The Cost of Hepatitis C Testing Strategies in Primary Care Patients with Abnormal Transaminases

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INTRODUCTION

Hepatitis C virus antibody (HCV Ab) testing of patients born between 1945 and 1965 has dramatically improved HCV diagnosis in primary care.¹ HCV Ab tests are highly sensitive, widely available, and low cost, but require confirmation with HCV RNA when positive. HCV Ab testing is the most cost-effective strategy for screening birth cohort (1945–1965) patients given their anti-HCV prevalence of 3.25%.² Abnormal alanine and aspartate aminotransferases (ALT and AST) are another indication for HCV testing, but with higher anti-HCV prevalence, the most cost-effective strategy for testing patients with these lab findings is not clear.³

To evaluate costs associated with different HCV testing strategies, we modeled (1) *reflex* testing, a positive HCV Ab immediately followed by confirmatory RNA test without a second blood draw; compared with (2) *direct* HCV RNA testing for all patients with elevated ALT and AST.⁴ We hypothesized that a direct HCV RNA testing strategy would be more efficient and cost-effective for diagnosing HCV in patients with abnormal transaminases.

METHODS

Using EHR data from a PCMH, we identified all patients with HCV testing results (Ab or RNA) between 2007 and 2018. Patients were the unit of observation, only included once in the sample, and categorized into 2 groups: (1) 1945–1965 birth cohort and (2) elevated transaminases. Patients were allocated to the elevated transaminase group if they possessed at least one elevated ALT (> 45 U/L) or AST (> 34 U/L) result during the study period. We compared testing strategies by cost per patient tested and cost per HCV diagnosis for patients with elevated transaminases and HCV Ab results. Not knowing the RNA status for those patients without follow-up testing, we presumed a similar proportion of positive RNA tests to those with confirmation (75.7% in the birth cohort, 80.0% in the elevated transaminase sample).

We also projected the costs of both strategies for PCMH birth cohort patients and those with elevated transaminases not already tested for HCV. We assumed an anti-HCV prevalence of 3.25% in the untested birth cohort, and considered prevalence estimates of 12%, 8.4%, and 5.5% in the untested patients with elevated transaminases, based on estimates from previously published data.^{2, 3} Median charges from the 2019 Clinical Laboratory Fee Schedule from the Centers for Medicare and Medicaid Services were used to measure costs.⁵ This study was approved by MUSC's IRB.

RESULTS

Of the 36,841 patients visiting the PCMH between 2007 and 2018, 10,973 (29.8%) patients had elevated aminotransferases. Of these, 4873 (44.4%) had HCV Ab tests and 585 (12.0% of those tested) had positive results.

Using the HCV testing results previously obtained, and assuming the completion of confirmatory testing, HCV Ab with reflex RNA testing would cost less overall, less per patient tested, and less per HCV diagnosis (Table 1). When the testing strategies were applied to unassessed PCMH groups, HCV Ab with reflex RNA testing led to lower overall cost, cost per patient tested, and cost per diagnosis.

With costs of testing remaining the same, it would require a patient sample prevalence of 53.8% for direct RNA testing to equal the cost of HCV Ab with reflex RNA (Fig. 1).

DISCUSSION

HCV Ab testing with reflex RNA was more cost-effective than direct RNA testing for all anti-HCV prevalence projections in PCMH patients with abnormal transaminases. With current cost estimates, direct RNA testing would be more costly in most settings with the possible exceptions of hepatology and needle exchange clinics. This study does not incorporate the psychological harm possibly associated with falsely positive HCV Ab tests, a consideration deserving attention in future work. Analyzing the costs of different testing strategies is necessary as HCV testing expands beyond the birth cohort in primary care.

Table 1 Costs of HCV Testing Strategies by Patient Group and Anti-HCV Prevalence

	Retrospective	Projected			
	Elevated transaminases (HCV Ab + 12.0%)	Birth cohort (HCV Ab + 3.25%)	Elevated transaminases (HCV Ab + 12.0%)	Elevated transaminases (HCV Ab + 8.4%) ³	Elevated transaminases Trans (5.5%)*
	n = 4873	n = 8698	n = 6100	n = 6100	n = 6100
HCV Ab with reflex RNA					
Total cost [†]	\$100,146.68	\$151,851.64	\$125,352.56	\$117,594.09	\$111,344.22
Cost/pt tested	\$20.55	\$17.46	\$20.55	\$19.28	\$18.25
Cost/ diagnosis [‡]	\$214.45	\$709.61**	\$214.09***	\$286.87***	\$414.84***
Direct RNA testing					
Total cost	\$172,163.09	\$307,300.34	\$215,513.00	\$215,513.00	\$215,513.00
Cost/pt tested	\$35.33	\$35.33	\$35.33	\$35.33	\$35.33
Cost/ diagnosis [‡]	\$368.66	\$1436.03	\$368.02	\$525.74	\$802.95

HCV Ab testing was \$15.85 (CPT 86803) and HCV RNA testing was \$31.22 (CPT 87520).⁵ Specimen collection tubes cost \$0.46 and \$4.11 for the HCV Ab and RNA tests respectively (<https://www.fishersci.com>). Phlebotomy costs were assumed equal. Total cost for HCV Ab negative patients was \$16.31, \$51.64 for HCV Ab positive patients (Ab + RNA), and \$35.33 for patients with direct RNA testing

*This prevalence that would be expected in the remaining, untested individuals if we assume an overall anti-HCV prevalence of 8.4% for all patients with elevated aminotransferases and account for the 585 already testing positive

[†]Cost = $16.31n + 35.33(\text{anti-HCV prevalence} \times n)$

[‡]= 76 pts with missing RNA. Assuming an additional $0.8 \times 76 = 60$ HCV RNA diagnoses. Total HCV diagnosis now 467

**Assuming 75.7% of HCV Ab-positive birth cohort patients were HCV RNA positive ($8698 \times .0325 \times 0.757$)

***Assuming 80.0% of HCV Ab-positive patients with HCV RNA testing were HCV RNA positive ($6100 \times \text{prevalence} \times 0.8$)

Figure 1 HCV testing cost per patient by anti-HCV prevalence for (1) Ab with reflex RNA and (2) direct RNA strategies.

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Compliance with Ethical Standards:

This study was approved by MUSC's IRB.

Conflict of Interest: The authors declare that they do not have a conflict of interest.

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