Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Am J Med. Author manuscript; available in PMC 2021 November 01.

Published in final edited form as:

Am J Med. 2020 November ; 133(11): e641–e658. doi:10.1016/j.amjmed.2020.05.029.

Hepatitis C Management at Federally Qualified Health Centers during the Opioid Epidemic: A Cost-Effectiveness Study

Sabrina A. ASSOUMOU, MD, MPH[1,2], **Shayla NOLEN, MPH**[1], **Liesl HAGAN, MPH**[3], **Jianing WANG, MSc**[1], **Golnaz EFTEKHARI YAZDI, MSc**[1], **William W. THOMPSON, PhD**[3], **Kenneth H. MAYER, MD**[4,5], **Jon PURO, MPH/HA**[6], **Lin ZHU, PhD**[7], **Joshua A. SALOMON, PhD**[8], **Benjamin P. LINAS, MD, MPH**[1,2,9]

[1.]Section of Infectious Diseases, Department of Medicine, Boston Medical Center, Boston, MA, USA

[2.]Section of Infectious Diseases, Department of Medicine, Boston University School of Medicine, Boston, MA, USA

[3.]Prevention Branch, Division of Viral Hepatitis, Centers for Disease Control and Prevention, GA, USA

[4.]The Fenway Institute, Fenway Health, Boston, MA, USA

[5.]Beth Israel Deaconess Medical Center, Harvard Medical School, Infectious Diseases, Boston, MA, USA

[6.]OCHIN, Inc., Portland, OR, USA

[7.]Department of Global Health and Population, Harvard TH Chan School of Public Health, Boston, MA, USA

[8.]Stanford University School of Medicine, Stanford, CA, USA

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

Abstract

Background: The opioid epidemic has been associated with an increase in hepatitis C virus (HCV) infections. Federally qualified health centers (FQHCs) have a high burden of hepatitis C disease and could serve as venues to enhance testing and treatment.

Methods: We estimated clinical outcomes and the cost-effectiveness of hepatitis C testing and treatment at US FQHCs using individual-based simulation modeling. We used individual-level

(corresponding author) Sabrina A. Assoumou, MD, MPH, Assistant Professor, Department of Medicine, Section of Infectious Disease, Boston University School of Medicine, Boston Medical Center, 801 Massachusetts Ave., Crosstown Center, 2nd Floor, Boston, MA 02118, P: 617-414-2896, F: 617-414-3534, sabrina.assoumou@bmc.org.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of Interest Statement: None.

All authors had access to the data and a role in writing the manuscript

Ethics: This study was approved by the BUMC Institutional Review Board.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

data from 57 FQHCs to model 9 strategies including permutations of HCV antibody testing modality, person initiating testing and testing approach. Outcomes included life expectancy, quality adjusted life years (QALY), hepatitis C cases identified, treated and cured, and incremental cost-effectiveness ratios (ICERs).

Results: Compared to current practice (risk-based with laboratory-based testing), routine rapid point-of-care testing initiated and performed by a counselor identified 68% more cases after (non-reflex) RNA testing in the first month of the intervention, led to a 17% reduction in cirrhosis cases, and a 22% reduction in liver deaths among those with cirrhosis over a lifetime. Routine rapid testing initiated by a counselor or a clinician provided better outcomes at either lower total cost or at lower cost per QALY gained, when compared to all other strategies. Findings were most influenced by the proportion of patients informed of their anti-HCV test results.

Conclusions: Routine anti-HCV testing followed by prompt RNA testing for positives is recommended at FQHCs to identify infections. If using dedicated staff or point-of-care testing is not feasible, then measures to improve immediate patient knowledge of antibody status should be considered.

Keywords

Hepatitis C; health centers; computer simulation; testing; treatment

Introduction

The US opioid epidemic has led to an increase in hepatitis C virus (HCV) infections due to transmission via injection drug use (1-4). Federally qualified health centers (FQHCs) care for approximately 24 million patients often from underserved communities disproportionally affected by hepatitis C and opioid use disorder (5, 6). Therefore, FQHCs may be an attractive venue for expanding hepatitis C testing and treatment. The US federal government funds FQHCs to provide comprehensive primary care and supportive services such as assistance with housing, food and transportation to address social determinants of health. These health centers accept private as well as publicly-funded insurance programs while also relying on income and family size-based sliding scales for uninsured patients. FQHCs are also mandated to serve all patients regardless of their ability to pay (7).

Rapid HCV antibody (anti-HCV) testing of 15 to 30-years-olds in urban settings with a large number of reported cases of hepatitis C is cost-effective (8). The generalizability of this conclusion to settings and populations with a lower prevalence of hepatitis C is not known. Additionally, although new guidelines recommend testing for adults 18 years and older, the relative costs and comparative outcomes of various implementation models for HCV testing is uncertain (9). Thus, we aimed to evaluate the clinical benefit and cost effectiveness of routine testing among all individuals receiving care at FQHCs, determine the best anti-HCV testing modality (rapid vs. laboratory-based without reflex HCV RNA testing), and estimate the economic value of employing a dedicated hepatitis C testing counselor/tester. Prior data show that dedicated counselor/testers achieve higher testing rates compared to clinicians who have many other competing priorities (10). The current model accounts for these differences in testing rates and compares outcomes for various scenarios.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Methods

Analytic overview

The Hepatitis C Cost-Effectiveness (HEP-CE) model is an individual-level transition model simulating hepatitis C testing, treatment and linkage to care (8, 11). We used individual-level data from a network of FQHCs in the United States, OCHIN (previously known as the Oregon Community Health Information Network). The data set included approximately two million patients seen between 2012 and 2017 in 19 states. We compared 9 strategies representing permutations of the following components: 1) anti-HCV test modality (rapid point-of-care vs. laboratory-based without reflex HCV RNA testing); 2) individual initiating testing (dedicated counselor vs. clinician); 3) testing approach (risk-based targeted vs. expanded risk-based targeted with an intervention to increase testing vs. routine) (Table 1). Outcomes included life expectancy; quality adjusted life years (QALY); hepatitis C cases identified, treated, and cured; and incremental cost-effectiveness ratios (ICER).

Model structure

Cohort characteristics——The model simulates adults characterized by age, sex, and identified drug use history at OCHIN FQHCs. Person-level traits influence survival, hepatitis C prevalence, testing probability, and linkage to care after diagnosis.

HCV natural history——At simulation start, each HCV-infected individual is assigned a Meta-analysis of Histological Data in Viral Hepatitis (METAVIR) liver fibrosis stage estimated using aspartate aminotransferase-to-platelet ratio index (APRI) from OCHIN laboratory data (12). Liver fibrosis progresses among HCV-infected persons and infection is associated with decreased quality of life and increased costs (Supplementary Figure 1).

Risk behaviors——Individuals are classified as “active person who inject drugs (PWID)”, “former PWID,” or “never PWID” with an age-stratified monthly probability of transitioning between these states. “Active PWID” status increases mortality and health care costs, and decreases quality of life, related to drug use status. It is also associated with incident HCV-infection or re-infection after cure.

Hepatitis C testing and linkage to care——Laboratory-based anti-HCV testing (LBT) could be initiated by either clinicians or dedicated counselor/testers. A counselor/tester is a technician trained to provide HCV-related information to patients and collect samples for testing either by finger stick for rapid testing (RT) or by phlebotomy for LBT. All testing initiated by clinicians is ultimately performed by a phlebotomist (LBT) or a counselor/tester (RT). In contrast, counselor/testers perform testing on patients they approach (Table 1).

We model the LBT algorithm as a serum HCV antibody test without reflex HCV RNA testing. HCV RNA testing is usually only performed following reactive HCV antibody and detectable RNA indicates chronic HCV infection. In the base case, patients must return to the clinical site following antibody testing to obtain an HCV RNA test and to seek additional care. In sensitivity analyses, we considered a scenario in which laboratory testing included “reflex” or automatic HCV RNA testing among those with detectable HCV antibody. This

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

approach increases identification of chronic HCV cases and movement along the cascade of care. In the “RT” algorithm, patients wait for results provided on the same day as testing. Among those with positive HCV rapid test, we assume immediate RNA testing.

We analyzed the OCHIN data to estimate the testing rate in the risk-based current practice strategy (see base case inputs below). We define “expanded targeted testing,” as an effort to improve adherence to CDC hepatitis C testing recommendations at the time of the analysis, namely one-time testing of individuals born between 1945-1965 and PWID testing (13). We define “routine testing” as all individuals having the same test offer probability regardless of identified risk or age; however, the testing probability is less than 100% as no testing strategy is perfectly implemented in practice.

Throughout their lifetimes, simulated individuals experience a “background” rate of hepatitis C testing outside of FQHCs (14), which is estimated from a commercially insured population as limited information are available for FQHC patients (14).

Following a positive HCV RNA test result, individuals identified with HCV viremia must link to care to be eligible for treatment. The linkage to care base case value is derived from OCHIN data (Table 1 and supplementary material). Individuals who do not link to care after initial diagnosis retain a probability of re-presenting to care in the future.

Hepatitis C treatment regimens are listed in Table 2(15-17). Hepatitis C cure results in a 50% reduction in HCV-attributable healthcare costs according to fibrosis stage and improvement in quality of life (18). Among those who were cirrhotic at the time of hepatitis C cure, liver-attributable mortality decreases by 94% (19).

Base case inputs

Demographics and hepatitis C epidemiology—Table 2 describes cohort characteristics and hepatitis C epidemiology of the simulated cohort (20-25). We used the OCHIN data set to characterize simulated individuals and the Substance Abuse and Mental Health Services Administration (SAMHSA) estimates to impute missing injection drug use status (26).

Hepatitis C testing at FQHCs—For the current practice strategy, we used hepatitis C testing proportions derived from the OCHIN data set where individuals in the 1945-1965 birth cohort and those in the complement cohort (i.e., outside the 1945-1965 birth cohort) had similar hepatitis C testing offer rates. For expanded targeted testing, we adjusted the current practice testing proportions with findings from an intervention study aimed at increasing testing in primary care settings (27). In this intervention, clinicians were prompted to test individuals with hepatitis C risk factors. Offer rates for routine testing were derived from a randomized controlled trial focused on HIV testing, since analogous hepatitis C testing data were unavailable (10). For background testing we used estimates from a commercially insured population (14).

Health-Related Quality of Life and Cost—Health state utilities were derived from published literature (28, 29). HCV infection at all fibrosis stages was associated with

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

decreased quality of life. Hepatitis C testing costs and treatment were informed by Medicare reimbursement schedules and the Federal Supply Schedule for pharmaceutical spending (30). In our model, all rapid tests initiated by a clinician took place during a scheduled visit and patients were referred to the onsite counselor/tester. There was no additional cost for the clinician visit as it was part of a previously scheduled appointment.

Analyses

We simulated the lifetime of an FQHC cohort until death. We assumed a scenario in which each individual presented at an FQHC at the start of the simulation and a decision was made whether or not to test the patient based on alternative testing strategies. Then, we simulated the person's subsequent lifetime clinical outcomes and cost-effectiveness under each anti-HCV testing strategy. We eliminated strategies that were dominated— strategies costing more and providing less clinical benefit as well as strategies delivering less clinical benefit for the same amount of money (31). We calculated all ICERs assuming a lifetime time horizon and a healthcare sector perspective. We discounted all costs and benefits by 3% annually. ICERs were expressed as the cost per QALY gained and we interpreted cost-effectiveness using a commonly-cited US willingness-to-pay threshold of $100,000/QALY gained (31, 32). We then performed deterministic sensitivity analyses to assess the stability of our findings and identify factors influencing our conclusion.

Results

Base case

Clinical and cost outcomes—Rapid testing always identified more cases and generated more cures than laboratory-based anti-HCV testing without HCV RNA reflex testing. In addition, strategies initiated by counselors always outperformed clinician-initiated, phlebotomist-performed approaches. For example, compared to current practice, counselor-initiated routine RT with follow-up RNA testing identified 75% of cases at the FQHC visit compared to only 7% identified by current practice (Supplementary Table 2). Having a dedicated counselor initiate and perform testing increased the percentage of cases identified by 41% compared to approaches where clinicians offered testing (Supplementary Table 2). In addition, targeted testing missed patients with no identified substance use. For example, current practice (risk-based targeted testing performed by a clinician) only identified 7% of HCV infections in the first month of the intervention whereas clinician-initiated phlebotomist-performed routine LBT identified 25% of infections.

As a result of background testing over the lifetime in venues other than FQHCs, 87% of all cases were ultimately identified under the current practice strategy, compared to 89% under the counselor-initiated and performed routine RT (Supplementary Table 2 and Supplementary Figure 2). The primary benefits of employing FQHCs for testing rather than background testing were earlier detection of infection and cure, prevention of disutility and cost reduction. Counselor-initiated and performed routine RT followed by non-reflex RNA testing reduced the number of lifetime cirrhosis cases by 17% and reduced liver-related death by 22% when compared to current practice due to earlier diagnosis and cure (Table 3).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Incremental Cost-Effectiveness Ratios—Strategies incorporating RT led to greater life expectancy than LBT at either lower lifetime medical cost or lower cost/QALY gained (i.e. RT dominated LBT) (Figure 1). Similarly, routine testing dominated all targeted testing strategies. Eliminating dominated strategies resulted in only two cost-effectiveness remaining strategies: 1) clinician-initiated, counselor-performed routine RT (ICER of $5,500/QALY gained compared to current practice), and 2) counselor-initiated and performed routine RT (ICER = $5,800/QALY gained compared to clinician-initiated routine RT) (Table 4).

Sensitivity analyses

Testing program characteristics: The finding that RT dominated LBT was sensitive to variation in the probability of test result delivery (Supplementary Table 2). When we increased the probability of result delivery for LBT by 25%, clinician-initiated, phlebotomist-performed routine LBT was no longer dominated, although counselor-initiated routine RT remained the preferred strategy.

Incidence of HCV re-infection: Routine testing strategies were consistently below $100,000 per QALY gained even when we assumed high incidence of HCV re-infection among active PWID who attain hepatitis C cure. Even when the incidence of HCV re-infection was 18.5 cases/100 person-years (base case 12.3 cases/100 person-years) among those who were active PWID, the ICER of counselor-initiated RT remained <$100,000/QALY gained (Supplementary Table 2). When we decreased the incidence of new HCV infection by 40%, targeted strategies were no longer dominated; however, routine RT continued to be preferred.

Hepatitis C prevalence: Counselor-initiated and performed routine RT was the preferred strategy unless the prevalence of hepatitis C at FQHCs was less than 0.11% (base case hepatitis C prevalence 3.2%) (Figure 2).

Additional analyses: In additional sensitivity analyses including the proportion of active PWID, liver fibrosis progression rates, background HCV testing, reflex HCV RNA testing for strategies including laboratory-based testing, and treatment cost, the ICER for counselor-initiated RT remained <$100,000/QALY gained when parameters were varied within reasonable estimates (Supplementary Table 2). Nevertheless, it was notable that in some analyses the ICER associated with clinician-initiated, phlebotomist-performed LBT was below <$100,000/QALY gained. (Supplementary Table 2).

Conclusion

We found that routine testing in FQHCs would improve diagnosis rates and health outcomes for hepatitis C-infected persons in the United States. This finding is important given the ongoing opioid epidemic, where persons who inject drugs are becoming infected with HCV at increasing rates, and utilizing FQHCs as a source of healthcare. We competed several strategies and demonstrated that including routine RT and investing in dedicated counselors/testers identifies the highest number of HCV infections with QALY gained of $100,000 or below. This intensive approach to testing in FQHCs shifts the timing of cure to early disease

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

stage, thereby preventing liver-related morbidity and reducing HCV-attributable deaths, even when there is substantial ongoing hepatitis C testing at venues elsewhere. If use of dedicated counselors or RT is not feasible, then it is important to ensure prompt reflex HCV RNA testing following LBT for those for whom hepatitis C testing is recommended, and also increase the hepatitis C offer rate by clinicians.

Importantly, we showed that targeted testing provides worse outcomes at a higher cost than routine testing. Testing according to risk factors is imperfect (8) as PWID may not report that risk. We also demonstrated that RT provides better outcomes at either lower total cost or at a lower cost per QALY gained (Figure 1) compared to standard LBT. The likely reason for this finding is that RT reduces loss to follow-up related to delivery of positive anti-HCV test results to patients. Studies have shown that RT has been successfully implemented at some US health centers (33). Where RT is not feasible or affordable, it is important to implement measures to improve test result delivery to reduce loss to follow up.

We also demonstrated that strategies using a dedicated counselor/tester to initiate and perform hepatitis C testing costs $100,000 per QALY gained or less. Dedicated counselors improve testing effectiveness, generating economic value by increasing fidelity to the intended testing strategy and increasing the probability that everyone will be tested under a universal/routine testing strategy. This approach increases the proportion of individuals with linkage to HCV care, treatment initiation and could prevent costly complications of such as cirrhosis and end-stage liver disease.

Our findings were robust across broad ranges of assumptions. Although LBT without HCV RNA reflex testing was never favored in our base case, sensitivity analyses showed that improving test result delivery influenced outcomes by reducing loss to follow-up.

Study limitations include the lack of information on risk factors and hepatitis C prevalence for individuals who were not tested for HCV infection. We used national data and the OCHIN data set to impute drug use and hepatitis C status for individuals who were not tested. This approach might underestimate these parameters given the reliance on self-report; however, sensitivity analyses showed that these assumptions did not significantly influence our conclusions. There was also limited information on background hepatitis C testing rates at FQHCs; therefore, we used information available from a commercially insured population. We performed sensitivity analyses to determine the robustness of these assumptions and our conclusions remained stable. Our base case estimates for the offer rates for routine testing by counselor and clinician were derived from a randomized trial focused on HIV testing; however, given similar risk factors between HIV and hepatitis C, we believe that these values provided reasonable estimates (10). In addition, our current model is unable to perform probabilistic sensitivity analyses to measure uncertainty; however, we performed extensive sensitivity analyses of all model input parameters and identified key parameters influencing our findings.

In conclusion, FQHCs are an attractive venue for expanding hepatitis C testing in the United States, even when testing is occurring elsewhere. We considered multiple implementation models, and provide evidence that utilizing RT using a counselor/tester focused in part on

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

hepatitis C testing would likely result in more complete follow-up care, reduce the burden of end-stage liver disease, and avoid future spending on advanced liver disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding Source: This project was funded by the U.S. Centers for Disease Control and Prevention (CDC), National Center for HIV, Viral Hepatitis, STD, and TB Prevention Epidemiologic and Economic Modeling Agreement (NU38PS004644) which contributed to the conception, design and analysis and the decision to submit the manuscript for publication. Support was also obtained from the National Institute of Drug Abuse (K23 DA044085, R01 DA046527, P30 DA040500). The findings and conclusions are those of the authors and do not necessarily represent the official position of the CDC or the NIH.

Abbreviations:

CA	California
GA	Georgia
MA	Massachusetts
OR	Oregon
US	United States

Text References:

1. Zibbell JE, Iqbal K, Patel RC, Suryaprasad A, Sanders KJ, Moore-Moravian L, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged ≤30 years – Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. MMWR Morb Mortal Wkly Rep. 2015;64(17):453–8. [PubMed: 25950251]
2. Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. Clin Infect Dis. 2014;59(10):1411–9. [PubMed: 25114031]
3. Notes from the field : hepatitis C virus infections among young adults--rural Wisconsin, 2010. MMWR Morb Mortal Wkly Rep. 2012;61(19):358. [PubMed: 22592276]
4. Notes from the field: risk factors for hepatitis C virus infections among young adults--Massachusetts, 2010. MMWR Morb Mortal Wkly Rep. 2011;60(42): 1457–8. [PubMed: 22031220]
5. National Association of Community Health Centers. America's Health Centers. Fact Sheet 3 2016. Accessed on January 6, 2019. Available at http://www.nachc.org/wp-content/uploads/2015/06/Americas-Health-Centers-March-2016.pdf.
6. DeVoe JE, Gold R, Cottrell E, Bauer V, Brickman A, Puro J, et al. The ADVANCE network: accelerating data value across a national community health center network. J Am Med Inform Assoc. 2014;21(4):591–5. [PubMed: 24821740]
7. National Association of Community Health Centers. Research Fact Sheets and Infographics. Available at http://www.nachc.org/research-and-data/research-fact-sheets-and-infographics/. Accessed on April 19, 2020.
8. Assoumou SA, Tasillo A, Leff JA, Schackman BR, Drainoni ML, Horsburgh CR, et al. The cost-effectiveness of one-time hepatitis C screening strategies among adolescents and young adults in primary care settings. Clin Infect Dis. 2017.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

9. Force USPST, Owens DK, Davidson KW, Krist AH, Barry MJ, Cabana M, et al. Screening for Hepatitis C Virus Infection in Adolescents and Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2020.
10. Walensky RP, Reichmann WM, Arbelaez C, Wright E, Katz JN, Seage GR 3rd, et al. Counselor- versus provider-based HIV screening in the emergency department: results from the universal screening for HIV infection in the emergency room (USHER) randomized controlled trial. Ann Emerg Med. 2011;58(1 Suppl 1):S126–32 e1-4. [PubMed: 21684391]
11. Linas BP, Barter DM, Morgan JR, Pho MT, Leff JA, Schackman BR, et al. The cost-effectiveness of sofosbuvir-based regimens for treatment of hepatitis C virus genotype 2 or 3 infection. Ann Intern Med. 2015;162(9):619–29. [PubMed: 25820703]
12. Chou R, Wasson N. Blood tests to diagnose fibrosis or cirrhosis in patients with chronic hepatitis C virus infection. Ann Intern Med. 2013;159(5):372. [PubMed: 24026329]
13. Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, et al. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. MMWR Recomm Rep. 2012;61(RR-4):1–32.
14. Barocas JA, Wang J, White LF, Tasillo A, Salomon JA, Freedberg KA, et al. Hepatitis C Testing Increased Among Baby Boomers Following The 2012 Change To CDC Testing Recommendations. Health Aff (Millwood). 2017;36(12):2142–50. [PubMed: 29200354]
15. Curry MP, O'Leary JG, Bzowej N, Muir AJ, Korenblat KM, Fenkel JM, et al. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. N Engl J Med. 2015;373(27):2618–28. [PubMed: 26569658]
16. Kwo PY, Poordad F, Asatryan A, Wang S, Wyles DL, Hassanein T, et al. Glecaprevir and pibrentasvir yield high response rates in patients with HCV genotype 1-6 without cirrhosis. J Hepatol. 2017;67(2):263–71. [PubMed: 28412293]
17. Bourliere M, Gordon SC, Flamm SL, Cooper CL, Ramji A, Tong M, et al. Sofosbuvir, Velpatasvir, and Voxilaprevir for Previously Treated HCV Infection. N Engl J Med. 2017;376(22):2134–46. [PubMed: 28564569]
18. Davis KL, Mitra D, Medjedovic J, Beam C, Rustgi V. Direct economic burden of chronic hepatitis C virus in a United States managed care population. J Clin Gastroenterol. 2011;45(2):e17–24. [PubMed: 20628308]
19. Bruno S, Zuin M, Crosignani A, Rossi S, Zadra F, Roffi L, et al. Predicting mortality risk in patients with compensated HCV-induced cirrhosis: a long-term prospective study. Am J Gastroenterol. 2009;104(5): 1147–58. [PubMed: 19352340]
20. Coffin PO, Jin H, Huriaux E, Mirzazadeh A, Raymond HF. Trends in use of health care and HIV prevention services for persons who inject drugs in San Francisco: Results from National HIV Behavioral Surveillance 2005–2012. Drug and Alcohol Dependence. 2015;146:45–51. [PubMed: 25468816]
21. Smith DJ, Combellick J, Jordan AE, Hagan H. Hepatitis C virus (HCV) disease progression in people who inject drugs (PWID): A systematic review and meta-analysis. International Journal of Drug Policy. 2015;26(10):911–21. [PubMed: 26298331]
22. Galai N, Safaeian M, Vlahov D, Bolotin A, Celentano DD. Longitudinal Patterns of Drug Injection Behavior in the ALIVE Study Cohort, 1988–2000: Description and Determinants. American Journal of Epidemiology. 2003;158(7):695–704. [PubMed: 14507606]
23. Yehia BR, Schranz AJ, Umscheid CA, Lo Re V 3rd. The treatment cascade for chronic hepatitis C virus infection in the United States: a systematic review and meta-analysis. PLoS One. 2014;9(7):e101554. [PubMed: 24988388]
24. Freiman JM, Tran TM, Schumacher SG, White LF, Ongarello S, Cohn J, et al. Hepatitis C Core Antigen Testing for Diagnosis of Hepatitis C Virus Infection: A Systematic Review and Meta-analysis. Ann Intern Med. 2016;165(5):345–55. [PubMed: 27322622]
25. Boeras D, Amini A, Falconer J, Kelly H, Peeling R, Tang W, et al. PICO 4: Diagnostic strategies for Hepatitis C antibody detection: A meta-analysis and review of the literature. Summary report for the HIV Department of the World Health Organization to inform the WHO Hepatitis Screening Guidelines; 2015.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

26. Substance Abuse and Mental Health Services Administration (SAMHSA). 2016 National Survey on Drug Use and Health (NSDUH). Accessed on February 2nd, 2018. Available at https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf
27. Litwin AH, Smith BD, Drainoni ML, McKee D, Gifford AL, Koppelman E, et al. Primary care-based interventions are associated with increases in hepatitis C virus testing for patients at risk. Dig Liver Dis. 2012;44(6):497–503. [PubMed: 22342471]
28. Sullivan PW, Ghushchyan V. Preference-Based EQ-5D Index Scores for Chronic Conditions in the United States. Medical decision making : an international journal of the Society for Medical Decision Making. 2006;26(4):410–20. [PubMed: 16855129]
29. McLernon DJ, Dillon J, Donnan PT. Health-State Utilities in Liver Disease: A Systematic Review. Medical Decision Making. 2008;28:582–92. [PubMed: 18424560]
30. United States Department of Health and Human Services Center for Medicare Services. Physician Fee Schedule. Available from: http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/index.html?redirect=/PhysicianFeeSched. Accessed August 3rd, 2017.
31. Neumann PJ SGD, Russell LB, Siegel JE, Ganiats TG Cost-Effectiveness in Health and Medicine, 2nd Edition. Oxford, UK: Oxford University Press; 2016.
32. Neumann PJ, Cohen JT. ICER's Revised Value Assessment Framework for 2017-2019: A Critique. Pharmacoeconomics. 2017;35(10):977–80. [PubMed: 28791663]
33. Porter JC, Lusk HM, Katz AR. Prevalence of HCV infection among clients in community-based health settings in Hawaii, 2002-2010: assessing risk factors. Am J Public Health. 2014;104(8):1534–9. [PubMed: 24028267]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

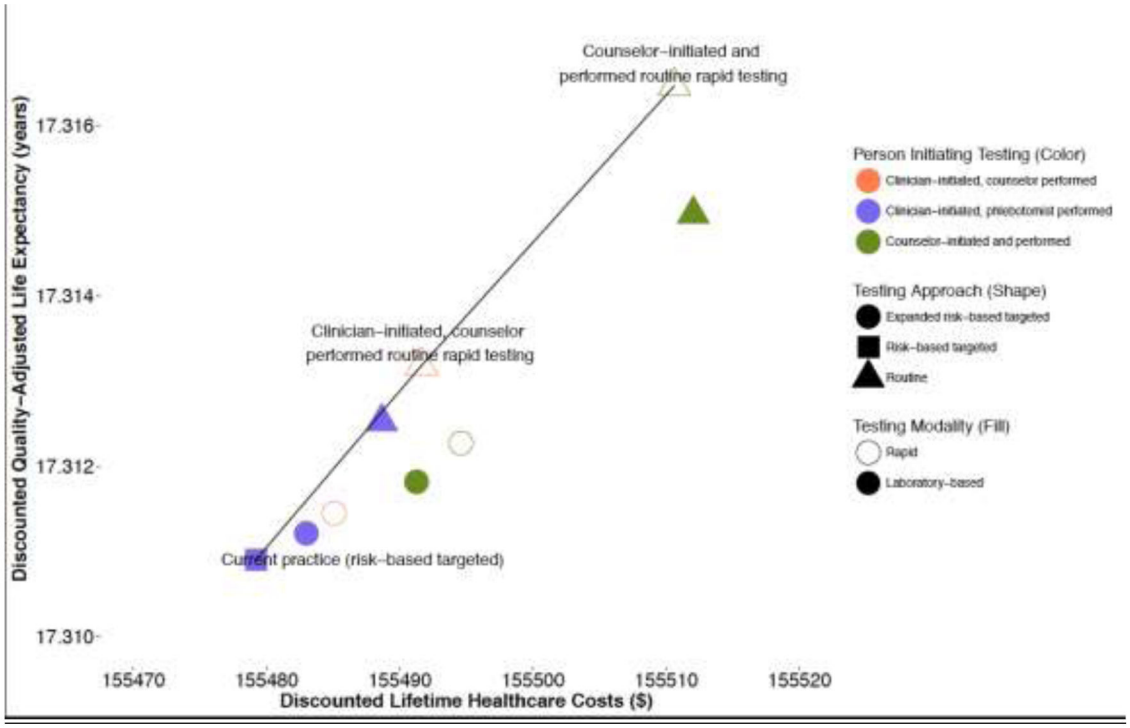

Figure 1: Cost-effectiveness frontier for hepatitis C virus infection testing and treatment at federally qualified health centers

The figure illustrates the cost, effectiveness and incremental cost-effectiveness of all 9 strategies considered. The color of each shape represents the person initiating and performing testing (clinician-initiated, counselor-performed vs. clinician-initiated, phlebotomist-performed vs. counselor-initiated and performed). Shapes (circle vs. square vs. triangle) represent the testing approach (expanded risk-based targeted vs. risk-based targeted vs. routine). The filling of the shape represents the testing modality (rapid vs. laboratory-based). The line represents the efficiency frontier. Strategies located to the right of the efficiency frontier result in either lower quality-adjusted life expectancy at higher cost than an alternative strategy or a higher cost per quality-adjusted life-year gained. Figure 1 shows that overall strategies with “counselor-initiated routine testing” provide better clinical outcomes than other testing approaches. “Clinician-initiated routine testing” also improves outcomes. The two strategies located on the cost-effectiveness frontier are “clinician-initiated, counselor-performed routine rapid” and “counselor-initiated and performed, routine rapid testing.”

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

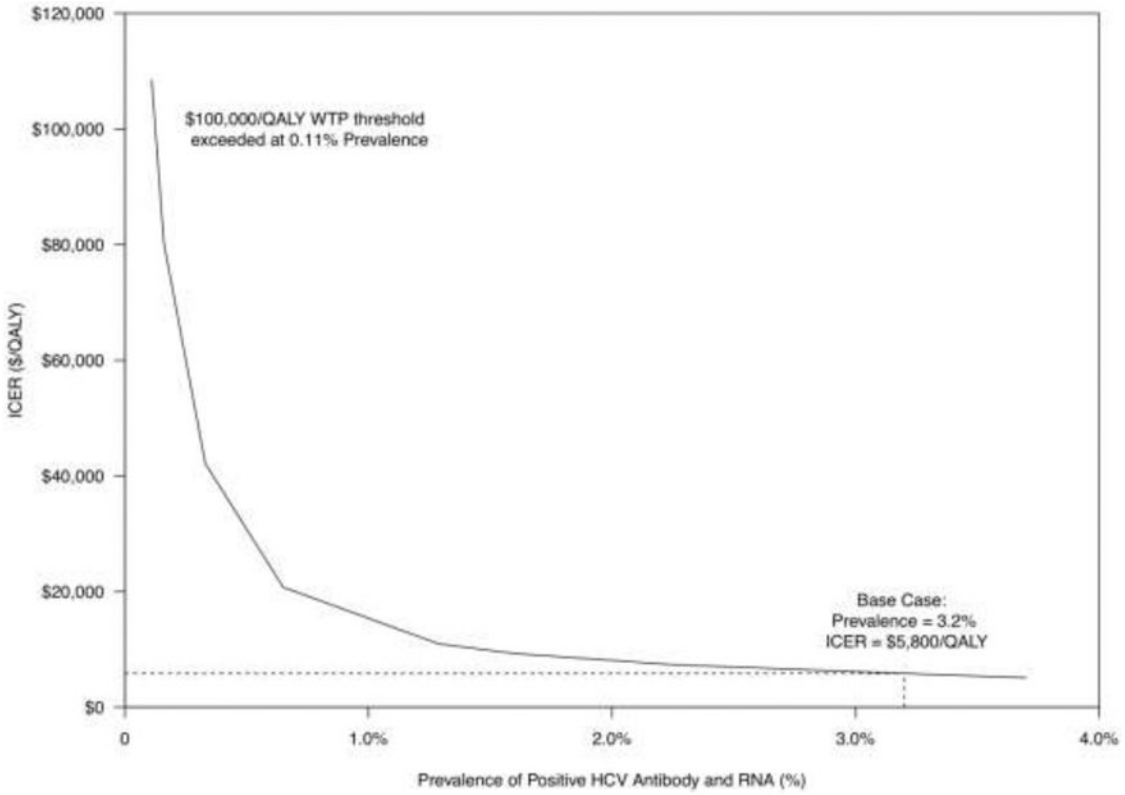

Figure 2: Incremental cost-effectiveness ratios for counselor-initiated routine rapid testing as a function of the prevalence of hepatitis C virus RNA positivity in the population

The line graph illustrates the ICER for "counselor-initiated routine rapid testing" compared to the next best alternative across a range of percentage of HCV RNA positivity in the population.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1.

Strategies considered

Test type	Person initiating the test	Strategy
Laboratory-based HCV antibody testing without reflex HCV RNA testing	Clinician	1. Current practice (risk-based targeted)
		2. Clinician-initiated, phlebotomist-performed expanded risk-based targeted * LBT
		3. Clinician-initiated, phlebotomist-performed routine LBT
	Counselor	4. Counselor-initiated and performed expanded risk-based targeted * LBT
		5. Counselor-initiated and performed routine LBT
Rapid	Clinician	6. Clinician-initiated, counselor-performed expanded risk-based targeted * RT
		7. Clinician-initiated, counselor-performed routine RT
	Counselor	8. Counselor-initiated and performed expanded risk-based targeted * RT
		9. Counselor-initiated and performed routine RT

* Clinicians used a validated hepatitis C screening checklist.

HCV=Hepatitis C virus; LBT=laboratory-based testing; RT=Rapid testing

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2.

Model input parameter

Variable	Base Case Value	Range Evaluated	Reference
Cohort characteristics			
Mean age, years	41	38-48	OCHIN FQHC Data set
Proportion male (%)	43	36-52	OCHIN FQHC Data set
Baseline proportion of current PWID (%)	0.51	0.3-0.8	OCHIN FQHC Data set
SMR, active PWID	6	1-12	(34)
SMR, former PWID	2	1-4	(34)
Monthly probability of initiating to drug use	0.0004	0.0002-0.0005	(26)
Monthly probability of recovery from drug use	0.0139	0.0070-0.0209	(22)
Monthly probability of relapse to drug use	0.0329	0.0165-0.0494	(22)
Baseline prevalence of chronic hepatitis C based on reactive anti-HCV antibody and detectable HCV viral load (%)	3	2-5	OCHIN FQHC Data set
Overall	32	16-48	
Identified history of active PWID	23	11-34	
Identified history of former PWID	0.84	0.4-1.3	
Not identified history PWID			
HCV infection in PWIDs (cases/100 person-years)	12	6 −18	(35)
(Detectable HCV RNA)			
Probability of clearing acute infection	0.2600	0.1300-0.3900	(36)
Hepatitis C testing and other cascade of care parameters			
Background testing (tests per 100 person-years)	39	0–49	(20, 37)
Active PWID	3	0-3	
Negative former or no PWID	5	0-6	
Positive former or no PWID	11	0-13	
Positive former or no PWID in birth cohort			
Percentage receiving antibody test results (%)			
Rapid testing	99	74-99	(38)
Laboratory-based testing	74	55-92	(39)
Intervention linkage to care (%)	53	25-75	OCHIN FQHC Data set
Background linkage to care (%)	47	35-59	(40)
Probability of re-engaging with care after being lost to follow-up[†] (%)	0.0011	0.0008-0.0014	Expert Opinion
Hepatitis C testing program-related inputs			
Laboratory-based HCV antibody test ($/test)	20	10-30	(30)
Rapid HCV antibody test ($/test)	15	7-22	(30)
Counselor/tester hourly wage ($/hour)	25	12-37	(41)
Estimated time to perform rapid test (minutes)	26	13-39	(42)

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Variable	Base Case Value	Range Evaluated	Reference
Hepatitis C disease progression			
Monthly liver fibrosis progression rate			
F0-F1	0.0107	0.0054-0.0161	(43)
F1-F2	0.0049	0.0025-0.0074	(43)
F2-F3	0.0065	0.0034-0.0098	(43)
F3-F4	0.0097	0.0048-0.0145	(43)
F4-decompensated cirrhosis	0.0098	0.0049-0.0146	(43)
Liver mortality (deaths/100 person years)			
F4 (Cirrhosis)	3	2-4	(19)
Decompensated cirrhosis	21	16-26	(19)
Therapy			
Therapy initiation (%)	92	86-100	(44)
Treatment completion (%)			(17, 45-47)
Sofosbuvir/velpatasvir	99	99-100	
Glecaprevir/pibrentasvir	99	98-100	
Sofosbuvir/ velpatasvir/ voxilaprevir	99	98-100	
Sofosbuvir/ velpatasvir/ voxilaprevir + ribavirin	84	68-100	
Withdrawal due to toxicity (%)			(17, 45-47)
Sofosbuvir/velpatasvir	25	0-50	
Glecaprevir/pibrentasvir	0.1	0-0.2	
Sofosbuvir/ velpatasvir/ voxilaprevir	33	0-67	
Sofosbuvir/ velpatasvir/ voxilaprevir + ribavirin	100	0-100	
SVR after treatment completion, non-cirrhotic (%)	95-100	48-50	(17, 45)
SVR after treatment completion, cirrhotic (%)	88-100	44-50	(46, 47)
Costs			
Routine medical costs per month with active HCV infection, F0-F2 ($)	302	151-453	(18)
Routine medical costs per month with active HCV infection, F3-F4 [§] ($)	538	269-755	(18)
Routine medical costs per month with active HCV infection, decompensated cirrhosis [§] ($)	1,020	510-1,530	(18)
Hepatitis C therapy costs per month			
Complete course per month, no cirrhosis			(48)
Glecaprevir/pibrentasvir (8-week course) ($)	9,830	4,915-14,745	
Complete course per month, cirrhosis			(48)
Sofosbuvir/velpatasvir (12-week course) ($)	8,090	4,145-12,135	
Complete course per month, non cirrhosis			(48)
First re-retreatment	19,285	9,643-28,928	
Sofosbuvir/velpatasvir/voxilaprevir (12-week course) ($)			
Complete course per month, cirrhosis			(48)
First re-treatment	22,798	11,399-34,197	
Sofosbuvir/velpatasvir/voxilaprevir + ribavirin (12-week course) ($)			

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Variable	Base Case Value	Range Evaluated	Reference
Managing hepatotoxicity ($)	240	120-360	
Quality of life			
Without history of PWID or HCV infection (age-specific) ¶	0.79-0.92	(0.72-0.84)-(0.87-1.00)	
With history of active PWID	0.68	0.36-1.00	
With history of past PWID	0.82	0.64-1.00	
With history of HCV infection, by fibrosis stage			
F0-F3	0.94	0.84-1.00	(28)
F4	0.75	0.65-1.00	(28)
Decompensated	0.60	0.50-1.00	(28)
After treatment, by fibrosis stage			
F0-F3	0.97	0.87-1.00	Expert opinion
F4	0.94	0.84-1.00	(49)
Decompensated	0.75	0.65-1.00	(29)

FQHC= Federally Qualified Health Center; OCHIN= formerly known as the Oregon Community Health Information Network and now referred to as OCHIN after it expanded to other states; HCV= Hepatitis C Virus; Laboratory-based testing=LBT; PY = person-years; PWID= Person Who Injects Drugs; RT= Rapid testing; SMR= standardized mortality ratio; SVR = sustained virologic response.

Note: costs are in 2017 US dollars

*HCV-related care is defined testing or work-up related to HCV treatment (HCV RNA testing, fibrosis staging).

†Twenty-year probability of re-engaging with care assumed to be half of original linkage probability (15% probability over 20 years).

§Costs varied as a function of age and sex.

¶The less than 1.0 utility for those living without HCV infection reflects lower quality of life for individuals with HCV risk-factors such as substance use.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3.

Base case cost-effectiveness analysis results

Strategies	Undiscounted Remaining Life Expectancy (years)	Total Discounted Cost per Person ($)	Discounted Remaining QALY per Person (QALY)	Incremental cost-effectiveness ratio ($/QALY)	Lifetime sustained virologic response (%)	Reduction in cirrhosis cases when compared to current practice (%)
a. Current practice (risk-based targeted) (1ai)	38.55	155,480	17.3111	--	73	--
b. Clinician-initiated, phlebotomist-performed expanded risk-based targeted* LBT (1bi)	38.55	155,490	17.3114	Extended dominance	73	1
c. Clinician-initiated, counselor-performed expanded risk-based targeted* RT (1bii)	38.55	155,490	17.3117	Extended dominance	73	2
d. Clinician-initiated, phlebotomist-performed routine LBT (1ci)	38.55	155,490	17.3127	Extended dominance	74	5
e. Counselor-initiated and performed expanded risk-based targeted* LBT(2bi)	38.55	155,500	17.3120	Dominated	74	3
f. Clinician-initiated and counselor-performed routine RT (1cii)	**38.55**	**155,500**	**17.3134**	**5,500**	74	7
g. Counselor-initiated and performed expanded risk-based targeted* RT(2bii)	38.55	155,500	17.3125	Dominated	74	5
h. Counselor-initiated and performed routine RT (2cii)	**38.56**	**155,510**	**17.3167**	**5,800**	75	17
i. Counselor-initiated and performed routine LBT (2ci)	38.56	155,520	17.3152	Dominated	75	12

LBT=laboratory-based testing; RT=Rapid testing; QALY = Quality Adjusted Life-Year

Strategy shorthand key: clinician (1), counselor (2); risk-based targeted (a), expanded risk-based targeted (b), routine (c); laboratory-based testing (i), rapid testing (ii).

Costs are rounded to nearest $10, QALYs to nearest 0.0001, ICERs to nearest $100/QALY. Small inconsistencies may be present due to rounding.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 4.

Base case clinical outcomes results

Strategies	Infections Identified in the first month of the intervention (%)	Infections Identified in the cohort's lifetime (%)	Sustained virologic response achieved (%)	Number of individuals with cirrhosis	Reduction in cirrhosis cases when compared to current practice (%)	Reduction in liver deaths among cirrhotics when compared to current practice (%)
a. Current practice (risk-based targeted) (1ai)	7	87	73	9,863	--	--
b. Clinician-initiated, phlebotomist-performed expanded risk-based targeted* LBT (1bi)	15	87	73	9,760	1	1
c. Clinician-initiated, counselor-performed expanded risk-based targeted* RT(1bii)	20	87	73	9,683	2	2
d. Clinician-initiated, phlebotomist-performed routine LBT (1ci)	25	88	74	9,384	5	6
e. Counselor-initiated and performed expanded risk-based targeted* LBT (2bi)	33	88	74	9,546	3	3
f. Clinician-initiated, counselor-performed routine RT (1cii)	**34**	**88**	**74**	**9,178**	7	**9**
g. Counselor-initiated and performed expanded risk-based targeted* RT (2bii)	44	88	74	9,399	5	5
h. Counselor-initiated and performed routine RT (2cii)	**75**	**89**	**75**	**8,186**	17	**22**
i. Counselor-initiated and performed routine LBT (2ci)	56	88	75	8,639	12	16

LBT=laboratory-based testing; RT=Rapid testing

Strategy shorthand key: clinician (1), counselor (2); risk-based targeted (a), expanded risk-based targeted (b), routine (c); laboratory-based testing (i), rapid testing (ii).