



HAL
open science

Model-based cost-effectiveness estimates of testing strategies for diagnosing hepatitis C virus infection in people who use injecting drugs in Senegal

Léa Duchesne, Gilles Hejblum, Ndèye Coumba Toure Kane, Richard Njouom, Toni Thomas-d'Aquin, Raoul Moh, Babacar Sylla, Nicolas Rouveau, Alain Attia, Karine Lacombe

► To cite this version:

Léa Duchesne, Gilles Hejblum, Ndèye Coumba Toure Kane, Richard Njouom, Toni Thomas-d'Aquin, et al.. Model-based cost-effectiveness estimates of testing strategies for diagnosing hepatitis C virus infection in people who use injecting drugs in Senegal. *International Journal of Drug Policy*, 2020, 75, pp.102613. 10.1016/j.drugpo.2019.102613 . hal-02543434

HAL Id: hal-02543434

<https://hal.science/hal-02543434>

Submitted on 15 Apr 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**MODEL-BASED COST-EFFECTIVENESS ESTIMATES OF
TESTING STRATEGIES FOR DIAGNOSING HEPATITIS C VIRUS INFECTION
IN PEOPLE WHO USE INJECTING DRUGS IN SENEGAL**

Léa Duchesne^a, Gilles Hejblum^a, Courba Toure Kane^b, Richard Njouom^c, Thomas-D'aquin
Toni^d, Raoul Moh^{e,f}, Babacar Sylla^g, Nicolas Rouveau^h, Alain Attiaⁱ, Karine Lacombe^{a,j}

^aSorbonne Université, INSERM, Institut Pierre Louis d'Épidémiologie et de Santé Publique,
F75012, Paris, France

^bLe Dantec CHU, Laboratoire de Bactériologie Virologie, Dakar, Sénégal

^cPasteur Center of Cameroun, Virology Department, Yaoundé, Cameroon

^dTreichville CHU, Centre de Diagnostic et de Recherches sur le SIDA (CeDReS), Abidjan,
Côte d'Ivoire

^eProgramme PAC-CI, Abidjan, Côte d'Ivoire

^fUniversité FHB, Unité Pédagogique de Dermatologie et Infectiologie, UFR SMA, Abidjan,
Côte d'Ivoire

^gIMEA, Paris, France

^hANRS, International Research and Collaboration unit, Paris, France

ⁱYopougon CHU, Service d'Hépatologie, Abidjan, Côte d'Ivoire

^jAP-HP, Hôpital Saint-Antoine, Service des Maladies Infectieuses et Tropicales, F75012,
Paris, France

Corresponding author:

Léa Duchesne

Inserm UMR-S1136

27 rue Chaligny 75012, Paris, France

E-mail: lea.duchesne@iplesp.upmc.fr

Title: Model-based cost-effectiveness estimates of testing strategies for diagnosing hepatitis C virus infection in people who use injecting drugs in Senegal

ABSTRACT

Background: Scaling-up the access to hepatitis C virus (HCV) diagnostics for people who use injecting drugs (PWID) is essential to reduce the HCV incidence in low and middle-income countries.

Methods: A decision tree model was developed to compare the cost-effectiveness of 12 strategies for diagnosing HCV in Senegal with a health sector perspective. Strategies included HCV-Ab screening and confirmation of viraemia (based on HCV-RNA or HCV core antigen detection) or only the latter step. Laboratory assays and decentralized tools (point-of-care (POC) tests and dried blood spot (DBS) samples) were included. The base-case assumed a 38.9% seroprevalence, as reported in the PWID population of Dakar.

Results: Compared to the cheapest strategy (POC HCV-Ab followed by POC HCV-RNA (S_5)), one strategy remained un-dominated in the base-case: POC HCV-Ab followed by venepuncture-based laboratory HCV-RNA (S_3). Above a lost to follow-up testing rate of 2.3%, combining POC HCV-Ab with HCV-RNA on DBS (S_4) became more cost-effective than S_3 . Above this threshold, a single-step POC HCV-RNA (S_{12}) was also found un-dominated (ICER to S_5 =€3,297.50). S_5 , S_{12} and S_4 cost €14.21, €17.03 and €36.55/screened individual. Incremental cost-effectiveness ratios (€/additional true positive case) were 2,164.82 (S_{12} versus S_5) and 3,297.50 (S_4 versus S_{12}). Whenever HCV seroprevalence reached 55.5%, S_{12} became more cost-effective than S_5 . Moreover, S_4 required a budget 2 to 2.5 times higher than S_5 or S_{12} for diagnosing 90% of HCV-infected PWID in Dakar.

Conclusion: A two-step POC-based strategy (S₅) would be the most cost-effective option among those proposed in this study for diagnosing HCV in PWID in Senegal. This study illustrates how the lack of secure financing and of data on PWID in LMICs, render difficult to identify the most sustainable strategy in those countries, as well as its implementation.

Keywords: hepatitis C, cost-effectiveness analysis, diagnosis, Africa, drug users

BACKGROUND

In high-income countries, ongoing and new HCV infections are mainly diagnosed in people who use injecting drugs (PWID) (Hajarizadeh et al., 2013). PWID have therefore been identified as a key group to target for reaching HCV elimination in those countries (AASLD-IDS A HCV Guidance Panel, 2018). In low and middle-income countries (LMICs), where the majority of HCV-infected people worldwide lives (WHO, 2017), the HCV epidemic is mostly caused by iatrogenic transmission of HCV, through unsafe medical procedures or blood transfusion for instance (Thursz & Fontanet, 2014). However, an increase in injecting drug use –by injection but also with straw or crack pipes– have been observed (Degenhardt et al., 2017) in LMICs, especially in sub-Saharan Africa (Nelson et al., 2011). Implementing HCV care and management models in this highly susceptible population is therefore essential for containing the spread of the virus (Easterbrook & WHO Guidelines Development Group, 2016; WHO, 2018).

Although enhancing access to HCV treatment for PWID was reported as cost-effective in several high-income countries (Scott et al., 2016; van Santen et al., 2016) and in LMICs (Morgan et al., 2017), the rate of treatment initiation in PWID remains low worldwide (Grebely, Hajarizadeh, et al., 2017). One major reason to this low rate is the widespread unavailability of HCV testing which has globally hampered scaling-up the access to HCV care. All in all, about 80% of HCV-infected individuals are estimated to remain undiagnosed worldwide (WHO, 2017b). In LMICs, only 6% of them are aware of their status (WHO, 2017b).

Historically, the reference procedure for diagnosing HCV infection is based on a two-step approach combining the detection of anti-HCV antibody (HCV-Ab) followed by the detection of HCV-RNA to confirm viral replication in individuals tested positive for HCV-Ab. This testing sequence was adopted in order to avoid unnecessary viraemia test and reduce the cost

of HCV diagnosis, given that HCV-RNA testing accounts for the major share of the testing expenditure. However, both steps are based on laboratory techniques requiring highly-skilled technicians and a complex equipment. In LMICs, such facilities are available only in centralized laboratory structures (i.e., in major cities). Moreover, as both tests must be run sequentially, completing the whole diagnosis procedure implies that the patient has to return several times to the laboratory. Consequently, this two-step procedure led to a high lost to follow-up (LTFU) rate between the two testing steps (Luma et al., 2018; Mohamed et al., 2018; Viner et al., 2015), especially in marginalized populations with a restricted access to health infrastructures, such as PWID. In addition, in most LMICs, HCV diagnostics are expensive, especially HCV-RNA testing (Etard et al., 2003; Sonderup et al., 2017). Yet, given that testing expenditures are generally out-of-pocket in these countries, the cost of laboratory testing represents an economic barrier for the major part of their populations.

Several innovative technologies provide opportunities for building alternative approaches, more adapted to LMICs and PWID. First, using dried blood samples (DBS)—blood samples collected on filter paper—that can be transported at room temperature from the field to a central laboratory enables a decentralized sample collection and therefore reduces the required number of visits to the laboratory. DBS-based strategies have been reported to be effective in reducing the rate of LTFU (Coats & Dillon, 2015). Second, point-of-care (POC) tests -portable devices able to detect biomarkers in 20 to 60 minutes at the site of patient care- are now available for HCV testing (Chevaliez, 2019). HCV-Ab POC tests are based on a mechanical mechanism whereas HCV-RNA POC tests require an electrical power supply. However, depending on the manufacturer and the model, HCV-RNA POC tests can be battery operated. This, added to their compatibility with finger-prick blood sampling, enables the use of POC tests in decentralized settings, such as in peripheral or community health centers, by minimally trained workers. POC tests were found effective in reducing LTFU and in increasing linkage to care among drug users

(Schackman et al., 2015). Third, decreasing the cost of HCV diagnosis is crucial to enhance access to testing. In line with such a perspective, tests based on the detection of HCV core antigen (HCV-cAg), a biomarker of HCV replication easier and cheaper to detect than HCV-RNA, have been developed (Freiman et al., 2016).

Evidence-based recommendations are now required to guide policy makers from LMICs in their choice between different testing strategies, taking into account the economic and technical constraints. However, most economic studies on HCV testing in PWID conducted to date aimed at assessing if an increased access to treatment through an increased testing uptake rate would be cost-effective in high-income countries. Very few studies have focused on the comparison of alternative testing algorithms with the reference strategy. A model-based study conducted in Switzerland found that a screening program based on rapid detection test and DBS would be cost-effective as compared to the reference screening program (Girardin et al., 2018). To our knowledge, only one study about the cost-effectiveness of HCV testing has been conducted in a LMIC but focused on the general population of Egypt and not on PWID (Kim et al., 2015).

Senegal is one of the first countries in sub-Saharan Africa to officially consider PWID as a key population to target for the management of infectious diseases and to give them access to testing infrastructures and opioid substitution programmes (UNODC, 2014). Moreover, the Senegalese government has shown willingness to implement a viral hepatitis national plan (Ndiaye, 2019). Senegal is also one of the few countries in sub-Saharan Africa for which data regarding the HCV epidemic in drug users are available (Degenhardt et al., 2017). A capture-recapture study estimated the HCV seroprevalence at 38.9% in the specific population of PWID in the Dakar area (Leprêtre et al., 2015). Given this political context, and the current need for scaling-up HCV diagnosis in LMICs and PWID, we designed the present study comparing the cost-

effectiveness of a range of HCV diagnostic strategies, based on the aforementioned technologies, in order to provide insights regarding, first, the economic impact that a publicly-funded intervention would have and, second, which strategies would provide the best value for money if such an intervention was to be implemented.

METHODS

This study report follows the Consolidated Health Economic Evaluation Reporting Standards statement (Husereau et al., 2013).

Diagnostic strategies

Twelve testing strategies were evaluated (Table 1). Strategies included one or two testing steps. Two-steps strategies included HCV-Ab screening followed by a viraemia test among individuals who tested positive for HCV-Ab screening. Single-step strategies included only a viraemia test. Viraemia test were either based on HCV-RNA detection or on HCV-cAg detection. The reference strategy (Sref[Ab_lab_Ven→RNA_lab_Ven]) corresponds to the standard procedure for diagnosing hepatitis C infection in Senegal. The compared strategies could involve laboratory and/or POC tests. Antibody rapid detection testing and HCV RNA POC testing will be referred to as POC tests. As the diagnostic performance of laboratory assays depend on the type of sample used, two strategies were modelled for each testing sequence including a laboratory test: one based on venepuncture blood samples and the other on DBS samples. Reflex testing has been recommended for several years by in the United States in order to decrease LTFU (CDC, 2013). In Africa, the current lack of storage capacities of laboratories would likely prevent the routine implementation of such a strategy. Reflexive strategy was therefore not considered.

Table 1: Description of the HCV testing strategies evaluated in the cost-effectiveness analysis

Strategy	Strategy label	Description
S _{ref}	Ab_lab_Ven→RNA_lab_Ven	HCV-Ab testing followed by HCV-RNA testing, both conducted in laboratory on blood samples collected by venepuncture
S ₂	Ab_lab_DBS→RNA_lab_DBS	HCV-Ab testing followed by HCV-RNA testing, both conducted in laboratory on DBS samples
S ₃	Ab_POC→RNA_lab_Ven	HCV-Ab testing performed with a POC followed by HCV-RNA testing conducted in laboratory on blood samples collected by venepuncture
S ₄	Ab_POC→RNA_lab_DBS	HCV-Ab testing performed with a POC followed by HCV-RNA testing conducted in laboratory on DBS samples
S ₅	Ab_POC→RNA (POC)	HCV-Ab testing performed with a POC followed by HCV-RNA testing performed with a POC device
S ₆	Ab_lab_Ven→cAg_lab_Ven	HCV-Ab testing followed by HCV-cAg testing, both conducted in laboratory on blood samples collected by venepuncture
S ₇	Ab_lab_DBS→cAg_lab_DBS	HCV-Ab testing followed by HCV-cAg testing, both conducted in laboratory on DBS samples
S ₈	Ab_POC→cAg_lab_Ven	HCV-Ab testing performed with a POC followed by HCV-cAg testing conducted in laboratory on blood samples collected by venepuncture
S ₉	Ab_POC→cAg_lab_DBS	HCV-Ab testing performed with a POC followed by a HCV-cAg testing conducted in laboratory on DBS samples
S ₁₀	cAg_lab_Ven	HCV-cAg testing on blood samples collected by venepuncture
S ₁₁	cAg_lab_DBS	HCV-cAg testing on DBS samples
S ₁₂	RNA_POC	HCV-RNA testing performed with a POC device

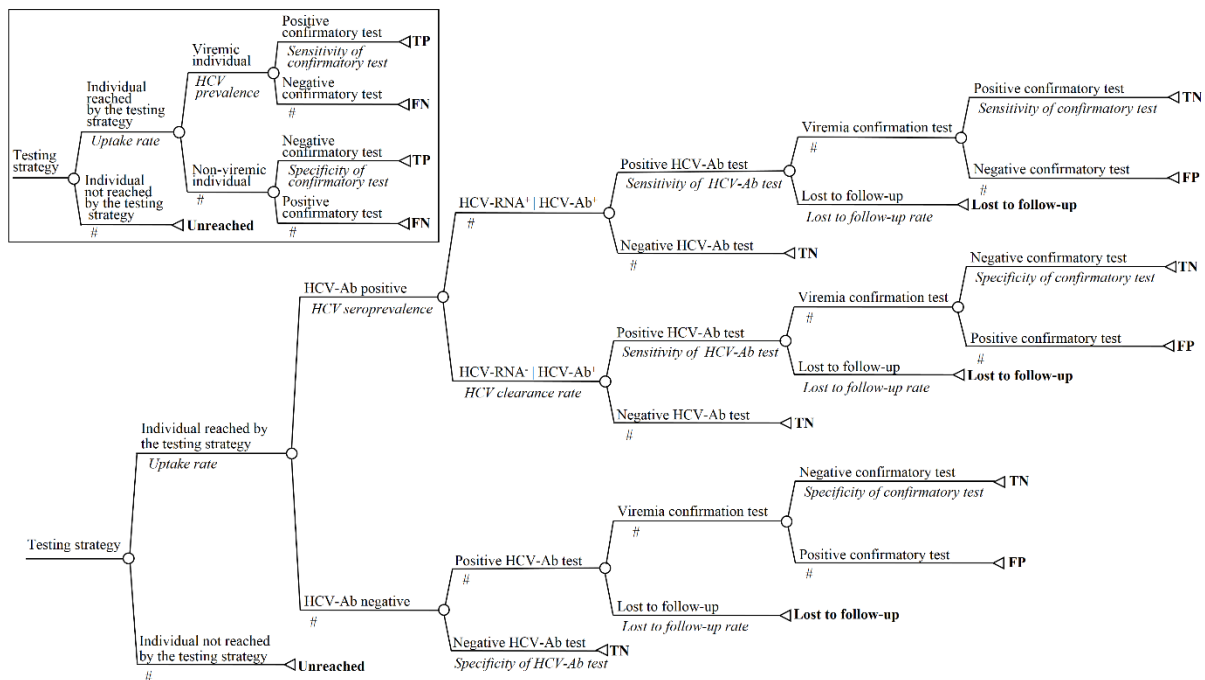
Ab=antibody. cAg=core antigen. DBS=dried blood spot. HCV-Ab=anti-HCV antibody. HCV-cAg=HCV core antigen. HCV-RNA=HCV ribonucleic acid. lab=laboratory. POC=point of care. RNA=ribonucleic acid. Ven=Venepuncture.

Model's assumptions

Decision trees were used to model the twelve strategies (Figure 1). The HCV prevalence was estimated as follows: HCV seroprevalence x (1 - clearance rate) (Figure 1, Tableau 2). Strategies involving a first step either based on POC or DBS testing are hereinafter referred to as “decentralized” strategies. “Centralized” strategies use a venepuncture-based laboratory test as a first-line test. Due to the restricted access of PWID, and a great part of the population in LMICs, to centralized health care facilities, we assumed that decentralized strategies would have a higher uptake rate than centralized strategies. This was modelled by including two different uptake rate probabilities in the model (Table 2).

Lost to follow-up (LTFU) was allowed for two-step strategies involving a venepuncture-based laboratory test for the confirmation of viraemia but we assumed that there was no LTFU in the two-step strategies including only POC testing (S5[Ab_POC→RNA_POC]), DBS testing (S2[Ab_lab_DBS→RNA_lab_DBS], S7[Ab_lab_DBS→cAg_lab_DBS]), or a combination of both (S4[Ab_POC→RNA_lab_DBS], S9[Ab_POC→cAg_lab_DBS]).

Figure 1: Structure of the decision tree used to model the studied strategies



Main panel: tree used for two-step strategies. Inset: tree used for single-step strategies. Two-step strategies included viraemia testing only in individuals who previously tested positive for HCV-Ab. Single-step strategies were only based on viraemia testing. Chance nodes and terminal nodes are represented by circles and triangles, respectively. The corresponding label and probability of occurrence appear above and below the branch, respectively, for each branch of the tree. The sum of a branch's probabilities of each chance node must equal 1; the # symbol corresponds to 1-probability of the alternative branch. The final effectiveness outcome of a decision pathway is shown to the right of each corresponding terminal node; the associated cost was also estimated. For single-step strategies, the HCV prevalence is equal to the product of the HCV seroprevalence and the HCV clearance rate. Abbreviations: Ab, antibody; HCV, hepatitis C virus; FN, false negative; FP, false positive; LTFU, lost to follow-up; TN, true negative; TP, true positive.

Health outcome and measurement of effectiveness

The health outcome of each strategy was the number of true positive (TP) cases identified, a TP case being defined as a chronically-HCV-infected individual tested positive with a viraemia test. Based on the estimation of the TP, false positive (HCV-negative individual tested HCV-RNA positive), true negative (HCV-negative individual whether tested HCV-Ab negative or HCV-Ab positive and HCV-RNA negative) and false negative (HCV-infected individual tested as HCV-Ab negative and HCV-RNA negative) rates (Figure 1), the sensitivity, specificity and diagnostic accuracy of each strategy were also estimated. In some analyses, the proportion of HCV-infected individuals diagnosed was reported. It corresponds to the estimated TP rate for the given situation divided by the estimated HCV prevalence. The diagnostic performances of all assays were taken from the literature.

Costs

PWID are usually economically vulnerable. Scaling-up HCV diagnostic in this population will therefore likely require an external intervention as, for instance, a public testing campaign. We therefore adopted a public health system perspective in order to estimate what would be the cost of each strategy if it was to be implemented within the current HCV testing system in Dakar. However, currently, most hospitals in this area usually do not routinely perform HCV testing and, hence, outsource it. All the costs included in this analysis (Table 2), except those of HCV-RNA POC and HCV-cAg testing, were communicated by the Fann Hospital of Dakar (€1 = FCFA655.96, €1 = US\$0.86) in 2018 and correspond to the prices private laboratories charged it for performing HCV testing. They include the costs associated to reagents, laboratory operating costs, technician time and the profit margin realized by the private laboratories. The cost per HCV-RNA POC cartridge was taken from the literature (Treatment Action Group, 2017). To be consistent with the costs communicated by the Fann hospital, the import tax on

medical products (2.5%), an estimated labor cost (including the employer and employee contributions) for performing the HCV-RNA POC test and an estimated profit margin were included in the analysis, as explained in Table 2. HCV-cAg testing has not yet been widely implemented in sub-Saharan Africa and is not available in the Dakar area. However, HCV-cAg testing is used in Cameroon, a nearby country classified, like Senegal, as a lower-middle income country, by the Pasteur Centre of Cameroon and billed at half the price of HCV-RNA testing. We therefore used the same ratio for inferring the cost of HCV-cAg in our analysis. Patients' costs, such as time and travel expenditures were not considered. The cost outcome estimated for each strategy corresponded to its cost per targeted individual. When a 100% uptake rate and no LTFU were applied, this cost is equivalent to the cost per individual screened. The aim of the study being to evaluate these strategies in a one-off intervention approach, an immediate time horizon was considered. Therefore, no discount rate was applied.

Analytic methods

Base-case and sensitivity analyses

The values used for estimating the health and cost outcomes of each strategy are shown in Table 2. The profit margin corresponding to HCV-RNA POC testing was set, based on a published case for a medical laboratory in Dakar, at 15% (World Bank, 2008). In the absence of data regarding the uptake or LTFU rates achievable in the study population with the proposed strategies, the base-case analysis was parameterized to estimate the model outcomes in an “ideal situation” (i.e., a 100% uptake rate and no LTFU) which then served as a reference for sensitivity analyses exploring the impact of these variables. Strategies which both cost more and were less effective than a comparator were said to be “dominated”. Un-dominated strategies were compared based on their incremental cost-effectiveness ratio (ICER) calculated as the difference in cost between one strategy and the next least expensive strategy divided by the

corresponding difference in the number of TP cases diagnosed. ICER were therefore expressed as an additional cost per supplementary TP case identified.

Deterministic sensitivity analyses were conducted on all variables, as well as a probabilistic sensitivity analysis (PSA) based on 10,000 iterations. The ranges and distributions used for those analyses are reported in Table 2. When the lowest and highest plausible values (confidence interval or ranges of prices published by the manufacturer), triangular distributions were used (Muenning & Bounthavong, 2016). If nothing was known, normal distributions were used. The result of the PSA was presented with a cost-effectiveness acceptability curve (CEAC) representing the probability of a strategy being cost-effective as a function of willingness-to-pay (WTP) thresholds. The WTP refers to the maximum cost the health system would accept to pay per TP case detected. The thresholds of 1 to 3 times the national GDP-per-capita per quality-adjusted life years (QALY) gained are commonly used to evaluate the affordability of health interventions in LMICs. Such thresholds must be viewed with caution in the present study since the health outcomes retained were not expressed in QALY. However, as gains in QALYs are mainly due to treatment, it must be acknowledged that using lower thresholds would probably better indicate the affordability of a diagnostic procedure in LMICs.

Table 2: Values, ranges and distributions of the model parameters used in the base-case and sensitivity analyses

Variables	Base-case	Range considered in the sensitivity analyses	Distribution type in the PSA	Reference
Health outcome and setting, %				
HCV seroprevalence	0.389	0.15 – 0.60	Triangular	Leprêtre et al., 2015
HCV clearance rate	0.30	*	*	Micallef, Kaldor, & Dore, 2006
Screening uptake rate of centralized strategies	1	0.05 – 0.60	*	Assumption
Screening uptake rate of decentralized strategies	1	0.30 – 0.80	*	Assumption
Loss to follow-up testing rate between the first and second-line tests for strategies using a venepuncture-based laboratory test to confirm viraemia	0	0 – 0.50	Triangular	Assumption
Test performance, %				
<i>Sensitivity</i>				
Laboratory HCV-Ab test on serum samples	0.995	0.930 – 1.000	Triangular	Product insert ^a
Laboratory HCV-Ab test on DBS	0.974	0.943 – 0.988	Triangular	Muzembo, Mbendi, & Nakayama, 2017
HCV-Ab POC test	0.995	0.989 – 0.998	Triangular	Khuroo, Khuroo, & Khuroo, 2015
Laboratory HCV-RNA test on serum samples	0.999	0.995 – 1.000	Triangular	Product insert ^b
Laboratory HCV-RNA test on DBS	0.980	0.950 – 0.990	Triangular	Lange et al., 2017
HCV-RNA POC test	0.955	0.845 – 0.994	Triangular	Grebely, Lamoury, et al., 2017
Laboratory HCV-cAg on serum samples	0.934	0.901 – 0.964	Triangular	Freiman et al., 2016
Laboratory HCV-cAg test in laboratory on DBS	0.767	0.667 – 0.850	Triangular	Mohamed et al., 2017
<i>Specificity</i>				
Laboratory HCV-Ab test on serum samples	0.990	0.930 – 1.000	Triangular	Product insert ^a
Laboratory HCV-Ab test on DBS	0.996	0.985 – 0.999	Triangular	Muzembo et al., 2017
HCV-Ab POC	0.998	0.996 – 0.999	Triangular	Khuroo et al., 2015
Laboratory HCV-RNA test on serum samples	0.997	0.990 – 1.000	Triangular	Product insert ^b
Laboratory HCV-RNA test on DBS	0.980	0.950 – 0.990	Triangular	Lange et al., 2017
HCV-RNA POC test	0.981	0.934 – 0.998	Triangular	Grebely, Lamoury, et al., 2017
Laboratory HCV-cAg test on serum samples	0.988	0.974 – 0.995	Triangular	Freiman et al., 2016
Laboratory HCV-cAg test on DBS	0.973	0.840 – 1.000	Triangular	Mohamed et al., 2017
Costs, €				
Laboratory HCV-Ab test	23.0	+/- 50%	Normal	^c
HCV-Ab POC test	7.6	+/- 50%	Normal	^c
Laboratory HCV-RNA test	68.6	+/- 50%	Normal	^c
HCV-RNA POC cartridge	14.02 ^d	10.12 – 14.02	Triangular	(‘HCV World CAB Report Treatment Action Group’.; Senegalese Customs)
Healthcare worker time for HCV-RNA POC	0.9	+/- 50%	Normal	^e
Profit margin	0.15 ^f	0.05 – 0.30	Normal	(World Bank, 2008)
Laboratory HCV-cAg test	34.3	+/- 50%	Normal	^g
DBS sampling	2.9	+/- 50%	Normal	^c
DBS transportation from POC to laboratory	3	+/- 50%	Normal	^c

DBS=dried blood spot. HCV=hepatitis C virus. HCV-Ab=anti-HCV antibody. HCV-cAg=HCV core antigen. HCV-RNA=HCV ribonucleic acid. POC=point of care. PSA=probabilistic sensitivity analysis.

*The base-case value was used in the corresponding sensitivity analysis.

^a Vitro anti-HCV Assay (Ortho Clinical Diagnostics).

^b Abbott Real Time HCV Viral Load (Abbott Diagnostics).

^c Personal communication from the study sites.

^d Calculated as the price of the POC cartridge * 1.025. The coefficient corresponds to the import tax on medical products in Senegal.

^e Calculated on the basis of : a monthly wage of FCFA 150,000, a contribution rate of 27.5% (CLEISS, 2019) and a working time for performing the test of 30 minutes.

^f This coefficient was applied to the following sum : cost of the HCV-RNA POC cartridge (tax included) + cost of healthcare worker time.

^g Calculated as half the price of HCV-RNA testing.

Budget analyses

In 2016, the World Health Organisation (WHO) released targets for combating viral hepatitis including an 80% reduction in HCV incidence by 2030 which would imply to diagnose 90% of HCV-infected individuals (WHO, 2017a). The impact of potential budget constraints on the achievement of this goal was estimated by calculating, based on the results of the base-case analysis, which percentage of HCV-infected individuals would be achieved by each of the dominant strategies previously identified in the cost-effectiveness analysis, when assuming different thresholds of budget per individual screened. In addition, we aimed to evaluate the affordability of the aforementioned strategies by extrapolating from the base-case analysis the budgets required for their implementation in the PWID population of Dakar. Given that the only size estimate available regarding this population concerned all drug users (n=1324), including PWID, the budget estimations were conducted based on the HCV seroprevalence estimate corresponding to this population (23.3%) (Leprêtre et al., 2015).

The model was developed with TreeAge Pro software (© 2018, TreeAge Software, Inc. Williamstown, MA, USA).

RESULTS

Base-case analysis

Table 3 presents the cost, effectiveness and cost-effectiveness of each strategy under the base-case assumptions. Compared to S5[Ab_POC→RNA_POC], which was the cheapest strategy with a cost per screened individual of €14.21, only one other strategy remained un-dominated: the strategy S3[Ab_POC→RNA_lab_Ven] which displayed a higher sensitivity than S5[Ab_POC→RNA_POC] (99.4 and 95.02, respectively) but had a substantially more

expensive cost per screened individual (€34.24). As a result, the ICER of S3[Ab_POC→RNA_lab_Ven] to S5[Ab_POC→RNA_POC] was high with a cost of €1,679.79/additional TP case identified. S12[RNA_POC] was extensively dominated by S3[Ab_POC→RNA_lab_Ven] As shown in Table S1, all one-step strategies resulted in higher false positive (FP) rates than two-step strategies. Due to its lower sensitivity, S5[Ab_POC→RNA_POC] missed more infections than S3[Ab_POC→RNA_lab_Ven] (136 and 16 false negatives (FN)/10,000 individuals screened, respectively).

Table 3: Base-case estimates of cost, effectiveness, and cost-effectiveness of testing strategies for detecting chronic hepatitis C cases

Strategy	Cost / targeted individual (€)	Number of true positive cases / 10,000 targeted individuals	ICER (€ / additional true positive case detected)	Cost / true positive case detected (€)	Diagnostic accuracy (%) [*]	Strategy sensitivity (%) [†]	Strategy specificity (%) [‡]
S ₅ : Ab_POC → RNA_POC	14.21	2587		50.80	98.42	95.02	99.69
S ₁₂ : RNA_POC	17.03	2600	**	54.91	97.39	95.50	98.10
S ₈ : Ab_POC → cAg_lab_Ven	20.92	2531	**	82.66	97.93	92.93	99.81
S ₉ : Ab_POC → cA_lab_DBS	23.23	2078	**	111.78	93.23	76.32	99.56
S ₃ : Ab_POC → RNA_lab_Ven	34.24	2707	1679.79	126.49	99.80	99.40	99.95
S ₁₀ : cAg_lab_Ven	34.30	2543	**	134.87	97.33	93.40	98.80
S ₆ : Ab_lab_Ven → cAg_lab_Ven	36.49	2531	**	144.18	97.93	92.93	99.80
S ₄ : Ab_POC → RNA_lab_DBS	36.55	2655	**	137.64	99.09	97.51	99.68
S ₁₁ : cAg_lab_DBS	40.25	2089	**	192.72	91.69	76.70	97.30
S ₇ : Ab_lab_Ven → cA_lab_DBS	42.03	2034	**	206.64	92.79	74.69	99.57
S _{ref} : Ab_lab_Ven → RNA_lab_Ven	49.97	2707	**	184.62	99.80	99.40	99.95
S ₂ : Ab_lab_Ven → RNA_lab_DBS	55.10	2599	**	212.05	98.52	95.43	99.68

*Diagnostic accuracy: cumulated percentage of true positive and true negative cases. **dominated strategy. Sensitivity: percentage of HCV-infected individuals in the population tested as positive cases. ‡Specificity: percentage of HCV-negative individuals in the population tested as negative cases.

Ab=antibody. cAg=antigen core. DBS=dried blood spot. ICER=incremental cost-effectiveness ratio. lab=laboratory. POC=point of care. RNA=ribonucleic acid. Ven=Venepuncture.

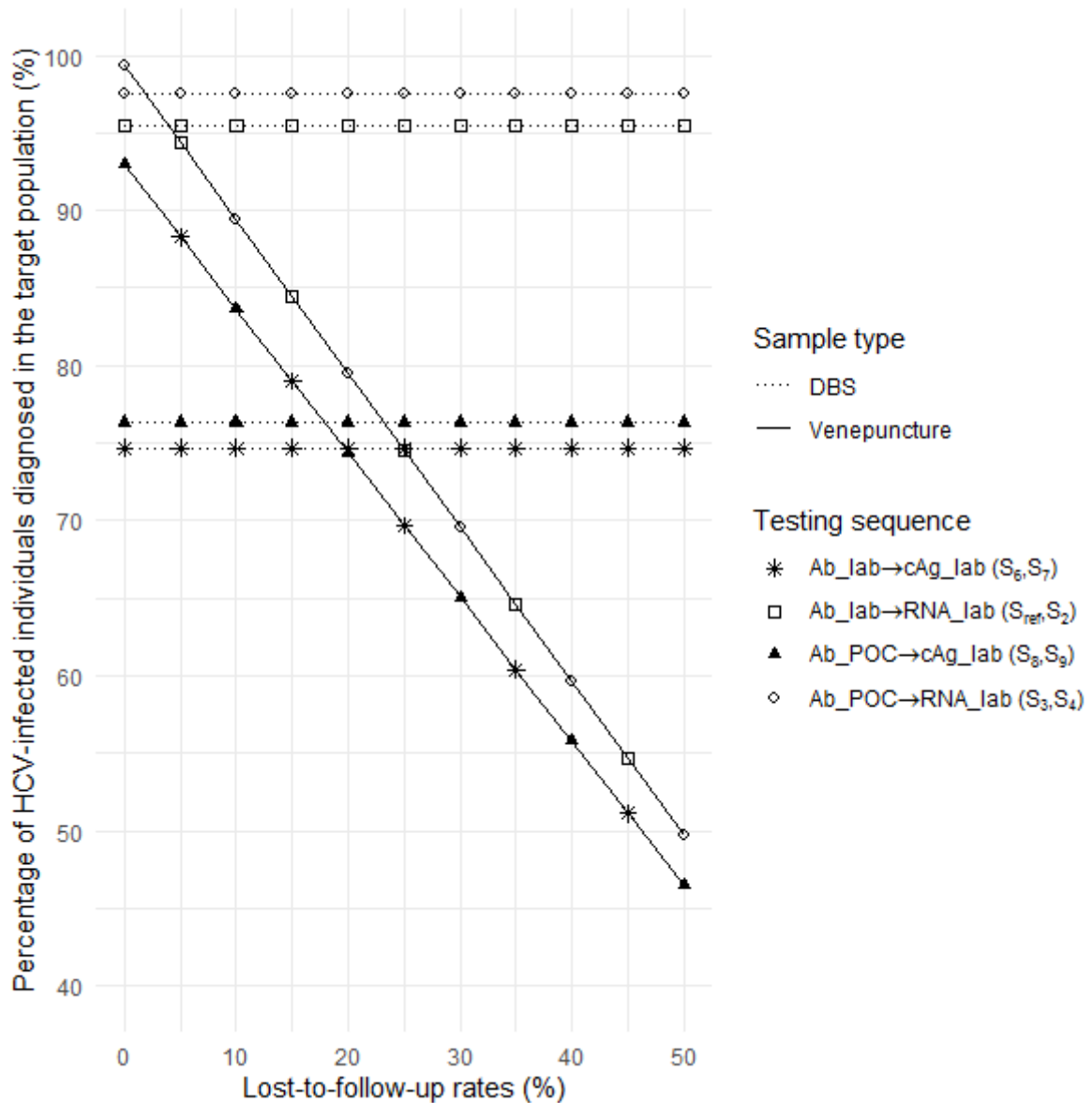
Deterministic sensitivity analyses

A two-way sensitivity analysis exploring the impact of variations in the ratio of the screening uptake rates of both centralized and decentralized strategies was conducted. Table S2 presents, for each scenario, the un-dominated strategies, as well as their cost, effectiveness and ICER. For all possible combinations of input values within the proposed ranges, S5[Ab_POC→RNA_POC], S12[RNA_POC] and S3[Ab_POC→RNA_lab_Ven] remained un-dominated. When the uptake rate of centralized strategies was at least 2.6 times inferior to that of decentralized strategies, S10[cAg_lab_Ven] was also found dominated: given its reduced uptake rate compared with the decentralized strategies, its effectiveness and cost fell below those of the two un-dominated strategies. As a result, the ICER of S5[Ab_POC→RNA_POC] to S10[cAg_lab_Ven] was in all cases very favourable (€3.12-45.12, Table S2).

When LTFU occurs in two-step strategies involving a venepuncture-based laboratory test for the confirmation of viraemia (Sref[Ab_lab_Ven→RNA_lab_Ven], S3[Ab_POC→RNA_lab_Ven], S6[Ab_lab_Ven→cAg_lab_Ven] and S8[Ab_POC→cAg_lab_Ven]), fewer individuals undergo this second step and, consequently, fewer HCV-infected individuals are identified. Figure 2 shows how the effectiveness of two-step strategies decreases with an increasing LTFU. Above a corresponding LTFU value, venepuncture-based strategies become less effective than their DBS-based equivalent; leading to a change in the cost-effectiveness ranking of the strategies. Most importantly, it was found that a change in the preferred strategy from S3[Ab_POC→RNA_lab_Ven] to S4[Ab_POC→RNA_lab_DBS] occurred at a very low LTFU rate (2.3%). S4[Ab_POC→RNA_lab_DBS] would produce almost twice less FNs and 6 times less FPs than S5[Ab_POC→RNA_POC]. Moreover, above this threshold, S12[RNA_POC] also became un-dominated with an ICER to S5[Ab_POC→RNA_POC] of €2,164.82. Compared to

S12[RNA_POC], S4[Ab_POC→RNA_lab_DBS] had an ICER of €3,566.59. As S5[Ab_POC→RNA_POC], S12[RNA_POC] and S4[Ab_POC→RNA_lab_DBS] are not subject to LTFU testing, these ICER would remain constant across all values of LTFU.

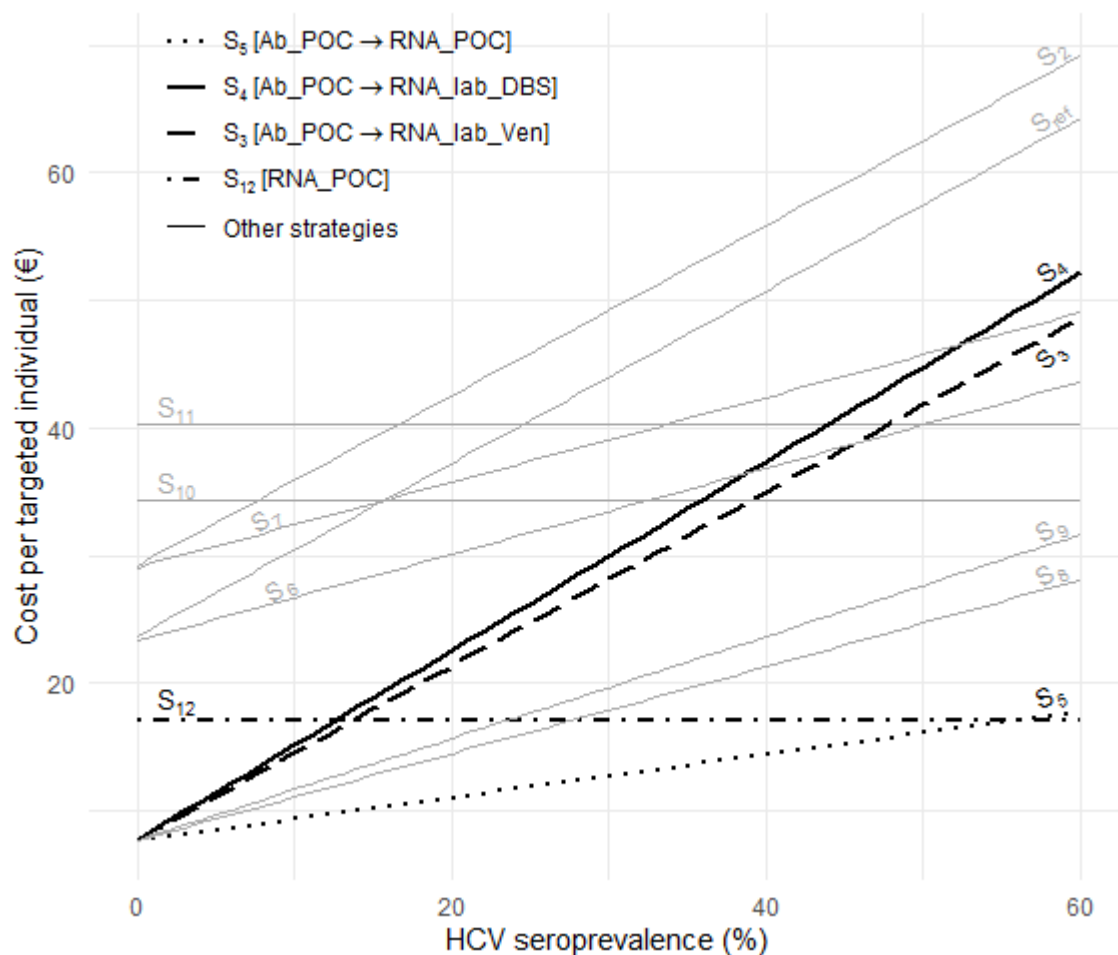
Figure 2: Percentage of HCV-infected individuals in the target population diagnosed by the studied two-step strategies according to different loss to follow-up rates and the type of samples used



Except the LTFU rates, all other parameters of the model were set at their base case values. Ab=antibody. DBS=dried blood spot. lab=laboratory. POC=point of care. RNA=ribonucleic acid. S=strategy. Ven=venepuncture.

The model results were also found to be sensitive to variations in HCV seroprevalence. The number of viraemia test to be performed in two-step strategies increases with an increasing HCV seroprevalence, resulting in an increased cost per targeted individual (Figure 3). Consequently, for HCV seroprevalence values greater than 55.5%, S12[RNA_POC] became less costly than S5[Ab_POC→RNA_POC]. Yet, as S12[RNA_POC] is more effective than S5[Ab_POC→RNA_POC], a change in the preferred strategy from S5[Ab_POC→RNA_POC] to S12[RNA_POC] was observed above this threshold value.

Figure 3: Cost per screened individual of each studied testing strategy according to different levels of HCV seroprevalence



Except HCV seroprevalence, all the parameters of the model were set at their base case values. DBS=dried blood spot. lab=laboratory. POC=point of care. RNA=ribonucleic acid.

Small variations in the costs of tests had an impact in the cost-effectiveness ranking of the strategies. S12[RNA_POC] became more cost-effective than S5[Ab_POC→RNA_POC] for HCV-Ab POC cost values superior to €10.41 (+37% compared to base-case) and for HCV-RNA POC cost values inferior to €9.78 (-28.5% compared to base-case). Regarding HCV-RNA laboratory testing, a really important decrease in its cost (-84%, which corresponds to a cost of €11) would lead to the dominance of S4[Ab_POC→RNA_lab_DBS] over S5[Ab_POC→RNA_POC].

One-way sensitivity analyses also revealed that the results of the model were sensitive to small variations in the diagnostic performances of the tests. The analysis exploring the range of sensitivity of the HCV-Ab POC (98.9%–99.8%) resulted in an ICER of S5[Ab_POC→RNA_POC] to S12[RNA_POC] ranging from €997.90 to €5,373.84/additional TP detected, with an increased sensitivity resulting in an increased ICER. Likewise, for sensitivity values of HCV-RNA testing on DBS below 96.0% (base-case estimate = 98.0%), S4[Ab_POC→RNA_lab_DBS] was dominated by S12[RNA_POC]. In contrast, for values above this threshold–96.0% to 99.0%–the ICER of S4[Ab_POC→RNA_lab_DBS] to S12[RNA_POC] steadily decreased with an increasing sensitivity value, with a corresponding ICER ranging from €2,385.64 to €358,442.

No other parameters were found to have an impact on the cost-effectiveness ranking of the studied strategies.

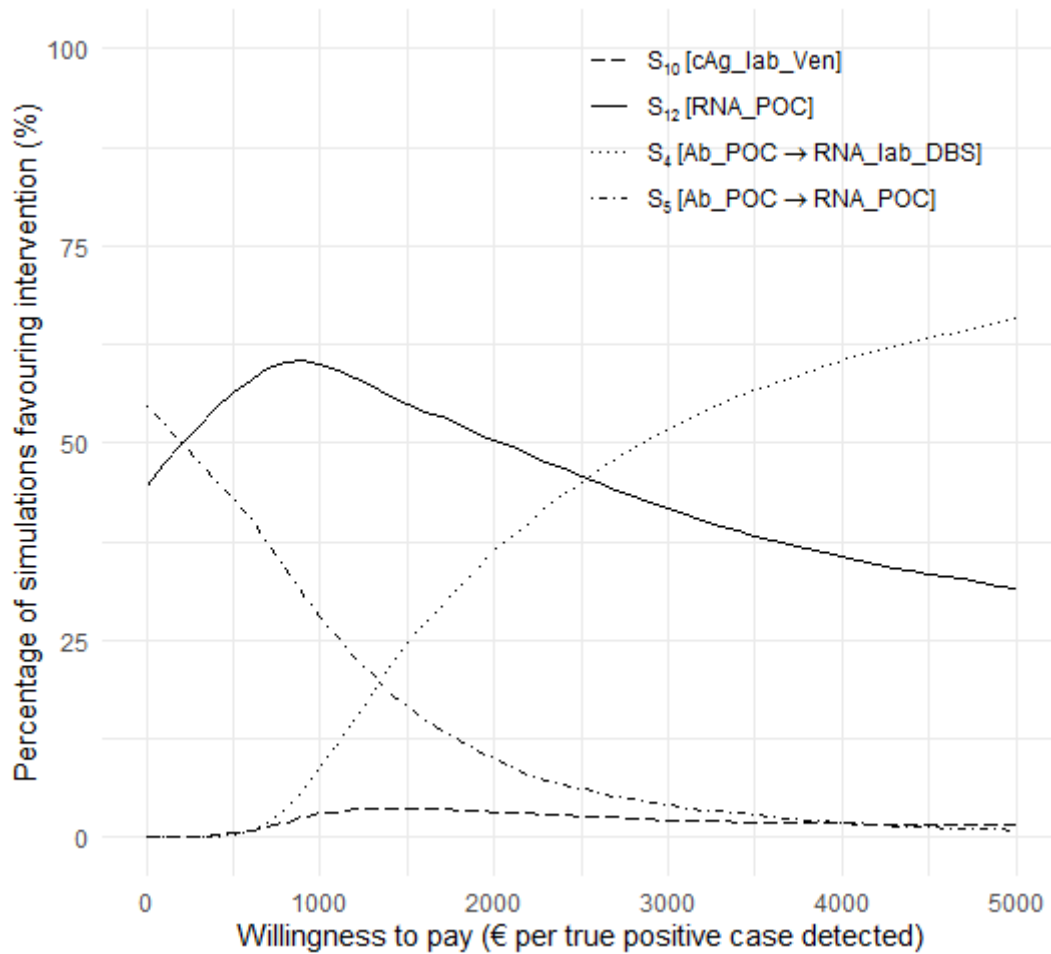
Most of the diagnostic tests included in the base-case analysis had similar diagnostic performance estimates and overlapping confidence intervals, with the exception of those based on the detection of HCV-cAg on DBS which had a substantially lower sensitivity than the other viremia tests (Table 2). The differences in cost-effectiveness between strategies observed in the base-case may therefore only reflect sampling fluctuations between the studies which reported

the aforementioned diagnostic performance estimates. In order to study the impact of this hypothesis on the cost-effectiveness outcomes, an alternative scenario was explored, with the sensitivity and specificity of all tests set at 98.0% and 99.0%, respectively. In this scenario, S5[Ab_POC→RNA_POC] and S12[RNA_POC] were the only strategies to remain undominated. Both strategies having similar costs (€14.19 and €17.03/screened individual for S5[Ab_POC→RNA_POC] and S12[RNA_POC], respectively) and effectiveness (2,615 and 2,668 TPs/10,000 individuals screened for S5[Ab_POC→RNA_POC] and S12[RNA_POC], respectively), the ICER of S12 to S5[Ab_POC→RNA_POC] was relatively low (€530.42/additional TP case detected). However, S12[RNA_POC] would produce more FPs than S5[Ab_POC→RNA_POC] (72 and 12/10,000 individuals screened, respectively). As S4[Ab_POC→RNA_lab_DBS] would have the same effectiveness than S5[Ab_POC→RNA_POC] but a higher cost, S5[Ab_POC→RNA_POC] would dominate S4[Ab_POC→RNA_lab_DBS].

Probabilistic sensitivity analysis

Figure 4 shows the CEAC derived from the PSA. Below a WTP value of €1,000, most simulations favoured S5[Ab_POC→RNA_POC]. When considering WTP values ranging between €1,000 and €2,100, S12[RNA_POC] was the strategy with the highest probability of being favoured by the simulation. For any WTP value greater than €2,100, the percentage of simulations favouring S4[Ab_POC→RNA_lab_DBS] exceeded that of simulations favouring S12 (and steadily increased with the WTP value). When considering the threshold of 1 time the GDP per capita of Senegal (€975), the proportions of simulations favouring S12[RNA_POC] and S5[Ab_POC→RNA_POC] were similar (about 44% and 45%, respectively). At a WTP value of 3 times the GDP per capita of Senegal (€2,925), 36% of the simulations favoured S12[RNA_POC] and 54% of them favoured S4[Ab_POC→RNA_lab_DBS].

Figure 4: Cost-effectiveness acceptability curve showing the probability favouring a given strategy according to different thresholds of willingness-to-pay



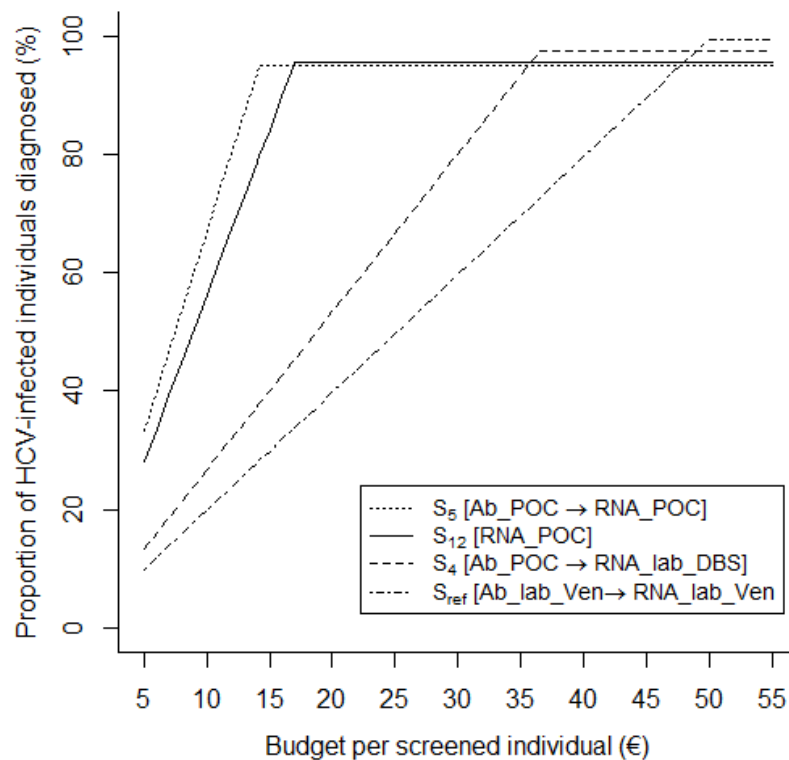
Ab=antibody. cAg= core antigen. DBS=dried blood spot. lab=laboratory. POC=point of care. RNA=ribonucleic acid.

Budget analyses

Figure 5 presents the variations in the percentage of HCV-infected individuals identified in the targeted population according to different fixed budget value per individual screened. These results were derived from the base-case estimates. The proportion of HCV-infected individuals identified with S5[Ab_POC→RNA_POC] and S12[RNA (POC)] was similar across all of the considered fixed budget values. In contrast, for budget values below the threshold of €35, S4[Ab_POC→RNA_lab_DBS] implementation would lead to a number of diagnosed infections substantially lower than that issued from S5[Ab_POC→RNA_POC] or

S12[RNA_POC] implementation. For any budget values inferior to €50, Sref[Ab_lab_Ven→RNA_lab_Ven] would achieve a lower coverage rate than the other mentioned strategies. Diagnosing 90% of the HCV-infected PWID population with S5[Ab_POC→RNA_POC], S12[RNA_POC], S4[Ab_POC→RNA_lab_DBS] and Sref[Ab_lab_Ven→RNA_lab_Ven] would require a minimal budget per screened individual of €13.46, €16.04, €33.73 and €45.25, respectively.

Figure 5: Percentage of HCV-infected individuals in the target population diagnosed by S₅, S₁₂ and S₄ according to different fixed budget per screened individual



Ab=antibody. DBS=dried blood spot. lab=laboratory. POC=point of care. RNA=ribonucleic acid.

Testing the whole estimated population of drug users in the Dakar area (n=1324, HCV seroprevalence=23.3%) would cost approximately €15,323, €22,541, €33,097 and €52,205 using S5[Ab_POC→RNA_POC], S12[RNA_POC], S4[Ab_POC→RNA_lab_DBS] and Sref[Ab_lab_Ven→RNA_lab_Ven], respectively (Table 4).

Table 4: Extrapolated costs for potential implementation of S₅, S₁₂ and S₄ in the estimated population of drug users in the Dakar area (n=1324 individuals)

Strategy	Cost / screened individual (€)	Diagnostic cost (€)
S ₅ : Ab_POC → RNA_POC	11.57	15,322.89
S ₁₂ : RNA_POC	17.03	22,541.50
S ₄ : Ab_POC → RNA_lab_DBS	25.00	33,096.90
S _{ref} : Ab_lab_Ven → RNA_lab_Ven	39.43	52,205.38

Except the HCV seroprevalence (23.3%), the parameters of the model were set at their base-case values. Ab=antibody. DBS=dried blood spot. DAA=direct-acting antivirals. FP=false positive. lab=laboratory. POC=point of care. RNA=ribonucleic acid. Ven=Venepuncture.

DISCUSSION

A decision tree model was designed to compare the cost-effectiveness of 12 strategies for diagnosing HCV in PWID in Senegal from a health sector perspective. The results of the present study suggest that none of the proposed centralized strategies, given the impact of LTFU on their effectiveness, would provide the best value for money. Three decentralized strategies stand out, namely, listed by increasing cost and effectiveness, S₅[Ab_POC→RNA_POC], S₁₂[RNA_POC] and S₄[Ab_POC→RNA_lab_DBS]. Compared to the sequential use of two POC tests (S₅[Ab_POC→RNA_POC]), implementing HCV-RNA POC testing alone (S₁₂[RNA_POC]) would result in a slightly increased effectiveness but also in a substantially higher cost as shown by the ICER of S₁₂[RNA_POC] to S₅[Ab_POC→RNA_POC]: €2,164.82 per additional TP case identified. This increased effectiveness is, however, at the expense of a decreased diagnostic specificity. Replacing the HCV-RNA POC test by a DBS-based HCV-RNA laboratory test as the 2nd-line test after HCV-Ab POC testing would be more effective but would also result in a substantially higher cost with an ICER of S₄[Ab_POC→RNA_lab_DBS] to S₅[Ab_POC→RNA_POC] of €3,297.51 per additional TP case identified. Sensitivity analyses showed that in some settings (HCV seroprevalence > 55.5%, an increased cost of HCV-Ab POC test, a decreased cost of HCV-RNA POC test or a

decreased sensitivity of the laboratory HCV-RNA test on DBS compared to their base-case values), using directly the HCV-RNA POC test (S12 [RNA_POC]) would be more cost-effective than when used after HCV-Ab POC testing.

In terms of budget, diagnosing 90% of HCV-infected individual in the population of PWID of Dakar by implementing S5[Ab_POC→RNA_POC], S12[RNA_POC] or S4[Ab_POC→RNA_lab_DBS] would require a budget about 3.5, 2.9 and 1.4 times lower than that required if the standard reference for diagnosing HCV was to be implemented. Yet, in settings such as LMICs, for which budget constraints are critical for building public health policies, the choice of a testing strategy is likely to be determined by the coverage rate achievable with each strategy under a certain fixed budget. This study showed that in case of budget constraints (corresponding to a fixed budget per screened individual < €50), any of the three strategies highlighted in this study would allow a greater part of the population to be diagnosed for HCV infection compared to the reference strategy. The budget value of €35 per screened individual was also a key threshold below which S4 would enable the diagnosis of a substantially lower number of HCV-infected individuals than S5 and S12. When taking the drug users population of Dakar as an illustrative example, we found that diagnosing this whole population with a decentralized strategy would require a budget ranging between €15,323 and €33,097, depending on the selected strategy. This would represent a very minor portion of the national public health expenditures (i.e., about €200 million (IMF, 2018; WHO, 2015)). However, given the present state of funding for policies targeting drug users, this is not a guarantee of financing.

Indeed, funding for implementing healthcare policies or promoting research that targets this population is scarce or, when available, financially unsustainable; this makes difficult to determine cost-effectiveness thresholds for such programs. Globally, PWID suffer from

restricted access to health infrastructures due to the stigmatization, discrimination and, above all, criminalization of drug use. Consequently, very few countries among LMICs have set up harm reduction programs or included drug users in their national plans against viral diseases common among PWID, such as HIV/AIDS. However, a political will to address drug issues with a non-criminalizing approach in sub-Saharan Africa seems to be emerging. For instance, the West Africa Commission on Drugs called governments to shift their funding from law enforcement to public health interventions (IDPC, 2018). In Senegal, PWID are considered since 2014 as a key population to target in the National Strategic Plan in Response to AIDS. Moreover, a Centre for integrated management of addictions (called CEPIAD) was launched in 2014 in Dakar and became the first health centre in delivering a methadone maintenance programme in West Africa. However, such encouraging political initiatives remain scarce. Moreover, the majority of harm reduction programs developed in LMICs are funded by international organizations or non-governmental organizations and those funds have tended to decrease over the recent years (HRI, 2018). The CEPIAD of Dakar, although partially funded by the Senegalese government, relies mainly on external funding. Yet, a recent modelling study showed that diagnosing HCV in PWID without simultaneously implementing harm reduction programs would not enable to achieve the 90% WHO target by 2030 (Heffernan et al., 2019). Reaching this goal will therefore require to implement an integrated program of HCV care and ensure the sustainability of its funding.

Looking beyond financial considerations, there are operational pros and cons to each of the three key strategies highlighted in this study that should be acknowledged. First, a large-scale intervention based on DBS sampling will require to increase the capacity of central laboratories and transportation infrastructures. Considering the shortage of health personnel and transportation infrastructures in Africa (Ghebreyesus et al., 2013; Gwilliam, 2011; Kinfu et al., 2009), this may limit the implementation feasibility of S4[Ab_POC→RNA_lab_DBS].

Moreover, the time required for sending the DBS samples to the central laboratory, performing the analysis and returning the results to the peripheral health centers, represents a risk factor for reduced linkage to care. On the contrary, both S5[Ab_POC→RNA_POC] and S12[RNA_POC] can be completed in a single visit of less than two hours, enabling immediate referral to care if necessary. Second, the GeneXpert cartridges contain a toxic chemical compound and must therefore be incinerated at 850°C minimum after use. Yet, many LMICs do not possess incinerators able to reach those temperatures. Adopting strategies based on these cartridges will require to address this waste management issue. In this case, HCV-Ab POC tests containing non-toxic materials, S5[Ab_POC→RNA_POC] might be more sustainable than S12[RNA_POC]. However, the Genedrive platform –the second POC platform currently available for HCV-RNA testing– use cartridges containing non-toxic materials. Currently limited by its requirement for serum or plasma samples, its use could overcome the aforementioned issue, if validated on finger-stick samples.

This study has several limitations. First, it must be recalled that the differences in effectiveness that we observed in the base-case analysis may only reflect sampling fluctuations of the source studies instead of solid performance differences between the tests. Therefore, a rigorous simultaneous assessment of the performance of the different assays used in the strategies identified as dominant in this study would be required to draw precise recommendations. Second, the costs of most HCV assays came from only one health center in one city in Senegal. Moreover, as some assays were not routinely used in this center, some costs had to be inferred from published projected costs (GeneXpert HCV viral load assay) or according to data of a neighboring country (HCV-cAg laboratory assay). The cost of biological assays can vary considerably across countries and even within a country. Yet, as the sensitivity analyses showed that variations in the assays' costs could lead to a change in the cost-effectiveness ranking, our results may not be generalizable to the whole country. This also highlights that even a slight

discount in the costs of assays could represent an efficient lever for improving the feasibility of some strategies. Third, our results reflect what would be the cost of scaling-up HCV testing for PWID within the current practice for public institutions. However, it must be acknowledged that outsourcing the diagnostic of HCV is not the only, and may not be the better, solution for implementing a publicly-funded intervention in the studied context. Indeed, in the mark of a large-scale program, the public sector would probably obtain lower tests cost than those considered in this study, through bulk-billing rates for instance. Furthermore, public hospitals in Dakar have already developed the capacity of their laboratories, in the mark of HIV or tuberculosis programs for instance; they would therefore probably be capable of strengthening their own testing system. Comparing the required investment, given the existing resources –in terms of personnel and equipment–, for implementing the proposed strategies within the public system to our results would therefore be valuable. Contrary to the strategy based on outsourcing, the latter would require not only a financial commitment from policymakers but also a logistical and political one. Fourth, our model did not evaluate the long-term effects of testing strategies on the transmission of HCV and, therefore, on the achievement of the WHO elimination goals. Yet, depending on the capacity of countries to implement ongoing testing and monitoring among PWID, false testing results may have a substantial impact on the mid- to long-term cost-effectiveness of the interventions and, therefore, on the nature of the more preferable strategy for the initial diagnosis. This aspect should be further developed. To achieve this, the data gap regarding some setting-specific parameters among PWID in LMICs should be filled, such as HCV transmission and re-infection rates, as well as the coverage rate and effectiveness achievable, considering the human and economic resources available in those countries, by prevention programs.

In conclusion, this study found that a two-step strategy based on POC tests would be the most cost-effective option compared to the other strategies proposed in this study for a one-off HCV

screening program in PWID in Senegal. A two-step strategy combining POC and DBS-based laboratory testing was also found cost-effective, as well as a one-step POC-based strategy. However, under budget constraints, only the two aforementioned POC-based strategies would be the most effective. Our model also indicates that any extension of this work to PWID in other settings requires the corresponding HCV seroprevalence and costs of assays to be precisely determined for assessing which strategies would be the most appropriate. In the end, the absence of sustainable funding for interventions targeting PWID makes difficult to determine whether implementing these strategies would be economically feasible for LMICs. The involvement of governments is therefore required for ensuring a proper environment for the implementation of such interventions and encourage HCV research among drug users as well as national or external funding.

REFERENCES

- AASLD-IDS A HCV Guidance Panel. (2018). Hepatitis C Guidance 2018 Update: AASLD-IDS A Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 67(10), 1477–1492. <https://doi.org/10.1093/cid/ciy585>
- CDC. (2013). *Testing for HCV Infection: An Update of Guidance for Clinicians and Laboratorians*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4605020/>
- Chevaliez, S. (2019). Strategies for the improvement of HCV testing and diagnosis. *Expert Review of Anti-Infective Therapy*, 17(5), 341–347. <https://doi.org/10.1080/14787210.2019.1604221>
- CLEISS. (2019). *Les cotisations au Sénégal*. Centre of European and International Liaisons for Social Security. <https://www.cleiss.fr/docs/cotisations/senegal.html>
- Coats, J. T., & Dillon, J. F. (2015). The effect of introducing point-of-care or dried blood spot analysis on the uptake of hepatitis C virus testing in high-risk populations: A systematic review of the literature. *The International Journal on Drug Policy*, 26(11), 1050–1055. <https://doi.org/10.1016/j.drugpo.2015.05.001>
- Degenhardt, L., Peacock, A., Colledge, S., Leung, J., Grebely, J., Vickerman, P., Stone, J., Cunningham, E. B., Trickey, A., Dumchev, K., Lynskey, M., Griffiths, P., Mattick, R. P., Hickman, M., & Larney, S. (2017). Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: A multistage systematic review. *The Lancet. Global Health*, 5(12), e1192–e1207. [https://doi.org/10.1016/S2214-109X\(17\)30375-3](https://doi.org/10.1016/S2214-109X(17)30375-3)
- Easterbrook, P. J., & WHO Guidelines Development Group. (2016). Who to test and how to test for chronic hepatitis C infection—2016 WHO testing guidance for low- and middle-income countries. *Journal of Hepatology*, 65(1 Suppl), S46-66. <https://doi.org/10.1016/j.jhep.2016.08.002>
- Etard, J.-F., Colbachini, P., Dromigny, J.-A., & Perrier-Gros-Claude, J.-D. (2003). Hepatitis C antibodies among blood donors, Senegal, 2001. - PubMed—NCBI. *Emerging Infectious Diseases*. <https://www.ncbi.nlm.nih.gov/pubmed/14725259>
- Freiman, J. M., Tran, T. M., Schumacher, S. G., White, L. F., Ongarello, S., Cohn, J., Easterbrook, P. J., Linas, B. P., & Denking, C. M. (2016a). Hepatitis C Core Antigen Testing for

- Diagnosis of Hepatitis C Virus Infection: A Systematic Review and Meta-analysis. *Annals of Internal Medicine*. <https://doi.org/10.7326/M16-0065>
- Ghebreyesus, T. A. [editor, Scheffler, R. M., & Soucat, A. L. B. (2013). *Labor market for health workers in Africa: New look at the crisis* (No. 77020; pp. 1–383). The World Bank. <http://documents.worldbank.org/curated/en/305871468009988200/Labor-market-for-health-workers-in-Africa-new-look-at-the-crisis>
- Girardin, F., Hearmon, N., Negro, F., Eddowes, L., Bruggmann, P., & Castro, E. (2018). Increasing hepatitis C virus screening in people who inject drugs in Switzerland using rapid antibody saliva and dried blood spot testing: A cost-effectiveness analysis. *Journal of Viral Hepatitis*. <https://doi.org/10.1111/jvh.13023>
- Grebely, J., Hajarizadeh, B., & Dore, G. J. (2017). Direct-acting antiviral agents for HCV infection affecting people who inject drugs. *Nature Reviews Gastroenterology & Hepatology*, *14*(11), 641–651. <https://doi.org/10.1038/nrgastro.2017.106>
- Grebely, J., Lamoury, F. M. J., Hajarizadeh, B., Mowat, Y., Marshall, A. D., Bajis, S., Marks, P., Amin, J., Smith, J., Edwards, M., Gorton, C., Ezard, N., Persing, D., Kleman, M., Cunningham, P., Catlett, B., Dore, G. J., Applegate, T. L., & LiveRLife Study Group. (2017). Evaluation of the Xpert HCV Viral Load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: A cohort study. *The Lancet. Gastroenterology & Hepatology*, *2*(7), 514–520. [https://doi.org/10.1016/S2468-1253\(17\)30075-4](https://doi.org/10.1016/S2468-1253(17)30075-4)
- Gwilliam, K. (2011). *Africa's transport infrastructure: Mainstreaming maintenance and management* (No. 60803; pp. 1–576). The World Bank. <http://documents.worldbank.org/curated/en/728801468191665263/Africas-transport-infrastructure-mainstreaming-maintenance-and-management>
- Hajarizadeh, B., Grebely, J., & Dore, G. J. (2013). Epidemiology and natural history of HCV infection. *Nature Reviews. Gastroenterology & Hepatology*, *10*(9), 553–562. <https://doi.org/10.1038/nrgastro.2013.107>
- HCV World CAB Report | Treatment Action Group*. (n.d.). Retrieved 10 September 2018, from <http://www.treatmentactiongroup.org/content/hcv/hcv-world-cab-report>
- Heffernan, A., Cooke, G. S., Nayagam, S., Thursz, M., & Hallett, T. B. (2019). Scaling up prevention and treatment towards the elimination of hepatitis C: A global

- mathematical model. *Lancet (London, England)*. [https://doi.org/10.1016/S0140-6736\(18\)32277-3](https://doi.org/10.1016/S0140-6736(18)32277-3)
- HRI. (2018). *The lost decade: Neglect for harm reduction funding*. <https://www.hri.global/harm-reduction-funding>
- Husereau, D., Drummond, M., Petrou, S., Carswell, C., Moher, D., Greenberg, D., Augustovski, F., Briggs, A. H., Mauskopf, J., Loder, E., & CHEERS Task Force. (2013). Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, 16(2), e1-5. <https://doi.org/10.1016/j.jval.2013.02.010>
- IDPC. (2018, September). *Model drug law for West Africa: A tool for policy makers*. <https://idpc.net/publications/2018/09/model-drug-law-for-west-africa-a-tool-for-policy-makers>
- IMF. (2018). *Report for Selected Countries and Subjects*. https://www.imf.org/external/pubs/ft/weo/2018/01/weodata/weorept.aspx?sy=2016&ey=2023&scsm=1&ssd=1&sort=country&ds=.&br=1&pr1.x=65&pr1.y=2&c=622%2C722%2C662&s=NGDP_R%2CNGDP_RPCH%2CNGDP%2CNGDPD%2CPPPGDP%2CNGDP_D%2CNGDPRPC%2CNGDPRPPPPC%2CNGDPPC%2CNGDPDPC%2CPPPPC%2CPPPSH%2CPPPEX%2CNID_NGDP%2CNGSD_NGDP%2CPCPI%2CPCPIPCH%2CPCPIE%2CPCPIEPCH%2CTM_RPCH%2CTMG_RPCH%2CTX_RPCH%2CTXG_RPCH%2CLP%2CGGR%2CGR_NGDP%2CGGX%2CGGX_NGDP%2CGGXCNL%2CGGXCNL_NGDP%2CGGSB%2CGGXONLB%2CGGXONLB_NGDP%2CGGXWDN%2CGGXWDN_NGDP%2CGGXWDG%2CGGXWDG_NGDP%2CNGDP_FY%2CBCA%2CBCA_NGDPD&grp=0&a=
- Khuroo, M. S., Khuroo, N. S., & Khuroo, M. S. (2015). Diagnostic accuracy of point-of-care tests for hepatitis C virus infection: A systematic review and meta-analysis. *PloS One*, 10(3), e0121450. <https://doi.org/10.1371/journal.pone.0121450>
- Kim, D. D., Hutton, D. W., Raouf, A. A., Salama, M., Hablas, A., Seifeldin, I. A., & Soliman, A. S. (2015). Cost-effectiveness model for hepatitis C screening and treatment: Implications for Egypt and other countries with high prevalence. *Global Public Health*, 10(3), 296–317. <https://doi.org/10.1080/17441692.2014.984742>

- Kinfu, Y., Dal Poz, M. R., Mercer, H., & Evans, D. B. (2009). The health worker shortage in Africa: Are enough physicians and nurses being trained? *Bulletin of the World Health Organization*. <https://www.who.int/bulletin/volumes/87/3/08-051599/en/>
- Lange, B., Roberts, T., Cohn, J., Greenman, J., Camp, J., Ishizaki, A., Messac, L., Tuillon, E., van de Perre, P., Pichler, C., Denkinger, C. M., & Easterbrook, P. (2017). Diagnostic accuracy of detection and quantification of HBV-DNA and HCV-RNA using dried blood spot (DBS) samples—A systematic review and meta-analysis. *BMC Infectious Diseases*, *17*(Suppl 1), 693. <https://doi.org/10.1186/s12879-017-2776-z>
- Leprêtre, A., Ba, I., Lacombe, K., Maynard, M., Toufik, A., Ndiaye, O., Kane, C. T., Gozlan, J., Tine, J., Ndoye, I., Raguin, G., & Girard, P.-M. (2015). Prevalence and behavioural risks for HIV and HCV infections in a population of drug users of Dakar, Senegal: The ANRS 12243 UDSEN study. *Journal of the International AIDS Society*, *18*, 19888. <https://doi.org/10.7448/IAS.18.1.19888>
- Luma, H. N., Eloumou, S. A. F. B., Noah, D. N., Eyenga, B. A., Nko'Ayissi, G., Taku, T. S., Malongue, A., Donfack-Sontsa, O., & Ditah, I. C. (2018). Hepatitis C Continuum of Care in a Treatment Center in Sub-Saharan Africa. *Journal of Clinical and Experimental Hepatology*, *8*(4), 335–341. <https://doi.org/10.1016/j.jceh.2018.01.001>
- Micallef, J. M., Kaldor, J. M., & Dore, G. J. (2006). Spontaneous viral clearance following acute hepatitis C infection: A systematic review of longitudinal studies. *Journal of Viral Hepatitis*, *13*(1), 34–41. <https://doi.org/10.1111/j.1365-2893.2005.00651.x>
- Mohamed, Z., Mbwambo, J., Shimakawa, Y., Poiteau, L., Chevaliez, S., Pawlotsky, J.-M., Rwegasha, J., Bhagani, S., Taylor-Robinson, S. D., Makani, J., Thursz, M. R., & Lemoine, M. (2017). Clinical utility of HCV core antigen detection and quantification using serum samples and dried blood spots in people who inject drugs in Dar-es-Salaam, Tanzania. *Journal of the International AIDS Society*, *20*(1), 21856. <https://doi.org/10.7448/IAS.20.1.21856>
- Mohamed, Z., Rwegasha, J., Kim, J. U., Shimakawa, Y., Poiteau, L., Chevaliez, S., Bhagani, S., Taylor-Robinson, S. D., Thursz, M. R., Mbwambo, J., & Lemoine, M. (2018). The hepatitis C cascade of care in people who inject drugs in Dar es Salaam, Tanzania. *Journal of Viral Hepatitis*, *25*(12), 1438–1445. <https://doi.org/10.1111/jvh.12966>

- Morgan, J. R., Servidone, M., Easterbrook, P., & Linas, B. P. (2017). Economic evaluation of HCV testing approaches in low and middle income countries. *BMC Infectious Diseases*, 17(Suppl 1), 697. <https://doi.org/10.1186/s12879-017-2779-9>
- Muenning, P., & Bounthavong, M. (2016). *Cost-Effectiveness Analysis in Health: A Practical Approach* (3rd Edition). Wiley. <https://www.wiley.com/en-us/Cost+Effectiveness+Analysis+in+Health%3A+A+Practical+Approach%2C+3rd+Edition-p-9781119011262>
- Muzembo, B. A., Mbendi, N. C., & Nakayama, S. F. (2017). Systematic review with meta-analysis: Performance of dried blood spots for hepatitis C antibodies detection. *Public Health*, 153, 128–136. <https://doi.org/10.1016/j.puhe.2017.08.008>
- Ndiaye, M. (2019). *Investing in the fight against hepatitis B and C in Senegal. National Strategic Plan (2019-2023). Policy brief*. <http://hepatites.sn/index.php/combattre-les-hepatites/le-plan-strategique-national>
- Nelson, P. K., Mathers, B. M., Cowie, B., Hagan, H., Des Jarlais, D., Horyniak, D., & Degenhardt, L. (2011). Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: Results of systematic reviews. *Lancet (London, England)*, 378(9791), 571–583. [https://doi.org/10.1016/S0140-6736\(11\)61097-0](https://doi.org/10.1016/S0140-6736(11)61097-0)
- Schackman, B. R., Leff, J. A., Barter, D. M., DiLorenzo, M. A., Feaster, D. J., Metsch, L. R., Freedberg, K. A., & Linas, B. P. (2015). Cost-effectiveness of rapid hepatitis C virus (HCV) testing and simultaneous rapid HCV and HIV testing in substance abuse treatment programs. *Addiction (Abingdon, England)*, 110(1), 129–143. <https://doi.org/10.1111/add.12754>
- Scott, N., Iser, D. M., Thompson, A. J., Doyle, J. S., & Hellard, M. E. (2016). Cost-effectiveness of treating chronic hepatitis C virus with direct-acting antivirals in people who inject drugs in Australia. *Journal of Gastroenterology and Hepatology*, 31(4), 872–882. <https://doi.org/10.1111/jgh.13223>
- Senegalese Customs. (n.d.). *Taxation Mission*. Retrieved 4 November 2019, from <https://www.douanes.sn/fr/node/1>
- Senegalese customs. (2019). <https://www.douanes.sn/fr/node/1>
- Sonderup, M. W., Afihene, M., Ally, R., Apica, B., Awuku, Y., Cunha, L., Dusheiko, G., Gogela, N., Lohouès-Kouacou, M.-J., Lam, P., Lesi, O., Mbaye, P. S., Musabeyezu, E., Musau, B.,

- Ojo, O., Rwegasha, J., Scholz, B., Shewaye, A. B., Tzeuton, C., ... Gastroenterology and Hepatology Association of sub-Saharan Africa (GHASSA). (2017). Hepatitis C in sub-Saharan Africa: The current status and recommendations for achieving elimination by 2030. *The Lancet. Gastroenterology & Hepatology*, 2(12), 910–919. [https://doi.org/10.1016/S2468-1253\(17\)30249-2](https://doi.org/10.1016/S2468-1253(17)30249-2)
- Thursz, M., & Fontanet, A. (2014). HCV transmission in industrialized countries and resource-constrained areas. *Nature Reviews Gastroenterology & Hepatology*, 11(1), 28–35. <https://doi.org/10.1038/nrgastro.2013.179>
- UNODC. (2014). *Senegal—Drug Monitoring and Rehabilitation*. <https://www.unodc.org/westandcentralafrica/en/senegal---drug-monitoring-and-rehabilitation.html>
- van Santen, D. K., de Vos, A. S., Matser, A., Willemse, S. B., Lindenburg, K., Kretzschmar, M. E. E., Prins, M., & de Wit, G. A. (2016). Cost-Effectiveness of Hepatitis C Treatment for People Who Inject Drugs and the Impact of the Type of Epidemic; Extrapolating from Amsterdam, the Netherlands. *PLoS ONE*, 11(10). <https://doi.org/10.1371/journal.pone.0163488>
- Viner, K., Kuncio, D., Newbern, E. C., & Johnson, C. C. (2015). The continuum of hepatitis C testing and care. *Hepatology (Baltimore, Md.)*, 61(3), 783–789. <https://doi.org/10.1002/hep.27584>
- WHO. (2015). *Global Health Observatory | Domestic general government health expenditure (GGHE-D) as percentage of gross domestic product (GDP) (%)—Data by country*. WHO. <http://apps.who.int/gho/data/node.main.GHEDGGHEDGDPSHA2011?lang=en>
- WHO. (2016). *Global health sector strategy on viral hepatitis 2016-2021*. <http://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/>
- WHO. (2017). *Global hepatitis report, Web Annex B, WHO estimates of the prevalence and incidence of hepatitis C virus infection by WHO region, 2015*. <http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/>
- WHO. (2018). *Progress report on access to hepatitis C treatment*. <http://www.who.int/hepatitis/publications/hep-c-access-report-2018/en/>
- World Bank. (2008). *The business of health in Africa: Partnering with the private sector to improve people's lives*. The World Bank.

<http://documents.worldbank.org/curated/en/302121467990315371/Investir-dans-la-sante-en-Afrique-Le-secteur-prive-un-partenaire-pour-ameliorer-les-conditions-de-vie-des-populations>

APPENDIX

Table S1: Expected numbers of true positive, false positive, false negative and true negative cases per 10,000 targeted individuals of testing strategies under the base-case assumptions

Strategy	True positives	False positives	False negatives	True negatives
S ₅ : Ab_POC → RNA_POC	2,587	22	136	7,255
S ₁₂ : RNA_POC	2,600	138	123	7,139
S ₈ : Ab_POC → cAg_lab_Ven	2,531	14	192	7,263
S ₉ : Ab_POC → cA_lab_DBS	2,078	32	645	7,245
S ₃ : Ab_POC → RNA_lab_Ven	2,707	4	16	7,273
S ₁₀ : cAg_lab_Ven	2,543	87	180	7,190
S ₆ : Ab_lab_Ven → cAg_lab_Ven	2,531	15	192	7,262
S ₄ : Ab_POC → RNA_lab_DBS	2,655	23	68	7,254
S ₁₁ : cAg_lab_DBS	2,089	196	634	7,081
S ₇ : Ab_lab_Ven → cA_lab_DBS	2,034	31	689	7,246
S _{ref} : Ab_lab_Ven → RNA_lab_Ven	2,707	4	16	7,273
S ₂ : Ab_lab_Ven → RNA_lab_DBS	2,599	23	124	7,254

Ab=antibody. cAg= core antigen. DBS=dried blood spot. lab=laboratory. POC=point of care. RNA=ribonucleic acid. Ven=Venepuncture.

Table S2: Estimates of cost, effectiveness, and cost-effectiveness of un-dominated strategies depending on the values of the uptake rates for decentralized and centralized strategies

		Uptake rate for centralized strategies (%)															
		0.1				0.2				0.3				0.4			
		Un-dominated strategies	Cost	Eff.	ICER	Un-dominated strategies	Cost	Eff.	ICER	Un-dominated strategies	Cost	Eff.	ICER	Un-dominated strategies	Cost	Eff.	ICER
Uptake rate for decentralized strategies (%)	0.2	S ₅ [Ab_POC→RNA_POC]	2.84	517	0												
		S ₃ [Ab_POC→RNA_lab_Ven]	6.85	541	1679.79												
	0.3	S ₁₀ [cAg_lab_Ven]	3.43	254	0	S ₅ [Ab_POC→RNA_POC]	4.26	776	0								
		S ₅ [Ab_POC→RNA_POC]	4.26	776	15.96	S ₃ [Ab_POC→RNA_lab_Ven]	10.27	812	1679.79								
		S ₃ [Ab_POC→RNA_lab_Ven]	10.27	812	1679.79												
	0.4	S ₁₀ [cAg_lab_Ven]	3.43	254	0	S ₅ [Ab_POC→RNA_POC]	5.68	1035	0	S ₅ [Ab_POC→RNA_POC]	5.68	1035	0				
		S ₅ [Ab_POC→RNA_POC]	5.68	1035	28.88	S ₃ [Ab_POC→RNA_lab_Ven]	13.69	1083	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	13.69	1083	1679.79				
		S ₃ [Ab_POC→RNA_lab_Ven]	13.69	1083	1679.79												
	0.5	S ₁₀ [cAg_lab_Ven]	3.43	254	0	S ₁₀ [cAg_lab_Ven]	6.86	509	0	S ₅ [Ab_POC→RNA_POC]	7.11	1294	0	S ₅ [Ab_POC→RNA_POC]	7.11	1294	0
		S ₅ [Ab_POC→RNA_POC]	7.11	1294	35.36	S ₅ [Ab_POC→RNA_POC]	7.11	1294	3.12	S ₃ [Ab_POC→RNA_lab_Ven]	17.12	1353	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	17.12	1353	1679.79
		S ₃ [Ab_POC→RNA_lab_Ven]	17.12	1353	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	17.12	1353	1679.79								
0.6	S ₁₀ [cAg_lab_Ven]	3.43	254	0	S ₁₀ [cAg_lab_Ven]	6.86	509	0	S ₅ [Ab_POC→RNA_POC]	8.53	1552	0	S ₅ [Ab_POC→RNA_POC]	8.53	1552	0	
	S ₅ [Ab_POC→RNA_POC]	8.53	1552	39.26	S ₅ [Ab_POC→RNA_POC]	8.53	1552	15.96	S ₃ [Ab_POC→RNA_lab_Ven]	20.54	1624	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	20.54	1624	1679.79	
	S ₃ [Ab_POC→RNA_lab_Ven]	20.54	1624	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	20.54	1624	1679.79									
0.7	S ₁₀ [cAg_lab_Ven]	3.43	254	0	S ₁₀ [cAg_lab_Ven]	6.86	509	0	S ₅ [Ab_POC→RNA_POC]	9.95	1811	0	S ₅ [Ab_POC→RNA_POC]	9.95	1811	0	
	S ₅ [Ab_POC→RNA_POC]	9.95	1811	41.86	S ₅ [Ab_POC→RNA_POC]	9.95	1811	23.7	S ₃ [Ab_POC→RNA_lab_Ven]	23.97	1895	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	23.97	1895	1679.79	
	S ₃ [Ab_POC→RNA_lab_Ven]	23.97	1895	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	23.97	1895	1679.79									
0.8	S ₁₀ [cAg_lab_Ven]	3.43	254	0	S ₁₀ [cAg_lab_Ven]	6.86	509	0	S ₁₀ [cAg_lab_Ven]	10.29	763	0	S ₅ [Ab_POC→RNA_POC]	11.37	2070	0	
	S ₅ [Ab_POC→RNA_POC]	11.37	2070	43.72	S ₅ [Ab_POC→RNA_POC]	11.37	2070	28.88	S ₅ [Ab_POC→RNA_POC]	11.37	2070	8.25	S ₃ [Ab_POC→RNA_lab_Ven]	27.39	2165	1679.79	
	S ₃ [Ab_POC→RNA_lab_Ven]	27.39	2165	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	27.39	2165	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	27.39	2165	1679.79					
0.9	S ₁₀ [cAg_lab_Ven]	3.43	254	0	S ₁₀ [cAg_lab_Ven]	6.86	509	0	S ₁₀ [cAg_lab_Ven]	10.29	763	0	S ₅ [Ab_POC→RNA_POC]	12.79	2329	0	
	S ₅ [Ab_POC→RNA_POC]	12.79	2329	45.12	S ₅ [Ab_POC→RNA_POC]	12.79	2329	32.58	S ₅ [Ab_POC→RNA_POC]	12.79	2329	15.96	S ₃ [Ab_POC→RNA_lab_Ven]	30.81	2436	1679.79	
	S ₃ [Ab_POC→RNA_lab_Ven]	30.81	2436	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	30.81	2436	1679.79	S ₃ [Ab_POC→RNA_lab_Ven]	30.81	2436	1679.79					

Ab=antibody. DBS=dried blood spot. lab=laboratory. Eff=Effectiveness. ICER=Incremental cost-effectiveness ratio. POC=point of care. RNA=ribonucleic acid. Ven=Venepuncture.