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Cost-effectiveness of rapid HCV testing and simultaneous rapid HCV and HIV testing in substance abuse treatment programs

Bruce R. Schackman, PhD¹, Jared A. Leff, MS¹, Devra M. Barter, MS², Madeline A. DiLorenzo, AB^{3,4}, Daniel J. Feaster, PhD⁵, Lisa R. Metsch, PhD^{5,6}, Kenneth A. Freedberg, MD, MSc^{3,4,7,8,9}, and Benjamin P. Linas, MD, MPH^{2,9}

¹Department of Healthcare Policy and Research, Weill Cornell Medical College, New York, NY, USA

²HIV Epidemiology and Outcomes Research Unit, Section of Infectious Diseases, Department of Medicine, Boston Medical Center, Boston, MA, USA

³Division of General Medicine, Massachusetts General Hospital, Boston, MA, USA

⁴The Medical Practice Evaluation Center, Massachusetts General Hospital, Boston, MA, USA

⁵Department of Public Health Sciences, Miller School of Medicine, University of Miami, Miami, FL, USA

⁶Department of Sociomedical Sciences, Mailman School of Public Health, Columbia University, New York, NY, USA

⁷Division of Infectious Diseases, Massachusetts General Hospital, Boston, MA, USA

⁸Department of Health Policy and Management, Harvard School of Public Health, Boston MA, USA

⁹Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA

Abstract

Aims—To evaluate the cost-effectiveness of rapid hepatitis C virus (HCV) and simultaneous HCV/HIV antibody testing in substance abuse treatment programs.

Design—We used a decision analytic model to compare the cost-effectiveness of no HCV testing referral or offer, off-site HCV testing referral, on-site rapid HCV testing offer, and on-site rapid HCV and HIV testing offer. Base case inputs included 11% undetected chronic HCV, 0.4%

Corresponding Author: Bruce R. Schackman, Ph.D., Professor of Healthcare Policy and Research, Department of Healthcare Policy and Research, Weill Cornell Medical College, 425 East 61st Street, Suite 301, New York, NY 10065, Tel: 646-962-9302, Fax: 646-962-0105, brs2006@med.cornell.edu.

Clinical trial registration

Clinical trials.gov identification number for the trial upon which these data were obtained is: NCT00809445.

Declarations of interest

There are no author conflicts of interest.

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undetected HIV, 35% HCV co-infection among HIV-infected, 53% linked to HCV care after testing antibody positive, and 67% linked to HIV care. Disease outcomes were estimated from established computer simulation models of HCV (HEP-CE) and HIV (CEPAC).

Setting and Participants—Data on test acceptance and costs were from a national randomized trial of HIV testing strategies conducted at 12 substance abuse treatment programs in the USA.

Measurements—Lifetime costs (2011 US dollars) and quality-adjusted life years (QALYs) discounted at 3% annually; incremental cost-effectiveness ratios (ICERs)

Findings—On-site rapid HCV testing had an ICER of \$18,300/QALY compared with no testing, and was more efficient than (dominated) off-site HCV testing referral. On-site rapid HCV and HIV testing had an ICER of \$64,500/QALY compared with on-site rapid HCV testing alone. In one and two-way sensitivity analyses, the ICER of on-site rapid HCV and HIV testing remained < \$100,000/QALY, except when undetected HIV prevalence was <0.1% or when we assumed frequent HIV testing elsewhere. The ICER remained <\$100,000/QALY in approximately 90% of probabilistic sensitivity analyses.

Conclusions—On-site rapid hepatitis C virus and HIV testing in substance abuse treatment programs is cost-effective at a <\$100,000/ quality-adjusted life years threshold.

Keywords

cost-effectiveness; economic evaluation; hepatitis C testing; rapid HIV testing; substance abuse treatment

INTRODUCTION

There are an estimated 3.2 million individuals in the United States who are chronically infected with hepatitis C virus (HCV), of whom only half have had an HCV antibody test and less than a quarter have had a confirmatory HCV RNA test [1]. The US Centers for Disease Control and Prevention (CDC) has set a goal to reduce the proportion of HCV-infected individuals unaware of their status from 55% to 33% [2]. In 2013, the US Preventive Services Task Force (USPSTF) changed its HCV screening recommendation to include screening for all individuals born between 1945 and 1965, in addition to individuals with identified risk factors previously recommended for screening [3, 4]. Current or former injection drug use is the most important identified risk factor for HCV infection in the US [5].

Learning one's HCV antibody status is an extremely important first step in the HCV treatment cascade. Subsequent steps include confirmatory testing, receiving the confirmatory test results, further medical evaluation (e.g. HCV genotype and HIV tests), and initiating treatment. Testing substance abuse treatment program clients for HCV represents an important opportunity to identify and cure chronically infected individuals [6] in order to fully realize the potential of new, highly effective, and well-tolerated HCV therapies [7]. Yet in a survey of community-based substance abuse treatment programs participating in the National Drug Abuse Treatment Clinical Trials Network (CTN), only 28% of programs offered HCV antibody testing on-site or through referral to other testing sites, and in a

survey of outpatient substance abuse treatment programs only 29% of clients had received HIV testing on-site or off-site [8, 9]. A more recent survey found a significant reduction in the proportion of opioid treatment programs conducting HIV testing between 2005 and 2011 and a significantly higher likelihood of testing in publicly-owned programs [10], suggesting that lack of reimbursement may be playing an increasing role in decisions about whether to offer testing in private for-profit and non-profit programs.

In 2009, the CTN conducted a randomized trial that evaluated the feasibility, efficacy, and cost-effectiveness of on-site rapid HIV testing in 12 community-based substance abuse treatment programs [11, 12]. Compared to off-site referral, on-site rapid testing was found to be more effective in delivering HIV test results and had a cost-effectiveness ratio of \$60,300/QALY. In 2011, a rapid point-of-care HCV antibody test was approved for marketing in the US, presenting the opportunity to conduct on-site rapid HCV testing in community-based substance abuse treatment programs [13]. Our objectives were to estimate the cost-effectiveness of rapid HCV testing in substance abuse treatment programs, and to examine the cost-effectiveness of conducting rapid HIV testing in substance abuse treatment programs if HCV testing is already being conducted.

METHODS

Analytic Overview

We used a decision analytic model to evaluate the cost-effectiveness of four strategies for HCV and simultaneous HCV and HIV testing in substance abuse treatment centers for clients who do not report being HCV-infected or HIV-infected: 1) no HCV test referral or offer (no intervention); 2) referral to an off-site HCV antibody test; 3) offer of an on-site rapid HCV antibody test; and 4) offer of on-site rapid HCV and HIV antibody tests. For the HCV and HIV testing strategy, we assumed that both tests would be offered together and that clients would accept either both tests or neither test [14, 15]. HIV tests offers were assumed to take place without brief risk-reduction counseling because trial results have shown that brief counseling adds cost without improving efficacy [11, 12, 16]. All clients receiving reactive results were assumed to receive counseling and referral for confirmatory testing [17]. Clients who reported being HIV-infected were excluded because HCV testing for these individuals should be conducted as part of their HIV care [18], but clients unaware of being HIV-infected were included. We assumed that HCV/HIV co-infected individuals would be identified as HIV-infected in follow-up HCV care even in the absence of an initial HIV test, based on standard clinical practice for HCV treatment evaluation [19].

Model inputs for undetected HCV antibody prevalence, proportion of HCV-antibody positive with chronic HCV, HCV/HIV co-infection prevalence, and the cascade of care (HCV and HIV test acceptance, receipt of test results, and linkage to care inputs) were from the literature (Table 1) [20–23]. The cohort characteristics, test acceptance and receipt of test results, and undetected HIV prevalence were from the CTN randomized trial of rapid HIV testing in substance abuse treatment programs [11]. Disease outcomes were estimated from established computer simulation models of HCV (Hepatitis C Cost-Effectiveness model: HEP-CE) [24, 25] and HIV (Cost-Effectiveness of Preventing AIDS Complications model: CEPAC) [12, 26].

Outcomes included lifetime costs (2011 US dollars) and quality-adjusted life years (QALYs), both discounted at 3% annually [27], and incremental cost-effectiveness ratios (ICERs). Costs were estimated from the health system perspective, including costs to substance abuse treatment programs (which may or may not be reimbursed) and downstream costs for HCV and HIV healthcare. ICERs were calculated as the additional cost per QALY gained compared to the next least expensive strategy after eliminating strategies due to dominance (when one strategy is more effective and costs less) or extended dominance (when a combination of alternative strategies is a more efficient use of resources than the dominated strategy) [28, 29]. We assumed a societal willingness-to-pay of \$100,000/QALY, a commonly used threshold in the US, although some have argued for an even higher threshold [30, 31].

Decision Analytic Model

For each strategy, the decision analytic model describes test offer, test acceptance and linkage to care and calculates costs and quality of life outcomes that depend on disease status and disease status awareness. We define being aware of chronic HCV infection or HIV infection as having received a confirmatory test result after linking to care (Figure 1). HCV and HIV test sensitivity and specificity are included in the model (Table S1). We assume that individuals who receive false positive reactive results (or true positive HCV reactive results but do not have chronic HCV infection) experience a short-term negative quality of life impact [32–34]. The on-site rapid HCV testing and simultaneous rapid HCV and HIV processes and costs are based on the on-site rapid HIV testing conducted without risk behavior counseling in the trial [12]. Off-site HCV testing referrals are assumed to be made to a clinical setting where a non-rapid HCV antibody test would be conducted [17]. The decision analytic model was programmed in TreeAge Pro 2013 (Williamstown, MA).

HEP-CE Model

Lifetime costs and QALYs for simulated individuals who are and are not aware of their disease status were estimated using the HEP-CE Monte Carlo simulation model [24, 25]. We estimated outcomes separately for 7 categories of individuals: HCV and HIV-uninfected; HCV-infected and HIV-uninfected (aware and unaware); HCV-uninfected and HIV-infected (aware and unaware); and HCV/HIV co-infected (aware and unaware). The proportion of individuals in each category varies by testing strategy, as determined by the decision analytic model (Table S2). The HEP-CE model simulates chronic HCV disease progression through 3 stages of liver disease: mild to moderate fibrosis, cirrhosis, and decompensated cirrhosis. Each disease stage is associated with a decrease in quality of life and an increase in health care costs (Table 1). If simulated individuals with chronic HCV become cirrhotic they have an increased risk of mortality attributable to their liver disease [35, 36].

Simulated individuals with chronic HCV who are linked to HCV care and receive confirmatory test results have a probability of initiating HCV treatment, and if they achieve sustained viral response (SVR) their health care costs, quality of life, and risk of mortality revert to those of HCV-uninfected individuals [37–40]. Consistent with treatment guidelines at the time of the analysis, individuals with HCV genotype 1 were treated with pegylated interferon (PEG), ribavirin (RBV), and telaprevir (TPV), while those with genotypes 2 or 3

were treated with PEG/RBV [19, 41] (Table S3). Duration and efficacy of treatment depended on genotype, presence of cirrhosis, and HIV co-infection status. In an alternative analysis consistent with current treatment guidelines [42], individuals with HCV genotype 1 were treated with sofosbuvir (SOF), PEG and RBV for 12 weeks, those with genotype 2 were treated with SOF and RBV for 12 weeks, and those with genotype 3 were treated with SOF and RBV for 24 weeks. Finally, we considered a hypothetical 12-week interferon-free treatment for all patients (Table 1).

Simulated individuals who refuse testing, who accept testing but do not receive results, or who accept testing and are found to be HCV-uninfected, have a probability of being tested for HCV elsewhere. Simulated individuals who become aware of their chronic HCV infection but do not initiate HCV treatment have a probability of returning to HCV care. Those without chronic HCV infection at baseline or who achieve SVR after treatment have a probability of HCV infection or re-infection. All simulated individuals in the model have an elevated mortality risk compared to the general population, reflecting their overall risk profile, with a higher risk assigned to individuals with a history of injection drug use [43, 44].

Simulated individuals who are HIV-infected or HCV/HIV-infected have HIV-attributable mortality, HIV-related health care costs, and quality of life weights assigned annually. We used the CEPAC model to estimate these HEP-CE model inputs for individuals who are unaware and aware of their HIV infection. The CEPAC model simulates HIV disease progression and treatment effects on immune status (CD4 count) and circulating viral burden (HIV RNA), depending on use of antiretroviral therapy, treatment adherence, and retention in care (Table 1). For HCV/HIV co-infected individuals, HIV-related costs were added to HCV-related costs, and quality of life estimates were calculated using a multiplicative assumption.

Simulated Cohort Base Case Inputs

We derived cohort age and sex characteristics from those substance abuse treatment program clients screened for participation in the CTN HIV testing trial who would be eligible for HCV testing (i.e. excluding individuals who indicated that they knew that they were HCV-infected and/or HIV-infected) (Table 1). There were 1,954 individuals in this population, of whom 61% were white, 29% black, and 10% Hispanic. One third of individuals reported a lifetime history of injection drug use.

Because the CTN trial did not conduct HCV testing, we estimated a base case prevalence of undetected chronic HCV of 11% [20] and varied this widely in sensitivity analyses [19, 45]. Although higher HCV prevalence has been reported in methadone treatment programs [46, 47], 11% prevalence may be more representative of substance abuse treatment programs employing diverse treatment modalities nationally [48, 49]. HCV test acceptance and receipt of results inputs were derived from off-site referral and on-site rapid HIV testing offer results for the 1,032 trial participants who would be eligible for HCV testing (i.e. excluding individuals who reported that they knew that they had been diagnosed with HCV). For treatment with interferon-containing regimens, we assumed 53% of individuals with chronic HCV infection would be linked to care after testing antibody positive and 27% of those

linked would initiate treatment [21, 50]. For treatment with interferon-free regimens, we conservatively assumed the same percentage would be linked to care but increased the treatment initiation rate to 50%. Because information on multiple HCV tests was not available from trial participants, the probability of being HCV tested elsewhere was based on twice the median time since the most recent HCV test reported by HCV-uninfected trial participants.

In the CTN trial, 0.4% of individuals with previously unknown HIV status were detected as HIV-infected; we used this as our base case model input and varied it widely in sensitivity analyses, along with the proportion of these individuals who were HIV/HCV co-infected (35% in the base case [22]). In the base case, 67% of individuals with a reactive HIV test (whether or not HCV co-infected) were linked to care [23], and approximately 85% of these individuals were eligible for immediate initiation of antiretroviral therapy (ART) at a threshold for ART initiation of <500 CD4 cells/ μ l [18]. The probability of being HIV tested elsewhere was based on the median time between HIV tests reported by the trial participants who would be eligible for HCV testing and who reported having previously received two HIV tests.

Sensitivity Analyses

In one-way sensitivity analyses we varied the following parameters: age, sex, elevated mortality risk compared to the general population, chronic HCV disease progression rate, liver-related mortality rate, untreated HIV disease progression rate, probability of being tested for HCV or HIV elsewhere, cascade of care inputs (test acceptance, receipt of test results, and linkage to care), HCV re-infection rate, HCV and HIV treatment efficacies and costs, ART initiation criteria, non-HCV/HIV background medical costs, and quality of life. In two-way sensitivity analyses evaluating the on-site HCV testing offer alone strategy, we varied HCV prevalence and linkage to care inputs. In two-way sensitivity analyses evaluating the on-site simultaneous HCV and HIV testing offer strategy, we varied HIV prevalence and the proportion of HIV-infected who are HCV-co-infected. We also simultaneously varied the efficacy and cost of interferon-free treatment. In probabilistic sensitivity analyses, we varied all decision analysis model inputs simultaneously across relevant ranges (Table 1) using gamma distributions for cost and quality of life inputs, beta distributions for probability inputs derived from the CTN trial data, and uniform distributions for other inputs derived from the literature [51].

RESULTS

Base Case

The referral for off-site HCV testing strategy resulted in a mean per person discounted lifetime cost of \$109,020 and quality-adjusted life expectancy of 16.546 QALYs, corresponding to an incremental \$120 cost and 0.004 QALYs compared to no intervention (Table 2). The incremental cost include the costs of making the referral (\$3), initial and confirmatory testing for those who accept the referral (\$47), and subsequent HCV care costs for those successfully engaged in care (\$70). The low incremental cost and quality-adjusted life expectancy reflect the small proportion of individuals who are HCV-infected, accept the

referral, link to care, initiate treatment, and achieve SVR. An offer of on-site rapid HCV testing had an incremental cost of \$390 (including \$37 incurred by the substance abuse treatment program) and yielded approximately five-fold higher incremental QALYs (0.021) compared to no intervention. This strategy resulted in greater quality-adjusted life expectancy than off-site referral at a lower cost, indicating that the off-site referral strategy was dominated because any resources directed towards off-site referral would be more efficiently employed offering on-site rapid testing. The ICER of on-site rapid testing compared to no intervention was \$18,300/QALY (Table 2). On-site rapid HCV and HIV testing had an ICER of \$64,500/QALY compared to on-site rapid HCV testing alone. Overall cost-effectiveness conclusions about screening did not depend on the treatment regimen used. When we considered HCV treatment with PEG/RBV/SOF (genotype 1) or SOF/RBV (genotypes 2/3), for example, on-site rapid testing continued to dominate off-site referral. The ICER for on-site rapid testing compared to no intervention was \$22,000/QALY, and the ICER for on-site rapid HCV and HIV testing compared to on-site rapid HCV testing alone was \$64,000/QALY. When we assumed a future, interferon-free regimen for all genotypes, results were similar (Table 2).

Sensitivity Analyses

Offer of on-site rapid HCV testing dominated off-site referral in all one-way and two-way sensitivity analyses using plausible ranges for off-site referral acceptance and receipt of results derived from the CTN trial. In one-way sensitivity analyses, the ICER for on-site rapid testing compared to no intervention varied between \$8,200/QALY and \$37,800/QALY (Table S4). In two-way sensitivity analyses when we assumed undetected chronic HCV prevalence was the same as the US national average of 0.5% (versus 11% in the base case), the ICER for on-site rapid testing compared to no intervention remained below \$100,000/QALY as long as at least 20% of those identified through rapid HCV testing were linked to care (Figure 2). The ICER was \$39,800/QALY when we assumed the lowest efficacy and highest cost for SOF-based regimens.

In one-way sensitivity analyses, the ICER for an offer of on-site rapid HCV and HIV testing compared to on-site rapid HCV testing alone remained <\$100,000/QALY, except when undetected HIV prevalence was <0.1% or we assumed frequent HIV testing elsewhere (more than four-fold increase from base case; Table S4). In two-way sensitivity analyses, if 80% of HIV-infected individuals in this population were HCV co-infected (versus 35% in the base case), the ICER for an offer of on-site rapid HCV and HIV testing compared to on-site rapid HCV testing alone varied from \$63,400/QALY with 1.0% undetected HIV prevalence to \$148,300/QALY with undetected HIV prevalence of 0.1% (Figure 3). The ICER was \$63,300/QALY when we assumed the lowest treatment efficacy and highest cost for SOF-based treatment.

At a willingness-to-pay threshold of \$100,000/QALY, an offer of on-site rapid HCV and HIV testing was the preferred strategy in 91% of probabilistic sensitivity analyses and an offer of on-site rapid HCV testing alone was preferred in 9% of these analyses (Figure 4). At a willingness-to-pay threshold of \$50,000/QALY, offer of on-site rapid HCV testing alone

was preferred in >99% of these analyses. Results were similar with SOF-based treatment and hypothetical interferon-free regimens.

DISCUSSION

Using a decision analytic model in conjunction with published models of HCV and HIV disease, we found that on-site rapid HCV testing in substance abuse treatment programs has a cost-effectiveness ratio <\$20,000/QALY, even with imperfect linkage to care and treatment regimens containing interferon, and <\$30,000/QALY with more effective and more expensive regimens. These ratios compare favorably to recent modeling studies that have examined the cost-effectiveness of birth cohort and general population HCV screening in the US and have reported cost-effectiveness ratios of \$28,600/QALY-\$65,700/QALY in 2010 US dollars [52–54]. Combined on-site rapid HCV and HIV testing has an ICER < \$100,000/QALY, generally considered good value for money in the US, under reasonable assumptions about undetected HIV and HIV/HCV prevalence and HIV testing elsewhere in this population.

Our results were consistent in sensitivity analyses when we varied model inputs individually and in combination. These results show the value of conducting HCV testing for all age groups in substance treatment programs, where there is a high prevalence of undetected chronic HCV and low levels of awareness of HCV status.

Our findings are subject to several limitations. Model inputs for acceptance of on-site rapid testing and off-site testing referral and for subsequent receipt of results in each scenario are from a randomized trial of HIV testing that did not include HCV testing options. Based on this trial, we assumed >80% acceptance of an offer of on-site HCV rapid testing or an offer of both HCV and HIV rapid testing. In contrast, we assumed only about one-half of individuals identified as HCV antibody-positive are linked to care, about one-quarter of those linked to care initiate interferon-based HCV treatment, and about one-half initiate interferon-free HCV treatment. Taken together, these assumptions are conservative with regards to the value of on-site HCV testing, because we assume most individuals are tested but less than one quarter with chronic HCV initiate treatment and achieve SVR. The rapid pace of new drug development for HCV will yield several new, more effective and less toxic treatment options and their cost is not fully known. Nevertheless, our results indicate that even if new treatments have significantly higher costs and treatment initiation rates improve modestly, HCV testing in substance abuse treatment programs will still be an attractive public health investment.

We also assumed that approximately two-thirds of newly-identified HIV-infected individuals would link to care, and most of those linked would initiate ART despite having relatively high CD4 cell counts. However, in the CEPAC model we accounted for heterogeneity in adherence to ART and retention in HIV care, and we varied the level of adherence in sensitivity analyses. Our analysis also did not incorporate potential future benefits of reduced secondary HCV and HIV transmission from HCV and HIV treatment, which could result in more attractive cost-effectiveness ratios for on-site rapid testing [55, 56].

Despite the value of HCV and HIV testing of substance users, there are important implementation challenges along the HCV cascade of care. Implementing on-site testing in substance abuse treatment programs has some start-up costs and requires personnel who are able to provide supervision and training [57]. These requirements may be particularly challenging, however, because of the limited organizational and administrative infrastructures and high employee turnover that characterize many programs [58]. Although the Affordable Care Act requires both tests to be covered by health insurers based on USPSTF recommendations [4, 59], some substance abuse treatment programs lack the capacity to bill for these services. Care coordination interventions may need to be established to link HCV-infected individuals to HCV providers [60], and these providers must be willing to treat these patients and accept their insurance coverage [61].

Based on available evidence, we conclude that on-site rapid HCV and HIV testing in substance abuse treatment programs represents good value as a public health investment. Policymakers should identify ways to improve the capacity of substance abuse treatment programs to implement on-site rapid HCV and HIV testing, bill for these services, and ensure that individuals testing positive for either virus receive further evaluation and treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Decision analytic model schematic

Figure 2.
Cost-effectiveness of on-site rapid HCV testing compared to no intervention varying linkage to HCV care (2011 US dollars)

Figure 3.

Cost-effectiveness of on-site simultaneous rapid HCV and HIV testing compared to on-site rapid HCV testing varying HIV prevalence and proportion of HIV co-infected with HCV (2011 US dollars)

Figure 4.
Cost-effectiveness acceptability curve for on-site testing strategies compared to no intervention

Table 1

Model input parameters

Variable	Base case	Range	Reference
Baseline cohort characteristics			
Mean age, years (SD)	36 (9)	26 (9)–56 (9)	CTN-0032
Sex, male (%)	61	0–100	CTN-0032
Undetected chronic HCV (%)	11	1–65	[19, 20, 45]
HCV incidence (new infections/100 PYs)	0.66	0.33–1.32	[20]
Proportion of HCV antibody positive with chronic HCV infection (%)	74	71–78	[20, 62, 63]
HCV-infected with genotype 1 (%)	73	60–90	[62, 64–66]
Undetected HIV (%)	0.4	0.1–1.0	[12]
HIV-infected who are co-infected with chronic HCV (%)	35	25–100	[22]
Test acceptance, receipt of results, and linkage to care			
Accept antibody test (%)			
Off-site non-rapid HCV	22	11–33	CTN-0032
On-site rapid HCV or HCV and HIV	83	54–100	CTN-0032, [57]
Receive antibody test results (%)			
Off-site non-rapid HCV	74	18–84	CTN-0032, [67]
On-site rapid HCV or HCV and HIV	99	95–100	CTN-0032
Linkage to care			
Link to HCV care (%)	53	24–77	[21, 68–71]
Receive HCV RNA confirmatory test result (%)	98	75–100	[72, 73]
Initiate HCV treatment if linked to care (%)	27	25–45	[50, 74, 75]
Link to HIV care (%)	67	53–85	[21, 23, 76]
Initiate HIV treatment if linked to care (%)	85	85–100	See text
Return to care			
Re-engage with HCV care within 10 years after being lost to follow-up (%)	27	0–53	assumption
Rate of return to HIV care per 100 PYs	16.7	8.4–25.1	<i>a</i>
HCV and HIV test costs (\$)			
Off-site HCV antibody test referral	50	25–75	Table S1
On-site rapid HCV antibody test offer	44	22–67	Table S1
On-site rapid HCV and HIV antibody test offer	71	36–107	Table S1
HCV disease history and progression			
Mean age of infection (years)	26	16–36	[77]
Median time from infection to cirrhosis (years)	25	10–40	[78, 79]
Median time from cirrhosis to decompensated cirrhosis (years)	11	6–19	[35, 80]
Rate of liver-related mortality with cirrhosis (deaths/100 PYs)	2.7	1.4–4.1	[36]
HIV disease history and progression			
CD4 count at HIV infection, cells/μl (SD)	751 (267)	–	[81]
CD4 count at time of test offer, cells/μl (SD)			
Previously tested for HIV	637 (256)	200–700	<i>b</i>
Never tested for HIV	489 (243)	200–700	<i>b</i>

Variable	Base case	Range	Reference
Rate of CD4 decline when not on ART (cells/ μ l/month) ^c	3.0–6.4	1.5–9.6	[82]
HCV treatment efficacy and cost			
Genotype 1, regimens with interferon (PEG/RBV/TPV)			
SVR, HIV-uninfected (%)			
Non-cirrhotic	75	60–95	[83]
Cirrhotic	63	60–95	[83]
SVR, HIV-infected (%)			
Non-cirrhotic	79	65–86	[84]
Cirrhotic	61	50–70	[84]
Genotypes 2 or 3, regimens with interferon (PEG/RBV)			
SVR, HIV-uninfected (%)			
Non-cirrhotic	74	55–95	[85, 86]
Cirrhotic	58	55–95	[85, 86]
SVR, HIV-infected (%)			
Non-cirrhotic	79	74–89	[87–89]
Cirrhotic	55	48–69	[87–89]
Genotype 1, regimens with sofosbuvir (PEG/RBV/SOF)			
SVR, HIV-uninfected and HIV-infected non-cirrhotic (%)	92	88–95	[90]
SVR, HIV-uninfected and HIV- infected, cirrhotic (%)	80	66–89	[90]
Genotype 2, regimens with sofosbuvir (RBV/SOF)			
SVR, HIV-uninfected and HIV-infected non-cirrhotic (%)	98	91–100	[91]
SVR, HIV-uninfected and HIV- infected, cirrhotic (%)	91	59–100	[91]
Genotype 3, regimens with sofosbuvir (RBV/SOF)			
SVR, HIV-uninfected and HIV-infected non-cirrhotic (%)	94	86–98	[92]
SVR, HIV-uninfected and HIV- infected, cirrhotic (%)	92	64–100	[92]
All genotypes, interferon-free regimens			
SVR, HIV-uninfected and HIV-infected non-cirrhotic (%)	90	80–100	[7, 93, 94]
SVR, HIV-uninfected and HIV- infected, cirrhotic (%)	81	70–90	[7, 93, 94]
HCV treatment cost (\$)			
Provider visit cost ^d	120	60–180	[95, 96]
Complete course of HCV treatment ^e			
Genotype 1, regimens with interferon (PEG/RBV/TPV)			
HIV-uninfected	67,000–89,400	33,900–134,100	[95, 97]
HIV-infected	89,400	44,700–134,100	[95, 97]
Genotypes 2 or 3, regimens with interferon (PEG/RBV)			
HIV-uninfected	19,800	9,900–29,700	[95, 97, 98]
HIV-infected	39,000	19,500–58,500	[95, 97, 98]
Genotype 1, sofosbuvir-based regimens with interferon (PEG/RBV/SOF)	99,000	49,500–148,500	[95, 97, 98]
Genotype 2, sofosbuvir-based interferon-free regimens (RBV/SOF)	91,500	45,700–137,200	[95, 97, 98]
Genotype 3, sofosbuvir-based interferon-free regimens (RBV/SOF)	182,900	91,500–274,400	[95, 97, 98]
All genotypes, interferon-free regimens	131,000	65,500–196,500	[24]
HIV treatment efficacy and cost			

Variable	Base case	Range	Reference
HIV RNA suppression at 6 months (%)	84	–	[99]
Adherence < 5%; >95%	0; 91	<i>f</i>	derived from [99]
Virologic failure rate after 6 months, per 100 PYs			
Adherence < 65%; >95%	60.7; 1.5	<i>f</i>	derived from [99]
Monthly treatment regimen costs (\$) Rate of loss to follow-up from HIV care, per 100 PYs	1,930–3,190	960–4,790	[97]
Adherence <50%; 50–95%; > 95%	84.5; 15.4; 0.1	<i>f</i>	derived from [99]
Background medical costs (\$/month)^g			
HCV-uninfected, HIV-uninfected	140–920	70–1,380	[100]
HCV-infected, HIV-uninfected	250–1,500	125–2,250	[100, 101]
HCV-uninfected, HIV-infected	310–6,050	160–9,080	[95, 102]
HCV-infected, HIV-infected	440–8,470	220–12,700	[95, 102, 103]
Non-HCV, non-HIV mortality			
Standardized mortality ratio reflecting elevate risk of mortality compared to general population ^h			
Male	4.1	1.0–8.0	[43, 44]
Female	5.3	1.0–10.3	[43, 44]
Quality of life weights (0=death, 1.00=best possible health)			
HCV- and HIV-uninfected (current/former substance abuser)	0.90	0.80–1.00	[104–106]
HCV-infected			
No to moderate fibrosis	0.89	0.75–0.95	[107–109]
Cirrhosis	0.62	0.55–0.75	[107–109]
Decompensated cirrhosis	0.48	0.40–0.60	[107–109]
On interferon-based HCV-treatment (multiplier) ⁱ	0.90	0.84–0.96	[110]
On interferon-free HCV-treatment (multiplier) ⁱ	0.95	0.90–0.99	See text
Major toxicity (decrement applied to month of event)	0.16	0.09–0.25	[111]
HIV-infected	0.83–0.87	0.74–0.96	[112]

SD = standard deviation; HCV = hepatitis C virus; PY = person year; HIV = human immunodeficiency virus; RNA = ribonucleic acid; CD4 = cluster of differentiation 4; ART = antiretroviral therapy; PEG = pegylated-interferon; RBV = ribavirin; TPV = telaprevir; SVR = sustained viral response; SOF = sofosbuvir; CEPAC = Cost-Effectiveness of Preventing AIDS Complications; AIDS = acquired immunodeficiency syndrome

Note: all costs are in 2011 US dollars.

^aFleishman J, 2013, HIV Research Network, personal communication.

^bWe used the CEPAC model to estimate CD4 counts at the time of the testing intervention for HIV-infected individuals previously tested for HIV and never tested for HIV based on data from the Multicenter AIDS Cohort Study (MACS) on CD4 count progression from the time of infection in the absence of treatment [113].

^cDepending on HIV RNA levels.

^dCost in first month is higher (\$750).

^eBased on the Average Wholesale Price [97] less 23% discount [114], assuming a standard dosage while on treatment except for sofosbuvir, which is valued at the wholesale acquisition price [97], consistent with reported estimates [115] (Table S3).

^fIn sensitivity analyses the proportion of the population with low versus high adherence was varied such that average HIV RNA suppression at 6 months on first-line ART was 75% and 90%.

^gFor HCV-uninfected and HIV-uninfected individuals, background medical costs are from the Medical Expenditure Panel Survey or the general population [100] and are stratified by age and sex. For HCV-infected and HIV-uninfected individuals, additional HCV-related costs are added to the costs for the general population. These HCV-related costs are applied both before and after diagnosis and are stratified by HCV disease stage (mild, moderate, or severe fibrosis) [101]. For HCV-uninfected and HIV-infected individuals, background medical costs are from the CEPAC model and vary by HIV disease stage. For HCV-infected and HIV-infected individuals, a multiplier of 1.7 is applied to costs from the CEPAC model representing the additional cost among HIV-infected individuals of being HCV-infected [101].

^hWeighed average of 5.79 for males with injection drug use history, 3.57 for heterosexual males without injection drug use history, 0.71 for men who have sex with men, 9.2 for females with injection drug use history, and 3.57 for females without injection drug use history.

ⁱThis utility weight was multiplied by an individual's health state utility during the month(s) that a patient was receiving HCV therapy without major toxicity.

Table 2

Base case cost-effectiveness results

Strategy	Total Cost per Person	Total QALY per Person	Incremental Cost per Person	Incremental QALY per Person	Incremental cost-effectiveness Ratio (\$/QALY)
Treatment with interferon-containing regimens					
No intervention	\$108,900	16.542	---	---	---
Off-site referral	\$109,020	16.546	\$120	0.004	dominated ^a
On-site rapid HCV	\$109,290	16.563	\$270 ^b	0.017 ^b	\$18,300
On-site rapid HCV and HIV	\$109,430	16.565	\$140	0.002	\$64,500
Treatment with SOF-based regimens					
No intervention	\$110,660	16.599	---	---	---
Off-site referral	\$110,850	16.605	\$190	0.007	dominated ^c
On-site rapid HCV	\$111,390	16.632	\$550 ^d	0.027 ^d	\$22,000
On-site rapid HCV and HIV	\$111,540	16.634	\$140	0.002	\$64,000
Treatment with hypothetical interferon-free regimens					
No intervention	\$113,420	16.645	---	---	---
Off-site referral	\$113,710	16.654	\$290	0.009	dominated ^e
On-site rapid HCV	\$114,680	16.691	\$970 ^f	0.037 ^f	\$27,100
On-site rapid HCV and HIV	\$114,820	16.694	\$140	0.003	\$64,300

HCV = hepatitis C virus; HIV = human immunodeficiency virus; QALY = quality-adjusted life year; SOF = sofosbuvir

Note: all costs are in 2011 US dollars. All costs and QALYs are lifetime and discounted at an annual rate of 3%. Cost-effectiveness ratios may not match previous columns due to rounding.

^a Cost-effectiveness ratio of offer of off-site non-rapid HCV test compared to no intervention is \$27,900 per QALY and cost-effectiveness ratio of on-site rapid HCV test compared to offer of off-site non-rapid HCV test is \$15,800 per QALY; offer of off-site non-rapid HCV test is dominated (extended dominance) [28, 29].

^b Compared to no intervention, the incremental cost per person is \$390 and the incremental QALY per person is 0.021, resulting in a cost-effectiveness ratio of \$18,300/QALY.

^c Cost-effectiveness ratio of offer of off-site non-rapid HCV test compared to no intervention is \$28,200 per QALY and cost-effectiveness ratio of on-site rapid HCV test compared to offer of off-site non-rapid HCV test is \$20,500 per QALY; offer of off-site non-rapid HCV test is dominated (extended dominance) [28, 29].

^d Compared to no intervention, the incremental cost per person is \$740 and the incremental QALY per person is 0.033, resulting in a cost-effectiveness ratio of \$22,000/QALY.

^e Cost-effectiveness ratio of offer of off-site non-rapid HCV test compared to no intervention is \$31,400 per QALY and cost-effectiveness ratio of on-site rapid HCV test compared to offer of off-site non-rapid HCV test is \$26,000 per QALY; offer of off-site non-rapid HCV test is dominated (extended dominance) [28, 29].

f Compared to no intervention, the incremental cost per person is \$1,260 and the incremental QALY per person is 0.046, resulting in a cost-effectiveness ratio of \$27,100/QALY.