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BRIEF REPORT

Preliminary Screening Results Outside the 1945–1965 Birth Cohort: A Forgotten Population for Hepatitis C?

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In December 2017, our academic medical center implemented universal hepatitis C virus screening among adult hospitalized patients. We reviewed charts of patients screening positive outside the birth cohort (1945–1965) in the first 6 months after implementation. Documented risk factors were common in younger patients but rare in patients born before 1945.

Keywords. HCV epidemiology; hepatitis C infection; quality improvement; social vulnerability; universal screening.

Historically, hepatitis C virus (HCV) infection was most prevalent among those born between 1945 and 1965, with an estimated seroprevalence of 3.25% in this population. As a result, the Centers for Disease Control and Prevention (CDC) currently recommend targeted screening for HCV only among this birth cohort or in patients with known risk factors, such as injection drug use (IDU) or those who were ever on long-term hemodialysis [1]. Recent data show increasing HCV incidence among younger patients; for example, the notification rate for acute HCV among those aged 25–39 increased from 0.68 per 100 000 person-years in 2010 to a rate of 2.47 in 2016—a more than 3-fold increase—likely reflecting the ongoing epidemic of opioid use disorder (OUD) [2–4]. However, patients with OUD and other people who inject drugs face significant stigma at many levels of society, including among health care institutions [2–5]. Therefore, some younger patients may be reluctant to disclose their IDU status, resulting in missed opportunities for targeted HCV screening by health care providers [5]. Universal screening may therefore facilitate earlier recognition among infected individuals.

One-time universal HCV screening has been shown to be cost-effective across a variety of settings in the United States, but it becomes cost-saving when the population HCV prevalence exceeds 1% [6]. The average HCV seroprevalence in New York City is estimated to be 2.5%, and our hospital, New York Presbyterian-Columbia University Irving Medical Center (CUIMC), serves 3 of the 4 neighborhoods with highest incidence of newly reported cases of HCV infection [7]. A similar pattern to national data has been observed in New York City, with a bimodal distribution of new HCV diagnoses characterized by a "distinct peak" among younger individuals born after 1964 [7]. In response to data locating CUIMC at a nexus of the NYC epidemic, the hospital implemented universal screening for HCV on hospital admission.

METHODS

In keeping with CDC recommendations and New York State public health law, an electronic medical record–based intervention was first enacted in 2014 at our large, urban academic medical center. This intervention embedded an element within the admission order set prompting all providers to order HCV antibody screening with reflex to qualitative HCV RNA polymerase chain reaction––or provide justification for not doing so––for all patients being admitted who were within the birth cohort (described as "a hard stop"). Since 2016, this intervention has been combined with a coordinated linkage program, in which a dedicated team follows up any positive HIV and HCV screening results and proactively attempts to link patients to specialty care after discharge. The linkage coordinators participate in a wide array of activities designed to enhance postdischarge engagement in care, including actively monitoring HCV test results throughout the hospital system to identify HCV-positive patients, meeting with patients during their hospitalization to discuss follow-up needs, discussing follow-up plans with inpatient medical providers, arranging postdischarge appointments in infectious diseases and hepatology specialty clinics, contacting patients after discharge to confirm follow-up plans and identify barriers to linkage, and tracking linkage status for all positive HCV tests. In December 2017, CUIMC expanded this screening protocol to include all patients who are 18 years of age or older, as part of a quality improvement effort to address the rising HCV prevalence in non–birth cohort populations.

In this preliminary study, we compared rates of HCV screening and positivity during the first 6 months of this policy with the same months in the preceding year. We conducted a

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retrospective chart review of HCV RNA–positive patients outside the birth cohort to identify documented risk factors and forms of social vulnerability, including age; status of housing, immigration, insurance, and employment; criminal justice involvement; history of transactional sex; self-identification as a transgender woman or man who has sex with men; IDU and other mental health comorbidities. Charts were also reviewed to determine the admission diagnosis, whether the diagnosis of HCV was previously known at the time of admission, and linkage status at the time of publication. Treatment status was not assessed, as a substantive portion of patients elected to follow up outside our hospital system. Using R 3.1.2 [8], chi-square test and Fisher exact tests (where appropriate) were performed to assess differences in risk factors and other characteristics between patients born before 1945 and those born after 1965.

This research was deemed exempt by the institutional review boards at Columbia University Medical Center.

RESULTS

From December 2017 through May 2018, a total of 8305 patients were screened on admission to our hospital center, with 112 (1.3%) positive results, compared with 3823 patients and 121 (3.2%) positives during the same months in 2016–2017. Outside the birth cohort, 60 of 5484 (1.1%) patients tested on admission were HCV RNA–positive in 2017–2018 compared with 30 of 994 (3.0%) in 2016–2017. Out of 60 HCV RNA–positive patients born outside the birth cohort, 35 (58.3%) had no documented risk factors. Among the cohort born after 1965, 20 out of 27 (74.1%) patients had documented risk factors, compared with only 5 out of 33 (15.2%) patients born before 1945. Documented factors associated with social vulnerability were highly prevalent among those born after 1965, but uncommon in patients born before 1945. Specifically, compared with those born before the birth cohort, individuals born after 1965 were significantly more likely to have a history of IDU, mental health comorbidities, homelessness, unemployment, and criminal justice involvement (Table 1).

Admission diagnoses directly related to substance use disorders and mental health comorbidities were also relatively common among individuals born after 1965, including severe bacterial infections (n = 6), suspected overdose (n = 3), and depression/suicidality (n = 6). Only 1 such admission diagnosis (severe bacterial infection) was found among individuals born before 1945 in a patient presenting with *Streptococcus viridans* endocarditis from a presumed oral source.

Thirty-seven percent of patients born after 1965 and 51.5% of patients born before 1945 had a known HCV diagnosis at the time the screening antibody test was ordered (Table 1). However, this includes 3 patients born before 1945 who had previous HCV treatment and were believed to be cured. An additional patient born after 1965 had known about his HCV diagnosis for many years but reported he had never been offered treatment. He was incidentally found to have evidence of cirrhosis and engaged follow-up care with both infectious diseases and hepatology after discharge. Eighteen out of 27 previously unknown cases of HCV were in patients with previous hospitalizations in our system.

Table 1. HCV Risk Factors and Forms of Social Vulnerability Among Those Testing Positive and Born Outside the 1945–1965 Birth Cohort

	Born Before 1945 (n = 33), No. (%)	Born After 1965 (n = 27), No. (%)	*P* Value
Documented CDC-defined risk factors			<.001
IDU	4 (12.1)	18 (66.7)	
Hemodialysis	1 (3.0)	0 (0)	
Prior transfusions	0 (0)	2 (7.4)	
Housing status			<.05
Housed	32 (97.0)	14 (51.9)	
Unstably housed/homeless	1 (3.0)	12 (44.4)	
Unknown	0 (0)	1 (3.7)	
Employment status			<.001
Employed/student	4 (12.1)	3 (11.1)	
Retired	26 (78.8)	0 (0)	
Disability	1 (3.0)	11 (40.7)	
Unemployed	0 (0)	12 (44.4)	
Unknown	2 (6.1)	1 (0)	
Mental health comorbidities	8 (24.2)	22 (81.5)	<.001
Transactional sex	0 (0)	2 (7.4)	.19
MSM	0 (0)	2 (7.4)	.19
Criminal justice involvement	2 (6.1)	16 (59.3)	<.001
Previously unknown diagnosis	17 (51.5)	10 (37.0)	.39
Prior hospitalizations	12/17 (70.6)	6/10 (60.0)	

Abbreviations: CDC, Centers for Disease Control and Prevention; HCV, hepatitis C virus; IDU, injection drug user; MSM, men who have sex with men.

Eight out of 60 patients found to be HCV RNA–positive died or were terminally ill: 6 born before 1945 and 2 born after 1965. The majority of the remaining 52 patients had received some of the services provided by the care coordination team and were at various stages in the process of establishing definitive HCV care. Three patients (all born before 1945) declined linkage activities. Eighteen patients had been seen in a clinic to discuss treatment options with a provider and/or initiate the pretreatment evaluation. Four patients had only incorrect contact information available, and 9 patients were lost to follow-up despite multiple attempts to arrange care. The remaining patients had some contact with the care coordination team and were in the process of establishing definitive care at the time of this report.

DISCUSSION

Expanding hospital admission–based HCV screening to include universal testing led to a more than 5-fold increase in screening outside the CDC-recommended birth cohort, with a doubling of the number of cases detected in the affected age groups. However, 2 substantially different populations were discovered among the patients. Documented substance use disorders and social vulnerability were highly prevalent in HCV-positive patients born after 1965, which was consistent with our expectations, given the association of HCV infection with OUD among younger patients [4]. In fact, the admitting diagnosis was directly related to substance use or psychiatric comorbidities in over half of the patients in this group. It is possible that many of these patients would have been offered screening regardless of the intervention. However, for a substantial proportion of these patients (33.3%), a specific history of injection drug use was not documented. Eighteen out of 27 previously unknown HCV cases detected outside the birth cohort would have been missed based strictly on documented CDC risk factors, and the same proportion had been missed on prior hospitalizations. Furthermore, in several cases where injection drug use was documented, patients reported this history inconsistently, denying it to some providers and endorsing it to others––or only disclosing a remote history upon discovery of the HCV diagnosis. Short of universal screening, therefore, expanding the criteria for risk-based screening to include other forms of social vulnerability associated with drug use may be warranted.

A substantial proportion of the HCV RNA–positive cases detected on admission screening were in patients previously known to have been diagnosed with HCV. Some of these patients reported previous treatment and were erroneously believed to be cured, representing an opportunity to re-engage in HCV care. Indeed, both for those with known risk factors and for those with prior known HCV diagnoses, admission screening provided an opportunity for enhanced linkage to HCV care. At the time of publication, our initial experience with care coordination for the patients detected via expanded screening demonstrates both the challenges and opportunities inherent in working to engage highly vulnerable and hard-to-reach populations such as those born after 1965. Although a number of patients have established HCV care––including, for example, 1 patient incidentally discovered to have cirrhosis and 2 out of 3 who previously received HCV treatment and were believed to be cured––a large number are still in the process of establishing care. In response to these challenges, our linkage protocols have been modified continually throughout the first year of implementation, improving our ability to reach patients over time. We are also currently in the process of expanding our HCV screening and linkage program to the emergency department. We suspect that this will provide an additional opportunity to reach a wider population of HCV-infected patients––who may be seeking care for minor unrelated complaints not meeting criteria for hospital admission––and attempt to engage them in treatment.

CDC guidelines note that only 76.6% of chronic HCV cases fall within their recommended birth cohort, and nationwide data demonstrate prevalent cases born both before and after the selected years [1, 9]. As the epidemiology of HCV has continued to shift toward younger patients, additional attention has been given to this younger cohort [10]. Our expansion of HCV screening was intended as a means to increase detection and linkage in this age group as well. Though many of the HCV-positive patients born after 1965 may have been screened on the basis of risk factors before our intervention, the successful increase in case detection after the intervention and the high rate of prior hospitalizations among those with previously undiagnosed HCV highlight an important gap in the care cascade.

Our finding of a comparable number of patients with HCV infection born before 1945––the majority of whom had no risk known risk factors––is also consistent with the existing epidemiologic literature [1, 9]. However, there is a relative paucity of data about HCV in this age group, making our finding somewhat suggestive of a "forgotten population" of older adults with occult chronic HCV infection [11]. For a number of patients in this age group, the diagnosis of HCV was previously known, so it may more accurately have represented a "forgotten diagnosis"; yet even for these patients, there was a subset for whom the detection of HCV RNA, indicative of active infection, was unexpected after having previously received treatment.

Because we relied on a retrospective chart review, an important limitation of our study is our inability to determine if the relative paucity of documented risk factors among patients born before 1945 reflected a true absence or simply a reluctance on the part of providers to ask sensitive social history questions in elderly patients (in whom it was also less likely to be relevant based on admission diagnoses). Four patients in this group reported a remote history of IDU, including 1 who disclosed this only while discussing the positive HCV result with his care team.

Little is known about the course of HCV infection in this older population. Early reports suggest similar efficacy of direct-acting antiviral (DAA) therapy in older patients but increased risk of adverse events in those over the age of 75 [12]. Given the rarity of documented risk factors in this cohort, it is unclear how and when the majority of these patients were initially infected. It is conceivable that these patients represent a subset of patients who are less likely to progress to cirrhosis and have thereby avoided prior detection of their HCV status. On the other hand, patients infected in the distant past may be at higher risk of having undiagnosed fibrosis or cirrhosis. More research is needed to better characterize the epidemiology, natural history, and outcomes of HCV disease in this population. However, unless a patient's life expectancy is severely limited, current guidelines from the Infectious Diseases Society of America and the American Association for the Study of Liver Diseases recommend initiating HCV treatment [13].

In this study, we provide initial striking evidence of 2 distinct populations reached by implementing universal HCV screening among patients being hospitalized in a large urban medical center. In keeping with the distinction between these populations, the value of screening appears to differ as well. For those born after 1965, the greatest value of our screening program was seemingly in the enhanced opportunities for linkage to HCV care offered to a highly vulnerable population that is generally hard to reach. For those born before 1945, risk factors for HCV appear to be infrequently and inconsistently assessed on a routine basis, so screening provides additional opportunities for detection of occult disease or disease that was evaluated before the DAA era. Previously diagnosed patients may benefit from a reassessment of viral load if they were treated in the past, while those once deemed poor candidates for older treatments may be good candidates for DAAs. Our center's early experience demonstrates that these aims can be achieved relatively quickly and with minimal interruption to routine patient care by the use of an of an electronic medical record–based intervention, though doing so also presents challenges in engaging a vulnerable, hard-to-reach population, even with resources devoted to linkage. As HCV's epidemiology shifts and funding for treatment becomes increasingly available, universal screening may serve as a valuable tool to reach not only populations with limited access to care, but also those who may be otherwise overlooked.

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