

Evaluating HCV Screening, Linkage to Care, and Treatment Across Insurers

eAppendix

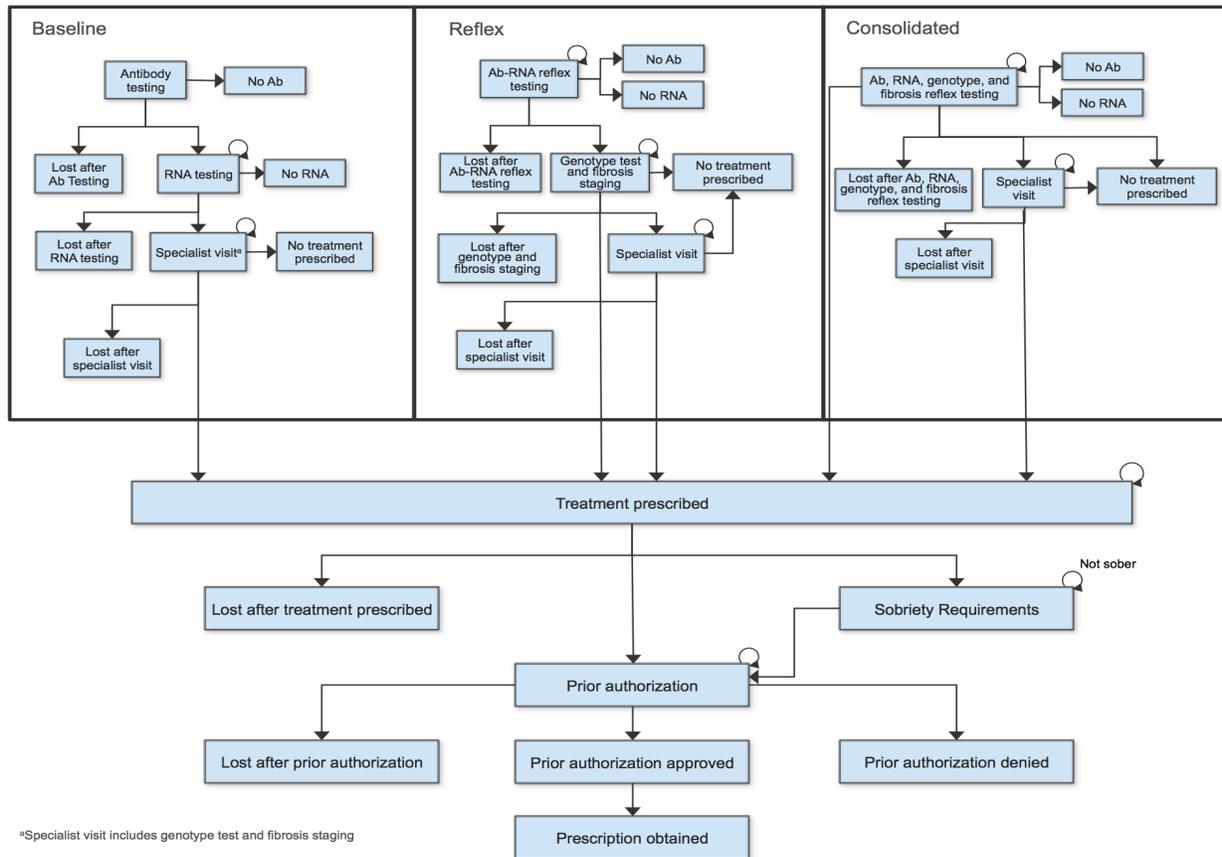
1. Conceptual model

Current guidelines recommend a 1-time screening for hepatitis C virus (HCV) for individuals born between 1945 and 1965 and individuals with increased risk of HCV infection, but initial screening only represents the first stage in the screening and linkage-to-care (SLTC) process.¹ The SLTC process includes: an initial HCV-antibody test, confirmatory RNA testing for patients who test positive for HCV antibodies, and additional diagnostics for those who test RNA positive, which means the patient has chronic HCV. Additional diagnostics include genotype testing and fibrosis staging. Whether a specialist is required in the SLTC is a function of patient fibrosis stage since current guidelines still recommend subspecialty care and consultation for patients with advanced fibrosis or cirrhosis.¹ Later stages in the SLTC process may include meeting sobriety requirements or prior authorization (PA), which depend on insurance status. We developed a discrete time Markov model to simulate the HCV SLTC process, and estimate three model scenarios as described in Section 2. Model states were adapted from HCV management and treatment guidance for clinicians and laboratorians published by the Centers for Disease Control and Prevention (CDC).² A cohort of 10,000 patients begins in the initial antibody screening stage, and patients are followed until they complete the screening process or are lost to follow-up (henceforth “lost”).

2. Model scenarios and outputs

We estimated three model scenarios, altering the minimum number of visits required to obtain a treatment recommendation: Baseline, Reflex, and Consolidated. Baseline requires four visits for a patient with chronic HCV to receive a treatment decision, and represents the least efficient screening process compared to the two scenarios with fewer visits. In Reflex, chronically infected patients require a minimum of three visits for a treatment decision, and in Consolidated, a minimum of two visits is required. Each model cycle is 1 week, and we do not include mortality in the model.

Figure 1. Model Schematics



2.1. Baseline scenario

The Baseline scenario states and transitions are shown in Figure 1, and it was adapted from the guidance for clinicians and laboratorians published by the Centers for Disease Control and Prevention (CDC).² The Baseline model includes the SLTC steps recommended in the current HCV guidelines, in which each step in the screening process requires an entirely separate visit and patients must receive their treatment decision from a specialist. All patients are required to see a specialist for genotype testing and fibrosis staging.

We assume a cohort of patients enter the model and receive an antibody test. Patients who are HCV antibody-negative have not been exposed to HCV and do not require additional testing; they are therefore considered to have completed the screening process. Patients who are antibody-positive (Ab+) have been exposed to HCV, but their disease status is as yet unknown. They either continue to HCV RNA testing or are lost.

The second stage in the screening process is HCV RNA testing for patients who have tested Ab+. RNA testing is the confirmatory, definitive test for the presence of active disease.

Patients who are HCV RNA-negative do not have active disease, require no further testing, and are considered to have completed the screening process. Patients who test HCV RNA-positive have chronic HCV, and either continue to a specialist visit for further testing or are lost.

In the specialist visit stage, chronically infected patients are tested for genotype and receive non-invasive liver fibrosis staging. At this stage, patients receive a ‘no treatment recommended’ decision, or prescription for HCV treatment, or are lost. Patients who receive a ‘no treatment recommended’ decision have completed the screening process.

Once a treatment recommendation is provided and a prescription for medication is written, patients must transition through additional stages before receiving actual drug therapy. Preliminary findings from the National Viral Hepatitis Roundtable (NVHR) show that at least 29 states require some degree of sobriety, ranging from 1-12 months.³ Medicaid patients must meet sobriety requirements to confirm they are not active users. Once patients have passed the requirement, they must obtain PA before they receive treatment. Medicare and commercial patients do not face sobriety requirements, but they must obtain PA from their health plans before they receive treatment. Patients who reach the PA stage are either denied, approved, or lost to follow-up. Patients who are denied PA may submit an appeal. Rather than model the appeals process explicitly, we generated the final set of PA-related transition probabilities for patients who are approved, denied, or lost based on the final decisions after appeal in our data. Patients who are denied PA are assumed to have completed the screening process. Patients who are approved for PA initiate treatment in the next model cycle. We assume no patients who are approved for prior authorization are lost.

2.2. Reflex scenario

Reflex (shown in Figure 1) also includes the SLTC steps recommended in the current HCV guidelines, but introduces reflex testing for the antibody and HCV RNA tests (that is, two blood samples are drawn at the first visit, and if the first sample is Ab+, the second sample is automatically tested for HCV RNA without requiring a separate visit and blood draw).^{5,6} By consolidating these two steps with reflex testing, it is possible to complete Reflex in 3 visits rather than 4.

Reflex also assumes patients receive genotype testing and fibrosis staging prior to an optional specialist visit. Rather than use cirrhosis as the cutoff for complex cases, we assumed

patients with fibrosis scores below F2 are less complex to be conservative in our estimate of the number of patients who do not see a specialist. The Kaiser Permanente Mid-Atlantic States⁵ (KPMAS) screening pathway provides 1 example of using F2 as a cutoff value in the SLTC. Although the KPMAS pathway does require all patients who initiate treatment to see a specialist, patients with fibrosis below F2 see a PCP for monitoring and those with scores F2 or higher see a specialist. In our model, if a patient does not require a specialist visit, then their treatment recommendation is given by a PCP. We assume 60% of patients require a specialist visit.⁸ All states in Reflex after the treatment recommendation are the same as in Baseline.

2.3. Consolidated scenario

Consolidated is shown in Figure 1 and represents a hypothetical “best case” scenario, in which all tests (antibody, RNA, fibrosis staging, and genotype testing) are reflexed and a specialist visit is only required for patients with fibrosis score F2 or higher. All states in Consolidated after the treatment recommendation are the same as in Baseline. This scenario requires a minimum of 2 visits for chronically infected patients to receive a treatment decision, and therefore provides the fewest opportunities for patients to be lost before completing the screening process.

3. Model parameters and outcomes

3.1. Transition parameters

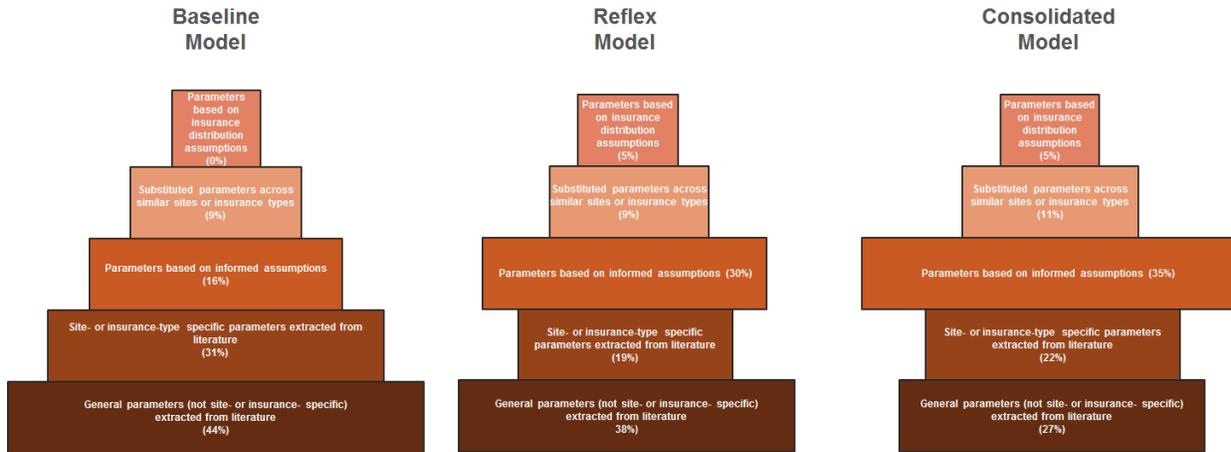
3.1.1. Baseline Scenario

Baseline required estimates for 30 different transition probabilities. A hierarchy was used in selecting model parameters which would allow for insurance stratifications, or that represented the population more generally. The specific hierarchy for selecting model transition parameters is as follows: 1) insurance-type specific parameters; 2) general parameters (ie not specific to any insurance); 3) substituted parameters across similar insurance types; and 4) parameters based on informed assumptions.

While ideally, we would select parameters based on this hierarchy alone, to construct and run a model that would produce results, it was necessary to assure that the transition parameters leading out of a model state summed to 1.0. This requirement implied that combining parameters from different references could potentially violate mathematical constraints. In order to mitigate this possibility, we attempted to identify 1 published source that contained multiple

parameters in the screening process. When we had to select parameters piecewise across different sources, we selected parameters that did not violate the summing-to-one constraint. Each transition matrix was normalized to account for small differences resulting from numerical precision.

Figure 2. Visual distribution of Parameter Sources for Baseline, Reflex, and Consolidated



3.1.2. Reflex and Consolidated scenarios

Transition parameters for the first steps of the Reflex and Consolidated models were generally not available in the literature due to the slow adoption of reflex testing in sites other than the VA; therefore, transition parameters were derived using Baseline parameters and assumptions. We assumed HCV prevalence is not impacted by reflex testing; we therefore used prevalence parameters from Baseline in Reflex and Consolidated. Second, we assumed the proportion of patients lost in Reflex and Consolidated should be lower relative to Baseline since these scenarios do not require a specialist visit. Accordingly, we modified the Baseline parameters for Reflex and Consolidated as described in Section 3.1.2.1.

Table 1. Summary of Model Scenarios and Steps

	Baseline – Worst Case (4-visit minimum)	Reflex – Moderate Case (3-visit minimum)		Consolidated – Best Case (2-visit minimum)	
		Fibrosis: F0-F1	Fibrosis: F2+	Fibrosis: F0-F1	Fibrosis: F2+
Step 1	Ab testing ^a	Ab testing with HCV RNA reflex testing ^b		“Visit 1”: Ab testing with reflex HCV RNA testing, followed by reflex GT testing and fibrosis staging (no specialist required) ^c	

Step 2	HCV RNA testing Lost parameters from literature	Genotype test and fibrosis staging (no specialist required) ^d		Treatment recommendation ^e from PCP	Specialist visit
Step 3	Specialist visit (including genotype test and fibrosis staging) ^f	Treatment recommendation ^e from PCP	Specialist visit		Treatment recommendation ^e from specialist ^g
Step 4	Treatment recommendation ^e		Treatment recommendation ^e from specialist ^g		

Notes: ^aLost parameters from Armstrong et al.⁴; ^bLost parameter from Jonas et al⁵; ^cLost parameter calculated using Reflex Model genotype lost parameter and Baseline Model parameters. See equations (1)-(3).; ^dLost parameter calculated using Baseline Model parameters and Jonas et al⁵ See equations (1)-(2).; ^eTreatment recommendation includes both “No prescription” and “Treatment prescribed”; ^fLost parameter from Butt et al⁶; ^gLost parameter equal to 0.01 by assumption.

3.1.2.1. Reflex and Consolidated Lost Parameter Derivations

For Baseline, we defined the lost parameters associated with steps 1 and 2 in Table 1 as:

$$P(X_{t+1} = Lost | X_t = RNA\ Test)^i$$

$$= \textit{proportion lost after RNA testing for site/insurer } i$$

$$P(X_{t+1} = Lost | X_t = Specialist\ Visit)^i$$

$$= \textit{proportion lost after specialist visit for site/insurer } i$$

The RNA test (step 1) and specialist visit (step 2) in Baseline are analogous to Ab-RNA reflex testing and genotype/fibrosis staging in Reflex, respectively. Similarly, step 1 in Baseline is analogous to “Visit 1” (ie, fully reflexed Ab-RNA-genotype-fibrosis) in Consolidated. The lost parameter that corresponds to Ab-RNA reflex testing in Reflex is available in the literature (25% according to Jonas et al).⁵

However, the lost parameter associated with genotype/fibrosis staging in Reflex is not available in the literature, nor is the lost parameter that corresponds to “Visit 1” for

Consolidated. We derive these two missing parameters using analogous lost parameters from Baseline, which were available in the literature.

3.1.2.1.1. Reflex scenario: proportion lost after genotype/fibrosis staging

According to Jonas et al⁵, 25% of patients are lost after Ab-RNA reflex testing (before receiving genotype testing and fibrosis staging). We therefore define the lost parameter following Ab-RNA reflex testing (ie, step 1 in Table 1) for Reflex:

$$P(X_{t+1} = Lost|X_t = AbRNA)^i = \text{proportion lost after AbRNA reflex testing} \quad (1)$$

$$= 0.25$$

We assume the percent change in the proportion of patients lost following steps 1 and 2 in Table 1 will be the same across Baseline and Reflex. Since this value is known for Baseline, we can apply it to Reflex. The percent change in proportion lost for the RNA and specialist states from Baseline is given by:

$$\% \Delta Lost_{RNA,Spec}^i = \frac{P(X_{t+1} = Lost|X_t = Specialist\ Visit)^i - P(X_{t+1} = Lost|X_t = RNA\ Test)^i}{P(X_{t+1} = Lost|X_t = RNA\ Test)^i} * 100 \quad (2)$$

where $P(X_{t+1} = Lost|X_t = RNA\ Test)^i$ and $P(X_{t+1} = Lost|X_t = Specialist\ Visit)^i$ are from the literature.

The proportion lost following genotype/fibrosis testing (ie, step 2 in Table 1) in Reflex reflects the proportion lost following Ab-RNA reflex (step 1), 25%, and the percent change in proportion of patients lost following steps 1 and 2 as calculated from Baseline:

$$P(X_{t+1} = Lost|X_t = Genotype)^i$$

$$= \text{proportion lost after genotype/fibrosis staging for site/insurer } i$$

$$= 0.25 * (1 - \% \Delta Lost_{RNA,Spec}^i) \quad (3)$$

3.1.2.1.2. Consolidated scenario: proportion lost after "Visit 1"

For Consolidated, we assume the proportion lost following "Visit 1" should be less than the proportion lost after the genotype/fibrosis test in Reflex since patients have only had one visit in Consolidated after genotype/fibrosis testing compared to two in Reflex.

To construct the lost parameter associated with “Visit 1”, we assume the unadjusted proportion lost after “Visit 1” will equal the proportion lost after genotype/fibrosis testing in Reflex ($P(X_{t+1} = Lost|X_t = Genotype)^i$). We then adjust the baseline proportion lost downward by the percent change in proportion of patients lost following steps 1 and 2 as calculated from Baseline:

$$P(X_{t+1} = Lost|X_t = Visit1)^i = P(X_{t+1} = Lost|X_t = Genotype)^i * (1 - \% \Delta Lost_{RNA,Spec}^i) \quad (4)$$

where i indexes insurance type.

All transition parameters after the treatment recommendation are the same across the three scenarios. Transition parameters are provided in Table 2 below.

Table 2. Transition Parameters (%)

	Medicaid	Medicare	Commercial
Disease Prevalence			
Proportion Ab Positive	16.0% ⁷	9.0% ⁸	5.0% ^{b 8}
Proportion RNA Positive	79.7% ^{a 4}	79.7% ^{a 4}	79.7% ^{a 4}
Treatment Decision			
Treatment prescribed	54.8% ^{a 9}	54.8% ^{a 9}	54.8% ^{a 9}
No Treatment prescribed	25.2% ^d	25.2% ^d	25.2% ^d
Drug Testing and Prior Authorization			
Probability of drug testing	99.0% ^d	0.0%	0.0%
Probability of pass drug test	71.0% ^{a 10}	N/A	N/A
Probability of PA approved ^e	51.1%	81.0%	40.0%
Probability of PA denied ^e	45.9%	13.2%	55.4%
Lost to Follow Up (<i>Baseline</i>)			
Lost after Ab Testing	21.2% ^{b 4}	21.2% ^{b 4}	21.2% ^{b 4}
Lost after RNA Testing	83.0% ^{f 11}	72.7% ^{b 9}	72.7% ^{b 9}
Lost after Specialist	20.0% ^{d 6}	20.0% ^{d 6}	20.0% ^{d 6}
Lost after treatment prescribed	1.0% ^{b 12}	1.0% ^{b 12}	1.0% ^{b 12}
Lost after PA ^e	3.0%	5.8%	4.6%

Lost to Follow Up (<i>Reflex</i>)			
Lost after Genotyping and Fibrosis Test ^g	6.0%	6.9%	6.9%
Lost to Follow Up (<i>Consolidated</i>)			
Lost after Ab, RNA, Genotype, and Fibrosis Test ^g	1.5%	1.9%	1.9%
Treatment Recommendation and Optional Specialist Parameters (<i>Reflex</i>)			
Treatment prescribed by PCP ^h	19.1%	20.0%	7.2%
No Treatment prescribed by PCP ^h	15.8%	16.5%	22.8%
Optional specialist visit ^h	52.4%	54.7%	45.0%
Treatment Recommendation and Optional Specialist Parameters (<i>Consolidated</i>)			
Treatment prescribed by PCP ^h	20.5%	21.2%	9.6%
No Treatment prescribed by PCP ^h	16.9%	17.5%	30.4%
Optional specialist visit ^h	56.1%	58.1%	60.0%
Notes: We assume prevalence is the same for Baseline, Reflex, and Consolidated.			
^a Insurance-specific parameter not available; general parameter used. ^b Commercial-specific parameter used, but was taken from PCP setting ^c Uninsured-specific parameter used, but was taken from ED setting ^d Calculated ^e Gilead PA adjudication data ^f Medicaid parameters derived from a source focused on emergency room patients ^g Parameters derived from Baseline model. The proportion of patients lost after the (optional) specialist visit is assumed to be 0.01 in both Reflex and Consolidated Models. Once treatment is prescribed, the states and transitions for the Reflex and Consolidated Models are the same as the Baseline Model. ^h The proportion of patients who visit a specialist and are not prescribed treatment is 0.06 ¹³ . We assume the proportion of patients lost after seeing a specialist is 0.01, and therefore the proportion of patients who receive prescriptions is 0.93 so that the transitions sum to 1.			

3.2. Timing parameters

A model with more narrowly defined states would have required more nuanced parameters.

Given that we were unable to populate all model transitions without relying on assumptions to

fill in gaps in the literature, it is unlikely we would have been able to populate a more nuanced version of the model for many of the insurance types. Rather than model these intermediate steps explicitly, we implicitly capture them by incorporating wait times (implemented using transitions of the form $P(X(t+1)=A|X(t)=A) > 0$ for each state A that has a wait time longer than one cycle) for each screening state.

Few timing parameters were available in the literature. Time for prior authorization was calculated using adjudication data provided by Gilead. We relied on various assumptions about timing to fill in gaps. The following table shows the Baseline timing parameters for each insurance type selected based on literature and assumption.

Table 3. Baseline Timing Parameters

	Medicaid	Medicare	Commercial
Ab test to RNA test	51 days ⁹	51 days ⁹	51 days ⁹
RNA test to Specialist Visit ^a	2.5 months	2.5 months	2.5 months
Specialist Visit to Treatment Recommendation ^b	0 days	0 days	0 days
Treatment Recommendation to Drug and Alcohol Testing ^b	0 days	N/A	N/A
Time between Failed Drug and Alcohol Test and Subsequent Test	4.5 months	N/A	N/A
Prior Authorization request to prior authorization decision ^c	8.5 days	20.2 days	19.4 days
<p>^a Assumed to have PCP; Assumed 2.5 months for specialist referral. These assumptions are consistent with published estimates for time between RNA testing and specialist visit for the VA population (9 weeks)¹⁴</p> <p>^b Specialist visit, treatment recommendation, and drug and alcohol testing (if required) are assumed to take place during the same visit. For patients who receive a ‘clean’ result for their drug test, we assume they move to the prior authorization step immediately.</p> <p>^c Based on adjudication data provided by Gilead</p>			

3.3. Cost parameters

Costs were assigned to each state in the screening process based on the test conducted in that state. Costs were obtained using the CMS Physician Fee and Laboratory Fee schedules.^{15,16} The specific testing procedure was identified by the appropriate *Current Procedural Terminology* (CPT) or Healthcare Common Procedure Coding System (HCPCS) code to distinguish these tests from related tests, given in Table 4.

Table 4. Model Costs and Sources

Cost	CPT Code	Model Parameter
HCV antibody test	86803	\$19.44
Quantitative HCV RNA test	87521 (amplified probe technique)	\$47.80
Genotype test	87902	\$350.69
Non-invasive liver fibrosis staging	76700	\$124.69
Specialist Visit	99204	\$166.73
Alcohol and/or drug screening with brief intervention, Medicaid	H0050 (HCPCS code)	\$48

As the model ends with treatment initiation, treatment costs were not included in the analysis.

We assumed there was no direct cost associated with PA. Since we assume a patient perspective for cost, we do not incorporate the overhead cost associated with screening site operation or other health system costs.

3.4. Model outcomes

The following key outcomes were measured in the model: yield, yield conditional on HCV infection, number lost to follow-up, and costs. Yield was defined as the percentage of patients entering the model for HCV antibody screening who complete the process and initiate treatment. Conditional yield was defined as the percentage of patients who are either Ab+ or chronically infected with HCV who complete the process and initiate treatment. The number of patients lost to follow-up is calculated after each stage and for the entire process. We also calculated total cost

(which includes screening cost and treatment cost), total cost of screening, total cost of screening per person treated, and total cost of screening per person screened.

4. Additional Results

4.1. Yields

Table 5 presents the same yield results from the main manuscript, and additionally presents yield conditional on Ab+ status. The key difference between a chronically infected patient and a patient who is Ab+ but not chronically infected is that the chronically infected patient requires treatment, but an Ab+ patient who is not chronically infected only needs a confirmatory RNA test to successfully complete the SLTC process.

Table 5. Yield and conditional yield results

		Medicaid	Medicare	Commercial
Yield	Baseline	0.5%	0.7%	0.2%
	Reflex	3.5%	3.1%	0.9%
	Consolidated	4.9%	4.4%	1.2%
Conditional yield (Ab+ patients)	Baseline	2.9%	7.5%	3.7%
	Reflex	22.1%	34.6%	17.1%
	Consolidated	30.9%	48.6%	24.0%
Conditional yield (RNA+ patients)	Baseline	3.7%	9.5%	4.8%
	Reflex	27.7%	43.5%	21.6%
	Consolidated	38.7%	61.1%	30.2%

4.2. Costs

Table 6. Screening costs for a cohort of 10,000 patients entering the screening process

		Medicaid	Medicare	Commercial
Total screening cost (total patients treated)	Baseline	\$368,598 (47)	\$328,648 (68)	\$269,337 (19)
	Reflex	\$819,606 (354)	\$523,952 (312)	\$377,585 (86)
	Consolidated	\$1,012,774 (494)	\$628,475 (438)	\$436,164 (120)
Cost of screening, per-person treated	Baseline	\$7,843	\$4,833	\$14,176
	Reflex	\$2,324	\$1,680	\$4,430
	Consolidated	\$2,049	\$1,446	\$3,615
Cost of screening, per-person screened	Baseline	\$37	\$33	\$27
	Reflex	\$82	\$52	\$38
	Consolidated	\$101	\$63	\$44
Cost to identify one additional	Baseline	\$1,586	\$1,539	\$2,546
	Reflex	\$283	\$441	\$730

chronically infected patient and link to care	Consolidated	\$212	\$331	\$548
-----------------------------------------------	--------------	-------	-------	-------

Notes: All costs are in 2016 USD. Total screening cost includes the cost of diagnostic tests, the cost of a specialist visit (when applicable), and the cost of drug testing (Medicaid population only). Diagnostic tests include: antibody testing, RNA testing, non-invasive fibrosis staging, and genotype testing.

4.3. Timing Results

Table 7 presents total treated, yield, and yield conditional on RNA+ for three-, six-, and twelve-month time horizons. These results provide insight into how quickly patients are able to complete the SLTC process. Note that most patients are have completed the process within the first year; therefore, the 12-month results are similar to the full lifetime horizon results presented in the manuscript.

Table 7. Timing results: 3-month, 6-month, and 12-month horizons

		Number Treated (% of Total Ultimately Treated)			Yield (Yield, Conditional on RNA+)		
		3 months	6 months	12 months	3 months	6 months	12 months
Commercial	Baseline	5 (29%)	14 (75%)	18 (98%)	0.1% (1%)	0.1% (3%)	0.2% (5%)
	Reflex	56 (66%)	77 (90%)	85 (99%)	0.6% (14%)	0.8% (19%)	0.8% (21%)
	Consolidated	83 (98%)	110 (99%)	119 (99%)	0.8% (21%)	1.1% (28%)	1.2% (30%)
Medicaid	Baseline	10 (22%)	34 (72%)	46 (98%)	0.1% (1%)	0.3% (3%)	0.5% (4%)
	Reflex	212 (60%)	314 (89%)	350 (99%)	2.1% (17%)	3.1% (25%)	3.5% (27%)
	Consolidated	217 (64%)	444 (90%)	490 (99%)	3.2% (25%)	4.4% (35%)	4.9% (38%)
Medicare	Baseline	19 (29%)	205 (66%)	303 (69%)	0.2% (3%)	0.5% (7%)	0.7% (9%)
	Reflex	51 (75%)	282 (90%)	400 (91%)	2.1% (29%)	2.8% (39%)	3.1% (43%)
	Consolidated	66 (98%)	310 (99%)	435 (99%)	3.0% (42%)	4.0% (56%)	4.4% (61%)

5. Alternative analyses and results

We estimated three alternative scenarios for each model: 1) Fixed Ab prevalence: to evaluate the effect of prevalence on model outcomes, we used a fixed prevalence across all insurers; 2) No Genotype Testing: assumed the genotype test was not required as part of the screening process (ie to estimate results if a pan-genotypic treatment is available); 3) No Sobriety Requirements: assumed Medicaid patients did not face sobriety requirements.

5.1. Fixed Ab prevalence

The fixed Ab prevalence analysis allows us to compare the efficiency of the SLTC process across insurance types net of differences in prevalence. Table 8 shows the difference in prevalence (ie, the proportion of patients who are Ab+) across the main analysis and this alternative analysis. The prevalence estimate for the fixed Ab analysis was derived using the average of prevalence across multiple sources that incorporated patients with various insurance types who were screened at different sites.^{7,11,14,17-22}

Table 8. Proportion Ab+, by analysis and insurance type

	Medicaid	Medicare	Commercial
Main analysis	0.160	0.090	0.050
Fixed Ab prevalence	0.128		

Table 9. Fixed Ab Prevalence: Lost to follow-Up and yield results for a cohort of 10,000 patients entering the screening process

		Medicaid	Medicare	Commercial
Number of patients lost to follow-up (% of Ab positive)	Baseline	969	908	906
	Reflex	329	354	348
	Consolidated	46	78	69
Yield	Baseline	0.4%	1.0%	0.5%
	Reflex	2.8%	4.5%	2.2%
	Consolidated	3.9%	6.2%	3.1%
Conditional yield (Ab+ patients)	Baseline	2.7%	7.5%	3.7%
	Reflex	20.1%	34.6%	17.1%
	Consolidated	27.9%	48.3%	23.9%
Conditional yield (RNA+ patients)	Baseline	4%	9%	5%
	Reflex	28%	43%	21%
	Consolidated	38%	60%	30%
Required # of patients screened	Baseline	25	20	20

to get 1 additional HCV patient into treatment	Reflex	13	13	13
	Consolidated	10	10	10

Table 10. Fixed Ab Prevalence: Cost results for a cohort of 10,000 patients entering the screening process

		Medicaid	Medicare	Commercial
Total screening cost (total patients treated)	Baseline	\$334,217 (38)	\$383,338 (96)	\$383,177 (47)
	Reflex	\$696,751 (280)	\$666,083 (446)	\$667,503 (220)
	Consolidated	\$838,441 (389)	\$812,488 (623)	\$808,152 (308)
Cost of screening, per-person treated	Baseline	\$8,795	\$3,993	\$8,153
	Reflex	\$2,488	\$1,493	\$3,034
	Consolidated	\$2,155	\$1,304	\$2,624
Cost of screening, per-person screened	Baseline	\$33	\$38	\$38
	Reflex	\$70	\$67	\$67
	Consolidated	\$84	\$81	\$81
Cost to identify one additional chronically infected patient and link to care	Baseline	\$646	\$521	\$521
	Reflex	\$336	\$332	\$332
	Consolidated	\$256	\$251	\$251

5.2. Removal of genotype testing

With the recent availability of a pan-genotypic treatment, the genotype testing stage might eventually become unnecessary for patients. To evaluate the effect of the genotype testing stage on model outcomes, we removed this requirement for all insurers. Since genotype testing occurs during the same visit as non-invasive fibrosis staging, removing genotype testing only impacts costs in our model. Table 11 shows the costs associated with screening a cohort of 10,000 patients, with and without a required genotype test.

Table 11. No Genotype Testing: Screening costs for a cohort of 10,000 patients entering the screening process

		Medicaid	Medicare	Commercial
<i>Main Analysis</i>				
	Baseline	\$368,598 (47)	\$328,648 (68)	\$269,337 (19)
	Reflex	\$819,606 (354)	\$523,952 (312)	\$377,585 (86)

Total screening cost (total patients treated)	Consolidated	\$1,012,774 (494)	\$628,475 (438)	\$436,164 (120)
Cost of screening, per-person treated	Baseline	\$7,843	\$4,833	\$14,176
	Reflex	\$2,324	\$1,680	\$4,430
	Consolidated	\$2,059	\$1,446	\$3,615
<i>Removal of Genotype Testing</i>				
Total screening cost (total patients treated)	Baseline	\$ 308,312 (47)	\$ 273,499 (68)	\$ 238,296 (19)
	Reflex	\$ 552,851 (354)	\$ 378,257 (213)	\$ 295,064 (86)
	Consolidated	\$ 660,613 (494)	\$ 428,435 (438)	\$ 324,741 (120)
Cost of screening, per-person treated	Baseline	\$ 6,510	\$ 4,033	\$ 12,809
	Reflex	\$ 1,564	\$ 1,211	\$ 3,445
	Consolidated	\$ 1,336	\$ 978	\$ 2,701

5.3. Removal of sobriety requirements

Finally, we removed the sobriety requirement for the Medicaid group. Since we assume patients who reach the sobriety requirement state in the model cannot be lost between the sobriety requirement and prior authorization, yields do not change relative to the main analysis.

Removing sobriety requirements impacts the cost of screening, which is presented in Table 12. Specifically, we find that removing sobriety requirements reduces total costs by 1% in Baseline and 4.5% in Reflex and Consolidated. Comparing total costs across the main results and no sobriety requirements analysis, the overall effect of removing sobriety requirements in a cohort of 10,000 patients may make it seem that sobriety requirements have a relatively small impact. However, if we apply the cost-savings to a cohort equal to the total estimated number of adults enrolled in Medicaid in January 2017 for states with sobriety requirements (approx. 23.4 million), removing sobriety requirements in all these states would save Medicaid \$9.2 million in Baseline, \$86.0 million in Reflex, and \$106.7 million in Consolidated.

Table 12. No Sobriety Requirements: Screening Costs Associated with Removal of Sobriety Requirements for the Medicaid Population

		Medicaid
<i>Main Analysis</i>		
Total screening cost (total patients treated)	Baseline	\$368,598 (47)
	Reflex	\$819,606 (354)
	Consolidated	\$1,012,774 (494)
	Baseline	\$7,843

Cost of screening, per-person treated	Reflex	\$2,324
	Consolidated	\$2,059
<i>No Sobriety Requirements</i>		
Total screening cost (total patients treated)	Baseline	\$ 364,656 (47)
	Reflex	\$ 782,803 (354)
	Consolidated	\$ 967,144 (494)
Cost of screening, per-person treated	Baseline	\$ 7,759
	Reflex	\$ 2,211
	Consolidated	\$ 1,958

References

1. AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. <http://www.hevguidelines.org>. Accessed February 2017.
2. Testing for HCV infection: an update of guidance for clinicians and laboratorians. *MMWR Morb Mortal Wkly Rep.* 2013;62(18):362-365.
3. National Viral Hepatitis Roundtable. *Hepatitis C: The State of Medicaid Access, Preliminary Findings: National Summary Report.* 2016.
4. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Annals of internal medicine.* 2006;144(10):705-714.
5. Jonas MC, Rodriguez CV, Redd J, Sloane DA, Winston BJ, Loftus BC. Streamlining Screening to Treatment: The Hepatitis C Cascade of Care at Kaiser Permanente Mid-Atlantic States. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* 2016;62(10):1290-1296.
6. Butt AA, Wagener M, Shakil AO, Ahmad J. Reasons for non-treatment of hepatitis C in veterans in care. *Journal of viral hepatitis.* 2005;12(1):81-85.
7. Coyle C, Viner K, Hughes E, et al. Identification and Linkage to Care of HCV-Infected Persons in Five Health Centers - Philadelphia, Pennsylvania, 2012-2014. *MMWR Morb Mortal Wkly Rep.* 2015;64(17):459-463.
8. Geboy A, Cha H, Perez I, et al. Low HCV Testing Uptake of the Current Birth Cohort Guidelines. 22nd Conference on Retroviruses and Opportunistic Infections; 2015; Seattle, WA.
9. Viner K, Kuncio D, Newbern EC, Johnson CC. The continuum of hepatitis C testing and care. *Hepatology (Baltimore, Md).* 2015;61(3):783-789.
10. Russell M, Pauly MP, Moore CD, et al. The impact of lifetime alcohol use on hepatitis C treatment outcomes in privately insured members of an integrated health care plan. *Hepatology (Baltimore, Md).* 2012;56(4):1223-1230.
11. Galbraith JW, Franco RA, Donnelly JP, et al. Unrecognized chronic hepatitis C virus infection among baby boomers in the emergency department. *Hepatology (Baltimore, Md).* 2015;61(3):776-782.

12. Lo Re V, Gowda C, Urick P, et al. Incidence and Determinants of Denial of DAA Therapy by Type of Insurance During the First 6 Months of the Modern HCV Treatment Era. Paper presented at: AASLD2015.
13. Yawn BP, Wollan P, Gazzuola L, Kim WR. Diagnosis and 10-year follow-up of a community-based hepatitis C cohort. *The Journal of family practice*. 2002;51(2):135-140.
14. Groom H, Dieperink E, Nelson DB, et al. Outcomes of a Hepatitis C screening program at a large urban VA medical center. *Journal of clinical gastroenterology*. 2008;42(1):97-106.
15. Centers for Medicare and Medicaid Services. Physician Fee Schedule. 2015.
16. Centers for Medicare and Medicaid Services. Laboratory Fee Schedule. 2015.
17. Morano JP, Zelenev A, Lombard A, Marcus R, Gibson BA, Altice FL. Strategies for hepatitis C testing and linkage to care for vulnerable populations: point-of-care and standard HCV testing in a mobile medical clinic. *Journal of community health*. 2014;39(5):922-934.
18. White DA, Anderson ES, Pfeil SK, Trivedi TK, Alter HJ. Results of a Rapid Hepatitis C Virus Screening and Diagnostic Testing Program in an Urban Emergency Department. *Annals of emergency medicine*. 2016;67(1):119-128.
19. Geboy A, Cha H, Perez I, et al. Low HCV Testing Uptake of the Current Birth Cohort Guidelines. 22nd Conference on Retroviruses and Opportunistic Infections; 2015; Seattle, WA.
20. Mark KE, Murray PJ, Callahan DB, Gunn RA. Medical care and alcohol use after testing hepatitis C antibody positive at STD clinic and HIV test site screening programs. *Public health reports (Washington, DC : 1974)*. 2007;122(1):37-43.
21. Akyar E, Seneca KH, Akyar S, Schofield N, Schwartz MP, Nahass RG. Linkage to Care for Suburban Heroin Users with Hepatitis C Virus Infection, New Jersey, USA. *Emerging infectious diseases*. 2016;22(5):907-909.
22. Devries J, Rucker M, Glick N. Implementation of an HCV linkage-to-cure program at an urban safety-net hospital. Paper presented at: The National Summit on HCV and HIV Diagnosis, Prevention and Access to Care 2015.