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Brief Report

High-impact hepatitis C virus testing for injection drug users in an urban $ED^{\stackrel{\star}{\wedge},\stackrel{\star}{\wedge}\stackrel{\star}{\wedge},\stackrel{\star}{\wedge},\stackrel{\star}{\wedge}}$

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ABSTRACT

Objectives: We implemented the "High-Impact Testing for Injection Drug Users", or the "HIT IDU" initiative, an emergency physician (EP)-based hepatitis C virus (HCV) testing program. The objective of this study was to evaluate the outcomes of this clinical protocol.

Methods: This was a prospective observational pilot study. The HIT IDU initiative encouraged EPs to integrate targeted HCV testing into care, with an emphasis on screening all people who inject drugs (PWID). Physicians selected the primary indication for HCV testing from a drop-down menu integrated into the electronic ordering process. The primary outcome was the absolute number and overall proportion of EP-based HCV antibody positive tests, further stratified by the indication for testing.

Results: Over the 3-month study period, 14,253 unique patients were evaluated, and EPs tested 155 patients for HCV (1.1%; 95% confidence interval [CI], 0.9%-1.2%), of which 40 (26%, 95% CI, 19%-33%) were HCV antibody positive. The proportion of HCV antibody positivity by testing indication was as follows: PWID 47% (34/73; 95% CI, 35%-59%), patient requested test 10% (4/40; 95% CI, 3%-24%), confirm patient report 67% (2/3; 95% CI, 9%-99%), liver disease of uncertain etiology 0% (0/3; 95% CI, 0%-71%), and other 0% (0/36; 95% CI, 0%-10%). There were 22 patients chronically infected, 19 had a follow-up appointment arranged, 3 attended their follow-up appointment, and 1 patient was treated at 1 year of follow-up.

Conclusions: Although the overall number of EP-based HCV tests performed was low, high rates of infection were identified, particularly among PWID. There were significant challenges with linkage to care.

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1. Introduction

Hepatitis C virus (HCV) affects an estimated 4 million persons in the United States, and more than half of those chronically infected are unaware of their diagnosis [1,2]. Hepatitis C virus infection is the leading

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cause of hepatocellular carcinoma and liver transplantation and is responsible for more US deaths per year than the human immunodeficiency virus [3,4]. With the advent of novel direct-acting antiviral treatments, there is renewed interest in HCV screening, linkage to care, and treatment.

Patients with a history of injection drug use have the largest HCV prevalence of any risk group, and patients actively using account for the highest incidence of new infections [1,5,6]. Furthermore, people who inject drugs (PWID) tend to be high utilizers of emergency departments (EDs) [7–9]. The potential impact of screening efforts that focus on PWID is significant: if providers were to ask all of their patients about their injection drug use history and offer HCV testing to all who report current or past use, an estimated 47% of all active HCV infections in the United States would be detected [1].

With this in mind, we designed an emergency physician (EP)-based HCV testing program that targeted PWID called High-Impact Testing of Injection Drug Users or HIT IDU.

The purpose of this study was to assess the proportion of unrecognized HCV infection through a targeted physician-led testing program with an emphasis on PWID in an urban ED.

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2. Methods

2.1. Study design and setting

This observational cohort study evaluated a clinical protocol at the Alameda Health System, Highland Hospital, a publically funded, urban ED with a census of 90,000 patients that supports a 4-year emergency medicine residency and serves predominately adult patients of racial and ethnic minorities. The HIT IDU pilot project took place over a 3-month period from March 1 through May 31, 2015. The study received institutional review board approval from the Alameda Health System, with a waiver of written informed consent.

2.2. Selection of participants

The HIT IDU initiative was a pilot project that encouraged EPs to screen patients for HCV and to focus on offering testing to all PWID. Attending physicians and residents received a 30-minute didactic presentation during mandated educational time. The presentation discussed risk factors for HCV infection, the high burden of disease among PWID, and mechanisms for test ordering and coordination of care with the Alameda Health System HCV clinic. For the first 2 months of the program, bimonthly emails were sent to providers by study investigators as reminders to screen PWID for HCV.

The ED had recently concluded a triage-based HCV screening program [10], and at the time of the HIT IDU pilot study, all HCV tests were EP initiated. The computerized order entry for HCV testing required that providers identify a single reason for ordering the test in a drop-down menu that included (1) injection drug use, (2) liver disease of unknown etiology, (3) patient request, (4) confirm patient report, and (5) other (specify). Injection drug use status was determined by patient report. Emergency physicians were not required to document when a patient refused HCV testing. Blood was then obtained using existing staff and laboratory procedures. All patients who had an HCV test ordered had an additional tube of blood drawn and held at the bedside in the event that confirmatory ribonucleic acid (RNA) viral load testing was indicated.

Laboratory technicians notified the attending EP of any positive antibody test results. When possible, the treating physician disclosed positive HCV antibody results and ordered a confirmatory RNA viral load test. When disclosing positive HCV antibody test results, physicians used a scripted disclosure handout and completed an HCV-positive intake form. Emergency department clerks were able to directly schedule follow-up appointments in our hospital's HCV clinic. The HCV program coordinator collected these forms weekly and contacted patients who were not disclosed their results, did not have confirmatory testing performed, or did not have a follow-up appointment scheduled. The HCV program coordinator also canceled appointments for patients if their confirmatory RNA test result was negative. All patients who were HCV antibody positive were included in the analysis to reflect the requisite program workload taken on by the staff.

2.3. Data collection and processing

All HCV tests performed during the pilot study period, as well as the indication for testing, were captured from the electronic medical record (Wellsoft Corporation, Somerset, NJ). In addition, data routinely collected during an ED visit, including demographic information (age, sex, race, ethnicity), housing status (homeless or address listed), insurance status (Medical, Medicare, private, or self-pay), and primary care provider, were exported into Excel spreadsheets (Microsoft Excel 2010; Microsoft, Redmond, WA). Patient-specific laboratory data including the results of the HCV antibody test and the RNA viral load test were captured from the laboratory electronic medical record (Novius; Siemens Healthcare, Malvern, PA) and linked to the same Excel spreadsheet. Longitudinal outcomes (follow-up attendance and treatment

information) were collected 1 year after the start of the pilot project by chart review by 2 investigators (ESA, LD). Both investigators reviewed all chronically infected patients' charts, and there were no disagreements. Any missing data were addressed by individual chart review by study investigators, and any discrepancies were reviewed and adjudicated by investigator consensus. Patients were deemed lost to follow-up if they missed 2 appointments in the HCV clinic or the linkage to care coordinator was not able to contact them after 3 attempts.

2.4. Main outcome measures

The primary outcome was the proportion of positive HCV antibody test results and the absolute number of HCV infections detected. We stratified these results by the indication for testing. Secondary longitudinal outcomes included the absolute number and proportion of patients who had confirmatory RNA viral load testing performed, who were chronically infected (defined as having a detectable RNA viral load), who had follow-up arranged, who successfully attended follow-up, and who received treatment.

2.5. Data analysis

Descriptive analyses were performed for all variables, and unique patient data, rather than visit-level data, are presented. There were no patients in the cohort who had multiple HCV tests performed, although many had multiple ED visits, and the demographic data analyzed are from the ED visit when HCV testing was performed. Continuous data are reported as means with standard deviations, and categorical data are presented as percentages. We performed no a priori sample size calculations, as this is a descriptive analysis of a clinical protocol. All statistical analysis was performed using Stata (Version 13; StataCorp, College Station, TX).

TableResults of EP targeted HCV screening, March 2014-May 2014

	Screening tests performed N = 155 (%)
Age, mean (SD), y	40.2 (13)
Reason for testing	
Injection drug use	73 (47)
Patient request	40 (26)
Confirm patient report of diagnosis	3 (2)
Liver disease unknown etiology	3 (2)
Other	36 (23)
Sex	
Male	107 (69)
Female	47 (31)
Unknown	1(1)
Race/ethnicity	
Black	55 (35)
White	55 (35)
Hispanic	33 (21)
Asian	11 (7)
Other	1(1)
Primary care provider ^a	
Yes	63 (41)
No	92 (59)
Insurance	
Medicare	9 (6)
Medicaid/Medical	113 (73)
Uninsured/self-pay	22 (14)
Private	11 (7)
Homeless	15 (10)
Area of care	
ED	116 (75)
Fast track	39 (25)
Acuity	
High (ESI 1,2)	31 (20)
Moderate (ESI 3)	70 (45)
Low (4,5)	54 (35)

ESI, Emergency Severity Index.

^a As documented in the electronic health record.

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3. Results

Over the 3-month study period, 14,253 unique patients visited the ED, of whom 155 (1.1%; 95% confidence interval [CI], 0.9%-1.2%) underwent HCV testing. Table shows the demographic characteristics and ED visit information for HCV tested patients. Of the 155 tested, 107 (69%) were male, 55 (35%) were black, 55 (35%) were white, 15 (10%) were homeless, 63 (41%) had a primary care provider, 22 (14%) were uninsured, and 122 (79%) had public insurance (Medicare or Medicaid). The most common indication for EP-based HCV testing was PWID (47%), followed by patient requested test (26%), other (23%), confirming patient report of HCV infection (2%), and liver disease of uncertain etiology (2%). Sixty-three tests were performed in the first month of the pilot period, 34 were performed in the second month, and 58 were performed in the third month.

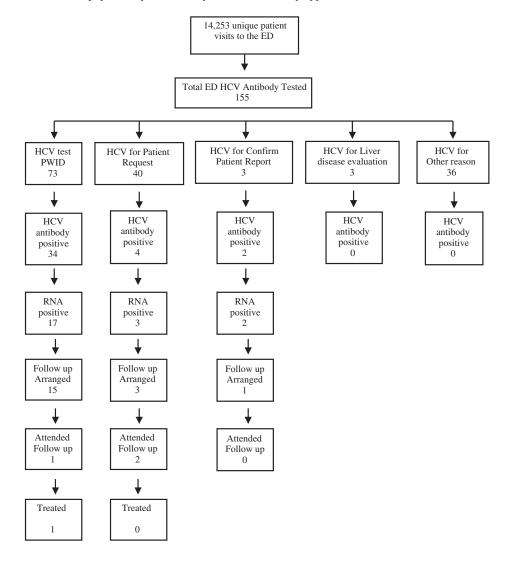
Of the 155 patients tested, 40 (26%; 95% CI, 19%-33%) were HCV antibody positive (Figure). The proportion of positive HCV antibody tests by indication for testing was as follows: PWID 47% (34/73; 95% CI, 35%-59%), requested HCV test 10% (4/40; 95% CI, 3%-24%), confirm patient report 67% (2/3; 95% CI, 9%-99%), liver disease of uncertain etiology 0% (0/3; 95% CI, 0%-71%), and other 0% (0/36; 95% CI, 0%-10%). Thirty-two (80%) of the 40 HCV antibody–positive patients completed

confirmatory RNA testing, of which 22 (69%) had detectable viral loads and were chronically infected. Twenty-six (65%) of the 40 HCV antibody-positive patients had repeat ED visits within 1 year, of which 4 (15%) never received confirmatory RNA testing.

Of the 22 chronically infected patients, 19 (86%; 95% CI, 65%-97%) had follow-up appointments arranged, 3 (14%; 95% CI, 3%-35%) successfully attended follow-up, and 1 (5%; 95% CI, 0%-22%) patient was treated at 1 year of follow-up. The patient that received treatment was in an outpatient substance abuse treatment program. Of the chronically infected patients, 7 had prior antibody positive testing on chart review, but none had been in care for HCV infection.

4. Discussion

Emergency physician–based targeted HCV testing identified patients with high rates of infection, exceeding 25% overall and approaching 50% among PWID. During the HIT IDU pilot period, approximately 1% of the unique ED patients were tested. Despite arranging appointments for 86% of chronically infected patients, only 3 successfully attended a follow-up appointment, and 1 was treated.



HCV, hepatitis c virus; ED, emergency department; PWID, people who inject drugs *Patient-level data for patients ≥ 18 years of age

Figure. Results of physician targeted HCV screening program*.

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The HIT IDU model was efficient in identifying patients with undiagnosed HCV but averaged fewer than 2 HCV tests per day and only 1 test every other day for PWID. In contrast, when our ED implemented an integrated, triage-based HCV screening program, we were able to perform more than 13 tests per day [10]. Expecting EPs to screen greater numbers of patients, however, may be unrealistic. Haukoos et al [11] reported the results of an EP-initiated HIV screening program using existing ED resources, and they were able to test 0.64% of their total patient census over a 30-month period.

Although this strategy of EP-based targeted testing resulted in far fewer tests being performed than ED triage–nurse screening programs [10,12], models such as HIT IDU have clinical value. Our experience with integrated, triage-based HCV screening required a significant time commitment from study staff, while the HIT IDU model required little infrastructure and fewer departmental resources. Many other EDs have implemented screening, brief intervention, and referral for treatment programs that integrate public health measures into ED care [13–15], and the HIT IDU model adds to this culture and may provide a simple, generalizable approach to ED-based HCV testing.

Patients screened for HCV infection in the ED likely have significant social and economic barriers to engaging in outpatient care, and all published ED-based HCV screening programs have struggled with linkage to care [10,12,16]. We found that PWID were less likely to attend follow-up compared with patients who requested testing, and had high rates of ED recidivism. Despite these challenges, focusing screening and linkage to care efforts on PWID could have significant public health benefit: according to mathematical models using the new direct-acting antiviral treatments, treating 1%-7% of chronically infected PWID annually could halve the prevalence of disease within 15 years [17]. Future research ought to focus on how to reliably connect the high number of newly diagnosed HCV infections, particularly PWID, to outpatient medical care for their disease.

Certain limitations of our study should be recognized. We were unable to report the proportion of PWID that were screened for HCV, as the total number of PWID in our ED is unknown (this data is not routinely collected in the electronic health record and some patients may not disclose their status). Patients also may have had more than one indication for HCV testing, though our drop down menu only allowed for EPs to select one option. This was a small pilot study, and how well HCV testing was truly integrated into provider practice cannot be assessed; however, there were no providers in our department that voiced concerns about the HIT IDU program. Our ED has significant experience with HIV and HCV screening as well as a streamlined process for referral to HCV-specific care; therefore, EP willingness to screen may be higher than in other EDs, which may limit the generalizability of our findings.

5. Conclusions

The HIT IDU pilot study shows that EPs can successfully integrate HCV testing into clinical practice and focus testing on PWID. Although the absolute number of HCV tests performed was small, the prevalence of disease was high, exceeding 25% overall and nearly 50% among PWID. There were significant difficulties with linkage to care for patients tested in the ED. The HIT IDU initiative represents a simple model for integrating targeted HCV screening into clinical ED practice that uses few departmental resources.

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References

- 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. Ann Intern Med 2006;144(10):705–14.
- [2] Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition examination survey 2001–2008. Hepatology 2012;55(6):1652–61.
- [3] Moyer VA. Screening for hepatitis c virus infection in adults: U.S. Preventative Services Task Force recommendation statement. Ann Intern Med 2013;159: 349–57.
- [4] Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW, Holmberg SD. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. Ann Intern Med 2012;156(4):271–8.
- [5] 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.
- [6] Valdiserri R, Khalsa J, Dan C, Holmberg S, Zibbel J, Holtzman D, et al. Confronting the emerging epidemic of HCV Infection among young injection drug users. Am J Public Health 2014;104(5):816–21.
- [7] Fairbairn N, Milloy MJ, Zhang R, Lai C, Grafstein E, Kerr T, et al. Emergency department utilization among a cohort of HIV-positive injecting drug users in a Canadian setting. J Emerg Med 2012;43(2):236–43.
- [8] Palepu A, Tyndall MW, Leon H, Muller J, O'Shaughnessy MV, Schechter MT, et al. Hospital utilization and costs in a cohort of injection drug users. Can Med Assoc J 2001;165(4):415–20.
- [9] Gebo KA, Fleishman JA, Moore RD. Hospitalizations for metabolic conditions, opportunistic infections, and injection drug use among HIV patients: trends between 1996 and 2000 in 12 states. J Acquir Immune Defic Syndr 2005;40(5):609–16.
- [10] White DAE, 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. Ann Emerg Med 2016;67(1):119–28.
- [11] Haukoos JS, Hopkins E, Eliopoulos VT, Byyny RL, LaPerriere KA, Mendoza MX, et al. Development and implementation of a model to improve identification of patients infected with HIV Using diagnostic rapid testing in the emergency department. Acad Emerg Med 2007;14(12):1149–57.
- [12] Galbraith JW, Franco RA, Donnelly JP, Rodgers JB, Morgan JM, Viles AF, et al. Unrecognized chronic hepatitis C virus infection among baby boomers in the emergency department. Hepatology 2015;61(3):776–82.
- [13] Cunningham RM, Bernstein SL, Walton M, Broderick K, Vaca FE, Woolard R, et al. Alcohol, tobacco, and other drugs: future directions for screening and intervention in the emergency department. Acad Emerg Med 2009;16(11):1078–88.
- [14] Bernstein SL, D'Onofrio G. A promising approach for emergency departments to care for patients with substance use and behavioral disorders. Health Aff (Millwood) 2013;32(12):2122–8.
- [15] Bernstein E, Bernstein JA, Stein JB, Saitz R. SBIRT in emergency care settings: are we ready to take it to scale? Acad Emerg Med 2009;16(11):1072–7.
- [16] Waridibo AE, Chiang W, Rubin A, O'Donnell L, Saldivar MA, Maurantonio M, et al. Hepatitis C virus infection in the 1945–1965 birth cohort (baby boomers) in a large urban emergency department. Am J Emerg Med 2016;34(4):697–701. http://dx.doi.org/10.1016/j.ajem.2015.12.072 [available online].
- [17] Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, et al. Hepatitis C virus treatment for prevention among people who inject drugs: modeling treatment scale-up in the age of direct-acting antivirals. Hepatology 2013;58(5): 1598–609.