Supplemental Material: The cost-effectiveness of hepatitis C virus screening in hemodialysis patients

Supplemental Table 1: CHEERS 2022 Reporting Checklist

Topic	No.	Item	Location where item is reported
Title			
	1	Identify the study as an economic evaluation and specify the interventions being compared.	Title, Page 1
Abstract			
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Abstract, Page 3
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Introduction, Last Paragraph
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Methods, Paragraphs 2 and 13
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Methods, Paragraph 4
Setting and location	6	Provide relevant contextual information that may influence findings.	Methods, Paragraph 5
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Methods, Paragraph 11
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Methods, Paragraph 4
Time horizon	9	State the time horizon for the study and why appropriate.	Methods, Paragraph 11

Topic	No.	Item	Location where item is reported
Discount rate	10	Report the discount rate(s) and reason chosen.	Methods, Paragraph 12
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Methods, Paragraph 13
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Methods, Paragraph 13
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Methods, Paragraph 13
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Methods, Paragraph 12
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Methods, Paragraph 12
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Methods, Paragraph 1-2
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Methods, Paragraphs 4, 5, 7, and Supplemental Materials
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Methods, Last paragraph
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Methods, Last paragraph
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Methods, Last paragraph

Topic	No.	Item	Location where item is reported
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Not applicable
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Table 2, Supplemental Materials
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure.	Results, Paragraph 1
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Results, Paragraphs 2-7
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	Not applicable
Discussion			
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Discussion
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	End of manuscript

Topic	No.	Item	Location where item is reported
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	End of manuscript

From: Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022;25. doi:10.1016/j.jval.2021.10.008

Supplemental Exhibit 1: HEP-CE Model Structure

Model Description:

The Hepatitis C Cost Effectiveness (HEP-CE) model is an individual-based stochastic microsimulation model programmed in C++. A cohort of individuals enters the model with a user-programmed age and liver disease (fibrosis) distribution, and injection-drug use, HCV seropositivity, and chronic infection prevalences. These individuals cycle through various health, disease, and care states, accrue costs and utilities (quality-adjusted life years; QALYs), and are exposed to background and HCV-related mortality each one-month cycle. The major disease and care states are represented in the model diagram below with additional detail on modules explained below and on hemodialysis-related HCV outbreaks detailed in Supplemental Table 3.
HCV Screening, Linkage, and Treatment:

All individuals who are not already diagnosed with and in care for HCV are exposed to HCV screening at a frequency determined by the strategy programmed (never, one-time, or periodic at a specified interval). Each time an individual is screened for HCV, they accrue testing costs. Testing occurs as reflex testing with HCV antibody followed immediately (the same cycle) by HCV RNA, only if HCV antibody testing is positive. False negative and false positive antibody and RNA tests can occur, at rates according to literature-informed test sensitivity and specificity, respectively. When a hypothetical individual enters the model, he/she has a true HCV infection status assigned, and a flag indicating whether that diagnosis (if positive) is known. Each time he/she is screened for HCV, the model calculates, based on test sensitivity and specificity, whether the test will reveal to the patient and clinician the true infection status, or a false negative/positive. If a false negative, the patient continues to have progression of liver disease until either re-screening with a true positive occurs or they die from liver-related or background mortality. If a false positive occurs, the patient goes on to have further HCV evaluation, including a genotype test. The genotype test should then reveal lack of HCV viremia, and the patient incurs the cost of the additional tests and evaluation and then returns to the susceptible pool and does not continue further in HCV care until the time of a new positive screen, if that occurs again.

If an individual has a positive HCV antibody and RNA on screening, they are then exposed to a probability of linking to care each cycle, and once linked to care they go through additional HCV evaluation including genotype testing, clinical visits, and liver disease (fibrosis) staging evaluation. This evaluation can occur the same cycle an individual is linked to care or can be programmed to take multiple cycles to complete. In this study, we programmed it to take at least 1 cycle (month) to complete. Once fibrosis evaluation is completed, individuals then enter the treatment module. In this module, they are exposed to a likelihood of starting treatment and assigned a treatment course and cost. Individuals can also be lost to follow-up any cycle that they are linked to care and/or in treatment. Once unlinked, they are also exposed to a lower, literature informed re-linkage rate each cycle, or they can be re-linked if they are screened again.

Treated individuals experience a literature-informed probability of completing treatment or withdrawing due to toxicity or a non-toxicity related reason. Those who complete treatment are

exposed to a literature-informed probability of achieving cure, and those who do not complete treatment can still clear spontaneously if within the first 6 months of infection.

HCV Infection:

Outside of a programmed hemodialysis center outbreak, HCV infection is possible only through injection drug use. Individuals with current injection drug use experience a monthly probability of HCV infection, and once infected can either spontaneously clear during the first 6 months after infection or can be treated as above.

Liver Disease:

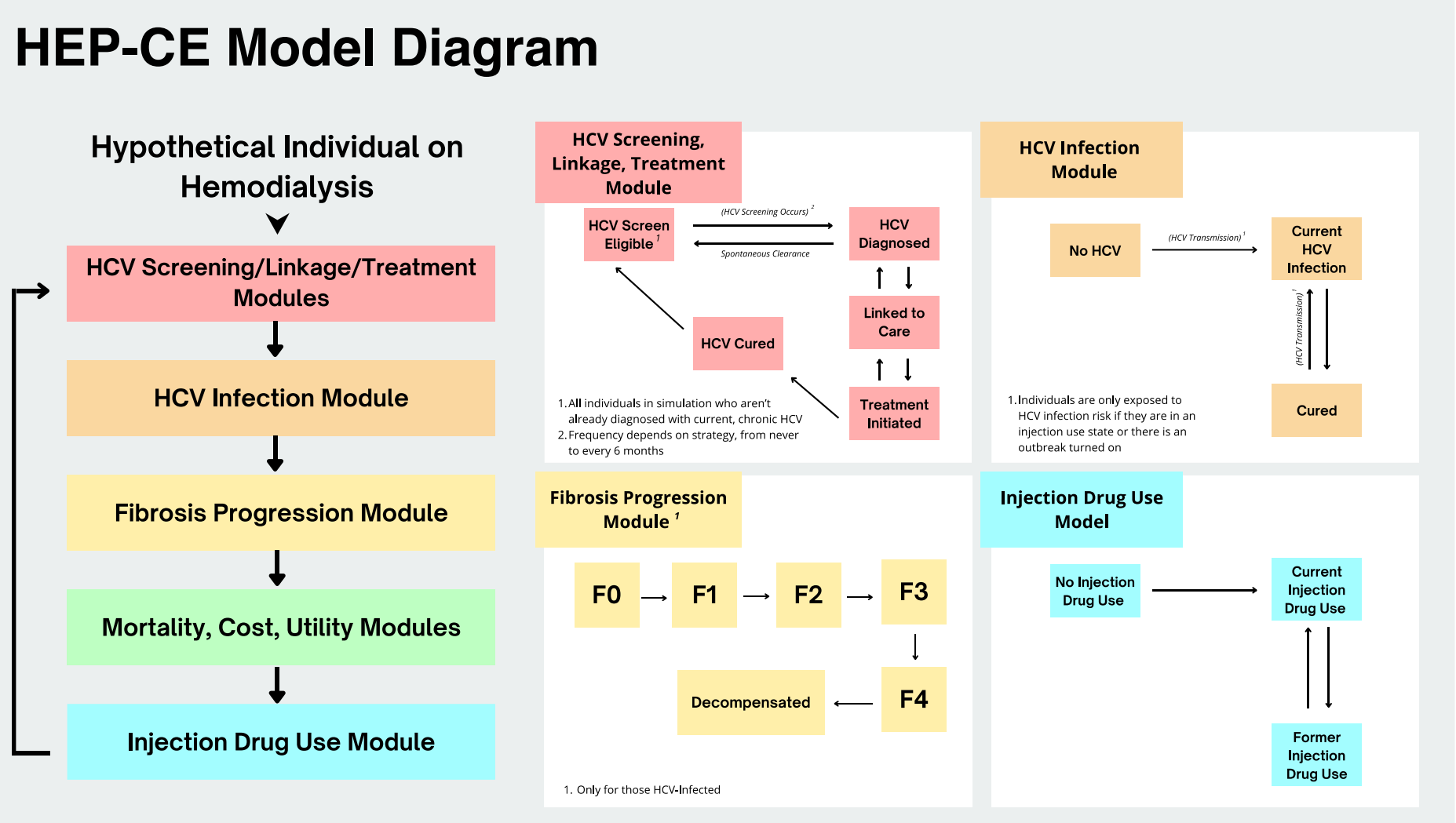
Only individuals with HCV infection enter the fibrosis progression module. In the fibrosis progression module, if they have current HCV infection, they experience a monthly probability of their fibrosis advancing to the next stage (F0 to F1, F1 to F2, F2 to F3, F3 to F4, and F4 to decompensated). Once HCV is cured, they remain in the fibrosis stage they reached prior to the last treatment month. If they are re-infected, fibrosis progression resumes. Their fibrosis stage determines their monthly costs due to liver disease, their mortality (higher only for F4 and decompensated stages), and their monthly utilities.
Mortality, Costs, Utilities:

Each cycle, each individual is exposed to a risk of background and liver-disease related mortality. For each individual still alive during a given cycle, the model sums the individual's current background healthcare costs with any costs incurred during the cycle from screening, care/treatment, and injection drug use or liver disease-related care. It also multiplies their age- and sex-defined background utility (QALY) by any disease- or treatment-related utilities they incur that cycle – i.e., from HCV infection, a particular fibrosis stage/liver disease, injection drug use, treatment or toxicity.

Injection Drug Use:

Individuals begin in one of three injection drug use states: never, current, or former. Once in current injection drug use, they move to former use at a literature-informed, age- and sex-stratified probability each month. Individuals can move into or back into current use from never or former states at a literature-informed probability each month as well. In this study's base case, we assumed no new injection drug use begins while on hemodialysis, so movement only occurs from current to former use states.

Model Diagram:



Supplemental Table 2: Hemodialysis Center Hepatitis C Virus Outbreak Literature Review and Calculations

Outbreaks described in literature that detail person-time:

Description of Source	N	HCV cases	Time Period (months)	Person-months followed	Outbreak Rate, monthly	Outbreak Probability, monthly	Source
NY State HD center outbreak 2001-2008	90	9	88	3590	0.002507	0.002504	[1]
2016 Cochrane Review of 1 trial that randomized HD centers to dedicated/ non-dedicated machines for those with HCV infection	254	4	9	2268	0.001764	0.001762	[2, 3]
	192	9	9	1688	0.005333	0.005319	[2, 3]
	160	2	9	1431	0.001397	0.001397	[2, 3]
	121	7	9	1058	0.006619	0.006598	[2, 3]
Mean					0.0035	0.0035	

We averaged the HCV incidence rates related to hemodialysis center outbreaks over the described New York state outbreak and the randomized trial arms (initial and subsequent 9 months of follow-up for each trial arm). We assumed all participants in the randomized trial were followed for the duration of the trial as only participants tested at the end of the trial were reported in the results. For the NY state outbreak, we assumed non-case tested individuals at the time of investigation had on average been utilizing the given center for half of the study period, similar to the cases average reported person-time in the center and given average lifespan. The overall mean outbreak HCV incidence was 0.0035 cases/person-month or 4.23 cases per 100 person-years. For sensitivity analyses, we varied this number between the lowest reported HCV incidence rate (0.001397 cases/person-month or 1.68 cases/100 person-years) and 4 times the highest reported incidence rate (0.02648 cases/person-month or 31.8 cases/100 person-years).

Determination of outbreak duration:

We estimated an antibody window period (time between infection and when HCV antibody is detectable on current assays) of 6 months/180 days based on the longest estimates from the literature.[4] We then used half the baseline screening period to account for the index case acquiring infection, on average, halfway through the screening interval (i.e. 6 months in if yearly strategy) and it therefore taking half the screening interval, on average, to pick up the index case. We then assumed that the index case could have transmitted HCV within that time period, and it would take up to 6 months for secondary cases to be detectable by antibody testing (given the window period and an outbreak screening interval of every 3 months). A case is then potentially contagious if the same infection prevention lapses continue until that case is linked to care and treated, which we estimate will take 4 months on average (1 month to make a referral, 2 months to link, complete fibrosis staging, and prior authorization for medications, and 1 month on treatment until viral load is undetectable). Altogether that equates to 16 months plus half the baseline screening interval, for periodic screening intervals as depicted in the formula and table

below. For the non-periodic screening intervals (no testing and testing only at dialysis center entry), we used literature-informed screening durations (multiple lasting approximately 5-7 years with variable screening practices occurring but usually less than guideline-recommended intervals)[5, 6] balanced with overall life-expectancy for the population from our simulations (about 5 years). For the screening at dialysis entry scenario, we assumed a shorter outbreak duration than no screening because of at least baseline known HCV status for an individual identified through likely diagnostic screening after elevated ALT or symptoms or background screening in another setting.

Outbreak Duration Formula:

Outbreak Duration = Antibody window period + 0.5*Baseline Screening Interval + 2*Outbreak Screening interval (3 months) + Time from diagnosis until 4 weeks into HCV Treatment, at which point HCV RNA should be undetectable

= 6 months + 0.5*Screening Interval (months) + 6 months + 4 months

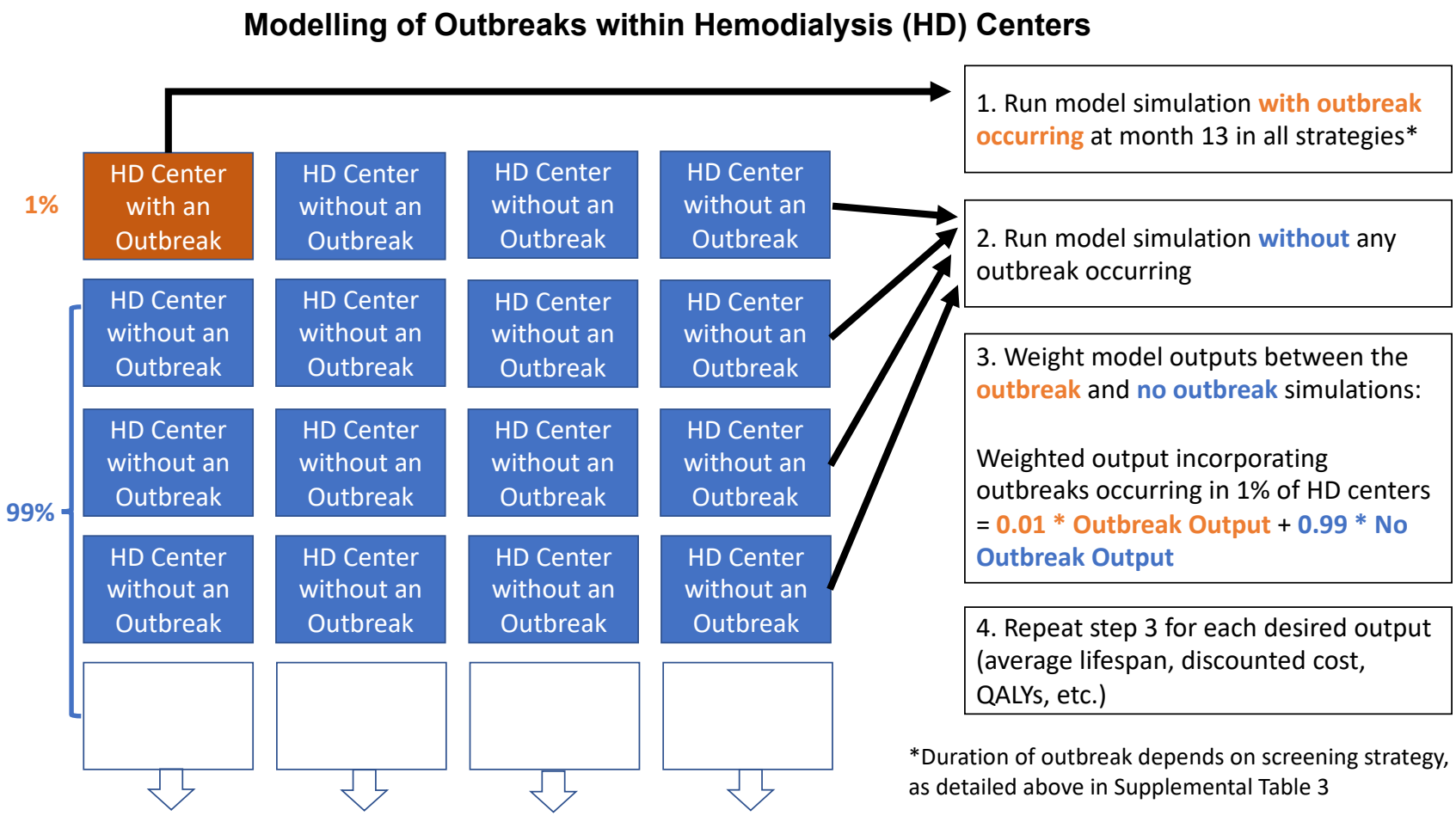
Outbreak duration based on Screening Interval:

Strategy	Outbreak Duration
No Screening	60 months
Screen only at HD Center Entry	42 months
Screen every 2 years	28 months
Screen yearly	22 months
Screen every 6 months	19 months

Outbreak duration in RNA testing only sensitivity analysis (no 'window period'):

Strategy	Outbreak Duration
No Screening	54 months
Screen only at HD Center Entry	36 months
Screen every 2 years	22 months
Screen yearly	16 months
Screen every 6 months	13 months

Outbreak Diagram:



Supplemental Table 3: HCV seropositivity and fibrosis stage data, initial cohort

Age	Sex	Proportion HCV Seropositive
18-24	male	0.01839978
18-24	female	0.02075406
25-29	male	0.03396505
25-29	female	0.02814523
30-34	male	0.04228198
30-34	female	0.03455368
35-39	male	0.05730906
35-39	female	0.04678727
40-44	male	0.08667965
40-44	female	0.06421291
45-49	male	0.13999133
45-49	female	0.09515614
50-54	male	0.18427662
50-54	female	0.10253617
55-59	male	0.17029166
55-59	female	0.09131393
60-64	male	0.11242212
60-64	female	0.06767342
65-69	male	0.06131423
65-69	female	0.04515619
70-74	male	0.03482455
70-74	female	0.03366514
75-79	male	0.02371474
75-79	female	0.02804273
80-84	male	0.01763923
80-84	female	0.02466199
85-99	male	0.01467136
85-99	female	0.01451613

Age	F0	F1	F2	F3	F4
18-24	0.54	0.41	0.02	0.02	0.01
25-29	0.43	0.43	0.05	0.05	0.03
30-39	0.43	0.43	0.06	0.06	0.03
40-49	0.34	0.34	0.13	0.13	0.06
50-59	0.24	0.24	0.20	0.20	0.13
60-69	0.17	0.17	0.23	0.23	0.20
70-99	0.11	0.1	0.26	0.26	0.27

Proportions HCV seropositive and with each METAVIR fibrosis stage (F0-F4) calculated from secondary data analysis from Sawinski et. al., 2019.[7] Fibrosis stages based upon Fibrosis-4 (FIB-4) scores, with cutoffs <1.45 for F0-F1, 1.45-3.25 for F2-F3, and >3.25 as F4.

Supplemental Figure 1: Calibration Results

A. Modeled Versus Predicted Survival

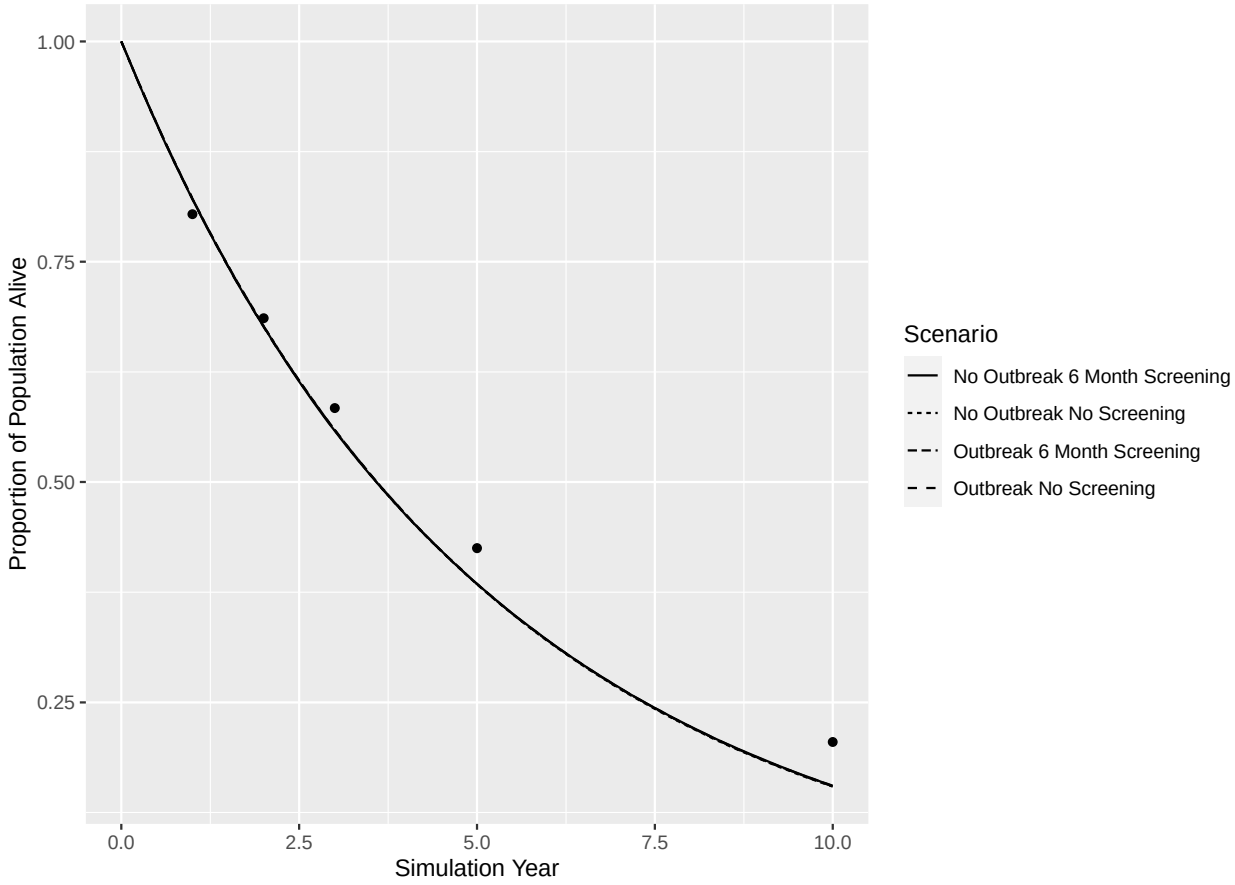


Figure Legend:

Lines represent proportion of population still alive in a given time step (month) in the base case simulation (Non screening or treatment and every 6-month screening strategies shown; results are very similar and lines overlap). Dots represent United States Renal Data System (USRDS) 2017 survival data for incident hemodialysis patients entering the USRDS cohort 1, 2, 3, 5, and 10 years before 2017.[11]

B. Hepatitis C Virus Incidence:

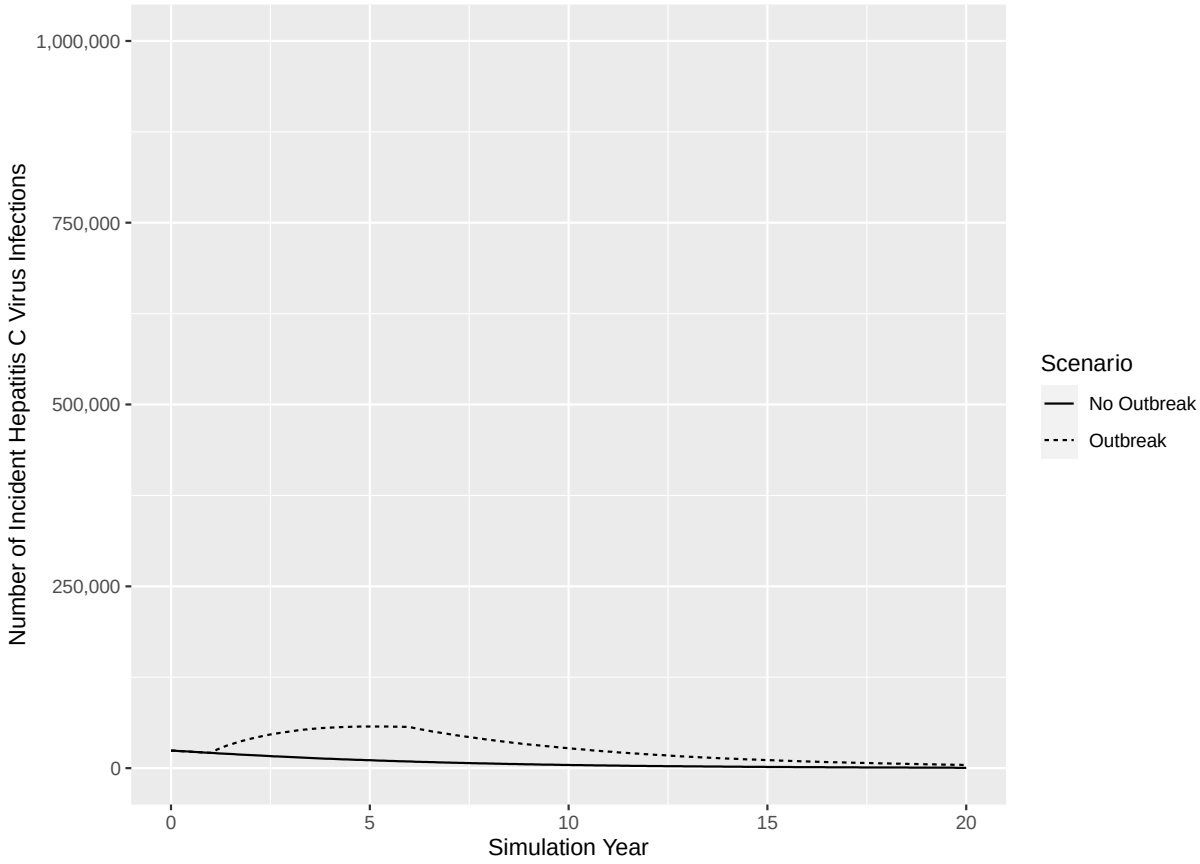


Figure Legend:

Absolute number of new hepatitis C virus (HCV) infections each cycle during outbreak and non-break scenarios in base case simulation, no screening, no treatment strategy with a total cohort size of 1,000,000 hypothetical individuals.

C. Cirrhosis Cases over Simulation

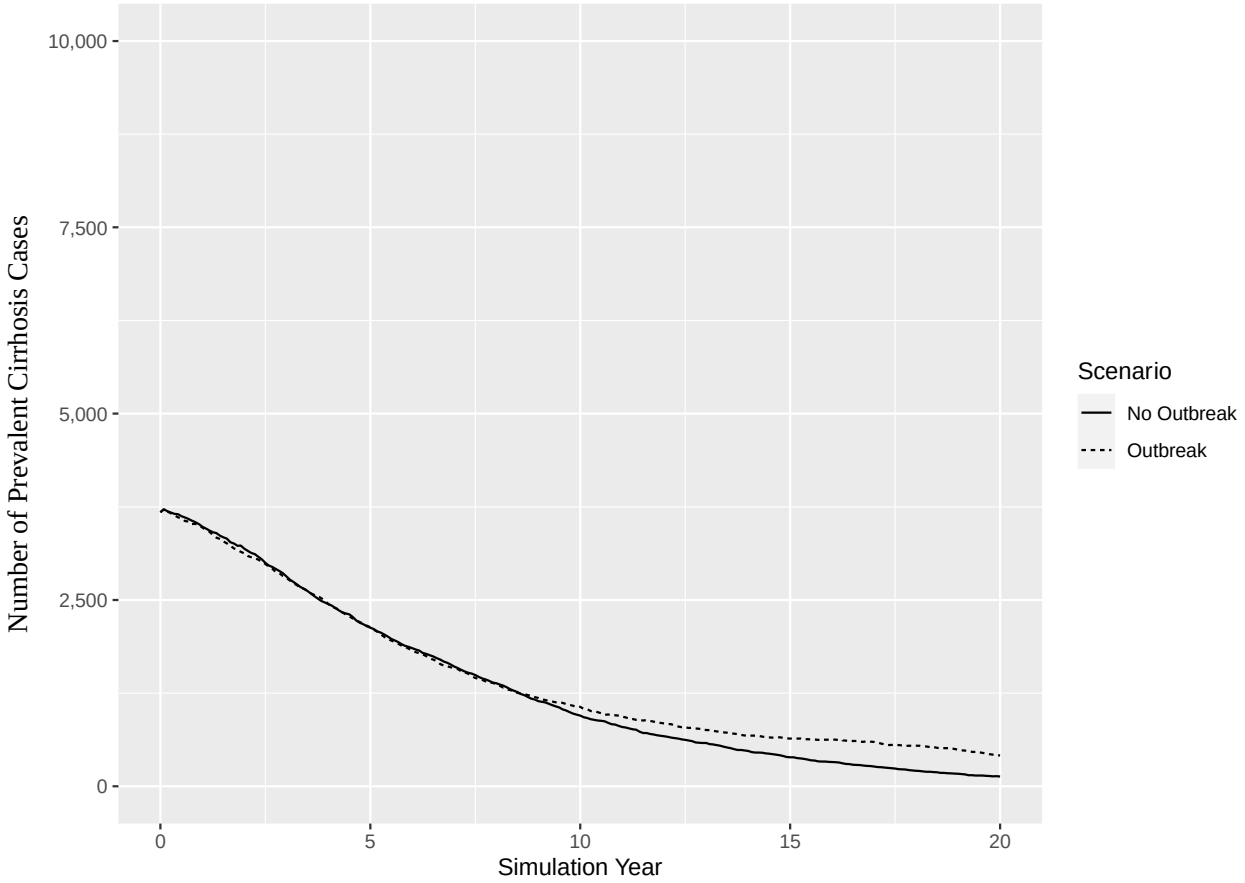


Figure Legend:

Absolute number of cirrhotic individuals each cycle during outbreak and non-break scenarios in base case simulation, no screening, no treatment strategy with a total cohort size of 1,000,000 hypothetical individuals.

D. Sample size needed to minimize stochastic variation

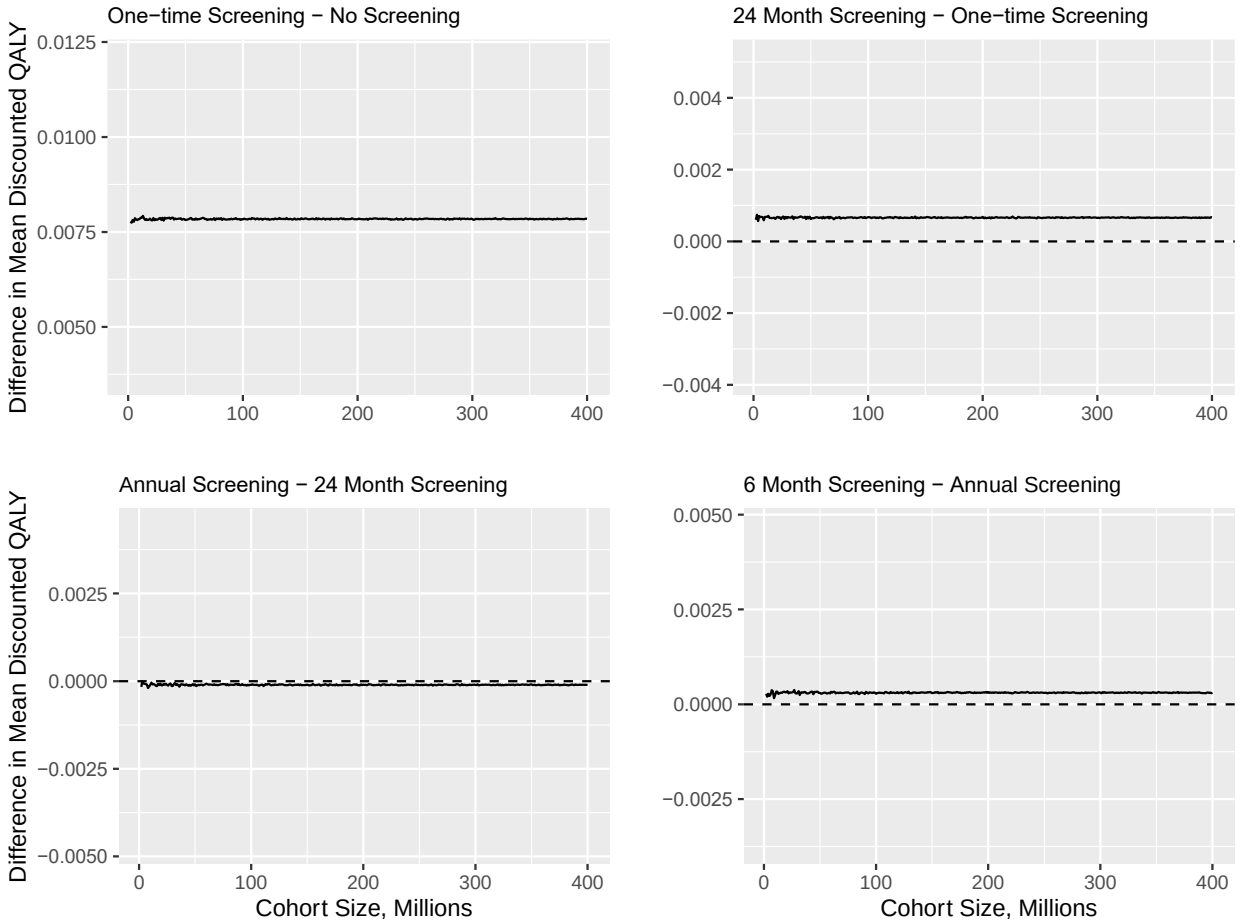


Figure Legend:

Panels each demonstrate the difference in mean quality-adjusted life years (QALYs) between the strategies noted when 1000 runs of increasing cohort sizes were used in the base case model simulation, up to a maximum of 400 million. The mean difference is graphed as the solid black line, and purple shaded area represents 95% confidence bands on the mean difference. The dashed black line indicates a mean difference of zero for reference (no difference in QALYs between strategies).

Abbreviations: QALY, quality-adjusted life year

Supplemental Table 4: Full list of model parameters

Parameter	Estimate[a]	Range/Distribution	Source
Population/Demography:			
Prevalence of Injection Drug Use (IDU)	Current: 0.3% Former: 6.0%	0.25-10x baseline current IDU rate	8-10
Distribution of METAVIR Fibrosis Stage	Varies by age/sex	See Supplemental Table 2	7
Mean Age (years)	63.4	18-99	11
Chronic HCV Infection	2.4%	0-5.4%	7, 12
Background Mortality Rates	Varies by age/sex[b]	0.5x baseline rates	11
Genotype Prevalence			13
One	0.745	--	
Two	0.102	--	
Three	0.153	--	
Injection Drug Use:			
SMR, former or current IDU	1.58	1.27-1.67	14
Probability of initiating IDU	0	0-0.000358	14
Probability of entering recovery	0.0139	--	14
Probability of relapsing to current IDU	0	0-0.0329	14
HCV Disease:			
IDU-Related HCV Incidence (cases/100 PY)	12.3	8.5-17.8	15
HD Center Outbreak-Related HCV Incidence (cases/100 PY)	4.23	1.68-31.8, Poisson	2, 3, 5
% of HD Centers with an HCV Outbreak	1%	1-50%	5
Probability of Clearing Acute Infection	26%	--	16
Monthly Fibrosis Progression Probability			
F0-F1	0.008877	--	17
F1-F2	0.00681	--	17
F2-F3	0.0097026	--	17
F3-F4	0.0096201	--	17
F4-Decompensated Cirrhosis	0.0097026	--	18
Monthly Cirrhosis Mortality			
F4 (Deaths/100 PY)	3	1-5, Poisson	19
Decompensated Cirrhosis (Deaths/100 PY)	21	3-30, Poisson	19
Post-SVR Mortality Multiplier:	0.06	0.01-1	20
Screening and Linkage:			
Background HCV Screening (outside HD)	0	0-20.8%	21
Referral to HCV-Specific Care	95%	--	Expert Opinion
Percent of Patients Successfully Linked to and Retained in Treatment	75%	50-100%	22-28
Monthly Voluntary Relinkage Probability	50% over 2 years	--	Expert Opinion;[29]
HCV Antibody Test Sensitivity/Specificity	98%/98%	88[c]-98%/98-99%, Beta	[30], [31, 32], [33-35]
HCV RNA Test Sensitivity/Specificity	99.3%/99.9%	98-100%/100%	36
Treatment (Glecaprevir/pibrentasvir 8-week course)			
Medication Cost	$9507.35	Gamma	37
Other Monthly Treatment Costs	$338.23	--	38
SVR Rate	97%	--	39
Toxicity Rate	2%	--	39

Cost of Treatment Toxicity	$224.74	--	[38]
Utility on treatment	0.99	--	Expert opinion
Utility if experience treatment toxicity	0.75	0.5-0.99	Expert opinion
Utilities:			
Background (Hemodialysis)	0.69	0.59-0.80	[40]
Current IDU	0.681	0.54-0.80	[41]
Former IDU	0.822	0.71-0.93	[41]
HCV Disease (Active Infection)			[42]
F0-F3	0.94	0.9-1.0	
F4	0.75	0.6-0.9	
Decompensated cirrhosis	0.6	0.48-0.75	
HCV Disease (Post-SVR)			Expert opinion
F0-F3	0.97	0.94-1.0	
F4	0.94	0.75-0.97	
Decompensated cirrhosis	0.75	0.6-0.94	
Costs (USD):			
Background Healthcare Costs (HD patients)	Age- and Sex-stratified	$7231-$8289	[11]
Background IDU Costs	$95.99	--	[43]
HCV Antibody Test	$15.85	Gamma	[38]
HCV RNA Test	$79.41	Gamma	[38]
Fibrosis Staging (Fibroscan)	$127.42	--	[38]
False-positive Test Result Cost[d]	$492.63	--	[38]
HCV Disease (Active Infection)			[44]
F0-F2	$345.54	--	
F3-F4	$615.58	--	
Decompensated cirrhosis	$1,167.06	--	
HCV Disease (Post-SVR)			Expert Opinion;
F0-F2	$172.77	--	assumed to
F3-F4	$307.79	--	decrease by 50%
Decompensated cirrhosis	$583.53	--	after SVR

[a] All probabilities, incidences, and costs are monthly unless otherwise indicated
[b] Based on age- and sex-stratified annual mortality rates from USRDS 2019 Reference Sheet H.8_1 with overall mortality across all ages of 183.4 deaths per 1000 person-years
[c] Lower antibody sensitivity range represents estimate halfway in between historical low HCV antibody sensitivity estimates[31, 32] and more recent, small studies with sensitivity 94-100% in dialysis patients[33-35]
[d] False positive test costs include an HCV genotype and two established physician visits

Abbreviations: IDU, injection drug use; HCV, hepatitis C virus; SMR, standardized mortality ratio; HD, hemodialysis; PY, person-years; SVR, sustained virologic response (cure); RNA, ribonucleic acid

Supplemental Table 5: Breakdown of HCV Testing and Treatment Costs, Base Case Model

Strategy	HCV Antibody testing costs per person[a]	HCV RNA testing costs per person[a]	HCV treatment costs per person[a]	HCV treatment toxicity costs per person[a]
No Screening	$ -	$ -	$ -	$ -
Screen once upon entering dialysis center	$ 16.90	$ 9.29	$ 215.50	$ 0.05
Screen every 2 years	$ 45.46	$ 34.50	$ 238.49	$ 0.05
Screen every year	$ 77.58	$ 79.63	$ 243.87	$ 0.05
Screen every 6 months	$ 134.22	$ 211.40	$ 248.90	$ 0.05

[a] All per person costs represent the total number of tests or treatments completed or toxicity events recorded, multiplied by the individual cost per test, treatment, or toxicity (treatment costs include drug costs as well as visit costs for 2 months), divided by the total cohort size (N=200,000,000).

Abbreviations: HCV, hepatitis C virus; RNA, ribonucleic acid

Supplemental Table 6: Comparison of testing using RNA versus antibody testing

Strategy	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	$ 434,932	3.08722	Reference
Base Case: Screen once upon entering dialysis center	$ 435,587	3.09514	$82,739
RNA Testing Only: Screen once upon entering dialysis center	$ 435,637	3.09496	Dominated
Base Case: Screen every 2 years	$ 435,680	3.09580	$140,193
Base Case: Screen every year	$ 435,719	3.09574	Dominated
RNA Testing Only: Screen every 2 years	$ 435,812	3.09555	Dominated
Base Case: Screen every 6 months	$ 435,904	3.09604	$934,757
RNA Testing Only: Screen every year	$ 436,028	3.09597	Dominated
RNA Testing Only: Screen every 6 months	$ 436,375	3.09600	Dominated

Strategy	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	$ 434,934	3.08688	Reference
Lower Ab Sensitivity (88%): Screen once upon entering dialysis center	$ 435,535	3.09603	$65,653
RNA Testing Only: Screen once upon entering dialysis center	$ 435,637	3.09496	Dominated
Lower Ab Sensitivity (88%): Screen every 2 years	$ 435,642	3.09636	$324,554
Lower Ab Sensitivity (88%): Screen every year	$ 435,713	3.09646	$683,807
RNA Testing Only: Screen every 2 years	$ 435,812	3.09555	Dominated
Lower Ab Sensitivity (88%): Screen every 6 months	$ 435,920	3.09611	Dominated
RNA Testing Only: Screen every year	$ 436,028	3.09597	Dominated
RNA Testing Only: Screen every 6 months	$ 436,375	3.09600	Dominated

Abbreviations: RNA, ribonucleic acid; QALYs, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; Ab, antibody

Supplemental Table 7: Additional Sensitivity Analysis Results

Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
A. Low HCV Prevalence in Initial Cohort (0%)						
No Screening	0.18%	0.0%	0.0%	$434,865	3.0998	Ref
Screen every 2 years	0.15%	74.4%	64.5%	$434,911	3.0997	Dominated
Screen once upon entering dialysis center	0.16%	46.6%	39.9%	$434,929	3.1001	$202,640
Screen every year	0.14%	79.4%	69.4%	$435,010	3.1000	Dominated
Screen every 6 months	0.14%	85.0%	73.8%	$435,132	3.0997	Dominated
B. High HCV Prevalence in Initial Cohort (75%)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	5.56%	0.0%	0.0%	$434,976	3.0711	Ref
Screen once upon entering dialysis center	5.54%	95.8%	80.6%	$436,389	3.0887	$80,413
Screen every 2 years	5.53%	98.6%	89.0%	$436,555	3.0902	$108,301
Screen every year	5.52%	99.1%	91.2%	$436,692	3.0910	$174,801
Screen every 6 months	5.52%	99.4%	93.1%	$436,857	3.0913	$548,326
C. Low SMR for Injection Drug Use (1.27)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.59%	0.0%	0.0%	$439,148	3.1121	Ref
Screen once upon entering dialysis center	2.58%	94.0%	79.3%	$439,802	3.1201	$82,158
Screen every 2 years	2.57%	97.8%	88.4%	$439,914	3.1209	$136,716
Screen every year	2.56%	98.5%	90.6%	$440,002	3.1212	$304,076
Screen every 6 months	2.55%	99.0%	92.6%	$440,186	3.1215	$606,217
D. High SMR for Injection Drug Use (1.67)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)

No Screening	2.59%	0.0%	0.0%	$433,922	3.0812	Ref
Screen once upon entering dialysis center	2.57%	94.3%	79.4%	$434,536	3.0889	$80,454
Screen every 2 years	2.56%	97.8%	88.2%	$434,664	3.0898	$140,428
Screen every year	2.55%	98.5%	90.5%	$434,744	3.0900	$346,064
Screen every 6 months	2.54%	99.0%	92.5%	$434,870	3.0899	Dominated

E. Injection drug use initiation based on literature rates (new initiation and relapse simulated)

Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	4.48%	0.0%	0.0%	$433,300	3.0467	Ref
Screen once upon entering dialysis center	4.52%	53.8%	45.3%	$433,949	3.0544	$84,032
Screen every 2 years	4.88%	81.0%	71.9%	$434,171	3.0554	$218,934
Screen every year	4.94%	86.0%	77.3%	$434,299	3.0558	$307,879
Screen every 6 months	5.00%	90.7%	82.0%	$434,570	3.0566	$361,532

F. Low Injection Drug Use-Related HCV Incidence (8.5 cases/100PY)

Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.57%	0.0%	0.0%	$434,910	3.0871	Ref
Screen once upon entering dialysis center	2.56%	94.9%	79.9%	$435,544	3.0949	$81,573
Screen every 2 years	2.54%	98.1%	88.5%	$435,655	3.0957	$138,950
Screen every year	2.53%	98.7%	90.7%	$435,747	3.0960	$276,793
Screen every 6 months	2.53%	99.2%	92.7%	$435,890	3.0960	$6,174,977

G. High Injection Drug Use-Related HCV Incidence (17.8 cases/100PY)

Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.62%	0.0%	0.0%	$434,952	3.0873	Ref
Screen once upon entering dialysis center	2.60%	93.3%	78.6%	$435,587	3.0951	$81,474
Screen every 2 years	2.60%	97.4%	87.8%	$435,629	3.0954	$149,583
Screen every year	2.59%	98.1%	90.1%	$435,736	3.0958	$243,427
Screen every 6 months	2.59%	98.8%	92.2%	$435,941	3.0962	$483,293

H. Low HD Center Outbreak-Related HCV Incidence (1.68 cases/100 PY)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.53%	0.0%	0.0%	$434,923	3.0873	Ref
Screen once upon entering dialysis center	2.53%	94.3%	79.4%	$435,575	3.0952	$82,795
Screen every 2 years	2.53%	97.9%	88.4%	$435,671	3.0958	$147,177
Screen every year	2.53%	98.6%	90.7%	$435,712	3.0958	Dominated
Screen every 6 months	2.53%	99.1%	92.7%	$435,897	3.0961	$986,339
I. High HD Center Outbreak-Related HCV Incidence (31.8 cases/100 PY)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	3.01%	0.0%	0.0%	$434,992	3.0866	Ref
Screen once upon entering dialysis center	3.09%	92.9%	78.7%	$435,695	3.0948	$86,128
Screen every 2 years	2.94%	96.8%	87.0%	$435,766	3.0955	$96,486
Screen every year	2.87%	97.6%	89.2%	$435,793	3.0955	Dominated
Screen every 6 months	2.83%	98.2%	91.2%	$435,969	3.0958	$691,330
J. Low Cirrhosis Mortality Estimate (1 case/100PY for F4, 3 cases/100PY for decompensated cirrhotics)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.59%	0.0%	0.0%	$435,413	3.0891	Ref
Screen once upon entering dialysis center	2.58%	94.2%	79.4%	$435,635	3.0952	$36,199
Screen every 2 years	2.57%	97.8%	88.5%	$435,731	3.0961	$113,170
Screen every year	2.56%	98.5%	90.7%	$435,748	3.0959	Dominated
Screen every 6 months	2.55%	99.0%	92.7%	$435,964	3.0964	$673,136
K. High Cirrhosis Mortality Estimate (5 cases/100PY for F4, 30 cases/100PY for decompensated cirrhosis; no improvement in mortality post-SVR)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.59%	0.0%	0.0%	$434,752	3.0865	Ref

Screen once upon entering dialysis center	2.58%	94.2%	79.2%	$435,236	3.0929	$75,329
Screen every 2 years	2.57%	97.8%	88.0%	$435,344	3.0937	$147,155
Screen every year	2.56%	98.5%	90.4%	$435,403	3.0938	$708,005
Screen every 6 months	2.55%	99.0%	92.4%	$435,646	3.0945	$343,574
L. Background HCV Screening Simulated (20.8% over 5 years)						
Strategy	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.59%	20.3%	17.2%	$435,060	3.0886	Ref
Screen once upon entering dialysis center	2.58%	95.1%	81.7%	$435,593	3.0952	$81,388
Screen every 2 years	2.57%	97.8%	88.4%	$435,643	3.0955	$153,458
Screen every year	2.56%	98.5%	90.6%	$435,756	3.0960	$249,146
Screen every 6 months	2.55%	99.0%	92.6%	$435,905	3.0960	$3,852,721
M. HCV Antibody and RNA Test Cost Lower Estimate (25th% Gamma Distribution)						
	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.57%	0.00%	0.0%	$435,268	3.0892	Ref
Screen once upon entering dialysis center	2.55%	94.20%	79.3%	$435,907	3.0970	$82,144
Screen every 2 years	2.54%	97.82%	88.2%	$436,070	3.0982	$135,548
Screen every year	2.53%	98.49%	90.5%	$436,111	3.0982	Dominated
Screen every 6 months	2.53%	99.01%	92.5%	$436,275	3.0985	$688,031
N. HCV Antibody and RNA Test Cost Higher Estimate (75th% Gamma Distribution)						
	HCV Infections (%)	HCV Infections Identified, Lifetime (%)	SVR Achieved (% of total infections)	Discounted Cost ($)	Discounted QALYs	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	2.57%	0.00%	0.0%	$435,265	3.0892	Ref
Screen once upon entering dialysis center	2.55%	94.22%	79.4%	$435,937	3.0972	$84,412
Screen every 2 years	2.54%	97.83%	88.2%	$436,069	3.0981	$147,171
Screen every year	2.53%	98.50%	90.5%	$436,188	3.0985	$269,120
Screen every 6 months	2.53%	99.02%	92.5%	$436,305	3.0982	Dominated

Abbreviations: HCV, hepatitis C virus; SVR, sustained virologic response (cure); QALYs, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; SMR, standardized mortality ratio; HD, hemodialysis

Supplemental Table 8: Probabilistic Sensitivity Analysis Results

Strategy	Median Average Lifespan	95% Confidence Estimates	Median Average Discounted Cost	95% Confidence Estimates	Median Average Discounted QALYs	95% Confidence Estimates	Incremental Cost-Effectiveness Ratio (ICER)
No Screening	5.2242	(5.2150, 5.2332)	$ 435,308	($434,611, $435,989)	3.0895	(3.0846, 3.0942)	--
Screen once upon entering dialysis center	5.2311	(5.2221, 5.2396)	$ 435,940	($435,304, $436,577)	3.0973	(3.0926, 3.1018)	$81,472
Screen every 2 years	5.2315	(5.2232, 5.2405)	$ 436,043	($435,381, $436,707)	3.0979	(3.0933, 3.1026)	$162,795
Screen every year	5.2317	(5.2232, 5.2401)	$ 436,131	($435,494, $436,762)	3.0982	(3.0937, 3.1027)	$315,644
Screen every 6 months	5.2318	(5.2233, 5.2404)	$ 436,293	($435,640, $436,943)	3.0983	(3.0937, 3.103)	$900,024

Abbreviations: HCV, hepatitis C virus; QALYs, quality-adjusted life years; ICER, incremental cost-effectiveness ratio

Supplemental Figure 2: Probabilistic Sensitivity Analyses Cost Effectiveness Acceptability Curve

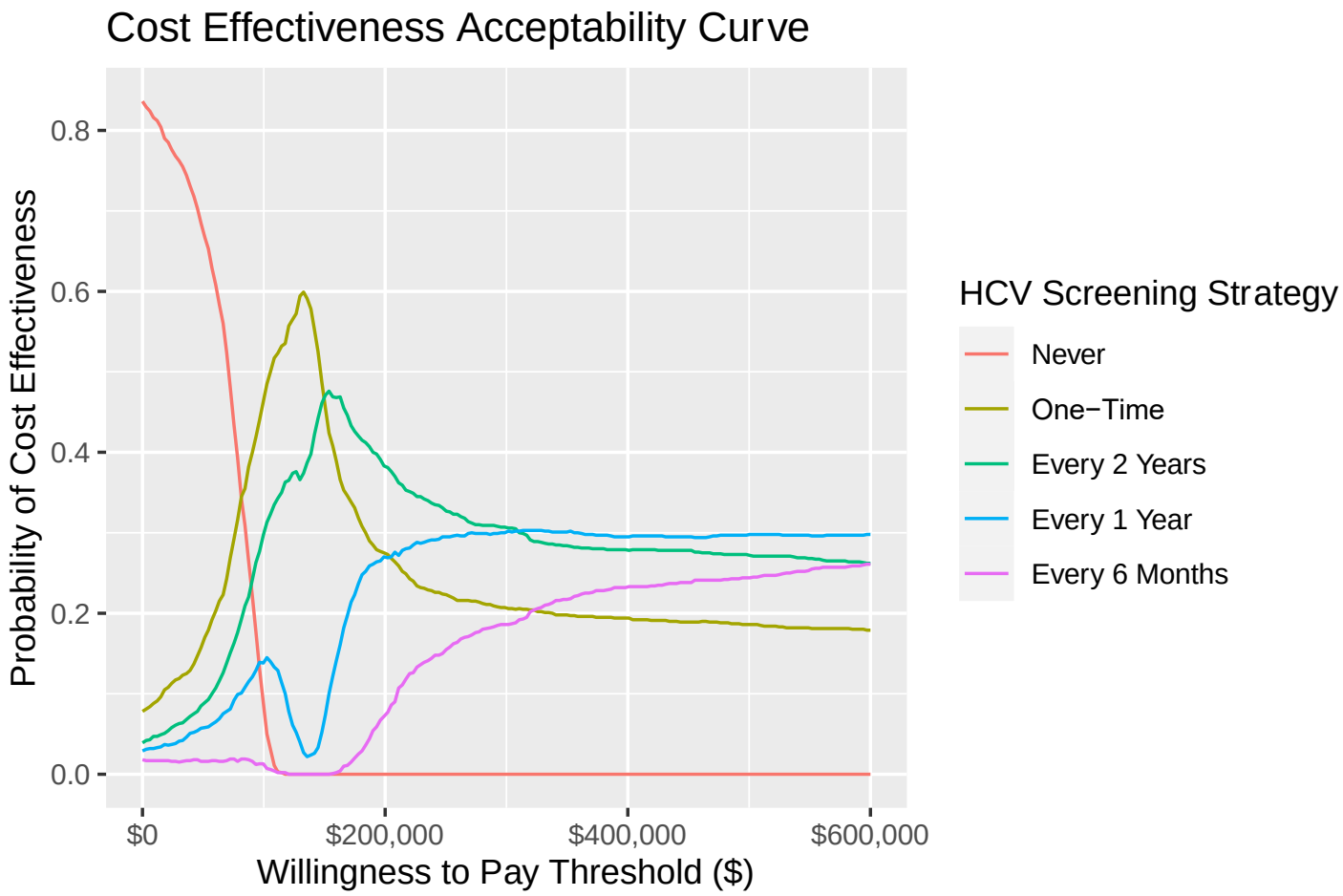


Figure Legend:

This graph represents the cost effectiveness acceptability curve (CEAC) for the probabilistic sensitivity analysis varying several parameters (HCV antibody and RNA test cost, treatment cost, outbreak-related HCV incidence, mortality from cirrhosis, and antibody and RNA test sensitivity and specificity). The x-axis is the willingness-to-pay threshold in $US and the y-axis is the probability that a given strategy will be the 'winner' at the corresponding willingness-to-pay threshold: the strategy that yields the highest number of quality adjusted life years (QALYs) for a cost under the willingness-to-pay threshold. The probability was determined by doing 1000 runs, each with a different set of parameters drawn from the probability distributions noted in Supplemental Table 5, and then calculating the strategy with the highest net monetary benefit (NMB; NMB = QALYs gained * willingness-to-pay threshold – incremental costs comparing each strategy to the next least expensive, non-dominated strategy) at each willingness-to-pay threshold.

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