nature portfolio

Peer Review File

Sociodemographic Disparities in Hepatitis C Care Utilization and Testing in the United States

Corresponding Author: Dr Adam Buckholz

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

Reviewer #2

(Remarks to the Author)
1. Unclear that the primary outcome is a valid measure of HCV care utilization. After reading the manuscript several times, I believe that the definition of HCV care utilization was any visit occurring any time after the existence of an HCV diagnostic code in any of five diagnostic fields. If so, it is a highly non-specific marker of care utilization that implicitly assumes that any and all visits following HCV diagnosis are indications of HCV care. That is not true. HCV is a chronic diagnosis and a person could carry that ICD code in their diagnostic fields for years while they pursue every other type of care they need. To pick an extreme example, if I have an HCV diagnosis and see the ophthalmologist for glaucoma, I might have the diagnostic code in my records, but was the ophthalmology visit HCV care utilization?

2. The discussion goes far beyond the data analyzed. For example:
“Between 2010 and 2019, 36.6 million HCV tests were performed”
this is far too definitive of a statement that overlooks many limitations of the analysis. These data provide a good look at HCV testing in traditional ambulatory care settings when the labs are processed by a traditional, CLIAA certified clinical diagnostic lab. The analysis can make no insight into how many tests were happening in harm reduction sites, criminal legal settings, temporary shelters, etc. Nor can it provide any estimate of POC testing that may not appear in the dataset. Those venues play a huge role in the strategy to end HCV transmission and this sentence ignores that reality. The discussion moves on to consider that ambulatory care settings alone cannot provide the screening needed to end HCV transmission – I agree – but why do you say that based on the data in this paper?

3. The second biggest finding – documenting disparities in access based on race, payer, and geographic region are over simplified. The comparisons of demographics and predictors of HCV care utilization are naïve to larger context. For example, older people are more like to have a visit for HCV. At the same time, older people are more likely to have just about any kind of visit other than prenatal care. So, are all of the findings about who is more likely to have an HCV visit simply reflections of larger trends in U.S. healthcare? Another good example of this is that having Medicaid as the payor and being a person who uses drugs were both associated with ED visits – that is true across diseases, not only HCV. The disparities are real and important – but it is arbitrary to say that the disparities are related to “HCV,” they are a specific realization of the larger structural problems with healthcare in the U.S.

4. Similar to the comment above, but slightly different example – the time trend analysis. The results show that HCV visit utilization went up over time. Is this really a difference in the likelihood that a person who is living with HCV infection was more likely to seek treatment in 2019 than in 2017? Or is it that there has been a major effort to diagnose HCV infection and that the pool of patients grew? That distinctions matters if you are planning a strategic response to eliminate HCV. If folks living with HCV infection really are more likely to seek care now than they used to be, that is wonderful and we really need to double/triple-down on screening. But if it is that the pool is getting larger, that suggests that we are making real progress with screening and need to focus sharply on linkage to care…probably, we need both things, but this analysis does not recognize the differences.

I have a few minor points as well:

1. Why exclude time while being pregnant from “at risk” for HCV testing? – I doubt very much that this in anyway changed the quantitative findings or the conclusions, but it jumped out at me because many people identify pregnancy and prenatal care period as being important for HCV elimination.

2. The discussion section opening is a little grandiose: “In this nationally representative study of ambulatory care use, our findings provide a comprehensive and contemporary evaluation of hepatitis C testing and ambulatory care utilization.” – I am not sure this is entirely fair. The data are more than 6 years old and we have had two presidential elections in the meantime! I understand that the data are what they are. I applaud the creative use of existing data to make public health and health policy insights. All of that being said, you can control how you talk about the data and this is not quite accurate.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
The authors have responded thoughtfully and addressed most of the suggested changes and the manuscript is improved as a result.

Reviewer #2

(Remarks to the Author)
The authors provided a thorough and thoughtful update and response to every comment from reviewers. The paper is improved and I think ready for publication.

To the reviewers, thank you for your very helpful feedback on our manuscript. We believe that having incorporated your suggestions, as detailed below, has improved the clarity and messaging of this study as well as forced us to examine the various strengths and limitations therein.

We hope that these revisions are to your standards and appreciate the opportunity to revise.

Reviewers' comments:

Reviewer #1 (Remarks to the Author):

Overall Summary and Evaluation

This is a well written, well-referenced paper describing the results of a nationwide survey analysis of both hepatitis C testing and care utilization in ambulatory and emergency settings in the US from 2010-2019. The authors report three key findings: demographic difference in the care settings utilized by people with HCV infection, increase in visits for those with HCV over the study period but primarily for White patients in the office setting, and overall low HCV testing rates. These findings specifically around HCV screening are important, timely and salient to the journal's readership given national HCV elimination goals that call for elimination by 2030, of which improved HCV screening is a large component. The paper's strengths include a substantial sample size, clear writing, reproducible methods, and a discussion well-tailored to the study's findings. Areas for improvement include placing a greater emphasis on the findings of low screening rates rather than on care utilization, as there is no suggestion that the "care" in question is specifically related to HCV, thus it has less relevance to the HCV cascade and therefore HCV elimination. In addition, enhanced discussion about why HCV screening rates are so low would be helpful.

Major Comments

Methods: It is unclear whether the care visits in question are a) visits in which HCV is addressed and HCV-specific care is provided, versus b) visits of any type for people who happen to have HCV. The findings are much less impactful if it's the latter, as these visits have questionable impact on the HCV care cascade and elimination. For example, page 3, line 110 describes "a care visit for a pt with identified CHC" and the primary variable of interest in the study, which seems like the visit is not necessarily related to HCV. Yet in the abstract (page 1, lines 22 and 32) the authors refer to "HCV visits,"

which implies visits where HCV is specifically addressed. Clarification here is very important in order to interpret and appreciate the paper's findings.

Thank you for the feedback. Upon reviewing the NAMCS documentation, visits included in our study were those that specifically addressed HCV and provided HCV specific care. We have updated wording in our methodology to provide some clarification for our readers.

"The primary variable of interest in this study was a care visit for a patient with identified CHC during which HCV-specific care was provided."

It's a strength of the paper that the authors use three decreasingly restrictive "tiers" of visit types to most accurately capture "true" HCV screening rates.

Discussion: More emphasis should be placed on the fact that the CDC's universal HCV screening recommendations were not released until 2020, after the study period. Thus, any discussion of the low screening rates among non-baby boomers should be interpreted in this context.

Thank you for this feedback, we have included the following sentence in our limitations to help put our findings into context and to avoid any confusions.

"Lastly, our most recent data were from 2019, a year prior to CDC's updated recommendation of universal screening for HCV."

Additional comments

Abstract:

Line 10, it's preferable to refer to HCV "elimination" rather than "eradication" here and throughout.

Thank you for this feedback, this has been updated.

Line 11, I would also mention that we have national treatment recommendations too.

Thank you for this feedback, we have included the following in our introduction. Unfortunately, due to the word limitations of the abstract we were not able to include this in the abstract.

"In response to such trends, the CDC and United States Preventive Services Task Force in 2020 released revised recommendations suggesting that all adults receive one-time screening for HCV regardless of risk factors. These efforts are in

accordance with national and international goal to eliminate HCV as a public health threat by 2030."

Line 12, I would suggest switching the order in which the two main variables of interest are reported, i.e. mention screening first followed by care utilization, as this order is more in line with the order of the HCV care cascade.

Your point is well taken. There's certainly a little bit of chicken and egg going on, whereby increased screening in a certain setting may increase care in that setting, and vice versa. Because utilization was the main thrust and our *a priori* primary variable of interest, we did not want to reverse the order at this time, but certainly on follow up manuscripts and utilization assessments using other sources, we could start with testing and move to care visits.

Introduction:

Page 2, line 50: consider rewording "undergo medical care." Something like "interface with a healthcare provider" (or healthcare system) may be more accurate.

Thank you for this feedback, we have made the following changes.

"In order to be treated, the disease must be identified, which generally requires an infected individual to interface with the healthcare system"

Line 52: instead of "HCV positive individuals," consider "individuals with HCV."

Thank you for this feedback, these changes have been made throughout the manuscript.

Line 68: It would be helpful to briefly describe the national/international HCV elimination goals for context.

Thank you for this feedback. We have made the following changes to include national / international HCV elimination goals.

"In response to such trends, the CDC and United States Preventive Services Task Force in 2020 released revised recommendations suggesting that all adults receive one-time screening for HCV regardless of risk factors. These efforts are in accordance with the national and international goal to eliminate HCV as a public health threat by 2030."

Line 71: Why did the authors hypothesize that increased utilization and screening would be among White insured baby boomers? Additional explanation would be helpful.

Thank you for this feedback. Studies have found that racial minorities and those with lower SES are more likely to face financial and non-financial barriers to accessing care, which is why we hypothesized White, insured, and older individuals are more likely to have higher care utilization.

Results:

Page 6, lines 209-210-the authors describe 2016-2018 as the years following FDA approval of DAAs and national screening recommendations. This seems late, as DAAs were approved 2013-14 and CDC baby boomer screening recommendations were in 2012, so the 2012-2015 timeframe would be more accurate.

Thank you for this feedback. We have made the following changes so our wording better reflects the timeline.

"the odds of an identified HCV visit were highest for the combined year period of 2016 and 2018 (OR 2.05, 95% CI [1.11, 3.78]). The largest increase in visit rate was observed between 2012-2014, from 0.22% to 0.43% or 98.8% increase. This is likely due to updated screening guidelines for baby boomers put forth by the CDC in 2012"

Discussion:

Page 8, line 316: The paper would benefit from additional discussion of the context of HCV screening in the ER. As the USPSTF Grade B HCV screening recommendations (and thus insurance coverage for screening) are specifically tied to the ambulatory setting, there has been a lack of clarity about coverage for (and therefore barriers to implementation of) HCV screening in the ER.

Thank you for this feedback. We have incorporated this in our discussions.

"One major barrier to improved HCV screening is the lack of insurance coverage for HCV testing in the ER. ER-based HCV screening has been shown to be cost-effective and has the opportunity to significantly reduce future complications, particularly for vulnerable patients."

Page 9, line 357: Consider "patients with HCV" instead of "HCV positive patients."

Thank you for this feedback, we have made this change.

Page 10, line 367: Clarify the statement that critical transition during the study period was "widespread adoption of universal screening." This recommendation was made by the CDC in 2020, so after the study period. Also, I would phrase this as a recommendation for universal screening, as the data from this paper shows screening

has not been widely adopted.

Thank you for this feedback. We have made the following changes to clarify.

“Finally, a critical transition in hepatitis C screening and management took place during this study period, including widespread adoption of screening in baby boomers.”

Additionally, we included the following in our discussions.

“Moving forward, it is critical to have updated HCV screening rates and to evaluate the effect of universal HCV screening put forth in 2020.”

Reviewer #2 (Remarks to the Author):

1. Unclear that the primary outcome is a valid measure of HCV care utilization. After reading the manuscript several times, I believe that the definition of HCV care utilization was any visit occurring any time after the existence of an HCV diagnostic code in any of five diagnostic fields. If so, it is a highly non-specific marker of care utilization that implicitly assumes that any and all visits following HCV diagnosis are indications of HCV care. That is not true. HCV is a chronic diagnosis and a person could carry that ICD code in their diagnostic fields for years while they pursue every other type of care they need. To pick an extreme example, if I have an HCV diagnosis and see the ophthalmologist for glaucoma, I might have the diagnostic code in my records, but was the ophthalmology visit HCV care utilization?

Thank you for your feedback. We recognize that the diagnostic code, and the context in which we’re describing it, needs improvement. Per the guidance for coding in NAMCS/NHAMCS, the variable Diag, which includes up to 5 diagnoses and were analyzed for HCV care use, refers to the provider’s primary, secondary, tertiary, etc. diagnosis and should be directly related to the reason for visit. While individual providers may in fact code incidental diagnoses, for example a history of hepatitis C despite the visit being for migraines, generally an HCV diagnosis code should reflect a direct association with hepatitis C and the present visit. We have updated language in the methods, results, and discussion sections to reflect this.

2. The discussion goes far beyond the data analyzed. For example:
“Between 2010 and 2019, 36.6 million HCV tests were performed”

this is far too definitive of a statement that overlooks many limitations of the analysis. These data provide a good look at HCV testing in traditional ambulatory care settings when the labs are processed by a traditional, CLIAA certified clinical diagnostic lab. The analysis can make no insight into how many tests were happening in harm reduction sites, criminal legal settings, temporary shelters, etc. Nor can it provide any estimate of POC testing that may not appear in the dataset. Those venues play a huge role in the strategy to end HCV transmission and this sentence ignores that reality. The discussion moves on to consider that ambulatory care settings alone cannot provide the screening needed to end HCV transmission – I agree – but why do you say that based on the data in this paper?

Thank you for this comment. We agree, these statements are too general and need to include clarifying language. We have made these changes throughout, specifically noting that this provides a broad look at testing and management only within the two most traditional ambulatory care settings. Non-traditional care settings and testing rates are not assessed by our study. We also included the following for further clarification.

"While not assessed in our study, others have found that Point of care (POC) HCV testing has shown promise in other countries and was recently approved by the FDA"

3. The second biggest finding – documenting disparities in access based on race, payer, and geographic region are over simplified. The comparisons of demographics and predictors of HCV care utilization are naïve to larger context. For example, older people are more like to have a visit for HCV. At the same time, older people are more likely to have just about any kind of visit other than prenatal care. So, are all of the findings about who is more likely to have an HCV visit simply reflections of larger trends in U.S. healthcare? Another good example of this is that having Medicaid as the payor and being a person who uses drugs were both associated with ED visits – that is true across diseases, not only HCV. The disparities are real and important – but it is arbitrary to say that the disparities are related to “HCV,” they are a specific realization of the larger structural problems with healthcare in the U.S.

Thank you for the feedback and thought-provoking questions. We agree that disparities faced by patients with HCV largely reflect trends in the US healthcare system. However, HCV is a curable infectious disease that if left untreated, can lead to significant comorbidities and major healthcare spending. This is why we wanted to specifically evaluate utilization disparities in patients with HCV. Additionally, one difference to note is that older patients, particularly those in the “baby boomer” cohort, may have higher healthcare utilization due to changes in screening guidelines. It would be interesting to evaluate changes in healthcare

utilization post 2020, after the updated universal screening guideline (unfortunately, as we noted in our limitations, data collection was discontinued post 2020). Another unique distinction in terms of disparities is that HCV screening in the ER setting is not covered by insurance, which further exacerbates existing disparities in the HCV diagnosis and treatment cascade, as minorities and patients with lower SES are more likely to utilize ER as a source of healthcare.

4. Similar to the comment above, but slightly different example – the time trend analysis. The results show that HCV visit utilization went up over time. Is this really a difference in the likelihood that a person who is living with HCV infection was more likely to seek treatment in 2019 than in 2017? Or is it that there has been a major effort to diagnose HCV infection and that the pool of patients grew? That distinctions matters if you are planning a strategic response to eliminate HCV. If folks living with HCV infection really are more likely to seek care now than they used to be, that is wonderful and we really need to double/triple-down on screening. But if it is that the pool is getting larger, that suggests that we are making real progress with screening and need to focus sharply on linkage to care…probably, we need both things, but this analysis does not recognize the differences.

I have a few minor points as well:

1. Why exclude time while being pregnant from “at risk” for HCV testing? – I doubt very much that this in anyway changed the quantitative findings or the conclusions, but it jumped out at me because many people identify pregnancy and prenatal care period as being important for HCV elimination.

Thank you for this comment. In this case, the reason we discounted pregnancy was that there are separte recommendations to test all patients who are pregnant for viral hepatitis including hepatitis B and hepatitis C. These being outside standard screening opportunities, we felt that these should not be included in the denominator of “eligible for screening” under the pre-defined criteria.

2. The discussion section opening is a little grandiose: “In this nationally representative study of ambulatory care use, our findings provide a comprehensive and contemporary evaluation of hepatitis C testing and ambulatory care utilization.” – I am not sure this is entirely fair. The data are more than 6 years old and we have had two presidential elections in the meantime! I understand that the data are what they are. I applaud the creative use of existing data to make public health and health policy insights. All of that being said, you can control how you talk about the data and this is not quite accurate.

Thank you for your comment. We have adjusted this sentence and recognize that contemporary may be misleading. Interestingly, it was our intent to include present-day data in the analysis. However, in the time since we started data collection, government funding priorities, COVID-19, etc. Have made it such that current and future NAMCS/NHAMCS data will be either inaccurate or unavailable. So, while not as contemporary as we'd like, it's as contemporary as we'll ever get. Regardless, we didn't want to mis-represent the data or the findings, so we have adjusted the sentence.