upfront investment in the machines and recurring cost of cartridges, albeit at a slightly lower cost than GeneXpert and with the potential to lower prices further in the case of pooled procurement/ volume guarantees.</p>	<p>The Molbio HCV test is registered in India and is being rolled-out in the private sector in India, with operationalisation in the public sector having also started (as they do not require WHO PQ or CE-mark). Once they receive WHO PQ and/or CE-mark the plan is to roll-out in other LMICs, starting with 31 priority LMICs where Molbio has existing distribution channels.</p>

Diagnostic pathway	Pre-grant status	FIND activities and counterfactual	Benefits	Next steps
Confirmation test – decentralised Xpert Fingerstick	Plasma HCV test available on near-POC GeneXpert platform but still requires infrastructure and specialised skill-set.	<p>FIND supported the clinical studies of the Xpert HCV viral load Fingerstick, which also enabled Cepheid to compile the data required for CE-mark and WHO PQ dossier.</p> <p>Thanks to the clinical data supported by FIND, the Fingerstick test received CE-mark in 2018.</p> <p>Counterfactual: The investment allowed the Fingerstick test to progress much faster along the pipeline than would have been possible in the absence of funding and technical support.</p>	<p>HCV viral load Fingerstick test uses capillary blood and is simpler to conduct, as it does not require a laboratory setting or specific skills, thereby allowing for greater decentralisation (e.g. mobile van testing), and has higher acceptability particularly, amongst high risk groups such as PWID.</p>	<p>Fingerstick registered in 22 countries including 14 LMICs and the EU.</p> <p>Developing an HCV viral load test for an existing platform such as GeneXpert, which is already in place in a number of countries for HIV and TB testing, also provides the potential for the process of greater integration of tests in the future.</p> <p>GeneXpert is expensive and requires upfront investment in the platform as well as the significant cost of the cartridges and the annual maintenance coverage.</p>
Confirmation test - centralised	<p>WHO 2017 HCV testing guidelines included a conditional recommendation on the use of DBS for HCV viral load testing. But there were only off-label approaches being used, which led to a lot of differences in performance.</p>	<p>FIND created a standard protocol and engaged three manufacturers to test and validate the protocol.</p> <p>Two manufacturers have already received WHO PQ in 2020 thanks to the FIND work on DBS.</p> <p>Counterfactual: In the absence of FIND's work manufacturers would have not prioritized PQ for their DBS products.</p>	<p>DBS sampling offers a number of benefits to increase testing rates by:</p> <ul style="list-style-type: none"> • allowing to reach rural and remote populations who would either wise not have access to confirmatory testing; • allowing the test to be run on existing platforms, offering the potential to increase machine throughput (and potentially negotiate lower prices) • allowing the test to be run at a similar price of the molecular test with a very minor cost-addition, given that DBS cards cost around US\$1/card. 	<p>Turnaround time is slightly longer than centralised testing due to sample transportation not using cold chain and sample reconstitution.</p> <p>Strong linkages to care need to be in place to avoid a large number of lost-to-follow-up.</p>

The FIND grant accelerated the development of HCV diagnostic products by providing incentives to diagnostic manufacturers to invest in HCV. Pre-2016 there were few incentives for diagnostic companies to invest in the development of new and innovative HCV diagnostic products due to a range of factors: (i) limited interest in diagnostic development due to few testing and treatment programmes in countries; and (ii) lack of clarity of the size of the HCV market and the use of diagnostics in countries in light of limited WHO guidelines (e.g. on HCV self-testing). For some of the diagnostics under development, it was noted that the investment risk was too high given the unclear returns due to uncertainty around the size of the market; Unitaid’s funding through the FIND grant thus provided an incentive for companies to invest in HCV diagnostics given the diminished risk. As one manufacturer stakeholder noted, the FIND grants work in HCV diagnostic R&D “*was a pull mechanism considering the uncertainty of diagnostics in HCV*”. Thus, the FIND grant was critical to signal to manufacturers that there is interest for a range of HCV tests. Furthermore, stakeholders, including manufacturers, noted that the investments accelerated the development of HCV diagnostic products. All consulted manufacturers noted that the FIND grant enabled them to move forward much quicker in the development/clinical trials of the products than would otherwise have been the case in the absence of the grant.

Quality – key access barrier

Through its work on R&D, the FIND grant has increased the number of HCV diagnostics which have received or applied for quality approvals such as WHO PQ and CE-mark by supporting data collection to facilitate manufacturer’s application to quality-assurance mechanisms. In 2016, the lack of available quality-assured diagnostics was a major gap. Overall, the number of pre-qualified HCV diagnostics grew from two in 2016 (one RDT and one centralised test) to 12 in October 2020, including 4 RDTs and 8 centralised tests, with a further 5 diagnostic tests undergoing review.⁷⁰ In this respect, FIND’s contribution has been important to stimulate the application of diagnostics to WHO PQ and CE-mark. The data collected through FIND’s clinical, feasibility and performance studies of the various diagnostic tools described under the Innovation and Availability section above has been used by manufacturers to support the dossier submission of five products through the WHO PQ and CE processes, including the Cepheid Fingerstick, two DBS products and two RDTs (see Table 5.3), with other products planning submission in due course. In particular FIND’s work has supported the introduction of quality HCV diagnostics by:

- Working closely with manufacturers on developing the clinical study designs, selection of clinical sites, study completion and dossier preparation, which enabled them to have the required data for complete dossier submission as well as for in-country registration;
- Highlighting the value of WHO PQ and stimulating the interest of diagnostic manufacturers to apply to WHO PQ, given that this is not usually a requirement to register their products in countries; and,
- Working closely with WHO PQ on developing the technical service requirements for HCVST for the planned submission of HCVST diagnostics.

Table 5.3: Key diagnostic products and stage of regulatory approval

	Manufacturer/ country	Technology	Status of PQ or CE
Approved	Cepheid/USA	HCV VL Fingerstick	Attained CE in 2018; submitted dossier to WHO PQ
	Abbott Molecular/USA	DBS for HCV RNA	Attained CE and PQ in July 2020
Dossier submitted	Premier Medical Corporation/India	HCV RDT	Submitted dossier to WHO PQ
	Beijing Wantai/China	HCV RDT	Submitted dossier to WHO PQ

⁷⁰ WHO PQ database, available online at https://www.who.int/diagnostics_laboratory/evaluations/en/

	Manufacturer/ country	Technology	Status of PQ or CE
	Fujireibo Europe/Japan	HCV EIA test for DBS	Submitted dossiers to WHO PQ and CE
Planned	OraSure/USA	HCV self-test	Submission envisioned/ planned for Q2 2021
	Premier Medical Corporation/India	HCV self-test	Submission envisioned/ planned for Q2 2021
	Molbio/ India	HCV VL test	Submission envisioned/ planned for 2022
	Roche/ USA	HCV DBS	Submission envisioned/ planned for 2022
	Commercialization partner	cAg RDT	Submission to be decided based on clinical studies outcomes

Affordability

The FIND HEAD-Start grant has contributed to improved affordability primarily by simplifying the diagnostic pathway. There have been some price negotiations for select HCV diagnostics, but overall these are not substantial and more needs to be done to lower the cost of HCV tests, particularly for confirmatory tests, to make them more affordable for countries.

The simplified algorithms introduced in some of FIND's in-country projects enabled a decrease in the price of the diagnostic pathway through the elimination of unnecessary steps, thereby making the diagnostic algorithm more affordable for the government⁷¹. For example, in Georgia, the 4th week of monitoring test has been removed from the testing algorithm and in Malaysia the total cost of the diagnostic pathway was reduced by 35%, from US\$176.50 in 2018 to US\$114 at the end of 2019 thanks to the simplification from a three-step to a two-step algorithm.⁷² In New Delhi, India, genotyping was removed from the diagnostic algorithm.

Through its work with manufacturers under Output 1, FIND has negotiated access prices for diagnostics in line with the affordability clause of its Global Access Policy. Manufacturers who are taking forward projects developed through the FIND HEAD-Start grant such as the cAg RDT have had to commit to FIND's Global Access pricing, thereby ensuring that when the product will come onto the market it will be affordable. Ensuring that the cAg RDT will be affordable is an important achievement which will help to amplify the game-changing nature of this tool. Furthermore, two of the RDTs which have applied for WHO PQ using FIND's data have committed to prices below US\$2/test, thus ensuring that they will be affordable, whilst also being competitive in the market. Smaller price reductions have been achieved through price negotiations and HCV diagnostic remain expensive and generally not affordable for LMICs. Table 5.4 shows the average cost of HCV test employed across the diagnostic pathway. These prices are ex-works averages and it is important to note that they vary significantly across countries. In particular, there is little price transparency of the final price paid by the end-buyer, as this will also need to include freight, taxes and duties, distribution costs and services and support cost, thereby making the final price much higher than the market price.

Table 5.4: Market price for selected HCV diagnostics

Country	RDTs (US\$)	Viral Load/ test (US\$)	Platform (US\$)
Global range	\$1-\$8	\$14-\$30*	\$ 10,000 - \$100,000

⁷¹ FIND (2019), 2019 Annual Report.

⁷² Malaysia diagnostic costs reported by FIND in 2019: screening US\$1.09; VL US\$20-40 (30); Staging US\$20; Genotyping US\$62.50.

Country	RDTs (US\$)	Viral Load/ test (US\$)	Platform (US\$)
Georgia national programme	\$0.5	\$21-\$50	
India national programme	\$0.3	\$14	

Source: WHO (2021) for Global range; CHAI (2020) for Georgia and India

Although FIND negotiated with manufactures to reduce the price of some HCV diagnostics, this was not a core area of the grant and more needs to be done to lower the cost of HCV tests, particularly for confirmatory tests, to make them more affordable for countries.⁷³ FIND together with other partners such as CHAI and the Treatment Action Group negotiated the price of US\$14.90/ test for the HCV VL GeneXpert cartridges for LMICs included on the list of countries with access to preferential prices,⁷⁴ thereby establishing a benchmark for HCV VL prices. FIND, together with CHAI, also negotiated with Roche for the inclusion of Hepatitis C and B in its Global Access Programme⁷⁵ as well as a price of less than US\$10/test for its HCV test for use on its newer molecular platforms (but these are not widely available in LMICs). As part of its country projects, FIND has also been able to bring down prices for diagnostics by increasing the volumes of patients screened and tested (lowering the price of the only PQ RDT available on the market from US\$1/ test to US\$0.80/test, as well as negotiating lower prices for reagents), but these prices were only project-related and not available to the countries per se.

Furthermore, FIND worked with WHO to produce the cost-calculator which is a costing tool to help decision-makers on testing approaches for HCV based on their cost-effectiveness in line with various diagnostic algorithms. The tool, which is available online⁷⁶ and linked to the existing HCV treatment calculator to maximise synergies, is expected to help countries to understand the cost-effectiveness of adopting various HCV testing approaches and is enable them to scale-up their HCV responses.

Overall, affordability of HCV diagnostics continues to be a challenge for countries, particularly in terms of the price of HCV confirmatory tests, and this is further exacerbated by a number of key issues which require attention: (i) lack of price transparency of HCV diagnostics across countries; (ii) need for better coordination across partners to enable stronger negotiations on price reductions with manufacturers; and (iii) potential of the role of integration of diagnostics to enable greater price reductions. On the latter point, we note that FIND has supported the demonstration of the feasibility of integrating HCV testing with other diseases (see Section on supply and delivery below) and there is the potential to improve affordability by negotiating with manufacturers across disease rather than through project-specific approaches.

Demand and adoption

FIND has contributed to improving demand and adoption by generating evidence at the global and country level which will inform revision of WHO guidelines as well as national guidelines. In particular, we note the following areas of contribution:

- *FIND's demonstration projects in countries have generated evidence that will be used in the process of updating the WHO guidelines on HCV testing and treatment, albeit with some limitations.* The data collected from FIND's demonstration in countries will be used to feed into the systematic review that WHO is undertaking in support of

⁷³ Stakeholders noted that in general, confirmatory test which are priced are sub-US\$10/test would be desirable for HCV diagnosis.

⁷⁴ Cepheid (2018), Cepheid announces expanded access to Xpert family of virology tests in global regions with the greatest need. Available at: <https://www.cephidlegacy.com/de/uber-uns/news-events/press-releases/319-cepheid-announces-expanded-access-to-xpert-family-of-virology-tests-in-global-regions-with-the-greatest-need>

⁷⁵ Roche (2019), Roche expands the Global Access Program beyond HIV to also include diagnostic tests for Tuberculosis, Hepatitis, and Human Papillomavirus. Available at: <https://www.roche.com/media/releases/med-cor-2019-07-22b.htm>

⁷⁶ Available at: <https://www.hepccalculator.org/>

its revision to the 2017 HCV Testing Guidelines. In particular, WHO is looking to update its guidelines on decentralisation and role of POC testing (as part of its update on service delivery), as well as issuing new guidelines on HCV self-testing. The systematic review on the role of POC testing will include evidence from the FIND studies that included GeneXpert (Manipur in India, Myanmar, and Georgia) and it is likely that WHO will make a recommendation on the use of POC testing. The inclusion of FIND's evidence in WHO guidelines will inform testing strategies for other non-project countries, thereby amplifying the reach of FIND's work. However, it was noted that not all studies could be included in the systematic review due to limitations in the study design and protocol used. The evidence on HCVST will include all of the data from the FIND studies on HCVST⁷⁷ which were conducted in 10 countries and the recommendation that will be issued by WHO will be solely based on the FIND data, which highlight the value and attribution of the FIND work in informing a revision to WHO's guidelines.

- *The research work and evidence generated by FIND's work in countries is also being used to update national guidelines and protocols on HCV testing.* In all four countries, select findings from the FIND projects are being used to update HCV testing guidelines and protocol. In Malaysia, the 2019 Clinical Practice Guidelines recommend the use of RDTs in the primary healthcare level, alongside centralised testing. Georgia is also currently working on the second HCV National Strategy for 2021-2025 and national consultees expressed that the experience accumulated through the FIND grant will be reflected. In Punjab (India), the state HCV testing Standard Operating Procedures are in the process of being updated and will reflect the decentralisation and simplification of HCV testing in ART centres and OST sites. They are planned to be published in April 2021. In Myanmar, the FIND/CHAI integration study protocol was shared with the NHCP, as during the dissemination meeting MoH decision makers noted that the integrated approach to testing should be considered in the ongoing drafting of the updated National Action Plan 2021-2025.
- *The FIND grant supported the development and publication of an advocacy tool to increase HCV diagnostic literacy especially amongst HCV affected communities.* Treatment Action Group in partnership with FIND developed and published the Activist Guide to Hepatitis C Virus Diagnostics in four languages; the guide offers HCV advocates, researchers etc. key information on HCV diagnostic algorithms and technologies to use for testing of HCV, as well as major barriers and challenges in the delivery and roll-out of HCV testing services. In India, for example, workshops with communities on the use of the guide have empowered community representatives and enabled them to better advocate with policymakers on HCV. The guide is an important tool to empower advocates on diagnostic literacy and was used in the FIND India project to increase diagnostic literacy amongst representatives of high-risk groups such as PWID, MSM and TGs, and in Georgia to conduct workshops for patient groups, affected communities and treatment activists.
- *FIND disseminated lessons learnt and best practices from its projects globally and in countries to support increased dialogue and focus on HCV diagnostics, although the reach of the dissemination events has been a challenge.* Evidence dissemination both in terms of the diagnostic technology pipeline from FIND R&D work as well as from its country work was done through publications in peer-reviewed journals and participation in major HCV and liver-related conferences, as well as webinars and grey literature. However, a key challenge has been to increase global interest in HCV outside of HCV-specific conferences and events; an approach taken by FIND has been to increase interest in HCV through the lens of HIV co-infection and integration of multi-disease diagnostics on existing platforms. In countries, FIND has held dissemination of findings workshops and events with government stakeholders, but in the absence of continuous follow-ups and dedicated funding, there is a risk of losing the focus on HCV, particularly given COVID-19 and other competing priorities.

Looking at the overall value add of the FIND work in this regard, our assessment is that the main contribution has been in terms of evidence-generation in support of future WHO guidelines. In addition, there have been focused

⁷⁷ The evidence package for WHO's Guideline Development Group included data from the feasibility and acceptability studies (completed in 7 countries), the values and preferences assessment (completed in 10 countries) and the cost effectiveness analysis (completed for 4 countries).

contributions to updating country-level policies and SOPs. Other work with regards to advocacy and diagnostic literacy for KPs has been more limited in nature, in line with the project’s focus.

Supply and delivery – key access barrier

Through the in-country projects, the FIND grant has demonstrated the feasibility of decentralized, simplified and integrated approaches that will improve delivery of HCV care in countries.

Table 5.5 provides an overview of the various models piloted by FIND in countries.

Table 5.5: Models piloted by the FIND grant in countries

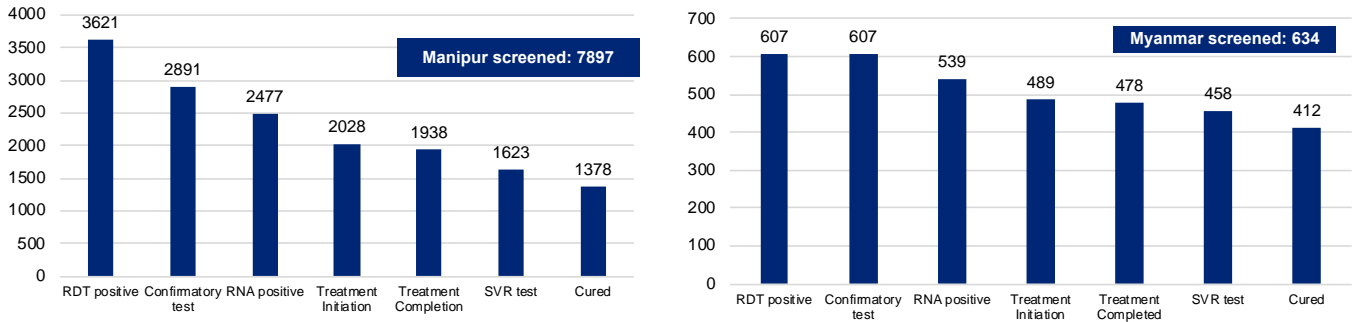
Country/ state	Intervention approach	Target population
Georgia	Decentralisation of HCV care and integration of HCV testing	PWID
New Delhi, India	Decentralisation of HCV care	General population
Punjab, India	Decentralisation and simplification of HCV care	PLHIV and later PWID
Manipur, India	Decentralization of HCV care	PWID and their partners
Malaysia	Decentralization and simplification of HCV care	High-risk groups including MSM, PLHIV, PWID and others
Myanmar, Burnet study	Decentralization of HCV care	PWID
Myanmar, CHAI study	Integration of HCV testing	General population

Key findings from the demonstration studies are as follows:

- Decentralisation and integration of HCV testing and treatment is feasible in primary health care facilities and non-traditional settings, such as ART centres, HRS and community health facilities, as opposed to going to specialised tertiary hospitals.** In Georgia, HCV testing was decentralised to Harm Reduction Sites (HRS) through the use of GeneXpert as well as via reflex sample referral to the centralised laboratory; similarly in Manipur and Myanmar (Burnet study) community-based models of decentralised testing were adopted to enable PWID to access HCV testing with GeneXpert in designated centres in a community-friendly manner. In Punjab, HCV testing and treatment for PLHIV was decentralised and integrated into existing ART centres. The projects demonstrated that when testing and treatment initiation is done in primary health care settings there is much better retention between HCV confirmatory and treatment initiation due: (i) cost and time savings to the patients who do not have to travel to hospital for treatment initiation; and (ii) reduced stigma and discrimination for high-risk groups compared to hospital settings. For example, in Punjab, during the initial phase of the project only approx. 10% of HCV-positive PLHIV were initiated on treatment due to the fact that they had to travel to the district hospital for treatment initiation, which they were not doing due to issues related to stigma and discrimination as well as distance, cost and time. Thus the project was course corrected to train and capacitate the medical staff at the ART centres to enable treatment initiation directly at ART centres, which increased retention across the care cascade. In New Delhi, the project compared the retention rate in the care cascade and treatment initiation time across three models and showed that the highest retention rate was for screening and treatment offered at the same district hospital site. A key lesson from all these demonstration studies is that for both high-risk groups and the general population there are significant advantages of delivering all HCV services, including testing and treatment initiation in the same decentralised location.
- Decentralisation of HCV testing and treatment also reduced LTFU and improved retention across the care cascade by reducing turnaround time between screening and confirmation and enabling more HCV patients to be started on treatment.** Through the use of GeneXpert, turnaround times between confirmatory testing and treatment initiation were significantly reduced (for example, in Georgia and Myanmar PWID who underwent confirmatory testing at the HRS with GeneXpert received the result the same day). All these models demonstrated that through decentralised testing there was good retention across the care cascade. In particular, in Manipur

82% of eligible PWID initiated treatment and 100% completed treatment, whilst in Myanmar 91% of eligible PWID started treatment and 98% completed it, as shown in Figures 5.2 and 5.3.

Figures 5.2 and 5.3: Retention in decentralised testing models targeting PWID in Manipur and Myanmar



Source: FIND HEAD-Start data - preliminary




- **The FIND projects also demonstrated the simplification of the HCV algorithm** by reducing the number visits along the testing and treatment pathway without the need for specialised doctors. Simplified models of HCV care are critical to enable wider testing and treatment in LMICs by minimising the number of visits and enabling greater retention across the care cascade, for example:
 - Malaysia simplified the diagnostic algorithm from three to two steps thereby halving the time between screening and treatment initiation from eight weeks to four weeks, and allowing individuals to be tested without having to travel to a tertiary level hospital;
 - New Delhi, India, demonstrated the reduced the number of visits between HCV screening and confirmation by demonstrating the use of reflex testing, whereby one extra blood sample for pre-treatment assessment is taken at the same time as the confirmation sample thereby combining two steps into one single visit. This has now been adopted in both Punjab and in Malaysia.
 - Trained non-specialist doctors to deliver HCV treatment thereby enabling treatment initiation in primary health care settings such as district hospitals in New Delhi, ART centres in Punjab and NGO-run community-clinics in Myanmar. The role of non-specialist doctors is critical to expand access to treatment to support the achievement of WHO elimination targets and through the projects FIND demonstrated that non-complicated cases can successfully be managed by trained non-specialist doctors, with referral protocols in place for complicated cases.

- **Integration of HCV testing with HIV and TB testing has demonstrated the operational feasibility to increase HCV testing using existing multi-disease platforms** without compromising testing targets of other diseases. Multi-disease testing on existing platforms offers a number of advantages: (i) to increase the utilisation of testing platforms, whilst enabling cost-sharing (purchase, service and maintenance, trainings, infrastructure investments etc); and (ii) spare capacity on existing machines can enable expansion of testing services for other diseases. Two FIND projects demonstrated the operational feasibility of multi-disease testing on existing platforms in country:
 - In Myanmar, FIND worked with CHAI and the National Health Laboratory to assess the feasibility and acceptability of integrating HCV viral load testing with HIV viral load testing on existing machines. The project evaluated the operational requirements needed to optimise laboratory workflow and to enable the utilisation of space capacity on the existing machines allocated to HIV. The findings demonstrated that it is operationally feasible to integrated HCV testing with HIV testing without impacting HIV testing targets and that there would still be spare capacity.
 - In Georgia, the FIND project piloted the integration of HCV testing with existing GeneXpert platforms used for TB testing at eight regional NCDC laboratories. The results demonstrated that HCV testing integration was possible without any risk to compromising TB testing, and it was acceptable to staff members of the

laboratories. Thus, the integration helped testing optimization and realization of unused potential of existing GeneXpert platforms at national laboratories.

Despite the successful demonstration, there are also challenges with the implementation of integration approach for multi-diseases testing, the main one being the collaboration required across the various diseases department, which can be a slow process.

5.3. SCALABILITY AND TRANSITION

Key findings	Strength of evidence
The extent to which project activities have transitioned varies across countries and is dependent on a number of factors, including inclusion in national/state-level programmes, extent of capacity building, funding availability and implications of COVID-19.	
FIND's diagnostics R&D work has been transformational in nature and helped unlock a very challenging HCV diagnostics market, although some further progress, and importantly funding, is needed to secure their scale-up.	
There is some evidence of small scale-up in some project countries, but no wide scale-up is currently happening mainly due to the lack of domestic and donor funding for HCV.	

Transition

The extent to which the FIND projects have transitioned, and will continue following project closure, varies by country. Of the project countries and states, three (Punjab, Malaysia and Georgia) out of six have allocated funding for HCV programmes to continue going forward.⁷⁸ Table 5.6 provides an overview of the project transition status and outstanding issues/ key challenges. Our assessment has highlighted the following key factors supporting or hindering transition:

- The adoption of FIND's pilot/ demonstration approaches through Government directives/ ordinances and/ or SOPs is enabling embedding in national strategies and programmes.
- Training of non-specialist doctors in primary health care settings, health care providers in ART and HRS, and laboratory technicians enables these settings to transition: building the capacity of medical staff working on HCV has been critical to ensure their sustainability post-project.
- Unclear domestic funding allocation is a factor hindering smooth transition.
- Limited mobilisation of external funding to support project continuation.
- High cost of diagnostic technologies (GeneXpert) is limiting uptake of the platforms.
- COVID-19 is causing delays and/or challenges to transition.

⁷⁸ In line with Unitaids' KPI 3.1, three out of six project countries/ states have secured funding to continue the grants' models. The evaluation team understands that the state NVHCP in Manipur have included the cost of cartridges and annual maintenance coverage for the two GeneXpert machines in their request to the National Health Mission through the Programme Implementation Plan (PIP) for 2021, but there has been a delay in the approval of the PIP due to the COVID-19 situation in India.

Table 5.6: Overview of project transition in countries

Country/ state ⁷⁹	Steps taken towards transition and sustainability	Challenges/ outstanding issues
Georgia	<ul style="list-style-type: none"> • Government ordinances issued to enable the continuation of the decentralization of HCV services at HRS and the Reinfection Testing project under HCV Elimination State Program. 	<ul style="list-style-type: none"> • Stock outs of GeneXpert cartridges have been observed which have halted confirmatory testing in HRS; the major reason for stock-outs being the system-level weaknesses in the overall planning process, which was affected by the pressure the COVID-19 pandemic.
New Delhi, India	<ul style="list-style-type: none"> • Dissemination workshop with HCV State Nodal Officer and commitment to take the Delhi Model forward. • ILBS was designated as a Model Treatment Centre for HCV. • At least 20 health workers were trained in the 5 district hospitals 	<ul style="list-style-type: none"> • COVID-19 has halted the transition progress due to all hospitals redirecting focus to COVID-19 testing and treatment. Only one hospital currently providing HCV testing and treatment.
Punjab, India	<ul style="list-style-type: none"> • Decentralised and simplified model of testing and treatment initiation in ART and OST centres adopted under state-NVHCP • SOPs are being updated to reflect this • Trained 31 ART staff to continue supporting HCV screening, diagnosis and treatment initiation 	<ul style="list-style-type: none"> • GeneXpert being returned to FIND as not cost-effective given that Punjab Government has been able to negotiate a PPP for centralised HCV viral load testing.
Manipur, India	<ul style="list-style-type: none"> • The GeneXpert machines have been handed over the state NVHCP with the plan to locate them in two very remote districts to fill the diagnostic gap for people living in remote locations. 	<ul style="list-style-type: none"> • Approval of the funding for the cost of cartridges and annual maintenance for 2021 still pending; the financial implications to run the GeneXpert machines as well as ability to sustain the cost of cartridges and annual maintenance.
Malaysia	<ul style="list-style-type: none"> • Circular from the MoH was issued providing information on “Upscaling of Hepatitis C Screening, Treatment and Care in Primary Health Care 2020”, thereby formalizing a guideline for the management of HCV in primary health care. • MoH have applied for US\$1.7m funding to support the takeover of MAC’s TEMAN project, providing HCV care to prisoners as they leave prison. 	<ul style="list-style-type: none"> • The expiration of the CL for SOF in October 2020 means that the upscaling of treatment will likely not progress as planned, unless it is renewed. • The MoH awaits confirmation from the government on funding for the TEMAN project.⁸⁰
Myanmar, Burnet study	<ul style="list-style-type: none"> • Dissemination workshop with MoH and NHCP who has accepted the results that test and treat can be decentralised and done through use of general practitioners but no commitment in place. • The government through the NHCP has started a Training of Trainers of general 	<ul style="list-style-type: none"> • Political situation • Burnet Institute also had planned to extend and continue the CT2 study (CT2 Extend), but this has been postponed due to COVID-19

⁷⁹ India is disaggregated by state, given that health is a federal state subject, so any progress will be made at the state level.

⁸⁰ The TEMAN project is a risk reduction programme for people returning to the community after incarceration.

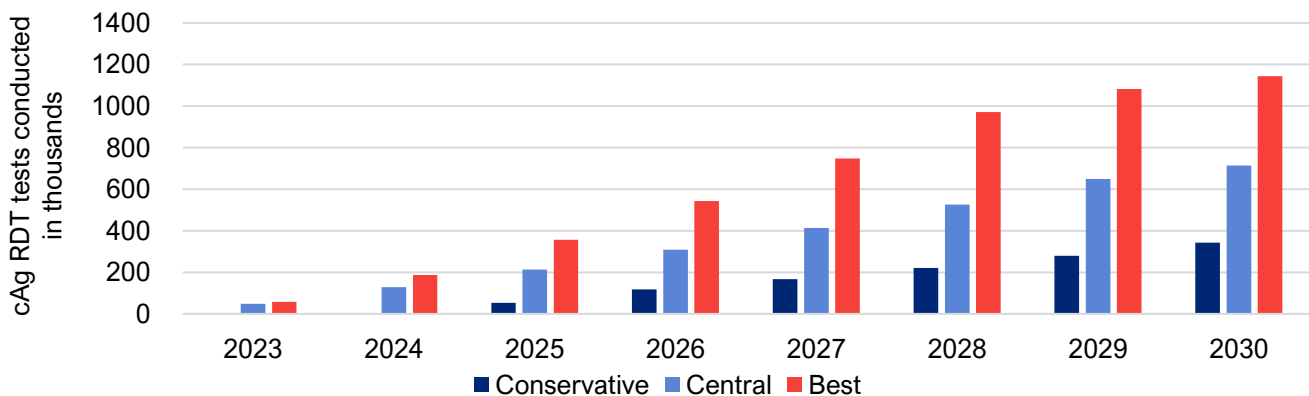
Country/ state ⁷⁹	Steps taken towards transition and sustainability	Challenges/ outstanding issues
Myanmar, CHAI study	<p>practitioners on the national treatment guidelines with the plan to train a large cohort of GPs to carry out screening and treatment at clinics and district hospitals.</p> <ul style="list-style-type: none"> Dissemination workshop with MoH and NHCP who requested study protocol to be shared to be considered in the ongoing drafting of the updated National Action Plan 2021-2025 	<ul style="list-style-type: none"> Political situation and COVID-19

Source: CEPA analysis.

Scalability

FIND’s diagnostics R&D work has been transformational in nature and helped unlock a very challenging HCV diagnostics market. The diagnostic pipeline has been much strengthened through the FIND work, and indeed there is a large diagnostic gap in the market to enable scale-up to happen. The market analysis commissioned by FIND as part of its work on cAg RDT estimates that demand could potentially exceed 1 million tests in the first five years following commercialisation for use as a confirmatory testing across five countries (Brazil, India, Nigeria, Pakistan and Thailand).⁸¹ The impact modelling conducted as part of the evaluation used the conducted market study to inform on input assumptions⁸² and received similar results, with potentially ~390,000 [~53,000 – ~ 602,000] testes conducted by 2025 and ~3 million [~1.2 million - ~5.1 million] by 2030. Figure 5.4 provides annual estimates separated by scenario:

Figure 5.4: Potential scale-up of cAg RDT usage in 19 countries between 2023 - 2030



Source: CEPA analysis

These estimates show that there is significant potential to scale-up the use of cAg RDT in LMICs, and it is important that the cAg RDT progresses through its final stages to enable it to be commercially available for countries to procure. As noted above in Section 5.2, there would also need to be further implementation support to ensure its fit within the

⁸¹ FIND (2020), FIND commissioned cAg market study: cAg rollout plan in LMICs

⁸² Overall, the market analysis was seen as well conducted and was used to inform input assumptions for the impact modelling work. Some key changes include: (i) change in years of when product will come to the market; (ii) more conservative approach on the total potentially market share that cAg can achieve; (iii) an expansion on the countries considered beyond the five focus countries of the study.

health systems in countries. The total number of additional patients that could be diagnosed and ultimately treated thanks to the use of cAg RDT is outlined in Section 5.4 further below.⁸³

Further progress, and importantly funding, is needed to secure scale-up of HCV diagnostics. Again as noted in Section 5.2, further implementation support is needed in order to: (i) demonstrate the marketing of HCVST and how to get the test into the hands of people who want to be screened without having to interact with the health system, whether the general population or high-risk groups; this is particular important given the limited awareness around HCV and the fact that it is asymptomatic for long periods of time; and (ii) show the potential of implementing HCVST programmes in countries and support countries with the inclusion of HCVST as a testing strategy in their national guidelines. As such, FIND’s work has helped unlock a very challenging diagnostics market, and while not fully ready to be scaled-up today, the progress made is substantial. The funding challenge for HCV programmes in country is another issue, which is discussed at length in Section 3 on the portfolio-level review.

There is some evidence that improved testing models are being expanded nationally/state-wide, but the lack of domestic and donors financing is a barrier to national scale-up. Scale-up is happening in some countries, with scale-up more likely to happen when: (i) projects are delivered through the existing health care system/ health facilities; and (ii) there are existing government champions in place. In Punjab the Government is a strong champion of the state NVHCP and has committed to continue and to scale-up the decentralised and simplified model of screening and treatment in ART centres and has been providing HCV services since April 2020 under the state NVHCP. Furthermore, in February 2021 it announced the expansion of the services to an additional four ART centres. In Malaysia, the MoH is in the process of scaling-up decentralized screening and treatment from the original 25 primary health clinics to 146 primary health clinics nationally, which includes all clinics with a resident primary healthcare physician. In Georgia, the Government is continuing the decentralised service delivery model in HRS, but is not planning to expand to more HRS sites due to existing regulation about minimal standards of care in HRS which is not expected to change in the near future. However, external funding from US CDC has been secured by Georgia to continue the Linkage to Care project and this will also enable scaled up beyond the public Health Centres.

5.4. IMPACT

Key findings	Strength of evidence
<p>The cAg RDT technology has the potential to lead to substantial increases in people being successfully diagnosed and treated, with potentially ~501,267 patients being successfully treated by 2030. As such, cAg RDT would offer one important tool towards reaching the WHO HCV elimination targets.</p> <p>The majority of the potential health and economic impacts would occur after 2025, with a total ~12,014 deaths averted, ~779,943 DALYs averted and US\$238 million in averted disease management costs by 2030.</p>	
<p>The Molbio Truenat HCV test can lead to an additional 180,000 people being diagnosed in India by 2025, by leveraging on the recent expansion of Molbio platforms due to COVID-19. A total of ~2800 deaths, ~185,725 DALYs and US\$21 million in averted disease management costs by 2025.</p> <p>There is further additional impact between 2026-30 in India as well as additional potential impact globally, once Molbio is successfully scaled-up in other countries.</p>	
<p>FIND’s in-country demonstration studies contributed to 9,563 patients being cured with an additional 3,792 expected to be cured within the next year. Within the next five years,</p>	

⁸³ From a modelling perspective, the numbers in the impact section provide various case scenarios of the role that the cAg RDT could play in helping to diagnose people with HCV. As the earliest entry for cAg RDT is expected in 2023, there are no additional people benefiting in the two years after the end of the grants (in line with KPI 3.2). Poor data availability on HCV testing and diagnosis also did not allow to quantify the scale-up of HCV testing more generally.

this will lead to 640 averted deaths, 39,924 averted DALYs and around US\$19 million in disease management costs savings.

There also additional public health and economic impacts from the expected adoption of decentralised and simplified HCV diagnosis and treatment models supported by the FIND grant.

This section provides an overview of the public health and economic impact of the FIND grant, separated out by impact under development of improved diagnostic tools (Output 1) and demonstration of improved diagnostic approaches/pathways (Output 2). For Output 1, we have focused on modelling the impact of cAg RDT globally and the Molbio Truenat HCV test in India, where the assumptions, data and extent of attribution to the FIND grant have facilitated more credible modelling. Challenges with modelling the impact of other technologies supported under Output 1 are discussed in Appendix D. For Output 2, we have focused on the patients directly accessing treatments through the FIND pilot studies and not considered wider impact through scale-up due to the tenuous nature of scale-up at present (and also the range of assumptions needed in linking the focused impact of FIND’s work in relation to the broad improvement in demand/ adoption/ delivery). It is therefore important to highlighted that the quantitative impact figures presented here **only cover a subset of the full public health and economic impact achieved through the FIND grant**, and should be viewed as ‘case studies’ of the impact of the FIND grant, rather than portraying the full impact of the grant.

CEPA constructed a range of Excel-based impact assessment models which accompany this report. All figures provided in this section are still subject to review as we continue to verify and improve on the input assumptions. A full description of the model design, input assumptions and limitations can be found in Appendix D.

Output 1 – public health and economic impact of cAg RDT

The impact of the cAg RDT technology has been modelled by comparing a factual scenario which includes access to a testing pathway with cAg RDT, with a counterfactual scenario in which only the current standard of care is available. Due to data availability, as well as the currently prototype-only nature of the cAg RDT, there is considerable uncertainty in the presented impact estimates. A conservative, a central, and a best-case scenario have been developed to capture some of this uncertainty around the input assumptions, such as (i) year of market entry, (ii) speed and magnitude of scale-up; (iii) technology impact on LTFU; (iv) sensitivity; and (v) costing. A detailed explanation of each step in the model design, as well as the input assumption by scenario, is provided in Appendix D. Table 5.7 below provides an overview of the key health outcomes in terms of additional people diagnosed and treated, as well as the public health impacts.

Table 5.7: Overview of the public health impacts (KPI 4.1) and health outcomes of cAg RDT

	Indirect impact (2021-2025)	Further potential impact (2026-2030)	Total contribution to WHO target achievement (2021-2030)
Additional people diagnosed [conservative – best case]	90,839 [7,677 - 189,605]	528,009 [138,895 - 1,240,768]	618,848 [146,572 - 1,430,373]
Additional people treated [conservative – best case]	73,580 [5,547 - 171,118]	427,687 [100,352 - 1,119,793]	501,267 [105,898 - 1,290,912]
Additional deaths averted [conservative – best case]	821 [36- 1,807]	11,194 [2,078 - 28,908]	12,014 [2,114 - 30,715]
Additional DALYs averted [conservative – best case]	57,065 [2,644 - 126,261]	722,878 [136,683 – 1,870,054]	779,943 [139,326 – 1,996,315]
Additional compensated cirrhosis averted [conservative – best case]	10,193 [730 - 23,557]	68,099 [15,240 – 177,814]	78,293 [15,970 – 201,371]

	Indirect impact (2021-2025)	Further potential impact (2026-2030)	Total contribution to WHO target achievement (2021-2030)
Additional decompensated cirrhosis averted [conservative – best case]	2,713 [190 - 6,251]	19,422 [4,243 – 50,617]	22,135 [4,433 – 56,868]
Additional hepatocellular carcinoma averted [conservative – best case]	573 [27- 1,271]	7,004 [1,334 – 18,127]	7,577 [1,362 – 19,397]

Source: CEPA analysis

These draft results indicate that the cAg RDT technology can have a substantial impact on the HCV diagnostic market leading to an increase in number of people diagnosed as well as treated. Within the five years of grant closure, the technology could help to diagnose an additional ~91,000 and help to treat an additional ~ 74,000. However, the majority of the impact would take place outside of the five-year post-grant period; most countries would reach the full scale-up of cAg RDT utilisation between 2026-30 leading to an additional ~ 528,000 diagnosed and 428,000 treated during that period. The key reason for this, is that the product is only assumed to come to the market in 2023 (immediately in Pakistan and India as priority countries without WHO PQ), and the year after in other countries. This modelling also showed that the delays in product prototype development (due to COVID-19 and, to a lesser extent, grant reprogramming and intensive checks through repeated Go / No Go decisions) had an influence on the public health impact realised within the five years after grant closure.

While the absolute numbers are heavily dependent on assumptions around the future development of national HCV programmes, the analysis shows that the cAg RDT technology can make a sizable contribution towards reaching the WHO target by 2030 in the 19 countries considered to be priority countries for the roll-out.⁸⁴ The modelling also focused on the impact from a reduction in loss-to-follow-up from the technology due to decentralisation of screening and confirmatory testing as well as increases in patients covered due to the reduced cost of testing. The figures, however, do not include any impacts from a shift in testing policy and guidelines in-countries (beyond an expansion due to cost reduction).⁸⁵ As such, the estimates can be considered to be conservative as they do not account for potential shifts in testing policies and guidelines that could significantly lead to further scale-up of HCV testing.

The additional public health benefits are estimated by calculating what would happen to patients that were successfully cured following diagnosis with the cAg RDT technology. Without the FIND grant, the HCV disease would have progressed over time, increasing the likelihood that patients would have developed severe morbidities or died from the disease. Curing these individuals could lead to health benefits of 859 averted deaths [36- 1,807] as well as 57,065 averted DALYs [2,644 - 126,261] within the next five years. Additionally, curing the patients would include averting 10,193 compensated cirrhosis, 2,713 decompensated cirrhosis and 573 cirrhotic cancers. Similar to the diagnosis and treatment numbers, the biggest public health impact would occur between 2026-2030. This is due to the additional treatments occurring in these years but also due to the additional adverse health outcomes that continued to be avoided from treatments within the five years of grant closure. The cAg RDT technology could potentially avert 12,014 deaths [2,114 - 30,715] and 779,943 DALYs [139,326 – 1,996,315] by 2030. There would also

⁸⁴ Algeria, Argentina, Brazil, Cambodia, Cameroon, Colombia, Ethiopia, Ghana, India, Indonesia, Kazakhstan, Malaysia, Morocco, Nigeria, Pakistan, Philippines, South Africa Thailand and Uzbekistan

⁸⁵ The modelling took this more conservative approach focusing on the areas with more robust data that are linked directly to the technology (e.g., loss-to-follow-up; cost reduction). In contrast, changes in testing policy are also highly depending on other country-specific factors (e.g., political willingness, financing etc.) and, thus, there is large uncertainty on how the new technology would influence countries testing policies.

be substantial health benefits after 2030 when the health conditions of patients would have continued to worsen in the absence of treatment.⁸⁶

The cAg RDT technology could potentially lead to substantial cost savings due to averted treatment costs that can make the implementation cost-saving over time. Additional costs between the factual and counterfactual scenario are due to the fact that the additional successfully diagnosed patients need to be treated. The cost savings have been calculated by incorporating the annual disease management costs that patients would occur in the absence of being cured. Table 5.8 provides an overview the economic impact and additional costs:

Table 5.8: Modelled economic impact and additional costs of cAg RDT technology (all costs below are in US\$)

	Indirect impact (2021-2025)	Further potential impact (2026-2030)	Total contribution to WHO target achievement (2021-2030)
Additional costs [conservative – best case]	US\$9.9 m [0.7 m – 17.9m]	US\$75.8 m [26.2 m – 160.2 m]	US\$85.7 m [26.9 m – 178.1m]
Disease management costs averted [conservative – best case]	US\$15.5 m [0.4 m – 33.2 m]	US\$222.7 m [29.0m – 566.8 m]	US\$238.2 m [25.7 m – 578.5 m]

Source: CEPA analysis

The additional costing figures have to be interpreted with care as they do not include non-commodity costs (e.g., distribution charges, imports, human resources for administration) and as such are likely an underestimate of the true additional costs of diagnosing and treating the additional patients. However, even in case that not all of disease management costs are actually taking place (e.g., in case patients do not receive care), the analysis suggests that the introduction of cAg RDT (similar to other current standard of care HCV treatment) will be cost-saving in the long-run.⁸⁷ This is particularly true as there are also further savings through averted productivity losses from morbidity and premature deaths.

Output 1 - public health and economic impact of the Molbio Truenat HCV test

The impact of the Molbio Truenat HCV test has been modelled by comparing a factual scenario which includes access to a testing pathway with the near-POC platform Molbio Truenat, with a counterfactual scenario in which only the current standard of care is available.⁸⁸ The impact has only been modelled for India, where the Molbio Truenat HCV test is already available on the market.⁸⁹ While India will be by far the largest market for Molbio Truenat testing in the short-to-medium term, there is further potential scale-up in other countries that has not been estimated. The public

⁸⁶ However, any more long-term benefits after 2030 would be based on the assumptions that patients that received treatment through cAg RDT would not receive treatment at a later stage. To be conservative, the impact after 2030 is therefore not reported.

⁸⁷ Aggarwal, Rakesh, et al. (2017), Cost-effectiveness of hepatitis C treatment using generic direct-acting antivirals available in India.

⁸⁸ The impact has been estimated using a similar modelling approach as for the cAg RDT testing, with the reduction in loss-to-follow-up due to decentralisation as well as the reduction in costs as key impact pathways. A conservative, a central, and a best-case scenario have been developed to capture some of this uncertainty around the input assumptions, such as (i) usage of Molbio Truenat platforms for HCV testing in factual scenario; (ii) market entry of Molbio Truenat HCV testing in the absence of the FIND project; (iii) technology impact on LTFU; (iv) costing. A detailed explanation of each step in the model design, as well as the input assumption by scenario, is provided in Appendix D.

⁸⁹ Molbio platforms have been installed across the country as part of the COVID-19 response that can be leveraged for HCV testing. Additionally, Molbio reportedly offered a volume-based price to the government of India which is below the standard testing price in laboratory settings.

health impact estimates presented in Table 5.9 below are therefore providing an underestimation of the full impact that the Molbio Truenat HCV test can have globally.⁹⁰

Table 5.9: Overview of the public health impacts (KPI 4.1) and health outcomes of Molbio Truenat in India

	Indirect impact (2021-2025)	Further potential impact (2026-2030)	Total contribution to WHO target achievement (2021-2030)
Additional people diagnosed [conservative – best case]	182,672 [36,154 - 469,449]	18,267 [0 - 117,362]	200,939 [36,154 - 586,811]
Additional people treated [conservative – best case]	147,964 [26,122 - 423,677]	14,796 [0 - 105,919]	162,761 [26,122 - 529,597]
Additional deaths averted [conservative – best case]	2,796 [565 - 7,129]	6,493 [1,048 - 20,700]	9,289 [1,613 - 27,829]
Additional DALYs averted [conservative – best case]	185,725 [37,182 - 476,826]	387,251 [61,827 – 1,248,038]	572,977 [99,009 – 1,724,864]
Additional compensated cirrhosis averted [conservative – best case]	22,120 [4,005 - 62,075]	10,401 [1,368 – 40,695]	32,522 [5,373 – 102,770]
Additional decompensated cirrhosis averted [conservative – best case]	6,104 [1,118 - 16,980]	4,204 [609 – 15,146]	10,308 [1,727 – 32,126]
Additional hepatocellular carcinoma averted [conservative – best case]	1,821 [363 - 4,693]	3,655 [584 – 11,797]	5,476 [946 – 16,490]

The draft results indicate that the Molbio Truenat HCV tests can have a substantial impact on the HCV diagnostic market in India leading to an increase in number of people diagnosed as well as treated. Within the five years of grant closure from 2021-25, the technology could help to diagnose an additional ~183,000 [~36,000 - ~470,000] and help to treat an additional ~ 147,000 [26,000 – 423,000]. This could lead to 2,796 [565 - 7,129] deaths averted and 185,725 [37,182 - 476,826] DALYs averted by 2025. This impact is considerable and leverages on Molbio rapidly expanding its platforms as part of the COVID-19 epidemic in India as well as competitive pricing of the Truenat HCV tests in India. The impact after 2025 is expected to be lower as it is assumed that Molbio would have brought the Truenat HCV test eventually to the market, even in the absence of the Unitaid project.⁹¹ However, there are continued health benefits that occur from the patients that have been cured between 2021-25 and whose conditions would have worsened further over time. By the end of 2030, the Molbio Truenat HCV test could potentially avert 9,289 [1,613 - 27,829] deaths and 572,977 [99,009 – 1,724,864] in India alone.

Similar to the cAg RDT test, the Molbio Truenat HCV test could lead to cost savings due to averted disease management costs that patients would otherwise occur in the absence of being cured. Additional costs between the

⁹⁰ The highest likelihood for additional usage of Molbio Truenat is in countries with a substantial HCV burden and political willingness to address it as well as with Molbio distribution networks due to the interest of expanding Molbio platform installation for other diseases such as TB. Depending on further data availability, we may model the impact in other countries for the final reiteration.

⁹¹ Based on stakeholder consultations, the assumes a delay in the market entry of 3 years in the conservative scenario, 4 years in the central scenario and 5 years in the best-case scenario.

factual and counterfactual scenario are due to the fact that the additional successfully diagnosed patients need to be treated. Table 5.10 provides an overview the economic impact and additional costs:⁹²

Table 5.10: Modelled economic impact and additional costs of Molbio Truenat in India (all costs below are in US\$)

	Indirect impact (2021-2025)	Further potential impact (2026-2030)	Total contribution to WHO target achievement (2021-2030)
Additional costs [conservative – best case]	US\$17 m [4 m –44 m]	US\$1.7 m [0 m – 11 m]	US\$18.7 m [4 m –55m]
Disease management costs averted [conservative – best case]	US\$21 m [3 m – 54 m]	US\$39 m [4m – 125 m]	US\$60 m [7 m – 179 m]

Source: CEPA analysis

The additional costing figures have to be interpreted with some care as they do not include non-commodity costs (e.g., distribution charges, imports, human resources for administration) and as such are likely an underestimate of the true additional costs of diagnosing and treating the additional patients. However, even in case that not all of disease management costs are actually taking place (e.g., in case patients do not receive care), the analysis suggests that the introduction of testing with the Molbio Truenat HCV test (similar to other current standard of care HCV treatment and cAg RDT) will be cost-saving in the long-run.

Output 2 - public health and economic impact

The work under Output 2 of the FIND project made direct contributions to public health by successfully diagnosing and successful treating HCV patients in the project countries (Georgia, India, Malaysia, and Myanmar). The contributions that the project made with regard to successfully curing patients is outlined in Table 5.11 below. The number of successful treatments is separated out between activities directly led by FIND (e.g., in-country studies) and activities to which FIND contributed more indirectly (e.g. through donations of testing equipment). Additionally, the table differentiates between successful treatments that have already been achieved and those that are expected to take place in 2021 or early 2022.⁹³

Table 5.11: Patients successfully cured through contributions from FIND under Output 2 (achieved and expected)

Country/State	Patients cured - Achieved		Patients cured - Expected		Patients cured - Total
	Studies	Donations	Studies	Donations	
Malaysia	889	734	446	205	2,274
Georgia	3,927	-	1,467	-	5,394
Myanmar	462	3,829	-	-	4,291
Punjab	2,068	-	1,878	419	4,365
Delhi	441	-	1	-	442
Manipur	1,752	-	-	118	1,870

⁹² The costing figures presented in this section are still subject to verification, in particular with regard to the inclusion of non-commodity related costing of HCV testing and treatment which so far have not been considered. As such, these numbers are still subject to change.

⁹³ For the FIND studies, future treatment includes diagnosed HCV patients that have not yet received treatment due to (COVID-19-related) delays but for which the national government guaranteed treatment. For donations, this includes donations that have been made before grant closure but where the products have not been used yet.

Country/State	Patients cured - Achieved		Patients cured - Expected		Patients cured - Total
Total	9,539	4,563	3,792	742	18,636

Source: CEPA analysis

The work conducted through the FIND studies led to 9,530 patients being cured with the majority of the share in Georgia, Punjab and Manipur. FIND's donations contributed to a further 4,563 successful treatments predominately due to cartridges donated to the government of Myanmar. Another 4,524 patients are still expected to be treated due to the work of FIND predominately due to expected treatment by the government of individuals identified through the FIND studies in Georgia and Punjab. While all of these successful treatments also rely on the contributions of in-country partners beyond FIND, this is more pronounced for the donations where FIND just contributed diagnosis products.⁹⁴ Without these received treatments, HCV would have progressed in these patients leading to increase morbidity (e.g. compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma) and death. Assuming that patients cured would have not received treatment from any other means within the next five years⁹⁵, the impact alone would be considerable and is detailed in Table 5.12 below.

Table 5.12: Public health and economic impact through contributions from FIND under Output 2 from 2018-2025

	FIND studies	FIND donations	Total
<i>Deaths averted</i>	640	278	918
<i>DALYs averted</i>	39,924	17,252	57,176
<i>Compensated Cirrhosis averted</i>	2,475	1,010	3,485
<i>Decompensated Cirrhosis averted</i>	760	314	1,074
<i>Hepatocellular carcinoma averted</i>	176	71	248
<i>Disease Management Costs Averted</i>	US\$18.9 million	US\$9.7 million	US\$28.7 million

Source: CEPA analysis

The impact through the FIND studies alone would include 640 averted deaths, 39,924 averted DALYs (including 305 cases of decompensated cirrhosis and 248 cases of hepatocellular carcinoma averted) and around US\$19 million in disease management costs savings. Including also impacts from FIND donations this could be as high as 918 deaths averted and US\$28.7 million disease management cost savings.

5.5. COUNTRY CASE STUDIES

This section provides summaries of the FIND HEAD-Start grant in each of the three country case studies: Georgia, India, and Malaysia.

⁹⁴ The analysis does not provide a comment on the additionality of the treatments provided though it seems reasonable to assume that the testing and treatment conducted by partners would have gone ahead (albeit at different scale) in the absence of the FIND product donations. As such, the FIND study results may provide a better approximation of the additionality of the FIND impact.

⁹⁵ While a simplifying assumption, the impact below does also not capture public health and economic benefits that would arise after 2025 in case the patients would continue to be left untreated. As such, this approach can serve an approximation of FIND's impact under output 2.

Georgia

Georgia, with an estimated population of 3.7 million people, is among the highest burden countries with an HCV prevalence estimated at 7.7% in the general population (95% CI = 6.7, 8.9) and HCV RNA prevalence at 5.4% (95% CI = 4.6, 6.4)⁹⁶ in 2015. High HCV burden in Georgia is largely driven by unsafe injection practices among PWID.⁹⁶ In 2015, the Government of Georgia approved its first HCV National Strategy and Action Plan 2016-2020⁹⁷ and became the first country in the WHO European Region to set targets for the elimination of HCV by 2020.⁹⁸ HCV elimination initiative is implemented by the National Centre for Disease Control (NCDC) with the technical support from the Division of Viral Hepatitis of US CDC and an extensive donation of DAAs from Gilead.

The FIND HEAD Start project in Georgia was implemented in October 2016 - December 2020, and aimed at achieving the following objectives:⁹⁹

- Facilitate decentralization of HCV care at Harm Reduction Sites (HRS);
- Generate evidence towards effective methods of HCV service delivery at HRS through evaluation against the standard of care, decentralized screening and confirmatory point of care (POC) testing on site, as well as screening on site and centralized confirmation of viremia using cAg RDT
- Generate evidence to contribute to the global evidence on the use of an HCV core antigen assay as test of cure.

The FIND grant implementing partners in Georgia were the NCDC, the governmental agency leading Georgia's HCV response, and the Georgian Harm Reduction Network (GHRN) - a Primary Recipient of the Global Fund HIV prevention project targeting PWID.

Unitaid's support in Georgia was perceived as timely, aligned with the national strategic priorities and responsive to the country specific needs. Health officials and other consultees note that despite the progress Georgia was making towards affordable HCV treatment, the HCV case finding was suboptimal and testing algorithm was complex and costly. Although Georgia has strong political commitment to HCV, the country was searching to identify best approaches for diagnostics and treatment, and the contribution of the HEAD Start project to this process was critical. The project success has been ensured through ongoing situation assessments and cross-sectional surveys to measure self-perceived barriers, acceptability and attitudes towards innovations the FIND grant intended to implement among various populations with the special focus placed on PWID – the most vulnerable and affected by HCV population group in Georgia.

The timeline of the FIND project was considered reasonable. Even though the FIND grant has had ambitious goals and was implementing several parallel projects, it has managed to achieve most of the outcome indicators set in the original grant proposal. However, the COVID-19 pandemic and subsequent lockdown affected project results for the two pilot projects that were initiated per the NCDC request at a later stage of the grant implementation: (1) *Linkage to Care project*, and (2) *HCV reinfection/relapse testing project* among previously treated PWID.

All consultees noted that one of the key success factors for the FIND grant in Georgia was unprecedented collaboration with the national authorities and implementing partners. The collaboration between FIND and NCDC, and the scope of the Unitaid's support was approved at the highest political level with the Government Ordinance.¹⁰⁰ Government officials and policy makers consulted believed that excellent interagency coordination of

⁹⁶ Hagan, L.M., Kasradze, A., Salyer, S.J. et al. (2019), Hepatitis C prevalence and risk factors in Georgia, 2015: setting a baseline for elimination.

⁹⁷ Georgia Ministry of Labour, Health and Social Affairs (2016), Strategic Plan for the Elimination of Hepatitis C Virus in Georgia, 2016-2020

⁹⁸ WHO (2021), Accelerating access to hepatitis C diagnostics and treatment. Overcoming barriers in low and middle-income countries. WHO. Global Progress Report. 2020.

⁹⁹ FIND (2018) Country Operational Plan, Georgia.

¹⁰⁰ Government Ordinance #2430; signed by the Prime Minister on Nov 22, 2017

the FIND grant with key HCV players in the country, including non-state actors and international development partners, such as the US CDC Office, and the Global Fund, has ensured complementarity and synergies.

The following were key achievements in terms of access barriers framework for Georgia:

Quality: Consultees note the FIND grant's contribution to expand the availability of quality assured HCV testing through validation and demonstration studies as substantial not only at the national, but also at the global level. It has demonstrated feasibility of HCV Core antigen as a test of cure. After the validation study, the Cepheid Xpert fingerstick HCV viral load testing was registered in Georgia. HCV RDT validation study conducted by the FIND grant has generated stronger evidence about the quality HCV tests, and the knowledge has become instrumental for informed policy making at the national level. Evidence of the performance of HCV RNA tests from DBS has been generated on four different platforms. Usability and feasibility of HCV self-tests was conducted among PWID and MSM in partnership with two NGOs. Due to the pandemic related lockdowns, publishing the results was delayed and is now in progress. Once all study findings are finalized and disseminated, the FIND grant's contribution to the global body of knowledge about HCV testing and diagnostics will be substantial.

Affordability: Consultees believed that even with unrestricted access to HCV DAA treatment in Georgia, the Unitaid support was important to improving the affordability of HCV diagnostic and testing services particularly for PWID. In 2017-2018, the FIND grant provided vouchers to PWID to cover the costs of HCV RNA, and SVR12 tests, which was subsequently discontinued as the government removed the co-payment requirement. Unitaid support has contributed to affordability of HCV testing through expanding, decentralizing and integrating HCV testing at four HRS and 8 NCDC laboratories in regions, which eventually improved geographic reach and saved cost related to transportation of blood samples from regions to the central Lugar Laboratory. The number of HCV confirmatory tests performed reached 10,719 instead of targeted 6,000. SVR testing among PWID has increased from 55.4%¹⁰¹ in 2015-2017 to 75%¹⁰² within the Head Start Project.

Demand and adoption: One of the sustainable impacts of the FIND grant in Georgia was empowering civil society organizations and expanding their role in the HCV response through decentralization of HCV testing and treatment. The Unitaid support was critical for improving HCV awareness and diagnostic literacy among key populations through a series of capacity building and advocacy interventions. The FIND in partnership with the Treatment Action Group (TAG) produced the Activist Guide to Hepatitis C Virus Diagnostics¹⁰³ and conducted workshops for patients' groups, affected communities and treatment activists in Georgia.

Supply and delivery:

- **Decentralization of HCV testing and treatment at HRS:** the FIND grant demonstrated that decentralization of POC molecular HCV RNA testing at harm reduction sites was feasible, which in turn, facilitated the Government's decision to initiate treatment decentralization at HRS. Almost all consultees from government institutions and civil society believed that treatment decentralization was a breakthrough in service delivery in Georgia that would not have happened without the Unitaid support.
- **HCV testing integration:** Unitaid support was critical for integrating HCV testing with existing GeneXpert platforms at 8 regional laboratories of NCDC. Before 2018, these GX platforms were used exclusively for TB testing. Consultees noted that there was no declared intention from the state for HCV/TB service integration until the FIND grant conducted a number of studies demonstrating that HCV testing integration was possible without any risk to compromising TB testing, and it was acceptable to staff members of involved laboratories.

¹⁰¹ Stvilija K, Spradling PR, Asatiani A, et al. (2018), Progress in Testing for and Treatment of Hepatitis C Virus Infection Among Persons Who Inject Drugs.

¹⁰² FIND (2020), HEAD Start: 2020 Semi-Annual Report

¹⁰³ FIND (2019), Activist guide to hepatitis C virus diagnostics; Treatment Action Group. FIND.

- **Linkage to care:** To respond to the country's emerging needs, the FIND grant implemented a demonstration study which aimed at outreaching to HCV RDT+ patients who have not advanced to the next step of testing for HCV viremia (i), or the patients with active HCV who have not initiated treatment (ii). The innovative model for patients' tracing was implemented in Jan - Dec 2020, and it managed to reach out to a total of 5,313 patients; of them 1,685 persons were found treatment eligible, and 887 (53%) initiated treatment.
- **Reinfection/ late relapse testing among PWID:** There was no strategy within the national HCV elimination program to assess the magnitude of reinfection among treated patients that might pose a challenge to HCV elimination efforts. In 2020, the FIND grant, per the NCDC request, initiated testing for two cohorts of previously treated PWID: with positive SVR 12/SVR 24 after 6 months from the last SVR testing (i), and those without known SVR results after at least 6 months of treatment completion (ii). Approximately 7% of all patients observed tested positive on HCV RNA with an overall incidence rate – 2.8 per 100 person-years. Consultees from key constituency groups believe that reinfection project implemented by the FIND grant has led to adoption of clear national policy about repeated treatment for re-infection at no cost to patients.

Transition and scale-up: Decentralized HCV POC testing and treatment at 4 HRS has been sustained under the state funding as documented through the Government Ordinances.¹⁰⁴ All GX machines in Georgia have been connected with the Cepheid c360 platform, which collects and aggregates real-time disease surveillance information from any GeneXpert system operational globally. The cAg as confirmation for HCV, first proposed in the FIND study, has been taken up as the standard of care in the country. Integration of HCV testing with existing GX platforms at 8 NCDC laboratories has been sustained within the HCV State Program. The Government secured funding from US CDC to continue Linkage to Care project which will be scaled up and beyond the public Health Centres, and Primary Health Care centres previously involved in case-findings, the Harm Reduction sites will be also engaged to work specifically with PWID who are lost to follow up. Reinfection/late relapse testing has become a part of the HCV Elimination State Program as documented in the Government Ordinance #677.¹⁰⁴

India

It is estimated that there are approximately 6-12 million people with HCV antibodies in India, with an estimate of 3-9 million people with active HCV infections.¹⁰⁵ Recognising HCV as a public health problem, the Ministry of Health and Family Welfare (MoHFW) of the Government of India launched the National Viral Hepatitis Control Programme (NVHCP) on 28 July 2018. The goal of the programme is to eliminate viral hepatitis by 2030, in line with the WHO 2030 elimination targets and the Sustainable Development Goal target.¹⁰⁶ The NVHCP provides free screening, testing and treatment for HCV to the whole population, including high-risk groups.

In India, the FIND HEAD-Start grant supported three pilot projects in New Delhi, Punjab and Manipur, each with separate objectives and different target populations:

- **New Delhi:** The aim of the Delhi project was to demonstrate decentralised screening, confirmation and treatment amongst the general population in the densely populated capital city of India in collaboration with the Institute of Liver and Biliary Sciences (ILBS), a tertiary care hospital in Delhi. In New Delhi, FIND also partnered with DNP+ to support advocacy and diagnostic literacy in the context of the project.
- **Punjab:** Given an existing government programme focussing on HCV in the general population, the aim of the project in Punjab was to demonstrate the integration and decentralisation of HCV services amongst high-risk groups, specifically PLHIV at ART centres and PWID at OST sites. FIND partnered with Government of the State of Punjab and the Punjab State AIDS Control Society (PSACS) to deliver the project.

¹⁰⁴ Government Ordinance #118 (dated March 7, 2018); Government Ordinance #356 (dated August 2, 2019); Government Ordinance #677 (dated December 31, 2019)

¹⁰⁵ MoHFW (2018) National Viral Hepatitis Control Program: Operational Guidelines.

¹⁰⁶ Ibid.

- **Manipur:** The state of Manipur has the highest burden of injecting drug use in India; the aim of the project in Manipur was to demonstrate the feasibility of providing partially decentralised HCV diagnosis and care for PWID and their sexual partners, through a community-based model. FIND partnered with a local organization, YRG CARE, who have been working with PWID in Manipur for many years.

Stakeholders agree that the grants were therefore very relevant and aligned with the country needs. The FIND grants started working in India in 2017/18, prior to the launch of the NVHCP in July 2018, at a time when the focus on HCV was intensifying at the national level. The focus of the FIND grant was found to be appropriate given the need to support and demonstrate the feasibility to implement the NVHCP. In terms of targeting of the interventions, the FIND projects focussed on both the general population and high-risk and vulnerable populations, who have some of the greatest needs for HCV testing and treatment.

The timelines of the FIND project were considered too short due to the delays in the start of the grant and the time required to set-up the projects on the ground, with extra efforts having to be made to achieve the project targets. Furthermore, the COVID-19 pandemic and consequent lockdown meant that patients that were supposed to return for SVR testing in first half of 2020, were not able to. Although the no-cost extension granted by Unitaid helped to mitigate this, project partners had to conduct a lot of follow-up to reach patients and get them to complete SVR testing.

Stakeholders noted a strong collaboration between the FIND and state level government in planning, design and implementation. Given India's federal structure, it is up to the individual states to manage the implementation of their HCV programmes under the NVHCP. FIND built strong relationships with state-level government stakeholders which has been critical to enable the smooth implementation of the projects, and in some cases to facilitate transition. However, stakeholders have noted that FIND's collaboration with the NVHCP at the national level was more limited, especially in the initial stages of the projects, due to the greater focus on collaboration with state-level NVHCP.

Key challenges in project implementation have included: (i) perceived stigma and discrimination of HCV can impact health seeking behaviour, especially for high-risk groups; (ii) limited awareness and diagnostic literacy of HCV amongst key population requiring extensive counselling to enable testing and treatment; and (iii) lack of robust project planning, including defined protocols and clarity around timelines and approval processes.

The following were key achievements in terms of access barriers framework for India:

Quality: In India there were no WHO PQ RDTs available on the market which was a constraint to enable the roll-out of the project in the three states. The FIND project worked with Unitaid and agreed to procure the Premier Medical Corporation (PMC) RDT given that it was undergoing performance testing by FIND under Output 1. The FIND grant showed PMC that there is a market for HCV RDTs in India and PMC has now applied to WHO PQ using the FIND Output 1 data.

Affordability: Given that affordability of DAAs has been largely achieved in India (through the local production of generic DCV and SOF), the contribution of the FIND grant to affordability of treatment was limited. However, stakeholders have noted that the grant demonstrated that decentralisation and simplification by reducing the number of tests through a simplified algorithm, resulting in more cost-effective and cost-saving models for Government programmes.

Demand and adoption: DNP+, as FIND's partner in New Delhi, supported demand and adoption efforts by:

- **Mobilising and empowering high-risk groups to enable them to access HCV services by linking them to the NVHCP.** Even though testing and treatment are offered free of charge under the NVHCP, uptake is still limited, especially amongst high-risk groups. This is due to the fact that awareness of HCV is still very low and even though services are offered free of cost, patients are still not accessing these services due to a combination of lack of knowledge and awareness, stigma and discrimination by health care workers, and challenging health seeking behaviours. DNP+ has been instrumental in enabling key populations, such as PWID, in accessing testing, treatment and care under the NVHCP. However, the limited availability of HCV testing continues to be an issue for access to HCV services, specifically in New Delhi and Manipur.

- **Empowering key populations through HCV diagnostic literacy and awareness raising so that they have the knowledge and capacity to access HCV services.** As part of the FIND grant, a series of workshops were organised on HCV diagnostic literacy amongst community representatives of key populations. These workshops were held in all three project states and helped mobilise the community and facilitated the formation of smaller groups of community representatives that now have the capacity to raise key HCV issues with government officers in charge of HCV programmes as well as with the communities themselves.

Supply and delivery: the FIND grant demonstrated the feasibility of decentralised, simplified and integrated models of HCV service delivery through the implementation of its projects in the three states.

- **In Punjab** the FIND grant demonstrated the feasibility of a decentralised and integrated approach to enable key populations such as PLHIV to access HCV testing and treatment. The project also had the objective of simplifying the diagnostic algorithm for PLHIV by minimising the number of visits for them to access testing and treatment. The project offered free testing and treatment for PLHIV in 13 ART centres and simplified the diagnostic algorithm, which was more time-efficient and more convenient for PLHIV, as they were offered a ‘one-stop-shop’ service at ART centres.
- **In New Delhi**, the FIND project demonstrated the feasibility of decentralising testing and treatment using a hub-and-spoke model whereby screening is done at the peripheral level (either district hospital, polyclinic or screening camp) with sample transported to ILBS for confirmatory testing and treatment initiation is done again at the peripheral level. The findings show that the highest rate of retention was for the model where screening and treatment are offered at the same site (i.e. screening and treatment at district hospitals); this shows that for the general population it is important to offer “one-stop-shop” services. The project also did successful capacity building of medical officers at the 5 district hospitals through trainings (20 health care workers trained with both pre and during the project) and demonstrated that medical officers can manage the treatment and cure process without the need for specialised training (and with referral mechanisms in place for complicated cases).
- **In Manipur**, FIND demonstrated the feasibility and effectiveness of decentralised testing and treatment through a community-based model targeting PWID and their sexual partners. Together with the local partner YRG Care, FIND established two HCV centres to deliver a community-based model of counselling, testing, treatment and care in two cities. Those who screened HCV antibody positive were then referred to one of the two centres set-up under the project for confirmatory testing using GeneXpert; if positive treatment could either be done at the local integrated community centres or at the GeneXpert site, in line with the patients’ preference and in a community-friendly environment. As part of the project, a core group of opinion leaders also worked to contact and follow-up with PWID to collect test results, support adherence to treatment and encourage SVR testing.

Transition and scale-up: The extent to which the activities supported by the projects have transitioned and will continue beyond the project life vary across the three states as follows: In New Delhi commitment was made to sustain the model for HCV service delivery and to continue the operations in 5 hospitals retaining ILBS as the site for confirmatory testing. However, in practice stakeholders have noted that due to COVID-19, HCV testing and treatment is currently only being provided at one hospital in New Delhi and it is unclear when it will restart in other hospitals (due to the five hospitals being designated as COVID-19 hospitals and not being able to provide any services beyond those for COVID-19). In Punjab, the model demonstrated has fully transitioned to the state NVHCP which has been providing screening, testing and treatment at the 13 ART centres since mid-April 2020 and was expanded to 4 additional ART centres in February 2021. The State Government has included budget to cover the cost of screening, VL testing and treatment in the state budget for all the general population, PLHIV, PWID and prison inmates. In Manipur, the two GeneXpert machines have been handed over to the state NVHCP who has communicated its intent to place them in two rural districts; however, approval of the funding for the cost of cartridges and annual maintenance for 2021 still pending.

Malaysia

Estimates of the national HCV burden vary; it was estimated in 2015 that there were 450,000 cases of HCV, with a 2.5% prevalence rate among the general population.¹⁰⁷ However, the 2020 National Health & Morbidity Survey found a 0.2% prevalence rate among the general population, suggesting that the national HCV burden may be much less than anticipated.¹⁰⁸ In recognition of the public health threat posed by HCV, the Malaysian government has implemented a number of steps towards the aim to eliminate viral hepatitis by 2030. This includes the 2017 “Hepatitis C screening, testing and treatment guidelines,” which details the national approach to HCV care.¹⁰⁹ It was later updated by the 2020 “Clinical Practice Guidelines: Management of Chronic Hepatitis C in Adults.”¹¹⁰ In addition, the “National Strategic Plan for Hepatitis B and C 2019-2023” presents the government’s strategy to achieve elimination by 2030.¹¹¹ From early 2018, SOF/DCV treatment for HCV was made free for patients under the public healthcare system.

From October 2018 to September 2019, FIND conducted a targeted screening program to high risk groups in 25 PHC sites, using SD Bioline HCV Rapid Tests. FIND funded confirmatory tests and pre-treatment assessments. Patients were then referred for treatment under the DNDi trial, or national treatment programme. In total, 26,946 individuals were screened, producing 1,308 RNA+ cases.¹¹²

In addition, FIND and its country-level partner DNDi advocated and supported the roll-out of its decentralised testing model. Such activities include:

- Collaborating with MAC and the MoH to organise a national screening campaign as part of World Hepatitis Day 2019. FIND worked with the MoH to implement screening in the 25 Klinik Kesihatan (KKs – the country’s PHC facility) used under the HEAD-Start pilot.
- Producing an abstract on its pilots across four countries, and presenting at the Asia-Pacific AIDS & Co-infections Conference 2020.¹¹³
- Donating the remaining stock of SD Bioline HCV RDTs and Roche HCV RNA VL tests to the MoH.¹¹⁴
- Presently, FIND is working with the MoH on two trials; the first is a one-stop diagnostic pathway using Gene Xpert in one health clinic. Thus far, the trial has tested 200 people over 3 months. The second is a clinical trial for self-testing, performed in 3 health clinics among 100 MSM and 100 of the general population, which was completed in February 2021.

Stakeholders agree that the grant was overall relevant and aligned with the country’s needs The FIND grant’s focus on the decentralisation of testing was important for overcoming the centralised approach, which took eight weeks to progress patients from screening to treatment initiation, and required patients to visit tertiary level hospitals.¹¹⁵ By piloting a decentralised approach, FIND was able to provide evidence to the government that more people could be tested and linked to treatment, significantly reducing LTFU as well as expanding testing to a wider number of people.

¹⁰⁷ McDonald, S. et al. (2015), Projections of the Current and Future Disease Burden of Hepatitis C Virus Infection in Malaysia.

¹⁰⁸ Institute for Public Health (forthcoming), National Health and Morbidity Survey 2020.

¹⁰⁹ MoH (2017), Hepatitis C screening, testing and treatment guidelines.

¹¹⁰ MoH (2020), Clinical Practice Guidelines: Management of Chronic Hepatitis C in Adults.

¹¹¹ MoH (2019), National Strategic Plan for Hepatitis B and C 2019-2023.

¹¹² FIND data

¹¹³ FIND (2020), Retention in the HCV care cascade for people living with HIV in Delhi and Manipur, India and Malaysia: The HEAD-Start Project.

¹¹⁴ FIND (2020), HEAD-Start Project: 2020 Semi-Annual Report.

¹¹⁵ FIND (2018), Assessing simplified decentralized HCV testing in Malaysia.

Stakeholders disagreed on whether the grant's implementation study design was adequate. The pilots conducted simple implementation studies in accordance with MoH priorities. However, it is unclear whether the grant should have implemented a randomised control trial (RCT), which if implemented appropriately could have provided stronger evidence to inform WHO global guidelines and other country stakeholders on how this decentralised approach compares with the standard of care.

In its screening pilot, FIND's targeted approach was successful. The FIND grant selected sites where they expected to test large numbers of KPs such as PWID. This approach resulted in a prevalence rate of over 13%, exceeding that of the general population.

FIND's collaboration with the concurrent DNDi treatment trial was particularly successful. This collaboration exploited the natural synergies between the HEAD-Start pilot and DNDi treatment trial; patients that were screened by FIND were referred to DNDi for treatment (subject to eligibility requirements). It also collaborated effectively with the MoH to implement its trial, incorporating its screening services into PHC harm reduction services as to integrate the care received by PWID and other KPs.

The following were key achievements in terms of access barriers framework for Malaysia:

Quality: If successful, the development of self-testing and a one-stop diagnostics pathway in PHC sites will improve the quality of HCV screening in Malaysia through the provision of a broader set of screening options; centralized testing will remain the most economical option in areas of low density of KPs, PHC site screening will provide a suitable option in areas of large density of PWID, and self-testing will help reach MSM populations who do not seek screening from PHC sites.

Affordability: The HEAD-Start pilot demonstrated the feasibility of decentralisation and simplification, reducing the number of tests through a simplified algorithm, resulting in more cost-effective and cost-saving models for Government programmes. Further developments in the future, through self-testing and the one-stop algorithm, will further reduce costs for government programmes. The resulting scale-up of the national screening programme, in part due to FIND's studies, will allow cost savings to be made through larger purchasing volumes.

Demand & Adoption: Stakeholders noted that the FIND grant has played a key role in advancing the national HCV programme to its current status of roll out. Without its demonstration study, the momentum that was previously built up and the government commitment, particularly from MoH, would be weaker.

If successful, the development of self-testing will help improve access to MSM. The development of the one-stop diagnostic pathway would further simplify and shorten the testing algorithm in PHC sites, further encouraging demand for HCV testing.

Supply & Delivery: The FIND pilot demonstrated the feasibility of a simplified, decentralised testing algorithm that has been adopted and scaled up by the MoH to 146 PHC sites. The simplified algorithm takes four weeks to progress from initial screening to treatment initiation, in comparison to eight weeks before, and patients no longer need to visit tertiary level hospitals to access testing services.

Transition and scale-up: The scale-up of the HEAD-Start pilot's screening algorithm to all 146 PHC sites with resident primary healthcare physicians by the MoH demonstrates the sustainability of FIND's impacts in Malaysia. The target of the MoH to scale up annual screening to 105,000 by 2030 highlights the MoH's commitment to scale-up its screening services further.¹¹⁶

The Malaysian MoH has adopted a proactive approach to addressing the Malaysian HCV burden, due to the work of both FIND and Coalition PLUS, in which the MoH is deciding on its next target KP, given the expectation that it would over time successfully screen enough PWID as to exhaust this targeting opportunity. This is exemplified by its

¹¹⁶ MoH (2019), National Strategic Plan for Hepatitis B and C 2019-2023.

research into a one-stop testing algorithm and self-testing, the latter of which is considered to be a favourable screening alternative for MSM.

Myanmar

With an estimated national prevalence of HCV of 2.65% amongst the general population¹¹⁷ and a reported HCV antibody prevalence of 47.7% amongst IDUs,¹¹⁸ HCV infection in Myanmar is a significant public health issue. Myanmar established the National Hepatitis Control Programme (NHCP) in 2014 and launched the National Strategic Plan for Viral Hepatitis (2016-2020) in 2017, followed by the Myanmar National Action Plan for Viral Hepatitis Response 2017-2020. In 2018, Myanmar launched the National Testing Guidelines for Viral Hepatitis, which were updated in 2019. Importantly these guidelines enable general physicians (GPs) to prescribe DAAs for non-complicated cases in Myanmar. In terms of confirmatory testing, the NHCP uses GeneXpert platforms for HCV VL testing.¹¹⁹ However, viral load testing machines and human resources for HCV confirmatory testing are limited to the National Health Laboratory (NHL) and other national centres.

FIND supported two projects in Myanmar under the HEAD-Start grant:

- **FIND/ Burnet Institute study:** Community-based point-of-care (POC) hepatitis C testing and general practitioner initiated direct-acting antiviral therapy in Yangon, Myanmar (the CT2 study). The aim of the CT2 study was to assess the feasibility, acceptability and effectiveness of a decentralised, simplified HCV care model in Myanmar.¹²⁰ The approached piloted decentralised, community-based POC testing and DAA treatment simplified model of care established at two sites in Yangon: at the Burnet Institute Site specifically for PWID and at the Myanmar Liver Foundation site for the general population.¹²¹
- **FIND/ CHAI study:** Optimising Utilization of Existing Abbott m2000 at the National Health Laboratory (NHL) to Expand Access to HCV Testing in Myanmar. The objective of the study, carried out in collaboration with CHAI, was to determine the feasibility and acceptability of introducing HCV VL testing on existing Abbott m2000 platform currently being used for HIV VL testing at the National Health Laboratory in Myanmar.¹²²

The two projects were very relevant to Myanmar's country needs for HCV: (i) given the significant HCV prevalence amongst both the general population and high-risk groups such as PWID, Myanmar's current hospital-based/ specialist-centred strategy of testing and treatment is limited in reaching the number of people infected with HCV and therefore support the country elimination efforts; (ii) there are only a limited number of GeneXpert machines in the country which can be used for testing of HCV (in line with the NHCP guidelines) thereby limiting the capacity and reach of the NHCP testing approach, meaning it would take years to reach the NHCP targets without additional testing capacity. Furthermore, stakeholders noted that the NHCP was reluctant to adopt any new strategies such as decentralisation of HCV testing and treatment and integration of HCV testing without evidence from the country.

The projects included a focus on vulnerable populations: The CT2 Study included one site specifically for the testing and treatment of PWID and showed that it was feasible to engage and test and treat this high-risk and marginalised group with good retention across the care cascade. Originally, the CT2 study protocol also included PWID co-infected with HIV, as the study wanted to show that testing and treatment of HIV/HCV co-infected patients

¹¹⁷ Government of Myanmar (2015) 2015 National prevalence survey for Hepatitis B and Hepatitis C.

¹¹⁸ Ministry of Health and Sport (2017) Myanmar National Strategic Plan on Viral Hepatitis 2016-2020, National Hepatitis Control Programme, July 2017 p.18-21

¹¹⁹ Ministry of Health and Sport (2019) National Simplified Treatment Guidelines of Viral Hepatitis C infection, Second Edition, July 2019, p.15-16

¹²⁰ Draper, B et al ILC 2020, AS037

¹²¹ Draper, B et al ILC 2020, AS037

¹²² FIND/CHAI Protocol

could be carried out in community settings; however, Myanmar's policy states that HIV co-infected patients have to be treated in hospitals, so the focus of the CT2 study refocussed on mono-infected PWID only.

Collaboration with national authorities was a challenging task, but was ultimately achieved and is a success of the project. The organizational structure of the Ministry of Health and Sports in Myanmar is very complex with many vertical programmes, including HCV, meaning that the project needed to interact and communicate with multiple levels of governance. The project therefore spent significant time and resources on ensuring coordination and collaboration amongst various programmes and departments (NHCP, NHL, National AIDS Programme etc). For example given that HIV testing platforms needed to be used under the FIND/CHAI project, this required to work closely with the National AIDS Programme as well as with NHL. This was perceived as critical to ensure there was a common understanding and buy-in across all stakeholders, not only to allow for smooth implementation but also to lay the foundations for future collaboration. The FIND/Burnet project collaborated with the Myanmar Liver Foundation, a local NGO. This collaboration was highlighted as particularly useful given their extensive local knowledge, level of experience and ongoing implementing efforts on the ground.

Timelines for project implementation were not considered adequate due to the time it took to secure government support and buy-in; this was particularly the case for the FIND/CHAI project which required extensive cross-departmental collaboration at the Ministry of Health and Sports. It was noted that Unitaaid should take into consideration for country-level issues faced by grantees and their effect on project timelines.

The following were key achievements in terms of access barriers framework for Myanmar:

Quality: Through the FIND/CHAI project, the NHL as a national reference laboratory received EQAS training. Laboratory technicians appointed under the CT2 studies were also trained on routine lab procedures and on EQAS.

Affordability: not a focus of the project, but stakeholder indicated that integration of HCV viral load testing with HIV viral load testing at the NHL offers potential for integration of procurement, which would make the procurement of both viral load tests cheaper, and more affordable for the government which relies on domestic financing for the purchasing of these tests.

Demand and adoption: the findings from the two studies have been accepted by the NHCP during the project dissemination workshops and stakeholders have noted that the evidence will be used to revise the current NHCP. The CT2 study protocol for decentralised testing and treatment and referral pathways was developed by experts from Myanmar with support from Burnet Institute and will be used as the basis for future guidelines on decentralisation of HCV care.

Supply and delivery: The FIND/ Burnet study proved the acceptability and feasibility of decentralisation, whilst the FIND/CHAI project proved the feasibility of integrating HCV and HIV testing in Myanmar. The projects provided proof of concept and demonstrated that:

- Decentralised RNA testing using GeneXpert is possible at community-based clinics, not just central/ hospital-based laboratories;
- Decentralised GP-led care was safe and effective for HCV; and,
- Integrating HCV testing into existing platforms currently in use for HIV testing was possible.

Transition and scale-up

The National Strategic Plan II 2021-2025 (NSPII) of the NHCP is current being developed and stakeholders have noted that the evidence and findings from the two studies will be included in the NSP II. The findings were considered particularly useful for the Myanmar policy updates given that they were carried out in Myanmar and reflect the specificities of the local context. In particular, the FIND/CHAI integration study protocol was shared with the NHCP, as during the dissemination meeting MoH decision makers noted that the integrated approach to testing should be considered in the ongoing drafting of the updated NSP II. In terms of transition and continuation of the projects, Burnet Institute was in the process of extending the project (CT2 Extend) but this has been delayed due to COVID-

19. In the meantime, the MLF will continue to provide this approach albeit on a more limited scale given the absence of donor funding.

5.6. CONCLUSIONS

The FIND grant aimed to increase the availability and adoption of new and existing HCV diagnostic technologies. FIND's work has been critical and transformational in this regard, specially noting the state of the diagnostics market at the start of the grant and where FIND's work has helped progress it today. In this sense, the work of FIND has been catalytic and helped kick-start the diagnostics market for HCV, and while some progress has been made with regards to mobilising the interest of the range of stakeholders involved – country governments, affected communities, manufacturers, etc. – more progress and financial commitment is needed to support larger scale scale-up.

PART C: GRANT EVALUATION – COALITION PLUS

6. COALITION PLUS

The Coalition PLUS HIV/HCV Drug Affordability Project was first approved by Unitaid in July 2015, following extensive discussions between Unitaid and the grantee. The overall goal, outcomes and outputs of the grant are summarised in Table 6.1 below.

Table 6.1: Summary of Coalition PLUS grant

Result level	Description	
	Up to 2018	2019-2020
Goal	Contribute to universal access to HCV care in low and middle income countries	Contribute to 2030 targets for HCV mortality reduction
Outcome	Improved government commitments, national protocols, budgets, and/or policies for HCV treatment access in target countries for hepatitis and HIV co-infected patients	Increased adoption of proactive and affordable HCV care policies aiming at elimination
Outputs	<ol style="list-style-type: none"> HCV movement networks are established or strengthened in target countries Awareness and education campaigns are performed in target countries Lessons learned are widely disseminated 	<ol style="list-style-type: none"> Increased commitment of national public authorities to well-funded and efficient HCV care. Increased focus on communities' needs in generating demand for and uptake of HCV services. Increased knowledge-building and coordination among national and international HCV stakeholders.

To achieve these results, Coalition PLUS partnered with both national and international civil society organisations (CSOs), to both advocate to governments as well as work with HCV communities to raise awareness of HCV and empower communities to know their HCV status and conduct advocacy to improve HCV services in countries. As discussed further below, this grant was largely implemented at the country level, although Coalition PLUS also undertook a number of international advocacy-related activities to support its country programmes as well as input into international policy dialogue.

Sections 6.1-6.4 present findings across the four pillars of the evaluation framework (relevance and implementation, effectiveness, impact, scalability and transition); Section 6.5 presents summary findings from the country case studies; and Section 6.6 concludes. For introductory information on this grant evaluation in terms of the evaluation background, scope and objectives as well as framework and methodology please refer to Section 1 included in Part A of this report.

6.1. RELEVANCE AND IMPLEMENTATION¹²³

Key findings	Strength of evidence
<p>Although not a “typical” Unitaid grant given its advocacy focus, the Coalition PLUS grant has been noted as highly relevant in terms of both addressing country needs and Unitaid’s mandate on market dynamics.</p> <p>A key value add of the grant has been its focus on representing marginalised groups.</p>	

¹²³ For a more detailed assessment of the relevance and initial implementation of the Coalition PLUS grant, see CEPA (2017), Mid-term evaluation of the HIV-HCV Drug Affordability Project.

Coalition PLUS has partnered with highly relevant organisations at the national level, enabling the grant to work closely with both national authorities and affected communities.

There have been numerous reprogrammings and extensions to the grant over its lifetime, which were of value in terms of content but inefficient in terms of process. But even with course correction, the level of ambition within the grant has often been above what was feasible in given timeframes.

Although not a “typical” Unitaid grant given its advocacy focus, the Coalition PLUS grant has been noted as highly relevant in terms of both addressing country needs and Unitaid’s mandate on market dynamics. There has been considerable debate, and even some apprehension, to Unitaid investment in advocacy through this grant, but it has been clear that this intervention was much needed in the context of the market dynamics for HCV where low demand and affordability have been key challenges. Indeed, some stakeholders have commented that the value of Unitaid’s market focused investments in HCV would not have been adequate in the absence of the advocacy through the Coalition PLUS grant. The Coalition PLUS grant has well accounted for the HCV policy status in countries. This holds for both the initial phases of the grant, as well as more recently following the restructuring of the grant for the 2019-20 period. For example, in the recent updates, Coalition PLUS structured its interventions in different countries based on the stage in which they were implementing HCV elimination plans, with the focus in Brazil and Colombia being on prioritising national advocacy efforts related to ensuring the programmes were affordable and appropriately funded, while in other countries, advocacy efforts also focused on ensuring programmes were designed with communities needs in mind and coordinating stakeholders (see Section 6.5 of this part for further details from the country case studies).

The selected countries for focus have largely been appropriate, given the affordability barriers many of these countries were facing. Some key countries such as China were not included, and consultees noted that this was one of the few “missing pieces,” although there are practical challenges of Unitaid funding CSOs in China. The focus of the countries covered within the Coalition PLUS grant has mainly been upper-middle income countries (UMIC). This differs from Unitaid’s typical focus across its portfolio, which is on countries at lower income levels. But given the issuance of VLs from Gilead and BMS for their DAAs, significant barriers to affordable treatments were reduced in LICs ahead of the grant being initiated. On the other hand, many of the Coalition PLUS countries, particularly Malaysia, Brazil and Colombia (as well as Thailand and Indonesia, which were previously included in the grant), were not included in the VLs offered by the companies and as a result could only obtain DAAs at considerably higher prices (see Section 3.2.3 of Part A of the report for further details). For the other countries, the rationale for their selection was that while generic manufacturers were available in some of the project countries, access to treatments was still limited by other barriers such as limited awareness and rollout of HCV programmes. Coalition PLUS considered not only the affordability and demand challenges in countries, but also other factors such as estimated HCV prevalence, the strength of CSOs in countries to advocate for change, the country’s history in issuing CLs, the extent to which governments had shown initial signs of commitment and the practicalities of working in countries. China was a key country not included in the programme, despite Coalition PLUS initially highlighting China as an important country to include given its HCV prevalence and the patent barriers on DAAs in the country. However, because of challenges related to funding CSOs in China and differing views on the extent to which policy changes could be achieved, it was not included in the overall programme.

Within the selected countries, Coalition PLUS has selected highly relevant local partners, with many being well respected and highly regarded in their respective country contexts. The mixture of supporting organisations with direct relationships with government and those with close contacts with HCV communities has meant that in-country organisations have been able to consider both perspectives in their advocacy work. Both in-country and global stakeholders have noted that Coalition PLUS’ partner selection has been highly appropriate, following some initial starting issues. This has drawn on the organisation’s own network and linkages to CSOs in the given countries from its previous advocacy work in HIV, as well as through Coalition PLUS’ initial due diligence work in establishing their country-based partnerships. In some countries, Coalition PLUS has partnered with multiple organisations, who each focus on different areas of advocacy such as: i) organisations which have direct

engagement with government MoHs and sub-national health authorities; ii) external, technical organisations focused on specific issues such as access to medicines; and iii) grassroots organisations with strong relationships with HCV communities. While in some countries not all these above partners have been directly funded by the grant, in practice Coalition PLUS partners have often had working relationships with other organisations to ensure that these different advocacy channels have been pursued. Through this approach, Coalition PLUS and its partners have been able to consider issues covering the technical and practical aspects of overcoming affordability and implementation barriers at the national policy level, practical challenges in the implementation of HCV programmes particularly when testing and treating marginalised populations, and garner the perspectives of key populations when considering how to address HCV challenges.

The Coalition PLUS grant is arguably one of the most effective grants for considering the views and issues facing marginalised groups in Unitaids' entire portfolio. This has drawn on Coalition PLUS' extensive experience and network of CSOs that have long advocated for the rights of marginalised groups in the context of HIV, and through this grant has been able to learn lessons on what has worked in these contexts while tailoring the focus for the key populations in HCV (for example, while still a relatively high proportion of PLHIV, PWID account for an even larger proportion of PLHCV in most contexts). This has continued throughout the implementation of the grant, including in recent years where under Output 2 Coalition PLUS aimed to specifically address HCV community needs, as well as support healthcare workers within countries address community needs.

Coalition PLUS worked effectively with other Unitaids grantees at the country level, with some exceptions. Within countries, Coalition PLUS and its partners have also been able to work effectively with national partners such as FIND, DNDi and MSF to offer a coordinated message to the national authorities on the design and rollout of HCV testing and treatment. In Malaysia, the coordination and collaboration between Coalition PLUS' local partners Third World Network, the Malaysia AIDS Council (MAC), FIND and DNDi was noted as a particularly important example of how coordination and collaboration between different organisations helped facilitate positive outcomes. In Manipur India, MSF and Coalitions PLUS's partner collaborated regularly, including with MSF directly training CoNE on treatment of PWIDs.¹²⁴ On the other hand, stakeholders noted that collaboration between FIND and local Coalition PLUS partners could have been better, especially given the overlapping timelines during which these grants were implemented.

Coalition PLUS partners have also worked with FIND in the implementation of its decentralised pilot projects, providing key educational materials to communities on this aspect of Unitaids' work, which has been important for raising awareness among these communities and policymakers of the need to provide services to these populations. More broadly, Coalition PLUS partners have been key advocates for decentralised testing, even in countries where FIND has not operated. Key examples of this include:

- In Malaysia, Coalition PLUS provided materials to support the FIND HEAD Start pilot programme that implemented decentralised testing models. This included MAC delivering a training course to family medicine specialists on the administration of decentralised testing, facilitating the wider rollout of this model.
- While FIND did not operate in Colombia, Coalition PLUS's local partner IFARMA advocated for decentralisation of testing and treatment of HCV and the MoH is creating conditions to support decentralisation (including establishing training courses, updating guidelines, etc.); however, in practice the specificities of decentralised community testing and treatment still need be taken into account.
- In Brazil, local partner FOAESP advocated for decentralisation of treatment, which was approved by the Federal MoH and is now being implemented in primary health care facilities. This was part of FOAESP's more comprehensive advocacy efforts to make the procurement, delivery, distribution and surveillance systems of DAAs more efficient and equitable.

¹²⁴ Dalberg (2019) Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs. Evaluation for Unitaids; Final Report.

- In Morocco, advocacy by local partner ALCS contributed to MoH agreeing to establish a system with additional referral centres to which HCV+ persons will be referred for treatment. Furthermore, whilst prior to the project HCV viral load testing was only available in Marrakech and Casablanca, thanks to ALCS' advocacy, all regional hospitals are now equipped with GeneXpert machines and are able to offer decentralized HCV viral load testing.

At the country level, Coalition PLUS has demonstrated its effectiveness in engaging and integrating its work with that of national authorities and implementing partners. National stakeholders noted that local Coalition PLUS partners have played an important role in taking forward HCV programmes, including the development of national testing and treatment guidelines and training national healthcare workers on approaches for testing and treating patients. In Colombia and Morocco, local partners sit on the National Technical Advisory Boards on Viral Hepatitis which enables them to influence national policy making and contribute to the development of national guidelines. In India, both DNP+ and CoNE built strong relationships with state-level government stakeholders which has been critical to enable the smooth implementation of the projects, and in some cases to facilitate transition. There are also examples of Coalition PLUS partners being directly integrated within the health systems of countries and delivering HCV services, as is the case with India, where local partner CoNE has been the sole organisation responsible for providing HCV referral for PWID in 2020 to healthcare facilities, while in Morocco ALCS is the sole organisation authorised to test high-risk groups and link them to care.



One key area where the Coalition PLUS grant has experienced challenges throughout the grant has been on the timeliness of achieving results. External factors have mostly influenced this, including changes of governments and key staff within ministries, but the long start-up period for the grant was also a contributory factor. Since the grant's inception, rollout has been hampered by several delays to activities. As noted in CEPA's mid-term evaluation of the Coalition PLUS grant, there was an extensive lag in the establishment of the grant, given the need for Coalition PLUS to recruit new staff and effectively build its HCV capacity from scratch. More recently, the COVID-19 pandemic has seriously limited the implementation of Coalition PLUS partners activities, with some key events cancelled and others either delayed or carried out virtually. Several countries, including Brazil, Morocco and Colombia, have also suffered from political instability and turnover of senior government staff. As discussed further in Section 6.2 below, these various delays have significantly impacted the ability of the grant to achieve its ultimate objectives.

There have been numerous reprogrammings and extensions to the grant over its lifetime, which have taken considerable time and effort from Unitaid and Coalition PLUS staff. This mix of reprogrammings and extensions have mostly been appropriate, and reflect the changing nature of the environments in which the grant has operated in and the fact that advocacy takes time and efforts. But even with course correction and extensions, the level of ambition within the grant has often been above what was feasible in given timeframes. Several extensions have been made during the course of the grant (including long discussions to agree the initial design). These have been viewed as useful, but the processes have been highly burdensome for both Unitaid and the grantee. While COVID-19 has ultimately impacted the extent to which grants could achieve their results since 2020, in the majority of Coalition PLUS countries, achieving the grant's overall targets may have been too ambitious. In most countries, progress has been made to achieving the overall outcome of country programmes working towards HCV elimination, but in many cases this has involved iterative rather than all-encompassing progress. A key factor behind this is that policy change can take decades to achieve, and even though the grants have been implemented for several years, achieving such objectives in the countries being considered would require even more years to truly see the impacts of the advocacy efforts that the grant has been undertaking.

6.2. EFFECTIVENESS

Table 6.2 provides a summary of our assessments including level of progress (i.e. the extent of achievements as significant/ good/ limited), strength of effect (i.e. the magnitude/ value of the progress given the market context as well extent of attribution to the grant, considered along a scale of high, moderate and low) and key areas of contribution as well as the strength of evidence of the finding. This is followed by a detailed consideration by access barriers.

Table 6.2. Summary of Coalition PLUS's grant key contribution to Unitaid's access barriers

Access barrier	Key areas of contribution	Level of progress	Strength of effect	Strength of evidence
Affordability	<ul style="list-style-type: none"> • Technical support to Malaysian government on various areas related to issuing to CL. • Ongoing discussions with government departments to address key intellectual property as well as health system barriers limiting affordability. • National advocacy campaigns to raise awareness of DAA costs and ways in which these could be reduced. 	<p>Good progress – Significant price reductions in some countries for DAAs, while others there has been reductions but not significant enough to make DAAs affordable for widespread procurement.</p>	<p>Moderate¹²⁵: CL issuance in Malaysia key example of how advocacy work of Coalition PLUS contributed to reduced prices. In other countries, advocacy activities have been noted for contributing to reduced prices as well.</p>	
Demand and adoption	<ul style="list-style-type: none"> • Participation in guideline development groups and national policy dialogue to inform elimination plans and guidance • Implementation of pilot programmes and support activities for PLHCV to enable them to access services • Support for national and regional screening campaigns to test and link patients to care • Dissemination of best practice guidance and evidence for engaging with HCV communities to generate demand 	<p>Good progress – Most countries are closer towards HCV elimination than when the Coalition PLUS grant was first initiated. Continued efforts are needed to ensure full implementation takes place.</p>	<p>Moderate: Combination of advocacy activities as well as direct implementation of pilot projects in countries have contributed to progressing the HCV programmes in terms of policy development and implementation</p>	

¹²⁵ Strength of effect rated as moderate as there were already VL in place before Unitaid's grant.

Affordability

Coalition PLUS and its partners have been important in facilitating more affordable treatments, with the issuing of the compulsory licence (CL) in Malaysia being a key example that resulted in far more affordable SOF being available in the country (which also had indirect implications for other countries). While Malaysia has significantly reduced the price of DAAs, these results may not be sustained in future without continued efforts to advocate for further competition in the country, including potential through the reissuance of the CL. As shown in Table 6.3 below, some of the Coalition PLUS countries were not included in either of the VLs provided for SOF or DCV at the outset of Unitaid’s support in this area, leading to countries having to pay significant amounts to procure these products that prevented widespread treatment programmes. Even in countries with access to generic medicines such as Morocco and India, prices were still significantly high that widespread treatment programmes would have been difficult to achieve.

Table 6.3: Coalition PLUS country inclusion in voluntary licenses of key DAAs in 2015/16 and estimated cost

Country	SOF	DCV	Estimated cost ¹²⁶
Brazil	No	No	US\$9,425
Colombia	No	No	US\$8,100 (SOF/VEL in 2017)
India	Yes	Yes	US\$825
Malaysia	No	No ¹²⁷	US\$12,000 (SOF only)
Morocco	Yes (added 2015)	Yes	US\$1,513

Source: CEPA analysis based on Coalition PLUS data for treatment cost; voluntary licence data taken from Simmons et al. (2019)

As part of its support in these countries, Coalition PLUS partnered with key civil society organisations (CSOs) to advocate for more affordable treatments in countries. In many countries, this involved a multi-pronged approach of working with CSOs focused on different areas, including: i) organisations with expertise in IP-related issues; ii) organisations with historic collaborations and links to country MoHs; and iii) grassroots-based organisations with close connections to people living with HCV, including key marginalised populations.

In the context of Malaysia, where Gilead had previously been granted a patent for SOF, the cost to the government of procuring such treatment meant that during the initial years of the grant treatment with DAAs in public health facilities were almost non-existent. However, the country took a major step towards obtaining more affordable DAAs in September 2017 when it issued a compulsory licence (CL), the first country in the world to issue a CL for HCV treatments, which enabled the country to be able to access generic treatments. Up to the end of 2020, Malaysia was able to access SOF for as little as US\$80. Having access to treatments at this price was noted by stakeholders as overcoming the “key blockage to unlocking the HCV programme”. Key examples of activities that were carried out as by Coalition PLUS partners included:

- TWN advising government on technical issues related to the issuance of the CL, enabling the government to have confidence to go ahead with its issuance.
- TWN offering technical support in light of pressure from the US pharmaceutical companies and other US trade representatives to remove the CL.
- Advocacy from MTAAG+ and MAC in terms of speeding up the process of access to DAAs.

¹²⁶ Treatment costs are for 12 week courses of treatment with SOF/DCV unless stated otherwise. Treatment costs listed above include costs for innovator drugs in some countries, whereas others (India and Morocco) are costs for generic manufacturer products. Costs are displayed in US dollars, though in many contexts countries will have paid in local currencies.

¹²⁷ For DCV in Malaysia, data exclusivity rights were not granted to BMS and no patent was filed in the country, which essentially enabled generic manufacturers to supply the market.

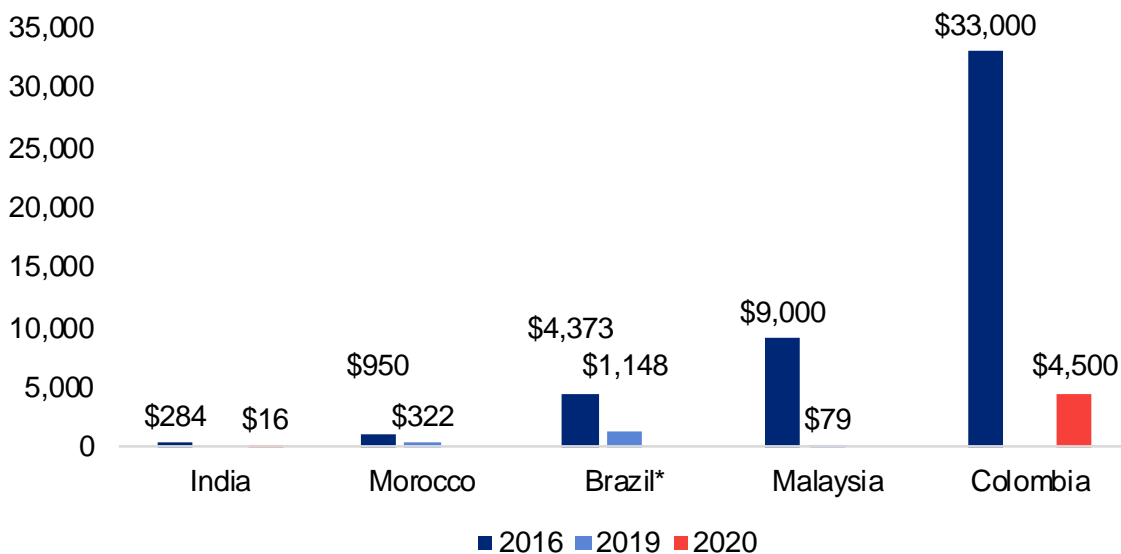
Country stakeholders noted that Malaysia benefits from strong CSOs which have ensured that these affordability issues were emphasised. In addition, extensive advocacy work was done by both Coalition PLUS and other in-country organisations such as FIND and DNDi, with all working collaboratively on advocating for the CL to be issued. The country also benefits from the MoH being highly committed to addressing HCV as a key health challenge in the country. That said, stakeholders noted that without the collaboration of in-country partners, it is likely that the issuance of the CL would have been much slower, with the support by all organisations speeding up the issuance by 2-3 years (i.e. the counterfactual).

Following the issuance of the CL in Malaysia, the country was included in the SOF VL, along with Thailand, Belarus and Ukraine, highlighting the indirect effect that this had in enabling affordable treatment that many believe would not have happened without the Malaysian CL being issued. In addition, consultees noted that lessons and experiences of issuing the CL in Malaysia could be used by other countries, including those that have not been supported by Coalition PLUS, should these countries wish to pursue this option in future.

When the CL was first issued in September 2017, this was only to apply for a three-year time period, and as a result needed to be renewed in September 2020. However, due to the unstable political environment, competing interests in the country and the COVID-19 pandemic, the CL lapsed, meaning that the country could only obtain SOF going forward from sublicensees of the innovator VL. In Thailand, where only one company covered under the VL is currently registered, the cost of full treatment for SOF/DCV is estimated to be US\$750 by project stakeholders. While Malaysia may still benefit from prices of SOF/DCV under the VL, these will be significantly higher than the US\$80 for SOF cost they obtained when the CL was issued. Thus, despite the initial successes, big risks remain to the Malaysia programme going forward that could hinder its wider rollout.

Across all Coalition PLUS countries supported by Unitaids’ investments, prices of key DAAs have fallen over the period that the grants have been operating, although in some contexts they continue to be unaffordable for meaningful rollout to take place. Figure 6.1 below summarises how key DAA prices have changed over time in Coalition PLUS countries. As shown, in some markets, prices have fallen significantly, particularly in India and Malaysia, with the former having access to generic competition in its domestic market, while the latter, as mentioned previously, has been able to facilitate competition through the issuance of the CL and being included in the VL for SOF, with the support of Coalition PLUS.

Figure 6.1: Price changes for 12-week SOF Coalition PLUS countries in US\$ (2016 to 2019/20)¹²⁸



Source: Coalition PLUS * Brazil and Colombia 2019 price refers to SOF/LED.

¹²⁸ Prices quoted in countries are based on the latest available data.

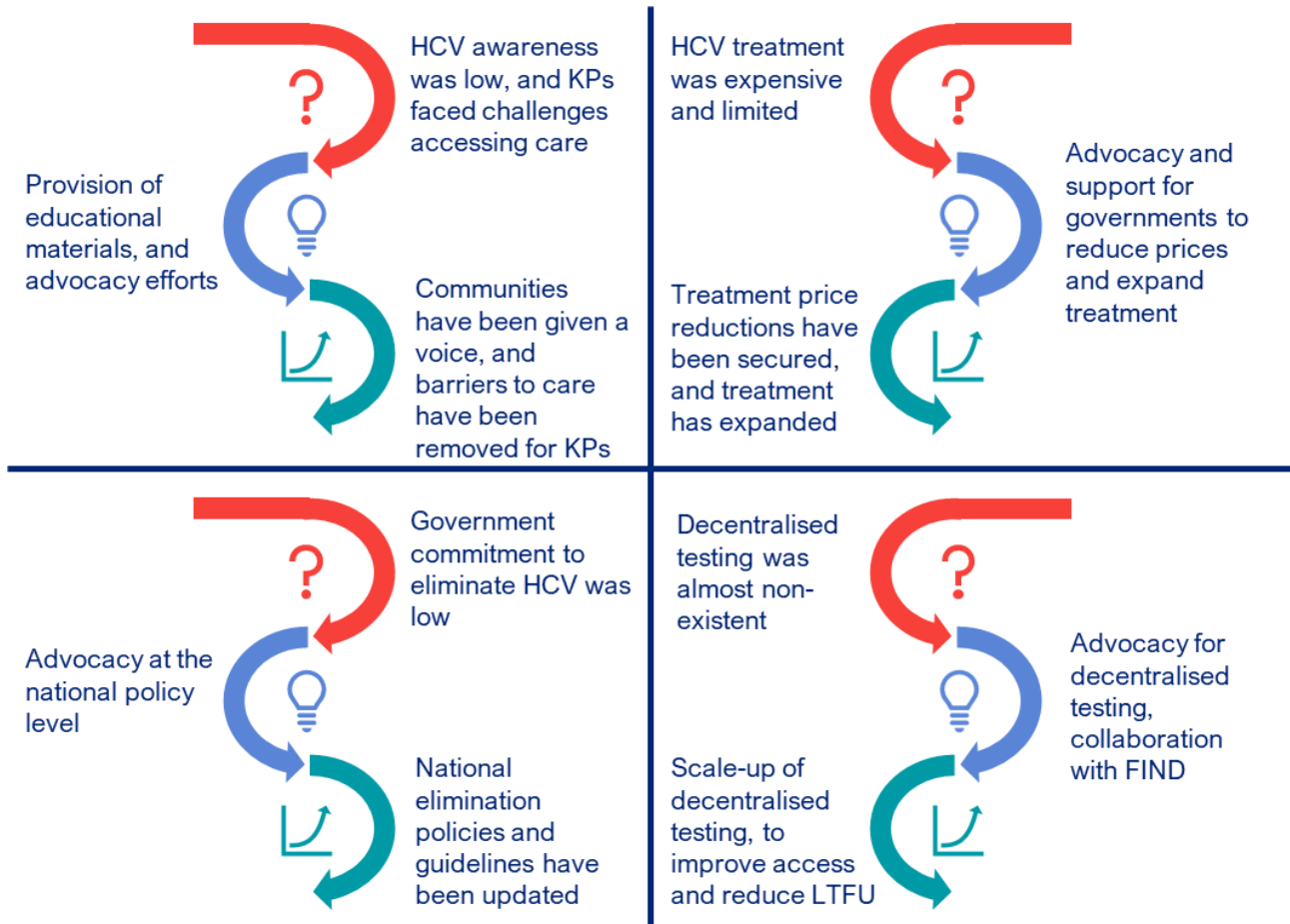
For other countries, particularly Brazil and Colombia, prices have fallen significantly, with advocacy by local partners noted as being key contributors to this. For example, in Colombia the move to centralise DAA procurement was long advocated for by local partner IFARMA through meetings with government, published articles and legal actions. Similar advocacy in Brazil also contributed to the transfer of DAAs into the strategic component of pharmaceutical assistance, which allowed to centralize different competences around procurement and supply (which were previously the competence of different departments at the MoH). In Brazil, parliament has prepared a law to enable the Federal MoH to issue CL when a public health emergency has been declared, which could result in prices reducing further going forward. But prices in both countries remain comparatively high, which is limiting the extent to which these countries can roll out wider HCV programmes.

Demand and adoption

At the outset of the Coalition PLUS grant, despite countries having national plans and policies in place to address HCV, awareness and commitment to HCV was low, the rollout of testing and treatment was very limited and programmes were only being implemented on a small scale. Awareness of HCV at the policy and community level was very low, and a number of KPs faced particular challenges accessing HCV services due to stigma and discrimination. This was particularly the case in South East Asia countries such as Thailand and Malaysia, the first two countries supported by Coalition PLUS, where PWID have particularly struggled to access health services due to the criminalisation of their activities and the unwillingness of governments and health services providers to offer them support. Most of the countries had some form of national plan in place at the start of Coalition PLUS' support, but actual implementation of services was very limited, often provided by the private sector and subsequently relied on out-of-pocket expenditures of patients. Of the five countries included at the end of the Coalition PLUS grant, India had the highest absolute number of patients treated at 38,000 patients in 2016 (mainly in Punjab), largely driven by the availability of more affordable DAAs and domestic manufactures, but in relation to annual incidence estimated to be 200,000, treatment levels here were still low.¹²⁹ Decentralised testing models were almost non-existent, with most countries relying on centralised forms of testing and treatment at centralised laboratories and hospitals in larger cities respectively. Figure 6.2 summarises some of the key pathways to which the grant intended to increase demand and adoption of HCV services.

¹²⁹ Based on Coalition PLUS project data.

Figure 6.2: Summary of Coalition PLUS' intended contribution to demand and adoption



Source: CEPA analysis

The main achievement of Coalition PLUS' interventions across countries has been the role it has had in giving communities a voice at the national and global level. Coalition PLUS partners have also been important in connecting people living with HCV to access HCV services and care at health facilities.

Successful examples of how Coalition PLUS partners have raised awareness include:

- In Malaysia, MTAAG+ and MAC have actively encouraged community participation in workshops linked to HCV alongside MoH, enabling these partners to discuss key issues between one another and facilitate dialogue in the implementation of the HCV programme. MAC also developed community brochures that were delivered as part of a national screening campaign in 2019, which helped raise awareness of the campaign among affected communities and ensure that over 11,000 people were tested. Country stakeholders also noted that MTAAG+ and MAC have undertaken important outreach activities for PLHCV to ensure they are well-linked to national health services, acting as a key link that may have otherwise not been in place in the absence of Unitaids' funding. MAC and MTAAG+ have also been important in piloting projects related to supporting prison populations have access to HCV services, including:
 - The **TEMAN Project, initiated by MAC in 2015**, is a risk reduction programme for people returning to the community after incarceration. As an example of its activities, from September 2016 the TEMAN Project helped women who inject drugs in Kajang Prison, reaching out to 36 women by 2017.¹³⁰

¹³⁰ MAC (2017), Annual Report 2017.

- In 2018, **MTAAG+ conducted a screening pilot across three prisons**, screening 180 prisoners and finding 72 positive cases.
- In India, both DNP+ and CoNE have been working on increasing HCV literacy and awareness of HCV through the delivery of workshops as well as educational materials to help communities understanding HCV-related issues. DNP+ and CoNE have been instrumental in enabling key populations, especially PWID, in accessing testing, treatment and care under the NVHCP. For example, to support demand and adoption of services, DNP+ has helped PWID reach the HCV unit at the Model Treatment Centre (MTC) in New Delhi and supported them throughout all processes of being screened, viral load confirmation testing, treatment initiation and adherence, and complete SVR testing. This support has been critical for PWID who are more likely not to seek health services and more likely to be lost to follow-up. Furthermore, DNP+ successfully advocated for the provision of testing and treatment to homeless vulnerable populations at a MTC in New Delhi, which was continuously being refused due to their inability to present an ID card. Similarly, in Manipur CoNE has played an important role in increasing demand and adoption for HCV services by PWID; importantly, the state government accepts the referral of HCV screening done by CoNE. CoNE also supports PWID patients who are referred to MTC throughout the whole process of testing and treatment to minimise loss to follow-up. One stakeholder described the work of these organizations as “*enabling the state NVHCP to function*”.
- In Morocco, ALCS is recognised by the government and health sector stakeholders as a trusted technical partner with expertise and capacity in reaching marginalised communities for HIV, STI and HCV prevention and testing and for accompanied referral to government health facilities for treatment and care. ALCS have been nominated as the only organisation authorised by government to conduct community testing once the screening campaign is launched nationally (after the government procures DAAs for the public sector). Advocacy by ALCS contributed to convincing the MoH to include PWID in the government list of key populations, which has resulted in drug users now being able to access free healthcare, including HCV services, through the government health insurance scheme RAMED (régime d’assistance médicale) targeting the informal sector and the poor. ALCS has worked on improving HCV literacy and awareness amongst key and vulnerable populations, including male and female sex workers, drug users, gay men and other men who have sex with men and people in prison, through workshops, peer education and outreach. Furthermore, ALCS has not only increased capacity of its own health facility staff but also of general practitioners and specialists in public and private health facilities in HCV testing, care and treatment and in working with vulnerable communities.
- In Brazil, members of local partner network organisation FOAESP have integrated HCV into their routine HIV awareness raising activities with KPs and communities and assist in referral to health care facilities. FOAESP have furthermore ensured that civil society voices are heard in national coordination bodies, which enables them to alert policy makers on gaps at implementation level and request them to address the issues, for example evidence on stockouts of tests or treatment medicines or on suspension of HCV screening in public facilities during the COVID-19 pandemic. FOAESP also facilitated the establishment of a multi-party Parliamentary Front to lobby on increasing access to HIV and HCV prevention, testing and treatment services for all populations, including marginalised groups. The Front has prepared a law authorising the federal MoH to automatically issue CLs in case of public health emergencies, which is awaiting discussion and approval in the parliamentary plenary. Once this law is approved it is hoped that the MoH will use it to issue CL for DAAs. Following grant advocacy, Brazil also approved a law to institutionalise awareness raising and screening campaigns by FMOH and implementing States, targeting key and vulnerable populations.
- In Colombia, advocacy by local partner IFARMA convinced the government that HCV is a public health issue, that the MoH should also centrally procure DAAs for populations covered by the subsidised health insurance regime targeting the informal sector to achieve lower prices, and that the subsidised insurance regime should include persons without any income, including key and vulnerable populations. In 2019, MoH approved these new policies and is currently implementing them, which is expected to greatly improve the access of poor and marginalised populations to HCV testing and treatment. Through these initiatives, stakeholders noted that

awareness among PLHCV in these countries has improved significantly, and that populations are more empowered to demand HCV testing and treatment services going forward.

At the national and state policy level, Coalition PLUS country partners have played an important role in supporting updates to national elimination policies and guidelines, including through participation on HCV steering committees. Key examples of this include:

- In Malaysia, MAC has been a participating member of the steering committee in the **development of the 2020 Clinical Practice Guidelines**. As a result of MAC advocacy, the guidelines: i) enforce notification of HCV diagnoses to District Health Offices; ii) recommend screening for key populations (including PWID and prisoners) and outreach testing; and iii) enforce the provision of DAAs to those diagnosed within a year; and iv) describe treatment procedures for those co-infected with HIV/HCV. MAC also contributed to the development of the 2019 National Strategic Plan. MAC and MTAAG have also been important in piloting projects related to supporting prison populations have access to HCV services.
- In Manipur in India, CoNE, with support from TreatAsia developed **state-level HCV Standard Operating Procedures (SOP)** which are more detailed and extensive than the National Viral Hepatitis Control Programme (NVHCP) guidelines and include specific testing strategies for key populations. CoNE advocated for the adoption of the SOPs, which have been approved by the State Government and are only awaiting to become state law. In practice, however, stakeholders noted that the SOPs are already being used and that the Government has requested CoNE to undertake mobile testing and screening camps on its behalf. Furthermore, CoNE is the community member representing the voice of the communities on the state level NVHCP Steering Committee, which provide an additional advocacy platform for CoNE to engage with policy makers and advocate for increased roll-out of the state NVHCP.
- In Colombia, IFARMA lobbied for and contributed to the development of an **integrated HIV and HCV strategic plan** and of HCV testing and treatment guidelines. It also developed training programmes for health professionals on HCV screening in preparation for scale up by government of rapid testing, which is currently under consideration by the MoH.
- In Brazil, FOAESP contributed to the public consultations on the updating of national HCV screening and treatment guidelines. Lobbying by FOAESP has furthermore contributed to the transfer of DAAs into the strategic component of pharmaceutical assistance, which allowed to centralize different competences around procurement and supply **of HCV treatment** through the federal MoH. This in turn has contributed to empowering the federal government to negotiate procurement prices and have better control and monitoring of distribution of commodities across states. Advocacy efforts by FOAESP and partners also led to the approval of a law institutionalising an annual Hepatitis awareness raising month.
- In Morocco, ALCS developed an **HCV investment case** which was instrumental in demonstrating to government and health sectors stakeholders the economic impact of not scaling up HCV testing and treatment.¹³¹ This reportedly convinced government to update its national HCV elimination plan, establish a network of regional HCV treatment and care centres, prepare procurement orders for DAAs, and simplify the HCV algorithm.

Despite some progress, wider rollout of HCV services has not been fully implemented across any of the countries. Progress between countries has varied considerably, with implementation of services being further along in Malaysia and India. But even for these countries, stakeholders noted that considerable momentum is needed to ensure these countries are truly on the path towards HCV elimination. For example:

- In Malaysia, consultees noted that a number of key population groups have still not been adequately addressed by the programme, particularly MSM, prisoners and trans-gender populations. Migrants and refugees have also

¹³¹ Hecht R, Kaddar M, Resch S, et al. Morocco investment case for hepatitis C: using analysis to drive the translation of political commitment to action. *Journal of Global Health Reports*. Vol. 3 2019.




not been adequately covered by HCV services to date, with many stakeholders noted could be potentially high-risk groups. In addition, the government has so far not been able to commit to its National Strategic Plan budget targets of US\$50 million being allocated to testing and treating hepatitis over the period 2019-23.¹³²

- In India, implementation of HCV services varies considerably by state. Although the advocacy and community awareness work done by Unitaids’ investments have been critical in raising awareness of HCV amongst key populations, in increasing the attention to key populations and establishing diagnostic literacy amongst high risk groups, due to the low health seeking behaviour of high risk and vulnerable populations, there is still limited access to testing and treatment in the absence of continuous community outreach and support.

For the other Coalition PLUS countries, key affordability barriers continue to affect the widespread rollout of HCV services, particularly in Colombia and Brazil. In Morocco, the key challenges faced have been in maintaining political commitment for HCV services, with the government cancelling several DAA procurement orders resulting in no DAAs being available in public facilities and therefore HCV treatment not having been rolled out by MoH. In addition, local partners in Morocco have had to continuously restart advocacy work with new senior government officials due to high MoH staff turnover, which has ultimately meant that progress in rollout of HCV services has not been significant for a number of years.

Progress remains fragile in many instances, and has been severely hampered by the COVID-19 pandemic. Going forward government commitment to addressing HCV will be essential in order for any of the countries to achieve WHO elimination targets. In all the Coalition PLUS countries, the implementation of activities has been halted or significantly scaled back as a result of the COVID-19 pandemic. While Coalition PLUS grantees have played an important role across countries in ensuring that PLHCV can continue to access treatment services, there was a clear agreement that COVID-19 has set back the rollout of many programmes, given that resources such as testing capacity and staff have been shifted in many countries to tackling the pandemic. In some countries such as Malaysia, stakeholders noted that the HCV programme is likely to continue long-term given the commitment from government to address it. But in other countries who face several barriers to wider adoption, it is unclear whether HCV will be prioritised ahead of other things, given the further limitations that countries are likely to face given COVID-19’s economic impact. This highlights that despite the efforts of Coalition PLUS and its partners, wider adoption going forward will depend on a range of factors that have been made even more challenging.

6.3. SCALABILITY AND TRANSITION

Key findings	Strength of evidence
The critical challenges to the scalability of national HCV responses are partly related to high prices of treatment, which means that governments cannot afford to expand treatment services to the scale required to address the WHO 2030 elimination targets.	
In addition to the challenges related to affordability, actual rollout across almost all Coalition PLUS countries needs to be scaled up significantly in order for countries to move towards elimination, which will require political commitment from governments to do so in the absence of large-scale donor funding.	
There are clear examples of where the activities under the grant have been or will be transitioned. That said, stakeholders highlighted that many key advocacy-related activities will be scaled back following the closure of the grant.	

The critical challenges to the scalability of national HCV responses are partly related to high prices of treatment, which means that governments cannot afford to expand treatment services to the scale required to address the WHO 2030 elimination targets. This has indirect consequences for other activities; stakeholders

¹³² Source: Coalition PLUS M&E data.

noted that many countries are reluctant to expand screening services without sufficient capacity to treat those that test positive for HCV. Specific examples of outstanding challenges limiting scale-up include:

- In Malaysia, the failure to renew the CL for SOF, which expired in October 2020, presents a major obstacle to the continued progress of the HCV response. Stakeholders expect the cost per SOF/DCV treatment under the VL to increase to US\$700 in line with other countries in the region with access to the VL, compared to the US\$300 under the CL.
- In India, despite free testing and treatment under the NVHCP, access to HCV care remains low among KPs and the general population, due to low awareness and low health-seeking behaviour.
- In Brazil, the government faces the challenges of high drug costs and an under-resourced national health service. As such, little can be done to expand testing and treatment services, unless external funding is mobilised to bear the treatment costs.
- In Colombia, treatment remains expensive, and the health system has a fragmented financing strategy. In conjunction with strong lobbying pressure from the pharmaceutical industry, the government is hesitant to authorise the use of generics for the treatment of HCV.
- In Morocco, MoH malpractice cases have made the government reluctant to issue medicine procurement orders representing large sums of money. As a result, the MoH has preferred not to publicly launch its current HCV elimination strategy, which would result in it being held accountable for not procuring the DAAs required to reach the elimination targets, and has cancelled two previously prepared orders for procuring DAAs for the public sectors.

In addition to the challenges related to affordability, actual rollout across almost all Coalition PLUS countries needs to be scaled up significantly in order for countries to move towards elimination, which will require political commitment from governments to do so in the absence of large-scale external funding. A key barrier across countries that is likely to remain is level of funding required to rollout HCV elimination programmes, which will largely be determined by the level of political commitment by government to reduce the prevalence and incidence of HCV in these countries. For this commitment to be realised, continued advocacy will be needed beyond the current Unitaidd grant. In particular, CSOs and international organisations will need to demonstrate to governments the issues HCV are creating, and that elimination can be achieved provided that effective and targeted rollout of HCV programmes is carried out. In light of the COVID-19 pandemic, it is unclear to what extent governments will be committed to achieving this within their limited health budgets, and as such there are clear risks that countries will not scale-up their programmes going forward, particularly those where treatment remains unaffordable. The findings from the country case studies indicate that Brazil, India and Malaysia have made some budgetary commitments to support continued roll-out of their HCV programmes.¹³³

There are clear examples of where the activities under the grant have been or will be transitioned as part of the project.¹³⁴ Key examples of how activities will be continued going forward include:

- In Malaysia, Coalition PLUS are collaborating with the Global Fund and MAC to design a protocol for a community care model for chem-sexers, defined as gay and bisexual men who use specific drugs in sexual contexts. After the close of the grant, the Global Fund will take over Coalition PLUS' activities in this project. In addition, MAC's work under the TEMAN project that has supported prison populations with risk-reduction activities related to

¹³³ In line with Unitaidd's KPI 3.1, three (Brazil, India and Malaysia) out five project countries have made some budgetary commitments.


¹³⁴ Due to the unavailability of data, it is not possible to calculate the number of additional people benefitting, as per Unitaidd's KPI 3.2.

contacting HCV, is expected to be taken over by the MoH, with a proposed investment of US\$1.7 million, which is currently awaiting approval.

- In India, we understand that CoNE has applied for funding to a pharmaceutical company to enable it to continue its advocacy, awareness raising and community mobilisation work with a decision expected in the coming months.
- In Brazil and Colombia, the capacity of the national partners FOAESP and IFARMA has been strengthened in terms of technical expertise on HCV, and HCV has also become part of their mandates. Therefore, these partners will likely be interested and able to continue to lobby their governments to plan and support the national HCV response after finalisation of the grant. Although, IFARMA and FOAESP have not yet been able to mobilise additional resources, they are pursuing various avenues in order to continue their advocacy efforts: for example, FOAESP adheres to Coalition PLUS lusophone network which might ensure some continuity in their HCV-related work; whilst IFARMA plans to participate in a call for proposal by the Global Fund on HIV and HCV co-infection and have already applied for a United National Democracy Fund grant as well as a for a grant by the national Ministry of Science.
- In Morocco, while ALCS will not receive programme funding for HCV advocacy after finalisation of the grant, it is a well-established NGO with capacity to mobilise resources, including from the government and external donors. It is therefore expected that ALCS will be able to sustain a reasonable level of advocacy on HCV at central level following the grant end, although the level may reduce as ALCS programme staff are allocated back to its core business of the HIV response.

However, stakeholders highlighted that many key advocacy-related activities will be scaled back following the closure of the grant. Despite these activities transitioning, stakeholders at the global and country level recognised that the extent to which CSOs will be able to continue their activities at the level implemented during the grant, let alone scale up these activities, is likely to be limited. This is particularly concerning for countries such as Colombia, Brazil and Morocco, where considerable results have yet to materialise in terms of rolling out sustainable HCV treatment programmes. In all countries, CSOs have played a critical role in connecting HCV communities with the national health services, and without sustained funding it is likely that such services will either have to be reduced, or resources reallocated within these organisations from other priority areas.

6.4. IMPACT¹³⁵

Key findings	Strength of evidence
<p>There are clear examples of Coalition PLUS's impact through the grant, in particular: (i) the role played by Coalition PLUS and its partners in enabling key populations, particularly PWID, in accessing HCV testing and treatment services in project countries; and (ii) in facilitating more affordable treatment. It should be noted that the evaluation presents the impact of the Coalition PLUS grant qualitatively, as opposed to through a robust impact modelling assessment.</p>	<p>Qualitative evidence only</p>
<p>The Coalition PLUS grant has clearly had an equity enhancing impact in terms of offering communities and CSOs in-country a voice to advocate for improved access to testing and treatment of HCV, which is likely to have a long-term effect in the countries where the grant has operated.</p>	

There are clear examples of how the Coalition PLUS grant has been able to achieve impact through the grant, both in terms of public health and economic impacts:

¹³⁵ As discussed between CEPA and Unitaaid, given the nature of the Coalition PLUS grant it has not been possible to accurately calculate quantitative impacts in terms of public health and economic impacts.

- **Public health impact:** Across the different countries, through their outreach work and pilot projects, Coalition PLUS' in-country partners have directly linked individuals living with HCV to healthcare services. For example, in India, stakeholders have noted that CoNE has played an important role in identifying the high prevalence of HCV among PWID in Manipur, and also helped identify the key issues that were inhibiting PWID from accessing treatment. Much of this work was carried out during the COVID-19 pandemic when access to healthcare services across countries was limited. Stakeholders have highlighted that without these services, the patients would not have been treated. In addition to these direct public health impact, in-country stakeholders in Malaysia highlighted that Coalition PLUS partners ensured that treatment could be expanded in the country with the cumulative number of people treated increasing from 331 in 2017 to 7,000 in 2020. While all of this cannot be attributed solely to the grantees, these partners had a clear contributory role in ensuring that these benefits were realised.
- **Economic impact:** As with public health impacts, economic impacts of Coalition PLUS' grant are also difficult to quantitatively measure. That said, the example from Malaysia of the issuance of the CL has ultimately led to the country being able to obtain treatments at more affordable prices. Such prices are lower than both the price being offered for SOF compared to previously, as well as the typical cost of Peg-IFN treatment, which in 2015 was US\$9,500 on average for a full course globally in 2013.¹³⁶ Based on expenditure data in Malaysia, treatment expenditure fell from more than US\$3.7 million in 2013 to less than US\$2 million in 2019, despite treating more than 3,000 patients in 2019 compared to less than 300 in 2013. This shows that when considering the counterfactual for both of these, the CL is likely to have resulted in significant government cost savings.¹³⁷ The exact extent to which this was achieved would be dependent on assumptions on how many patients the government would have treated in the absence of the CL, which is difficult to fully determine, though it is likely that less budget would have been allocated to the programme that what was the case. At beneficiary level, the decentralisation and simplification of HCV testing and treatment implemented by governments following advocacy by Coalition PLUS partners are likely to have generated savings for clients in terms of transport and opportunity costs.
- **Benefits to marginalised populations:** Stakeholders were unanimous in their view that Coalition PLUS and its in-country partners have been critical for ensuring that marginalised groups have been targeted for testing and treatment services, and noted that a number of the pilot programmes run in countries were critical for linking these groups to care. In particular, the grant has targeted PWID, prisoners and MSM as part of its work, which are key population groups that were previously overlooked on HCV programmes in a number of countries.
- **Strategic benefits and positive externalities:** As noted previously, a key value-add of the grant has been the role it has played in empowering communities and CSOs to advocate for greater coverage of HCV testing and treatment, with many noting that these partnerships are likely to be sustained after the end of the grant. A key example of this is in Malaysia, where the strong partnership created among CSOs in the country has been key to the achievements seen to date. In addition, Unitaids' support for Coalition PLUS has enabled the organisation to establish its presence in the HCV space, enabling it and its members to advocate globally for more inclusive and widespread HCV programmes. Contributions the Coalition PLUS grant has also helped build community networks and CSO capacity across different countries, enabling them to be advocate for improved HCV testing and treatment at both national and global levels. In some contexts such as Malaysia, the Coalition PLUS grant was also noted as being an important contributor to local CSOs being included as part of key in-country mechanisms such as the Global Fund CCM, where partners have and stated they will continue to advocate for greater HCV funding and integration with other disease responses as part of this.

¹³⁶ Unitaids (2013), Hepatitis C Medicines and Diagnostics in the context of HIV/HCV Co-Infection: a scoping report.

¹³⁷ Chan et al. (2019), Treatment coverage and drug expenditure in Hepatitis C patients from 2013-2019: A journey of improving treatment accessibility in Malaysia through government-led initiatives.

6.5. COUNTRY CASE STUDIES

This section summarises the findings from the detailed case studies carried out in India and Malaysia of the Coalition PLUS grant, as well as a summary of how access barriers have been addressed for the high-level case studies for Brazil, Colombia and Morocco.

Malaysia

The Coalition PLUS grant in Malaysia supported the work of three partners:

- **Third World Network (TWN)**, an international research and advocacy organisation. Within the project, TWN's main activity was advocacy to policymakers and implementers on issues regarding access, IP and trade. Since 2018, TWN has been funded directly by Unitaaid to address wider IP-related issues across all Unitaaid's diseases areas and in multiple countries. TWN has maintained close collaboration with the Coalition PLUS grantees in Malaysia during the implementation of this grant.¹³⁸
- **Malaysian AIDS Council (MAC)**, an umbrella organisation that supports and coordinates the efforts of non-governmental and other organisations working on public health issues. Within the project, their work focused on raising awareness, diagnosis, the support of building of community capacity, and the opening of dialogue with parliamentarians. Stakeholders highlighted their strong working relationship with the MoH as a key stakeholder for issues on AIDS, HIV and HCV.
- **Positive Malaysian Treatment Access and Advocacy Group (MTAAG+)**, an organisation that advocates national implementation of TRIPS flexibilities for access to generic treatments, and amplifies the voice of KPs through its PLHIV network. Within the project, MTAAG+ were community focused, helping to empower these groups to undertake their own advocacy.

From July 2020, MAC and MTAAG+ also maintained a minimum package of HCV prevention services and therapeutic care for vulnerable populations during the COVID-19 pandemic. In addition, Coalition PLUS have also been supported by **TREAT Asia**, who has been offering support throughout the region for grantees on access to medicine-related issues.

Coalition PLUS selected an appropriate set of project partners which complemented each other's activities. TWN's focus on national drug pricing issues, MAC's focus on government engagement and diagnosis, and MTAAG+'s work on demand generation and the involvement of KPs created a multi-pronged approach to national advocacy.

Coalition PLUS partners engaged with national stakeholders to ensure that activities remained relevant. They conducted biannual roundtable discussions in order to agree activities to be performed. This ensured that activities were targeted at KPs. Examples of this include the projects that screened prison populations run by MTAAG+ and a wider scale screening programme run in prisons implemented by MAC, known as the TEMAN project. HCV issues among PWID were discussed as part of an HCV diagnostics workshop convened by MTAAG+, TAG and FIND in March 2019.¹³⁹

Stakeholders noted the strong relationship between Coalition PLUS partners and state-level government stakeholders, which were critical to the grant's success. Collaboration between the MoH, MAC and TWN has been instrumental in the adoption of the CL for SOF in September 2017, and the training of Family Medicine Specialists to facilitate decentralisation of HCV screening.

¹³⁸ Further details of Unitaaid's direct funding to TWN can be found at: <https://unitaid.org/project/using-trips-flexibilities-to-make-medicines-affordable/#en>

¹³⁹ MTAAG, TAG and FIND (2019), Hepatitis C Virus Diagnostics Advocacy Workshop.

Despite this, some stakeholders noted that some of the advocacy work became irrelevant to the country's needs, particularly the grassroots-level advocacy that continued to advocate to government for more affordable DAAs after the issuance of the CL. This view was not shared by a wide number of stakeholders.

Affordability: The key success in Malaysia has been **the introduction of the CL for SOF in September 2017**, which reduced the cost of treatment by 97.5%, from US\$12,000 to US\$300 per SOF/DCV course.¹⁴⁰ The role of Coalition PLUS partners in this is as follows:

- **Stakeholders argued that TWN played a critical role in the introduction of the licence,** through training, advocacy efforts and education to government departments (including the Ministry of Domestic Trade and Consumer Affairs, as well as the Ministry of Health) on the mis-information from international pharmaceutical companies related to the country's rights under the implementation of the TRIPS Flexibilities and issuing the CL.
- **Coalition PLUS partners campaigned for the introduction of the CL** through media outreach and workshops with the MoH and general public. Visibility was given to the campaign through its appearance on talk shows, the TV and news.
- **Coalition PLUS partners continued to support the government after the licence introduction,** in face of pressure from Gilead and the American Embassy, through public declarations of support.

Overall, the conditions in Malaysia to facilitate the introduction of the CL for SOF were good, even in the counterfactual that the Unitaid portfolio did not act. Thus, the work the **Unitaid portfolio is likely to have had a catalysing effect in speeding up the introduction of the CL for SOF.**

Demand & adoption: Coalition PLUS partners facilitated increased demand and adoption in the following ways:

- **As a member of the Steering Committee, MAC contributed to the development of the 2020 Clinical Practice Guidelines.** As a result of MAC advocacy, the guidelines: i) enforce notification of HCV diagnoses to District Health Offices; ii) recommend screening for key populations (including PWID and prisoners) and outreach testing; and iii) enforce the provision of DAAs to those diagnosed within a year; and iv) describe treatment procedures for those co-infected with HIV/HCV.
- **The Unitaid grantees have reshaped the HCV space in Malaysia to give civil society a more significant voice.** The HCV programme was once champion-led, heavily influenced by key hepatologists. This meant that HCV care was typically reliant on experts, and thus heavily centralised. However, through FIND's exemplification of the benefits of decentralisation, and advocacy work from Coalition PLUS and its partners, the programme increasingly listens to community voices, leading to a more decentralised, targeted HCV approach.
- **The Unitaid grantees have taken measures to empower grassroots organisations and community representatives.** For example, MTAAG+ and FIND provided a platform for healthcare workers at KKs, as well as representatives of the PWID, MSM, transgender and prisoner communities, to present in their national diagnostics workshop in 2019. This workshop was attended by CSOs, members of the Human Rights Commission and the MoH.

In addition, Coalition PLUS partners undertook a direct role in the supply of HCV treatment during the COVID-19 pandemic, to mitigate the effects this may otherwise have on LTFU and screening. MAC and MTAAG+ ensured the continued provision of HCV treatment, as well as the provision of prevention equipment and PPE.

Transition and scale-up: Coalition PLUS have secured transition of the following activities, to facilitate scale-up going forward:

- In 2018, Coalition PLUS assisted TWN in its successful application to Unitaid for a grant for an IP project, ensuring that they can continue their advocacy work after the Coalition PLUS grant has finalised.

¹⁴⁰ Coalition PLUS (2018), HIV-HCV Drug Affordability Project: 2018 Annual Report.

- The Coalition PLUS team have created a strong network of partners, including MAC, MTAAG+, FIND, TWN and DNDi. Coordination between this network will facilitate collaborative action on HCV in the future, leading to greater, sustainable change in the HCV space.
- The TEMAN project is planned to be taken over by the MoH once the Coalition PLUS project has ended. They have proposed an investment of US\$1.7m to the government, and is awaiting approval.
- Coalition PLUS are collaborating with the Global Fund and MAC to design a protocol for a community care model for chem-sexers, defined as gay and bisexual men who use specific drugs in sexual contexts. After the close of the grant, the Global Fund will take over Coalition PLUS' activities in this project.

However, following the conclusion of the grant, it is likely that the work of the CSOs will be reduced in the absence of alternative funding, which many stakeholders noted as being a key future risk to HCV remaining a priority for the government and being scaled up in future.

India

The Coalition PLUS grant in India supported the work of two partners on the ground:

- **The Delhi Network of Positive People (DNP+)** in New Delhi is a network of PLHIV which supports access to HIV and HCV treatment and care. The main focus of their work has been: advocacy with policy makers at the state level to support the delivery of HCV testing and treatment, and awareness raising on HCV and empowerment of PWID to access HCV services and care, amongst other.
- **Community Network for Empowerment (CoNE)** in Manipur is a network of 11 community-based organizations who support PWID. The main activities under the Coalition PLUS grant since 2017 have been: awareness raising of HCV amongst PWID; negotiations with the private sector to reduce the out-of-pocket cost of HCV testing and treatment; HCV advocacy at the state government level to support the roll-out of the state NVHCP, including to support development of state-level policies on HCV; HCV screening camps amongst PWID and support for PWID to access testing and treatment under the NVHCP; amongst others.

The Coalition PLUS projects in India were also supported by **TreatAsia**, a network of organisations to support the delivery of HIV and HCV treatment across Asia, who provided technical assistance to both DNP+ and CoNE in developing campaigns throughout the implementation of the grant.

Coalition PLUS started working in India in 2017, prior to the launch of the NVHCP in July 2018, at a time when the focus on HCV was intensifying at the national level. The design of the Coalition PLUS grants in India was found to be appropriate given that they aimed to support advocacy activities at a crucial time when the NVHCP was being launched and sought to mobilise communities to advocate for the implementation of the NVHCP. In terms of targeting of the interventions, the Coalition PLUS programme focussed on high-risk and vulnerable populations, who have some of the greatest needs for HCV testing and treatment: In Manipur the focus of the Coalition PLUS project has been on reaching PWID and their partners with testing and treatment of HCV, as well as prison inmates in Manipur. In New Delhi, DNP+ also worked to support PWID with HCV advocacy and access to HCV testing and treatment.

CoNE and DNP+ built strong relationships with state-level government stakeholders which has been critical to enable the smooth implementation of the projects. In Manipur, CoNE's collaboration with the state-level government was very strong and CoNE has collaborated closely with the government on various issues, from the training of health care workers on HCV to the organisation of screening camps for PWID in hard to reach areas.

Affordability: Given that affordability of DAAs has been largely achieved in India, the contribution of the Coalition PLUS grant to affordability has been limited since 2019. However, stakeholders have noted that in Manipur CoNE was able to organize meetings with the pharmaceutical industry and with local private sector labs in Manipur to negotiate the price of both DAAs and VL testing in the private sector: for the DAAs, the price of a 12-week course of SOF/DCV was lowered from US\$690 to US\$170 and the cost of HCV RNA confirmatory test was lowered from US\$145/test to US\$28/test. CoNE has in place an MoU with these private sector suppliers and these prices are still applicable. Even though from July 2019, when the NVHCP started being rolled out in Manipur, patients are generally linked to NVHCP for free testing and treatment, in some cases whereby patients do not want to be tested and treated under the NVHCP they can pay out-of-pocket and access these more affordable prices enabled through CoNE efforts.

Demand and adoption: The Coalition PLUS grant has significantly contributed to improving the demand and adoption of HCV testing, treatment and care; in particular the grants have:

- **Advocated for the availability of testing and treatment at designated public health facilities to enable roll-out of the NVHCP.** In Manipur, CoNE’s advocacy with the state level government has been successful in designating two Model Treatment Centres, which is an important achievement to enable the delivery of HCV services given the high burden of HCV in the state. In New Delhi the order of the high-court on the Public Interest Litigation case filed by DNP+ instructed the state government of New Delhi to provide HCV testing and treatment in 10 hospitals. The court case was a powerful advocacy tool used by DNP+ to achieve greater testing and treatment roll-out; however, in practice, only two hospitals in New Delhi were providing HCV services before COVID-19.
- **Mobilised and empowered high-risk groups to enable them to access HCV services by linking them to the NVHCP.** DNP+ and CoNE have been instrumental in enabling key populations, especially PWID, in accessing testing, treatment and care under the NVHCP. To support demand and adoption of services, DNP+ has helped PWID reach the HCV unit at MTC in New Delhi and supported them throughout all process of being screened, VL confirmation testing, treatment initiation and adherence, and complete SVR testing. Similarly, in Manipur CoNE has played an important role in increasing demand and adoption for HCV services by PWID; importantly, the state government accepts the referral of HCV screening done by CoNE.¹⁴¹ CoNE also supports PWID patients who are referred to MTC throughout the whole process of testing and treatment to minimise loss to follow-up. One stakeholder described the work of these organizations as “*enabling the state NVHCP to function*”. Given the low levels of awareness of HCV amongst health care workers, CoNE also worked to reduce stigma and discrimination towards patients with HCV by developing a booklet on HCV to train health care workers in hospitals and organizing regular trainings of health care workers.
- **In Manipur, CoNE with support from TreatAsia, developed and advocated for the adoption of the state-level HCV Standard Operating Procedures (SOP) which are more detailed and extensive than the NVHCP guidelines and include specific testing strategies for key populations.** The SOPs also have a stronger focus on key populations especially PWID, in line with the burden of the HCV epidemic in Manipur. In particular, CoNE advocated for the inclusion of mobile testing and screening camps as testing strategies in the SOPs, which is critical to reach key vulnerable populations such as PWID. CoNE supported the elaboration of the SOPs with technical assistance from TreatAsia under the Coalition PLUS grant.
- **CoNE and DNP, through the support of Coalition PLUS grant successfully demonstrated the feasibility of testing and treatment in prisons in New Delhi and Manipur.** CoNE undertook a pilot project to screen inmates in Manipur’s central jail. Although prisoners are included as target populations in the NVHCP guidelines, in practice they were not being actively tested. In Manipur this has now changed thanks to CoNE’s pilot project and related advocacy.

Furthermore, the earlier CEPA review of the Coalition PLUS granted noted that CoNE and DNP+ had also contributed to the development of the National Action Plan by ensuring it reflected the community voice as well as encouraging the inclusion of the provisions for vulnerable populations.

Transition and scale-up: the advocacy work of CoNE and DNP+ will continue, although it is unclear whether it will need to be scaled-back in the absence of further funding. CoNE has applied for funding to a pharmaceutical company to enable it to continue its advocacy, awareness raising and community mobilisation work with a decision expected in the coming months.

High-level case studies

For the high-level case studies on Brazil, Colombia and Morocco, we have focused our assessment on progress made in these countries against the access barriers, which is described in the table below.

¹⁴¹ This means that if a PWID doesn’t want to go to hospital for HCV screening but approaches CoNE instead, CoNE will do screening of HCV (using kits donated by FIND project leftovers) and the test result is accepted by the state government as the basis for the VL test.

Table 6.4: Overview of how Coalition PLUS countries addressed key access barriers

Access barrier	Country evidence
Affordability	<p>In Brazil, advocacy by Coalition PLUS local partner FOAESP and other in-country partners has helped empower the federal MoH to negotiate with pharmaceutical companies to lower the costs of diagnostics and treatment. MoH was also convinced to shift to centralised procurement of tests and treatment to public tenders open to drug manufacturers, which has helped reduce the prices of DAAs procured. FOAESP facilitated the establishment of a multi-party parliamentary committee to push for the development of a law allowing for government to issue a CL automatically when a public health emergency is declared. The law is awaiting approval. The COVID-19 pandemic has reportedly facilitated convincing stakeholders to be more flexible on the granting of CL for public health emergencies and this is expected to translate into the Parliament accepting the proposed CL law once it is tabled.</p>
	<p>In Colombia, advocacy by Coalition PLUS local partner IFARMA contributed to convincing the government and insurance providers to include key and vulnerable populations under the subsidised health insurance regime, which will enable these groups to access free HCV prevention and treatment services. Advocacy by IFARMA and other in-country partners also convinced government to centralise procurement of HCV diagnostics and treatment for both the contributory and the subsidised health insurance schemes, and to procure these via the PAHO Strategic Fund, which has resulted in lower procurement prices for DAAs. IFARMA advocated for the government to approve the issuing of CL for HCV medicines, so that the MoH can procure generic DAAs to further reduce procurement prices. However, this measure has not yet been approved by government and resistance against this remains high as the government is following the US health system model and lobbying by pharmaceutical companies remains strong.</p>
	<p>In Morocco, HCV prevention and testing services are free of charge for the users in the national health service. Treatment however is not yet available in the public sector as the government has so far not purchased DAAs for use in public health facilities. Advocacy by ALCS resulted in the MoH deciding to integrate their HCV response with the national HIV programme, generating economies of scale. Project advocacy convinced the government to negotiate with pharmaceutical companies to achieve lower prices. MoH has been procuring HCV tests for use in public health facilities and is reportedly able to afford the procurement of DAAs sufficient to meet the annual targets set in the HCV elimination plan. However, political instability and malpractices resulted in the MoH so far cancelling the two previous DAA orders. A new DAA procurement order was prepared last year by the national programme and partners and is currently awaiting approval by MoH.</p>
Demand and adoption	<p>In Brazil, updated national policies and guidelines are in place but implementation is slow. Through advocacy, FOAESP contributed to the public consultations for the updating of the national testing and treatment guidelines. Approval by government of the inclusion of HCV into the list of essential medicines and of procurement of HCV commodities via public tenders to drug manufacturers contributed to greater transparency on procurement and empowered MoH in its efforts to reduce procurement prices. Advocacy by FOAESP and partners convinced MoH to approve decentralisation of HCV treatment to primary care level, although the rollout of this decentralisation – particularly the training of health professionals on HCV treatment - has not yet started. Project partners have lobbied the government to adhere to testing and treatment targets set in the elimination plan and have taken the government to court when MoH performance was insufficient. So far, particularly since COVID-19 and due to political instability, implementation is considered to lag behind, and stakeholders consider that the government could do much more to scale up the response. FOAESP and partners advocacy resulted in MoH authorising the use of rapid tests and developing and approving guidelines and training programmes for rapid testing. However, it is yet unclear if the MoH will give the green light to scaling up testing in 2021.</p>
	<p>In Colombia, implementation of the updated national policies and guidelines is underway but scale up has not yet started. IFARMA's advocacy contributed to the MoH developing a new integrated HIV-HCV strategic plan and new guidelines for the decentralisation of HCV treatment</p>

Access barrier	Country evidence
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to GPs (still under consideration by the MoH and yet to be approved). IFARMA led on the development of a virtual training course for GPs on HCV treatment and on reaching out to communities, including underserved communities, and the course is currently under consideration by MoH. Advocacy resulted in MoH authorising the use of rapid tests in the country, and authorising CSOs to conduct rapid testing amongst hard-to-reach populations. The Global Fund is supporting a community HCV testing pilot, the results of which are supposed to feed into procedures and guidelines for community testing currently under development.

In **Morocco**, ALCS generated evidence on HCV infections amongst KPs in Morocco and Coalition PLUS produced an investment case for the HCV response, resulting in convincing the government to develop its integrated HIV-HCV response plan and increasing commitment to investing in the expansion of the HCV response. MoH has designated ALCS as the sole CSO provider authorised to conduct community screening for HCV. The national HCV testing and treatment guidelines are currently being updated. ALCS has developed a training programme for community HCV screening and is currently rolling out the training to ALCS staff. Regional authorities contracted ALCS to train prison employees on HCV screening and treatment of inmates, and have committed to procuring DAAs once HCV positive cases are identified. However, ALCS cannot scale up community screening in its facilities and outreach services as long as no HCV treatment medicines are available in public health facilities. ALCS lobbying for decentralisation and simplification of HCV treatment resulted in the MoH establishing additional regional referral centres for HCV care and treatment and approving simplification of diagnostics. Procurement of DAAs for the public health services is awaiting the approval of MoH. Previous orders were cancelled as the government was reluctant to issue medicine procurement orders representing large sums of money amidst political instability and malpractices in the MoH.

6.6. CONCLUSIONS

Overall, the Coalition PLUS grant has been vital for giving communities and CSOs a voice for advocating for improved access to HCV treatment in the countries that have been supported. The support Coalition PLUS and grantees have given to these countries has been essential for ensuring that national programmes have considered the needs of key and marginalised populations, particularly PWID and prisoners, where the work of in-country partners through its pilot programmes as well as direct engagements with government has ensured these groups are represented in government elimination plans.

The support given in Malaysia is a notable example of where, in combination with other actors and a committed government, the work of the grantees has been essential for overcoming affordability barriers and unlocking the programme that, in the absence of Unitaids' ongoing support, may have taken significantly longer to become a reality.

While some progress has been made in all countries, this has clearly not been uniform, and a number of outstanding challenges remain. These include:

- Ongoing affordability challenges of DAAs, which vary across different countries
- The need for more widespread implementation of HCV programmes across countries, with some countries within the portfolio still being in their infancy in terms of implementation, while in others some aspects related to implementation, such as reducing turnaround times for test results, as well as enabling access to HCV services, still need to be overcome.

Across all countries, stakeholders were almost unanimous in their view that significant progress has been made towards the objectives of the grant. However, they stressed that the objectives have not yet been fully achieved, with the need for continued advocacy to encourage further government policy and financing for HCV programmes.



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