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MAJOR ARTICLE

Prevalence of Hepatitis C Virus Infection Identified From Nontargeted Screening Among Adult Visitors in an Academic Appalachian Regional Emergency Department

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Background. We describe the initial results of an adult academic emergency department (ED) nontargeted hepatitis C virus (HCV) screening program serving Appalachia, which is disproportionately affected by the opioid epidemic.

Methods. The study was a retrospective screening study of ED systematic, nontargeted, opt-out HCV testing outcomes from July 2018 through September 2020. Eligibility requirements for "nontargeted" HCV testing included age ≥18 years, verbally able to communicate, receiving bloodwork already as part of routine clinical care, and not opting out of testing. For eligible individuals who did not opt out of testing, an HCV antibody (Ab) test was performed. Reactive Ab tests were confirmed with reflexive HCV RNA testing. The primary study outcome was the characterization of HCV Ab and RNA prevalence.

Results. There were 75 722 unique adult visitors during the period studied. Of these, 54 931 individuals were verbally engaged regarding testing and did not opt out. A total of 34 848 individuals received HCV Ab testing, with 3665 patients (10.5%) having reactive results. RNA confirmatory testing was reflexively performed in all Ab-positive patients, with 1601 (50.3%) positive. The majority of HCV Ab– and RNA-positive patients were young, born after 1965, and were more likely to be White, male, Medicaid insured, and report a history of injection drug use.

Conclusions. ED nontargeted, opt-out testing can identify a high prevalence of HCV infection among adult visitors. HCV infection was disproportionately high among younger, White individuals, likely reflecting the escalating syndemic of opioid injection and HCV transmission in Appalachia.

Keywords. emergency department; hepatitis C; HCV prevalence.

Identifying persons with chronic hepatitis C virus (HCV) infection is a public health priority in the United States (US) due to the high burden of HCV-related morbidity and mortality, low rates of awareness among persons infected, and the recent advent of curative treatment [1]. Chronic HCV infection is the leading cause of liver cirrhosis, hepatocellular carcinoma, and liver transplantation [2, 3]. Before the coronavirus disease 2019 pandemic, annual US HCV-related deaths exceeded those of 60 other communicable diseases combined [3]. However, the availability of well-tolerated, all-oral direct-acting antivirals (DAAs) has transformed this life-threatening, once difficult-to-treat infection into a curable condition [4, 5].

Despite this advancement in treatment, low HCV awareness among infected persons challenges treatment efforts to reduce the downstream burden of HCV-related complications and deaths. Among the 2.4 million Americans with chronic HCV infection, only 60% are aware of their condition [6]. For this reason, the National Academies of Sciences recently emphasized widespread HCV testing as an essential intervention as part of the strategy to eliminate HCV in the US by 2030 [7]. To meet this HCV elimination goal, identifying appropriate health care venues and best practices for HCV screening and testing is critical.

US emergency departments (EDs) are high-yield and well-positioned venues for identifying HCV infection among adults [8–12]. Populations known to be disproportionately affected by HCV (minorities, Medicaid recipients, and uninsured persons) are more likely to utilize emergency services, and ED-based targeted testing has revealed a high prevalence (6%–18%) of previously unrecognized HCV infections among persons born between 1945 and 1965 [13–15]. Furthermore, recent ED-based nontargeted HCV testing has identified a high prevalence (5.7%–15.2%) among all adult visitors—a finding driven

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by White persons born after 1965, the majority of whom were people who inject drugs (PWID) [9]. Based on results from these previous ED screening programs, US EDs may play a crucial role in raising HCV awareness for national elimination efforts.

While most ED-based HCV testing outcomes have been described from urban ED settings, little is known about HCV screening in nonurban locations. The purpose of the current analysis was to describe HCV testing outcomes from an adult, nontargeted, opt-out HCV screening program in an academic ED serving a large rural catchment area known to be disproportionately impacted by the opioid epidemic and associated injection drug use [16, 17].

METHODS

Setting and Population

The study was performed in a primary academic ED with 85 000 annual visits, including 40 000 unique adult patients. The University of Kentucky Chandler Medical center serves the greater Lexington area and the vast majority of Appalachian counties in Kentucky. Of Kentucky's 120 counties, 54 (45%) are designated as Appalachian and encompass much of the state east of Lexington. Most of these counties (74%) are considered economically distressed by the Appalachian Regional Commission, indicating that they are among the lowest 10% of counties in the US in terms of economic viability [18].

Patient Consent Statement

The Institutional Review Board at the University of Kentucky reviewed the protocol and determined that initial clinical service did not meet the federal definition of research. As such, patient consent was not required. However, all patients were verbally informed of the testing and had the option of opting out. Additionally, per Kentucky statute, the ED general consent form also contained language informing patients that they might be tested for HCV. Thus, 2 forms of acceptable clinical consent were obtained. An additional expedited protocol was generated once de-identified patient data were studied and was approved through the same institutional review board. Subsequent patient consent was not deemed necessary for the research aspect of this program.

Screening Program

A screening study was undertaken in an ED, whereby systematic, nontargeted, opt-out HCV antibody (Ab) testing was conducted between July 2018 and September of 2020. Eligibility requirements for "nontargeted" HCV testing included age ≥18 years, verbally able to communicate, receiving bloodwork already as part of routine clinical care, and not opting out of testing. The approach was a nurse-driven model integrated within the electronic health record (EHR). As part of the nursing workflow, a hard-stop, triage opt-out statement was communicated with each patient before the nursing workflow could continue declaring: "If you have blood drawn today, as part of your care, we will also do a hepatitis C test at no cost to you, unless you say no. If your test is positive, someone will contact you." The options available for the nurse to move on were: "continue" (did not opt out), "opt out," and "unable to consent." For eligible patients who did not opt out, an order to collect a single gold-topped tube for a screening HCV Ab test was generated and was automatically reflexed to an HCV RNA test in the event of a reactive Ab screen. During this study, the HCV tests utilized were the Abbot Architect anti-HCV and Abbott RealTime HCV RNA (Abbott Diagnostics, Lake Forest, Illinois) platforms. If an Ab test was noted in the EHR during the previous 6 months, the order was not generated, thus reducing duplicate orders.

Measures were taken to ensure minimal interference with the typical ED workflow. First, ordering was automated with a brief triage nursing interaction. Second, no additional blood draws were required for RNA confirmation if the Ab screen was positive, as the same tube of blood previously drawn was used for confirmation. Third, there was no expectation for results to be completed before ED discharge. Fourth, if screening results returned while the patient was still in the ED, it was optional for the primary team to disclose results to the patient while in the ED; however, many patients did receive standardized posttest counseling from physicians. Fifth, standardized follow-up was primarily handled by a linkage-to-care team, which consisted of a single administrator and 2 linkage navigators who were licensed social workers. The linkage navigators would call patients, disclose results, counsel them on the disease and risk reduction strategies, and arrange follow-up to an HCV treatment prescriber. Data were obtained directly from patient records in the EHR and from a REDcap database managed by the linkage navigators (supported by the National Institutes of Health National Center for Advancing Translational Sciences through grant number UL1TR001998). The University of Kentucky Institutional Review Board approved the study.

Data Collection

EHR data were utilized for this analysis. For patients with multiple encounters, the first HCV test is included in the dataset (if applicable). If a patient had multiple HCV Ab tests, the first positive test was included. Furthermore, among those with multiple positive Ab tests, the first positive RNA test was included in the final dataset. Consistent with those that did not opt out, if a patient with multiple encounters opted out each time, their first opt-out encounter is included in the dataset.

Variable Selection

Sociodemographic variables contained in the EHR included age, race, gender, county of residence, and insurance status. Age was analyzed as both a continuous and categorical variable (18–24, 25–34, 35–44, 45–54, 55–64, 65–74, and

≥75 years). Furthermore, given the association between birth cohort and HCV status, a dichotomous variable was created to represent those born between 1945 and 1966 (1) to those born after 1966 (0). The county of residence was dichotomized to Appalachian and non-Appalachian. There were >20 insurance types that were collapsed into 4 categories: private insurance, Medicaid, Medicare, and uninsured/self-pay. Each patient also had an indicator of whether they did not opt out, opted out, or were unable to consent to HCV screening. Among those who did not opt out, HCV Ab results are reported. As indicated above, only those with positive Ab results were tested for the presence of viral RNA. Among those testing Ab positive, additional risk data were collected from the EHR (human immunodeficiency virus [HIV] and hepatitis B virus [HBV], if available) and patient self-report upon linkage via a supplemental questionnaire that was administered after discharge. The supplemental questionnaire assessed injection drug use, self-reported HIV/HBV status, substance use disorder, mental health disorder, and whether they were homeless or incarcerated at the time of the positive test. While every attempt was made to ascertain additional information from all Ab-positive patients, these data were not systematically collected from all patients (30% are missing these data) and are therefore subject to bias. As such, these data were only utilized for a secondary analysis and not as the primary independent variables of interest.

Data Analysis

Comparisons were initially made between those who did not opt out, those who opted out, and those who were unable to consent to HCV Ab screening to identify potential demographic differences in screening. Among those who did not opt out, further analyses were conducted comparing Ab-positive and Ab-negative patients, as well as RNA-positive and RNA-negative patients. The dependent variable for "those who did not opt out" analysis was categorical (those who did not opt out, opted out, unable to consent), and contingency tables were constructed to examine patient choice around HCV testing for the sociodemographic variables that were dichotomous or categorical. The χ^2 statistic was used to determine whether there were significant ($P < .05$) differences in proportions in each choice category by sociodemographic variable. Differences in age across categories was compared using the nonparametric Mann-Whitney *U* test. Similar analyses were conducted when comparing sociodemographic characteristics among those with and without positive Ab tests and those with and without positive RNA tests. To determine the factors independently associated with RNA positivity (ie, DAA treatment eligible), logistic regression was employed. In brief, a forward selection process was utilized whereby the variables most significant at the bivariate level were entered into the model one at a time, noting any potential changes to the standard errors as each variable was added to the model until the most parsimonious model was achieved. Specific to this model, changes in the standard error for the Appalachian variable were noted when age and race were entered into the model. Appalachian patients were more likely to be significantly older and White. Therefore, the model was stratified by whether patients resided in an Appalachian county or not, and both models are presented in the results and Table 1. Results from the 2 logistic regression models are presented as adjusted odds ratios (aORs) and 95% confidence intervals (CIs), and only data from the EHR were considered for inclusion in the logistic model since they were systematically collected for all patients, regardless of HCV status. Stata software, version 16.0 (StataCorp, College Station, Texas) was utilized for all analyses.

Table 1. Factors Independently Associated With Hepatitis C Virus RNA Positivity Among Emergency Department Patients From Appalachian and Non-Appalachian Counties in Kentucky

	Appalachian (n = 1356)			Non-Appalachian (n = 1829)		
Factor	aOR	(95% CI)	*P* Value	aOR	(95% CI)	*P* Value
Male	2.22	(1.76–2.79)	<.001	1.69	(1.38–2.07)	<.001
Race/ethnicity						
White		referent			referent	
Black	1.99	(.62–6.35)	.243	1.13	(.83–1.52)	.420
Hispanic	1.75	(.40–7.61)	.451	0.24	(.12–.48)	<.001
Other	2.76	(1.06–7.20)	.037	2.21	(1.03–4.71)	.040
Age, y	0.97	(.96–.98)	<.001	0.97	(.97–.98)	<.001
Insurance						
Private		referent			referent	
Medicaid	2.20	(1.45–3.33)	<.001	2.79	(2.00–3.88)	<.001
Medicare	1.42	(.87–2.30)	.153	1.48	(.99–2.21)	.055
Uninsured/self-pay	1.24	(.64–2.39)	.515	2.21	(1.03–4.71)	.040

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval.

RESULTS

There was a total of 179 389 patient encounters between July 2018 and September 2020. Of those, 75 722 (42.2%) were unique patients and comprised the current analysis sample. The majority of these unique patients were White (80.1%) with public insurance (34% Medicaid, 24% Medicare). Of these, 54 931 (72.5%) individuals were verbally engaged about testing and did not opt out, of whom 34 848 (63.4%) unique individuals received HCV Ab testing, with 3665 patients (10.5%) having reactive results. Patients who did not opt out but did not have blood drawn as part of their routine care did not have an HCV Ab test performed. Patients who did not opt out for HCV testing were significantly more likely to be female and less likely to be White (Table 2). Those who did not opt out were younger and less likely to reside in an Appalachian county. Ab-positive patients were significantly more likely to be male and White, with a mean age of 44.5 years (Table 3). The age of those testing Ab positive were significantly younger than those testing Ab negative (mean, 48.5 years; $P < .001$). Figure 1 demonstrates that when examining the age and race of Ab-positive patients, White individuals skewed far younger, consistent with data suggesting that young, White PWID are driving the current HCV epidemic. Although less likely to be tested, patients from Appalachian counties were more likely to have been exposed to HCV, with a 13% prevalence rate in those from Appalachian counties vs 9.3% in those from non-Appalachian counties ($P < .001$). Medicaid recipients were also more likely to be HCV Ab positive than those with other types of insurance.

RNA confirmatory testing was reflexively performed in all Ab-positive patients, with 1601 (50.3%) testing RNA positive (Table 4). The comparison of sociodemographic characteristics between RNA-positive and negative patients is not remarkably different from the analyses of Ab positives and negatives. Those who are RNA positive, and therefore treatment eligible, are more likely to be younger, White, male, Medicaid insured, and reside in an Appalachian county. A subsample of Ab-positive individuals was queried about risk behaviors, and not surprisingly, PWID were significantly more likely to have viral RNA ($P < .001$), as were those with a self-reported substance use disorder (41.5% vs 19.3%; $P < .001$).

Results from the logistic regression indicate that men are twice as likely as women to test RNA positive, and for every year increase in age, the odds of being RNA positive are 3% lower (aOR, 0.97 [95% CI, .97–.98]). Compared to those with

Table 2. Characteristics of Emergency Department Patients Who Did Not Opt Out, Those Who Opted Out, and Those Who Were Unable to Consent to Hepatitis C Testing, 2018–2020 (N = 75 722)

	Did Not Opt Out (n = 54 931)		Opted Out (n = 11 560)		Unable to Consent (n = 9231)		
Characteristic	No.	(%)	No.	(%)	No.	(%)	*P* Value
Gender							
Female	28 043	(51.1)	5760	(49.8)	4337	(47.0)	<.001
Male	26 886	(48.9)	5800	(50.2)	4891	(53.0)	
Race/ethnicity							
White	43 474	(79.1)	9374	(81.1)	7834	(84.9)	<.001
Black	6877	(12.5)	1373	(11.9)	900	(9.7)	
Hispanic	2966	(5.4)	451	(3.9)	257	(2.8)	
Other	1614	(2.9)	362	(3.1)	249	(2.6)	
Age category, y							
18–24	8670	(15.8)	1887	(16.3)	1080	(11.7)	<.001
25–34	10 170	(18.5)	2070	(17.9)	1404	(15.2)	
35–44	9512	(17.3)	1747	(15.1)	1226	(13.3)	
45–54	8470	(15.4)	1642	(14.2)	1195	(12.9)	
55–64	8272	(15.1)	1613	(18.9)	1452	(15.7)	
65–74	5849	(16.6)	1346	(11.6)	1280	(13.8)	
≥75	3988	(7.3)	1255	(10.9)	1593	(17.3)	
Age, y, mean (SD)	45.4 (18.5)		46.3 (20.1)		51.9 (21.0)		<.001
Rurality (residence)							
Appalachian	17 413	(31.7)	3907	(33.8)	4054	(43.9)	<.001
Non-Appalachian	37 518	(68.3)	7653	(66.2)	5177	(56.1)	
Insurance							
Private	18 749	(34.1)	4106	(35.5)	2754	(29.8)	<.001
Medicaid	17 635	(32.1)	3235	(28.0)	2533	(27.4)	
Medicare	12 722	(23.2)	3044	(26.3)	3173	(34.0)	
Uninsured/self-pay	5824	(10.6)	1175	(10.2)	807	(8.7)	

Abbreviation: SD, standard deviation.

Table 3. Characteristics of Emergency Department Patients Tested for Antibodies to Hepatitis C Virus, 2018–2020 (n = 34 848)

	HCV Ab Positive (n = 3665)		HCV Ab Negative (n = 31 183)		
Characteristic	No.	(%)	No.	(%)	*P* Value
Gender					
Female	1519	(41.5)	16 840	(54.0)	<.001
Male	2146	(58.5)	14 343	(46.0)	
Race/ethnicity					
White	3249	(88.6)	25 052	(80.3)	<.001
Black	282	(7.7)	3610	(11.6)	
Hispanic	63	(1.7)	1673	(5.4)	
Other	71	(1.9)	848	(2.7)	
Age category, y					
18–24	151	(4.1)	4168	(13.4)	<.001
25–34	857	(23.4)	4789	(15.4)	
35–44	993	(27.1)	4795	(15.4)	
45–54	715	(19.5)	5000	(16.0)	
55–64	655	(17.9)	5234	(16.8)	
65–74	226	(6.2)	4202	(13.5)	
≥75	68	(1.9)	2995	(9.6)	
Age, y, mean (SD)	44.5 (13.6)		48.5 (19.0)		<.001
Rurality (residence)					
Appalachian	1597	(43.6)	10 730	(65.6)	<.001
Non-Appalachian	2068	(56.4)	20 453	(34.4)	
Insurance					
Private	357	(9.7)	10 539	(33.8)	<.001
Medicaid	2394	(65.3)	8862	(28.4)	
Medicare	671	(18.3)	9094	(29.2)	
Uninsured/self-pay	243	(6.6)	2687	(8.6)	

Abbreviations: Ab, antibody; HCV, hepatitis C virus; SD, standard deviation.

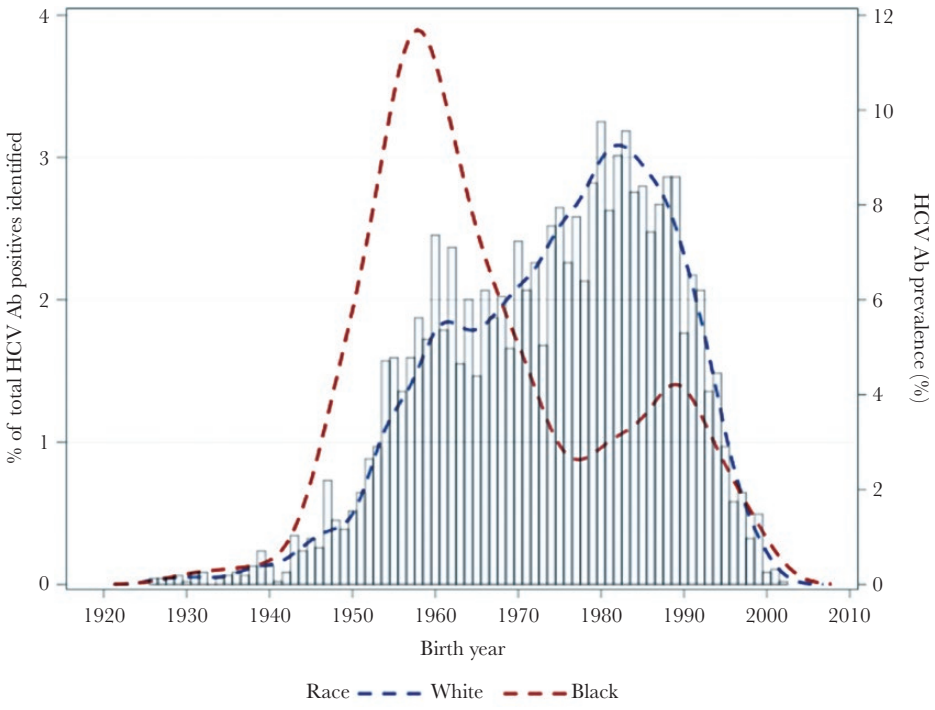

Figure 1. Chronic hepatitis C virus (HCV) birth year distribution and prevalence by birth year and race. Gray bars indicate % of total; dashed lines indicate kernel density curve of HCV antibody (Ab) prevalence by birth year and race (red = Black; blue = White).

Table 4. Characteristics of Emergency Department Patients Tested for the Presence of Viral RNA for Hepatitis C Virus, 2018–2020 (n = 3185)

	HCV RNA Positive (n = 1601)		HCV RNA Negative (n = 1584)		
Characteristic	No.	(%)	No.	(%)	*P* Value
Gender					
Female	575	(35.9)	758	(47.8)	<.001
Male	1026	(64.1)	826	(52.2)	
Race/ethnicity					
White	1430	(89.3)	1387	(87.6)	<.001
Black	111	(6.9)	136	(8.6)	
Hispanic	16	(1.0)	44	(2.8)	
Other	44	(2.7)	17	(1.1)	
Age category, y					
18–24	56	(3.5)	62	(3.9)	<.001
25–34	438	(27.4)	300	(18.9)	
35–44	481	(30.0)	355	(22.4)	
45–54	331	(20.7)	304	(22.4)	
55–64	231	(14.4)	354	(19.2)	
65–74	52	(3.2)	158	(10.0)	
≥75	12	(0.8)	51	(3.2)	
Age, y, mean (SD)	42.2 (12.1)		48.5 (19.0)		<.001
Rurality (residence)					
Appalachian	714	(44.6)	642	(40.5)	.020
Non-Appalachian	887	(55.4)	942	(59.5)	
Insurance					
Private	105	(6.6)	212	(13.4)	<.001
Medicaid	1166	(72.8)	874	(55.2)	
Medicare	211	(13.2)	398	(25.1)	
Uninsured/self-pay	119	(7.4)	100	(6.3)	

Abbreviations: HCV, hepatitis C virus; SD, standard deviation.

private insurance, Medicaid patients are 2.6 times more likely to have viral RNA (aOR, 2.55 [95% CI, 1.98–3.30]) and those who are uninsured/self-pay are 2 times more likely to be chronically infected and are therefore HCV treatment eligible. While Medicaid patients accounted for only 30% of overall ED visits during the study period, they accounted for 69% of persons confirmed with chronic HCV infection. Finally, rurality was an important factor in RNA positivity. The odds of detectable viral RNA among those residing in an Appalachian county were 22% higher than those residing in non-Appalachian counties (aOR, 1.22 [95% CI, 1.05–1.43]).

DISCUSSION

Our study identified a high prevalence of previously unrecognized HCV infection in the ED, with 1 of every 10 adult visitors testing HCV Ab reactive—6 times the estimated community prevalence in Kentucky [19]. Among the ≥34 000 patients tested as part of this program, almost 5% are RNA positive and eligible for HCV treatment. Additionally, the majority of HCV infections identified were among younger White individuals born after 1965. These findings are similar to and support the growing body of evidence that US EDs are high-yield, target-rich venues for detecting HCV infection, especially among younger individuals [9, 12].

The high HCV prevalence identified among younger White persons is consistent with the syndemic of HCV infection and opioid use disorder known to have a disproportionate impact within rural Appalachia [17]. However, most existing literature on HCV screening in EDs has arisen from urban settings, and little has been known about HCV screening in ED's serving largely rural regions, including Appalachia. Our study is consistent with a recent HCV screening study in a rural ED where most HCV Ab–positive patients were young and White, likely due to the high prevalence of PWID and opioid use disorder within the region [20].

Numerous challenges must be overcome to implement systematic HCV testing in the ED setting, including operationalizing screening in an environment with competing priorities, overcoming the effects of HCV stigma on patients and providers, referral of HCV-infected persons to treatment, and the reimbursement associated with testing and linkage services. Third-party billing for these services is not standard and external funding remains necessary for clinical programs such as the one described herein. Similar challenges

have been overcome over the last decade with the advent of standard-of-care HIV testing in the ED [21]. Similar to HIV, nontargeted HCV testing offers advantages in the ED setting where systematically identifying risk factors is difficult to operationalize, and patients may not disclose risks due to a lack of patient–provider rapport. Early systematic ED-based HCV testing primarily targeted persons born between 1945 and 1965. It has been recognized that up to 50% of HCV-infected persons will be missed by this birth cohort screening strategy alone [22].

Ultimately, the efficacy of ED-based HCV testing will be measured in the uptake of HCV treatment by persons identified with HCV infection. Prior ED reports demonstrate that ED-based navigation to HCV care success is similar to other outpatient settings [23–25]. One of the most significant financial challenges to ED-based HCV testing is care navigation costs. Optimal navigation to care often includes a dedicated person to provide additional in-person or phone HCV counseling after the ED visit regarding HCV confirmatory RNA results and referral and tracking to both primary care and subspecialty appointments (ie, HCV treatment provider or substance use treatment). Due to the large number of HCV-infected persons identified in the ED setting, these personnel costs for care navigation can be prohibitive.

Compounding care navigation challenges, we identified a high prevalence of previously unrecognized HCV infection among Medicaid enrollees—a finding previously described in other ED-based HCV testing reports [9, 10]. This population, known to be disparate users of ED services, faces the most significant HCV identification and treatment barriers. While Medicaid enrollees have both a higher HCV prevalence and mortality than persons with other insurances, Medicaid enrollees face the most significant barriers to DAA treatment due to costs [26]. Due to state Medicaid restrictions, Medicaid enrollees have the highest HCV DAA claim denials compared to those with Medicare or commercial insurance [27]. For these reasons, ED-based programs will require robust navigation to care plans and community partnerships to support the critical Medicaid population. The purpose of any HCV screening program is to identify those in need of curative treatment. Our data further add to the growing body of evidence that ED-based nontargeted screening programs identify a large number of treatment-eligible adults. Increased testing and linkage services specific to PWID have been viewed as the most critical interventions needed to reach World Health Organization goals for HCV eradication by 2030 [28]. As payor restrictions for DAAs continue to loosen, efficient case finding coupled with efficient treatment initiation programs are essential [29]. Additionally, if HCV elimination will ever be realized, there must be replicable models of testing and treatment that serve urban and rural areas, especially due to the impact of the opioid epidemic and rising HCV incidence in the rural US. While there are no known studies of ED-based HCV testing and treatment initiation during a single ED encounter, the extensive infrastructure of EDs may prove to be an important avenue for not only testing but also treatment—especially for hard-to-reach individuals.

Results from this study are subject to several limitations. First, this was not universal screening, given that some patients opted out and others were unable to consent. Not all patients had venipuncture performed as part of their care and thus were not screened. Further, 20 000 high-acuity patients did not have their HCV triage questionnaire performed due to competing clinical priorities. This exception was not by design and was uncovered as part of a routine quality improvement assessment. The attrition from eligibility to testing in this program is consistent with reported findings from other ED-based targeted HCV screening programs [10]. To our knowledge, there are no truly universal ED-based HCV screening programs in the US, but the results presented here represent one of the most comprehensive ED-based screening programs to date in our country.

Additional research is needed to see if further eliminating screening barriers and moving toward a truly universal approach could be achievable in the ED setting and whether such an intervention would add clinical value. Finally, study findings are limited to a single academic ED serving the Appalachian region, and therefore the results may not be generalizable. However, given the absence of ED-based screening studies in rural areas, the results presented here are an important contribution to the evidence for ED-based HCV testing and may inform future policy decisions endorsing ED-based HCV testing in nonurban communities as risk of an outbreak of HCV infection [16].

CONCLUSIONS

ED-based, nontargeted, opt-out testing identifies a high prevalence of HCV infection among adult visitors. HCV infection was disproportionately high among younger, White individuals born after 1965, likely reflecting the opioid use disorder epidemic and injection drug use in Appalachia. These findings support the role of ED-based HCV testing, especially in EDs serving rural communities at risk for outbreaks of HCV infection.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. MMWR Morb Mortal Wkly Rep **2012**; 61:1–32.
2. Lingala S, Ghany MG. Natural history of hepatitis C. Gastroenterol Clin North Am **2015**; 44:717–34.
3. Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising mortality associated with hepatitis C virus in the United States, 2003-2013. Clin Infect Dis **2016**; 62:1287–8.
4. Afdhal NH, Zeuzem S, Schooley RT, et al; New Paradigm of HCV Therapy Meeting Participants. The new paradigm of hepatitis C therapy: integration of oral therapies into best practices. J Viral Hepat **2013**; 20:745–60.
5. Ward JW, Valdiserri RO, Koh HK. Hepatitis C virus prevention, care, and treatment: from policy to practice. Clin Infect Dis **2012**; 55(Suppl 1):S58–63.
6. Ryerson AB, Schillie S, Barker LK, et al. Vital signs: newly reported acute and chronic hepatitis C cases—United States, 2009-2018. MMWR Morb Mortal Wkly Rep **2020**; 69:399–404.
7. National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Committee on a National Strategy for the Elimination of Hepatitis B and C. A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report. Buckley GJ, Strom BL, eds. Washington, DC: National Academies Press; **2017**.
8. Galbraith JW. Hepatitis C virus screening: an important public health opportunity for United States emergency departments. Ann Emerg Med **2016**; 67:129–30.
9. Galbraith JW, Anderson ES, Hsieh YH, et al. High prevalence of hepatitis C infection among adult patients at four urban emergency departments—Birmingham, Oakland, Baltimore, and Boston, 2015-2017. MMWR Morb Mortal Wkly Rep **2020**; 69:569–74.
10. Galbraith JW, Franco RA, Donnelly JP, et al. Unrecognized chronic hepatitis C virus infection among baby boomers in the emergency department. Hepatology **2015**; 61:776–82.
11. White DA, Anderson ES, Pfeil SK, et al. Results of a rapid hepatitis C virus screening and diagnostic testing program in an urban emergency department. Ann Emerg Med **2016**; 67:119–28.
12. Schechter-Perkins EM, Miller NS, Hall J, et al. Implementation and preliminary results of an emergency department nontargeted, opt-out hepatitis C virus screening program. Acad Emerg Med **2018**;25:1216–26.
13. Tsui JI, Maselli J, Gonzales R. Sociodemographic trends in national ambulatory care visits for hepatitis C virus infection. Dig Dis Sci **2009**; 54:2694–8.
14. Hsieh YH, Patel AV, Loevinsohn GS, et al. Emergency departments at the crossroads of intersecting epidemics (HIV, HCV, injection drug use and opioid overdose)—estimating HCV incidence in an urban emergency department population. J Viral Hepat **2018**; 25:1397–400.
15. Yin S, Barker L, Teshale EH, Jiles RB. Rising trends in emergency department visits associated with hepatitis C virus infection in the United States, 2006-2014. Public Health Rep **2019**; 134:685–94.
16. Van Handel MM, Rose CE, Hallisey EJ, et al. County-level vulnerability assessment for rapid dissemination of HIV or HCV infections among persons who inject drugs, United States. J Acquir Immune Defic Syndr **2016**; 73:323–31.
17. Zibbell JE, Iqbal K, Patel RC, 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**; 64:454–8.
18. Appalachian Regional Commission. Classifying economic distress in Appalachian counties. Available at: https://www.arc.gov/classifying-economic-distress-in-appalachian-counties. Accessed 21 May 2021.
19. Rosenberg ES, Rosenthal EM, Hall EW, et al. Prevalence of hepatitis C virus infection in US states and the district of Columbia, 2013 to 2016. JAMA Netw Open **2018**; 1:e186371.
20. Wojcik EM, Sharon MJ, Davis SM, et al. Centers for Disease Control and Prevention recommendations for hepatitis C testing: the need to adopt universal screening in an Appalachian emergency department. Acad Emerg Med **2020**; 27:844–52.
21. Branson BM, Handsfield HH, Lampe MA, et al; Centers for Disease Control and Prevention. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep **2006**; 55:1–17; quiz CE1–4.
22. Hsieh YH, Rothman RE, Laeyendecker OB, et al. Evaluation of the centers for disease control and prevention recommendations for hepatitis C virus testing in an urban emergency department. Clin Infect Dis **2016**; 62:1059–65.
23. Anderson ES, Galbraith JW, Deering LJ, et al. Continuum of care for hepatitis C virus among patients diagnosed in the emergency department setting. Clin Infect Dis **2017**; 64:1540–6.
24. Blackwell JA, Rodgers JB, Franco RA, et al. Predictors of linkage to care for a nontargeted emergency department hepatitis C screening program. Am J Emerg Med **2020**; 38:1396–401.
25. Franco RA, Overton ET, Tamhane AR, et al. Characterizing failure to establish hepatitis C care of baby boomers diagnosed in the emergency department. Open Forum Infect Dis **2016**; 3:ofw211.
26. Canary LA, Klevens RM, Holmberg SD. Limited access to new hepatitis C virus treatment under state Medicaid programs. Ann Intern Med **2015**; 163:226–8.
27. Re Lo V III, Gowda C, Urick PN, et al. Disparities in absolute denial of modern hepatitis C therapy by type of insurance. Clin Gastroenterol Hepatol **2016**; 14:1035–43.
28. Grebely J, Dore GJ, Morin S, et al. Elimination of HCV as a public health concern among people who inject drugs by 2030—what will it take to get there? J Int AIDS Soc **2017**; 20:22146.
29. Kapadia SN, Jeng PJ, Schackman BR, Bao Y. State Medicaid hepatitis C treatment eligibility criteria and use of direct-acting antivirals. Clin Infect Dis **2018**; 66:1618–20.
30. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform **2009**; 42:377–81.
31. Harris PA, Taylor R, Minor BL, et al; REDCap Consortium. The REDCap consortium: building an international community of software platform partners. J Biomed Inform **2019**; 95:103208.