Hepatitis C Testing Increased Among Baby Boomers Following The 2012 Change To CDC Testing Recommendations

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Abstract

In 2012 the Centers for Disease Control and Prevention recommended routine testing for hepatitis C for people born in the period 1945–65. Until now, the recommendation's impact on hepatitis C screening rates in the United States has not been fully understood. We used an interrupted time series with comparison group design to analyze hepatitis C screening rates in the period 2010–14 among 2.8 million commercially insured adults in the MarketScan database. Hepatitis C screening rates increased yearly between 2010 and 2014, from 1.65 to 2.59 per 100 person-years. A 49 percent increase in screening rates among people born during 1945–65 followed the release of the recommendation, but no such increase was observed among adults born after 1965. The effect among the target population was sustained, and by twenty-four months after the recommendation's release, screening rates had increased 106 percent. We conclude that the hepatitis C testing policy change resulted in significantly increased testing among the target population and may have decreased the magnitude of the hepatitis C epidemic.

Infection with the hepatitis C virus is associated with significant morbidity and mortality, with more than 19,000 annual deaths related to hepatitis C in the United States.[1,2] In the

period 2003–13 the number of deaths related to hepatitis C exceeded those related to sixty other infectious diseases combined.[1] In 2015 people ages 55–64 accounted for half of the deaths related to hepatitis C in the United States.[2] The cost of hepatitis C in the United States in 2011 was estimated to be $6.5 billion, a figure that is projected to increase to $9.1 billion by 2024.[3]

In 1998 the Centers for Disease Control and Prevention (CDC) recommended that people at high risk for transmission of hepatitis C be tested for the virus.[4] However, the risk-based testing strategy had limited effectiveness, as shown by the substantial proportion of people who were unaware that they were infected.[5] In recognition of the disproportionately high prevalence of hepatitis C among people born in the period 1945–65,[6,7] the CDC released a new recommendation in August 2012: All people in this birth cohort should receive a one-time test for hepatitis C without previous assessment of their risk for the disease.[8] In 2013 the US Preventive Services Task Force gave this recommendation a "B" rating, which motivated insurers to provide coverage for screening in the birth cohort.[9]

Despite these changes, birth cohort screening rates vary depending on patient population.[10–12] Analyses of national trends in hepatitis C testing have shown significant increases in testing among the birth cohort in the period following the recommendation change,[13,14] but the specific causal impact of this policy change on clinical practice has not been evaluated. Improvements in testing can lead to increased case finding, decreased hepatitis C transmission, and earlier initiation of antiviral treatment among infected persons, thus reducing morbidity and mortality related to hepatitis C.[15–17] We analyzed hepatitis C screening rates in the United States in the period 2010–14, using a strong quasi-experimental design to determine the causal impact of the 2012 recommendation on rates of testing among people with commercial insurance in the birth cohort.

Study Data And Methods

Data Source

We analyzed data for the period 2010–14 from the MarketScan Commercial Claims and Encounters database, a commercial health insurance database managed by Truven Health Analytics. This database includes approximately one billion insurance claims per year from more than a hundred US commercial insurance plans for the continuum of outpatient and inpatient care for people younger than age sixty-five. While the database does not include information about every person in the United States, it does cover all enrollees in nearly half of the employer sponsored health insurance plans in the US. Previous studies have found that the people in the database are representative of the commercially insured US population.[18] The claims data include *Current Procedural Terminology* (CPT) codes and dates of service and are linked to patient demographic characteristics such as age, sex, and geographic region of residence (Northeast, North Central, South, and West).

Inclusion And Exclusion Criteria

We included claims for hepatitis C screening events for all adults ages eighteen and older. We studied two cohorts: the *birth cohort*, defined as adults born in the period 1945–65 (as

explained above), and the *complement cohort*, defined as adults born after 1965 but at least age eighteen. We defined a *hepatitis C screening event* as a claim for an hepatitis C virus antibody test (using CPT codes 86803, for a hepatitis C virus antibody test; 86804, for a hepatitis C virus antibody confirmatory test; and 80059, for a hepatitis panel test) that occurred at least thirty days after the most recent previous hepatitis C virus antibody test for a given individual.

We assumed that two or more hepatitis C tests obtained within a thirty-day period would represent a single screening event. Two or more hepatitis C tests obtained within a subsequent thirty-day period would represent another screening event. For example, an antibody test for the virus obtained by one provider might represent the true screening test, while a subsequent referral to a subspecialist might elicit a second antibody test if records for the first test were unavailable. The second test should be considered a confirmatory test rather than a screening test.

We calculated the number of times that two or more antibody tests were obtained in a thirty-day period for people born in 1964 or 1966. We found that this phenomenon occurred 601 times for people born in 1964 and 549 times for persons born in 1966. Given the relatively small number of occurrences, we concluded that excluding these occurrences as screening events would probably not impact our overall findings.

We defined hepatitis C diagnostic testing and evaluation as antibody tests that were likely ordered to either confirm a recent positive test or as part of preparation for hepatitis C treatment. We excluded from analysis the following claims: those for people whose first claim in the database related to hepatitis C was for hepatitis C RNA, hepatitis C genotype, or a clinic visit for hepatitis C; and those for people who had previous claims for hepatitis C treatment, RNA, or genotype.

Statistical Analysis

We used an interrupted time series with comparison group design to analyze quarterly hepatitis C screening rates in the MarketScan data for the period January 2010–December 2014. This particular quasi-experimental design is regarded as one of the strongest designs to assess causal inference based on observational data.[19]

The August 2012 release of the CDC recommendation for one-time hepatitis C testing among US adults in the birth cohort was the intervention of interest. The quarterly hepatitis C screening rate was the outcome of interest. We determined the number of months per year that people were enrolled in a health plan in the database by age cohort. This resulted in person-months, which we divided by 12 to calculate person-years. We used Akaike information criteria to determine that a negative binomial regression model provided the best fit, compared to other models.[20]

Because the CDC's hepatitis C testing recommendation was released in August 2012, we defined the third quarter of 2012 as the transition quarter and excluded it from the analysis. The pre-intervention period began on January 1, 2010, and ended on June 30, 2012 (the end of the second quarter), and the post-intervention period began on October 1, 2012 (the

beginning of the fourth quarter), and ended on December 31, 2014. The final models included nineteen time points (ten for the pre-intervention quarters and nine for the post-intervention quarters).

We fit a series of regression models. The initial model included terms for year of birth (birth cohort versus complement cohort), intervention (pre-intervention period versus post-intervention period), and secular time trends for periods before and after the intervention, as well as interaction terms for these individual terms (for regression model results, see online Appendix Exhibit A1).[21] Our second model assessed whether there were significant differences after the intervention between men and women in the birth cohort. Our final model estimated the relationship between screening rates and region of residence for people in the birth cohort.

We modeled the screening rates in the first post-intervention quarter (immediate) as well as twelve and twenty-four months after the intervention. To quantify the impact of the recommendation on screening rates, we compared the expected rate of screening over time (calculated from the model) to the projection of pre-intervention trends (as if the guidelines had not changed). As a result, our analysis accounted for secular trends that were present before the recommendation was released. Rate ratios of the estimated and expected rates and the percentage changes were calculated.

A two-sided *p* value of less than 0.05 was considered significant. Statistical analyses were performed using R version 3.3.2 and SAS version 9.4.

Limitations

There were several limitations to our study. First, hepatitis C screening events were identified based on CPT codes and our definition of a *screening event*, which could be subject to miscategorization. However, antibodies are the preferred screening test in the United States, and we included CPT codes that contained the hepatitis C virus antibody. In addition, we found very few instances in which there was more than one screening test ordered in a single thirty-day period. This would indicate that we were selecting only true screening events and not simply confirmatory testing or testing by a different provider.

Second, the MarketScan database includes only people with commercial insurance—not those with governmental insurance such as Medicare or Medicaid. Nor does the database include information on race or ethnicity, so no evaluation of confounding by these variables was possible. Previous studies in key populations have demonstrated that there are racial and ethnic differences in hepatitis C screening, so our results might not be generalizable to populations less well represented in the MarketScan database.[11] Future studies of hepatitis C screening trends and the impact of recommendations should use databases that include information on these demographic characteristics.

Finally, while we used a strong quasi-experimental design for causal inference, we could not rule out the possibility of unmeasured confounders that may exist in any observational study.

Study Results

In the period 2010–14, there were 3,204,010 hepatitis C screening events in the MarketScan database (Exhibit 1). Thirty-three percent of the events were for people in the birth cohort, and 67 percent were for those in the complement cohort. The total number of yearly screening events increased from 479,399 in 2010 to 791,787 in 2014. In the study period, the birth cohort accounted for 43 percent of the total person-years, and the complement cohort accounted for 57 percent.

Hepatitis C screening rates in the US population increased each year in the study period, from 1.65 per 100 person-years in 2010 to 2.59 per 100 person-years in 2014 (Exhibit 1). The screening rates in the birth cohort initially increased modestly, but they increased markedly from 2012 to 2014 (Exhibits 1 and 2). In comparison, the screening rates in the complement cohort increased only modestly throughout the study period, although this cohort started with higher screening rates.

In the two-group interrupted time series model, there was a significant change in hepatitis C screening rates following the recommendation in the birth cohort but not in the complement cohort. While screening rates in both age groups increased during the period, there was a 49 percent additional increase in the immediate post-intervention period in the birth cohort (risk ratio: 1.49) that was not observed in the complement cohort (RR: 1.00) (Exhibit 3).

As noted above, the trend in rising screening rates within the birth cohort turned sharply higher in the years following the 2012 recommendation, whereas there was no significant change in trend within the complement cohort (Exhibit 2). We examined two additional specific time points, twelve and twenty-four months after the intervention. In the birth cohort, there was an increase of more than a 100 percent in screening rates at twenty-four months, relative to what would have been predicted in the absence of the intervention (RR: 2.06) (Exhibit 3). No difference was observed in the complement cohort at that time point, relative to what would have been predicted in the absence of the intervention (RR: 0.99).

We next evaluated whether in the birth cohort the intervention had a different impact among men and women, and among people in different geographical regions. We found no difference in the screening rates between men (1.07 per 100 person-years) and women (1.11 per 100 person-years) in the pre-intervention period (data not shown). We also found no difference in the impact of the intervention on screening rates by sex: Men and women both had significant increases in screening rates in the post-intervention period compared to the pre-intervention period, but they did not differ from each other at any time point (for example, in the fourth quarter of 2012, the risk ratios were 1.42 for men and 1.47 for women) (Exhibit 3).

The 2012 recommendation that members of the birth cohort be tested for hepatitis C resulted in increases in screening rates in all regions of the United States, although different patterns of change were observed across regions (Exhibit 4). In the Northeast, there was only a 29 percent increase in screening rates in the immediate post-intervention period, but at twenty-four months after the intervention, screening rates had increased by 134 percent. Conversely, in the West there was an initial increase of 73 percent in screening rates, but the longer-term

change in trend was less pronounced than in the Northeast (an increase of 55 percent at twenty-four months). The North Central and South regions had gradual, modest increases in screening rates over the post-intervention period.

Discussion

We assessed the impact of the 2012 CDC recommendation that all adults born in the period 1945–65 be tested once for hepatitis C, and we found a significant increase in and acceleration of hepatitis C screening uptake among the target population. We confirmed that there was no significant change after 2012 in the screening trends among adults born after 1965, which supports to the conclusion that the observed changes are likely related to the CDC recommendation rather than to a general secular trend. Based on the birth cohort's estimated 3.2 percent prevalence of hepatitis C,[6] the overall testing effect may be translated into an estimated 118,000 additional cases of hepatitis C identified among the birth cohort by the end of 2014 that were attributable to the change in testing recommendations. This is a substantial number of cases, given the estimated total burden of hepatitis C in the birth cohort.[6]

We used a robust quasi-experimental design that provides strong evidence for a causal effect of the recommendation on the observed increases in screening. Our findings complement those of Cheryl Isenhaur and coauthors, who observed a 2.5-fold increase in hepatitis C virus antibody testing in the period 2005–14—with the greatest increases seen in the birth cohort.[13] Our findings also complement another analysis that demonstrated increases in hepatitis C testing among the birth cohort following the release of the 2013 US Preventive Services Task Force recommendation.[14] We note that there was a secular trend of increasing screening rates in the US population and in each age group before the CDC's recommendation. Possible drivers of the observed change could include increasing awareness of hepatitis C among patients and clinicians, the availability of new oral medications, and the expansion of the number of people with health care under the Affordable Care Act.

We found a steep increase in screening rates among the birth cohort in the quarter immediately following release of the CDC's recommendation that did not appear in the complement cohort. Furthermore, we found that the difference in trends between the two groups became greater over time: While the rate of increase continued to grow in the birth cohort, the complement cohort experienced no change in the rate of increase. Our analysis allowed for a continued secular trend in both age groups, but we identified and quantified the independent effect of the hepatitis C testing recommendation on screening rates.

We also observed that before 2012, the complement cohort had higher screening rates than the birth cohort. The higher initial screening rates in the complement cohort likely reflect previous recommendations for risk-based screening. The large increase that we observed in the birth cohort screening rates after the CDC's guidance changed demonstrates the potential for recommendations for routine hepatitis C screening to expand the reach of hepatitis C diagnosis. Furthermore, the fact that screening rates among the complement cohort did not go down after 2012 suggest that there has not been detrimental competition between routine

and risk-based testing guidelines. Studies of the impact of other policy changes that used similar methodology have also observed abrupt changes in the post-intervention period.[22,23] Our study is significant because it further demonstrates, on a national level, both an immediate and sustained impact of hepatitis C testing guidelines on clinical practice.

Our findings differ from smaller studies that have evaluated the impact of interventions to improve screening. These studies show gradual increases in screening rates that are often not sustained after, for example, the implementation of electronic reminders.[24–26] These studies cite patient, provider, and societal barriers to the implementation of guidelines, which can include a lack of knowledge about the guidelines.[24–27] We acknowledge that such barriers exist and could explain why the post-intervention screening rates we found were not higher. Perhaps if those barriers had been addressed, screening rates in the post-intervention period would have increased even more.

We also evaluated the effect of the testing recommendation on sex and geographic region of residence. We found no disparities based on sex in the change in screening rates following the intervention, which is consistent with a previous study that found only slightly higher screening rates among female veterans than males (58.2 percent versus 54.5 percent).[11] However, another study found that male veterans were more likely than females to be tested for hepatitis C.[28] Both studies reported screening rates that were considerably higher than the national screening rates we found. These differences may be a result of the effective programs that the Department of Veterans Affairs has implemented to reduce barriers to implementation of the testing recommendation. Our findings highlight the need to address systemic barriers to further improve hepatitis C screening rates on the national level.

The guidelines had a more sizable effect in the Northeast, compared to the other three regions of the United States. This may be due to issues related to access to medical care, including preventive services, and availability of health insurance. Regional variation in the uptake of recommendations on a number of health interventions has previously been documented.[29,30] Additionally, Sourik Sarkar and coauthors found significant regional variability in hepatitis C testing.[28] Taken together, these findings suggest the need for region-specific programs to augment guidelines to further improve screening.

The screening recommendation appears to have been a success, raising the question of whether screening rates would similarly increase if hepatitis C recommendations were expanded to include additional age groups. When the birth cohort recommendation was released, it was widely known that the highest hepatitis C prevalence in the United States was among people in that cohort.[31] At the time, it was estimated that three-quarters of all people living with hepatitis C and 70 percent of all those whose deaths were associated with hepatitis C were in this cohort.[32] This recommendation was appropriate given the high prevalence and cost-effectiveness of birth cohort screening.[33] The hepatitis C epidemic has changed, however, and the greatest incidence of infection is now among young people who inject drugs, due to the tremendous spike in injection opioid use among that population.[34–38] For instance, 77 percent of the young people who had nearly 1,200 incident hepatitis C infections in the period 2006–12 reported using injection drugs.[39] While people who inject drugs are included in CDC recommendations as members of a high-risk group who should

be screened, we know from previous studies that risk-based screening has been inadequate in the past in identifying hepatitis C infection.[40] With the knowledge that guidelines do affect clinical practice, now may be the time to consider expansion of the hepatitis C screening guidelines. We acknowledge that achieving universal screening will be difficult given the growing syndemic of hepatitis C and opioid use disorder.

Conclusion

We found that the 2012 CDC recommendation that people born in the period 1945–65 be tested for hepatitis C had a significant impact on screening trends. Our causal design allowed us to separate the impact of the recommendation from the secular screening trends attributable to other factors. These results contribute to the body of evidence that health policy recommendations can affect clinical practice. However, screening for and identifying hepatitis C infection are just the first steps in the continuum of care. Further expansion of hepatitis C testing recommendations and the development of region-specific approaches to address barriers to implementation could lead to increased treatment and significantly improve clinical outcomes associated with hepatitis C in the United States.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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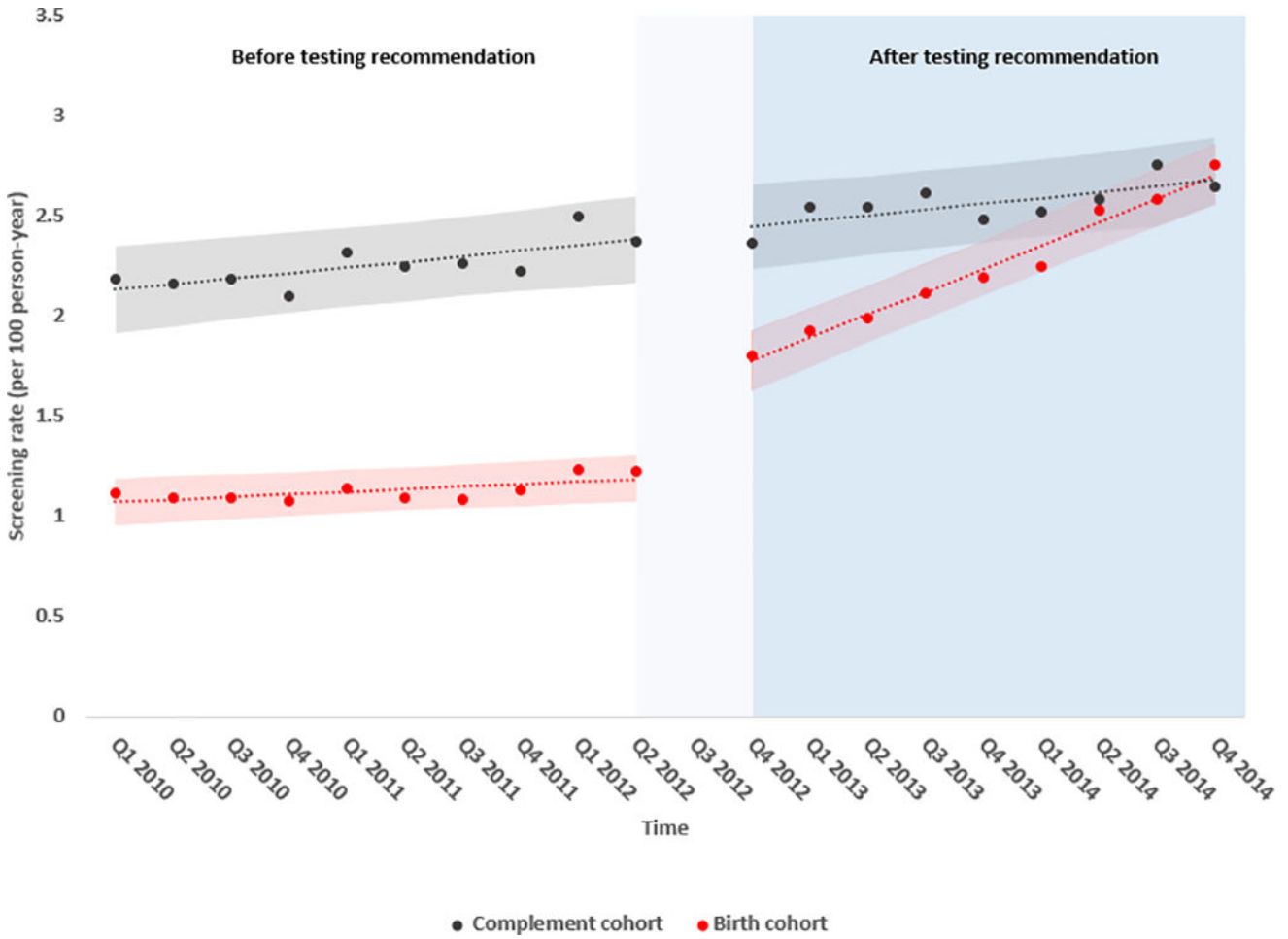
Exhibit 2.

Trends in quarterly hepatitis C screening rates in the United States per 100 person-years in 2010–14, by age group

Source/Notes: SOURCE Authors' analysis of data from the MarketScan Commercial Claims and Encounters database managed by Truven Health Analytics. NOTES "Person-years," "birth cohort," and "complement cohort" are defined in the Notes to Exhibit 1. "Q" indicates quarter-year. Because the Centers for Disease Control and Prevention released its recommendation that all members of the birth cohort be tested for hepatitis C in August 2012, we treated the third quarter of 2012 as the transition quarter and excluded it from our analysis. The trend lines show observed data. The 95% confidence intervals (the shaded areas around each trend line) were modeled using a negative binomial regression model.
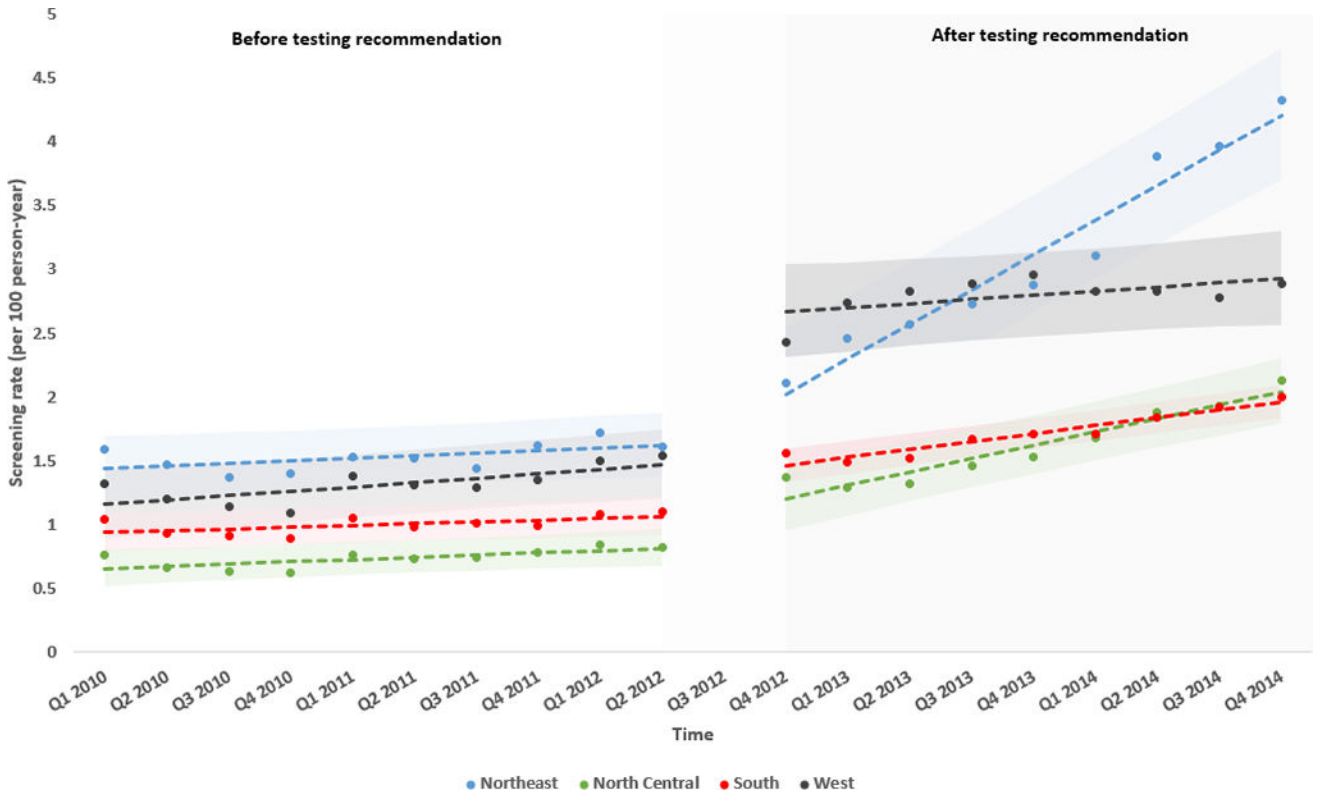
Exhibit 4.
Trends in quarterly hepatitis C screening rates per 100 person-years in the United States in 2010–14 for people in the birth cohort, by geographic region of residence
Source/Notes: SOURCE Authors' analysis of data from the MarketScan Commercial Claims and Encounters database managed by Truven Health Analytics. NOTES "Person-years" and "birth cohort" are defined in the Notes to Exhibit 1. "Q" indicates quarter-year. The transition quarter is explained in the Notes to Exhibit 2. The trend lines show observed data. The 95% confidence intervals (the shaded areas around each trend line) were modeled using a negative binomial regression model.

Exhibit 1

Characteristics of adults in a US national database who were screened for hepatitis C in 2010–14, by age group

	All adults		Birth cohort		Complement cohort	
	Number	%	Number	%	Number	%
Total	2,785,300	100	947,715	34	1,837,585	66
Sex ****						
Male	993,303	36	429,231	45	564,072	31
Female	1,791,997	64	518,484	55	1,273,513	69
Geographic region ****						
Northeast	762,617	27	259,479	27	503,138	27
North Central	411,354	15	153,186	16	258,168	14
South	921,075	33	280,895	30	640,180	35
West	636,237	23	233,939	25	402,298	22
Unknown	60,707	2	21,760	2	38,947	2
Screening events						
2010	479,399	15	153,259	14	326,140	15
2011	583,606	18	167,937	16	415,669	20
2012	684,629	21	207,434	20	477,195	22
2013	664,589	21	233,188	22	431,401	20
2014	791,787	25	292,728	28	499,059	23
Total	3,204,010	100	1,054,546	33	2,149,464	67
Person-years						
2010	29,106,099	19	14,000,123	21	15,105,976	17
2011	33,487,881	21	15,130,755	23	18,357,126	21
2012	34,154,777	22	14,415,367	22	19,739,410	22
2013	28,290,002	18	11,344,350	17	16,945,652	19
2014	30,592,258	20	11,590,468	17	19,001,790	21
Total	155,631,017	100	66,481,063	43	89,149,954	57
Screening rates						

	All adults		Birth cohort		Complement cohort	
	Number	%	Number	%	Number	%
2010	1.65		1.09		2.16	
2011	1.74		1.11		2.26	
2012	2.00		1.44		2.42	
2013	2.35		2.06		2.55	
2014	2.59		2.53		2.63	
Total	2.06		1.59		2.41	

SOURCE Authors' analysis of data from the MarketScan Commercial Claims and Encounters database managed by Truven Health Analytics. NOTES "Birth cohort" refers to people born in the period 1945–65. "Complement cohort" refers to people age eighteen or older who were born after 1965. Numbers of people are those screened during the study period (some people were screened more than once, and some may have been screened in more than one geographic region). "Person-years" refers to the number of years people were enrolled in a health plan included in the MarketScan database. Screening rates are the number of screening events divided by 100 person-years. The Centers for Disease Control and Prevention recommended in August 2012 that all members of the birth cohort be tested for hepatitis C. Significance refers to differences in overall demographic characteristics between the birth cohort and complement cohort.

****
$p < 0.001$

Exhibit 3

Risk ratios (RRs) of hepatitis C screening in the United States before and after the birth cohort testing recommendation

	Fourth quarter of:		
	2012	**2013**	**2014**
Age group (overall)			
Birth cohort	1.49**	1.75**	2.06**
Complement cohort	1.00	0.99	0.99
Birth cohort by sex			
Females	1.47*	1.68**	1.93**
Males	1.42**	1.61**	1.82***
Birth cohort by geographic region			
Northeast	1.29**	1.74***	2.34***
North Central	1.45*	1.71**	1.99**
South	1.36**	1.48**	1.62**
West	1.73*	1.64**	1.55**

SOURCE Authors' analysis of data from the MarketScan Commercial Claims and Encounters database managed by Truven Health Analytics. NOTES The Centers for Disease Control and Prevention recommended in August 2012 that all members of the birth cohort be tested for hepatitis C. Because the fourth quarter of 2012 was the first full quarter of the intervention period, we assessed the intervention's impact in the fourth quarters of subsequent years. "Birth cohort" and "complement cohort" are defined in the Notes to Exhibit 1. Risk ratios are calculated by comparing the screening rate at each time point in the presence of the intervention to the predicted screening rate at each time point in the absence of the intervention. Significance refers to differences between the screening rate in the presence of the intervention and the predicted screening rate in the absence of the intervention.

*
$p < 0.10$

**
$p < 0.05$

***
$p < 0.01$