

Title: Population level outcomes and cost-effectiveness of expanding the recommendation for age-based hepatitis C testing in the United States

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Running title: Expanding age-based HCV testing

Main point:

Routine hepatitis C virus (HCV) testing is recommended for persons born 1945-1965, but HCV incidence has increased among younger adults. We used simulation modeling to demonstrate that routine testing in adults ≥ 18 increases lifetime identification, cure rates, and is cost-effective.

ABSTRACT

Background: The U.S. Centers for Disease Control and Prevention and the U.S. Preventive Services Task Force recommend one-time hepatitis C virus (HCV) testing for persons born 1945-1965 and targeted testing for high-risk persons. This strategy targets HCV testing to a prevalent population at high risk for HCV morbidity and mortality, but does not include younger populations with high incidence. To address this gap and improve access to HCV testing, age-based strategies should be considered.

Methods: We used a simulation of HCV to estimate the effectiveness and cost-effectiveness of HCV testing strategies: 1) standard of care (SOC) – recommendation for one-time testing for all persons born 1945-1965, 2) recommendation for one-time testing for adults ≥ 40 years (≥ 40 strategy), 3) ≥ 30 years (≥ 30 strategy), and 4) ≥ 18 years (≥ 18 strategy). All strategies assumed targeted testing of high-risk persons. Inputs were derived from national databases, observational cohorts and clinical trials. Outcomes included quality-adjusted life expectancy, costs, and cost-effectiveness.

Results: Expanded age-based testing strategies increased U.S. population lifetime case identification and cure rates. Greatest increases were observed in the ≥ 18 strategy. Compared to the SOC, this strategy resulted in an estimated 256,000 additional infected persons identified and 280,000 additional cures at the lowest cost per QALY gained (ICER = \$28,000/QALY).

Conclusions: In addition to risk-based testing, one-time HCV testing of persons 18 and older appears to be cost-effective, leads to improved clinical outcomes and identifies more persons with HCV than the current birth cohort recommendations. These findings could be considered for future recommendation revisions.

Keywords: Hepatitis C virus, testing, cost-effectiveness

INTRODUCTION

Half of the estimated 3.5 million people with chronic hepatitis C virus (HCV) are unaware of their status [1]. HCV treatments provide cure rates >90% [2], highlighting the importance of diagnosis. Current U.S. HCV testing recommendations by the U.S. Centers for Disease Control and Prevention and U.S. Preventive Services Task Force include routine one-time testing of persons born 1945-1965, 'the birth cohort,' and concurrent targeted testing for high-risk persons [3, 4]. While prevalence remains highest among those in the birth cohort [5], incidence is rising in younger persons [6] exposed primarily through injection drug use (IDU).

The current strategy targets the high prevalence population with advanced liver disease at near-term risk of HCV-associated mortality and is cost-effective [7], but misses younger, more recently infected persons. Risk-based strategies are currently employed to identify persons with HCV not in the birth cohort. Risk-based testing in addition to birth cohort testing is more effective than either strategy alone [8]. The value of expanding routine HCV testing among adults born after 1965 in the U.S. is unknown. In this study, we used a simulation model of HCV disease to investigate population-level outcomes and cost-effectiveness of expanding HCV testing recommendations to age-based testing that could replace birth cohort testing.

METHODS

Analytic Overview

We used the Hepatitis C Cost-Effectiveness (HEP-CE) model, a Monte Carlo microsimulation model of HCV infection, screening and treatment [9], to estimate the cost-effectiveness of four strategies for HCV testing: 1) standard of care (SOC) – one-time testing for all persons born 1945-1965, 2) recommendation for one-time testing for adults ≥ 40 years (≥ 40 strategy), 3) adults ≥ 30 years (≥ 30 strategy), and 4) adults ≥ 18 years (≥ 18 strategy). All strategies assumed targeted testing of PWID. We chose to compete these strategies because

age-based strategies may enhance national implementation [10] and the effectiveness and costs of early screening are unknown.

We simulate outcomes including HCV cases identified, linked to care, initiated treatment and cured over a lifetime; fibrosis stage at diagnosis; liver-attributable mortality; and quality-adjusted life years (QALYs). We projected lifetime medical costs assuming a healthcare system perspective and a 3% discount rate to both costs and benefits [11].

We used standard methods to calculate the incremental cost-effectiveness ratio (ICER) of each testing strategy as the additional cost per person for the total population divided by the QALYs gained compared to the next less expensive strategy [11]. We assumed a willingness-to-pay (WTP) threshold of \$100,000/QALY [11].

We used data from national databases, clinical trials, and observational cohorts to inform parameter values (Table 1). We repeated the analysis under alternative scenarios: 1) inefficient testing, in which identifying the same number of cases as were identified in the base case requires twice as much testing among uninfected persons, and 2) payer restrictions on HCV treatment such that individuals must have at least METAVIR stage F2 fibrosis and ≥ 6 months of sobriety prior to being treated. With regards to the inefficient testing strategy, an argument against recommending routine testing is that such an approach generally requires a greater number of persons tested to find one infected person. Since our base case testing rates assumed targeting that improves yield, we varied assumptions about the efficiency of such targeting to reflect the possibility of lower yield with broader testing strategies. Second, payer restrictions continue to exist in most states; therefore, it is important to explore these real-world scenarios. We conducted one-way deterministic sensitivity analyses on the base case.

HEP-CE Model Structure and Inputs

Model structure

The model is a closed cohort microsimulation, meaning that there are no new entrants to the simulation. It simulates the lifetime course of a hypothetical cohort that has the same demographics and HCV epidemiology of the U.S. population (see Supplementary Appendix [12]). The model includes several modules described below:

HCV infection, risk factors and natural history

HCV prevalence is stratified by age, sex, and risk behaviors. We simulate initiation, duration and cessation of IDU behavior. Incidence of HCV, mortality from non-HCV causes, health care costs, and quality of life (QoL) depend on current drug use status (Supplementary Appendix). There is an incidence of new infections among simulated people that is conditional on current IDU. In the model, this corresponds to higher HCV incidence among young people due to higher prevalence of IDU in that group, and the tendency for individuals to leave IDU as they age.

As individuals advance through METAVIR stages of fibrosis, QoL decreases, and health care costs increase. Liver-attributable mortality occurs only among individuals who have reached METAVIR stage F4 (cirrhosis). Individuals with decompensated cirrhosis face a higher mortality probability than those with compensated cirrhosis, which reflects real-world findings [13].

HCV Testing

Individuals have a monthly probability of HCV testing that varies by age, sex, and drug use status. We model the effect of a recommendation for routine HCV testing as an increase in the monthly probability that a person in a group is tested. Recommending routine one-time

testing does not ensure that all receive an HCV test, nor does it prevent some individuals from being tested multiple times in a lifetime.

HCV Treatment

When an individual is identified as HCV infected, (s)he is first linked to HCV care, with a probability according to age. Individuals who do not link to care upon diagnosis may do so in the future (Supplementary Appendix). After successful linkage, individuals have a probability of accepting and completing HCV treatment.

HCV cure halts fibrosis progression [14, 15], HCV-attributable costs decrease by 50% of the individual's disease stage-specific cost before therapy [16], and HCV-related health utility reverts to that of the previous untreated stage. Finally, following cure, liver-related mortality among cirrhotic individuals is reduced by 94% [17]. Residual risk of liver death reflects ongoing risk of decompensation or HCC [13].

Costs

During each month, persons accrue age- and sex-stratified “background costs” attributable to non-HCV-related health care [18], HCV-specific costs that vary by disease state [16], and IDU in PWID [19].

Utilities

“Background” utility, a function of age and unrelated to HCV, which was derived from the Medical Expenditure Panel Survey (MEPS) [20] is multiplied by HCV-specific utility [21, 22], IDU-related utility, and, when applicable, temporary disutility from treatment-ending major toxicity events (see Supplementary Appendix).

Model data

HCV infection, risk factors and natural history

We estimated age- and sex-stratified HCV prevalence among active PWID using published literature, whereas prevalence for other risk behavior groups was derived from the National Health and Nutrition Examination Survey (NHANES) (see Supplementary Appendix).

We modeled movement between IDU states over the course of the simulation using AIDS Linked to the Intravenous Experience (ALIVE) cohort data (see Supplementary Appendix).

HCV testing

We estimated HCV testing rates among active PWID using data from cohorts of PWID [23] and assigned a constant testing rate to all active PWID in the simulation. We estimated testing rates and the effect of recommendation changes in the non-drug using cohort using the MarketScan claims database (see Supplementary Appendix) [24].

HCV Treatment

We modeled an oral, pan-genotypic HCV regimen for all genotypes and fibrosis stages [25]. In the base case, there were no treatment restrictions. Duration and treatment outcomes were derived from cohort studies and clinical trials [25, 26].

Costs

We assessed costs from the healthcare system perspective in 2016 U.S. dollars. We derived costs from the 2016 laboratory and physician fee schedules from Centers for Medicare and Medicaid Services (CMS) for reimbursement [27, 28]. HCV treatment costs were derived by

using the average wholesale price minus 23%. We explored HCV-attributable costs in sensitivity analysis (Supplemental Tables 4 and 5).

Utilities

We used a combination of MEPS data and published health utility literature estimates to derive health state-related utilities [18, 21, 29].

Monte Carlo variance reduction

We developed a strategy that enabled us to improve the precision of estimates since results would otherwise be subject to substantial Monte Carlo error (Supplementary Appendix). Briefly, we simulated a large cohort and noted infection status over time for each individual. For those individuals who never became infected, we recorded key health and economic outcomes and we did not re-simulate their life courses under each of the comparator strategies in the analysis. We deterministically calculated life expectancy and healthcare costs for this subgroup. For those who were infected, we simulated life courses following infection under each of the various screening strategies to determine health outcomes, life expectancy and costs. For all cost and health outcomes used in the cost-effectiveness calculations, we computed population-weighted averages that combined outcomes among the never-infected group and the infected group.

IRB Approval

This secondary analysis of published literature and de-identified data sources did not require IRB approval.

RESULTS

In the SOC strategy, 71% of all HCV infected persons were identified and 44% of HCV-infected persons were cured over a lifetime (Figure 1). The proportion of individuals in the total U.S. population diagnosed prior to cirrhosis was 58%, and 32% of those who were HCV-infected ultimately died from liver disease (data not shown). Among HCV-infected persons born outside the birth cohort, 67% of cases were diagnosed prior to developing cirrhosis, and liver-related mortality among HCV-infected persons was 27% (Table 2).

Clinical outcomes

Expanded age-based testing strategies increased lifetime case identification and cure rates in the U.S. population, with the greatest increases observed in ≥ 18 strategy (Figure 1). Compared to the SOC, the ≥ 18 strategy resulted in an estimated 256,000 additional infected persons identified, 280,000 additional cures, and an estimated 4400 fewer cases of HCC in the US (assuming an HCC incidence rate of 2.49 per 100 person-years with cirrhosis) [30] over the lifetime of this cohort. The average number of lifetime tests increased from 2.35 tests per person to 4.63 in the SOC strategy and the ≥ 18 strategy, respectively (Supplementary Table 2 and Supplementary Figure 1). Clinical outcomes over different time horizons are included in the Supplementary Appendix (Supplementary Figures 2 and 3).

Among the HCV-infected population born outside of the birth cohort, case detection rates increased from 74% to 85% and cure rates from 49% to 61%, which resulted in a 31% reduction in the proportion reaching cirrhosis before diagnosis, and a 21% reduction in liver-attributable mortality in the ≥ 18 strategy compared to the SOC (Table 2).

The ≥ 18 strategy resulted in an increase in life expectancy from 67.2 to 68.2 years compared to the SOC in this population (Table 2) and one discounted quality adjusted life day across the general population (Table 3).

Cost outcomes

As testing began at younger ages, HCV-related costs comprised a smaller portion of the incremental cost of each strategy compared to the next most inclusive (Figure 2). All strategies resulted in decreased costs related to managing chronic HCV and advanced liver disease including HCC. The cost of HCV testing in the SOC strategy corresponds to approximately \$2500 per case diagnosed. In the ≥ 18 strategy, the cost of testing increases to \$4400 per case diagnosed. The additional cost of testing per case diagnosed is \$1900.

Incremental cost-effectiveness ratio

In the base case, the ≥ 18 strategy provided the greatest quality adjusted life expectancy and the lowest cost/QALY gained. This strategy dominated all other expanded testing strategies by extended dominance with an ICER compared to the SOC of \$28,000/QALY (Table 3).

Scenario Analysis

In the inefficient testing scenario that required twice as much testing among uninfected persons to identify the same cases, the average discounted cost of the ≥ 18 strategy increased minimally to \$126,170 (from \$126,150 in the base case). That strategy remained cost-effective, with an ICER compared to ≥ 30 strategy of \$44,000. In the treatment restriction scenario, the

≥ 18 strategy ICER remained cost effective but increased to \$34,000/QALY (Supplementary Tables 22-23).

Sensitivity Analysis

In one-way sensitivity analyses, the ≥ 18 strategy had an ICER less than \$100,000/QALY compared to its next best alternative across broad parameter ranges (Supplementary Tables 4-21), except for the scenario when an individual can only link to care when first identified as infected and never again (Supplementary Table 20). In other scenarios, specifically, when there was no improvement in QoL and costs decreased following early stage cure, when cost of early stage disease was \$0, and when treatment costs were varied, the ≥ 30 strategy dominated the ≥ 40 strategy by extended dominance, but the ≥ 18 strategy remained cost-effective (Supplementary Tables 6, 12-13, 21). We note that the ≥ 18 strategy remained cost-effective with an ICER of \$30,000 when there was no mortality benefit from SVR (Supplementary Table 8).

CONCLUSIONS

We used a simulation model of HCV to investigate the clinical outcomes, costs, and cost-effectiveness of age-based strategies for routine HCV testing that could replace current cohort-based guidance in the U.S. We found that a recommendation for one-time testing of all adults, with continued risk-based testing throughout life, improved clinical outcomes and was cost-effective in the U.S.

The birth cohort recommendation focuses the testing effort among the group that have had the highest HCV prevalence [31]. The HCV epidemic is changing with an increasing proportion of persons with HCV outside of this cohort. The shift is multifactorial, including premature mortality in the birth cohort [32]; persons treated and cured of their infection in the birth cohort [33]; and higher incidence of new HCV infections among younger PWID [6]. A substantial number of undiagnosed cases exist outside of the birth cohort, and might never be diagnosed under the current strategy [8]. Expanding the recommendation for routine testing to include all adults would increase the probability of testing and identify more people with HCV.

Other analyses have demonstrated that HCV testing is cost-effective in high prevalence settings such as among baby boomers [7], in substance use disorder treatment programs [34], or in prisons and jails [35], as well as in subpopulations including adolescents and young adults [36] or HIV-infected men who have sex with men [37]. Our study takes the next step in this evolution of thought and policy about HCV testing to consider routine HCV testing all adults.

The value of screening all adults lies in the value of early diagnosis. In our base case, routine testing of adults ≥ 18 years dominated the other age-based strategies by extended dominance. The ≥ 18 strategy identifies cases sooner than the other strategies, thereby increasing QoL and decreasing costs associated with HCV, since there is disutility and cost for the years that a person lives with HCV, even with early stage disease. When we assume no

QoL improvement or cost decrease associated with treating early stage HCV, the ≥ 18 strategy no longer dominates the ≥ 30 strategy, but does prevent enough liver-attributable morbidity and mortality to remain cost-effective. Ultimately, the cost-effectiveness of expanding testing to ≥ 18 is driven by reductions in cirrhosis and liver-related mortality including HCC while the reason it dominates other strategies is driven by QoL improvements and cost reductions associated with treating early stage HCV. New recommendations should continue to include targeted testing among PWID, which effectively serves as a “backstop” to catch later incident cases missed by the ≥ 18 strategy.

Findings from our alternative scenarios deserve discussion. First, while an argument against routine testing is that it is a resource intensive effort to find a small number of cases, our findings demonstrate that routine testing is cost-effective even when we test twice as much to find the same number of cases. Second, though testing in our treatment restriction scenario was cost-effective, this conclusion is not an endorsement of these restrictive policies. Rather, this scenario recognizes the status quo in many states and demonstrates that even if patients are treated only once they reach advanced fibrosis, it remains cost-effective to test all adults.

There were limitations to our study. First, the use of cohort studies and large national databases to derive estimates may not be representative of the overall U.S. population; however, our detailed analysis of testing rates in Marketscan [24] are in line with previously published reports [38-40]. Second, there is relatively little evidence on the cost of early-stage HCV and the magnitude of the change in health-related utilities derived from treating early-stage HCV. Our sensitivity analyses demonstrated that earlier testing remained cost-effective even in the setting in which treating early stage disease had no implications for cost or QoL. Third, differences between strategies are small and could be suspected to reflect Monte Carlo variance. We anticipated this because the life expectancy change in the general population attributable to expanded HCV testing is expected to be small even at a high general population

prevalence of 3% because the majority remain uninfected and get no benefit from testing. We minimized Monte Carlo error in our results with a variance reduction strategy outlined in the methods and supplementary appendix. We empirically assessed the degree of variance between runs to ensure that the differences between strategies expected from random variance is smaller than the difference in outcomes seen between strategies (Supplementary Figures 4-12). Fourth, we use a closed cohort, but allowed individuals who are <18 to age into guidance. Using a closed cohort in this way will be biased by omitting some future consequences of different screening strategies. Because the omitted consequences occur two decades or more into the future, the impact of the omission will be relatively small compared to the overall magnitude of the population-level cumulative outcomes, especially given uncertainties about long-term changes in demography and HCV epidemiology, and in the presence of a positive discount rate, as in our main analyses. Fifth, the rate of fibrosis progression with HCV is uncertain. We used one appropriate estimate of fibrosis progression rates and performed sensitivity analyses to ensure that such uncertainty did not have a major impact on the qualitative conclusions. Finally, while we did not incorporate incident infection explicitly related to factors such as tattoos, HCV incidence in the US due to these risk factors is small in comparison to IDU [6]. We explored the impact of non-drug use related HCV on cost-effectiveness conclusions and our results remained robust.

In conclusion, in addition to risk-based testing, routine, one-time HCV testing of persons 18 years and older is cost-effective, could lead to improved clinical outcomes and is likely to identify more persons with HCV than the current birth cohort recommendations. These findings should be considered for future recommendation revisions.

Author Contributions:

J.A.B. conceived of the design of the work; led the acquisition, analysis, and interpretation of the data; and drafted the initial and revised manuscript.

A.T. conceived of the design of the work; performed the acquisition, analysis and interpretation of the data; and contributed to the initial and revised manuscript.

G.E.Y. implemented computer simulation model; assisted with model design; analysis of data; and manuscript revision.

J.W. assisted with acquisition, analysis and interpretation of data; and manuscript revision.

C.V. assisted with project design; interpretation of data; and manuscript revision.

S.H. assisted with project design; interpretation of data; and manuscript revision.

C.I. assisted with interpretation of data and manuscript revision.

L.R. assisted with project conception; analysis and interpretation of data; and manuscript revision.

J.W.W. assisted with analysis and interpretation of data; and manuscript content and revision.

J.M. assisted with analysis and interpretation of data; and manuscript content and revision.

J.A.S. conceived of the design of the work; was involved with the acquisition, analysis, and interpretation of the data; and assisted with drafting the initial and revised manuscript.

B.P.L. conceived of the design of the work; was involved with the acquisition, analysis, and interpretation of the data; and assisted with drafting the initial and revised manuscript.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Funding Sources: This work was supported by the National Institute on Drug Abuse at the National Institutes of Health [5T32DA013911-15 and 1R25DA037190-01 to J.A.B] and [R01DA031059 and P30DA040500 to B.P.L. and J.A.S.], the Massachusetts General Hospital Fund for Medical Discovery [to J.A.B], and the U.S. Centers for Disease Control and Prevention [5U38PS004642 to J.A.B, J.W, G.E.Y, A.T, J.A.S, and B.P.L].

Conflicts of Interest: We report no conflicts of interest.

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Figures Legend

Figure 1. HCV continuum of care over the lifetime, by strategy.

The bar graph illustrates the percent of the HCV infected population attaining clinical outcomes along the HCV continuum of care. Each bar shading represents a specific testing strategy.

Figure 2. Incremental healthcare utilization costs, by strategy over the lifetime

The bar graph illustrates the incremental costs relative to the previous strategy by type of healthcare expenditure for each testing strategy. The first grouping of bars are the incremental costs of the ≥ 40 strategy compared to the standard of care. The next are the ≥ 30 strategy compared to the ≥ 40 strategy followed by the incremental costs of the ≥ 18 strategy compared to the ≥ 30 strategy. In all 3 strategies, HCV testing, HCV therapy, and other non-HCV healthcare are costs (positive value), which outweighed the cost savings from HCV management (negative value). Non-HCV healthcare costs become a larger proportion of the overall incremental costs in younger testing strategies.

Table 1. Selected Model Inputs for Analysis of Cost-Effectiveness of Expanding Recommendations for Age-Based HCV Testing^a

Parameter	Estimate	Range	Source
Population			
Median age (years)	38	25-55	[12]
Mean age of infection (years)	23	18-28	[41, 42]
SMR ^b , active PWID ^c	11	4.8-17	[43]
SMR, former PWID	6.5	4.8-17	[44-46]
HCV Infection			
Liver mortality (deaths/100 p-y)			
<i>F4</i>	3	1-5	[13]
<i>Decompensation</i>	21	3-30	[13]
Infection, PWID (cases/100 p-y)	12	1.7-35	[47]
Testing, Linkage, Treatment			
Background testing (tests per 100 person-years)			[24]
<i>Birth Cohort</i>	2.7	1-5	
<i>Complement</i>	2.6	1-5	
<i>PWID</i>	33.1	15-50	[23]
Linkage (%)			[48]
<30	17.9	8.5-86	
≥30	28.9	8.5-86	
Relink ^d			[48]
<30	17.9	8.5-86	

≥30	28.9	8.5-86	
Voluntary relink	0.00142	0-0.01	Expert opinion ^e
Treatment completion (%)	96.7-96.8	--	[25]
Hepatotoxicity (%)	0.08	--	[25]
SVR ^f after completion, non-cirrhotic (%)	99	50-99	[25]
SVR after completion, cirrhotic (%)	93	93-96	[25]
Post-SVR mortality multiplier	0.06	0.01-1	[17]

Healthcare Costs

Cost with active infection (\$/month) [16]

<i>f0</i>	256	128-384
<i>f1</i>	256	128-384
<i>f2</i>	256	128-384
<i>f3</i>	256	128-384
<i>f4</i>	455	228-683
<i>decompensated</i>	867	434-1301

Cost with SVR (\$/month) [16]

<i>f0</i>	128	64-192
<i>f1</i>	128	64-192
<i>f2</i>	128	64-192
<i>f3</i>	128	64-192
<i>f4</i>	227	114-341
<i>decompensated</i>	433	217-650

Testing and Eligibility Costs (\$)

HCV Antibody test	19	10-30	[28]
HCV RNA test	78	50-100	[28]
Fibroscan	135	--	[28, 49]
False positive ⁹	683	300-1000	
Treatment Costs (\$)			
Sofosbuvir/velpatasvir (per month)	23026	0-38000	[50]

Health State Utilities⁸

Age-specific utility for persons
without infection or injection drug
use

Utility for active injection drug			[29]
Utility for former injection drug use	0.76-0.92		[29]
Utility for active HCV infection, by METAVIR fibrosis stage	0.68	0.54-0.8	[51]
<i>f0</i>	0.82	0.71-0.93	
<i>f1</i>			
<i>f2</i>	0.94	0.9-1.0	
<i>f3</i>	0.94	0.9-1.0	
<i>f4</i>	0.94	0.9-1.0	[21]
<i>decompensated</i>	0.94	0.9-1.0	
Utility for HCV infection after effective treatment, by stage	0.75	0.6-0.9	Expert opinion
<i>f0</i>	0.60	0.48-0.75	
<i>f1</i>			
<i>f2</i>	0.97	0.94-1.0	
<i>f3</i>	0.97	0.94-1.0	

<i>f4</i>	0.97	0.94-1.0
^a <i>decompensated</i>	0.97	0.94-1.0
^a <i>B</i>		
^a Utility with hepatotoxicity	0.94	0.75-0.97
^s		
^e	0.75	0.60-0.94
ⁱ		
ⁿ	0.75	0.50-0.99
^e		

estimates used in Baseline estimates used in the analysis are reported, with ranges used for sensitivity analysis, when applicable. Costs are in the 2016 U.S. dollars.

^bSMR denotes standardized mortality rate

^cPWID denotes people who inject drugs

^dIndividuals identified as HCV-infected for the first-time have a probability of linking to care (i.e., “linkage”). If such individuals do not link to care at that time, they may be identified with subsequent testing. Therefore, they have a probability of linking to care with each subsequent identification. The “relink” parameter refers to this subsequent linkage probability.

^eExpert opinion includes methodological consultation with the Center for Health Economics of Treatment Interventions for Substance Use Disorders, HCV, and HIV (CHERISH)

^fSVR denotes sustained virologic response, a commonly accepted marker of HCV cure measured 12 weeks following completion of treatment

^gAll individuals are subject to an age-adjusted utility without injection drug use or HCV infection. Active or former injection drug use, and active or treated HCV infection are then applied multiplicatively. Final absolute utilities are relative to a hypothetical individual in perfect health (utility=1.0).

Table 2. Selected cost and clinical outcomes by strategy for various populations^a

Strategy ^b	Total U.S Population			HCV-Infected Persons		HCV-Infected Persons Born Outside Birth Cohort			
	Average Lifetime Healthcare Cost \$ ^c	Life Expectancy <i>LY</i>	Quality- Adjusted Life Expectancy <i>QALY</i>	Life Expectancy <i>LY</i>	Quality- Adjusted Life Expectancy <i>QALY</i>	Life Expectancy <i>LY</i>	Quality- Adjusted Life Expectancy <i>QALY</i>	Proportion Identified Prior to Cirrhosis %	Proportion with HCV- Attributable Death %
Standard of Care	\$287,760	81.319	74.476	69.888	62.411	67.157	58.162	66.5	27.0
Test ≥40	\$287,880	81.326	74.482	70.414	62.896	67.976	58.918	75.4	22.1
Test ≥30	\$287,900	81.327	74.483	70.517	62.994	68.136	59.070	76.5	21.4
Test ≥18	\$287,900	81.327	74.484	70.564	63.038	68.209	59.138	76.8	21.3

^a All values in this table are undiscounted; averages of costs and life expectancy are per person

^b Additional details of the sensitivity analyses as well as the inefficient testing and payer restriction alternative scenarios are provided in the Supplementary Appendix.

^c Values that appear the same differed beyond the 3rd decimal place

LY = life years; QALY = quality adjusted life years; ICER = incremental cost effectiveness ratio

Table 3. Results of Cost Effectiveness Analysis

Strategy^a	Average Discounted Cost \$ ^c	Incremental Average Discounted Cost \$	Discounted Quality Adjusted Life Years <i>QALY</i>	Incremental Discounted Quality Adjusted Life Days <i>QALD</i>	ICER ^b (\$/QALY)
Standard of Care	\$126,080	--	56.840	--	--
Test ≥40	\$126,140	--	56.842	--	Dominated
Test ≥30	\$126,150	--	56.843	--	Dominated
Test ≥18	\$126,150	\$74.50	56.843	0.964	\$28,000

^a Additional details of the sensitivity analyses as well as the inefficient testing and payer restriction alternative scenarios are provided in the Supplementary Appendix.

^b The overall incremental cost-effectiveness ratio was calculated as the difference in the average discounted costs for the total U.S. population divided the difference in the discounted quality adjusted life expectancy for the total U.S. population, all discounted at 3% per year.

^c Values that appear the same differed beyond the 3rd decimal place

^d Dominated = extended dominance means that the strategy was more costly and more effective, but have a lower incremental cost effectiveness ratio compared to other strategies

LY = life years; QALD = quality adjusted life days; QALY = quality adjusted life years; ICER = incremental cost effectiveness ratio

Figure 1.

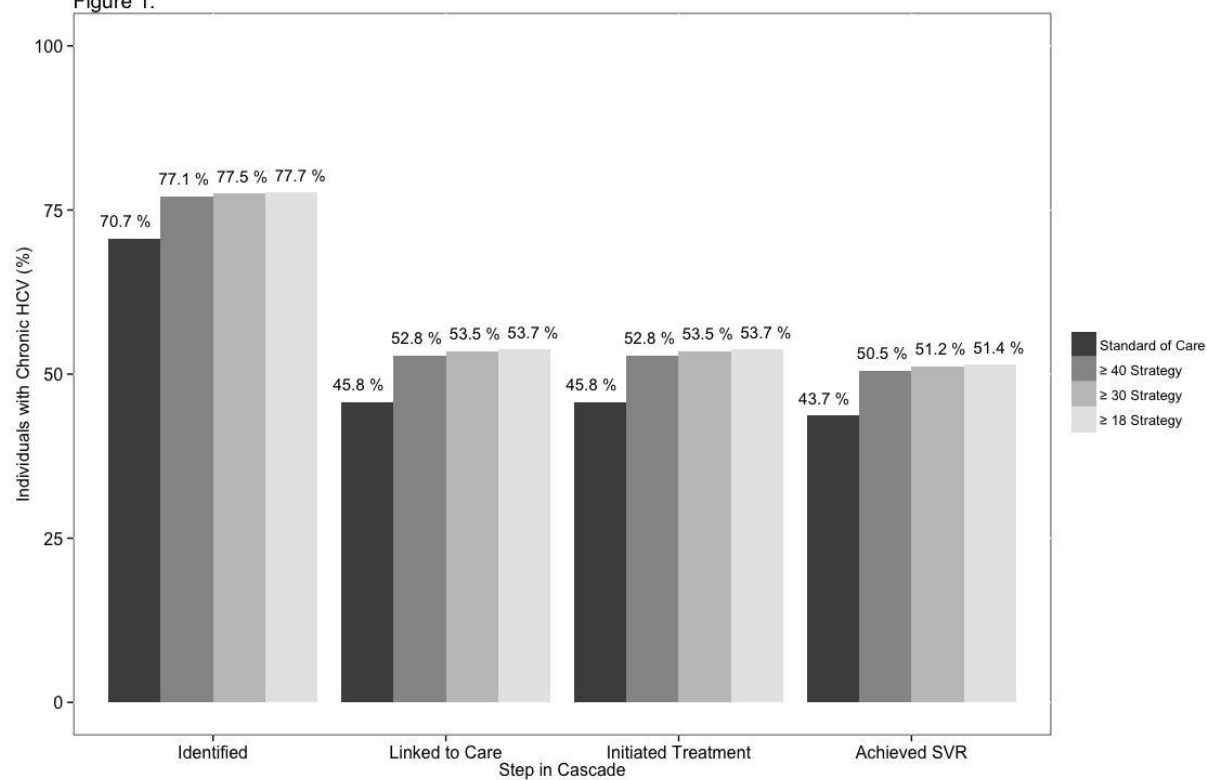


Figure 2.

