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Cost and cost-effectiveness of a real-world HCV treatment program among HIV-infected individuals in Myanmar

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ABSTRACT

Introduction Over half of those hepatitis C virus (HCV)/HIV coinfected live in low-income and middle-income countries, and many remain undiagnosed or untreated. In 2016, Médecins Sans Frontières (MSF) established a direct-acting antiviral (DAA) treatment programme for people HCV/HIV coinfected in Myanmar. The purpose of our study was to evaluate the real-world cost and cost-effectiveness of this programme, and potential cost-effectiveness if implemented by the Ministry of Health (MoH).

Methods Costs (patient-level microcosting) and treatment outcomes were collected from the MSF prospective cohort study in Dawei, Myanmar. A Markov model was used to assess cost-effectiveness of the programme compared with no HCV treatment from a health provider perspective. Estimated lifetime and healthcare costs (in 2017 US$) and health outcomes (in disability-adjusted life-years (DALYs)) were simulated to calculate the incremental cost-effectiveness ratio (ICER), compared with a willingness-to-pay threshold of per capita Gross Domestic Product in Myanmar ($1250). We evaluated cost-effectiveness with updated quality-assured generic DAA prices and potential cost-effectiveness of a proposed simplified treatment protocol with updated DAA prices if implemented by the MoH.

Results From November 2016 to October 2017, 122 with HIV/HCV-coinfected patients were treated with DAAs (46% with cirrhosis), 96% (n=117) achieved sustained virological response. Mean treatment costs were $1229 (without cirrhosis) and $1971 (with cirrhosis), with DAA drugs being the largest contributor to cost. Compared with no treatment, the program was cost-effective (ICER $634/DALY averted); more so with updated prices for quality-assured generic DAAs (ICER $488/DALY averted). A simplified treatment protocol delivered by the MoH could be cost-effective if associated with similar outcomes (ICER $316/DALY averted).

Conclusions Using MSF programme data, the DAA treatment programme for HCV among HIV-coinfected individuals is cost-effective in Myanmar, and even more so with updated DAA prices. A simplified treatment protocol could enhance cost-effectiveness if further rollout demonstrates it is not associated with worse treatment outcomes.

Key questions

What is already known?

- Estimates show that implementing hepatitis C virus (HCV) screening and treatment programmes with generic direct-acting antivirals (DAAs) would be cost-saving within a 10-year period.
- HCV treatment is likely cost-effective in low/middle-income country (LMIC) settings where DAAs are available at low costs.

What are the new findings?

- Using Médecins Sans Frontières programme data, we found that compared with no treatment, HCV treatment with quality-assured DAA among HIV-coinfected individuals is cost-effective in Myanmar.
- Access to affordable, quality-assured generic DAAs improved cost-effectiveness.
- A simplified treatment protocol delivered by the Ministry of Health could be highly cost-effective among HIV/HCV-coinfected individuals if combined with an HCV screening programme.

What do the new findings imply?

- A simplified treatment protocol could enhance cost-effectiveness if not associated with worse treatment outcomes.
- National HCV programmes in Myanmar and similar LMIC settings should no longer consider DAA cost a barrier, but rather consider these data along with simplified models of care as a means to cure people with HCV infection and progress towards WHO HCV elimination goals.

INTRODUCTION

Among people living with hepatitis C virus (HCV) infection, coinfection with HIV can lead to accelerated liver cirrhosis, liver cancer and death compared with those with HCV monoinfection.[1–3] Globally, an estimated 6.2% of people living with HIV show serological evidence of HCV antibody (2.3 million individuals), the majority residing in low/

middle-income countries (LMICs).[4] In Myanmar, an estimated 5.3% of the 222 000 HIV-infected individuals are HCV-seropositive,[5–7] but in the rural Southern township of Dawei, HCV seroprevalence rises to 8% among people living with HIV (data unpublished), and as high as 23% among male HIV-infected fishermen.[8]

Promisingly, HCV treatment with new direct-acting antivirals (DAAs) is highly effective among HCV/HIV-coinfected individuals (>90% cure rate).[9] Yet the previous high cost of DAAs restricted many individuals in LMIC settings from accessing treatment in these highest burdened areas.[10] Few studies have evaluated the cost-effectiveness of HCV treatment in LMIC settings where healthcare management of liver disease and costs of providing DAA treatment differ dramatically from high-income countries. Existing evaluations are limited to theoretical analyses of DAA-containing regimens for HCV monoinfection in Egypt, India, Pakistan and Thailand; and have not evaluated real-world programme implementation costs or cost-effectiveness.[11–14] Evaluating real-world HCV treatment programmes in low-income settings is critical to designing and implementing cost-effective HCV treatment programmes to achieve the global HCV elimination targets set by the WHO as it provides real data of current programmes which allow a better understanding of which components are driving cost and where cost-savings can be made.[15]

In 2016, Médecins sans Frontières (MSF) began a UNITAID-funded HCV treatment programme within an HIV cohort in Dawei, Myanmar using interferon (IFN)-free DAA-based regimens, and in 2018, obtained updated prices for quality-assured generic DAAs.[16] With programmatic experience treating HCV/HIV-coinfected patients in Dawei, MSF subsequently proposed a simplified HCV treatment protocol as a potential HCV model of care that aligns with the 2017 Myanmar Ministry of Health (MoH) National Hepatitis Guidelines.

The purpose of this primary research, performed in collaboration with MSF, was to evaluate the cost of providing DAA treatment in the MSF programme and assess the cost-effectiveness of the programme compared with no treatment among HCV/HIV-coinfected patients in Myanmar. Additionally, we use these data to evaluate the potential cost-effectiveness of HCV treatment using generic DAAs and a simplified treatment protocol as proposed by MSF to the Myanmar MoH. To our knowledge, this is the first study to conduct a cost and cost-effectiveness analysis of a real-world HCV treatment programme for HIV-infected individuals in an LMIC.

METHODS

Setting and model of care

The MSF-Dawei HIV clinic was established in 2004, targeting patients in Dawei and the entire Thanintharyi division in Southern Myanmar. In 2014, MSF began screening all HIV-positive patients attending the MSF-Dawei HIV clinic (87% of HIV-positive patients in the region) for HCV, initially providing IFN-based treatment. In late 2016, a UNITAID-funded prospective cohort study evaluating IFN-free HCV regimens with DAAs was initiated in the clinic. Within the MSF-Dawei clinic, there were 73 local staff members and 2 expatriate staff. Data including patient characteristics, outcomes and costs were collected from this UNITAID study, which was part of a larger multicentre cohort study to evaluate the effectiveness and cost-effectiveness of HCV screening and treatment programmes in LMICs.[17]

We assessed costs and outcome data among chronically HCV-infected (HCV RNA-positive) patients from the MSF-Dawei HIV cohort initiated on IFN-free DAA treatment between November 2016 and October 2017. There were no restrictions on treatment eligibility by HCV disease stage or substance use criteria. Prior to initiation, patients underwent liver disease staging and testing for comorbidities. Patients were classified by METAVIR stage (F0, F1, F2, F3, F4) based on transient elastography with those classified as having cirrhosis (F4) if they had a liver stiffness measure of ≥11 kPa. Decompensated cirrhosis (DC) was defined as liver stiffness ≥11 kPa and Child-Pugh score ≥6 based on values for HCV/HIV-coinfected patients.[18] All patients were screened for hepatocellular carcinoma (HCC) via abdominal ultrasound. Patients were treated with sofosbuvir+daclatasvir (SOF+DAC) without or with ribavirin (RBV) as per the 2015 European Association for the Study of the Liver recommendations.[19] During treatment, patients returned every 2–4 weeks (or more frequently, if necessary) for routine clinical monitoring and biological testing (figure 1). Patients were evaluated for sustained virological response (SVR), defined as a negative HCV RNA test 12 or more

Examination	Baseline (Pre-treatment)	Ongoing Monitoring (week of treatment)					Post-treatment follow-up (weeks)		
		Initiation	2	4	8	12	12	14	24
Consultation type									
Medical doctor	◆	◆	■	■	■	■	■	▲	▲
Nurse	■	■	■	▲	■	◆	■		
Counseling	◆	◆	◆	■	■	◆		▲	◆
Clinical and lab investigations									
HBsAg	◆								
CD4 count	◆					■			
HIV Viral load	◆								
ALT	◆		■	◆		■	■		
AST	◆								
Creatinine	◆		■	◆		■			
Haemoglobin	◆		■	■	■	■			
Platelets	◆								
Glucose	◆			■					
HCV Viral Load	◆					■	◆		
HCV genotype	■								
TSH	■					■			
INR	■								
Albumin	■			■		■			
Bilirubin total	■					■			
Pregnancy Test	◆			◆	■	◆	▲		
FibroScan	◆								

Legend ■ Full model of care ▲ Simplified model ◆ Both models of care

Figure 1 Treatment protocols for the MSF full model of care and simplified model of care for patients on a 12-week treatment regimen. Mandatory appointments shown, optional appointments excluded. ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; INR, international normalised ratio (coagulation test); MSF, Médecins Sans Frontières; TSH, thyroid stimulating hormone.

weeks after the end of treatment. Patients who did not achieve SVR12 with DAAs were not retreated. Patients were considered as lost to follow-up if they did not return within 2 months after a scheduled appointment and were not noted as dead or transferred out. Intention-to-treat SVR rates were calculated that included patients who were lost to follow-up or died.

Costing methods

Overall costing approach

We performed a patient-level microcosting analysis of HCV treatment delivery from a programme provider's perspective, incremental to the standard twice-yearly HIV visits. Data on costs were obtained from MSF's financial records, receipts and price lists from a 12-month period (January 2017–December 2017), when the majority of the HCV-related costs were incurred. Records prior to 2017 were used to allocate a proportion of capital equipment costs obtained in previous years based on expected service lives estimated by interviewing local staff. Using an ingredients approach, patient-level resource use (in terms of type and frequency of visit) was combined with cost information for each patient interaction type. Patient-level data on number and type of visits, clinical examinations, laboratory investigations, treatment regimens and treatment outcomes were extracted from electronic medical records.[20] Resources were valued from MSF financial records, invoices, price lists and additionally informed through interviews with key staff (finance, logistics, pharmacy manager, medical activity manager). We present costs stratified by HCV-related visit components, HCV-related lab costs, DAA costs and coordination costs, as described below. Results are presented in 2017 US$.

HCV-related visit components

HCV-related visits were classified as: (1) *pre*-treatment (2) *on*-treatment and (3) *post*-treatment as per the MSF protocol (figure 1). All HCV-related labs costs were excluded from visit costs and costed separately (see below). Each HCV visit included personnel time specific to the visit (patient-interacting and administrative time, determined by staff diaries), space/materials depending on which area of the clinic was used (laboratory, medical, counselling, pharmacy), and proportion of usage for HCV treatment. For each location, the visit cost incorporated recurrent costs (general personnel costs, medicines (excluding HCV), medical and laboratory supplies, non-medical supplies, transport operating costs, building rental and insurance, maintenance, utilities and bills, freight and clearance, travel and training) and capital costs (buildings, vehicles, medical equipment including FibroScan transient elastography machine, laboratory equipment including GeneXpert real-time PCR system, cold chain equipment, non-medical equipment, construction and rehabilitation, and furniture). Building space for each location visit was determined through site maps and visual inspection and allocated as HCV related by determining the proportion of all consultations which were HCV related from records. Personnel effort by visit type was determined by general staff category (coordination, nursing, medical doctor, individual counselling, pharmacy, registration, human resources, support staff), involvement in HCV-related activities and allocated to proportion of staff, budget, floor space or consultations. Group counselling for HCV treatment, in which patients shared HCV treatment experiences and served as a discussion group for treatment preparation (including counselling on HCV infection, transmission, encouragement for family testing, lifestyle, treatment and monitoring plan, and contact tracing to minimise loss to follow-up), was costed separately.

HCV-related laboratory costs

Costs of HCV-related laboratory investigations as per the MSF protocol (figure 1) were obtained from invoices and price lists.

DAA costs

Unit costs were determined from MSF invoices (online supplemental table S1). Patient-specific DAA costs were calculated based on observed length of treatment and treatment regimen.

Coordination costs

Per visit MSF coordination costs were included from the local coordination site (Dawei) and country coordination (Yangon) using a top-down method (see online supplemental material). For Dawei, HCV-related coordination costs were estimated through obtaining the remaining personnel, recurrent and capital costs associated with the HCV programme, after extracting specific costs attributable to direct HCV visits by type. For Yangon, coordination costs included the proportion of personnel effort attributed to the Dawei programme by staff type and non-personnel costs (eg, all HCV-related activities) and were allocated as a proportion of the total budget.

Cost-effectiveness methods

Disease progression model

We developed a compartmental, deterministic Markov model of liver disease progression in a closed cohort of diagnosed HCV/HIV-coinfected adults (figure 2), based on the liver disease distribution in the MSF cohort (online supplemental table S1). We simulated disease progression through each stage of HCV-related hepatic fibrosis (METAVIR stages F0, F1, F2, F3), compensated cirrhosis (CC, METAVIR F4), DC and HCC. Liver-related mortality was assumed to only occur from DC or HCC. The model did not include liver transplantation, as this is not commonly performed in Myanmar. The model was additionally stratified by treatment history and outcome (untreated, treated and cured, or treated and failed). Individuals with F3 or milder liver disease who were treated and achieved SVR were assumed not to have further liver fibrosis progression. Those with CC, DC or HCC who were treated and achieved SVR could progress

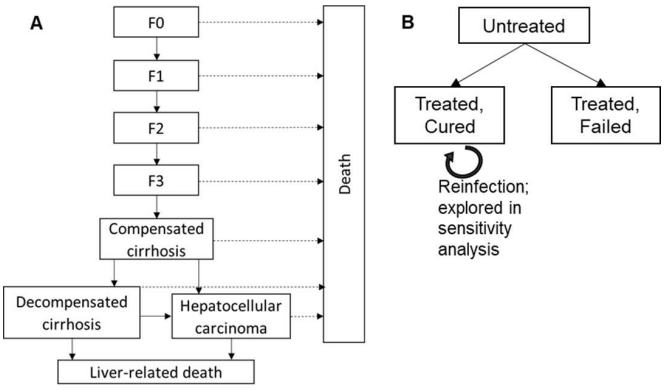

Figure 2 Schematic of Markov model showing (A) untreated chronic HCV disease progression by liver disease states and (B) stratification of the model by treatment. For those who are cured (achieve SVR), further liver disease progression is halted (if in stages F0–F3) or reduced compared with those who do not achieve SVR (if in stages CC, DC, HCC). F0–F3 are METAVIR hepatic fibrosis scores determined by transient elastography (<11.0 kPa); cirrhosis: METAVIR score ≥11.0 kPa; DC: METAVIR score ≥11.0 kPa and Child-Pugh score ≥6. HCC was determined by abdominal ultrasound. CC, compensated cirrhosis; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; SVR, sustained virological response.

to more severe liver disease states or liver-related death but at reduced rates. We assumed those who achieved SVR cannot be reinfected and those who did not achieve SVR with DAAs were not retreated. The model was developed in Matlab R2018a.

Disease progression rates and mortality

Liver disease state transition probabilities (online supplemental table S3) were based on previous studies among HCV/HIV-coinfected individuals which suggest faster acceleration to more advanced hepatic fibrosis stages and mortality among HCV/HIV-coinfected individuals off antiretroviral therapy (ART) compared with HCV/HIV-coinfected individuals on ART.[1 21–26] Background (non-HCV related) mortality rates were estimated given the CD4 count distribution, ART status of the cohort and estimated life expectancy based on mean age of the cohort weighted by sex[27] (This information references 1.3 Background (non-HCV related) mortality rate calculation in the online supplemental text).

Costs

HCV treatment and routine HIV care and treatment costs were obtained through our patient-level analyses. Due to a lack of information available on patient access to care for advanced liver disease associated with HCV outside of the HIV clinic, for the baseline analysis we use estimates of HCV-related disease management costs from similar income settings (Cambodia), adjusted for Gross Domestic Product (GDP; online supplemental table S3). Patients who achieved SVR were assumed to remain in their disease stage and continue to accrue disease stage costs despite being cured.

Health utilities

Health outcomes were evaluated in disability-adjusted life-years (DALYs). Health disutilities for HIV and liver disease stages were obtained from the Global Burden of Disease (online supplemental table S3)[28] and coinfection disutility values calculated as: [1−(1−HIV disability weight)×(1−HCV disability weight)].[26]

Cost-effectiveness analyses

We evaluated the cost-effectiveness of HCV treatment for HCV/HIV-infected individuals compared with no HCV treatment. We evaluated the following treatment protocol scenarios:

- 'Observed MSF': data from observed full MSF protocol from the implemented UNITAID HCV DAA study in 2016/2017, using 2017 DAA prices.
- 'MSF updated DAA cost': costs estimated from full MSF protocol, but with updated DAA prices based on the outcomes of the MSF HCV tender for quality-assured generic DAAs (reduces 12-weeks SOF+DCV from US$493 to US$120) negotiated after the study in 2018.
- 'Simplified MoH': we estimate costs of a simplified treatment protocol (as proposed by MSF to the Myanmar MoH after the study in 2018, figure 1) if implemented by the MoH. The simplified protocol reduced the number of visits and laboratory measurements and incorporated partial task-shifting from doctors to nurses. To represent implementation by the MoH, we also use local staff costs (26% less expensive than current staff costs), no MSF coordination costs, quality-assured generic DAA prices and updated HCV test costs (previously OraQuick rapid test, and now SD Bioline HCV rapid test resulting in a~US$5 reduction per test). We simulate cost-effectiveness of the proposed simplified protocol assuming the same SVR as observed with the full protocol.

The model was run for 100 years, with cost and utilities discounted at 3%/year. To account for parameter uncertainty, we performed a probabilistic sensitivity analysis, sampling 1000 parameter sets from parameter distributions (online supplemental table S3). We calculated the mean incremental cost-effectiveness ratio (ICER, mean incremental costs divided by mean incremental DALYs averted) for the intervention compared with no treatment. Interventions with an ICER less than a willingness-to-pay (WTP) threshold of one times per capita GDP of Myanmar (US$1250 in 2017) were considered cost-effective.[29 30]

One-way sensitivity analyses

We performed several one-way sensitivity analyses on the ICER for each of the 'Observed MSF', 'MSF updated DAA cost' and 'Simplified MoH' strategies compared with no treatment. We varied the discount rate (0% and 6% compared with 3% at baseline), time horizon (20 and 50 years vs 100 years at baseline), SVR rate (90% and 98% vs 96% at baseline), initial distribution of fibrosis stage

(30% and 60% patients with cirrhosis vs 46% at baseline), HCV/HIV coinfection disutility values (lower and upper bounds vs mean values at baseline), transient elastography costs (cost in Cambodia observed with higher volume of use compared with Dawei: $4 compared with $115), reinfection among those who achieved SVR (5%/year vs 0% at baseline), no cost for care for all hepatic fibrosis stages (vs F0: $0; F1: $35; F2: $80; F3: $137; F4: $207; DC: $314; HCC: $378 at baseline), no coordination cost (vs $98 for patients without cirrhosis and $142 for patients with cirrhosis at baseline), and accelerated liver disease progression among patients with genotype (GT) 3 (HR: 1.31 for cirrhosis (95% CI 1.22 to 1.39); HR: 1.80 for HCC (95% CI 1.61 to 2.03)[31] ; among 56% of patients). Additionally, for the 'Simplified MoH' strategy, we examine task-shifting to nurse-led care only during treatment, reducing overall physician interactions by 56% (nine visits vs four; and nurse interaction by 66% from six interactions to two) and examine equal SVR rates as observed in the MSF trial or those reduced to SVR rates to 70% in the event the simplified model results in reduced SVR.

HCV screening and treatment sensitivity analyses

Because screening occurred several years prior to the UNITAID intervention, our base case evaluates the cost-effectiveness of the DAA treatment programme only. For a sensitivity analysis, we explored the cost-effectiveness of a combined screening and treatment programme for the 'Simplified MoH' scenario compared with no screening and treatment across various HCV seroprevalences (0.5%–10%), reflecting likely geographical heterogeneity across Myanmar (see online supplemental information for details). We estimated associated screening costs based on testing yields for each prevalence scenario, assuming HCV antibody testing using the SD Bioline HCV rapid test (US$2.33) and GeneXpert HCV RNA test (US$21.09) with staff costs included.

Patient and public involvement

Study participants and the public were not involved in the design, conduct or reporting of this study. However, study findings will be disseminated through publications and presentations at conferences and other public events.

RESULTS

Treatment outcomes

From November 2016 to October 2017, all 122 HIV-infected patients (mean age 43 years) who screened positive for HCV were treated with DAAs (56/122 (46%) with cirrhosis (CC or DC)). No HCC was detected among those treated or untreated. Roughly half of the treated cohort were GT3 (51%), followed by GT1 (46%) and GT6 (3%). Of these, 96% (n=117) achieved SVR. The majority of patients with cirrhosis (n=50; 89%) were treated with 24 weeks of SOF+DAC, but six were treated with 12 weeks of SOF+DAC+RBV resulting in lower costs (all six patients achieved SVR; GT1: n=1; GT3: n=4; GT6: n=1). One patient was previously treated with IFN-based HCV treatment (peg-IFN+RBV) prior to the availability of IFN-free DAA therapy and retreated with DAAs once available. Of those who did not achieve SVR (n=5), one died, one did not complete treatment and three completed treatment. There was no difference in SVR by liver fibrosis stage (online supplemental table S2).

Treatment delivery cost

The average cost of HCV treatment per patient was $1229 (95% CI $848 to $1829) for patients without cirrhosis and $1971 (95% CI $1307 to $2686) for patients with cirrhosis (online supplemental figure S1). Variations in cost were predominantly due to differences in durations of treatment and drug regimens, with minor differences in monitoring. DAA drug cost was the largest cost component and main driver of difference in cost by liver disease stage (without cirrhosis: $524 vs with cirrhosis: $1122; table 1). The second largest driver of cost was laboratory costs, with minimal difference by liver disease stage (without cirrhosis: $421 vs with cirrhosis: $437). Of these laboratory costs, transient elastography costs comprised $115, which was high because of the initial purchase price (~US$49 037) and relatively low usage (159 measurements in 2017). Visit costs were the third largest contributor to cost (breakdown by visit type in online supplemental table S4). Within the personnel component of visit costs, 61% of the personnel costs were due to physician costs (three local, one foreign), as the protocol incorporated physician-led treatment. Coordination costs were on average $98 per treatment for patients without cirrhosis and $142 per treatment for patients with cirrhosis (45% from Dawei, and 55% from Yangon; This corresponds to 1.1 Valuation of coordination costs in the online supplemental text).

Updated quality-assured generic DAA costs were obtained after the end of our study ($120 for 12 weeks of SOF/DAC before MSF-overhead charges (online supplemental table S1). With these updated costs, the total estimated DAA costs when incorporating RBV (included in 54% of treatments) were $184 for 12 weeks, $453 for 24 weeks, reflecting variations in dose). With these costs, based on the observed treatment protocol, the total cost per treatment would be $889 for patients without cirrhosis and $1302 for patients with cirrhosis (table 1). In this scenario, the highest contributors to overall cost would be the laboratory and monitoring costs.

Cost-effectiveness of HCV treatment among HIV-infected individuals

The 'Observed MSF' treatment programme (mean treatment costs: $1229 (patients without cirrhosis), $1971 (patients with cirrhosis)) resulted in an average incremental cost of $2121 per patient treated including annual HIV care costs (online supplemental table S5), and 3.35 DALYs averted per patient. This led to a mean ICER of $634/DALY averted compared with no treatment, cost-effective compared with a WTP threshold of one times the per capita GDP of Myanmar ($1250) (table 2). In

Table 1 Cost of HCV treatment by component type among HIV-infected individuals in Myanmar, with the 'Observed MSF' treatment protocol and proposed alternative protocols

	HCV visit costs per patient	HCV laboratory costs per patient	DAA costs per patient	HCV coordination costs per patient	Total HCV treatment costs per patient
Observed MSF intervention*					
Non-cirrhotic	186.60 (95% CI 158.65 to 292.94)	420.80 (95% CI 194.80 to 718.94)	523.53 (95% CI 411.60 to 663.81)	97.60 (95% CI 82.74 to 153.66)	1228.53 (95% CI 847.79 to 1829.35)
Cirrhotic	270.47 (95% CI 225.45 to 419.17)	436.73 (95% CI 251.62 to 697.04)	1122.01 (95% CI 711.58 to 1349.37)	141.84 (95% CI 118.20 to 220.15)	1971.05 (95% CI 1306.85 to 2685.72)
MSF with updated DAA costs†					
Non-cirrhotic	186.60 (95% CI 158.65 to 292.94)	420.80 (95% CI 194.80 to 718.94)	183.69 (95% CI 169.03 to 198.35)	97.60 (95% CI 82.74 to 153.66)	888.69 (95% CI 742.41 to 827.62)
Cirrhotic	270.47 (95% CI 225.45 to 419.17)	436.73 (95% CI 251.62 to 697.04)	453.02 (95% CI 413.51 to 492.53)	141.84 (95% CI 118.20 to 220.15)	1302.06 (95% CI 1102.84 to 1219.49)
Simplified MoH‡					
Non-cirrhotic	80.92	216.33	120	–	417.25
Cirrhotic	89.54	271.25	240	–	600.79

*'Observed MSF intervention' presents summary data from observational study, including 2017 DAA prices.
†'MSF with updated DAA costs' estimates costs with updated DAA prices for quality-assured generic DAAs negotiated in 2018.
‡'Simplified MoH' strategy estimates costs with generic DAAs and a proposed simplified protocol (figure 1), with local staff costs and no overheads. The 95% CIs are presented for the observed cost data reflecting patient variations in observed costs. For estimations of costs using updated cost data or simplified strategies, patients were assumed to adhere to the exact clinical schedule (see figure 1) and so no uncertainty is provided. Non-cirrhotic: METAVIR F0–F3, cirrhotic: F4 as measured by transient elastography.
DAA, direct-acting antiviral; HCV, hepatitis C virus; MoH, Ministry of Health; MSF, Médecins sans Frontières.

Table 2 Incremental cost-effectiveness of HCV treatment among HIV-infected individuals in Myanmar compared with no treatment, as observed and with proposed simplified protocols and newly negotiated DAA costs

	Cost (US$ 2017) per capita		DALYs per capita		ICER mean
Strategy	Total mean (95% CI)	Incremental mean compared with no treatment (95% CI)	Total mean (95% CI)	Incremental mean compared with no treatment (95% CI)	$/DALY averted compared with no treatment
No treatment	3991.71 (3133.86 to 4955.87)	–	21.89 (20.77 to 22.92)	–	–
Observed MSF treatment programme*	6112.72 (5019.45 to 7170.54)	2121.01 (1885.59 to 2214.67)	18.54 (17.48 to 19.50)	−3.35(−3.29 to −3.42)	633.60
MSF programme with updated DAA costs†	5624.94 (4550.21 to 6738.39)	1633.23 (1416.35 to 1782.52)	18.54 (17.48 to 19.50)	−3.35 (−3.29 to −3.42)	487.89
Simplified MoH strategy‡	5050.30 (4009.81 to 6128.90)	1058.59 (875.95 to 1173.03)	18.54 (17.48 to 19.50)	−3.35 (−3.29 to −3.42)	316.23

Estimates for interventions include cost of annual HIV care and treatment.
*'Observed MSF intervention' presents summary data from observational study, including 2017 DAA prices.
†'MSF with updated DAA costs' estimates costs with updated DAA prices for quality-assured generic DAAs negotiated in 2018.
‡'Simplified MoH' strategy estimates costs with generic DAAs and a proposed simplified protocol (figure 1), with local staff costs and no overheads.
DAA, direct-acting antiviral; DALYs, disability-adjusted life-years; HCV, hepatitis C virus; ICER, incremental cost-effectiveness ratio; MoH, Ministry of Health; MSF, Médecins sans Frontières.

this analysis, 100% of the simulations fell under the WTP threshold.

The 'MSF updated DAA cost' analysis (with updated DAA prices, mean treatment cost $889 (patients without cirrhosis), $1302 (patients with cirrhosis)) produced a mean ICER of $488/DALY averted compared with no treatment, cost-effective under the WTP threshold (all simulations fell under the WTP threshold).

Finally, a 'Simplified MoH' strategy (also with cheaper drugs) could result in substantial reductions in treatment cost (patients without cirrhosis: $417, patients with cirrhosis: $601), and if resulting in equal treatment outcomes, could be highly cost-effective (mean ICER $316 DALY averted compared with no treatment, all simulations fell under the WTP threshold).

One-way sensitivity analyses

The 'Observed MSF' treatment programme remained cost-effective across all scenarios, if the discount rate was reduced to 0% or increased to 6%, there were no costs of care for hepatic fibrosis stages, coordination costs were excluded, GT3 patients were assumed to have accelerated liver disease progression, transient elastography costs were decreased, there was a time horizon of 20 or 50 years, they achieved a reduced SVR rate, there was different disutility estimates used, cirrhosis prevalence varied or reinfection rate was 5%/year (figure 3).

The 'MSF updated DAA cost' and 'Simplified MoH' scenarios remained cost-effective for all sensitivity analyses (online supplemental figures S2 and S3). Furthermore, the 'Simplified MoH' scenario remained cost-effective with SVR rates of 70% (ICER: $372).

Screening and treatment sensitivity analyses

A combined screening and treatment programme among HIV-infected individuals implemented by the MoH using the 'Simplified MoH' strategy could be cost-effective at all HCV seroprevalences considered examined, including the lowest prevalence (0.5%; ICER: $489), below the national monoinfection estimate (2.7%) and

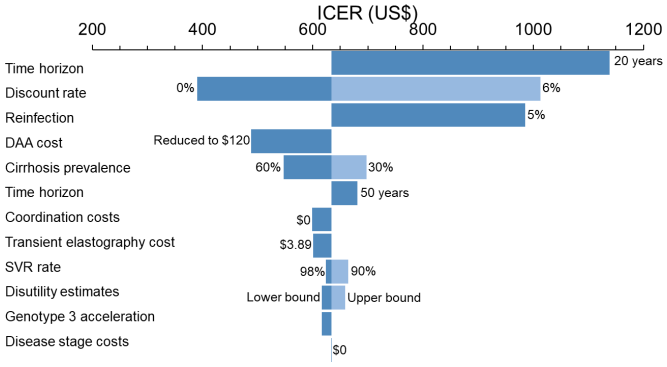

Figure 3 Sensitivity analysis of the cost-effectiveness of the 'Observed MSF' model of care with 2017 DAA costs compared with no treatment. Costs shown in US$. The reduced FibroScan cost (US$3.89) scenario reflects the FibroScan cost estimated in similar income country setting with higher volume (GDP adjusted cost from Cambodia, US$2017; $4.31). Dark and light blue bars displayed when two values of a parameter were examined and resulted in ICER values lower and above the baseline ICER value (US$634). DAA, direct-acting antiviral therapy; GDP, Gross Domestic Product; ICER, incremental cost-effectiveness ratio; MSF, Médecins sans Frontières; SVR, sustained virological response (at 12 weeks).

the 8% observed among HIV-infected individuals in Dawei (ICER: $334; online supplemental figure S4).[6] The 'Simplified MoH' strategy was cost-effective for HCV seroprevalences above 0.1% (ICER: $1152 at 0.1%; online supplemental figure S4).

DISCUSSION

Main findings

Our study found that the DAA treatment programme among HCV/HIV-coinfected patients in Myanmar implemented by MSF is cost-effective, particularly with quality-assured generic DAAs. Moreover, a simplified model of care (proposed by MSF to the Myanmar MoH, incorporating fewer visits and task-shifting) implemented by the MoH with local staff could be highly cost-effective (ICER <$400/DALY averted compared with no treatment), if not associated with worse treatment outcomes, and could be cost-effective if combined with an HCV screening programme among HIV-infected individuals. These findings hold even with lower than observed (90%) SVR rates and reinfection rate was 5% per year. With quality-assured generic DAAs, treatment remained cost-effective even over 20-year time horizons.

The majority of treatment costs in our study were comprised of DAA costs in 2017, which were negotiated to lower prices after the study period in 2018 by the MSF Supply Centers and MSF Access campaign ($120 for 12-week course),[16] underscoring the importance of generic competition to reduce drug prices and improve access to HCV treatment. The cost of transient elastography also contributed markedly to cost of treatment delivery because of the high purchase price and low annual use. These costs could be reduced if used in a higher volume clinic or if non-invasive methods for determining hepatic fibrosis were used (eg, Fibrosis-4 Index for Hepatic Fibrosis, aspartate aminotransferase-to-platelet ratio index or FibroSure).

Comparisons with existing literature

To our knowledge, our study is the first to evaluate the real-world costs and cost-effectiveness of DAA treatment in an implemented HCV treatment programme among HIV-infected individuals in a clinical setting in an LMIC. However, our study supports previous analyses indicating that HCV treatment is likely cost-effective in LMIC settings where DAAs are available at low costs. One study in Egypt found that implementing an HCV screening programme with IFN-based DAA therapy compared with no screening would be cost-effective.[11] Compared with IFN-based therapy, IFN-free DAA therapy is superior in efficacy, has shorter treatment duration and better tolerability,[32–35] yet in many settings historically more costly, though costs continue to fall.[36 37] Similarly, two cost-effectiveness studies in India showed that implementing HCV screening and treatment with generic DAAs would be cost-saving within about a decade, but these studies did not use programmatic treatment delivery or outcome data.[12 38] Importantly, none of these studies, ours included, incorporated data on access to healthcare, which may be low in LMICs, and therefore it is possible that treatment is less cost-effective than estimated if fewer medical costs are associated with untreated HCV infection. While our sensitivity analyses indicated that HCV treatment remained cost-effective with no cost of care for hepatic fibrosis stages, further work is warranted to assess real-world medical utilisation for liver disease in LMICs.

Strengths and limitations

The main strength of our study is that it was based on real-world programmatic costs and outcome data. However, as with all modelling studies, there were numerous uncertainties in the parameter values. Nevertheless, we incorporated these uncertainties in our analysis, conducted sensitivity analyses, and our results were generally robust to most of these uncertainties. First, no patients in our cohort received additional care for HCV within the MSF-Dawei HIV clinic, but it was unknown whether they received care at other medical facilities and so was not included in our analysis. Future work in this area is warranted to refine our estimates.

Second, we used published data on disease progression from other settings, while it is unclear whether these are truly generalisable to Myanmar. Our baseline analysis did not simulate differential disease progression by GT. Half our cohort was GT3, which has been associated with accelerated liver disease progression in HCV-monoinfected individuals,[31 39 40] yet it is unclear if this is true in HCV/HIV coinfection. A sensitivity analysis incorporating accelerated disease progression among GT3 patients improved the cost-effectiveness.

Third, reinfection rates among HIV-infected individuals in Myanmar are unknown, however we note that our analyses with quality-assured generic DAA prices indicated that treatment was cost-effective even with reinfection rates of 5%.

Fourth, although we used observational data for our main analysis ('Observed MSF'), our analyses examining a simplified model of care as proposed by MSF to the MoH are theoretical. The MoH strategy assumed equal SVR rates and projected costs based on adherence to the planned visits and monitoring plan. The true cost of an MoH strategy is unknown and could be different between HCV treatment programmes implemented at the hospital versus clinic level, due to variation in staff and clinical monitoring costs. Real-world data on costs and treatment outcomes are required to confirm these findings, although our sensitivity analyses show that treatment with generic DAA costs was cost-effective when including lower SVR and higher treatment costs, indicating that it is likely that our results would hold in other settings with worse treatment outcomes. Furthermore, compared with no treatment, treatment with DAAs would likely remain cost-effective in other real-world settings even with lower SVR rates. Additionally, the MoH may be able to acquire DAAs at even lower prices than the updated DAA costs

included in our analyses, if purchased in bulk, which would further increase cost-effectiveness.

Fifth, the Markov model that we developed to describe HCV disease progression simulated an average population behaviour and thus did not incorporate individual-level heterogeneity. Sixth, both the study and model did not account for retreatment after DAA failure as retreatment was not available during the study period and is currently not recommended by national guidelines. We note however that within the MSF cohort, select individuals have been eligible for retreatment since 2019.

Finally, our study was based on data from a cohort receiving care from an MSF clinic in a single, rural setting (Dawei, Myanmar), so it is unclear whether our results are generalisable to the country or if scaled up to the broader population of people living with HIV. Additionally, our treated cohort were all on ART with well-controlled HIV and had access to consistent HIV counselling which may have resulted in greater adherence levels and follow-up than in a larger healthcare system without available counselling. Integrating HCV treatment into existing ART programmes and HIV clinics may be an effective strategy to reach HCV/HIV-coinfected populations and should be considered. Additionally, we recognise the clinical and medical environments equivalent to that of MSF clinics, which offer intensive follow-up protocols and patient engagement, may not exist nationally. Non-MSF clinics in Myanmar may differ in resource allocation and availability such as human resources, logistics and supply chains, which may influence (1) access and support for patients seeking care and treatment, and (2) treatment adherence, patient retention and patient outcomes, which could impact cost-effectiveness.

CONCLUSION

In conclusion, we found the MSF treatment programme for HCV infection among HIV-infected individuals in Myanmar cost-effective, with the potential of being even more cost-effective when using a simplified protocol as long as this does not result in worse treatment outcomes. Access to affordable, quality-assured generic DAAs improved cost-effectiveness.

Practical implications

Given our cost-effectiveness projections, national programmes in Myanmar and similar settings should no longer consider DAA cost a barrier, but rather consider these data along with simplified models of care as a means to cure people with HCV infection and progress towards WHO HCV elimination goals. While this study evaluated the current HCV treatment programme implemented by MSF, these results can be informative to the MoH in Myanmar and other similar LMIC settings.

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Patient consent for publication Not required.

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Supplementary Information for "Cost and cost-effectiveness of a real-world HCV treatment program among HIV-infected individuals in Myanmar"

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1.1 Valuation of coordination costs

Yangon coordination: To determine the proportion of the Yangon country coordination budget attributable to the HCV treatment program in Dawei, we first separated out the budget which was attributable to the full Dawei program. First, we divided the total MSF Yangon budget into personnel and non-personnel. Staff interviews were performed to determine what proportion of personnel effort was attributable to the Dawei program, by staff type. The personnel budget was allocated accordingly by multiplying the personnel costs for each staff type by their stated proportion effort attributable to Dawei. Non-personnel costs were allocated to the Dawei program as a proportion of the total budget (e.g. roughly 45% of the total budget was comprised of Dawei costs).

Among the Yangon budget estimated to be attributable to Dawei coordination, we estimated what proportion of these costs were associated with HCV-related activities based on the proportion of all consultations in Dawei which were for HCV treatment in 2017 (14%). We then divided the Dawei HCV program coordination budget estimate by the number of HCV consultations in 2017 to obtain a per HCV consultation Yangon coordination cost ($5.23/consultation).

Dawei Coordination: The Dawei HCV-related coordination costs were estimated through obtaining the remainder of the personnel, recurrent and some capital costs (shared office supplies allocated to proportion of staff) associated with the HCV program, after extracting specific costs attributable to direct HCV visits by type (e.g. laboratory visit, pharmacy visit, etc). Some capital costs were fully allocated to coordination, such as general support items including cold chain and energy equipment, furniture, spare parts for vehicles, and construction/rehabilitation costs for building maintenance. The per HCV consultation coordination cost was obtained from dividing the total HCV-related Dawei coordination cost by the number of HCV consultations ($6.59/consultation).

1.2 Valuation of GeneXpert for HCV-related activities

GeneXpert costs were first costed separately by capital costs, personnel costs, consumables, and overheads. Since the GeneXpert was utilized to test for HIV and tuberculosis in addition to HCV, we multiplied shared costs by the proportion of HCV viral load tests performed in 2017 out of the total number of tests run on the GeneXpert for 2017. HCV viral load tests performed internally using the GeneXpert accounted for 29% of the total number of tests performed on the GeneXpert at the MSF-Dawei clinic in 2017.

1.3 Background (non-HCV related) mortality rate calculation

As all patients were on ART at HCV treatment initiation, we estimated a weighted background non-HCV related mortality rate based on the CD4 cell count distribution among the cohort at HCV treatment initiation (stratified by <200, 200-350, 350-500, >500 cells/μL, see **Table S4**), and expected survival on ART by stage, assuming a 3-4 fold increase in lifespan if on ART [1, 2]. With this calculation, the estimated average lifespan *excluding* HCV-related mortality among the HIV infected cohort was 30 years, only slightly less (3-4 years) than the expected lifespan among the general population in Myanmar [3]. The background death rate was then calculated as 1/weighted life expectancy.

1.4 HCV/HIV coinfection disability weights calculation

HCV/HIV coinfection disability weights were calculated as [1-((1-HIV disability weight)*(1-HCV disability weight))]. We obtained relevant disability weights from the WHO Global Burden of Disease Study 2013 [4]. For the HIV disability weight for this analysis, we use the disability weight for ART (0.078), as all were on ART in the treatment cohort. Disability weights for DC (0.178) and HCC (0.451) were obtained directly from the GBD. No disability weights were available for HCV METAVIR stages, so the weight for mild abdominopelvic problem (0.011) was

used for stages F0/F1, moderate abdominopelvic problem (0.114) was used for CC, and the midpoint between these two values was used for F2 (0.063) [4, 5].

1.5 HCV screening sensitivity analysis calculations

For a given HCV seroprevalence, we estimate chronic prevalence by assuming that 16% of individuals spontaneously clear their infection (as calculated from cohort data as 1- [Total # individuals HCV RNA-positive / Total # individuals HCV Ab tested]), and the remainder proceed to chronic infection. The number of antibody tests that would need to be performed to identify one chronic HCV case was calculated as the total number of individuals in the population divided by the number that were HCV RNA-positive, the number of RNA tests required to identify a single chronic case of HCV was calculated as the number of HCV Ab-positive individuals divided by the number of HCV RNA-positive individuals. For example, if there were 1000 total individuals in our population under a HCV seroprevalence of 8%, 80 individuals would be HCV Ab-positive, 67 would be HCV RNA-positive (assuming that 16% of HCV Ab-positive individuals spontaneously clear their HCV infection). Therefore, for each HCV RNA infection, we would need to test approximately 14.9 individuals for HCV antibody and 1.2 individuals for HCV RNA to identify a single chronic case of HCV.

1.6 HCV reinfection rate sensitivity analysis calculations

While not accounted for in our primary modeling analysis, we performed a sensitivity analysis to examine the impact of reinfection on the cost-effectiveness of the treatment scenarios. We implement a fixed annual rate of reinfection (5% per year) into the model which does not change over time. As such this fixed rate neglects change in risk over an individual's life, or changes in risk of acquiring HCV through treatment scale up (the latter of which requires a dynamic model).

SUPPLEMENTARY FIGURES

Figure S1. Distribution of patient-level HCV treatment costs (in 2017 US$) by liver disease stage among HIV-infected individuals in Dawei, Myanmar. Non-cirrhotic includes F0-F3, defined by METAVIR scores determined by transient elastography (<11.0 kPa); Cirrhotic includes CC: compensated cirrhosis (≥11.0 kPa); DC: decompensated cirrhosis (≥11.0 kPa and Child-Pugh score ≥6).

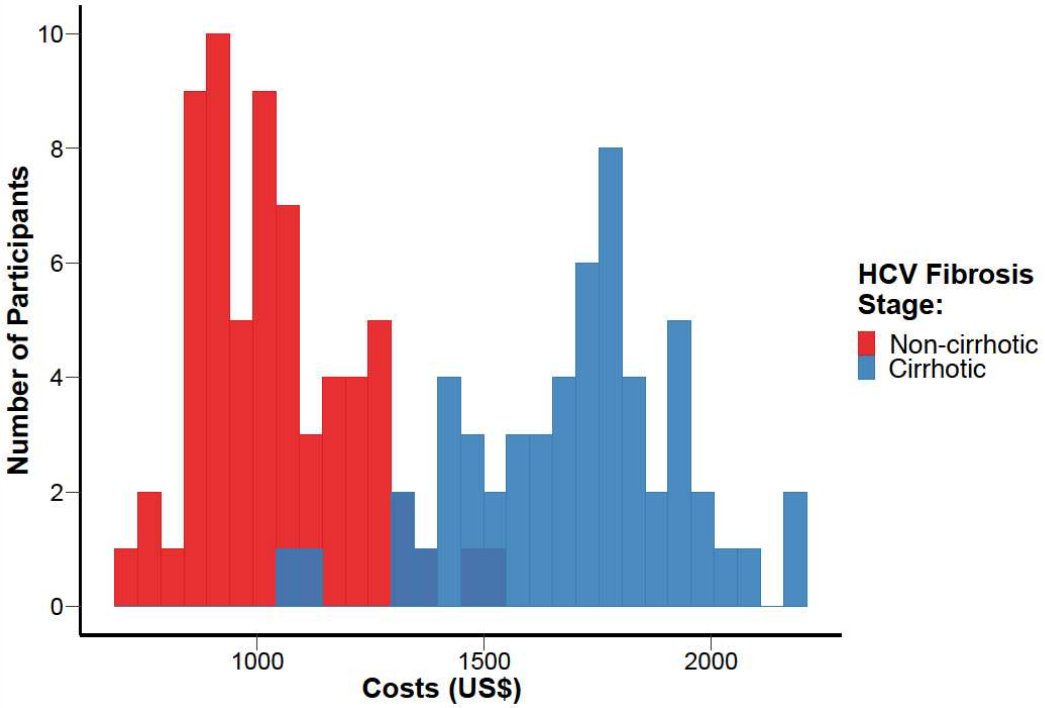


Figure S2. Sensitivity analysis of the cost-effectiveness of the "MSF updated DAA cost" model of care with 2018 DAA Access drug costs. 12-week Sofosbuvir/Daclatasvir treatment cost: US$120; 24-week Sofosbuvir/Daclatasvir treatment cost: US$240. DAA: direct-acting antiviral therapy; SVR: sustained virologic response at 12 weeks. Baseline parameter values are shown in Table 1. Fibroscan cost (US$3.89) reflects fibroscan cost estimated in similar setting (Cambodia, US$2017; $4.31; GDP-adjusted (Myanmar, US$1250/Cambodia, US$1385). Dark and light orange bars displayed when two values of a parameter were examined and resulted in ICER values lower and above the baseline ICER value (US$488).

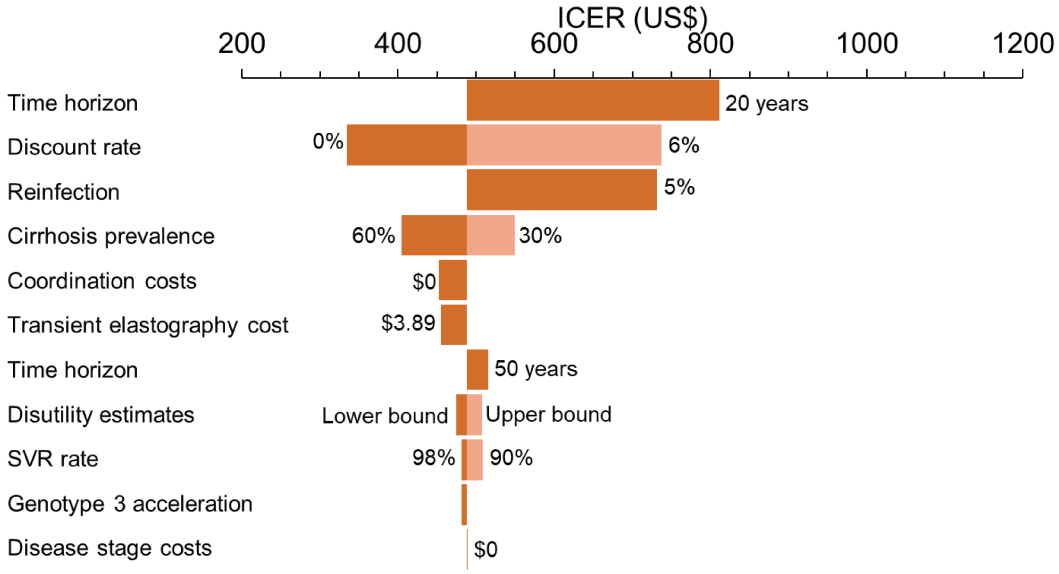


Figure S3. Sensitivity analysis of the cost-effectiveness of the "Simplified MoH" model of care with 2018 DAA costs. DAA: direct-acting antiviral therapy; SVR: sustained virologic response at 12 weeks. Task shifting to nurse-led care increased nurse-led consultations by 3 times. Dark and light green bars displayed when two values of a parameter were examined and resulted in ICER values lower and above the baseline ICER value (US$316).

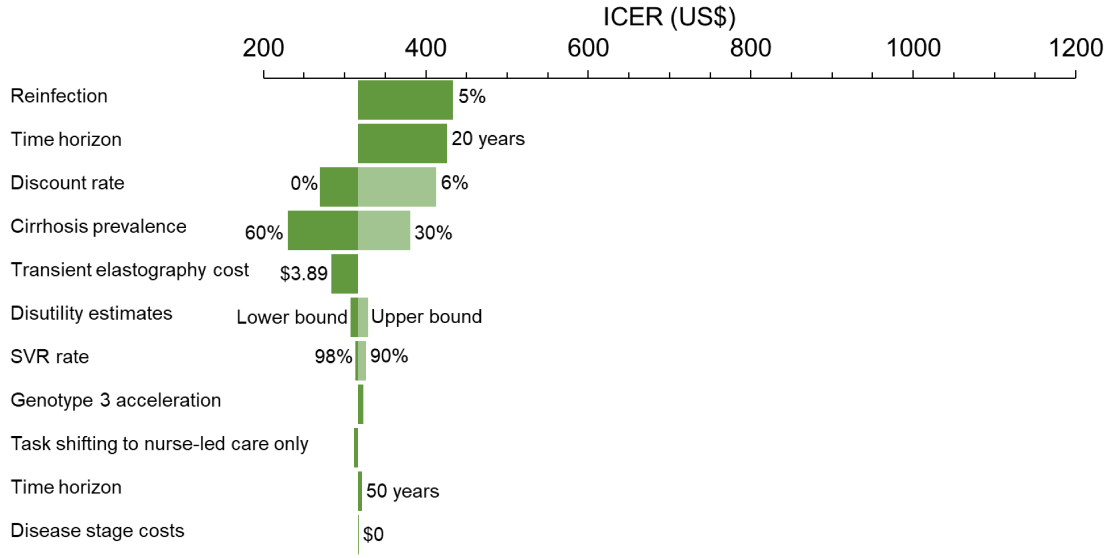
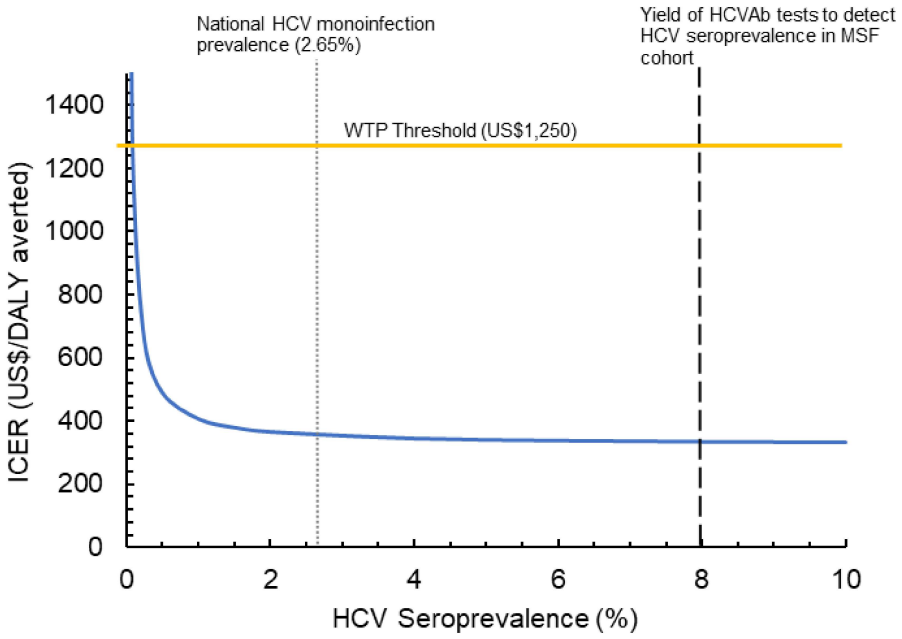


Figure S4. Incremental cost-effectiveness ratio (ICER) for HCV screening and treatment among HIV-infected individuals compared to no screening for various HCV seroprevalences. HCV treatment protocol examined is the proposed Myanmar Ministry of Health HCV treatment strategy. MSF cohort HCV seroprevalence (HCV Ab-positive) was 8%. ICER: incremental cost-effectiveness ratio; DALY: disability-adjusted life years; HCV: hepatitis C virus; Ab: antibody; MSF: Médecins sans Frontières.



SUPPLEMENTARY TABLES

Table S1. Unit cost in US$ of HCV therapy by drug type. 2017 drug costs are based on costs obtained from MSF invoices, which include MSF overhead charges. Updated unit drug costs from the Access campaign shown for sofosbuvir (400mg) and daclatasvir (60mg), excluding MSF overhead costs. †Ribavirin was not included in the Access campaign, but was prescribed in the "Observed MSF" intervention. Costs for Ribavirin were only included in the "Observed MSF" and "MSF with updated DAA costs" scenarios.

HCV treatment drug	2017 Cost	2018 Cost
Sofosbuvir (400mg)	3.52	1.04
Daclatasvir (60mg)	1.38	0.39
Ribavirin (200mg)	0.35	0.35†

Table S2. HCV treatment outcomes by liver fibrosis stage among cohort of HIV-infected patients in Dawei, Myanmar initiated on DAA treatment from 11/2016-10/2017. F0-F3 are METAVIR scores determined by transient elastography (<11.0 kPa); CC: compensated cirrhosis (≥11.0 kPa); HCV: hepatitis C virus; SVR: sustained viral response at 12 weeks; CC: compensated cirrhosis; DC: decompensated cirrhosis; HCC: hepatocellular carcinoma

HCV disease stage	N (% of total)	Number achieved SVR	SVR rate by HCV stage	Number failed treatment, lost-to-follow-up, or died
F0	39 (32%)	37	94.5%	2
F1	9 (7%)	8	88.9%	1
F2	6 (5%)	5	83.3%	1
F3	12 (10%)	11	91.7%	1
CC	54 (44%)	54	100%	0
DC	2 (2%)	2	100%	0
HCC	0 (0%)	0	-	0
Total	122 (100%)	117	95.9%	5

Table S3. Economic model parameters and their distributions. HCV: hepatitis C virus; SVR: sustained virologic response; ART: antiretroviral therapy; CC: compensated cirrhosis; DC: decompensated cirrhosis; HCC: hepatocellular carcinoma; GDP: gross domestic product. †2017 USD$

Variable	Sampled Value mean (95%CI)	Distribution and input parameters	Source
HCV disease stage costs† (annual)			
No hepatic fibrosis – F0	0	-	[6, 7] No Myanmar data; 2017 costs from Cambodia (Walker JG, unpublished) for F0-CC adjusted by GDP (Myanmar GDP $1250)/(Cambodia GDP $1385); Minimum/maximum values ±50% point estimate. Multiplier of 5.3 used from Cambodia cohort data for DC calculation; 6.5 for HCC.
Mild hepatic fibrosis– F1	34.87 (18.88, 51.85)	Uniform (min=17.64, max=52.92)	
Moderate hepatic fibrosis – F2	80.45 (41.89, 117.55)	Uniform (min=39.85, max=119.55)	
Severe hepatic fibrosis – F3	137.03 (71.72, 199.60)	Uniform (min=67.62, max=202.86)	
Compensated cirrhosis (F4, CC)	206.93 (109.23, 301.92)	Uniform (min=102.25, max=306.75)	
Decompensated cirrhosis (DC)	313.51 (161.53, 460.81)	Uniform (min=156.70, max=470.10)	
Hepatocellular carcinoma (HCC)	378.09 (202.34, 561.70)	Uniform (min=191.47, max=574.42)	
HIV care costs (annual)			
HIV care visit cost	191.70 (154.69, 227.36)	Uniform (min=152.74, max=229.12)	Dawei Cohort, including visit and ARV drug costs. See Table S4 for specific ARV costs. Bounds ±20% point estimate
Transition rates			
F0 to F1 (per year)	0.122 (0.094, 0.155)	Gamma (shape=61.95, scale=.00197)	[8]
F1 to F2 (per year)	0.115 (0.091, 0.142)	Gamma (shape=84.64, scale=0.00136)	[8]
F2 to F3 (per year)	0.124 (0.091, 0.16)	Gamma (shape=50.21, scale=0.0025)	[8]
F3 to CC (per year)	0.115 (0.096, 0.134)	Gamma (shape= 132.25, scale=0.0009)	[8]
CC to DC (per year)	0.039 (0.022, 0.062)	Beta (alpha=14.6168, beta=360.1732)	[5, 9-12] Transition probability sampled, converted to rate

CC or DC to HCC (per year)	0.015 (0.002, 0.04)	Beta (alpha=1.19326, beta=136.1074)	[5, 9-13] Transition probability sampled, converted to rate
Relative risk of CC to DC with SVR	0.078 (0.023, 0.190)	Lognormal (mean 0.07, 95%CI 0.03-0.2)	[14, 15]
Relative risk of CC/DC to HCC with SVR	0.236 (0.151, 0.352)	Lognormal (mean 0.23, 95%CI 0.16-0.35)	[16]
Background (non-HCV related) mortality	0.0336 (0.0292, 0.0378)	Uniform (min=0.029, max=0.038)	[1, 2] Weighted by CD4 status at HCV treatment initiation (Table S3), with all patients on ART as per cohort. See supplement for details.
Relative risk of DC to liver-related death in HIV/HCV coinfection compared to HCV monoinfection	2.3 (1.57, 3.38)	Lognormal (mean 2.26, 95%CI 1.51-3.38)	[5, 17-19]
DC to liver-related death for HCV monoinfection	0.130 (0.111, 0.150)	Beta (alpha=147.03, beta=983.97)	[9, 10] Transition probability sampled, converted to rate
HCC to liver-related death	0.429 (0.370, 0.482)	Beta (alpha=117.1, beta=155.23)	[5, 20-22] Transition probability sampled, converted to rate
SVR	96%	-	Dawei cohort
Discount rate	3%	-	[23]
Disability weights			
HCV/HIV coinfection (no SVR)			
F0/F1	0.088	-	Calculated as [1-((1-HIV disability weight)*(1-HCV disability weight))] using ART disability weight as all on ART in cohort. See supplement for details. [4, 5]
F2/F3	0.136	-	[5, 24]
Compensated cirrhosis (CC)	0.183	-	[4, 5]
Decompensated cirrhosis (DC)	0.242	-	[4, 5]
Hepatocellular carcinoma (HCC)	0.494	-	[4, 5]
HCV/HIV coinfection (achieved SVR)			
Disutility improvement on achieving SVR	0.045 (0.04, 0.05)	Uniform (min=0.05, max=0.05)	[25-27]

Table S4. Average unit cost in 2017 US$ of an HCV visit to Dawei clinic by cost category and visit component. Distribution of visit component by cost category expressed as row percentage. HCV: hepatitis C virus.

	Cost category		
Visit component	**Recurrent cost (%)**	**Personnel cost (%)**	**Capital cost (%)**
General coordination	20.31 (59.0)	13.46 (39.1)	0.66 (1.9)
HCV consultation	0.75 (65.2)	0.20 (17.7)	0.19 (17.1)
Laboratory	2.83 (90.5)	0.26 (8.4)	0.04 (1.2)
Pharmacy	0.22 (59.6)	0.13 (34.6)	0.02 (5.8)
HCV counselling	0.48 (74.2)	0.13 (20.2)	0.04 (5.6)

Table S5. Cost components by intervention scenario. †"Observed MSF intervention" presents summary data from observational study, including 2017 DAA prices. ‡"MSF with updated DAA costs" estimates costs with updated DAA prices for quality-assured generic DAAs negotiated in 2018. §"Simplified MoH" strategy estimates costs with generic DAAs and a proposed simplified protocol (Figure 1), with local staff costs and no overheads. HCV treatment costs are assumed to be standard for all patients ($120/12-week treatment course of sofosbuvir/daclatasvir for non-cirrhotic patients; $240/24-week treatment course of sofosbuvir/daclatasvir for cirrhotic patients). 95% confidence intervals are presented for the observed cost data reflecting patient variations in observed costs. For estimations of costs using updated cost data or simplified strategies, patients were assumed to adhere to the exact clinical schedule (see Fig 1) and so no uncertainty is provided. MSF: Médecins sans Frontières; DAA: direct-acting antiviral treatment; MoH: Ministry of Health; CI: confidence interval.

	Per patient cost (95% CI)		
Strategy	**HCV treatment**	**HIV treatment**	**HCV disease stage**
Baseline	0	2,306.63 (1,785.13, 2,868.67)	1,685.08 (1,106.88, 2,367.23)
Observed MSF treatment program†	1,563.92 (1,309.88, 1,855.96)	2,866.59 (2,252.05, 3,520.34)	1,682.21 (1,030.56, 2,346.50)
MSF program with updated DAA costs‡	1,076.13 (870.05, 1,314.11)	2,866.59 (2,252.05, 3,520.34)	1,682.21 (1,030.56, 2,346.50)
Simplified MoH§	501.50	2,866.59 (2,252.05, 3,520.34)	1,682.21 (1,030.56, 2,346.50)

Table S6. HIV characteristics of study participants at baseline enrollment (n=121). WHO HIV staging categories defined as: Stage 1: Asymptomatic; Stage 2: mildly symptomatic; Stage 3: moderately symptomatic; Stage 4: severely symptomatic/AIDS [28].TDF: Tenofovir (300mg daily); 3TC: Lamivudine (300mg daily); EFV: Efavirenz (600mg daily); AZT: Zidovudine (300mg twice daily); NVP: Nevirapine (200mg twice daily); ABC: Abacavir (600mg daily); LPV/r: Kaletra/ Lopinavir/Rionavir (400mg/100mg twice daily);

Characteristic	n	%
CD4 Count (cells/μL) upon HCV treatment initiation		
<200	13	10.7
200-350	23	18.9
350-500	24	19.7
>500	62	50.8
WHO HIV staging at HIV care enrollment		
Stage 1	10	8.3
Stage 2	20	16.5
Stage 3	73	60.3
Stage 4	17	14.1
Unknown	1	0.8
HIV treatment regimen		
AZT + 3TC + NVP	19	15.7
AZT + 3TC + EFV	5	4.1
TDF + 3TC + EFV	84	69.4
ABC + 3TC + EFV	3	2.5
LPV/r + 3TC + AZT	5	4.1
TDF + 3TC + LPV/r	4	3.3
AZT + TDF + 3TC + LPV/r	1	0.8

Table S7. Unit cost in US$ of HIV therapy by drug type. 2017 drug costs are based on costs obtained from MSF invoices, which include MSF overhead charges. TDF: Tenofovir (300mg daily); 3TC: Lamivudine (300mg daily); EFV: Efavirenz (600mg daily); AZT: Zidovudine (300mg twice daily); NVP: Nevirapine (200mg twice daily); ABC: Abacavir (600mg daily); LPV/r: Kaletra/ Lopinavir/Rionavir (400mg/100mg twice daily)

ARV regimen	2017 Cost (Annual)
AZT+3TC+NVP	34.23
AZT+3TC+EFV	54.32
TDF+3TC+EFV	79.40
ABC+3TC+EFV	152.45
LPV/r+3TC+AZT	239.63
TDF+3TC+LPV/r	219.00
AZT+TDF+3TC+LPV/r	301.08

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