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RESEARCH ARTICLE

# HCV universal EHR prompt successfully increases screening, highlights potential disparities

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# Abstract

# **Background & objectives**

Screening for hepatitis C virus is the first critical decision point for preventing morbidity and mortality from HCV cirrhosis and hepatocellular carcinoma and will ultimately contribute to global elimination of a curable disease. This study aims to portray the changes over time in HCV screening rates and the screened population characteristics following the 2020 implementation of an electronic health record (EHR) alert for universal screening in the outpatient setting in a large healthcare system in the US mid-Atlantic region.

### Methods

Data was abstracted from the EHR on all outpatients from 1/1/2017 through 10/31/2021, including individual demographics and their HCV antibody (Ab) screening dates. For a limited period centered on the implementation of the HCV alert, mixed effects multivariable regression analyses were performed to compare the timeline and characteristics of those screened and un-screened. The final models included socio-demographic covariates of interest, time period (pre/post) and an interaction term between time period and sex. We also examined a model with time as a monthly variable to look at the potential impact of COVID-19 on screening for HCV.

# Results

Absolute number of screens and screening rate increased by 103% and 62%, respectively, after adopting the universal EHR alert. Patients with Medicaid were more likely to be screened than private insurance ( $OR_{adj}$  1.10, 95% CI: 1.05, 1.15), while those with Medicare

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**Competing interests:** Dawn Fishbein, MD receives grant funding for this research from Gilead Sciences, Inc through her employer. She has stock ownership in Abbvie and Merck is a discretionary portfolio with a value less than \$10,000. This does not alter our adherence to PLOS ONE policies on sharing data and materials. were less likely ( $OR_{adj}$  0.62, 95% CI: 0.62, 0.65); and Black ( $OR_{adj}$  1.59, 95% CI: 1.53, 1.64) race more than White.

### Conclusions

Implementation of universal EHR alerts could prove to be a critical next step in HCV elimination. Those with Medicare and Medicaid insurance were not screened proportionately to the national prevalence of HCV in these populations. Our findings support increased screening and re-testing efforts for those at high risk of HCV.

### Introduction

Over the past two decades, viral hepatitis has become the foremost cause of global infectious disease related mortality, surpassing even HIV and tuberculosis [1]. The rapid increase in mortality, despite the availability of curative treatments, led international health leaders to develop action plans for the elimination of viral hepatitis [1]. Specifically, the World Health Organization presented the following aims regarding all hepatitis viruses by the year 2030: a 90% reduction in incidence, a 65% reduction in mortality, a 90% rate of diagnosing chronic cases, and an 80% treatment rate of individuals with chronic hepatitis [1].

An estimated 48% of global hepatitis-related mortality is attributable to hepatitis C virus infection, although a vast majority-between 75-90%-of hepatitis burden in the western hemisphere is HCV-related [1]. The approximate prevalence of HCV infection in the United States population is 1.7% (4.1 million people), based on 2013–2016 antibody (Ab) testing, which indicates either past or current infection [2]. The highest US prevalence was previously among those belonging to the Birth Cohort (BC), individuals born between 1945–1965, and the greatest single risk factor for HCV infection is current or historical intravenous drug use (IVDU) [3]. This led to guidelines which recommended one-time screening for the BC, more often for patients with risk factors such as IVDU, incarceration or substance use disorders [3]. However, based on cost-benefit analyses and the rising prevalence of HCV in younger populations, the guidelines were updated in March 2020 to recommend one-time universal HCV screening for those with risk factors [4–8]. This marked an important step in the elimination of HCV in the USA.

One goal under elimination is "micro-elimination", as in eliminating HCV in a given population; however, the first challenge of this aim is developing a strategy for improving screening efforts [5]. With the advent of universal screening, the healthcare provider still needs to recognize which patients require their screening, and if re-testing is appropriate based on risk factors [7, 8]. Fortunately, clinical decision support (CDS) alerts built into electronic health records (EHR) may lessen the burden of this responsibility [9–14]. Additionally, such alerts may improve screening rates and, ultimately, connection to care [14].

In the studied large academic healthcare system, with approximately 2.7 million outpatient visits annually, HCV screening CDS EHR alerts have reflected the changing recommendations over the past decade. A system-wide EHR alert for screening the BC began in 2015, was temporarily discontinued by January, 2017 during transition from one EHR to another, and then reimplemented in September, 2018. In May, 2020, less than two months after the update in US Preventive Services Task Force (USPSTF) and Centers for Disease Control (CDC) recommendations, a universal HCV screening CDS alert for eligible patients was adopted. This observational study aims to describe the changes over time in HCV screening rates and population characteristics in the period preceding and following implementation of an EHR alert across the health system, and to use this information along with comparisons to the unscreened population to suggest future avenues for HCV micro-elimination.

### Materials and methods

### **Extraction and variables**

Data was extracted from the EHR for patients who received an HCV antibody (HCVAb) screen between January 2017 and October 2021 and were seen in the outpatient setting. Data was extracted by biomedical informatics and provided to the team in an Excel or csv database. Variables included age, sex (female, male, other/unknown), race (White, Black, Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, Multiple, Other/Unknown), ethnicity (non-Hispanic, Hispanic, Other/Unknown), address including state and zip code, insurance name and type (government, Private, Medicare, Medicaid, Self-Pay, Other/ unknown), and date of antibody test.

A separate data set was extracted for all outpatient visits during the period January 1, 2020 and October 31, 2020, which included all variables above as well as whether the patient received an HCV Ab screen and the dates of the screenings, in addition to all outpatient visit dates. If any of the screening dates were 31 days before or after an appointment date, then the patient was considered screened for that appointment date. This measure was taken to account for providers ordering tests to be completed shortly before or after scheduled outpatient appointments. If a patient's closest appointment was before the alert implementation and the screening date was after, then the date of their screen was considered pre-alert to provide a more conservative estimate of the alert's effect.

Consent was waived for participants in our study as all data was deidentified. This study was approved by the MedStar Health Research Institute Institutional Review Board.

### Statistical analysis

We used frequencies and percentages to summarize the distribution of our categorical variables; and means with standard deviations or medians with interquartile ranges to summarize our continuous variables. To account for repeated measures of patients who had outpatient visits pre-alert and post-alert, we conducted bivariate and multivariable mixed effects logistic regression analyses with screened for HCV as the dependent categorical outcome variable. We evaluated two different models by adding an interaction term between time period and sex, and an interaction term between time period and race to examine if the relationship between the independent variable and the outcome was affected by time period. Any statistically significant interaction term was included in the final model. Our final models included socio-demographic covariates of interest (i.e. age, race, ethnicity, sex and insurance type), time period (pre/post) and an interaction term between time period and sex. We also examined a model with time as a monthly variable to look at the potential impact of COVID-19 on screening for HCV. We evaluated the inclusion of random effects versus a linear regression model using the likelihood ratio test. Statistical analyses were conducted on Stata version 17 (StataCorp LLC). Significance level was set at 0.05.

#### Results

### Absolute screening numbers and characteristics 1/2017-10/2021

During the study period, there were 155,012 HCV Ab screen recipients in outpatient locations. Between January 2017 and May 2020 (pre-alert), 84,139 screens were completed at a rate of



**Fig 1. HCV antibody screening over time.** Absolute HCV antibody screens, birth cohort (BC) vs. non-BC over time January 2017 to October 2021 for all MedStar outpatient sites. The first arrow (left) indicates the approximate re-implementation of the electronic health record (EHR) alert for the birth cohort in September 2018. The second arrow (right) indicates the approximate implementation of the universal screening EHR alert on May 28<sup>th</sup>, 2020.

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2,052 screens per month. Between June 2020 and October 2021 (post-alert), 70,873 screens were completed at a rate of 4,169 screens per month, representing a 103% increase in monthly screening rate (Fig 1). The mean age of HCV Ab screening recipients decreased from 53.8 in 2017 to 45.1 in 2021 (Table 1). The percent of HCV Ab screen recipients who did not belong to the BC (non-BC) increased from 56.8% in 2017 to 79.8% in 2021 of the total screened.

In the year prior to re-implementation of the system BC EHR alert for HCV screening in September 2018 (October 2017 –September, 2018), 20,514 screens were completed at a rate of 1,710 screens per month; the year following implementation (October 2018 –September 2019), 33,001 screens were completed at a rate of 2,750 screens per month. This represented a 60.9% increase in the mean monthly screening rate. The mean age of those screened from prior to the BC alert was 50.7 years, which increased to a mean age of 53.9 in the year after the BC alert; prior to the BC alert, 36.8% of all screened belonged to the BC; the year after, 50.0% of those screened were in the BC (Fig 1, Table 1).

Over the entire study period, 66.2% of all screened with an indicated sex (n = 146,564) were female; there was an absolute increase from 63.3% in 2017 to 67.7% in 2021. The two most prominent races of those with an identified race (n = 137,331) were White and African American/Black, which comprised 45.7% and 47.5% of the sample respectively. During 2017, 44.2% of those screened were White and 49.5% were African-American/Black; in 2021, 45.7% were White and 47.2% were African American/Black (Table 1).

Overall, 64.0% of the screened individuals with an indicated insurance type (n = 137,061) had private/commercial insurance, 11.9% Medicare, and 21.3% Medicaid. In 2017, 63.7% of those screened had private insurance which increased to 65.3% by 2021. In 2017, 11.4% of those screened had Medicare, which increased to 14.6% in 2020, then decreased to 10.5% in 2021 (Table 1).

Overall, 72.3% of those screened who indicated a state of residence (n = 152,107) lived in Maryland, 22.0% in Washington, District of Columbia and 5.7% in Virginia. In 2017, 66.9% of those screened lived in Maryland, which increased to 76.1% in 2019, then decreased to 70.6% in 2021.

	2017		2018		2019		2020		2021		Total	
	Absolute	Percent										
Total Screens	21,280		23,524		31,500		37,718		40,990		155,012	
Age (mean)	53.8		51.7		53.7		47.3		45.1		49.6	
Non-BC	12,096	56.8	13,909	59.1	15,864	50.4	27,634	73.2	10,084	79.8	102,228	65.9
BC	9,184	43.2	9,615	40.9	15,636	49.6	10,084	26.7	8,265	20.2	52,784	34.1
Sex												
Male	7,518	36.7	7,819	34.7	10,487	35.1	11,204	32.0	12,491	32.3	49,519	33.8
Female	12,967	63.3	14,725	65.3	19,425	64.9	23,782	68.0	26,146	67.7	97,045	66.2
Race/Ethnicity												
Black*	9,374	49.3	10,471	50.0	12,516	44.5	15,451	47.3	16,955	47.3	64,767	47.4
White	8,375	44.0	8,854	42.3	13,267	47.2	15,406	47.1	16,444	45.8	62,346	45.6
Hispanic/LA**	880	4.3	981	4.4	1089	3.7	910	2.6	1,250	3.3	5,110	3.5
Asian	544	2.9	713	3.4	868	3.1	1162	3.6	1,619	4.5	4,906	3.6
Insurance												
Private	11,747	63.7	13,552	64.7	18,004	64.3	20,870	62.2	23,560	65.3	87,733	64.0
Medicare	2,111	11.4	1,960	9.4	3,538	12.6	4,908	14.6	3,805	10.5	16,322	11.9
Medicaid	3,957	21.4	4,731	22.6	5,814	20.8	7,070	21.1	7,594	21.1	29,166	21.3
Location												
MD	13,815	66.9	16,491	72.0	23,538	76.2	27,575	74.2	28,578	70.6	109,987	72.3
DC	5,462	26.4	4,939	21.6	5,695	18.4	7,553	20.3	9,758	24.1	33,407	22.0
VA	1,390	6.7	1,474	6.4	1,672	5.4	2,040	5.5	2,137	5.3	8,713	5.7

Table 1. Absolute numbers and characteristics of HCV screened individuals from 1/2017-10/2021.

Percent is equal to the percent of HCV screened patients with a given characteristic over the total screened with the given characteristic.

\*Black race includes all individuals who indicated their race as 'Black,' 'African American' or 'Black or African American.'

\*\*Hispanic and Latin American represents all those with ethnicities listed as Hispanic, Latin American, Cuban, Dominican, Puerto Rican, South American, or

Colombian; race and ethnicity are collected separately, therefore Hispanic/LA is not independent from the races listed.

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# Screening rates per visit and demographic comparisons before and after HCV universal alert, January, 2020—October, 2020

To model the effect of the universal screening alert on the screening rate per outpatient visit and on the characteristics of those screened, a symmetric time period was analyzed which centered around the month of the implementation date. Absolute number and percentage of characteristics for the entire unique outpatient and the HCV screened populations from 1/1/2020-10/31/2020 are reported in the Table 2. The outcomes of a mixed effect multivariable analysis model are presented in Table 3. Adjusting for all other covariates, there was a 62% increased odds of being screened after the universal alert (post-alert) compared to prior to the universal alert (pre-alert) (OR<sub>adj</sub> 1.62, 95% CI: 1.54, 1.70; Table 3). Compared to January 2020, there was a statistically significantly decreased odds of screening in March–May 2020, no significant difference in June 2020, and then increased odds of screening thereafter (Table 3, Fig 2). March– May 2020 also represents a major clinic shutdown during the COVID-19 pandemic.

On multivariable analysis, there was a statistically significant interaction between sex and time period–females showed a 10%-decreased odds of being screened post-alert compared to male patients pre-alert ( $OR_{adj}$  0.90, 95% CI: 0.85, 0.95). Compared to patients who identified as White, patients that identified as Black, or any other race, were associated with a 59% ( $OR_{adj}$  1.59, 95% CI: 1.53, 1.64) and 61% increased odds ( $OR_{adj}$  1.61 95% CI: 1.52, 1.71), respectively, of being screened for HCV. Each one-year increase in age was associated with a 2% decreased

	All Pre-Alert** (n = 429,085)		All Post-Alert** (n = 501,076)		Screened Pre-Alert** (n = 10,717)		Screened Post-Alert** (n = 21,295)	
	N or Median	%/IQR	N or Median	% or IQR	N or Median	% or IQR	N or Median	% or IQR
Age	59	41-73	59	41-73	49	29-69	48	28-68
Sex								
Male	169,470	39.50%	198,082	39.53%	3,371	31.45%	6,789	31.88%
Female	259,556	60.49%	302,897	60.45%	7,343	68.52%	14,503	68.11%
Race								
White	217,342	50.65%	258,498	51.59%	4,371	40.79%	8,698	40.85%
Black/African American	141,955	33.08%	156,288	31.19%	4,612	43.03%	9,044	42.47%
American Indian/Alaska Native	1,036	0.24%	1,164	0.23%	33	0.31%	73	0.34%
Asian	10,022	2.34%	11,241	2.24%	331	3.09%	739	3.47%
Native Hawaiian/Pacific Islander	204	0.05%	249	0.05%	10	0.09%	17	0.08%
Multiple	2,947	0.69%	3,406	0.68%	84	0.78%	174	0.82%
Other	27,615	6.44%	31,905	6.37%	790	7.37%	1,579	7.41%
Unknown/Declined	27,964	6.52%	38,325	7.65%	486	4.53%	971	4.56%
Ethnicity								
Non-Hispanic	379,089	88.35%	437,714	87.35%	9,693	90.45%	19,227	90.29%
Hispanic	10,174	2.37%	11,314	2.26%	290	2.71%	659	3.09%
Other/Unknown	39,822	9.28%	52,048	10.39%	734	6.85%	1,409	6.62%
Insurance Category								
Government	4,542	1.06%	5,231	1.04%	92	0.86%	205	0.96%
Medicaid	61,786	14.40%	70,520	14.07%	2,282	21.29%	4,245	19.93%
Medicare	115,163	26.84%	124,708	24.89%	1,961	18.30%	3,264	15.33%
Private	187,298	43.66%	225,650	45.03%	5,225	48.75%	11,454	53.79%
Self-Pay	13,150	3.06%	19,500	3.89%	243	2.27%	414	1.94%
Other/Unknown	47,146	10.99%	55,467	11.07%	914	8.53%	1,713	8.04%

Table 2. Characteristics and percentages of all individuals (screened and unscreened) and all screened individuals seen in the MedStar outpatient setting for 10 months between 1/1/2020-10/31/2020.

\*\* Pre-alert: Jan 1<sup>st</sup> 2020 –May 31<sup>st</sup> 2020; Post-alert: June 1st 2020 –Oct 31<sup>st</sup> 2020.

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odds of being screened for HCV ( $OR_{adj}$  0.98, 95% CI: 0.97, 0.98). Compared to patients who had commercial or private insurance, patients who had Medicaid were associated with an increase in odds of screening ( $OR_{adj}$  1.10, 95% CI: 1.05, 1.15) whereas patients that had government ( $OR_{adj}$  0.83, 95% CI: 0.71, 0.97), or Medicare ( $OR_{adj}$  0.62, 95% CI: 0.62, 0.65) were all associated with a decrease in odds of screening (Table 3).

# Discussion

# Implementation of the HCV EHR alert and screening rates

The data presented here suggests that implementation of an EHR alert for HCV universal screening in a large health system is an effective strategy for accomplishing increased screening rates. Absolute number of screens per month was 2,052 before the universal screening guide-line and EHR alert were adopted, and this rate increased by 103% to 4,169 screens soon after the implementation of the EHR alert for universal screening at the end of May 2020, despite the COVID-19 pandemic. To determine whether it was a result of the change in USPSTF and CDC guideline recommendations alone or the addition of the alert which was associated with an increase in screening, screening rates among all outpatient appointments from a smaller

#### Table 3. Multivariable mixed effects logistic regression models for pre-post 6/1/2020 (model one) and by month 1/2020-10/2020 (model two).

Adjusted b estimates for outco	ome								
Random Effects Model 1 (n = variance 4.17 (0.06))	1,799,767, intercep	ot = 0.00 [0.0,0.01]	], constant	Random Effects Model 2 (n = 1,799,767, intercept = 0.01 [0.00, 0.01], Constant Variance 4.12 (0.06))					
			Fixed Effects						
Covariate	Coefficient	95% CI	p-value	Covariate	Coefficient	95% CI	p-value		
Time period				Time period					
Pre-alert	Ref			Jan 2020	Ref	[1.01, 1.12]	0.032		
Post-alert	1.62	[1.54, 1.70]	<0.001	Feb 2020	1.06	[0.87, 0.98]	0.010		
				March 2020	0.93	[0.44, 0.51]	<0.001		
				April 2020	0.47	[0.55, 0.63]	<0.001		
				May 2020	0.59	[0.95, 1.06]	0.938		
				June 2020	1.00	[1.18, 1.31]	<0.001		
				July 2020	1.24	[1.17, 1.29]	<0.001		
				Aug 2020	1.23	[1.29, 1.43]	<0.001		
				Sept 2020	1.36	[1.36, 1.51]	<0.001		
				Oct 2020	1.43	[0.97, 0.98]	<0.001		
Sex				Sex					
Male	Ref			Male	Ref				
Female	1.26	[1.20, 1.32]	<0.001	Female	1.18	[1.14, 1.22]	<0.001		
Interaction term time*sex									
Pre*male	Ref								
Post*female	0.90	[0.85, 0.95]	<0.001						
Age	0.98	[0.97, 0.98]	<0.001	Age	0.98	[0.97, 0.98]	<0.001		
Race				Race					
White	Ref			White	Ref				
Black/African American	1.59	[1.53, 1.64]	<0.001	Black/ African American	1.58	[1.53, 1.64]	<0.001		
Other	1.61	[1.52, 1.71]	<0.001	Other	1.60	[1.52, 1.70]	<0.001		
Ethnicity				Ethnicity					
Non-Hispanic	Ref			Non-Hispanic	Ref				
Hispanic	1.08	[0.97, 1.20]	0.177	Hispanic	1.07	[0.97, 1.19]	0.180		
Insurance type				Insurance type					
Private	Ref			Private	Ref				
Government	0.83	[0.71, 0.97]	0.022	Government	0.83	[0.71, 0.98]	0.023		
Medicaid	1.10	[1.05, 1.15]	<0.001	Medicaid	1.11	[1.06, 1.16]	<0.001		
Medicare	0.62	[0.60, 0.65]	<0.001	Medicare	0.63	[0.60, 0.66]	<0.001		
Self-Pay	0.71	[0.64, 0.78]	<0.001	Self-Pay	0.71	[0.65, 0.79]	<0.001		

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time period (1/1/20–10/31/20) were analyzed. This allowed for a symmetric time range surrounding the implementation date and a month-by-month analysis. Screening rates rose precipitously after May 2020 and remained at levels significantly higher than those in January 2020. Overall, there was an 162% increase in screening rate in the five months after the alert compared to the five months before. This leads us to conclude that the EHR alert adopted on 5/28/2020 was associated with a significant increase in screening rate, although not the only likely factor contributing to the rise in screening rate. This increase was not seen between March and May, when the universal screening guidelines had been published, but the system EHR alert had not yet been adopted.

As aforementioned, in March 2020 major USA guideline publishing organizations recommended changing practice to one-time universal screening for HCV in all patients ages 18–79,



# **Screening Rate and Total Outpatient Visits 2020**

**Fig 2. Screening rate and total outpatient visits 2020.** Screening rate per 1,000 outpatient visits and total outpatient visits, both screened and unscreened, between January 1<sup>st</sup>, 2020 to October 31<sup>st</sup>, 2020. The arrow indicates the approximate implementation of the universal screening electronic health record alert on May 28<sup>th</sup>, 2020.

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all pregnant women and with repeated testing in those with risk factors [7, 8]. Unfortunately, this drastic and promising change in elimination strategy coincided with the rise of the COVID-19 pandemic. In the month of March 2020, national outpatient visits began declining until they reached a 70% decline from the previous year in April 2020; afterwards, they began increasing again until they reached pre-COVID levels in August 2020 [15]. Our results are consistent with this finding, as absolute visits decreased rapidly between March and April; this could also explain the concurrent decrease in HCV screening rate, despite the coincidental adoption of universal screening guidelines. However, it does not likely explain the rapid increase in screening rates after May 2020, as an increase in the number of visits does not necessarily translate to an increase in how many individuals are screened per 1,000 visits. In addition, although the number of visits returned to pre-COVID levels in July 2020, screening rates were significantly higher than previously. These considerations support the conclusion that the EHR alert was driving the encouraging screening trends.

Even before the onset of the COVID-19 pandemic, the United States was not on track to achieve the elimination goals set out by the World Health Organization, according to recent modelling of HCV screening and connection to care [16]. Although global HCV prevalence decreased from 0.9% in 2015 to 0.7% in 2020, they estimated that 78% of HCV cases were undiagnosed [16]. This suggests that the first step of elimination, thoroughly screening the general population, may prove to be the most important. Thus, developing strategies such as EHR alerts to enhance population screening will play a significant role in HCV elimination.

There are several other reports in the literature of EHR prompts or alerts improving rates of screening, specifically for HCV [9-14, 17-19]. Most of the studies were completed when only

the BC screening guidelines were in place. Sidlow et al. (2015) reported a 254% increase in HCV screening after incorporating a clinical reminder into the EHR for primary care patients who belonged to the BC and still required a screen. Barter et al. (2021) systematically reviewed 11 studies and found that EHR utilization increased HCV screening rates across all of them. These findings are consistent with those presented here, as the re-implementation of the EHR alert for BC screening in September 2018 was followed by a 61% increase in absolute number of screens and 6.3% increase in age of those screened.

Only a few studies have observed screening data after the universal screening guidelines were published in March 2020 [17–19]. Of note, all of these studies were conducted in emergency departments. The largest of these studies looked at screening rates before and after implementation of a "Best Practice Advisory" (BPA) for universal screening; they found that 0.3% (218/69,604) of patients were screened for 11 months pre-BPA, and 22.0% (14,981/ 68,225) were screened in the 11 months post-BPA, representing a 73-fold increase in screening rate [17]. This increase is likely more drastic than the results found here as we measured screening rates in the outpatient setting, where baseline screening rates were already higher. Taking our findings and the previous literature into account, EHR alerts for universal screening, along with other clinical decision support tools, can play an important role in HCV elimination.

# Characteristics of screened and unscreened individuals: Who are we missing?

Regardless of universal screening and EHR alerts, the importance of identifying patients who are not getting screened cannot be understated. To understand this problem, we compared the basic characteristics of unique patients who were HCV screened to unique patients who were not screened by the universal alert over the 10-month period between 1/1/2020 and 10/31/2020 (pre- and post-alert). Multivariable fixed effects modeling revealed that patients identifying as female were 17% more likely to be screened than males, Black individuals 66% more likely than White, and Hispanic 16% more than non-Hispanic. According to national data from 2019, the majority of actively HCV-infected individuals identify as male (63.7%), thus representing one discrepancy between who is getting tested and who should be getting tested [20]. Older data found that the national prevalence of HCV was 1.0% among non-Hispanic White individuals and 2.3% among non-Hispanic Black individuals, suggesting that the higher screening rate of Black individuals may be warranted [21]. Consideration of these simple demographics in screening may help providers make clinical decisions while limiting bias.

A notable discrepancy we present here was that in insurance type. Patients with Medicare or Medicaid insurance were screened at a rate about 60% and 110%, respectively, of those with private insurance. One analysis of national data from 2001–2010 found that the prevalence of HCV in those with private insurance was 0.81%, while it was 1.24% in those with Medicare, and 2.58% in those with Medicaid [22]. This data indicates that HCV prevalence is approximately 300% higher in Medicaid patients compared to privately insured, while our data revealed only a 10% higher screening rate. Therefore, our results demonstrate that, although screening rates were slightly higher in patients with Medicaid than private insurance, they are not proportionate to the prevalence of HCV in these populations. Those with Medicare insurance were also tested at disproportionately low rates, though this could partially result from the increased screening of lower ages. Policies to improve screening could incorporate these disparities, perhaps with increased clinical decision support for those with Medicaid and Medicare insurance.

### Limitations

Many of the limitations of this study result from the vast size of the data sets and the lack of granularity on the unique patient level. Temporal observations of unique-screened patients over the 58-month period required us to only include the last appointment at which an individual was screened. This decision was made because a patient who is HCV Ab positive will always remain Ab positive, though a patient with a negative screen can later seroconvert and become positive. Although this could skew the results toward a later temporal distribution, a simple calculation of average screens per person was conducted to find that, among those screened, a vast majority were only screened once, with an average of approximately 1.3 screens per person. Therefore, the descriptive statistics presented here were unlikely affected by the choice of last versus first screening–this measure was not needed for the 10-month period analysis.

Our temporal analysis of unscreened versus screened individuals was limited by database software. The pre-post analysis for screening rates before and after the universal alert was conducted on a limited, symmetric time frame rather than the entire 58-month period. With approximately 2.7 million outpatient appointments annually, the size of the potential sample over a 58-month period exceeded the capacity of the database. Therefore, a five-month period preceding and following the alert implementation was chosen for a more statistically manageable, yet still large, sample size, as well as a historically meaningful period. For this analysis, univariable statistical comparison was not appropriate for pre-post analysis because individual patients could have been seen at multiple appointments before being screened; therefore, a multivariable mixed-effect analysis was completed. Additionally, the pre-post comparison of screening rate was possibly influenced by the low number of visits and screens at the beginning of the COVID-19 pandemic.

The size of the database also limited our ability to accurately collect and analyze certain variables. Given that pregnancy is a consideration in HCV screening, pregnancy status of participants could have impacted screening rates. Universal pregnancy screening was not recommended until June, 2021 by the American College of Gynecology nor the Society for Maternal Fetal Medicine, and thus this was not captured separately. Additionally, we were not able to differentiate whether patients' visits were at primary care or specialty clinic sites.

Another limitation of this study is that data before 2017 was not available to us, as the health system transitioned from one EHR to another. Thus, our analysis could not account for patients who were screened before 2017, and therefore would not necessarily need to be screened during this later time period unless they had continued risk factors.

One final limitation of this study is that we could not explore provider interaction with the screening alert, which prevented us from determining potential reasons patients went unscreened. With this data, we would have been able to observe which providers viewed the alert, and then how many indicated a reason for not screening the patient; for example, if the patient had previously been screened or treated for HCV in a different health system.

# Conclusions

Our findings support the universal adoption of an EHR prompt for universal HCV screening of adults 18–69. The absolute number and rate of HCV screening increased over time, and became dramatically higher with the implementation of the universal screening recommendation and EHR alert. Our findings also support screening and re-testing of individuals who are at higher risk of HCV infection. Females were tested more than males, despite data suggesting that males have a higher HCV prevalence. In addition, patients with Medicare or Medicaid insurance were not screened proportionately to the relative national prevalence of HCV in

these populations. Implementation of such practices could play a crucial role as the first step in identification and then elimination of HCV.

### Supporting information

S1 Data. (XLSX) S2 Data. (ZIP)

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#### References

- 1. World Health Organization. Combating Hepatitis B and C to reach elimination by 2030. WHO; Geneva, Switzerland, 2016.
- 2. Hofmeister MG, Rosenthal EM, et al. Estimating Prevalence of Hepatitis C Virus Infection in the United States, 2013–2016. *Hepatology*. 2019; 69(3). https://doi.org/10.1002/hep.30297 PMID: 30398671
- Smith BD, Morgan RL, et al. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945–1965. Morbidity and Mortality Weekly Report: Recommendations and Reports. 2012 Aug 17; 61(4):1–32. PMID: 22895429
- Carty PG, Fawsitt CG, et al. Population-Based Testing for Undiagnosed Hepatitis C: A Systematic Review of Economic Evaluations. *Applied health economics and health policy*. 2021 Dec. <u>https://doi.org/10.1007/s40258-021-00694-w</u> PMID: 34870793
- 5. Eckman MH, Ward JW, Sherman KE. Cost Effectiveness of Universal Screening for Hepatitis C Virus Infection in the Era of Direct-Acting, Pangenotypic Treatment Regimens. *Clinical Gastroenterology and Hepatology* 2019 April; 17(5):930–939.
- Barocas JA, Tasillo A, Eftekhari Yazdi G, Wang J, Vellozzi C, Hariri S, et al. Population-level Outcomes and Cost-Effectiveness of Expanding the Recommendation for Age-based Hepatitis C Testing in the United States. Clinical Infectious Diseases 2018 Aug 01,; 67(4):549–556. https://doi.org/10.1093/cid/ ciy098 PMID: 29420742

- Owens DK, Davidson KW, et al. Screening for Hepatitis C Virus Infection in Adolescents and Adults: US Preventive Services Task Force Recommendation Statement. JAMA: the Journal of the American Medical Association 2020 Mar 10,; 323(10):970–975. https://doi.org/10.1001/jama.2020.1123 PMID: 32119076
- Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC recommendations for hepatitis C screening among adults—United States, 2020. MMWR Recommendations and Reports. 2020 Apr 3; 69(2):1. https://doi.org/10.15585/mmwr.rr6902a1 PMID: 32271723
- Barter L, Cooper CL. The impact of electronic medical record system implementation on HCV screening and continuum of care: a systematic review. *Annals of Hepatology* 2021 Sep; 24. <u>https://doi.org/10.1016/j.aohep.2021.100322</u> PMID: 33549734
- Kruger DL, Rein DB, et al. Implementation of Birth-Cohort Testing for Hepatitis C Virus. Health Promotion Practice 2017 Mar; 18(2):283–289. https://doi.org/10.1177/1524839916661495 PMID: 27496859
- Hojat L, Avery A, Greco PJ, Kaelber DC. Doubling Hepatitis C Virus Screening in Primary Care Using Advanced Electronic Health Record Tools—A Non-Randomized Controlled Trial. *Journal of General Internal Medicine* 2019 Dec 02; 35(2):498–504. https://doi.org/10.1007/s11606-019-05536-z PMID: 31792863
- Sidlow R, Msaouel P. Improving Hepatitis C Virus Screening Rates in Primary Care: A Targeted Intervention Using the Electronic Health Record. *Journal for Healthcare Quality* 2015 Sep; 37(5):319–323. https://doi.org/10.1097/JHQ.00000000000010 PMID: 26186704
- Mulhem E, Brown I, Song K. Electronic Health Record Reminder Effect on Hepatitis C Antibody Screening. Journal of the American Board of Family Medicine 2020 Nov 01; 33(6):1016–1019. https://doi.org/ 10.3122/jabfm.2020.06.190440 PMID: 33219082
- Geboy AG, Nichols WL, Fernandez SJ, Desale S, Basch P, Fishbein DA. Leveraging the electronic health record to eliminate hepatitis C: Screening in a large integrated healthcare system. *PLOS ONE* 2019 May; 14(5).
- Chatterji P, Li Y. Effects of the COVID-19 Pandemic on Outpatient Providers in the United States. *Medi*cal Care 2021 Jan; 59(1):58–61. https://doi.org/10.1097/MLR.00000000001448 PMID: 33136711
- Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. *The Lancet. Gastroenterology & Hepatology*. 2022 Feb 15. https://doi.org/10.1016/S2468-1253(21)00472-6 PMID: 35180382
- Ford J, Chechi T, Toosi K, Mahmood B, Meehleis D, Otmar M, et al. Universal Screening for Hepatitis C Virus in the ED Using a Best Practice Advisory. *The Western Journal of Emergency Medicine*. 2021 Jun 09; 22(3):719–725. https://doi.org/10.5811/westjem.2021.1.49667 PMID: 34125052
- Martel-Laferriere V, Baril J, et al. Opt-out universal HCV and HIV screening in a Canadian emergency room: a cross-sectional study. *BMJ Open* 2022; 12.
- Burrell CN, Sharon MJ, et al. Using the electronic medical record to increase testing for HIV and hepatitis C virus in an Appalachian emergency department. *BMC Health Services Research*. 2021 May 29; 21 (1):524. https://doi.org/10.1186/s12913-021-06482-5 PMID: 34051774
- Reau N, Sulkowski MS, et al. Epidemiology and Clinical Characteristics of Individuals with Hepatitis C Virus Infection in the United States, 2017–2019. Adv Ther. 2021 Oct 27; 38(12):5777–5790. https://doi. org/10.1007/s12325-021-01928-y PMID: 34704194
- Bradley H, Hall EW, Rosenthal EM, Sullivan PS, Ryerson AB, Rosenberg ES. Hepatitis C virus prevalence in 50 US states and DC by sex, birth cohort, and race: 2013-2016. *Hepatology Communications*. 2020 Mar; 4(3):355–70.
- Bush H, Paik J, Golabi P, de Avila L, Escheik C, Younossi ZM. Impact of hepatitis C virus and insurance coverage on mortality. Am J Manag Care. 2019 Feb 1; 25(2):61–7. PMID: 30763036