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# An intensive model of care for hepatitis C virus screening and treatment with direct-acting antivirals in people who inject drugs in Nairobi, Kenya: A model-based cost-effectiveness analysis.

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**Abbreviations**

| | |
|---|---|
| AIDS | Acquired immunodeficiency syndrome |
| ART | Antiretroviral therapy |
| DAA | Direct Acting Antiviral |
| DALY | Disability adjusted life year |
| DOT | Directly-observed therapy |
| GDP | Gross Domestic Product |
| HCV | Hepatitis C |
| HIV | Human Immunodeficiency Virus |
| ICER | Incremental cost-effectiveness ratio |
| LMIC | Lower- and middle-income countries |
| MAT | Medically Assisted Therapy |
| NSP | Needle and syringe exchange program |
| PWID | People Who Inject Drugs |
| PWUD | People who use drugs |
| RNA | Ribonucleic acid |
| SVR | Sustained Viral Response |
| SVR12 | Sustained Viral response at 12 weeks |
| TLC-IDU | Testing and Linkage to care for injecting drug users |
| USD | United States dollar |

## Abstract

**Background and aims:** Hepatitis C virus (HCV) treatment is essential for eliminating HCV in people who inject drugs (PWID) but has limited coverage in resource-limited settings. We measured the cost-effectiveness of a pilot HCV screening and treatment intervention using directly-observed therapy among PWID attending harm reduction services in Nairobi, Kenya.

**Design:** We utilised an existing model of HIV and HCV transmission among current and former PWID in Nairobi to estimate the cost-effectiveness of screening and treatment for HCV, including prevention benefits, versus no screening and treatment. The cure rate of treatment and costs for screening and treatment were estimated from intervention data, while other model parameters were derived from literature. Cost-effectiveness was evaluated over a lifetime horizon from the healthcare provider's perspective. One-way and probabilistic sensitivity analyses were performed.

**Setting:** Nairobi, Kenya

**Population:** PWID

**Measurements:** Treatment costs, incremental cost-effectiveness ratio (cost per disability adjusted life year averted).

**Findings:** The cost per disability adjusted life year averted for the intervention was US$975, with 92.1% of the probabilistic sensitivity analyses simulations falling below the per capita gross domestic product for Kenya (US$1,509; commonly used as a suitable threshold for determining whether an intervention is cost-effective). However, the intervention was not cost-effective at the opportunity cost-based cost-effectiveness threshold of $647 per disability adjusted life year averted. Sensitivity analyses showed that the intervention could provide more value for money by including modelled estimates for HCV disease care costs, assuming lower drug prices ($75 instead of $728 per course) and excluding directly-observed therapy costs.

**Conclusions:** The current strategy of screening and treatment for hepatitis C virus (HCV) among people who inject drugs in Nairobi is likely to be highly cost-effective with currently available cheaper drug prices, if directly-observed therapy is not used and HCV disease care costs are accounted for.



**Key words:** HCV, direct-acting antiviral treatment, people who inject drugs, low-income setting, cost-effectiveness

## Introduction

Globally, 71 million people were chronically infected with hepatitis C virus (HCV) in 2015[1]; most of whom live in lower- and middle-income countries (LMIC) where there is limited testing and treatment[1, 2].

People who inject drugs (PWID) have a high prevalence of HCV infection (52% antibody positive)[3] globally and contribute an estimated 43% of incident HCV infections[4]. In Kenya, the estimated seroprevalence of HCV is 3% in the general population[5], but 11-36% among PWID[6-10]. To ensure Kenya can achieve the World Health Organisation HCV elimination targets[11], interventions to scale-up HCV case finding and directly-acting antiviral (DAA) treatment must target PWID. Despite international guidelines recommending these interventions for PWID[12, 13], coverage is limited in Kenya and LMICs[14, 15].

Testing, referral and treatment of PWID can be challenging due to patient-level and system-wide factors[16], particularly in LMIC with poor availability of services for PWID. However, the increasing acceptability and availability of harm reduction services in settings such as Kenya[17], and recent advances in the simplification of HCV testing and treatment presents opportunities for expanding HCV treatment among PWID in LMICs[18]. This could improve access and reduce the costs of expanding HCV treatment to PWID.

Recent systematic reviews highlight the cost-effectiveness of HCV treatment for PWID in high-income countries, but evidence from LMICs is limited[19, 20]. Model-based analyses evaluated the cost-effectiveness of HCV screening and DAA-based treatment among PWID in LMICs[21], including Tanzania[22], but relied mostly on data from literature and expert opinion. The lack of empirical data makes the realism of these analyses uncertain and their generalizability to other LMICs unclear. Cost-effectiveness analyses of 'real-world' HCV testing and treatment interventions for PWID in LMICs are needed for guiding policy on the expansion of these interventions. In this study, we evaluated the impact and cost-effectiveness of a pilot HCV screening and DAA-based treatment intervention among people who use drugs (PWUD) in Nairobi, Kenya.

## Methods

### Study design

The cost-effectiveness of the HCV screening and DAA-based intervention was assessed in comparison to usual care. Although the intervention was for PWUD, all HCV infections diagnosed in this setting were assumed to be through injecting drug use. Before the pilot program, there was negligible screening and treatment for HCV among PWID as confirmed by the Kenyan Ministry of Health (Helgar Musyoki, January 2021) and the Kenyan Testing and Linkage to care for injecting drug users (TLC-IDU) study survey from 2015 that found no PWID reported previously being treated for HCV[10]. We, therefore, used 'no screening and treatment' as the comparator. A healthcare provider's perspective was assumed as it estimates the costs and effects incurred from the health service, and so provides guidance to decision-makers on whether to invest in HCV screening and treatment in Kenya.

Ethical approval for this study was obtained from the Kenya Medical Research Institute Scientific and Ethics Review Unit (reference: KEMRI/RES/7/3/1).

**Setting and intervention**

Patient characteristics and resource utilization in the base-case analysis were collected from a pilot intervention aimed at demonstrating the 'real-world' effectiveness of DAA-based HCV treatment amongst PWID in Nairobi. The pilot treatment program was established in 2016 by Médecins Sans Frontières in collaboration with Médecins du Monde. Médecins du Monde offered point-of-care screening for HCV antibodies to PWUD as part of harm reduction services provided through its Drop-in Centre and outreach activities in Nairobi (**Figure 1** shows the model of care). Blood samples for all HCV seropositive clients were sent to an external laboratory for HCV confirmatory testing, genotyping and other pre-treatment tests. Patients received a transient elastography (Fibroscan) at a nearby private hospital. Treatment eligibility was based on international guidelines[23-25]. Eligible clients were treated with daclatasvir and sofosbuvir (86.4%) or ledipasvir and sofosbuvir (13.6%), delivered within the Drop-in Centre using directly-observed therapy (DOT). All clients on treatment attended the clinic every day, where a clinical officer dispensed and observed them taking drugs. The clinical officer provided counselling sessions or medical reviews at each visit, including family planning, pre-treatment, treatment initiation, and lifestyle and reinfection advice. Transport costs were reimbursed and included in the analysis. Peer support and defaulter tracing was facilitated through peer educators. After treatment completion, patients were followed up for ~12 weeks, whereupon the sustained virologic response (SVR12) was assessed to determine treatment success.

We also used data from the TLC-IDU study (NCT01557998)[8, 10] to estimate costs of an alternative HCV screening and treatment intervention in Kenya. The study cohort and intervention cost analysis are described in the Supplementary materials. These costs were used in the sensitivity analysis.

Figure 1

**Mathematical model structure**

We utilised an existing dynamic compartmental model of HIV and HCV transmission amongst current and former PWID in Nairobi[26] to evaluate health outcomes and costs of the HCV treatment intervention in comparison to no treatment. The model allowed us to capture both the individual (preventing or slowing down HCV disease progression) and population benefits (preventing new infections) of treatment.

The model incorporates the transmission of HIV and HCV due to injecting drug use as well as HIV transmission due to sexual risk behaviour (Supplementary Figure 1). The population is stratified by injecting status (PWID and former PWID), sex, HIV infection state (susceptible, acute HIV infection, chronic HIV infection, Pre-AIDS, AIDS), HIV treatment status (on/off anti-retroviral therapy; ART), HCV infection state (susceptible, previously exposed, chronic HCV infection, and chronic HCV undergoing treatment), HCV disease progression states (METAVIR fibrosis stages F0-F4, decompensated cirrhosis or hepatocellular carcinoma), and harm reduction state (on/off Medically Assisted Therapy (MAT) and/or needle and syringe exchange program (NSP)). The model was calibrated using Approximate Bayesian Computation to detailed data for Nairobi from the Kenya AIDS indicator surveys[27], national polling booth surveys among PWID from 2015 and 2016[28, 29], national MAT and NSP programme data, and a series of cross-sectional bio-behavioural surveys done over 2012-2015 by the TLC-IDU study[30]. Data on HIV and HCV disease progression rates and efficacy of NSP, MAT and ART came from the literature (Table 1). The calibrated model included uncertainty in all model parameters, which was propagated into all model projections. We used data on MAT status, current injecting status, HIV co-

infection and fibrosis stages of all patients treated in the intervention to parameterise treatment numbers within each compartment of the model (Table 1).

Table 1

**Intervention costs**

HCV screening and treatment costs were estimated from intervention data using a retrospective, cohort-based, micro-costing approach from the healthcare provider's perspective in 2018 US dollars. A detailed review of the treatment protocol and interviews with staff identified activities undertaken in the screening and treatment intervention. Resources accounted for each activity included staff time (doctors, nurses, counsellors), diagnostic and clinical tests, medicines, overheads (management, buildings, support staff, utilities and consumables) and reimbursed transport costs for patients. Staff time for clinical staff was estimated for each activity using staff time sheets, supplemented through interviews. Patient-level data on resource use including clinic visits, tests and medicines were obtained from the Research Electronic Data Capture clinical database[31].

Costs for staff, consumables, including test kits, were obtained from study financial records and supplemented through interviews with key personnel (finance, logistics, and program managers). Costs for the DAA medicines represent the prices paid by Médecins Sans Frontières in Kenya at the time. Unit costs for outsourced laboratory tests were obtained from relevant laboratories.

Up-to-date unit costs were applied for each resource. Historical costs were adjusted for inflation to 2018 prices[32]. Local currency prices were converted to USD using the average market-based exchange rate for 2016–2017[33](1 USD=103 Kenya Shillings). The cost of each activity is the sum of costs for all resources used for that activity, i.e. labour, consumables and overheads. The activity costs were multiplied by the frequency that a patient received each activity and summed to give the estimated total cost per patient.

The costs of HCV screening included the rapid test for HCV antibodies, and when positive, the HCV confirmatory test. The average cost per diagnosis was calculated based on the number of antibody and confirmatory tests done per individual diagnosed with chronic infection.

**Costs of HCV related disease**

Information on cost of health care for HCV-related disease was not available for Kenya, and so were not included in the base-case analysis.

**HCV Treatment Outcome**

We estimated the proportion of patients who achieved an SVR at 12 weeks among all those that initiated therapy using patient-level data from the intervention.

**HCV disability weights**

In the absence of Kenya specific health utility values, we applied the Global Burden of Disease estimates of disability weights to HCV disease states in the model to estimate disability adjusted life years (DALYs) as health outcomes (Table 1)[34]. We assumed that patients with METAVIR score F0 were not associated with disability. A linear increase in disability was modelled for F1-F3 based on the estimate for F4 (cirrhosis), which was assumed to be equivalent to the value for moderate abdominopelvic problem. The estimate

for decompensated cirrhosis was used. A direct estimate for hepatocellular carcinoma was not available and so a value for metastatic cancer was used.

**Cost-effectiveness**

We estimated the incremental cost-effectiveness ratio (ICER) in terms of cost per DALY averted. We used a 3% discount rate for both costs and DALYs, following current guidance for LMICs[35, 36]. We used a 50-year time horizon to capture the long-term effects of chronic HCV infection and population prevention benefits associated with disease transmission. The estimated ICER was compared to the 2018 Gross Domestic Product (GDP) per-capita for Kenya (US$ 1,509)[37] which is commonly used as a threshold for determining whether an intervention is cost-effective[38]. We also compared the ICER to an empirical opportunity cost-based cost-effectiveness threshold for Kenya of $647 per DALY averted[39]. This analysis was not pre-registered, however we followed standard guidelines for economic evaluations[35, 36] and methods we have used in previous analyses[26].

**Sensitivity analyses**

To quantify the effect of parameter uncertainty on model results, a probabilistic sensitivity analysis was conducted using the uncertainties of individual parameters and performing random independent parameter draws from their probability distributions to generate 3,000 simulations of costs and DALYs (Table 1 and Supplementary Table S2-S5). These simulation results were used to estimate the probability that the intervention was cost-effective over different cost-effectiveness thresholds.

Sensitivity analyses were performed to evaluate the impact of varying our assumptions for key parameters on cost-effectiveness. We performed one-way sensitivity analyses on the following model parameters: time horizon (25 or 100 years), discount rates (0 or 6%, as recommended by the World Health Organisation [35]), SVR12 (70/95%), higher HCV seroprevalence among PWID in Kenya (13%)[10], a lower cost of HCV rapid diagnostic test ($1.16) and HCV confirmatory test ($50) using estimates from the TLC-IDU study. We also evaluated the effect of varying HCV seroprevalence from 2.8% (observed in the general population)[5] to 70% (highest observed in PWID)[40] to reflect the likely variation across Kenya. We also evaluated the effect of including healthcare costs for HCV-related disease using modelled estimates from Tanzania[41], adjusted for Kenya using purchasing power parity conversion factors[42].

The intervention employed DOT to improve adherence to HCV treatment, however, evidence shows PWID can adhere to ART[43] and HCV treatment without DOT[44-47]. In addition, the costs for DOT could have been lower if it had been integrated with the provision of MAT, which 69.1% of treated patients were taking. Therefore, in two scenarios we explored the effects of either assuming a shorter time for each DOT (5 versus 20 minutes used in the base-case) or excluding the costs of DOT altogether. The shorter time was based on interviews with pharmacists in a local MAT clinic where a similar program (TLC-IDU) was piloted. We also evaluated the impact of assuming costs incurred by this other pilot intervention, assuming similar treatment outcomes (see Supplementary materials).

The average price of DAAs used by the intervention was US$728 per treatment. We assessed the effect of reducing DAA prices to levels currently being paid by Médecins Sans Frontières ($75 per 12-week treatment), but not in Kenya. We also evaluated the simultaneous effect of the cheaper DAA price, accounting for healthcare costs and the exclusion of DOT costs on cost-effectiveness of the intervention.

## Results

### Patient characteristics

The HCV cascade of care in the intervention is shown on **Figure 2**. A total of 1,673 people (33.8% PWID, 58.8% PWUD [non-injecting], 6.9% other key populations and 0.5% general population) were screened for HCV between January 2016 and April 2018, with 124 (7.7%) HCV seropositive and 96 (77.4%) HCV RNA positive. Eighty-one individuals (84.4%) initiated DAA treatment; their fibrosis distribution and treatment outcomes are shown in **Table 2**. The mean age for the diagnosed patients was 37.0 years and 88.9% were male. Nearly half (43.2%) of the patients who initiated treatment were co-infected with HIV, all of whom were receiving ART, and most had early stages of fibrosis (**Table 2**). Most patients (72%) had a history of past drug/substance use, 24.7% reported current use and data was missing for 2.5%. Because 90.6% of patients with past drug/substance use were on MAT, we assumed they had on-going drug use, while the remainder were assumed to be ex-PWID; 66.7% of current users were also on MAT. Of the 15 diagnosed clients not started on treatment, 9 were lost to follow-up before treatment initiation, 2 were excluded because of high HIV viral load, 3 for comorbidities and information was missing for 1 patient (data not shown in **Table 2**). A total of 79 clients completed treatment, 77 were assessed for SVR12 and 73 achieved SVR12 (90.1% of all patients who initiated treatment and 92.4% of those assessed for SVR12). SVR12 was 89.1% in HCV mono-infected versus 91.4% in HIV-HCV co-infected patients.

Figure 2

Table 2

### Treatment costs

The average cost per diagnosis was estimated to be $574 (accounting for testing HCV seronegative patients and HCV confirmatory tests in seropositive patients), while the cost of treatment was $5,164 (SD $785) per patient. The total cost of finding and treating HCV was $5,739 per patient treated. The distribution of costs is shown in **Table 3**. Visit costs include costs incurred during all visits made in preparation for, during and after treatment. These included baseline assessments, treatment initiation, on-treatment follow-up (excluding DOT), end of treatment, post-treatment follow-up and SVR assessment. DOT costs include the costs associated with daily visits made by patients to take medications under supervision. The major cost driver was DOT, contributing 57.2%% of the total intervention cost. Other contributing costs were DAAs (12.8%), clinic visits (10.9%), screening and diagnosis (10.0%), laboratory investigations (7.2%), and elastography (3.4%). Treatment costs were $429 higher for HCV/HIV coinfected compared to HCV mono-infected patients largely due to differences in DAA drugs used, laboratory and clinic visit costs (**Figure 3**).

Table 3

Figure 3

### Base-case cost-effectiveness

The calibrated model fit the data well suggesting slowly decreasing HIV and slowly increasing HCV epidemics among PWID in Nairobi, with an estimated chronic HCV prevalence of 6.7% (95%CrI: 5.9-8.2) in 2016. The intervention is estimated to avert 5.9% (95%CrI: 4.2-8.1%) of all new HCV infections over 2016-2030.

We estimated that the HCV screening and treatment intervention undertaken over 2016-2018 incurred a total cost of $463,629 and would avert 475 DALYs over 50 years, discounted at 3.0% per annum, resulting in an ICER of $975 per DALY averted (**Table 4**). The ICER is less than one times the 2018 GDP per capita for Kenya (US$ 1,509) demonstrating that this intervention is potentially cost-effective at this cost-effectiveness threshold. However, the intervention was not cost-effective at the opportunity cost-based threshold of $647 per DALY averted.

Table 4

**Sensitivity analysis**

In one-way sensitivity analyses, the base-case ICER was most sensitive to the time horizon (**Figure 4**). Reducing the time horizon to 25 years increased the ICER to $3,708/DALY averted, rendering the intervention not cost-effective, while increasing the time horizon to 100 years reduced the ICER to $355/DALY averted. Assuming discount rates of 0% or 6% improved (ICER=$342/DALY) or reduced (ICER=$2,514 /DALY) cost-effectiveness, respectively. Assuming a 13% HCV seroprevalence among PWID in Kenya reduced the cost of case-finding from $574 to $434, slightly improving cost-effectiveness of the intervention (ICER=$951/DALY). The intervention could remain cost-effective at the GDP per capita cost-effectiveness threshold over all the HCV seroprevalences evaluated including the lowest (2.8%; ICER=$1,114/DALY). Reducing the costs of HCV point of care and confirmatory tests reduced the cost per case diagnosed to $349 and $469, respectively, resulting in ICERs of $937 and $958 per DALY averted, respectively. Accounting for costs of HCV disease care reduced the ICER to $670 per DALY averted.

The ICER for the base-case scenario is reduced by a shorter time for DOT ($939/DALY), a reduced price for DAAs ($866/DALY), or a combination of both ($830/DALY). The ICER is further reduced ($418/DALY) if DOT is not used, assuming no adverse effect on HCV treatment outcomes. A reduction in DAA prices and the exclusion of DOT costs resulted in an ICER of $307/DALY averted. Lastly, accounting for HCV disease care costs, a reduction in DAA prices and the exclusion of DOT costs resulted in improved value for money ($2/DALY averted).

The probabilistic sensitivity analysis suggests that 92.1% of the simulated ICERs for the base-case scenario fall below the GDP per capita cost-effectiveness threshold (Supplementary Figures 3 and 4), but only 1.8% fall below the opportunity cost-based threshold. This increases to 36.7% when we account for HCV health care costs, 99.0% if we assume the cheaper DAA cost and no DOT and 100% if we account for all three.

Figure 2

## Discussion

### Main findings

This study provides important evidence that the implementation of testing and DAA-based HCV treatment interventions among PWID can be cost-effective in a LMIC setting. Our results suggest that the intervention undertaken in Nairobi, involving DOT), cost $975/DALY averted, less than the one times GDP per capita (US$1,509) cost-effectiveness threshold for Kenya. The intervention could provide improved value for money with simplification of the care pathway, integration with other services like MAT and lower prices for DAAs. The intervention would become nearly cost-saving (ICER=$2/DALY averted) if, in addition to

reduced DAA prices and accounting for HCV healthcare costs, DOT is eliminated altogether (assuming no drop in SVR).

**Strengths and limitations**

This study draws major strength from using 'real-world' data on PWID screened, diagnosed, and treated as part of a pilot intervention in Nairobi. This enabled collection of patient-level data on resource utilization and estimation of the full costs of screening and DAA-based HCV treatment. We used testing, linkage-to-care and effectiveness data (SVR12 rates) derived directly from the intervention. These strengths make our results likely transferable to PWID populations in other parts of Kenya and the SSA region. Secondly, a dynamic compartmental model allowed us to capture both the individual (prevention of HCV disease progression) and population benefits (reducing HCV transmission) of HCV treatment.

However, the interpretation of our findings requires consideration of potential limitations. Firstly, the generalizability of our results may be limited because they are based on a closely managed, intensive model of care for testing, linkage-to-care, treatment, DOT and follow-up using dedicated staff in a harm reduction service; all of which may have contributed to the observed successful treatment outcomes. However, they could be generalizable to other SSA settings with similar HCV prevalence in PWID, where PWID are provided harm reduction services through similar Drop-in centres and MAT services. Secondly, we did not evaluate the effect of including healthcare costs associated with HCV-related disease in the base-case analysis, which is likely to make our projections conservative. Accounting for these cost savings decreased the ICER by a third, reflecting improved value for money. Thirdly, the use of costs and outcome data from a single population of PWID may limit the generalisability of our results. Fourthly, in the absence of Kenya specific utility weights, we applied the Global Burden of Disease study disability weights to estimate DALYs. Some of these disability weights were not specific to HCV diseases states, possibly limiting their accuracy; however, they are widely used in the literature[48, 49], allowing comparison of our results with other studies, while previous analyses suggest they may not impact on decisions[50].

**Comparison with other studies**

To our knowledge, this is the first study to evaluate the cost-effectiveness of a 'real-world' implementation of HCV testing and DAA-based treatment among PWID in a LMIC setting. This represents a significant addition to existing evidence, which currently focusses on high income countries[19]. Model-based analyses have evaluated the cost-effectiveness of HCV screening and DAA-based treatment among PWID in LMICs[21] and recently in Tanzania[22], and found them to be cost-effective or cost-saving if DAA costs are low enough. However, unlike our study, their costs or outcomes were not derived from an actual intervention.

**Conclusions and implications**

Our analysis suggests that screening and treatment of HCV with DAA-based regimens among PWID in Nairobi, Kenya is associated with significant costs largely due to DOT and expensive DAAs. Despite this, the intervention is cost-effective in its current format. Large improvements in cost-effectiveness can be easily achieved through accessing cheaper DAAs and streamlining or removing DOT. In this study, therapy was dispensed by a clinical officer, which could be simplified through using trained peer educators who already support harm reduction services. Although eliminating DOT could improve cost-effectiveness, it is important to assess whether it would be similarly effective for treating PWID. Fortunately, prior studies suggest this should be the case, with 94.0% retention and 90.0% achieving

SVR12 in a randomized control trial setting in New York[45, 51], 94.9% retention in the TLC-IDU study in Kenya (NCT01557998) and 93-98% retention and 85-87% achieving SVR12 in other real-world studies not using DOT[46, 47, 52]. The development of innovative approaches to enhance and monitor adherence to DAAs in PWID that may be more cost-effective than DOT presents opportunities to further optimize models of care in this setting[53].

Our findings support the development of similar and optimized HCV screening and treatment strategies for PWID in Kenya and other LMIC. Numerous centres provide harm reduction services and MAT in Kenya. Such centres provide opportunities to establish similar treatment interventions for HCV that could enable Kenya and other LMIC with such services to substantially reduce their HCV burden.

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# Tables

**Table 1.** Key model parameters and calibration data. * indicates calibration data.

| Parameter | Prior Parameter Distribution/ Calibration range | Source |
|---|---|---|
| **Cohort characteristics** | | |
| PWID population Size* | 9750-17150 | [54] |
| Proportion of PWID that are female* | 14.7% (95% CI: 13.1-16.4) | TLC-IDU[10] |
| Average duration of injecting drug use (years) | Uniform: 1.75-7.0 | TLC-IDU[10] |
| HIV prevalence amongst male PWID in 2015* | 9.6% (95% CI: 8.2-11.0) | TLC-IDU[10] |
| HIV prevalence amongst female PWID in 2015* | 29.1% (95% CI: 19.8-38.4) | TLC-IDU[10] |
| ART coverage amongst HIV positive PWID **in 2015*** | 65.7% (95% CI: 60.3-71.0) | TLC-IDU[10] |
| Proportion of PWID on ART that are virally supressed | Normal: 34.3% (95%CI: 28.3-40.2) | TLC-IDU[10] |
| HCV antibody prevalence amongst PWID in **2015*** | 10.9% (95% CI: 8.4-13.3) | TLC-IDU[10] |
| Proportion of HCV infections that spontaneously clear | | |
| amongst HIV negatives | Uniform: 0.22 - 0.29 | [55] |
| amongst HIV positives | Uniform: 0.115 - 0.193 | [56] |
| **Efficacy of interventions** | | |
| Relative reduction in HCV transmission risk if on OST | Lognormal: 0.50 (95%CI: 0.40-0.63) | [57] |
| Relative reduction in HCV transmission risk if on NSP | Lognormal: 0.44 (95%CI: 24-0.80) | [57] |
| Relative reduction in HIV transmission risk if on OST | Lognormal: 0.46 (95%CI: 0.32-0.67) | [58] |
| Relative reduction in HIV transmission risk if on NSP | Lognormal: 0.42 (95%CI: 0.22-0.81) | [59] |
| **HCV disease progression rates** | | |
| from F0 to F1 (per year) | Normal(0.128, 0.0245) | [60]. |
| from F1 to F2 (per year) | Normal(0.059, 0.012) | [60] |
| from F2 to F3 (per year) | Normal(0.078, 0.0112) | [60] |
| from F3 to F4 (per year) | Normal(0.116, 0.0232) | [60] |
| Relative increase in HCV disease progression from F0 to F4 if HIV infected | | |
| Without ART | Lognormal: 2.489 (95% CI 1.811 – 3.420) | [61] |
| With ART | Lognormal: 1.723 (95% CI 1.059 – 2.804) | [61] |
| Annual probability of HCV progression from F4 to decompensated cirrhosis | Beta(14.6168,360.1732) | [62] |
| Annual probability of HCV progression from F4 to hepatocellular carcinoma | Beta(1.9326,136.1732) | [62] |
| Annual probability of HCV progression from decompensated cirrhosis to hepatocellular carcinoma | Beta(1.9326,136.1732) | [62] |
| Annual probability of mortality from decompensated cirrhosis | Beta(147.03,983.97) | [62] |

| | | |
|---|---|---|
| Factor increase in mortality rate from decompensated cirrhosis if HIV co-infected. | Lognormal: 2.26% (95% CI: 1.51-3.38) | [63, 64] |
| Annual probability of mortality from hepatocellular carcinoma | Beta(117.1033,155.23) | [62] |
| Relative risk of progression from F4 to decompensated cirrhosis following SVR | Lognormal: 0.07% (95%CI: 0.03-0.2) | [65] |
| Relative risk of progression from F4 to hepatocellular carcinoma following SVR | Lognormal: 0.23% (95%CI: 0.16-0.35) | [66] |
| **Disability Weights** | | |
| **HIV Disease States** | | |
| Acute Infection | Equal to ART Value | No GBD estimate so assumed equal to ART. |
| Chronic Infection | Equal to ART Value | No GBD estimate so assumed equal to ART. |
| HIV: symptomatic, pre-AIDS | Uniform(0.184,0.377) | [67] |
| AIDs: not on ART | Uniform(0.406,0.743) | [67] |
| HIV/AIDs: receiving ART | Uniform(0.052,0.111) | [67] |
| HCV Disease States | | |
| Metavir F0 | Not sampled | |
| Metavir F1 – F3 | | [67]Assumed linear disability increase from F0 to F4. |
| Metavir F4 | Uniform(0.078,0.159) | [67]No GBD estimate so used value for moderate abdominopelvic problem |
| Decompensated Cirrhosis | Uniform(0.123,0.250) | [67]Decompensated Cirrhosis of the liver |
| Hepatocellular Carcinoma | Uniform(0·307,0·600) | [67]Cancer: metastatic |
| HIV/HCV co-infection | Not sampled | Disability weights were compounded multiplicatively |
| **HCV Disease State costs ($US** | | |
| Metavir F0 | 38 | [41] Sensitivity analysis |
| Metavir F1 – F3 | 76 | [41] Sensitivity analysis |
| Metavir F4 | 89 | [41] Sensitivity analysis |
| Decompensated Cirrhosis | 994 | [41] Sensitivity analysis |
| Hepatocellular Carcinoma | 1,827 | [41] Sensitivity analysis |
| Abbreviations: AIDS, acquired immune deficiency syndrome; ART, antiretroviral therapy; GBD, Global Burden of Disease; HCV, hepatitis C virus; HIV, human immunodeficiency virus; KAIS, Kenya AIDS Indicator Survey; NSP, needle and syringe exchange program; OST, opioid substitution therapy; PWID, people who inject drugs; SVR, sustained virologic response; TLC-IDU, Test and Linkage to Care for injecting drug users | | |

1

**Table 2.** Distribution of cohort of diagnosed patients who initiated treatment and achieved SVR by fibrosis stages (n=81). F0-F4 are METAVIR scores estimated using APRI scores. HIV, human immunodeficiency virus; SVR, sustained virologic response.

| Disease stage | N (% of total) | HIV positive (% of group) | Finished treatment (% of group) | Assessed for SVR (% of group) | Achieved SVR (% of group) |
|---|---|---|---|---|---|
| F0 | 56 (69.1%) | 19 (33.9%) | 55[*] (98.2%) | 53[¥] (96.4%) | 50[Ω] (94.3%) |
| F1 | 11 (13.6%) | 4 (36.4%) | 10[+] (90.9%) | 10 (100%) | 10 (100%) |
| F2 | 3 (3.7%) | 1 (33.3%) | 3 (100%) | 3 (100%) | 3 (100%) |
| Unknown | 11 (13.6%) | 11 (100%) | 11 (100%) | 11 (100%) | 10[€] (90.9%) |
| Total | 81 (100%) | 35 (43.2%) | 79 (97.5%) | 77 (97.5%) | 73 (94.8%) |

[*]1 patient died during treatment; [+]1 patient lost to follow-up during treatment; [¥]2 not assessed for SVR; [Ω]1 patient died, 2 failed treatment; [€]1 patient failed treatment

**Table 3.** Average cost of HCV screening and treatment using DAA-based regimens. Costs are mean (SD) in 2018 USD. DAA, directly acting antivirals; DOT = directly-observed therapy.

| | Average cost (SD) | | | | | |
|---|---|---|---|---|---|---|
| **Fibrosis stage (n)** | **Visits** | **Laboratory** | **Fibroscan** | **DAA** | **DOT** | **Total cost*** |
| **Full cohort (64)** | **626.47 (73.15)** | **412.06 (104.51)** | **114.21 (13.01)** | **727.66 (301.08)** | **3284.54 (566.37)** | **5164.92 (785.34)** |
| *F0 (47)* | 622.12 (42.78) | 380.25 (74.44) | 115.67 (0) | 636.06 (154.95) | 3269.38 (492.63) | 5023.49 (560.17) |
| *F1 (10)* | 586.42 (42.01) | 417.36 (100.34) | 115.67 (0) | 600.46 (99.53) | 3122.74 (376.19) | 4842.66 (538.14) |
| *F2 (3)* | 599.09 (0) | 412.04 (45.81) | 115.67 (0) | 615.41 (113.79) | 3236.17 (0) | 4978.39 (142.91) |
| [¥]*Unknown (11)* | 695.31 (151.56) | 562.88 (121.75) | 105.15 (34.88) | 1335.12 (307.41) | 3533.91 (987.5) | 6232.37 (1169.54) |

[¥]1 patient was retreated on sofosbuvir/daclatasvir and the rest of the patients received sofosbuvir/ledipasvir which was more expensive.

* excludes diagnosis cost ($574 per patient treated) which varies according to HCV seroprevalence & HCV RNA prevalence – currently based on Ab prevalence of 7.7% and chronic prevalence of 77.4%.

**Table 4.** Base-case costs, effects and incremental cost-effectiveness ratios for HCV screening and DAA-based treatment compared to no treatment per person. CrI – credible interval; DALY – disability adjusted life year; DAA – direct acting antiviral, ICER = incremental cost-effectiveness ratio, US$ = United States dollar.

| | Costs, US$; mean (95% CrI) | | Effects$; mean (95% CrI) | | ICER$; mean (95% CrI) |
|---|---|---|---|---|---|
| **Treatment strategy** | **Total costs** | **Incremental costs** | **Total DALYs** | **DALYs averted** | **US$/DALY** |
| **Base-case** | | | | | |
| No treatment | 0 | - | 901,509 | - | - |
| DAA-based treatment | 463,629 (393,669-539,366) | 463,629 (393,669-539,366) | 901,034 (722,592-1,032,582) | 475 (296-673) | 975 (661-1,601) |

**Figures legends**

**Figure 1**
Summary representation of the model of care for HCV screening and treatment with directly acting antivirals in Nairobi, Kenya. HCV, hepatitis C virus; DAA, directly-acting antiviral; SVR12, sustained virological response 12 weeks post-treatment; DOT, directly observed therapy.

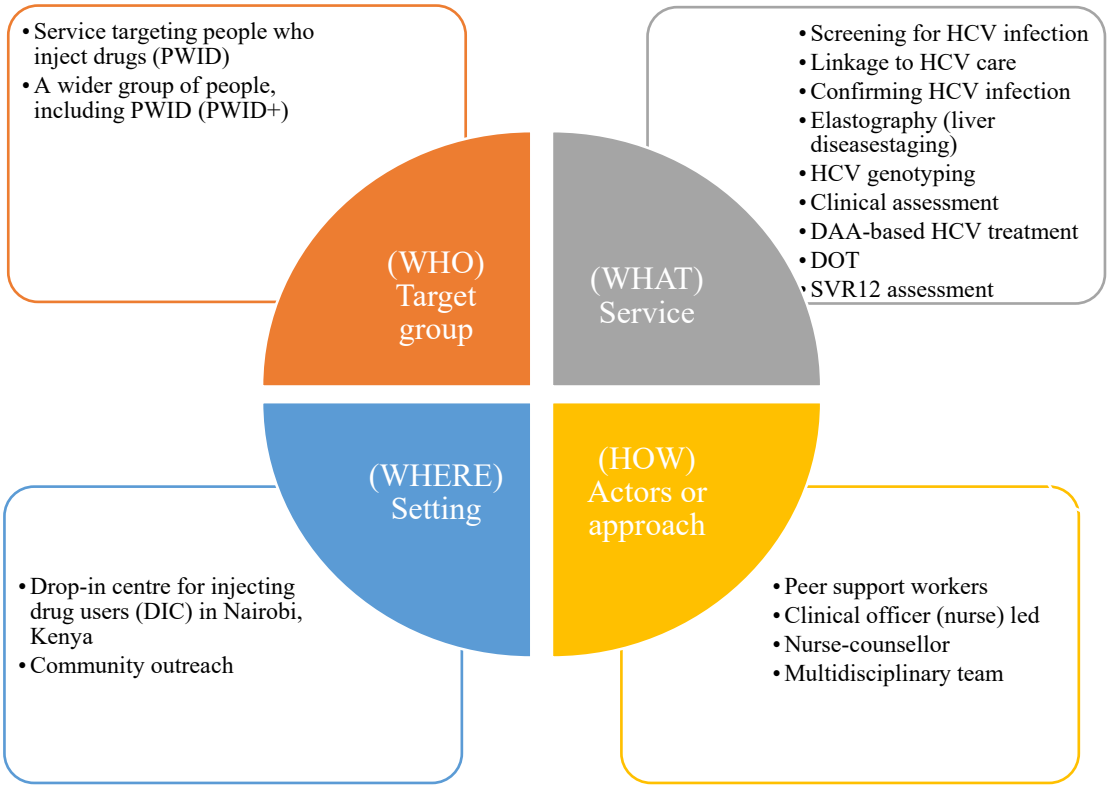

**Figure 2**

HCV cascade of care in the Médecins du Monde / Médecins Sans Frontières intervention in Nairobi, Kenya. DAA, directly-acting antiviral, SVR, HCV, hepatitis C virus; RNA, ribonucleic acid; sustained virological response. Arrows between bars represents the proportion of patients going from one step of the cascade to the next. e.g., 85.3% of those confirmed with chronic HCV initiated HCV treatment.

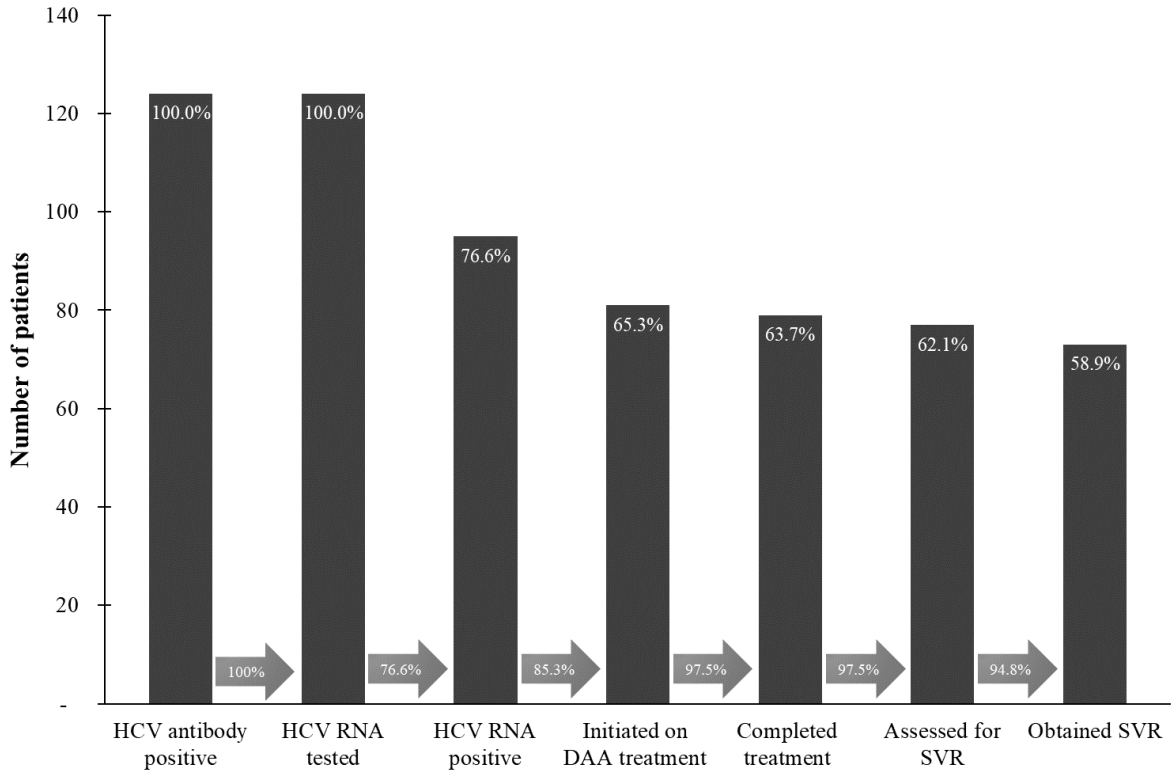

**Figure 3**

Average cost of HCV screening and treatment using DAA-based regimens by HIV status. Costs are presented in 2018 USD. DAA, directly-acting antiviral; DOT, directly-observed therapy; HCV, hepatitis C virus; HIV, human immunodeficiency.

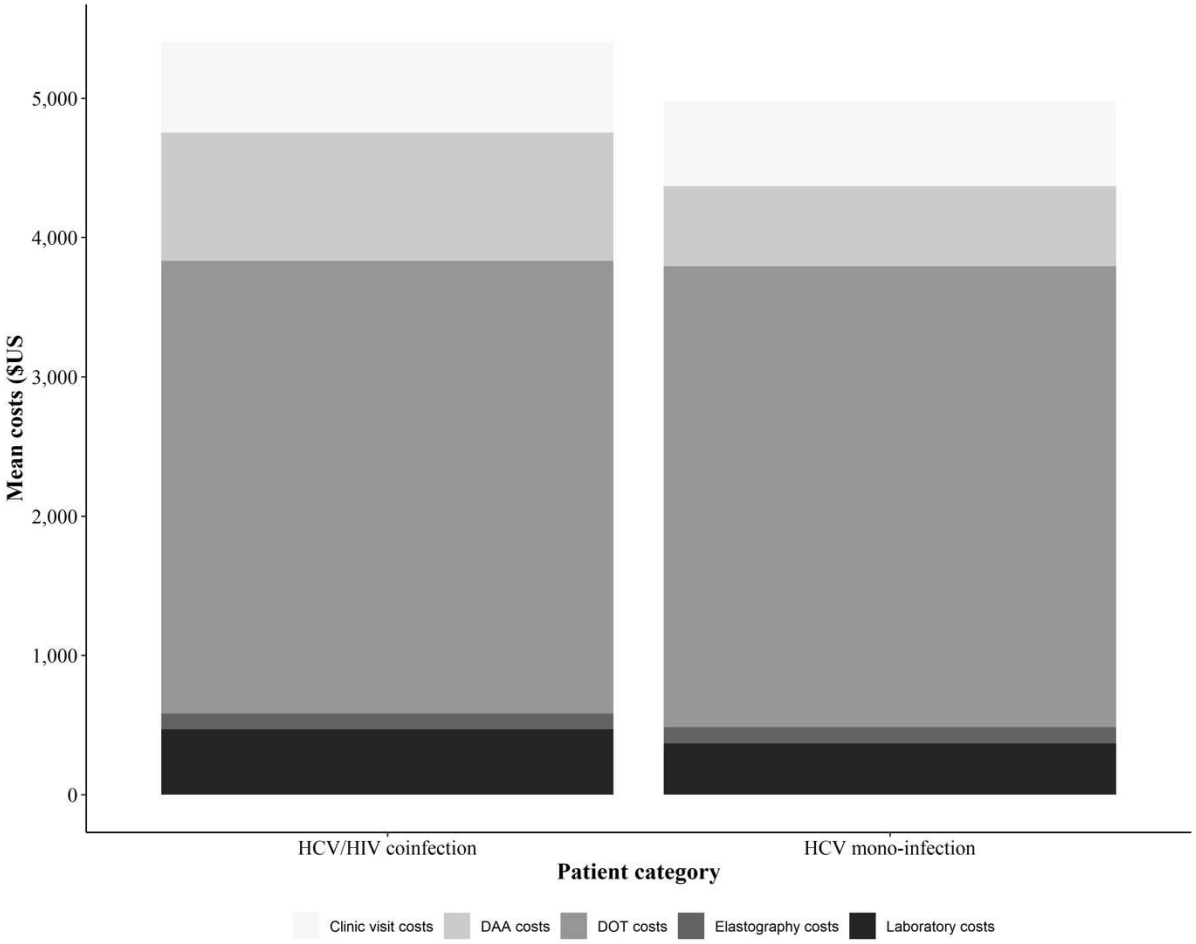

**Figure 4**

Univariate sensitivity analysis showing the effect of various changes in parameter values or model assumptions (listed on left hand side) on the incremental cost-effectiveness ratio (ICER, cost per DALY averted). The vertical line shows the base-case ICER per DALY averted. Numbers at the end of each bar are the new values used for each parameter, with grey bars giving the new ICER for decreases in parameters and black for increases in a parameter. The baseline cost of $5,739 is the estimated total cost per individual treated in the intervention. DAA=directly acting antivirals, DALY, disability adjusted life year; DOT, directly-observed therapy; SVR, sustained virological response; TLC-IDU, Test and Linkage to Care for injecting drug users.