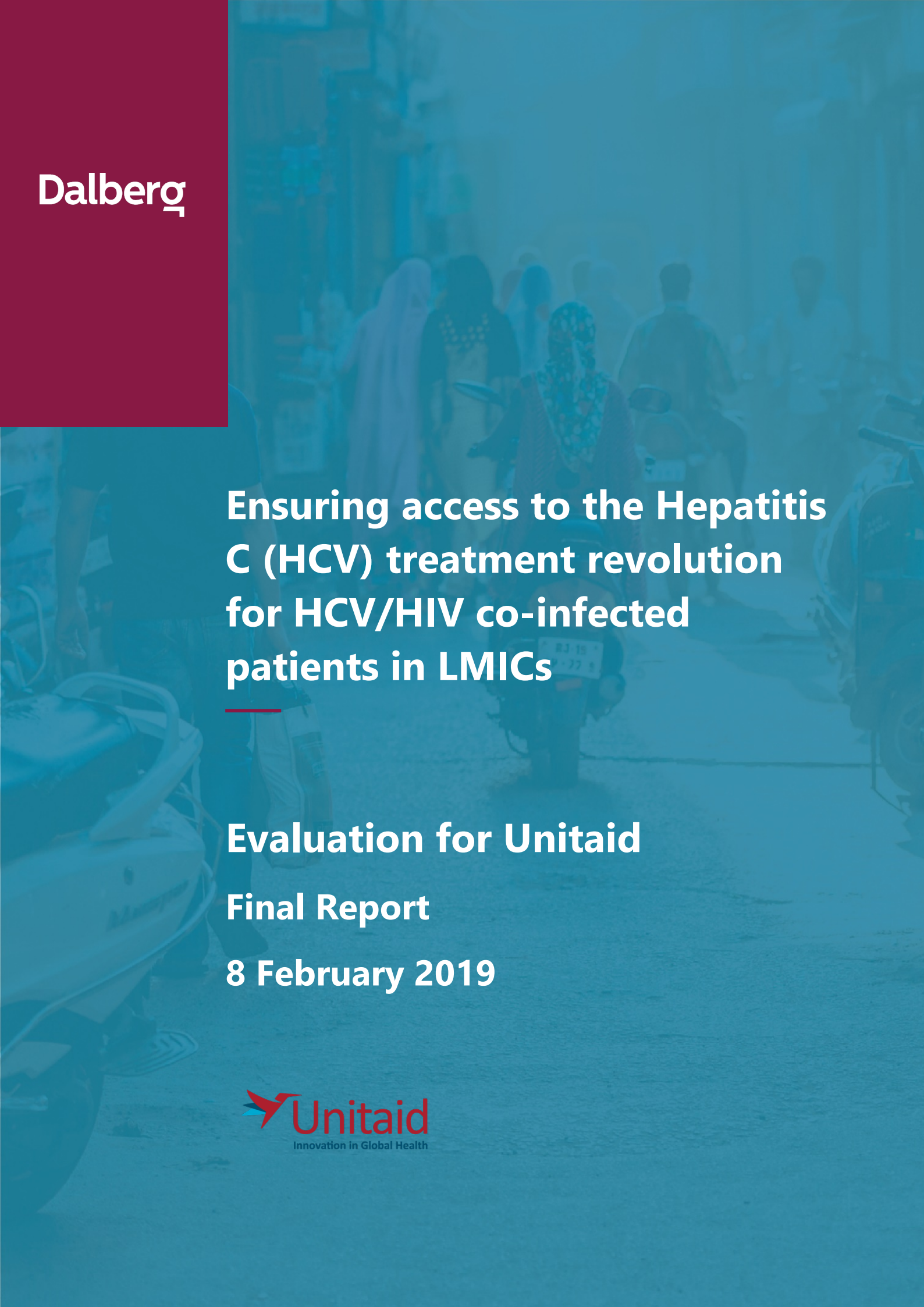


Dalberg

Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs

Evaluation for Unitaid

Final Report

8 February 2019

Unitaid
Innovation in Global Health

EXECUTIVE SUMMARY

Context

In 2014, Unitaid awarded Médecins sans Frontières (MSF) a US$15M grant to improve access to Hepatitis C Virus (HCV) diagnosis and treatment in Low and Middle-Income Countries (LMICs). MSF delivered several activities, including providing clinical care to HIV-HCV co-infected patients, developing and testing simplified models for this care, gathering and sharing evidence on treatment outcomes, and conducting local and global advocacy. The grant was implemented across seven countries: Cambodia, India, Kenya, Mozambique, Myanmar, South Africa, and Uganda. It was drawn to a close in June 2018.

The grant was one of the very first efforts to demonstrate the feasibility of HCV care in low-resource settings. In 2014, new Direct-Acting Antivirals (DAAs) remained too expensive for LMICs, and the existing HCV care protocols were too complex and burdensome for the health systems of these countries. The grant was designed to overcome three critical access barriers: the affordability of diagnosis and treatment, the supply and delivery of simplified care models, and the demand and adoption of these new models. In 2016, the grant's objective evolved to include a greater emphasis on the scalability of HCV care through national health systems, reflecting a shift in the Unitaid strategy.

This evaluation assessed the causal pathways by which the grant intended to reach its desired impacts. The report assesses the grant's progress against each of the three critical access barriers (as defined above), followed by an assessment of the grant's overall implementation and impact. Finally, there are a number of recommendations emerging from the evaluation findings.

Evaluation against critical access barriers

Barrier 1: Affordability

The grant aimed to ensure that DAAs became affordable enough for LMIC governments to scale procurement without causing unreasonable financial burden. To overcome this barrier, the MSF Access Campaign was active in two main areas: increasing price transparency and encouraging the production of affordable generic drugs. Overall, MSF (through the Access Campaign) had a moderate effect on the affordability of DAAs. However, current DAA prices remain unaffordable for most LMIC governments without funding from international donors.

MSF publicly announced their price of US$120 for Sofosbuvir/daclatasvir (sof/dac) to empower others to negotiate similar prices. MSF achieved this price through negotiation and activism led by the Access Campaign, helped significantly by the downward trend in DAA pricing over the last five years. MSF's announcement was the first of its kind, and was praised by other organizations as a signal for the need for greater transparency in the DAA market. Despite the announcement, ***"most countries are still nowhere close to hitting low prices such as $120: they are still paying $600-***

800 despite organizations like MSF attempting to provide market intelligence"[1]. The majority of DAA prices remain protected by non-disclosure agreements and countries are unaware of the lower prices they could access.

To drive affordability, MSF supported generics manufacturers, for instance by encouraging the expansion of existing voluntary licences. It is difficult to establish causality between MSF's work and the growth in generic production. However, MSF's advocacy partners such as Coalition Plus noted the valuable contribution of MSF advocating with governments to carefully assess patent applications related to DAAs. They stated ***"the Access Campaign's contribution was very valuable, they have access to data and evidence from real individuals getting treated which is essential to make the case to the government".***

Barrier 2: Supply and Delivery

The grant sought to develop and introduce simplified and cost-effective diagnosis and treatment methods, to reduce the burden of HCV care on LMIC health systems. In project countries, MSF worked to support DAA registration; field-test near PoC (Point of Care) virology and serology tests; develop effective simplified care models, and transition these capabilities to the local Ministries of Health (MoH). Overall, MSF had a strong effect on demonstrating the feasibility of HCV care in LMICs, and in influencing others through these best practices. However, MSF only made limited progress in integrating these care models into the local health systems in their project countries.

As one of the very first implementors, MSF developed best practices for improving the efficiency of HCV diagnosis and treatment in low resource settings. MSF screened almost 50,000 people across 10 treatment sites, as a way of iteratively testing possible simplifications to the 'full' HCV care model [as used in High Income Countries]. Evidence gathered from these treatment sites demonstrated that cure rates of 85% - 95% (similar treatment outcomes to High Income Countries) can be achieved with far fewer clinic visits and without the need for specialised hepatologists. Elements of the MSF models of care, such as removing genotyping from the diagnosis process, task-shifting treatment to nurses, and reducing clinical monitoring after the treatment, are being adopted and further built on by others. MSF shared these best practices through direct training of in-country actors and indirect knowledge transfer through publications and conferences. While these are not 'discreet care protocols' being adopted wholesale at scale, WHO argued that ***"MSF helped move the needle on simplified models of care globally, reducing steps that might not be necessary"[2].***

Integration of MSF's models into the local health systems of national countries varied by treatment site. The degree to which MSF have been able to hand over activities to the respective MoH depended on their ability and willingness to take up new activities, the availability of domestic funding for diagnostic tools and DAAs, and the extent of existing cooperation between MSF and the local MoH. For example, in Cambodia, MSF transitioned the full screening process to MoH staff at the Kossomak MoH Hospital. However, MSF still run confirmatory diagnostic tests for quality control of the MoH screening. In Manipur, India, MSF work within the Churachandpur District Hospital, but continue to run the full diagnosis and care process independently. Transition plans and timelines are

[1] Interview with CHAI

[2] Interviews with WHO, MPP, PharmAccess. CHAI.

undefined, and overall there is a sense that MSF will remain involved in the roll-out of HCV treatment at least for the medium term.

Barrier 3: Demand and Adoption

Finally, the grant sought to generate and share evidence on HCV care to inform national and international guidelines, and lobby nationally for adoption of HCV care across national health systems. Overall, the evidence generated by MSF made a strong contribution to national and global HCV guidelines, but only limited effect on driving the financing and implementation of HCV care at scale within countries. This is partly due to the fact that launching new national programmes in health within LMICs is a challenging, and lengthy process, typically requiring longer time scales than the grant provided.

MSF played a key role supporting countries to develop national guidelines on HCV, a first essential step towards national roll-out of treatment and care. In Cambodia, Kenya, Manipur (India) and Mozambique, MSF was directly involved in the technical advisory committees writing the national guidelines. In Cambodia, for example, MSF co-authored guidelines for the treatment of co-infected patients with the MoH, and has been a key driving force behind the creations of a Technical Working Group responsible for the development of National Guidelines and a national strategy. Other members of this group noted that ***"MSF brings technical expertise to the working group, as the only organisation with experience implementing HCV care in-country…their important work is helping to push the national strategy".***[3]

MSF also provided key evidence to the 2018 revised WHO HCV Guidelines, which shape HCV care protocols globally. MSF's contribution was particularly valuable in demonstrating the effectiveness of sof/dac on the less-researched HCV genotypes 5 and 6, rendering the sof/dac DAA regime pan-genotypic. This evidence removed the need for costly genotyping tests in LMICs, where other pan-genotypic regimes remain unavailable. While sof/dac is not yet registered in all LMICs, it is more affordable and accessible than other regimes. MSF also provided evidence on their model of care simplifications for the WHO Guidelines, which highlight ways to make HCV care possible in decentralised, low-resource settings. WHO noted that ***"MSF made an integral contribution to the WHO Guidelines in 2018".***

Despite advancing technical know-how and awareness of HCV both nationally and globally, the HCV space lacks a large donor to finance the scale-up of interventions. Although MSF conducted some high profile global advocacy efforts (e.g. writing an open letter to the Global Fund to increase HCV funding), the international financing landscape for HCV remains sparse. The grant activities hence raised some challenging questions concerning the availability of domestic financing as a route to scale for HCV, particularly in resource-constrained LMICs.

Overall Grant Assessment

Grant Implementation

MSF faced expected and unexpected delays throughout the grant which contributed to a large underspend: only US$8.2M of the original US$15M was spent at the end of the grant period. Many of these delays occurred because of a first mover disadvantage faced by MSF within HCV, and

[3] Interview with CHAI about MSF's work in Cambodia.

overcoming these barriers was an integral part of the original objective of the project. Stakeholders agreed that ***"Delivering HCV care in LMICs was just an idea in 2012, Unitaid accepted it as a challenge… they were really taking a risk".*** These implementation hurdles therefore should not detract from the grant's success, recognised by many as pioneering in tackling HCV within LMICs.

Operationally, the different project components could have been more joined up at country level, and between countries. Unitaid's funding was distributed to four MSF Operational Centres (Amsterdam, Geneva, Paris and Brussels), and then to their respective country missions in seven countries, as well as to the MSF Access Campaign and Epicentre. Fundamentally this grant was organised around MSF's organisational structure, rather than fully addressing pre-defined barriers or country-level needs. While some *ad hoc* cooperation did occur between the units of MSF, more strategic alignment could have led to more effective national interventions.

Grant Outcomes

The grant made some progress towards overcoming *all* the access barriers that inhibit the delivery of HCV care at scale: 'affordability', 'supply and delivery' and 'demand and adoption'. Externally, the main success of the grant is considered to be the demonstration that HCV care is possible in low-resource environments. WHO noted that thanks to MSF's work, ***"no one now believes that HCV cannot be treated effectively in LMICs through simplified models, the proof of concept is now clear'.***

The grant made mixed progress in securing the transition and scale-up of grant activities. In most project countries, MSF actively engaged MoH's on HCV, and has been largely successful in putting HCV on their public health agendas. Since the start of the grant, a number of governments including India, Myanmar and Cambodia have committed to launching HCV programmes. However, this progress cannot be exclusively attributed to MSF, and there are still critical challenges in mobilizing the political will and financing necessary to implement these programmes.

The grant's focus on co-infected patients raised some important practical, ethical and strategic questions, raised in several discussions between Unitaid and MSF. MSF found lower-than-expected HIV-HCV co-infection rates: under 1% in African countries, and around 2-3% in Cambodia and Myanmar. The focus on co-infected patients was *perceived* to raise ethical issues regarding not financing treatment for mono-infected HCV patients, and practical issues around re-infection of co-infected patients through mono-HCV-infected partners. Unitaid responded to these challenges by stretching their mandate as far as possible: agreeing to cover the screening of all patients regardless of their HIV status, financing treatment for certain mono-infected groups, and establishing a clear agreement with MSF whereby MSF would cover the cost of treatment of other mono-infected patients identified as part of the project. Despite these efforts, the grant highlighted the limitations of focusing on co-infection as a way to catalyze HCV care in the broader population.

Finally, the grant played an additional catalytic role within MSF, accelerating the development of HCV programmes. Beyond funding, Unitaid's involvement lent legitimacy to HCV, helping to secure buy-in from MSF management. HCV programming is now being implemented in 13 countries[4]. Following the end of the grant most programmes are continuing under MSF's own financing.

[4] Pakistan, Iran, Armenia, Kyrgyzstan, Ukraine, India, Cambodia, Myanmar, Mozambique, Kenya, South Africa, Uganda, South Sudan. In Armenia and Kyrgyzstan, screening and treatment is focused on the current TB cohorts, and in South Sudan, the programme is limited to MSF staff.

However, a few programmes will be scaled down or closed, including the treatment of co-infected patients in Kenya and the new HCV programme in Uttar Pradesh in India.

Recommendations

Dalberg's recommendations are based exclusively on the evidence emerging from the MSF grant. The grant-informed recommendations for Unitaid are clustered into two groups:

1. **Grantee-facing recommendations**
   - 1.1. The partnership model (points of contact, conversations, reporting) should be fit for purpose relative to the type of engagement that Unitaid has with the grantee.
   - 1.2. Unitaid should consider whether a focus on HIV-HCV co-infection fits with their positioning and level of ambition in the HCV space.

2. **Recommendations to inform new investments in HCV**
   - 2.1. The scalability of HCV care is still hindered by two main 'gaps': diagnostics and financing. Unitaid should reflect on whether it is doing enough on diagnostics, and should consider its role in financing.
   - 2.2. As part of its strategic thinking on taking HCV treatment to scale, Unitaid should ensure a 'systems change' lens is applied when designing grants and portfolio structures.

Table of Contents

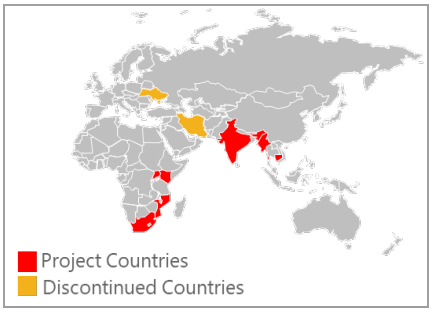
ACRONYMS

ANRS	[French] Agence nationale de recherches sur le Sida et les hépatites virales
CDC	[Cambodian] Centre for Disease Control
CHAI	Clinton Health Access Initiative
CoNE	Community Network for Empowerment
CSO	Civil Society Organisation
DAAs	Direct-Acting Antiviral
DNDi	Drugs for Neglected Diseases initiative
FIND	Foundation for Innovative New Diagnostics
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
LMIC	Low or Middle-Income Country
MACS	Manipur State AIDS Control Society
MdM	Médecins du Monde
MoH	Ministry of Health
MoU	Memorandum of Understanding
MSF	Médecins sans Frontières
NACO	[Indian] National AIDS Control Organisation
NCHADs	[Cambodian] National Centre for HIV/AIDS, Dermatology and STDs
NHVCP	[Indian] National Viral Hepatitis Control Program
OC [A,B,P,G]	[MSF] Operational Centre [Amsterdam, Brussels, Paris, Geneva]
OECD DAC	Organisation for Economic Co-operation and Development's Development Assistance Committee
PoC	Point of Care
PWIDs	People Who Inject Drugs
RDT	Rapid Diagnostic Test
RNA	Ribonucleic acid
SoE	Strength of Evidence
TB	Tuberculosis
ToC	Theory of Change
WHO	World Health Organisation

INTRODUCTION AND PRINCIPLES FOR THE EVALUATION

Grant overview

Figure 1: Countries where grant activities took place



In 2014, Unitaid awarded Médecins sans Frontières (MSF) a US$15M grant to improve access to Hepatitis C Virus (HCV) diagnosis and treatment in Low and Middle-Income Countries (LMICs). The project was implemented across seven LMICs: Cambodia, India, Kenya, Mozambique, Myanmar, South Africa, and Uganda[5]. Unitaid committed US$15M to supplement MSF's own funding, with a total budget of US$48M. By June 2018, when the grant was drawn to a close, Unitaid's contribution amounted US$8.2M out of a total US$28.2M spent[6].

MSF tested the feasibility of delivering quality HCV diagnosis and treatment in resource-limited settings, thus putting in place the building blocks for delivering HCV care at scale. Through its treatment sites in the seven project countries, MSF developed and tested adapted HCV models of care tailored to specific target populations, including HIV/HCV co-infected patients, People Who Inject Drugs (PWIDs), and urban populations. The objective of these small scale pilots was to demonstrate whether it was possible to treat individuals in LMICs with similar outcomes to those in High Income Countries. Beyond simplifying the treatment protocol, the grant also worked to secure other essential components/'building blocks' of HCV care, including registering Direct-Acting Antivirals (DAAs) in-country, negotiating low procurement prices, field-testing new virology/serology tests to improve the speed and quality of diagnosis, and advocating nationally and globally for the effectiveness, and urgent need, of HCV care. In 2016, the grant objectives evolved to include a greater emphasis on scalability.

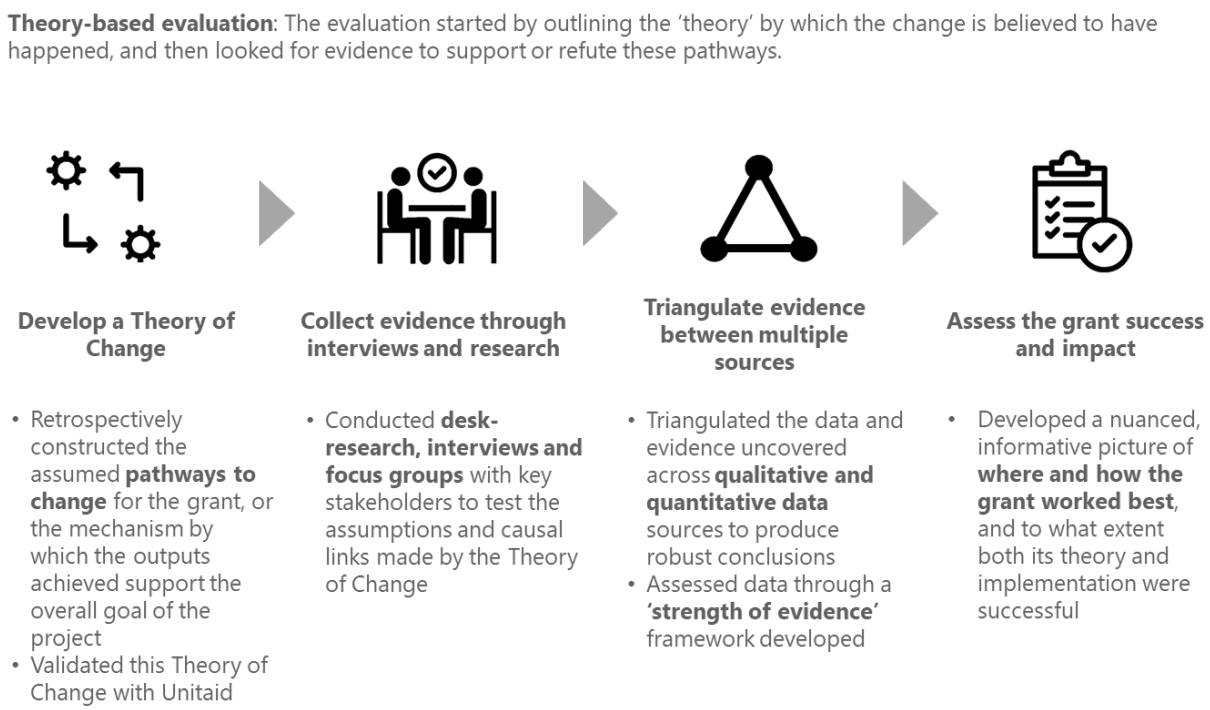
Unitaid funding was dispersed to four MSF Operational Centres (Amsterdam, Brussels, Geneva and Paris[7]) and two other MSF units. The four Operational Centres worked independently, receiving different sums of funding based on the size and scope of their project activities[8]. Overall, 52% of the budget covered diagnostics and treatment commodities, including Rapid Diagnostic Tests (RDTs), viral load tests, genotyping and fibro-scan equipment, and DAAs. 33% covered staff costs across all organisations, and 15% covered other costs, including operating and travel costs.[9] The Access Campaign received US$650,000 to conduct advocacy and support the production of affordable generic drugs, and Epicentre, the MSF-led epidemiological research centre, received US$1.3M to conduct a multi-centre cohort study and validate RDTs[10]. A central 'Unitaid pool', led by OCG, coordinated all the various units involved in the grant.

[5] Ukraine, Iran were discontinued in 2016, and Kenya, Uganda, Mozambique were scaled down
[6] MSF Final Report 2018, and consultation with MSF Grant Coordinator. Significant underspend occurred from both the Unitaid and MSF side, due to project delays and challenges (see Overall Summary).
[7] Respectively: OCA, OCB, OCG, OCP.
[8] Funding varied greatly, between US$87,171 received by OCB in Kenya to US$787,985 by OCA in Myanmar.
[9] MSF Project Documents: Budget Narrative, Budget version January 2015
[10] MSF Project Documents: Consolidated budged excel, Annual Report 2017

Methodology and evaluation principles

Dalberg conducted a mixed-methods, theory-based evaluation of this grant primarily through desk research and interviews (Figure 2). The evaluation started by retrospectively seeking to understand the 'theory' by which the change is believed to have happened throughout the grant, and then looked for evidence to support or refute these pathways. We collected evidence through field visits to Cambodia and India, interviews and desk research, involving a total of 35 experts and global and local stakeholders (excluding Unitaid staff). We triangulated evidence gathered between multiple sources and assessed its validly based on our strength of evidence framework (see Annex 3). Finally, we developed conclusions on the grant's overall success and limitations based on the evidence gathered. This mixed-method approach was deliberately selected for complex interventions, where the types of change envisaged are multi-faceted, with multiple influencing factors.

Figure 2: Methodology of the evaluation



I. THEORY UNDERPINNING THE MSF GRANT

Through its mandate to invest in HIV co-infections, Unitaid is supporting the global goal of eliminating viral hepatitis by 2030. Globally, 71 million people have chronic HCV, but only 20% are aware of their status and 4% are accessing treatment, due to challenges in the affordability, supply and delivery of care[11]. 73% of people with chronic hepatitis C live in LMICs[12], where these barriers are especially prominent. Unitaid seeks to unlock access for HCV treatment for all, acting within its mandate around co-infected HIV/HCV patients, to develop solutions for the HCV space more broadly. As part of its HCV strategy, Unitaid has made three complementary grants, to the Foundation for Innovative New Diagnostics (FIND), Coalition Plus and MSF. Each investment seeks

[11] UNAIDS, 2017: Global HIV & AIDS statistics in 2017; WHO, 2017: Global Hepatitis Report 2017.
[12] WHO, 2018: Progress report on access to Hepatitis C treatment.

to develop essential 'building blocks' for large-scale adoption of HCV care, focusing respectively on the development of new diagnostic tools, advocacy campaigns and simplified care models.[13]

The MSF grant aimed to demonstrate that it is possible to treat HCV patients in resource-limited settings. When the grant was conceived and co-designed in 2014 ***"…we had really no idea, very little understanding of the epidemiology of HCV. The burden was by very far exceeding the response that was possible at that time".***[14] Before the introduction of DAAs, HCV care through interferon-based therapy was challenging, causing high burden on health facilities and serious side effects for patients. Sofosbuvir/daclatasvir (sof/dac) were introduced 2014 but were only registered and available in the United States where they cost up to US$84,000 per treatment course[15]. The MSF grant was designed against this backdrop, with the aim of becoming the ***"early voice of a disease that was not taken seriously enough in the global health community",***[16] and demonstrating the feasibility of treating individuals through simple, affordable models.

MSF leveraged the rise in availability and affordability of diagnostic tests and DAAs to demonstrate effective care outcomes in LMICs. New (at the time) tools meant patients could be screened through RDTs[17] and viral load testing, and then treated in 12 or 24 week courses with 85% cure rates[18]. MSF sought to bring these developments to LMICs by testing a 'minimum viable product' for HCV care, which reduced the cost and burden of HCV care. These new 'models of care' streamline HCV protocols, reduce necessary steps, and use task shifting to lessen human resource bottlenecks. Evidence from MSF's outcomes were then shared broadly to influence national and global guidelines and demonstrate proof of concept for treating HCV in challenging settings.

Since the grant's conception in 2014 the global HCV context has changed radically. Global interest in HCV has risen. In 2016, the WHO published "Guidelines for the screening, care and treatment of persons with Hepatitis C infection", to encourage the use of DAA regimens for all persons with chronic HCV[19]. Soon after, the World Health Assembly endorsed the Global Health Sector Strategy on viral hepatitis, which proposes to eliminate viral hepatitis as a public health threat by 2030, through 90% reduction in incidence and 65% reduction in mortality[20]. A growing number of actors, including Drugs for Neglected Diseases initiative (DNDi), the Clinton Health Access Initiative (CHAI), FIND, and others have begun to support this global strategy. Across a handful of LMICs, including in Egypt, Mongolia and Georgia, governments have integrated free HCV treatment into existing health systems.

Mid-way through the grant, Unitaid's overall strategy evolved, and with that came a greater emphasis on scalability. In 2016 the Unitaid Executive Board agreed on a strategy for 2017-2021

[13] While the three grants tackle different, complementary parts of HCV care, cooperation was limited. Coalition Plus focused on advocacy within middle income countries where the conditions for scale were already in place, and hence only worked alongside the MSF Access Campaign in India. The FIND grant worked with different implementation agencies than MSF to trial diagnostics: even in Manipur where MSF is active, but they partnered with a CSO, YRG.

[14] Interview with former MSF-employee involved in the grant design.

[15] Wholesale acquisition cost of Sofosbuvir 12-week course in the US in 2015.

[16] Interview with MSF Staff in Mozambique

[17] RDTs were pre-qualified by WHO in December 2016, so they only can into use 2 years into the grant.

[18] WHO, 2018: Progress report on access to Hepatitis C treatment.

[19] WHO, 2016: "Guidelines for the screening, care and treatment of persons with Hepatitis C infection"

[20] WHO, 2016; "Combating Hepatitis B and C to reach elimination by 2030".

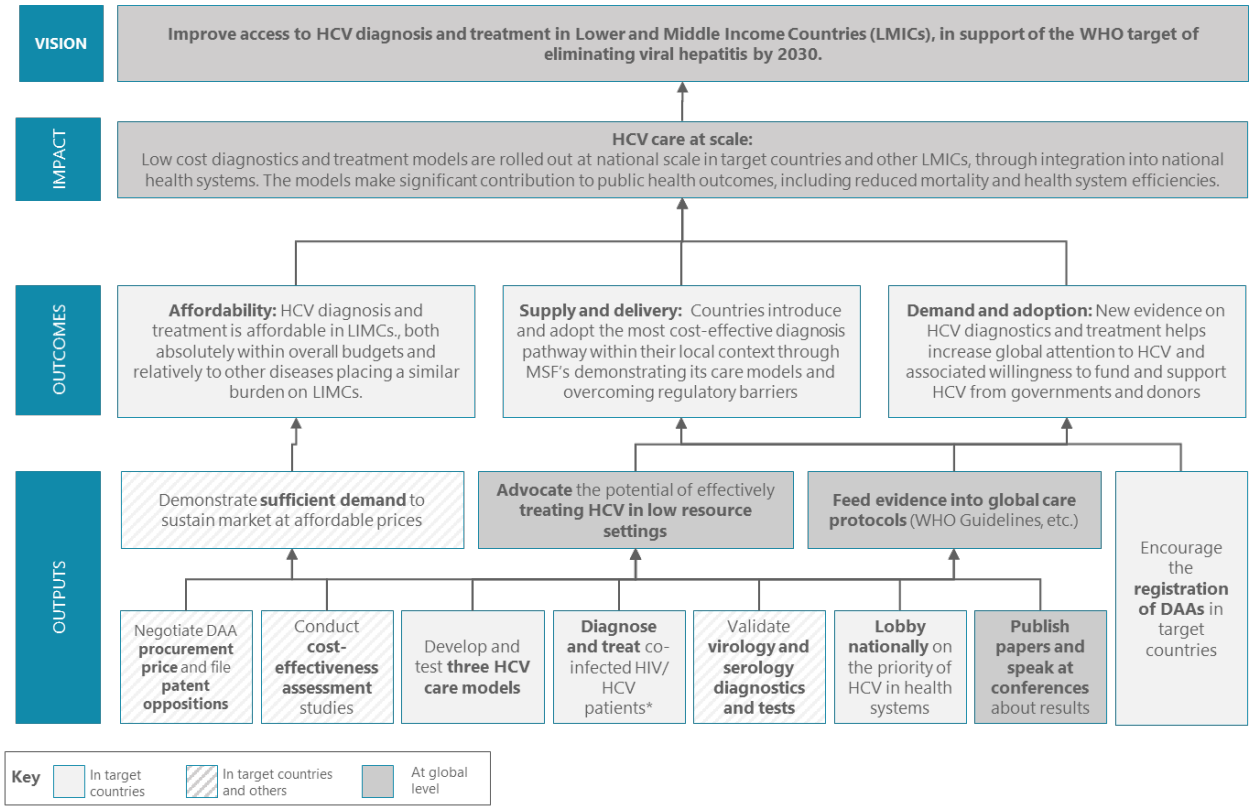
which included a greater focus scaling up innovations piloted under Unitaid grants. While the previous strategy included the scalability element which was integrated in the design of the MSF project, the greater emphasis on scalability in the new strategy led to a renewed focus and reprogramming of activities in the MSF project as from 2016 to reflect this. By 2016, the Unitaid team determined that the MSF grant had already accomplished the 'proof of concept' for HCV care in LMICs in its site in Manipur, India, and was hence ready to pivot towards a greater focus on scale[21]. Due to the lack of a large-scale donor active in HCV, Unitaid envisioned scale-up to occur primarily through domestic funding. Grant activities and metrics were changed to include the transition of MSF treatment sites to respective Ministries of Health (MoH) and national lobbying (see Annex for the Evaluation Terms of Reference). This evaluation will take into consideration both the original objectives around which the MSF programme was designed, as well as the later increase in focus on scalability as a target.

The evaluation tested a retrospectively constructed Theory of Change, which highlights the mechanisms by which the grant intended to reach its overall desired impact (Figure 3). The Theory of Change is underpinned by the three access barriers (as defined by Unitaid) the grant aimed to overcome:

- **Affordability:** Through price negotiations, advocacy and other strategies, MSF aimed to ensure DAAs are affordable at the lowest possible price that is sustainable for suppliers and does not impose an unreasonable financial burden on governments.
- **Supply and delivery:** The grant aimed to develop and introduce the most cost-effective diagnosis pathways and treatment models in LMICs, by overcoming barriers of DAA registration, field testing new virology and serology tests, developing local care models in MSF treatment sites and transitioning these capabilities to the Ministries of Health.
- **Demand and adoption**: MSF would generate and share evidence on HCV care to influence national and international guidelines, and lobby nationally to drive adoption of HCV care across national health systems.

[21] MSF project document, 2016: Annual Report 2016.

Figure 3: Theory of Change



These three barriers, as defined by Unitaid, are overlapping and interlinked. For example, there is a strong link between DAA registration and affordability, but these fall under different access barriers.[22] If only one or two suppliers of generic DAAs are registered in a country, this will affect the competitiveness of DAA pricing in that market, and therefore DAA affordability. While this evaluation is framed around the three Unitaid barriers, it will also highlight the interlinkages.

[22] DAA registration is considered part of 'Supply and Delivery', not 'Affordability'

II. EVALUATION OF GRANT OUTCOMES

This evaluation focused on testing the causal pathways between MSF's activities and overcoming the HCV access barriers in target countries. For each of the three barriers, there is a summary table which outlines the LMIC HCV context, MSF's activities under the grant, and a sense of their contribution to overcoming this barrier. This is all synthesised into an evaluation of overall progress against that barrier, accompanied by a strength of evidence assessment. This provides guidance (see the Annex 3 for further detail) on the type, number of sources, and consistency of the evidence underpinning the key finding.

Barrier 1: Affordability

The affordability of HCV treatment has improved dramatically, and MSF's efforts through the Access Campaign contributed towards this goal. (This section will only cover the improved affordability of DAAs, while diagnostics are covered in the following section.)

Figure 4: Overall assessment of MSF's progress on Affordability

Progress in the HCV Context	Since their introduction in 2014, the price of DAAs has steadily dropped, partially due to the issuance and negotiation of voluntary licenses to 112 low-income countries, and the large-scale production of generics in Egypt and India[23]. However, some interviewees felt the DAA market was still a de-facto monopoly, and markets will not be truly competitive until more generics are registered in each country. Despite this downwards trend, DAAs remain unaffordable for large-scale procurement through domestic resources in LMICs.	
MSF Activities	• The Access Campaign negotiated and publicly acknowledged their procurement price of US$120 for the sof/dac DAA combination regime. • The Access Campaign worked closely with generic manufacturers, providing information on securing the licenses needed to produce and sell DAAs. • The Access Campaign advocated for DAA affordability.	
MSF Contribution	**Decreasing Price**: MSF's US$120 procurement price was not available to other actors. The public announcement of this low price was one of the first of its kind. It empowered other organizations in their price negotiations and signaled the need to improve transparency around procurement prices. **Building a market for generics:** MSF's encouraged generic production of DAAs in India. 11 Indian generics manufacturers have since gained voluntary licenses from Gilead. **Lessons learnt:** The Access Campaign is considered a leader in this field, sharing their expertise with others. WHO remarked that ***"MSF provides critical input on issues such as transparency in drug and diagnostics pricing, procurement strategies including pooled procurement, diagnostic access and quality assurance".***	
		SoE*[24]

[23] WHO, 2018: "Progress report on access to Hepatitis C treatment".

[24] Causal linkages are especially hard to establish here, due to i) manufacturers declining to engage with the evaluation [to understand what role the Access Campaign played in influencing pricing], ii) the Access Campaign treated this grant akin to core funding, and so were not easily able to point to specific additionality

Evaluation of overall progress	**MSF had a moderate effect on improving the affordability of DAAs.** The Access Campaign's work has supported the downward trajectory of DAA prices in multiple ways including by improving price transparency. To ensure DAA affordability, different organizations will have to work on improving the transparency of current drug pricing, catalyzing genuinely competitive markets, and securing voluntary licenses for high-burden Middle-Income Countries.	◑

* Strength of Evidence (SoE) assessment - see above and Annex III

Price negotiations

MSF negotiated a DAA price of US$120 for their procurement. In 2015, MSF started procuring sof/dac from Gilead and Bristol-Myers Squibb through their 'access programmes' at a price of US$1,400 to US$1,800 per 12-week treatment. The original grant budget had earmarked around US$3M to procure treatment commodities for ~2,000 patients, to be treated through various regimens, including Sofosbuvir, pegylated interferon treatment or Ribavirin[25]. In 2017, however, MSF negotiated a new procurement price of US$120 per 12-week treatment, applicable to provide DAAs in any country where MSF is authorized to procure generics, greatly decreasing its treatment commodity budget needs. This price reflects both the success of the activism led by Access Campaign ahead of the tender negotiation, as well as the general downward trend in pricing of DAAs over the last five years. This price was negotiated by MSF for their own procurement, and is not directly transferrable to other entities, who have to negotiate their own price with manufacturers.

MSF's public announcement of the US$120 procurement price[26] sought to provide market signalling on HCV pricing, but this price remains inaccessible to most actors. Other international organizations have been able to use this price point as leverage in the own negotiations. While the causal link between the MSF price and other procurement prices is difficult to establish, CHAI noted that across their project countries knowledge of the MSF price did empower governments to negotiate further, particularly if purchasing DAAs through in-country distributors. In 2017, MSF also published a report sharing all public prices supplied by manufacturers[27]. However, actual negotiated price points remain protected by non-disclosure agreements and hence unknown. CHAI noted that ***"most countries that we work in are still nowhere close to hitting low prices such as $120. They are paying $600-800 despite organizations attempting to provide some global market intelligence ".***

from Unitaid, and iii) the nature of advocacy work - change is often non-linear, with multiple variables making contributions which are very hard to disentangle.

[25] MSF Budget Narrative, Budget version January 2015.

[26] Wise, 2017: "MSF pushes down price of generic Hep C drugs to new low level". British Medical Journal, v. 395; MSF Access, 2017; "MSF secures generic Hep C treatment at US$120 compared to US$147,000 launch price tag".

[27] MSF, 2017: "Hepatitis C: Not even close".

MSF's public announcement raised awareness on the need for greater price transparency. In the 2018 HCV Progress Report, the WHO noted that ***"Price transparency of DAA regimes remains inadequate... manufacturers use this method to bolster their position. Greater transparency is needed if countries are to succeed in negotiating affordable prices".*** Large variance exists between the prices that different countries are paying for DAAs.Supporting generics manufacturers on IP law

The Access Campaign encouraged the generic production of DAAs by highlighting legal barriers and coordinating with other activists. MSF promoted the expansion of territories for voluntary licenses and the removal of legal barriers to facilitate production and export of generic DAAs. MSF worked with generics companies to request voluntary licenses or on identifying other legal routes to produce DAAs.

Relative affordability of DAAs

Despite the downward price trajectory, current DAA prices remain unaffordable for most LMIC governments, who still struggle to fund anti-retrovirals. Limited health budgets in developing countries make it challenging for governments to take on HCV care. An official at the Cambodian MoH stated: ***"DAAs are not a priority for the government. We don't even have enough funds for ARVs yet and we have to sustain this cost first".*** The Cambodian MoH only began funding ARV treatment in 2016, providing 20% of the costs of the total HIV/AIDS programme. This came after 10 years of full Global Fund support to the Cambodian AIDS programme. Similarly, in Manipur, in India, the state MoH's total budget for HIV/AIDS is approximately US$800,000, with an additional ~US$150,000 promised by the federal government to treat HCV co-infection (which has not yet materialised). MSF staff stated that "***the Manipur MoH is so underfunded at the state level that they are having challenges funding ARVs, we don't see them taking up DAAs any time soon***"[28] (See India Case Study). DAA prices are expected to come down further, with growing economies of scale around purchase and the registration of an increasing number of generic DAAs across LMICS. However, the MoH's interviewed noted that donor investment would be necessary alongside domestic financing to scale DAA procurement.

Barrier 2: Supply and delivery

The grant sought to overcome barriers around the supply and delivery of quality HCV care in LMICs through demonstration of new tools and simplified treatment models.

Figure 5: Overall assessment of MSF's progress on supply and delivery

Context	Strong evidence on the feasibility of delivering quality HCV care in low-resource setting has emerged in the last five years. Originator or generic DAAs (sofosbuvir) are now registered in 56 LMICs. Improvement and simplifications to the full treatment model have increased the efficiency of care and reduced the burden on patients and health systems. ***"The feasibility of HCV care has***

[28] This is the up-to-date view on the state MoH's capacity to scale HCV, based on interviews with stakeholders and MoH in Manipur. It is a departure from the previous, optimistic view put forward in Annual Reports, which stated that *"A full catalytic policy change cycle (… full transition of services to MoH) will hence be completed by end of 2018"*

	been effectively been worked out"[29]. However, in many LMICs, care is still delivered by smaller scale non-state implementors, rather than through the national health system.	
MSF Activities	• MSF encouraged companies to register four DAAs in two countries • MSF delivered care to ~2,200 patients through simplified care models, which significantly reduced the steps required for HCV care • MSF field-tested two new diagnostic tests (SD Bioline and GeneXpert)	
MSF Contribution	• MSF's contribution to DAA registration was strong in India, moderate elsewhere • MSF's care model improvements (new diagnostics, reduced steps, task-shifting) have significantly helped demonstrate the feasibility of HCV care for low-resource settings, and are being introduced into care protocols by other actors • MSF's progress on transitioning HCV care to MoH varies across treatment sites from highly integrated, to little or no integration.	
Evaluation of overall progress	**MSF had a strong effect on demonstrating the feasibility of HCV care in LMICs through simplified models of care.** As one of the very first implementors, MSF developed some best practices for improving the efficiency HCV diagnosis and treatment in low-resource settings.	***SoE*** ●
	MSF's models of care had a moderate influence on those being provided by other organizations. Elements of the MSF models of care are being adopted and further built on by others, either through direct training, indirect knowledge transfer, or drawing inspiration from MSF's simplifications.	◑
	MSF made some progress on the integration of its HCV sites into local Ministries of Health. More needs to be done to transfer MSF's technical know-how to MoH staff and integrate HCV into national health systems.	***SoE*** ●

DAA registration

MSF's contribution to DAA registration varied by country, depending on the previous status of DAAs. MSF has encouraged the registration of DAAs in LMICs through of the Access Campaign. The difficulty of registration depends on the capacity of local regulatory agencies, including their requirements on safety and efficacy data, and requests for local clinical trials in each country of registration. MSF's involvement varied by country. In India the Access Campaign was involved in strong activism to support registration of two sofosbuvir generics as Sof/Vel from Gilead, including coordinating civil society protests, sending HCV patients to visit the Food and Drug Authority offices on a daily basis, and providing legal advice to manufacturers. In Uganda, the Access Campaign supported the registration of Sofosbuvir by engaging continuously with the generic producer - supporting them to register in countries where the government, MSF or other organisations require the drugs. In Cambodia and Myanmar, on the other hand, less stringent regulatory authorities meant that the main DAAs were already registered at the time of the grant start. MSF's role in registration was therefore very limited. In other countries the process of DAA registration is simply very slow, despite MSF's advocacy efforts. In South Africa, for example, pharmaceutical companies filed for the

[29] *Interview with DNDi*

registration of Sofosbuvir in 2014, but this has yet to be approved by authorities due to requests for additional local clinical trials, and lengthy bureaucracy.

In several countries, MSF used special import licenses as a way to procure drugs where registration was not possible, despite limitations for future scale-up. MSF deprioritized advocacy for DAA registration in countries with lower HCV burden, particularly countries in Africa. Pharmaceutical companies view these countries as less profitable markets, and therefore are less inclined to file for drug registration in them. This means it is more of an uphill struggle for MSF to advocate for, and support, registration. In Kenya, Mozambique and South Africa, MSF hence imported through special import licenses granted by the government. These special import licenses are not sustainable, long-term solutions, as they require the mediation of an international organisation like MSF[30]. Government willingness to scale-up HCV treatment would signal the growth of demand to manufactures and should increase their interest in seeking DAA registration. However, this might not be enough to ensure genuine affordability: according to WHO, the registration of at least five generics per country is essential to creating a competitive market and ensuring competitive prices[31]. Further, some countries, such as South Africa, fear that the registration of a single-brand DAA will in fact limit their ability to procure through a special licence, and hence drive up the cost of that DAA.[32]

Figure 6: List of generic DAAs registered and MSF's involvement[33]

Country	***Generic DAA regimens***	***MSF's role in registration***
Cambodia	*Sofosbuvir* *Sofosbuvir /Ledipasvir* *Daclatasvir*	MSF's involvement was limited as all 3 DAAs were already registered at the start of the grant in 2015-2016.
Myanmar	*Sofosbuvir* *Sofosbuvir /Ledipasvir* *Daclatasvir* *Velpatasvir*	MSF involvement was limited, as all DAAs were already registered and available by distributors in country by the start of the grant.
India	*Sofosbuvir* *Sofosbuvir /Ledipasvir* *Daclatasvir* *Sofosbuvir/ Velpatasvir*	The Access Campaign strongly supported the registration of Sofosbuvir (Hetero), Sofosbuvir (Mylan); SOF/VEL (Gilead), which was granted in 2016. MSF coordinated civil society protests, wrote a number of press releases, articles and briefs[34]
Kenya	*N/A*	N/A – MSF import using a special import license
Mozambique	*N/A*	N/A – MSF import using a special import license

[30] In some cases, such as South Africa, doctors can request special import licenses themselves for certain drugs.
[31] See 'Affordability', Interview with MSF Access Campaign.
[32] Daclatasvir from Gilead is expected to be registered in mid-2019 in South Africa. Doctors fear this will make it more difficult to procure generic versions through the 'Section 21' import exception mechanism, making the expensive originator the only drug available.
[33] TREATAsia, amfAR, 2017: Access to Hepatitis C treatment, Asia Pacific AIDS and Co-infection Conference,
[34] MSF Access Campaign, 2017: "MSF challenges Gilead's patent application for Hepatitis C combination"; MSF Access Campaign, 2016: "Patent challenge heading on Gilead Hepatitis C drug sofosbuvir starts in India"

South Africa	*N/A*	N/A – MSF import using a special import license. A new regulator has just been put in place in South Africa, who is currently faced with a large back-log of cases, therefore registration is slow. Sofosbuvir and Daclatasvir are expected to be registered in mid-2019[35]
Uganda	*Sofosbuvir*	MSF encouraged the registration of Sofosbuvir from Hetero for the Epicentre cohort study by supporting the Indian-manufacturer with the approval process.

Treatment models

The simplified treatment models developed by MSF made some of the first improvements to HCV care in LMICs, and were crucial to demonstrating the viability of HCV care in these contexts. The full care model for HCV treatment, as recommended by early WHO Guidelines, included 16 visits to a clinic, monthly doctor visits with specialist hepatologists and numerous follow-up consultations[36]. This process would place a high burden both on the clinical staff, as well as on patients, who would be required to travel several times to treatment site, often from distant locations. Rolling out at scale in LMICs would hence require a simplification of this model to a 'minimum viable product', which still maintains the quality of patient outcomes. MSF's early efforts to develop these simplified models were essential to demonstrate that HCV care could indeed be effective in LMICs. Through an iterative testing approach, MSF's treatment sites were some of the first to make some important changes needed for a leaner treatment model.

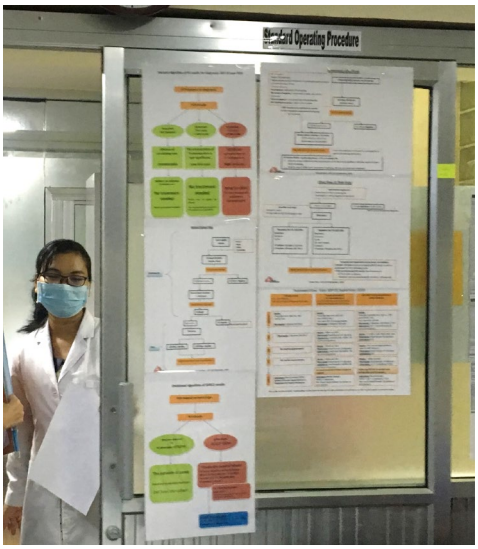


Figure 7: MSF clinician with the Cambodian care model

The main changes to HCV care piloted by MSF included:

- Removing genotyping from the diagnostic process;
- Eliminating the need for specialist hepatologists;
- Task-shifting fibro-scan exams, monitoring, and consultation during treatment to nurses;
- Reducing the need for clinical monitoring after the end of treatment.

While MSF developed three care models for target populations (co-infected patients, PWIDs and urban dwellers), these 'care models' are not rigid treatment protocols, and are continually being adapted to the realities on the ground. The MSF grant coordinator said ***"in the field they are not aware of discreet 'models of care', rather they focus on the simplification of care".*** In Cambodia, MSF reduced the HCV care model from 16 to 8 steps[37] for the general population in a tertiary hospital facility. As of early 2019, the process has been further reduced to 4 steps. In the rural Battambang clinic, MSF is now seeking to develop a 3-step rural care model, which requires fewer patient visits to the clinic. However, epidemiologists working with PWIDs in Manipur suggested that in settings where treatment is focused on marginalized and vulnerable communities at high risk of re-infection, a very light touch model is less effective due to higher risk of non-adherence to the

[35] Interview with MSF South Africa
[36] WHO, 2016: "Guidelines for the screening, care and treatment of persons with chronic Hepatitis c infection".
[37] MSF, World Hepatitis Summit 2017: "Identifying the optimal care model for HCV in Cambodia".

treatment course.[38] In Manipur the model is supplemented with additional counselling, psycho-social assessments and follow-up monitoring, as well as referrals to harm reduction programmes.

Other organisations have been influenced by the MSF models of care. MSF shared their findings through direct training and support and indirect knowledge transfer through publications or conferences. MSF's streamlined treatment models have influenced the way other organisations, including governments, think about HCV care. While it is difficult to identify the causal links between MSF's particular "care models" and those of other organisations, stakeholders broadly agreed that ***"MSF helped move the needle globally on simplified models of care globally, reducing steps that might not be necessary"[39].*** In Manipur, MSF directly trained the Community Network for Empowerment (CoNE) on treating PWIDs, while working in a joint clinic in Shalom. CoNE will soon start screening 2000 patients through an MoH funded programme, using the MSF care model. In Kenya, MSF trained Médecins du Monde (MdM) on simplified HCV care for HIV patients. MDM are now screening patients independently (although they are not implementing treatment). MSF also trained Kenyan MoH staff around the country on decentralised protocols for HCV care. In Cambodia, MSF helped the National Centre for HIV/AIDS, Dermatology and STDs (NCHADs) develop guidelines for the nation's HIV/HCV co-infected cohort based on MSF's treatment model. Elements of the Cambodian care model were also replicated in MSF's new HCV projects in five countries[40]. MSF published the evidence on simplified HCV care in numerous reports and conferences[41]. A number of other stakeholders, including CHAI and PharmAccess, used this evidence for their programmes.

Figure 8: MSF contribution to the adoption of simplified treatment models

Entity	***Size of project***	***MSF contribution to the treatment model***
CoNE (Manipur)	Screening 2000 patients	• Direct influence by working jointly on screening of PWIDs through MSF diagnosis protocols and transferring technical know-how.
MDM / MoH (Kenya)	Screening 1000 patients	• Direct influence by jointly screening of PWIDs through MSF diagnosis protocols, transferring technical know-how.
NCHADs (Cambodia)	Screening 60,000 patients	• Direct influence by co-developing guidelines for treatment of co-infected patients based on the MSF treatment model • Trainings of MoH staff on HCV care
MSF projects in 13 countries, including the 7 grant project countries and Iran, Armenia, Kyrgyzstan, Ukraine, South Sudan	Treated 5,926 patients in 2017[42]	• Direct influence through knowledge-sharing at MSF HCV workshops (organised through the Unitaid grant), informational trips between operational centres and published evidence in papers.

[38] Interview with MSF epidemiologist and clinical staff in Manipur and MoH MACS department, who found evidence that a more comprehensive care-model is necessary for PWIDs to achieve the same treatment cure rates are other patients, especially when suffering from compounded chronic illnesses such as liver cirrhosis.
[39] Interviews with WHO, MPP, PharmAccess. CHAI.
[40] Iran, Armenia, Kyrgyzstan, Ukraine South Sudan.
[41] See 'Demand and Adoption'.
[42] MSF International Activity Report, 2017: "Hepatitis C: pushing for access to the cure".

MoH (Myanmar)	Treating 2000 patients	• Inspiration, MSF were the first to demonstrate that HCV could be treated in low-resource ways in Myanmar. Today, MoH are not following the MSF model, and follow a protocol that has become more simplified than MSF's.
State MoH, Punjab	Treating 20,000 patients	• No influence, MoH is supported by the Mukh Mantri Punjab Hepatitis C Relief Fund and started treating patients in parallel to the MSF grant in Manipur.

New models for HCV care are emerging, providing even more simplified, decentralised solutions. By demonstrating that HCV care could be simplified, MSF paved the way for further improvement. Reflecting on the treatment model used in India, an MSF staff member told us ***"I would simplify the model further. It's a simple disease, treatment can be even more simplified".*** In Australia, the Kirby Institute is running a clinical trial of a two-step model of care, whereby all monitoring and follow-up is conducted by phone[43]. In Punjab, Mukh Mantri Punjab Hepatitis C Relief Fund has rolled-out a decentralised HCV model, whereby specialised hepatologists in tertiary hospitals act as 'hubs' to remotely train district hospitals in HCV care through an online platform called ECHO[44]. This model takes important steps towards decentralisation and knowledge transfer, but also relies on the availability to technology and specialised hepatologists[45]. Overall, care models reflect the context and resource constraints of the location they are implemented in, and build upon each other's learnings.

Diagnostics

There is a spectrum of delivery models for viral load testing, each with pros and cons. Viral load testing can be centralized (patient travels to referral centre); it can use decentralized sample collection (sample travels); or can be decentralized to lower-level health facilities. Centralized testing models offer the potential for use of high-throughput, lower cost-per-test technology, but can be slow and can mean high access barriers, especially for poorer patients.[46]

MSF verified the use of capillary blood rather than venous blood for the SD Bioline RDT. The validation of the use of capillary blood for the SD Bioline diagnostic was an important finding, making this affordable test accessible in resource-limited settings where venepuncture is difficult. SD Bioline is currently the cheapest RDT on the market, available for US$1 per test, and can be imported in the majority of LMICs. MSF India originally planned to carry out five other RDT validation tests. These were cancelled due to delays in gaining approval from the Ethical Review Board and operational issues around transporting laboratory samples. There is still the need for additional validation of competing RDTs, to avoid a monopoly and allow for different diagnostic methods. FIND remarked that ***"it is necessary for [diagnostics] technology to become yet more diverse. Only a***

[43] Kirby Insitute, 2018: "Trial of Simplified Treatment Monitoring for 8 Weeks Glecaprevir/Pibrentasvir in Chronic Hepatitis C Patients (SMART-C)"

[44] Dhiman et al, 2016: "Tackling the Hepatitis C Disease Burden in Punjab, India". Journal of Clinical and Experimental Hepatology, v.6, i.3.

[45] The success of the Punjab scale-up was due to a combination of factors, including bottom up pressure from civil society efforts, and top-down support from the Chief Minister due to a personal connection with HCV (for more, see Demand and Adoption section).

[46] See the CHAI/FIND HCV Diagnostics Market Intelligence Report 2017: First Report on Screening and Diagnosis Market Growth for a fuller discussion on diagnostics

handful of RDTs are available, of which only one is for oral use, which remains too expensive at $12 per test".

MSF also confirmed that GeneXpert (a cartridge-based nucleic acid amplification test from Cepheid AB) can be used for viral-load testing for all patients, including Genotype 6 patients[47]. GeneXpert is considered near PoC, and hence reduces issues with the transport of samples and long delays. GeneXpert is the only WHO pre-qualified HCV PoC viral-load testing platform available[48] Studies found GeneXpert to perform equally, if not better, than the existing market-leading laboratory-based platform Abbott RealTime HCV[49],[50]. By using these two tests and eliminating genotype testing, the time taken from initial screening to DAA initiation was reduced from two months to 5 days (Figure 9).

Figure 9: MSF's simplified diagnostic process

GeneXpert can work well in low prevalence contexts. For example, GeneXpert is successfully used across Cambodia as part of the national TB programme, with 75 machines enough to process all the necessary tests, at high speed and lower cost than the Abbott/Roche [centralized] equivalents.

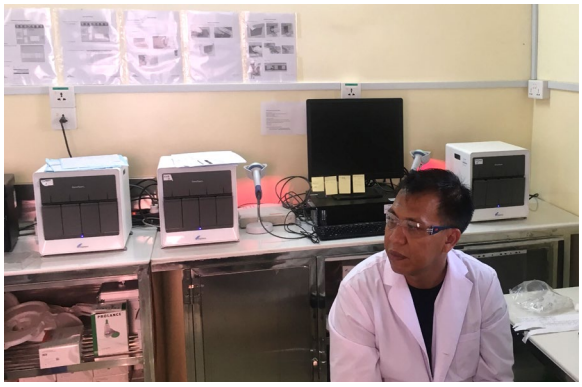


Figure 10: MSF lab technician in the MoH Hospital

Decentralized capacity on GeneXpert for all HCV testing needs should already exist, but the reality is somewhat different. The CHAI-FIND report provides evidence from a survey, demand modelling and analysis of Cepheid's sales data to show that enough capacity should exist on the GeneXpert platform to perform the necessary HCV viral load tests on existing machines.[51] However, this evaluation found a more mixed ground-level picture in terms of whether i) this 'theoretical' capacity was geographically located in the right place, and ii) whether HIV/HCV clinics could access the spare capacity e.g. very practical challenges like the machines being located in a different hospital department, so HCV-

[47] MSF Access, 2017: "Putting HIV/HCV to the rest".
[48] PoC Genedrice HCV is another near-PoC VL test currently undergoing CE-marking, but yet to be tested in the field.
[49] McHugh et al, 2017: "Multicenter Evaluation of the Cepheid Xpert Hepatitis C Virus Viral Load Assay". Journal of Clinical Microbiology, 55(5).
[50] Review of all laboratory-based HCV viral load tests can be found in MSF, 2017: 'Putting HIV and HCV to the test". Laboratory tests cost US$13-100 per test, but also have high running costs for the laboratory and transport.
[51] CHAI/FIND HCV Diagnostics Market Intelligence Report 2017: First Report on Screening and Diagnosis Market Growth

focused staff were unaware if/when they were free, or undefined processes for cost sharing with multiple users.[52]

Furthermore, GeneXpert is still expensive, and cannot be truly decentralized. The machine costs USD$12,000 - USD$71,000 upfront (depending on the number of modules), plus there are regular maintenance costs, and cartridges cost $14.90 each[53]. It cannot be fully decentralised to primary care facilities, due to the need for a constant electricity supply, back-up energy generation and a constant room temperature. This led one MSF interviewee to note, ***"GeneXpert is the answer for the moment, but it is not a good answer".***

There is still a technology-service model gap in diagnostics. Multiple interviewees expressed a concern that diagnostics have not moved enough over the last five years[54]. The solutions to this gap could be new technologies (where MSF[55] and Unitaid-grantee FIND are active[56]), and/or ways of better using existing technologies (whether centralised[57] or GeneXpert), and/or reducing the cost of technology, which both lowers costs overall but also reduces the downside of any unused capacity). In reality, the solutions will probably be all three, and more, across different contexts.

Integration with the Ministry of Health

MSF is working alongside the respective MoH in several treatment sites, but transition and integration is generally low and often varies (Figure 11). The level of MoH integration is based on a number of factors, which include the availability of technology, the capacity and willingness of the MoH staff to take on the additional workload, and the overall MSF relationship with the MoH. Transition plans and timelines are often undefined, and overall there is a sense that MSF will remain involved in the roll-out of HCV at least for the medium term.

[52] The CHAI/FIND report notes "However, the challenges on how to make this integration possible and acceptable across programs, given the situation around governance, funding, and oversight still remains to be addressed in most countries"

[53] Cepheid, 2018: "Cepheid announces expanded access to Xpert family of virology tests in global regions with the greatest need".

[54] Interviews with MSF HCV Referents, WHO India, WHO regional office in Western Pacific.

[55] MSF UK and Imperial College are currently preparing two publications on the minimum possible costs for RNA diagnostics in LMICs and simplified diagnostic algorithms. See MSF Project Documents, Annual Report 2018, Appendix 1: list of deliverables.

[56] Through a separate grant to FIND, Unitaid is supporting development of affordable, faster diagnostic tools on HCV, which provide PoC solutions that can be performed by less specialised health workers.

[57] In the Kossomak hospital in Phnom Penh, the MoH screens patients for HCV using their own, more dated, molecular testing. However, as this system is more imprecise and at risk of contamination, MSF uses GeneXpert in their own laboratory within the hospital for quality control of some samples, to periodically verify the outcomes of the MoH tests. This duplication of labour could be eliminated if MSF worked with the MoH to improve their own molecular testing capabilities

Figure 11: Varying levels of MoH integration at a sample of MSF treatment sites[58]

Integration within MOH	***Treatment site***	***Steps taken towards MoH integration***
Higher  **Lower**	**Battambang Clinic, Cambodia**	• MoH staff run the full process including diagnostic tests, treatment and follow-up with patients. • MSF runs laboratory testing due to lack of MoH capacity and technology • MSF pharmacy provides DAAs
	Kossamak Hospital, Cambodia	• MoH staff conduct diagnostic tests, MSF validate samples for quality control, and support when additional capacity is needed. • MSF staff treat patients, although in 2018 ~20 patients a day were transitioned to MoH doctors • MSF pharmacy provides DAAs • MSF and MoH staff discuss complex cases together
	Churachandpur District Hospital, Manipur	• MSF run the full process, within an MoH hospital • MSF pharmacy provides DAAs • MSF and MoH staff discuss complex cases together and MSF are training MoH on HCV care, with the aim of future transition
	Moreh and Chakpikarong Clinics, Manipur	• MSF runs diagnosis and treatment within their own HIV clinics with no clinical support from MoH • Plans for transition of activities to MoH facilities being discussed
	Yangon and Dawei MSF Clinic Myanmar	• MSF screen and treat patients in a separate location to MoH • No transition of services is planned to MoH

Barrier 3: Demand and adoption

The demand for, and adoption of, simplified HCV care models is the third barrier the project sought to overcome in its ambition to improve access to HCV diagnosis and treatment in LMICs.

Figure 12: Overall assessment of MSF's progress on demand and adoption

Context	The advent of DAAs as a simple and highly effective treatment of HCV revolutionized the HCV space. In 2016, the WHO first published global Guidelines encouraging the use of DAAs for all persons with chronic HCV. Global attention on HCV has been growing, with over 84 countries developing national guidelines for treatment, and a number of international organizations becoming interested in this issue. However, this growing interest has yet to unlock significant financing for HCV, whether through global donors or, as will be more likely the route to scale, through domestic resources.
MSF Activities	• MSF advised the MoH in Kenya on the content of the HCV national guidelines published in 2017, and led successful lobbying of the MoH in Cambodia, Mozambique and Manipur, which they are now supporting in the development of their guidelines (though this is not funded by Unitaid). • MSF's shared evidence on the positive outcomes of sof/dac in treating genotype 5 and 6 patients with the WHO for their Global Guidelines.

[58] All active MSF treatment sites are included except Uganda, where MoH staff carry out full treatment but only 4 HCV patients were ever served, and Mozambique and Kenya, where treatment has been interrupted.

	• MSF lobbied national governments on HCV, including presenting the findings of four cost-effectiveness studies • MSF shared the evidence from the pilot sites in 16 publications and 23 events	
MSF Contribution	• MSF brought technical expertise to the development National Guidelines, and they have also been a driving force for these guidelines in some countries • MSF's finding on sof/dac was one of the main findings of the 2018 WHO Guidelines update. • MSF has engaged several MoH's on HCV and raised its profile nationally and globally, but beyond additional MSF funds, financing options remain limited .	
Evaluation of overall progress	**Evidence generated by MSF had strong influence on national and global HCV guidelines.** MSF played a key role in supporting three countries and a state in developing their national guidelines on HCV and added key evidence to the WHO Guidelines on less-researched Genotypes 5/6 and on model of care simplifications. Their contribution to the WHO Guidelines was an important addition to global understanding and treatment of HCV, while national guidelines are a necessary first step towards National HCV programmes.	***SoE*** 
	MSF made limited progress on lobbying governments to finance HCV programmes. The grant has raised some challenging questions the lack of international financing options for HCV at scale (given the lack of large international donor), and long road ahead to secure domestic financing.	***SoE*** 

National and global guidelines

The evidence generated from MSF's studies has been shared widely, and incorporated into global WHO Guidelines. Marc Bulterys, co-author of the 2018 WHO Guidelines on HCV treatment, said ***"MSF made an integral contribution to the WHO Guidelines in 2018 in demonstrating the effectiveness [of] sof/dac DAA regime on Genotype 5 and 6 patients",***[59] a finding which makes the regime pan-genotypic[60]. This finding is highly significant because while sof/dac is one of four existing pan-genotypic regimens, it is the only regime of the four currently accessible in LMICs, where Genotype 5 and 6 patients are concentrated[61]. Pan-genotypic regimes remove the need for time-consuming and costly genotyping tests. MSF's findings on the simplification of care models will also feature in the WHO's forthcoming 'Systematic review of service delivery models', to be published in early 2019. MSF was part of the stakeholder consultation for the review, and the publication includes a description of the simplified care model developed in Phnom Penh. Care models from the MSF

[59] MSF tested Genotype 6 (prevalent in South-East Asia), through its treatment site in Cambodia, while Genotype 5 (prevalent in Africa) was tested by a local clinic in South Africa using DAAs procured and donated by MSF.

[60] MSF Epicentre also provided evidence on sof/dac for Gen 1-4 patients through their: "Report on effectiveness of the Sofosbuvir – Daclatasvir regimen in cirrhotic and non-cirrhotic patients with genotype 1-4 (A. Loarec, C. Fortas).

[61] Of the other pan-genotypic regimens, *Sofosbuvir/Velpatasvir* is only registered in 3 LMICs, *Glecaprevir/Pibrentasvir* is not registered in any LMICs and *Sofosbuvir/Velpatasvir/Voxilaprevir* is only available for re-infected patients, and remains prohibitively expensive.

sites in Battambang, Mozambique, Kenya and Myanmar were not included in the review, as it focuses on HCV care for mono-infected patients in primary care facilities. Evidence from the grant has also been showcased in 16 papers by MSF staff, which have been submitted to academic journals such as the Lancet, the Viral Hepatitis Journal, the Journal of Hepatology and JIAS[62]. These contributions have been significant in raising the profile of HCV elimination as a pressing, but achievable, global health target.

MSF has contributed to developing national guidelines for HCV care in a number of countries, a first essential step towards national roll out. Developing national guidelines for the cure of a particular disease signals the government's recognition of it as serious threat to public health, which should be addressed through national health services. Since the publication for the first WHO Guidelines recommending the treatment of HCV through DAAs in 2016, a number of governments have taken notice of HCV as a curable, and potentially eliminable, disease. By December 2018, at least 84 WHO member countries have published national guidelines on HCV care,[63] adapting the recommendations of the global guidelines to their contextual reality. Figure 13 details countries in which MSF contributed directly the development of national guidelines.

Across its project countries, MSF played an important role in driving and advising development of these guidelines, providing technical know-how in Kenya, Cambodia, Mozambique and Manipur. Being one of the first implementors of HCV care in LMICs, MSF possesses valuable technical evidence that can feed into national guidelines. In Cambodia, Kenya, Manipur and Mozambique, MSF has been a key participant of the technical working groups for the development of national guidelines. In Cambodia, CHAI remarked: ***"MSF brings the technical expertise to the working group, as the only organisation with experience implementing HCV care in the country…their important work at Kossamak hospital is helping to push the national strategy".*** Similarly, the MSF team in Kenya stated they ***"contributed greatly to national guidelines: the MoH was able to replicate the model of care and regimen we were using, and we were part of the trainers for the national team".*** In South Africa and Uganda, HCV is considered a very low government priority, and therefore the development of treatment guidelines is not being prioritised by the MoH.

Figure 13: Progress on National Guidelines for HCV and MSF's role

Country	***Status***	***Guidelines:***	***MSF's role***
Kenya	Published	2017: Published guidelines for the Treatment of Chronic Hepatitis B and C Viral Infections[64]	MSF contributed by sharing evidence on their model of care and treatment regimen for the guidelines, and supported the rollout by training MoH staff around the country
India	Published	2017: National Viral Hepatitis Control Program and guidelines launched[65] 2019: Manipur State plans to develop HCV guidelines	State-level: MSF will play a leading role in drafting state guidelines in Manipur National-level: No direct contribution, but in regular contact and collaboration

[62] MSF Project Documents, Annual Report 2018, Appendix 1: Publication list.
[63] WHO, 2018: "Progress report on access to Hepatitis C treatment"
[64] Gastroenterology Society of Kenya, 2017: "Guidelines for the treatment of chronic hepatitis B & C viral infections"
[65] Gov't of India, Ministry of Health & Family Welfare, 2018: "National Viral Hepatitis Control Program".

			with WHO focal person, who supported the guidelines
Cambodia	In progress	2017: Published guidelines for co-infected HIV/HCV patients[66] 2018: Summoned technical working group on National Guidelines	MSF's technical expertise leveraged for co-infection guidelines, and MSF is a driving force of the technical working group for national guidelines.
Mozambique	In progress	2019: National guidelines to be published	MSF is part of a technical working group for the development of these guidelines given their experience screening for HCV
Myanmar	Published	2016: Published the National Strategic Plan on Viral Hepatitis[67] 2017: Published simplified treatment guidelines for Hepatitis C infections[68]	No direct contribution, limited MoH engagement by MSF.
South Africa	In progress	2018**:** MoH is preparing the National Viral Hepatitis management guidelines and 5 year action plan	Limited MSF engagement with the government on HCV. MSF does not lead HCV care implementation and therefore does not hold technical expertise.
Uganda	No guidelines	No existing or upcoming national clinical guidelines on HCV care	Initial government engagement was stopped when only 8 HCV cases were identified from screening 10,000 individuals, making it a very low government priority.[69]

MSF has also conducted four cost effectiveness studies to help develop a strong business case for the scale up of HCV treatment, but results are yet to be published. The studies evaluated cost effectiveness of simplified HCV care, with the aim of developing economic evidence for discussions between MSF and various MoH's. These studies included assessments of the business case for treating PWIDs in Nairobi, co-infected patients in Myanmar, mono-infected patients through a simplified model in Phnom Penh, and the general population in Pakistan. Publications of these studies are planned, and preliminary results have already been shared at hepatitis conferences. A further study on rural patients in Cambodia was delayed beyond grant funding. Overall, due to delays and challenges in securing approval from Ethics Review Boards, the results of these studies have yet to be published, and used to influence government advocacy. Nonetheless, other organisations outside MSF see value in using economic analysis as an advocacy tool with government, highlighting the cost-savings implications of treatment, compared to long-term burdens on the health system. CHAI argued that these analyses can highlight to governments that HCV can lead to a large burden to health care burden down the line, unless tackled promptly. CHAI Cambodia is hence developing a cost-effectiveness analysis as a companion to the forthcoming National Strategy.

MSF OCs are focused on clinical care. Mobilising domestic resources through political willingness is outside of their core competencies. Government decisions around resource allocation and health priorities are affected by many factors beyond technical feasibility, or evidence

[66] NCHADs, 2017: "National Guidelines for Management of Persons with HIV and Hepatitis C coinfection, 1st edition"
[67] Myanmar Ministry of Health and Sports, 2016: "Myanmar National Strategic Plan on Viral Hepatitis 2016-2020"
[68] Myanmar Ministry of Health and Sports, 2017: "Simplified treatment guidelines for Hepatitis C Infection".
[69] Interview with MSF Epicentre Uganda

(however rigorous) on cost effectiveness. Organisations can seek to drive political willingness either top down, by advocating with high level government officials, or bottom-up, by coordinating civil society efforts. Marc Bulterys, WHO, noted MSF was active in advocating with government ***"the work that is done by MSF was really catalytic, from very early on urging the government to start providing access for everyone".*** MSF OC's were not always aware of the need for advocacy (beyond informing technical guidelines), and sometimes lacked access to the relevant top-level authorities. In India, for instance, MSF advocacy efforts were concentrated at the state-level through the Manipur AIDS Control Society (MACS), rather than at the federal level with the National Health Mission or the National Aids Control Organisation, who ultimately allocate large amounts of budget. Coalition Plus, who worked alongside the MSF in India, noted that "***advocacy is much easier at the state level, but it is federal government who set objectives and budgets for each state***". While the Access Campaign did hold these federal-level contacts in some countries, they did not work systematically to advance the agenda of the OCs. More fundamentally, the OCs are focused on delivering clinical care, and this is a very different mindset from organisations more focused and experienced in government advocacy. In Cambodia, a local CHAI staff member noted that ***"until there's top down pressure from the Director of the MoH communicable disease department, or someone tops up the salary of lower-down MoH staff, nothing will happen".***

Developing substantial bottom-up pressure can be an effective change mechanism. The Access Campaign has been active in organising civil society in a few project countries, but large-scale mobilization requires actors beyond just MSF. Generally, countries or states in which civil society have been most vocal about the need for HCV care, have moved quicker towards implementation at scale. In India, for example, MSF worked alongside Coalition Plus to organise two large seminars convening government and HCV stakeholders, along with CSOs who represent "the voice of the patients" such as Coalition Plus themselves. Coalition Plus and the Access Campaign stated that these seminars were crucial in bringing about the National Viral Hepatitis Control Program in 2017[70]. Mobilising coordinate civil society efforts goes beyond MSF's core capabilities, and requires a consortium of actors including research organisations, local civil society, international donors and relevant stakeholders on the same issue. Coalition Plus is focused on convening the 'voice of the patients' through civil society to mobilize government action. In Cambodia, this type of cooperation is emerging around a technical working group to advise the creation of National Guidelines, including MSF, CHAI, ANRS, WHO, local CSOs and the MoH. The group held their first meeting in late 2018.

[70] Interview with Coalition Plus.

Financing and scale-up

Global guidelines and advocacy efforts have yet to mobilize significant funding from donors or governments. The Global Fund estimated that the economic burden of treating HCV co-infected patients in Global Fund eligible countries would amount to US$440M-790M. However, donors have only been able to provide limited funding for HCV often tied to co-infection with HIV. The HCV space overall lacks a large donor to finance the scale-up of interventions. Unitaid was aware of this limitation: they described their efforts in HCV as ***"a foray into a new area, rather than our usual connect-the-dots strategy",***[71] whereby their role is to fund feasibility projects and connect them to larger investment from other donors, particularly the Global Fund. Despite the global advocacy efforts by MSF (e.g. writing an open letter to the Global Fund to increase HCV funding[72]) and by Unitaid, the international financing landscape for HCV remains sparse, and financing will primarily have to come from domestic resources.

MSF and other actors have been considering innovative, hybrid financing models to unlock domestic financing, yet these are still in early stages and have yet to demonstrate strong results. Most LMIC governments will be unable to bear the full cost of HCV treatment at current prices. CHAI stated that "***If HCV is to be financed publicly, then diagnostics and treatment costs need to come down further, or new hybrid financing will need to emerge".*** Some interesting financing models that seek unlock more domestic resources are starting to emerge. Cost-sharing models have emerged, whereby international organisations such as MSF or CHAI, or patients themselves, pay for particular drugs or part of the treatment which are made affordable. In other countries, HCV treatment has been included in national health insurance schemes. In Cameroon, PharmAccess is piloting a 'pay-for-results' financing scheme, whereby donors or governments only commit funds for positive health results. The Director of PharmAccess stated that ***"Pay-for-results is the best way to convince local governments to commit funds to HCV care, by limiting their risks".*** In Myanmar, public-private financing models are also emerging, whereby corporate companies subsidise the treatment of the employees at risk, with care delivered through MoH hospitals. Overall, financing remains the largest unanswered question to how HCV will scale-up in MSF's project countries, and beyond.

The Global Fund's position on HCV in the context of HIV co-infection has been debated. Before 2015, the Global Fund did not follow any specific guidance on the funding of co-infections and co-morbidities, prioritizing country-level decision making and allowing for case by case decisions. In 2015, however, a Board meeting acknowledged that the Global Fund would be open to financing co-infections, in situations that fit a particular framework. The financing would only be approved in countries where key interventions on HIV/AIDS, TB and malaria are already scaled; the intervention would impact a large number of people; not displace Global Fund funding from other sources; and demonstrate a strong investment case[73].

Although the Global Fund developed a policy around HCV treatment for co-infection, not all countries are clear on the application of the policy. This illustrates the difficulty of finding the right balance when addressing co-morbidities, and is good learning opportunity for Unitaid as it battles with similar issues**.**

[71] Focus group with Unitaid Senior Management Team

[72] MSF Access Campaign, 2016: "MSF open letter to the Global Fund to Fight AIDS, TB and Malaria".

[73] The Global Fund, 2015: "Thirty-Third Board Meeting Global Fund support for coinfections and co-morbidities".

One clear success of the Unitaid grant has been to catalyse momentum and financing from MSF themselves. Following the end of the grant, the vast majority of grant activities have continued through MSF core funding, and are being scaled to additional locations and treatment sites. Before the grant, there was already a growing interest in HCV within MSF, emerging in many locations directly from the demands of patients and MSF staff. However, HCV remained a low priority amongst competing demands. The availability of Unitaid funding to cover the upfront costs of HCV programming *"**created momentum and a dynamic within MSF. It would've been difficult to start [without Unitaid]".*** All MSF Operational Centres interviewed agreed that the grant accelerated HCV programming, and ***"made things happen that wouldn't have happened at the time".*** Following the grant, ***"nobody questions HCV in MSF".*** During the course of the grant, MSF committed US$20M to HCV care. MSF now implements HCV care independently in 13 countries[74]. Unfortunately, a cumulative figure on the total funding leveraged within MSF is not available.

[74] MSF now delivers HCV care in Pakistan, Iran, Armenia, Kyrgyzstan, Ukraine, India, Cambodia, Myanmar, Mozambique, Kenya, South Africa, Uganda, South Sudan.

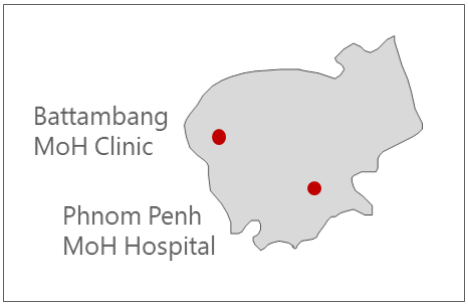
III. COUNTRY CASE STUDIES

These country case studies aim to i) highlight the results of the field visits to Cambodia and India, and ii) show how the three barriers to HCV treatment have or have not been overcome in a given national context. Unitaid's strategy on HCV (see Theory underpinning the MSF Grant) aimed to put in the place the 'building blocks' for HCV treatment at scale, but taking a country-level lens [rather than thinking globally by building block] shows how *all* of the barriers need to be overcome in one country before HCV diagnosis and treatment is unlocked at scale.

Cambodia

HCV was already a priority for Cambodia, and MSF Cambodia in 2015. Around 300,000 people are infected with HCV in Cambodia. These are mostly older citizens (median age 55), infected through unsafe healthcare practices or drug use during the Khmer Rouge regime. In 2015, MSF Cambodia started providing HCV diagnosis and treatment.

Figure 14: MSF sites in Cambodia

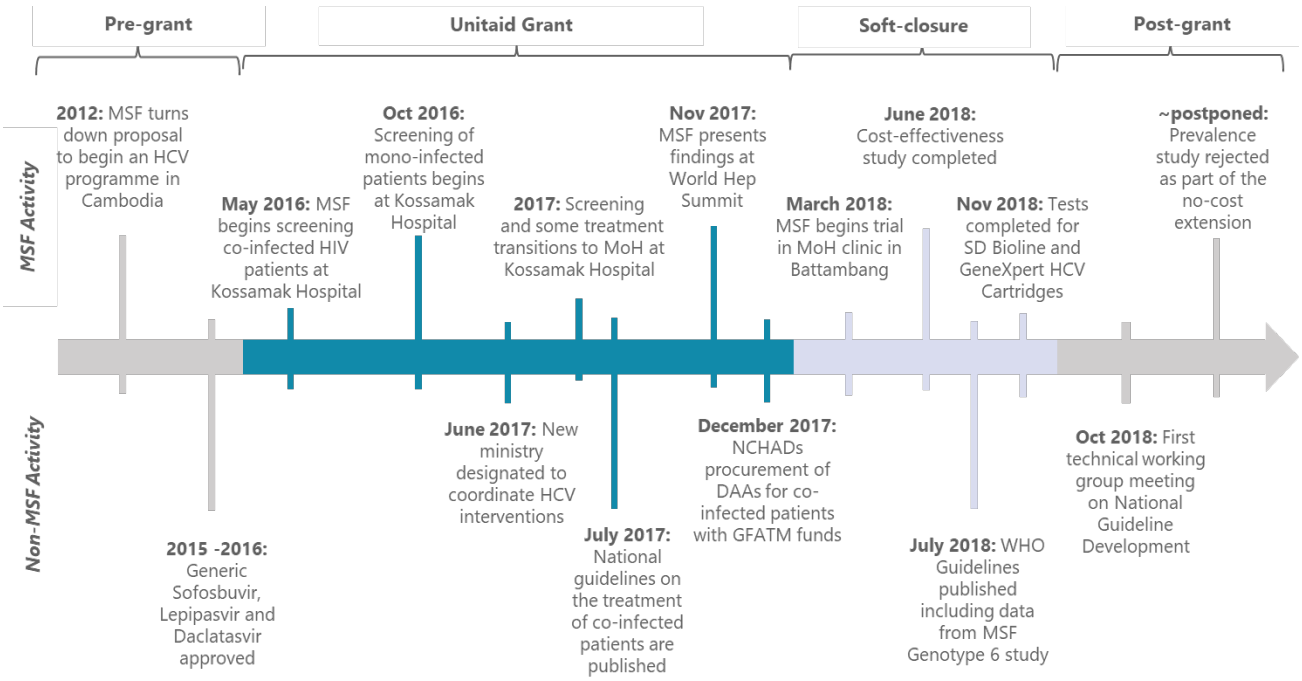


Unitaid started supporting HCV through MSF Cambodia in 2016. The grant began supporting work in Cambodia in 2016, after low-prevalence in African countries caused a pivot towards Asia. The Unitaid grant supported MSFs programmes in both Phnom Penh, where MSF operates within the state-run Kossamak hospital, and Battambang, where MSF works within a state-run clinic. Unitaid funds covered the purchase of some HCV commodities, two virology and serology field tests and the implementation of a cost-effectiveness study. The Head of the MSF mission in Cambodia noted that ***"HCV was already a priority for MSF in Cambodia, so we found a common interest with Unitaid"***.

Figure 15: Overall assessment of grant outcomes in overcoming HCV access barriers in Cambodia

Barrier	***Progress:***	***Evidence:***	***SoE:***
Affordability	Some progress	• DAA prices remain too high for the government to cover the without donor funding.	◑
Supply and Delivery	Strong progress	• MSF made important progress by developing an eight-step care model, now used by other organisations including NCHADs • MSF validated two diagnostic tests that reduce time needed for diagnosis from >1 month to five days • MSF's HCV programmes at the MoH hospital and rural clinic are both partially integrated with MoH staff	●
Demand and Adoption	Strong progress	• Evidence on Genotype 6 patients was included in WHO Global Guidelines • MSF is a key member of the technical working group on national guidelines for HCV • The ability of the MoH to scale HCV care is limited	●

Figure 16: Timeline of HCV care in Cambodia, relative to the Unitaid grant



MSF dramatically simplified the model of care relative to existing guidelines. Through a trial-and-error process, MSF pared down the 18-step model of care (based on international guidelines) to an 8-step process. The diagnostic process was shortened from over a month to five days, by decentralizing initial screening to the treatment sites, and by using GeneXpert for viral load testing. Doctors' work-load per patient was reduced through task shifting and decreasing the amount of clinical follow-up and biological monitoring. The new model only includes one visit to a doctor. MSF achieved the same patient outcomes (95% cure rate) and quality ratings for the simplified model as the full treatment. The results of this iterative process were shared widely at the World Hepatitis Summit in 2017 to support other stakeholders in finding simplified care pathways.

The grant was then used to test the pan-genotypic suitability of sof/dac. Screening and treatment to develop the model of care above found very few HIV/HCV co-infected patients: many fewer than expected. MSF and Unitaid therefore decided to repurpose the Unitaid funding to test the applicability of sof/dac to mono-infected Genotype 6 patients. Genotype 6 is restricted to South-East Asia and South China, and has been the subject of very limited research. Genotype 6 patients were treated with sof/dac and achieved the same treatment outcomes as other genotypes. This finding provided evidence that sof/dac is pan-genotypic, removing the necessity for lengthy, expensive genotype testing from the diagnostic process. These findings were included in the 2018 WHO Updated Guidelines on HCV.[75]

MSF's two treatment sites are partially integrated into state-run infrastructure. At the Battambang clinic, MoH staff run the full process, including screening, diagnosis, treatment and follow up with patients. At Kossamak Hospital, MSF work alongside the MoH staff, sharing tasks. In 2017 the MoH staff started conducting screening and diagnostic tests for HCV. MSF remains responsible for the treatment and monitoring of patients, as well as the procurement and disbursement of drugs. The MoH's involvement has increased in the last year: MSF has transitioned

[75] See 'Demand and Adoption'

around 20 patients per day to MoH doctors. However, there are some concerns about the state's capacity to keep up quality care. Diagnostic tests, for instance, are still validated through a separate MSF lab, using higher-quality viral load technology. Further, it is unlikely that the MoH will be able to take on the full cost of procuring drugs in the near term.

In parallel to the MSF clinics, the National Centre for HIV/AIDS, Dermatology and STDs (NCHADs) leads treatment of co-infected patients nationally. NCHADs has screened 20,000 individuals in the HIV cohort and initiated ~200 individuals on DAAs. Screening 20,000 people represents about 1/3 of the national HIV cohort. In contrast, MSF has initiated 10,700 mono-infected patients since 2015[76] . They leveraged existing HIV infrastructure to reduce the costs of diagnosis, and the transport of samples.

NCHADs and other actors leverage MSF's expertise and simplified care model. MSF trained NCHADs clinic staff on HCV treatment, and participated in writing national guidelines for the treatment of co-infected patients. Similarly, the WHO regional office for the Western Pacific expressed strong interest in using the evidence from the MSF model to start HCV care the other countries in the region.[77]

Questions remain around the MoH's capacity and willingness to scale up HCV care across Cambodia. In July 2017, the Cambodian MoH appointed the Centre for Disease Control (CDC) as the focal point for viral hepatitis, superseding NCHADs' role on co-infected patients. CDC has committed to development of national strategy, and brought together a technical working group to develop national guidelines for mono-infected HCV patients. 2020 is the earliest that HCV programming could be included in the health budget. However, the Cambodian government is hesitant to commit to investments with longer-term obligations. HCV does not have the high-level political support needed to catalyse action, and so it is unlikely significant national funding will be found before 2021.

Figure 17: Counterfactual - what might have happened in the absence of the Unitaid grant

MSF activities	There is strong evidence to suggest that without the Unitaid grant most MSF HCV activities in Cambodia would likely still have occurred. Unitaid's funding was additional and complementary to MSF's on-going work. When the grant began, MSF had already signed an MoU with the MoH to treat HCV patients at the Kossomak Hospital. The MSF Mission staff recall that they ***"were not seeking funds for HCV, but the Unitaid grant was a win-win situation".*** However, MSF staff did note that ***"we might not have had such a large or rapid impact had we engaged on our own, not just because of funds, but because of the partnership and legitimacy we gained through Unitaid's involvement".*** All treatment activities will continue fully under MSF funding following the grant closure. In fact, MSF have now treated 10,700 patients in Phnom Penh and Battambang, of which only 880 were treated with Unitaid-funded commodities. The grant did support cost-effectiveness and prevalence studies which were not originally planned by MSF, although the latter was cancelled under the no-cost extension.

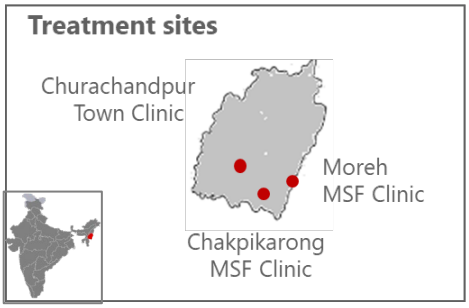
[76] Reporting from the MSF Mission in Cambodia

[77] Interview with WHO Western Pacific Region Medical Officer for Viral Hepatitis

Work by other organisations	A number of other international organisations (CHAI, ANRS, Pasteur Institute) are now active in Cambodia on HCV. Each organisation is working on different aspects of HCV care, from DAA forecasting and procurement (CHAI), testing HCV care protocols (ANRS) to clinical research on DAA resistance (Pasteur Institute). These organisations recognise MSF's ***"critical role from an implementation point of view"*** and its ***"important work in demonstrating how HCV care can work in Cambodia"[78].*** Nonetheless, these organisations would likely have engaged in HCV in Cambodia regardless of MSF's work, given the high burden in Cambodia, and that they are all active in HCV across other countries.
Government engagement	MSF's contribution is clear on initiating and catalysing government interest in HCV. MSF's research and care models were the first 'proof of concept' that HCV care was possible in Cambodia, and the government recognises that MSF has been instrumental in advocacy efforts. MSF's involvement in HCV was instrumental in supporting NCHADs to develop guidelines and to start providing HCV for the HIV cohort..

India

Figure 18: MSF sites in Manipur



In Manipur, MSF demonstrated the effectiveness of treating PWIDs through existing HIV infrastructure. MSF Amsterdam has been active in the Manipur since 2004, providing basic healthcare, HIV and TB programming. Demand for HCV care emerged bottom-up, as MSF and government staff identified the high prevalence of HCV within HIV cohorts, themselves made up of many PWIDs. PWIDs are a relatively large population group in Manipur due to proximity to the 'Golden Triangle' and associated drug trafficking**.** In 2016, MSF began diagnosing and treating HCV/HIV co-infected PWIDs through the Unitaid grant. MSF began treating HCV in the Town Clinic of Churachandpur, and subsequently in its own clinics in Chakpikarong and Moreh[79]. MSF also started self-funded projects in the Churachandpur District Hospital ART Centre and in Sholom. MSF found HIV/HCV co-infection of over 25% amongst PWIDs.

Figure 19: Overall assessment of grant outcomes in overcoming HCV access barriers in India

Barrier	***Progress***	***Evidence:***	***SoE***
Affordability	Some progress	• The MSF Access Campaign was very active in supporting the production of generics through advocacy working alongside Coalition Plus and other CSOs However, MSF still purchases at higher prices than Punjab, and the success of Indian low-prices cannot be linked solely to MSF	◑
Supply and Delivery	Some progress	• The Access Campaign played a strong role in DAA registration • MSF demonstrated high treatment outcomes for PWID co-infected patients	●

[78] Interview with CHAI in Cambodia

[79] MSF is also treating mono-infected drug-users through an NGO-run drop-in centre in Sholom, but this is not covered by the Unitaid grant.

		• MSF is delivering HCV care effectively, although the current treatment model places heavy burden on staff. • Integration of care into the state health system is limited	
Demand and Adoption	Some progress	• MSF is collaborating with Manipur State Aids Control Society (MACS) on state guidelines for HCV • MSF has limited engagement with the National Health Mission on the roll-out of the National Viral Hepatitis Control Programme (NVHCP) in Manipur.	◑

The Unitaid grant was catalytic within MSF India. *"The Unitaid grant gave us an opportunity to voice our concern around HCV, and helped us make things happen that wouldn't have happened at the time"*[80]. The grant funded the purchase of rapid diagnostic tests, GeneXpert machines, and fibroscan machines. These technologies allowed MSF to run diagnostic tests independently in Manipur, rather than outsourcing the tests to private labs in other Indian states, which had meant high costs and delays. The grant also covered a large proportion of the DAAs needed in Manipur and the salaries of seven new MSF staff members to lead the HCV treatment.

High levels of skepticism existed around the feasibility of treating intravenous drug users, who face higher risks of treatment failure and/or re-infection. MSF developed a treatment protocol for PWIDs, which differs from simplified models that that are effective elsewhere. The Manipur care model includes monthly doctor visits, psycho-social assessments, follow-up visits after 12 and 24 weeks, on-going counselling, and has recently also included harm reduction activities. The MSF epidemiologist in Manipur found evidence that a more comprehensive care-model is necessary for PWIDs to achieve the same treatment cure rates are other patients, especially when suffering from compounded chronic illnesses such as liver cirrhosis. Patient education is also a crucial cross-cutting component, as many patients demonstrate very low levels of health literacy.

MSF demonstrated the effectiveness of treating PWIDs for HCV through existing HIV infrastructure, but this model is time intensive. MSF managed to achieve high quality care outcomes (85% cure rates). However, the care model is far less simplified than in other MSF locations, and placed a heavy burden on the MSF staff. MSF staff at the district hospital reported spending over half their time treating HCV, compared to HIV and TB.

The government asked MSF to run a treatment centre in the local district hospital. In October 2016, MSF signed an MoU with the MACS to begin HCV treatment within the MoH town clinic and district hospital at Churachandpur. The MoU included a plan for transition, stating that by 2019 MACS would take-over the treatment of HCV patients, whilst MSF would continue to support diagnostic tests, and provide training to MACS staff.

Integration with the public health service "*is not as easy as it looks, as you get deeper you understand the complexity of the situation*".[81] MSF had predicted that by the end of 2018***,"a full catalytic policy change cycle from MSF pioneering HCV care to full transition of services to MoH".*** However, by late 2018 MSF continued to operate independently across all its treatment sites.

[80] Interview with MSF Programme Coordinator in Manipur
[81] Interview with MSF Programme Coordinator in Manipur

MACS is encouraging MSF to open treatment centres in additional districts, rather than planning scale-up through the national health system. The state's ability to take on HCV treatment is limited by a number of factors, including human resources, push back from hospital staff on the added burden of work, and limited financing. Further, while the state MoH has assigned a local civil society organization, the Community Network for Empowerment (CoNE), to screen up to 2,000 HIV patients in the state capital Imphal, this has yet to take place[82]. While the 2018 MSF semi-annual report portrays this as ***"solid proof of the willingness of the MoH to take over and scale up",*** it is yet to materialize. Overall, the prospect of state ownership of HCV care remains exceptionally limited.

MSF has focused its government engagement at state level, but it is the federal-level National Health Mission (NHM) who is likely to drive HCV diagnosis and treatment at scale. On World Hepatitis Day 2018, the NHM announced a NVHCP and the publication of National Guidelines on HCV[83]. The programme committed to implement HCV prevention, screening, diagnosis, treatment and monitoring across all Indian states, including Manipur. Initial plans for NVHCP stated that the Jawaharlal Nehru Institute of Medical Sciences in Imphal would be the first hospital to receive funding for staff training and active consumables. However, this programme has yet to be implemented. The state government noted small, distant states like Manipur are often the last to receive federal support.

In parallel to the clinical work in Manipur, the Access Campaign was very active in advocating for DAA access in India. In 2015, the Access Campaign began encouraging Indian generics companies to start producing DAAs locally. Furthermore, the Access Campaign played a strong role in coordinating civil society and activist efforts to advocate for the registration of three DAAs in India (Sofosbuvir (Hetero), Sofosbuvir (Mylan), SOF/VEL (Gilead)), which were officially registered in 2016. This work put in place one of the essential building blocks for HCV treatment across the country.

[82] MSF project documents, 2018: Semi-Annual Report.
[83]Ministry of Health and Family Welfare of India, 2018: "National Guidelines for the Diagnosis & management of Viral Hepatitis"

Figure 20: Counterfactual - what might have happened in the absence of the Unitaid grant

MSF activities	Without the grant, MSF staff believe that HCV care in Manipur would not have started in 2015, despite requests from patients and staff. The Head of Mission said "***the grant helped us make things happen that wouldn't have happened at the time"*** by covering the upfront costs of diagnostic technology, and financing staff and DAAs. In Maharashtra, however, a different MSF Operational Centre (OCB) started treating HCV independently of the Unitaid funding, following the Punjab model for patients in the general population [not PWIDs].
Work by other organisations	It is unlikely that local CSOs such as the CoNE and the Y.R. Gaitonde Centre for AIDS Research and Education would have started treating HCV patients independently in Manipur[84]. Across India, however, other NGOs such as the Mukh Mantri Punjab Hepatitis C Relief Fund have been highly successful in treating HCV independently of MSF.
Government engagement	The development of the National Viral Hepatitis Control Program (NVHCP) is likely to have occurred without MSF's work, as it is a ***"carbon copy of the model successfully rollout out in Punjab".*** However, the Access Campaign's strong advocacy work, alongside Coalition Plus, contributed to the mounting pressure on the government to provide HCV care. Further, MSF contributed to the affordability and registration of DAAs, two essential building blocks of large scale HCV treatment across India.

Highlights from non-visited countries

The grant was initially focused on Sub-Saharan Africa, where MSF led its strongest HIV/AIDS programmes. However, MSF found very low co-infection rates in these countries. In Kenya, for example, only 2 co-infected patients were identified amongst the original cohort of 2000 people.[85] The programme therefore pivoted to a greater focus on Asia. Scaled-down HCV pilots continued in the original African countries, focusing specifically on PWIDs.

This list provides a few highlights of particularly strong and weak contributions to overcoming the access barriers in Kenya, Uganda, Mozambique, South Africa and Myanmar. Evidence is lower in these countries, as they were not visited by the evaluators.

Figure 21: Highlights of MSF's outcomes across non-visited project countries

Barrier	***Evaluation:***	***Country Evidence:***	***SoE***
Affordability	No progress	In South Africa, MSF procured and donated DAAs to a local clinic, but no measures were developed to ensure future access to DAAs.	◑
	No progress	In Myanmar, the state acquired DAAs through a donation from CHAI, who is procuring at a higher price than MSF. However, there is no procurement plan in place for the government fund DAAs themselves.	◑
Supply and Delivery	Strong progress	In Kenya, MSF demonstrated the feasibility of treating HCV without specialist hepatologists in decentralised clinics.	◑

[84] Interview with MSF Project Coordinator in Manipur and YRG

[85] MSF project document: Annual Report 2016.

	Strong progress	In Mozambique, MSF developed a simplified model to treat PWIDs, which is now being rolled out by their civil society partners in a new project in the slums of Maputo.	
	No progress	In Kenya, Mozambique and South Africa, DAAs are not registered and MSF is importing DAAs on behalf of MoH using a special import license. In South Africa, this licence can also be accessed by doctors, but is a long and burdensome process.	
	No progress	In Myanmar, the MSF treatment model is less advanced that the MoH's (continued using Ribavirin longer than the MoH)	
Demand and Adoption	Strong progress	In Kenya, MSF advised the MoH on the content of the new HCV guidelines and trained staff around the country on their treatment model.	
	Strong progress	In Mozambique, MSF supported the government in including HCV in their 2016 Global Fund proposal. MSF also strongly advocated for the development of guidelines on viral hepatitis (B and C), and is now part of the technical working group for the development of these guidelines.	
	No progress	In Myanmar, although the MoH is implementing a National HCV plan, MSF is not engaging with them on this. MoH is rolling out a first phase of treatment for 2000 patients.	
	No progress	In South Africa and Uganda, MSF is not engaging the MoH on HCV as this is not a local priority.	

IV. OVERALL EVALUATION SUMMARY

Implementation

MSF faced expected and unexpected delays. MSF experienced delays due to manufacturers struggling to get DAAs registered across countries; finding lower co-infection rates than expected in sub-Saharan Africa and moving project activities to Asia; and longer-than-expected timelines for approval of research. Many of these delays occurred because of a first mover disadvantage faced by MSF within HCV, and overcoming these barriers was an integral part of the original objective of the project. Unitaid's flexibility as a donor was praised by multiple MSF counterparts, allowing them to make the most of the reality on the ground, pivoting their focus onto cohorts of higher HCV prevalence, as occurred in Kenya, or switching to the treatment of Genotype 6 patients, as in Cambodia. However, the delays and unexpected challenges, such as the low co-infection rate, contributed to a large underspend only US$8.2M of the original US$15M was spent at the end of the grant.[86]

Project components could have been more joined up at country level. Unitaid's funding was distributed to four Operational Centres (Amsterdam, Geneva, Paris and Brussels), and then to their respective country missions in seven countries, as well as to the MSF Access Campaign and Epicentre. The groups delivered (mostly) independent activities, each tackling different 'building blocks' of HCV treatment and diagnosis. Within a single country, at times 2-3 different MSF bodies operated simultaneously. The grant coordinator noted that ***"the country [OC] teams worked independently of each other, often even within the same country"***, though other MSF members stated ***"we work well together organically, coming together to solve common issues".*** The Operational Centres were particularly disjointed around national advocacy. In Myanmar OCA and OCG have separate MoUs with the government, different levels of engagement with government, with very little sight of each other's work. In India, OCA (working in Manipur and Uttar Pradesh) and OCB (active in Maharashtra) only advocate individually at state level, rather than collaboratively at federal level. Fundamentally this grant was partly a project, partly core support, and organised around MSF's organisational structure, rather than fully around the Unitaid-defined barriers or to address country-level barriers.

Overall outcomes might have been improved by focusing grant management as much on strategic questions as on reporting and accountability. Both Unitaid and MSF were taking a large risk in engaging in HCV at a time when the treatment for this disease was so new. Both Unitaid and MSF have donors to whom they have to report. Unitaid and MSF engaged frequently throughout the project, but these discussions too often focused on output delivery, accountability, and technical discussions around funding criteria for particular patients, rather than on the higher-level shared ambitions in HCV elimination. Across Operational Centres MSF noted ***"the level of reporting bureaucracy for the grant was high"*** and Unitaid ***"was too focused on log-frame and annual reports, rather than on maximizing their impact as a major player in HCV".*** Unitaid should ensure enough time is protected for the strategy discussions, which all too often come below the essential reporting and process conversations. This is especially true where the partnership model

[86] The underspend was also due to the drop in price of DAAs, following the $120 negotiated price.

includes core support (e.g. to the Access Campaign), and where the grantee is more like an equal partner e.g. providing lots of co-financing.

Demonstrating the feasibility of HCV care

The grant was successful in demonstrating the feasibility of HCV treatment and care in LMICs. A former MSF staff member involved at the start of the grant noted that ***"Delivering HCV care in LMICs was just an idea in 2012, Unitaid accepted it as a challenge. When we incubated the idea, others really could have thought Unitaid were just dreamers, they were really taking a risk"***. Similarly, WHO remarked that ***"No one now believes that HCV cannot be treated effectively in LMICs through simplified models, the proof of concept is now clear'***. MSF demonstrated that similar treatment outcomes to high-income countries (85%-95% cure rates) can be achieved in low-resource settings, with far fewer clinic visits and without the need for specialised hepatologists. This model reduced the burden of care on both local health facilities and low-income patients. The WHO Western Pacific office noted that ***"we are taking the results of MSF's HCV pilot very seriously. They are the only organisation demonstrating that a simplified service model can work in decentralised and limited resource settings, and this is very useful for other countries to learn from"***.

The grant made good progress against most of the 'building blocks' that underpin the ability to deliver treatment and care at scale, but diagnostics remain a challenge. As part of demonstrating the feasibility of treatment and care, MSF helped to put in place most of the 'building blocks' needed to ultimately take this to scale: technical know-how, affordable drugs, and policy guidelines. However, diagnostics remains the least 'complete' of the building blocks. While RDTs are now available at US$1 per test and easily administered in the field using capillary blood, GeneXpert remains too slow and expensive for use at real scale and requires certain operating conditions which make it difficult to decentralise. MSF missions also faced challenges with waste management of GeneXpert cartridges, which resulted in high costs to transport waste for safe disposal. Funded by Unitaid, FIND is one of the only organisations focusing on this challenge.

Enabling scale-up

The grant made mixed progress in securing the transition and scale-up of grant activities. The grant did not initially focus on putting in place HCV treatment at scale, and "***there was no structured thinking about what the route to scale would look like"***[87]**.** In 2016, with Unitaid's strategic refresh, MSF was encouraged to think about potential for scale-up, but the grant was not significantly re-designed. Unitaid recognized that the progress towards scale would be limited with a real focus on scale in place for only half of a three-year grant. MSF actively engaged MoH's on HCV, and has been largely successful in putting HCV on the public health agenda in their project countries. However they have not yet been successful in lobbying governments to secure domestic financing. The Head of the MSF Mission in India remarked that ***'It takes 10 years to eliminate a disease. We've had three years so far, and are making impressive progress compared to the scale-up of HIV'***. HCV programmes started in India in 2016 through MSF and other CSOs such as the Mukh Mantri Punjab Hepatitis C Relief Fund, and by 2018 India committed funding to a national hepatitis programme. However, this progress cannot be fully attributed to MSF. Cambodia has also seen some important progress, with a new Ministry department designated to spearhead HCV initiatives in 2017, and a

[87] Focus group discussion with Unitaid Senior Management Team

technical working group (including MSF) convened to develop a national strategy. In other countries, like Kenya, MSF is working to bring together HCV and HBV, which is a much bigger health burden.

The closing of the grant did not result in many activities stopping, but some opportunities have been missed. Most programmes are continuing under MSF's own financing, on account of the growing momentum around HCV within MSF, and MSF's commitment to delivering clinical care to those in need. In Cambodia, Unitaid interrupted the funding of the prevalence study, which was completed in August 2019 through MSF funds. A few programmes will be scaled down or closed, including the treatment of co-infected patients in Kenya at the Médecins du Monde PWID clinic, and the new HCV programme in Uttar Pradesh. However, the larger opportunity cost, as expressed by MSF staff, is Unitaid's potential to help sustain the momentum created around HCV in project countries. While this grant made important first steps, ***"it is very important for donors to remain involved to keep HCV in the spotlight and put pressure on governments to delivery the national strategies they have implemented or promised"***[88]**.** In Cambodia, Unitaid's legitimacy and advocacy efforts could help push forward the technical working group's progress towards a national strategy[89], and Unitaid's catalytic funding might help mobilise domestic resources in the 2020 national health budget. In India, Unitaid's involvement could help prioritise the more distant and challenging Indian states, such as Manipur, where the burden of HCV is particularly high, but the National Health Mission is unlikely to reach in the near future.

A catalytic role within MSF

The grant has played a catalytic role within MSF, accelerating the development of HCV programmes and increasing cooperation amongst its different bodies. Even before the grant, MSF's interest in HCV was growing because of the availability of DAAs as an affordable, simple cure. However, HCV still faced competition from other priorities within MSF, particularly from issues more closely aligned to MSF's core mission of serving in emergency crisis settings. Staff members across MSF noted that the Unitaid grant created momentum around HCV. Beyond funding, Unitaid's involvement lent legitimacy to HCV, helping to secure buy-in from MSF management. HCV programming is now being implemented in 13 countries[90]. MSF Holland noted that ***"starting HCV treatment had been a difficult topic within MSF before the grant. Positive treatment results, cheaper treatment and the availability of Unitaid funding all helped us engage".*** In addition, the grant supported collaboration between, and alignment of different Operational Centres, as well as the Access Campaign and Epicentre. MSF "HCV referents" noted that the grant ***"forced different MSF bodies to sit around a table and organise themselves around HCV, developing a common vision and easing cooperation".*** While was not necessarily an intended effect of the grant, Unitaid did play a strong part in kick-starting MSF's involvement in HCV, earlier than would have otherwise happened.

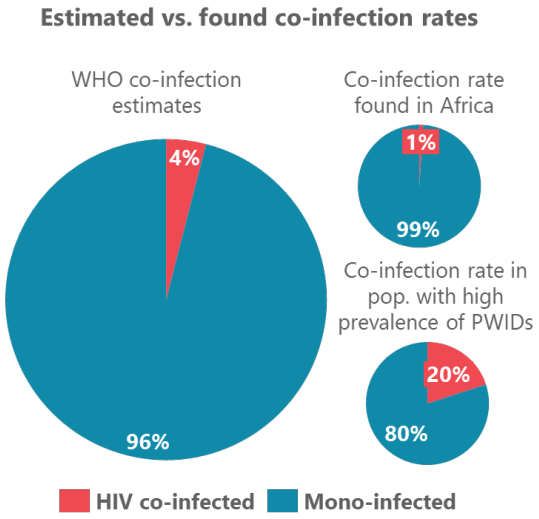
[88] Interview with FIND.

[89] While MSF's work has been instrumental in urging the government to set up a technical working group on HCV, more work will be required to spearhead this group and push forward the development of a national strategy. See Cambodia section for more.

[90] Pakistan, Iran, Armenia, Kyrgyzstan, Ukraine, India, Cambodia, Myanmar, Mozambique, Kenya, South Africa, Uganda, South Sudan

HIV/HCV co-infection

Figure 22: Co-infection rates



The lower than expected co-infection rates found in most project countries raise some important practical, ethical and strategic questions. The most recent estimates from WHO suggest that ~2.8M persons with HIV are co-infected with HCV, out of a total of 71M people infected with chronic HCV[91]. Within the general population in project countries, MSF found even lower co-infection rates: under 1% in African countries, and around 2-3% in Cambodia and Myanmar. In Manipur, MSF found 20% co-infection rates amongst the HIV cohort, but also noted that over 60% of these were PWIDs. MSF staff remarked that ***"it is easy to integrate HIV and HCV care for PWIDs, but for other patients it doesn't really make sense".*** Many MSF missions, as well as MSF's partners and local stakeholders, spoke of their concerns over the grant's focus on co-infected patients. Whilst the Unitaid Secretariat was perceived to have interpreted their organizational mandate as practically and openly as possible, and there was an agreement in place with MSF for them to cover the cost of any mono-infected patients identified, it still caused issues with perception. By focusing on screening HIV cohorts, MSF was concerned that they were being perceived as discriminatory in their treatment of HCV. The criterion on co-infection also created practical issues around re-infection, as turning away mono-infected partners or families of co-infected patients could result in the re-infection of that patient.[92] In short, a number of interviewees noted the grant highlighted the limitations of focusing on co-infection as a way to catalyze HCV care in the broader population.

Evaluation against Unitaid's KPIs

Dalberg evaluated the MSF grant against the Unitaid's KPIs. These KPIs were developed in 2016, after the start of the grant and are hence being applied retrospectively. The evaluation against the OECD DAC criteria (relevance, effectiveness, efficiency etc.) is embedded throughout this document e.g. putting in place most of the building blocks for HCV care shows the grant was highly relevant.

Figure 23: Evaluation of the grant against Unitaid KPIs

KPI 1: Adding Value to Global Response	
Metric	*MSF Contribution*
1.1 Increasing Public Health Impact (Additional number of lives saved and/or number of infections averted, 2-year projection)	- Projected public health impact cannot be determined for this project. - We have little evidence that HCV diagnosis and treatment will be scaled up over the next two year in the project countries. This is primarily due to the lack of financing options for HCV, which would require high amounts of domestic resources to be diverted to the issue by the MoH.

[91] WHO, 2018: "Progress report on access to Hepatitis C treatment"

[92] It is important to note that no mono-infected patients were denied treatment: simply the perception of starting from HIV-HCV co-infection caused challenges during the project implementation.

1.2 Generating efficiencies and savings (Financial savings ($) and health system efficiencies ($), 5 year projection)	- The project was not designed to generate financial savings, as scaling-up HCV care will result in more financing by donors or countries. - Some efficiencies can be expected if countries are able to purchase diagnostics and treatment at affordable prices, as a result of the MSF Access Campaign's efforts. Care model simplifications, such as reducing the number of clinical visits, can also reduce the resources needed.
1.3 Delivering Positive Returns (Return on Investment = $ Benefits / $ Costs)	– The return on investment for this grant could not be calculated due to uncertainties around public health impact.
KPI 4: Overcoming Market Barriers	
Metric	*MSF Contribution*
4 Total number of critical access barriers overcome during the strategic period	MSF contributed to progress against all three access barriers, making the most progress on 'Supply & Delivery'. - **Affordability:** MSF moderately contributed to improving the affordability of HCV care. Through their advocacy efforts and civil society engagement, the Access Campaign influenced the production of generic DAAs, particularly in India. **Supply and Delivery:** MSF successfully demonstrated the feasibility and technical 'know-how' of providing HCV care in LMICs, leading to best-practices which have been adopted widely by other organisations to provide quality, efficient treatment to patients in LMICs. **Demand and Adoption:** MSF drove the adoption of quality HCV care by contributing to national and global guidelines. However, the implementation of these guidelines at national scale was limited, given time and resource constraints.
KPI 5: Scalability	
Metric	*MSF Contribution*
5.1 Securing Funding (Proportion (%) of project countries where future funding has been secured at grant closure through partners and countries)	- At the end of the Unitaid grant, MSF secured internal funding to continue operations in their current sites across 4 of 7 project countries. MSF will fund the continuation and expansion of operations in Cambodia, Manipur and Myanmar, while in Mozambique treatment will resume under a new MSF project in the Maputo slums. In Kenya, Uganda and South Africa programmes were interrupted to do a limited HCV prevalence, rather than a lack of funding. Only one significant programme was discontinued due to lack of funding, being MSF's new HCV programme in Uttar Pradesh. - Beyond MSF's own funds, very limited additional financing was secured.
5.2 Scaling-up coverage (Additional number of people who benefit from a better health product or approach, 2 years after the grant end)	- MSF has contributed to putting in place the building blocks necessary for scaling up HCV care, including affordable DAA prices, treatment models, evidence on treatment outcomes and global and national guidelines. - However, lack of donor and/or national financing /commitment to HCV is preventing scale-up of HCV diagnosis and treatment.

V. RECOMMENDATIONS FOR UNITAID

Dalberg's recommendations are based exclusively on the evidence emerging from the MSF grant. We are aware that Unitaid is currently reviewing its strategic thinking on HCV, including its role in financing and how to address co-infection. These grant-informed recommendations will hopefully add something to this process. They are just one source of input, alongside other important considerations, including strategic fit with Unitaid's broader mission, the actions of other stakeholders, donor requirements and preferences, and more.

1. Grantee facing recommendations

1.1 **The partnership model (points of contact, conversations, reporting) should be fit for purpose relative to the type of engagement that Unitaid has with the grantee.** Unitaid was brave and bold when it decided to tackle HCV in 2014 and commit significant resources to answer important, new questions. The project designed was in essence a co-financing agreement with MSF to jointly pursue improved HCV care in LMICs. Unitaid actually contributed the minority of the project funding, around a third in total. Despite this co-financing set-up, Unitaid managed the project like a typical grant, whereby Unitaid covers costs for discreet activities. Unitaid's partnership model with MSF was not fit for purpose: reporting focused more on downward accountability than on higher-level conversations around maximizing the grant's impact and responding constructively to what both MSF and Unitaid were learning as partners. Of course, Unitaid must be able to oversee relevant parts of the project in order to safeguard Unitaid's key interests and ensure visibility on the use of its funding. But developing effective and efficient models for special engagements like this one that better reflect the nature of the engagement with each grantee can help unlock synergies between the two organizations, and bring about a more productive working relationship, ultimately increasing Unitaid's impact. This is a live discussion within Unitaid, with new guidelines from October 2018 on partnership models for Special Engagements.

1.2 **Unitaid should consider whether a focus on HIV-HCV co-infection fits with their level of ambition in the HCV space.** Unitaid's entry point to HCV is through HIV co-infection (though this perspective is broadening within the organization). During the MSF grant, it became apparent that this focus raises practical, perceived ethical and reporting complications both around screening and treating HCV mono-infected patients, and around treating those for whom HCV is just one part of their health challenges. Nowhere was this clearer than in treating PWIDs, who might be in need of much more holistic care than just HIV and HCV treatment. Unitaid responded to these challenges by stretching their mandate as far as possible, agreeing to cover the screening of all patients regardless of their HIV status, financing treatment for certain mono-infected groups, and encouraging MSF to fund treatment for the diagnosed mono-infected patients. Despite these efforts, questions remain around whether Unitaid's strategic ambitions for HCV can in fact be realized through an approach linked solely to co-infection. Moving forward, Unitaid should define and communicate externally its level of ambition within the HCV space, and consider whether a focus on co-infection is a barrier to achieving its objectives.

2. Recommendations to inform new investments in HCV

2.1 **The scalability of HCV care is still hindered by two main 'gaps': diagnostics and financing. Unitaid should reflect on whether it is doing enough on diagnostics, and should consider its role in financing.** This grant made significant progress in putting in place many of the 'building blocks' for HCV diagnosis and treatment in LMICs. As one interviewee mentioned, ***"effectively the feasibility has been pretty much worked out."***[93] However, two components of the HCV care model still lag behind: diagnostics and financing. Unitaid should consider focusing future HCV efforts on these issues, by assessing the existing gaps in the two areas, Unitaid's potential added value, and their current levels of engagement.

2.1.1 For diagnostics, there is still a gap at the intersection of technology and delivery models. A detailed review of the diagnostic landscape and role for Unitaid was not in scope, but should be prioritised given the limited progress relative to other areas.

2.1.2 Financing is hindered by the lack of a large international donor to take interventions to scale, leaving the burden to domestic health resources. Recent discussions have considered Unitaid's role within financing, and (assuming work on diagnostics is on track), this seems the key area to continue to discuss and debate.

2.2 **As part of its strategic thinking on taking HCV treatment to scale, Unitaid should ensure a 'systems change' lens is applied when designing grants and portfolio structures.** As Unitaid knows, taking HCV treatment to scale is fundamentally different to demonstrating the feasibility of HCV treatment[94]. Achieving national scale treatment is a systems challenge, and can be thought of like a chair: even if three legs are in place, without the fourth, the chair cannot stand. Treatment at scale requires funding, political willingness, staff capacity, technical know-how, effective drug markets, equipment, policy change and more. The MSF grant has put in place some of these building blocks, across different countries, but was structured in a way that fundamentally limited its ability to consider the way that all factors interacted in one country.

It not in Unitaid's remit to tackle all aspects of HCV care. However, as Unitaid moves towards a greater focus on sustainability it should adopt this 'systems-change lens' in designing its interventions. This will help map out a pathway to scale in much greater depth than for this grant, with potential implications (at grant and portfolio level) including:

- Grant/portfolio governance and strategy should focus at a country level[95] (Which legs of the chair are in place? Which are not?) rather than following the grantee's organizational chart.
- Grant/portfolio activities should focus (as much as is possible or needed) within one country. For example, without DAA registration, take-up of technical know-how at

[93] Interview with DNDi

[94] Unitaid recognises this, noting in 2017 a "strategic consideration to direct future Unitaid HCV investments towards a more holistic, but targeted elimination approach in specific countries" (Cited in the 2017 Annual Narrative Report)

[95] At a portfolio level, Unitaid may well want to work in multiple countries. In which case, the strategy and governance should include an overall coordination element, as well as focus at country level (across multiple countries)

scale is very unlikely. Similarly, without a push for funding, registering DAAs still will not lead to scale.

- It is very unlikely one organization will be able to put in place all of the building blocks on its own. A consortium (whether formal, or more of a loose alliance) is likely needed. For example, countries with strong civil society demand for treatment have tended to be effective in securing domestic resources. Similarly, Unitaid could strategically align its separate HCV grants into a single portfolio-level consortium, ensuring they complement each other and tackle different aspects in the same context (e.g. focus on advocacy and implementation in the same country).
- Grant/portfolio reporting should focus on the country level, with joint reporting on progress, gaps and strategies for 'standing up the chair' in that country.

ANNEX

Annex I: Interview list

In-country interviews	Dr. Ly Peng Sun	Cambodia MoH NCHADS
	Dr. Ny Chanty Dr. Dimanche	Cambodia MoH Kossamak Hospital Doctors
	Dr. Oliver Segeral	Cambodia ANRS
	Dr. Philippe Dupont	Cambodia Pasteur Institute
	Tour Sovannary	Cambodia Khana (CSO)
	Marie Ryan	Cambodia Global Fund
	Caroline Barret	Cambodia CHAI
	Mr Radhabinod Sharma	Manipur MoH MACS
	V. Vumlunmang	Principle secretary, government of Manipur
	Mr. Abhrahim	Manipur MoH MACS
	Dr. Tonsing and clinical staff	Manipur Ccpur MoH District Hospital,
Global stakeholders	Greg Dore	Kirby Institute
	John Simon	PharmAccess
	Isabelle Andrieux-Meyer	DNDi HVC Referent
	Sonjelle Shilton	FIND
	Mark Bulterys	WHO HQ
	Dr. Serongkea	WHO Cambodia
	Naoko Ishokawa	WHO Division of Communicable Diseases, World Health Organization Regional Office
	Nicole Seguy	WHO India
	Po-lin Chan	WHO Western Pacific
	Jessica Tepor	CHAI Global Hepatitis Programme
	Maria Donatelli	C Plus Coalition
	Esteban Burrone	Medicine Patent Pool
MSF staff	Camille Baillat, Sophie Arbona	Current and former grant coordinator
	Sabrina Sharmin	India Head of OCA Mission
	Mickael Le Paih, Jean Philippe Dousset	Cambodia Head of OCP Mission
	Francesca Quinto, Camilo Gomez	Myanmar Heads of OCG and OCA Missions
	Yvonne Nzomukunda	Kenya OCB Medical Coordinator
	Lucas Molfino,	Mozambique Head of OCG Mission
	Amir Shroufi	South Africa Head of OCB Mission
	Juliet Mwanga	Uganda Epicentre Director
	Jessica Burry, Leena Menghaney	Access Campaign
	Anne Loarec	Epicentre M&E officer
	Aude Nguyen, Suna Balkan	OCP HCV Referent
Unitaid staff	Vincent Bretin	Leader, Results Team
	Loveena Dookhony	M&E Manager, Results Team
	Jemmy Dopas	Grant Finance Officer, Finance & Administration Team
	Tijana Dragicevic	Officer, Results Team
	Janet Ginnard	Leader, Strategy Team
	Judith Polsky	Team Leader, Operations
	Romane Theoleyre	Programme Officer, Operations Team
	Karin Timmermans	Technical Manager, Strategy Team

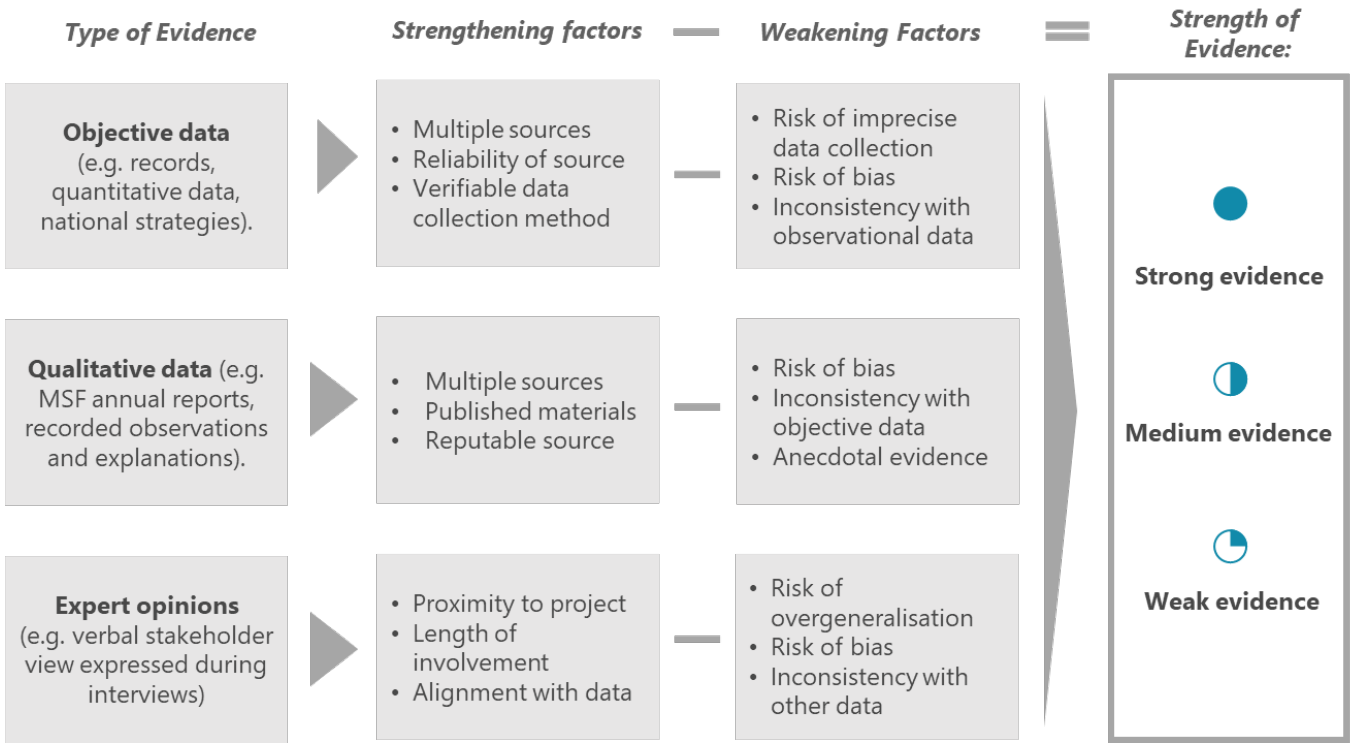
Annex II: OECD DAC Framework Evaluation

OECD DAC Framework	
Metric	*Grant Evaluation*
Relevance *The extent to which the activity is suited to the priorities and policies of the target group, recipient and donor.*	**Highly Relevant** The objective of the grant, to improve access to HCV care to LMICs, is still highly relevant. Globally, 71M people have chronic HCV, of which 73% are in LMICs and are highly unlikely to receive treatment. Global interest in HCV care has increased, particularly linked to the falling costs of treatment. In 2016, the World Health Assembly set the goal of eliminating viral hepatitis as a public health threat by 2030. MSF were amongst the first actors to implement a programme to reach this objective, and made a meaningful contribution to the space. The grant activities tackled three critical access barriers to HCV care: 'affordability', 'supply & delivery', and 'demand & adoption'. A wide variety of activities were conducted, including leading advocacy efforts and procurement negotiations to improve affordability, simplifying the delivery of care through new treatment models, and influencing national and global guidelines to adopt HCV care at scale. While the grant was not designed around these access barriers, (which were retrospectively fitted) overall the activities were well aligned with the intended outcomes.
Effectiveness *A measure of the extent to which an activity attains its objectives.*	**Mostly Effective** During the grant, MSF experienced several delays. These were caused by a number of factors, including: manufacturers struggling to get DAAs registered across countries; lower-than-expected co-infection rates in sub-Saharan Africa; project activities shifting to Asia; and longer-than-expected timelines for approval of research. However, many of these delays occurred because of a first mover disadvantage faced by MSF within HCV, and overcoming these barriers was an integral part of the original objective of the project. Despite these delays, the grant still achieved the majority of its outputs, including treating screening ~50,000 patients and initiated 2200 on DAAs, developing three simplified care models, field-testing two diagnostics tests, producing evidence on GT 5 and 6 patients and more. Unitaid's flexibility as a donor was praised by multiple MSF counterparts, allowing them to make the most of the reality on the ground, e.g. pivoting their focus onto cohorts of higher HCV prevalence, as occurred in Kenya, or switching to the treatment of Genotype 6 patients, as in Cambodia. Operationally, however, the programme faced some challenges due to the MSF's internal management structure. Unitaid's funding was distributed to four MSF Operational Centres (Amsterdam, Geneva, Paris and Brussels), and then to their respective country missions in seven countries, as well as to the MSF Access Campaign and Epicentre. While some ad hoc cooperation did occur between the units of MSF, more strategic alignment could have led to more effective national interventions.

Efficiency *Efficiency measures the outputs -- qualitative and quantitative -- in relation to the inputs. It is an economic term which signifies that the activity uses the least costly resources possible in order to achieve the desired results. This generally requires comparing alternative approaches to achieving the same outputs, to see whether the most efficient process has been adopted.*	**Somewhat Efficient (difficult to assess)** Overall, the grant achieved its intended objectives despite the large programme underspend: only US$8.2M of the original US$15M was spent at the end of the grant. This was partly due to the decreasing price of commodities, particularly the $120 price for DAAs negotiated in 2016, which made it increasingly cost-efficient to treat patients for HCV. It is very challenging to determine the relative efficiency of each activity within the grant. For HCV to be adopted at scale, different interventions needed to occur simultaneously. 'Systems change' can be thought of like a chair: even if three legs are in place, without the fourth, the chair cannot stand. Therefore, the grant resulted in a number of different outputs like 'apples and oranges', which cannot be directly compared. Some activities, such as advocacy, simply cost less than others, like developing and testing a clinical model. However, all these elements were necessary to pursue the objective of the grant.
Impact *The positive and negative changes produced by a development intervention, directly or indirectly, intended or unintended. This involves the main impacts and effects resulting from the activity on the local social, economic, environmental and other development indicators. The examination should be concerned with both intended and unintended results and must also include the positive and negative impact of external factors, such as changes in terms of trade and financial conditions.*	**Somewhat Impactful** The projected public health impact and financial savings of this project cannot be determined, as we have little evidence of where and how HCV diagnosis and treatment will be scaled up over the next few years. However, we can assess the fact MSF contributed to putting in place several building blocks necessary for scaling up HCV care, including affordable DAA prices, treatment models, evidence on treatment outcomes and global and national guidelines. <u>Affordability:</u> The grant aimed to ensure that DAAs became affordable enough for LMIC governments to scale procurement without causing unreasonable financial burden. The MSF Access Campaign was active in two main areas: increasing price transparency and encouraging the production of affordable generic drugs. However, current DAA prices remain unaffordable for most LMIC governments without funding from international donors. <u>Supply and Delivery:</u> The grant sought to develop and introduce simplified and cost-effective diagnosis and treatment methods, to reduce the burden of HCV care on LMIC health systems. Overall, MSF had a strong effect on demonstrating the feasibility of HCV care in LMICs, by developing three effective simplified care models, field-test near PoC (point-of-care) virology and serology tests, and encouraging DAA registration. However, MSF only made limited progress in integrating these care models into the local health systems in their project countries. <u>Demand and adoption:</u> Overall, the evidence generated by MSF made a strong contribution to national and global HCV guidelines, but only limited effect on driving the financing and implementation of HCV care at scale within countries. This is partly due to the fact that launching new national programmes in health within LMICs is a

	challenging, and lengthy process, typically requiring longer time-scales than the grant provided.
Sustainability *Sustainability is concerned with measuring whether the benefits of an activity are likely to continue after donor funding has been withdrawn. Projects need to be environmentally as well as financially sustainable?*	**Sustainable within MSF, but not readily scalable through MoH's.** The Unitaid grant successfully catalysed financing for HCV from MSF itself. Following the end of the grant, the vast majority of grant activities have continued through MSF core-funding, and are being scaled to additional locations and treatment sites**.** As of 2018, MSF is financing HCV care independently in 13 countries, including the grant-project countries and 6 new countries. However**,** the HCV space lacks a large donor to finance the scale-up of interventions. Although MSF conducted some high-profile global advocacy efforts, the international financing landscape for HCV remains sparse. The grant activities raised some challenging questions concerning the availability of domestic financing as a route to scale for HCV, particularly in resource-constrained LMICs.

Annex III: Framework for assessing the strength of evidence



Annex IV: Terms of reference for the evaluation

1. Background

Unitaid awarded Médecins sans Frontières (MSF) a 3 year grant (January 2015-December 2017) for the project "*Ensuring access to the Hepatitis C (HCV) treatment revolution for HCV/HIV co-infected patients in LMICs*". The overall cost of running the project was estimated at US$48 million, with US$15 million committed by Unitaid and MSF providing the rest.

The project was intended to demonstrate how simplified models of care can treat people co-infected with HIV and HCV in resource-limited settings. Note that the original project countries targeted included India, Iran, Kenya, Mozambique, Myanmar, Uganda and Ukraine. However, during the course of implementation, activities were scaled down in some African countries due to lower-than-anticipated HIV/HCV co-infection prevalence, were never launched in Iran, and activities were instead initiated in Cambodia and South Africa. From the outset, MSF committed to develop transition strategies for each country, and to track sustainability over the course of project implementation. Furthermore, MSF claimed, the project would generate evidence / impact that would inform policies beyond project countries.

The investment was approved as part of Unitaid's overall commitment to work with countries to simplify and decentralize the diagnosis and treatment of HCV within the context of HIV co-infection.

2. Goal, outcome and outputs

The goal, outcome and outputs of the Project were changed during the course of implementation. The original and revised definitions are presented below.

ORIGINAL (2015)	REVISED (2017)
Goal: Improve access to HCV diagnosis and treatment in Low & Middle Income Countries (LMIC)	Goal: *No change*
Outcome: Improved availability of products for HCV diagnostics and treatment in L&MICs	Outcome REVISED TO > Simplified, adapted and affordable HCV care models are developed for adoption in LMIC
Outputs - Output 1: Feasible treatment and diagnostics algorithms started in 7 L&MICs - Output 2: Build a market of affordable HCV products - Output 3: Quality-assured DAAs registered in beneficiary countries - Output 4: Validation of serology and virologic tests for co-infected patients - Output 5: Information on HCV treatment and diagnostic market made available	Outputs - Output 1: REVISED TO > Diagnosis and Treatment of HIV co-infected patients implemented in LMICs - Output 2: *No change* - Output 3: *No change* Output 4: *No change* - Output 5: *No change*

3. Objectives of the Consultancy

Under this Terms of Reference (ToR), the Evaluators will provide Unitaid with an assessment of the programmatic implementation of the project with a particular focus on the project's overall contribution to public health impact and the part it played in improving access to HCV diagnosis and treatment in project countries captured by the outcome, outputs and activities performed.

4. Scope of work

The Unitaid Grant Evaluation Framework aims to assess the grant relevance, effectiveness, efficiency, impact and lessons learned (see annex 1). These criteria are same as the Organisation for Economic Co-operation and Development's (OECD) Development Assistance Committee (DAC) standard evaluation criteria[96] and the Independent Commission for Aid Impact's (ICAI) updated assessment framework[97] with emphasis on lessons learned and value for money/impact.

The Evaluators will review the overall goal and outcome of the project, its outputs (listed above) and the activities against each output against the questions in Annex 1. The Evaluators should consider project achievements and lessons learnt as a result of the implementation of the project.

Specifically, the Evaluators are expected to

(1) Conduct an independent assessment of the results reported by MSF against the stated original and revised outcomes and outputs of the project.

(2) Assess contribution/attribution, i.e., causal linkage between MSF HCV grant activities and the significant results reported under the project. This should include a simulation of the counterfactual in the absence of Unitaid funding across all dimensions of the results.

(3) assess scalability by evaluating the extent to which MSF achieved their original stated aim to "bring about the necessary conditions for subsequent sustainable scale-up in project countries and beyond" (project plan 2015), paying particular attention to highlighting:

(i) the extent to which grant activities have been scaled up across project countries and beyond;
(ii) identified factors which may have contributed towards, or limited scalability and transition.

Moreover, among the Strategic Key Performance Indicators (KPIs) of Unitaid which demonstrate Unitaid's impact to support direction-setting and accountability, and to provide clarity on Unitaid's role and mandate within the global health response, KPIs 1.1, 1.2, 1.3, 4 and 5[98] are specifically in scope for this evaluation.

The main critical access barriers (as defined by Unitaid's strategic KPI) that the grant aimed to address were:

- Demand and adoption: Countries, programmes, providers (e.g. healthcare providers, retailers) and end users rapidly introduce and adopt the most cost-effective products within their local context through MSF's demonstrating its care models and overcoming regulatory barriers in registration;
- Affordability: The medicine or technology is affordable at the lowest possible price that is sustainable for suppliers and does not impose an unreasonable financial burden on governments, donors, individuals or other payers through MSF's work on price reduction of DAAs and simplified diagnosis and;
- Delivery of HCV diagnostics and treatment by generating evidence to inform national and international guidelines.

5. Target respondents

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

- The lead grantee – Médecins sans Frontières;

[96] http://www.oecd.org/dac/evaluation/dcdndep/39119068.pdf

[97] http://icai.independent.gov.uk/tag/assessment-framework/

[98] KPI 1.1: Increasing public health impact; KPI 1.2: Generating efficiencies and savings; KPI 1.3: Delivering positive returns; KPI 4: Overcoming market barriers and; KPI 5: Scalability. For more information, refer to https://unitaid.eu/assets/Unitaid-strategy-2017-2021_Dec-2017.pdf

- In country partners / stakeholders such as key decision makers at the country level, officials (high and mid-level) at relevant Ministries;
- Wider stakeholder group(s) that are indirectly involved with the MSF Grant such as World Health Organization, Donors, Technical Working Groups, and civil society groups and;
- Relevant staff at the Unitaid Secretariat.

➢ **ADDITIONAL NOTES on Target Respondents:**
  - To assess contribution of project activities, the focus of target respondents should be external stakeholders and partners rather than grantee or Unitaid secretariat;
  - Evaluators are encouraged to do focus group interviews when relevant and;
  - The Evaluators and Unitaid will agree on the 2-3 countries to do country visits.

6. Methodology, place of work and frequency of interaction

The grant evaluation methodology will involve a combination of document reviews and key informant interviews with the relevant stakeholders. Evaluators will undertake a review of the grants using the grant documents such as: Grant Agreement, and Annual and Semi Annual Reports and any other grant related material.

The evaluators will work remotely and will be required to travel to two or three of the project countries (India, Myanmar and Cambodia). Progress in the remaining countries where country visits will not be done will be assessed through a desk review including teleconference interviews. The Evaluators will take the lead to identify potential stakeholders to interview in all 7 project countries[99] and will be assisted by Unitaid and MSF if needed. It is preferred that the evaluators have either a local presence in the project countries or have access to local counterparts that can assist the Evaluators in understanding the HIV/HCV landscape of the country and help identify stakeholders to interview.

Evaluators will be expected to meet with the Unitaid team in Geneva for the purpose of the evaluation prior to the first draft and for presentation of the final findings. In addition, the Unitaid focal point for the evaluation will have weekly updates with the Evaluators.

7. Qualification and skills

The Evaluators will have prior experience in designing and leading evaluations, data analysis skills, and technical competence in the field of HIV/HCV diagnosis and treatment

Specific expertise in the following areas is required:
- Experience in conducting evaluations of grants in the HCV and/or HIV field and familiarity with WHO guidelines on HCV diagnosis and care
- Experience with assessment of public health and financial impact
- Experience in Monitoring & Evaluation in the public health sector;
- Proficiency in English language.

8. Deliverables

The Evaluators will be required to do around work over a time span of 12 weeks, with the indicative following dates:

Deliverable	**Time**
1. An Inception report outlining the process for the evaluation including a proposed methodology/approach to the review, draft assessment/evaluation tools, a work plan and timeline and a list of interviewees.	October 31st, 2018

[99] Cambodia, India, Kenya, Mozambique, Myanmar, South Africa and Uganda

2. Country visit (2-3 countries).	November 7th-16th, 2018
3. A first draft evaluation report for review and comments by Unitaid.	December 5th, 2018
4. A Second Draft evaluation report that incorporates Unitaid feedback to be shared with Unitaid and the grantee.	January 11th, 2019
5. A virtual or in-person presentation to Unitaid secretariat on key findings and recommendations.	January 18th , 2019
6. A final evaluation report.	January 25th, 2019

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

9. Payment Terms and schedule

For professional fees, payment will be made following satisfactory completion of the deliverables and of corresponding detailed invoices indicating number of days worked per team member and deliverables.

For travel costs, payment will be made in accordance with WHO rates and upon submission of invoices indicating actual travel costs with proof of payment. Evaluators are responsible to organize all logistics of travel, including hotel booking and local transportation.

ANNEX 1: Unitaid's Evaluation Framework

Relevance:
1. Are the outcome(s) and impact(s) of the grant aligned with Unitaid's overall mission to contribute to the scale up of and access to treatment for HIV/AIDS, malaria and TB for the most disadvantaged populations in developing countries using innovative global market based approaches? 2. How did the grant contribute to one or more of Unitaid's strategic objectives?
Effectiveness:
1. Are the outputs of the grant consistent with the objectives and expected outcomes as described in the project plan? If changes have been made, has the Unitaid Secretariat been involved in discussions and decision making on the changes? 2. Were the outputs of the project for the evaluation period fully achieved within the timeframe and budget specified in the initial project plan? 3. What are the main factors influencing the achievement or non-achievement of the outputs or overall outcomes across all countries and within each beneficiary country? 4. What factors have been considered to ensure that value for money has been achieved?
Efficiency:
1. Have the grant implementer and co-implementers ensured project planning, implementation and assessment in collaboration with the national authorities? Can the grant implementers and their partners demonstrate that national authorities were aware and participating in grant activities at the national level? 2. How cost efficient and cost effective was grant implementation? 3. Were challenges raised with the Unitaid Secretariat in a timely manner and did the Secretariat participate in resolving these challenges? 4. Was the grant's procurement model designed to identify and solve procurement-related problems (where applicable)? 5. Were there any concerns or reported instances related to potential diversion of products, counterfeit products or poor quality products? 6. Is the grantee implementation arrangement and coordination with co-implementers and national and sub-national authorities efficient?
Impact:
1. Has the grantee been able to report on impact as originally framed in the project plan and Log-Frame? If not, has the grant impact been measured in another way? 2. Where relevant, can the grantee attribute Unitaid's financial support for medicines, diagnostics or preventive products purchased to patients tested or treated in each beneficiary country?
Learning & Risk mitigation:
1. Have lessons learnt been documented and widely disseminated by grantees and Unitaid? 2. Have programmatic and financial risks been identified and tracked over the course of grant implementation? 3. Have the findings and recommendations of audits (where relevant) been used to improve grant performance?