

Health Affairs

At the Intersection of Health, Health Care and Policy

Cite this article as:

Fujie Xu, Xin Tong and Andrew J. Leidner
Hospitalizations And Costs Associated With Hepatitis C And Advanced Liver Disease
Continue To Increase
Health Affairs, 33, no.10 (2014):1728-1735

doi: 10.1377/hlthaff.2014.0096

The online version of this article, along with updated information and services, is available at:

<http://content.healthaffairs.org/content/33/10/1728.full.html>

For Reprints, Links & Permissions:

http://healthaffairs.org/1340_reprints.php

E-mail Alerts : <http://content.healthaffairs.org/subscriptions/etoc.dtl>

To Subscribe: <http://content.healthaffairs.org/subscriptions/online.shtml>

Health Affairs is published monthly by Project HOPE at 7500 Old Georgetown Road, Suite 600, Bethesda, MD 20814-6133. Copyright © 2014 by Project HOPE - The People-to-People Health Foundation. As provided by United States copyright law (Title 17, U.S. Code), no part of *Health Affairs* may be reproduced, displayed, or transmitted in any form or by any means, electronic or mechanical, including photocopying or by information storage or retrieval systems, without prior written permission from the Publisher. All rights reserved.

Not for commercial use or unauthorized distribution

By Fujie Xu, Xin Tong, and Andrew J. Leidner

DOI: 10.1377/hlthaff.2014.0096
 HEALTH AFFAIRS 33,
 NO. 10 (2014): 1728–1735
 ©2014 Project HOPE—
 The People-to-People Health
 Foundation, Inc.

Hospitalizations And Costs Associated With Hepatitis C And Advanced Liver Disease Continue To Increase

Fujie Xu (fax1@cdc.gov) is a team leader in the Division of Viral Hepatitis, Centers for Disease Control and Prevention (CDC), in Atlanta, Georgia.

Xin Tong is a statistician in the Division of Viral Hepatitis, CDC.

Andrew J. Leidner is a prevention effectiveness fellow in the Division of Viral Hepatitis, CDC.

ABSTRACT Disease burden models have predicted worsening morbidity of liver disease caused by hepatitis C in the United States. The aim of this study was to determine the trend in hospitalizations caused by hepatitis C and advanced liver disease. We analyzed data for the period 2004–11 from the Nationwide Inpatient Sample, the largest nationwide all-payer hospital inpatient care database. Hospitalization rates for hepatitis C per 100,000 people increased significantly from 4.76 in 2004–05 to 13.81 in 2010–11—an increase of 190 percent. Hospitalization rates for advanced liver disease also increased, particularly for hepatorenal syndrome (93 percent) and portal hypertension (62 percent). Hepatitis C was the principal diagnosis for 64,867 hospitalizations in 2010–11, resulting in a total charge of \$3.5 billion. We found nationwide trends in increasing morbidity and medical costs for advanced liver disease associated with hepatitis C. Our findings suggest that hepatitis C is a public health problem and has been growing in magnitude in recent years. Stakeholders and policy makers should implement both recommended screenings for people born in the period 1945–65 and more effective treatment for hepatitis C, which have the potential to reverse the rising morbidity and costs of hepatitis C.

An estimated 2.7 million people in the United States have chronic hepatitis C.¹ These people are at risk for progressive hepatic fibrosis and cirrhosis, which can lead to portal hypertension, ascites, gastrointestinal bleeding, hepatic encephalopathy, and liver cancer.²

The majority of people infected with hepatitis C were born between 1945 and 1965.^{3,4} Largely because of the aging of this birth cohort, disease burden models predict a substantial increase over the next thirty years in the morbidity associated with liver disease and hepatitis C.^{5,6} Deaths and liver transplants as a result of hepatitis C have increased,^{7,8} and a trend of increasing liver-related hospitalizations has been observed in recent years.⁹ These hospitalizations have con-

siderable costs^{6,9} and—in the absence of interventions that are more cost-effective than current practices—will continue to contribute to the projected vast economic burden of hepatitis C.⁶ With the implementation of recommended screening³ and treatment^{10,11} for hepatitis C in the United States, its growing burden can be reduced.¹²

Unfortunately, chronic hepatitis C is not widely acknowledged as an urgent public health issue. This lack of awareness becomes particularly apparent when the levels of diagnosis, evaluation, and treatment related to hepatitis C are examined. About 50 percent of people infected with hepatitis C remain undiagnosed.^{13,14} Many people who might otherwise qualify for therapy have not been tested and identified.¹⁵ In a large,

multicenter cohort study, only 18 percent of the population predicted to be infected had evidence of any treatment for hepatitis C.¹³

However, therapeutic agents for hepatitis C are advancing rapidly and are more effective at curing hepatitis C quickly—often within twelve weeks—with few side effects.^{16–18} A cure of hepatitis C after treatment is associated with reductions in all-cause mortality, not just mortality resulting from liver disease.¹⁹

This article investigates the recent trends in hospitalizations and costs associated with hepatitis C and advanced liver disease. We used representative data sets that recorded inpatient care discharges and patient characteristics during the period 2004–11.

Study Data And Methods

Using diagnosis and procedure codes from the *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM) (for a list of the codes, see online Appendix A),²⁰ we identified hospitalizations for which the principal diagnosis was either hepatitis C or advanced liver disease in the Nationwide Inpatient Sample (NIS) and State Inpatient Database (SID) annual data sets for the period 2004–11. For our trend analysis of hospitalizations related to hepatitis C, we also examined hospitalizations that were principally for advanced liver disease but whose secondary diagnoses included hepatitis C.

NATIONWIDE INPATIENT SAMPLE The NIS is drawn annually from the administrative databases of a nationally representative sample of hospitals.^{21,22} The NIS is the largest nationwide all-payer hospital inpatient care database available in the United States. It is maintained as part of the Healthcare Cost and Utilization Project (HCUP), which is sponsored by the Agency for Healthcare Research and Quality.

The NIS is a stratified sample of approximately 20 percent of all US community hospitals. Five characteristics are used to select the hospitals: location (rural or urban), hospital size, region, teaching status, and ownership. The NIS includes all discharges from sampled hospitals, providing information on five to eight million discharges from an average of 1,000 hospitals each year. Discharges are captured regardless of payer status—that is, patients with Medicare, Medicaid, private insurance, or no insurance are all included.

STATE INPATIENT DATABASE The SID is also maintained by HCUP.²³ Similar to the NIS, it includes inpatient discharge abstracts regardless of payer status.²⁴ The SID captures over 90 percent of all annual US hospital discharges.²⁴ For our state-specific analyses, we chose California,

Florida, and Michigan because their populations were the largest, and because data from them were available for the entire study period.

SCOPE AND OUTCOMES OF INTEREST We estimated national hospitalization rates and costs from the NIS during the period 2004–11. In addition to hospitalization rates associated with hepatitis C, we calculated hospitalization rates associated with hepatitis B because hepatitis B is an important cause of liver disease. In addition, we provided rates of hospitalizations associated with HIV as a comparison.

ICD-9-CM diagnostic or procedure codes (Appendix A)²⁰ were used to identify hospitalizations associated with hepatitis C, advanced liver disease such as liver cancer, hepatitis B, and HIV. This analysis focused on hospitalization rates calculated from principal diagnosis codes. Because there was only one principal diagnosis for each hospitalization, the hospitalizations included in our analyses were put in one of four mutually exclusive categories: hepatitis C, hepatitis B, HIV, or any of ten specific diagnoses of advanced liver disease.

Typically there were multiple secondary diagnoses for each hospitalization. To better estimate the burden of hospitalizations related to hepatitis C, we combined hospitalizations with hepatitis C as the principal diagnosis with those that had advanced liver disease as the principal diagnosis and also listed hepatitis C among the secondary diagnoses.

EMPIRICAL APPROACH The unit of analysis was the hospital discharge. We excluded hospital discharge records from the NIS and SID if the patient was younger than age eighteen at hospital admission. Patient characteristics included age, race or ethnicity, and first listed payment source. Hospital characteristics included geographic region and status as a teaching hospital. Discharge-specific characteristics included the charge or cost for the hospitalization, in-hospital death, the principal diagnosis or procedural code, and whether hepatitis C was listed as a secondary diagnosis.

National estimates were obtained by using individual discharge sampling weights. The weighted number of hospitalizations at the national or state level each year was then divided by the corresponding national (or state) population count based on the midyear (July) US census population estimates tabulated by HCUP.²⁵

The ratio of the estimated number of hospitalizations to the estimated population count is the hospitalization rate. To adjust costs incurred in earlier years to 2011 US dollars, we used the Personal Consumption Expenditure index for hospital services²⁶ (for inflation rates, see Appendix B).²⁰ We computed changes during the

period 2004–11 in hospitalization rates and average charge per hospitalization by comparing estimates for 2004–05 with those for 2010–11.

We estimated orthogonal polynomial coefficients both to summarize patient characteristics and to test hypotheses for trends over time across categories of patient characteristics. All statistical analyses were conducted using SAS 9.3-callable SUDAAN.

Because this study relied on existing data that were publicly available, it was exempt from review by an Institutional Review Board.

LIMITATIONS Our findings must be interpreted in light of some limitations.

First, some amount of the trends in hospitalization rates that we observed may be the result of changes in coding practice. Increased awareness of hepatitis C might have led to coding changes that increased the use of hepatitis C as the principal diagnosis for hospitalizations caused by advanced liver disease in more recent years.

Second, the number of states contributing data to the NIS has increased, which could introduce bias as the nationwide sample changed over time. From 2004 to 2011 the number of participating states increased from thirty-seven to forty-six. However, we found no evidence that people in the states newly added to the sample were more or less likely to have had hospitalizations for hepatitis C and liver disease than people in the states sampled before 2004. Furthermore, the stability of the proportions of patients from different regions suggests that any sampling bias attributable to geographic area was limited.

Finally, the unit of the analysis was the hospital discharge, not the patient. If a single patient had multiple hospital admissions in any one-year period, readmissions were counted as new hospitalizations. This could mean that if a small number of patients account for a large number of hospitalizations, this small number of patients could become overly influential in estimating the means and could distort the distribution of patient characteristics.

Study Results

NATIONAL TRENDS During the study period the number of hospitalizations for which hepatitis C was the principal diagnosis more than tripled, from 20,963 in 2004–05 to 64,867 in 2010–11 (Exhibit 1). All of these hospitalizations had one or more liver diseases listed among the secondary diagnoses. During the same period the nationwide rate of those hospitalizations per 100,000 people increased from 4.76 to 13.81, a relative percent change of 190 percent—that is, relative to the amount of hospitalizations in 2004–05, there were almost two times more hos-

With the implementation of recommended screening and treatment for hepatitis C, its growing burden can be reduced.

pitalizations in 2010–11.

Similar, though less dramatic, trends were observed for a number of advanced liver diseases, including liver cancer (Exhibit 1). Only modest changes in hospitalization rates were observed for liver transplant and hepatic encephalopathy. Interestingly, hospitalization rates for esophageal and other variceal bleeding and rates associated with cirrhosis of the liver (both alcoholic and without mention of alcohol) declined during the study period.

After we adjusted for inflation, the average per hospitalization charge for hepatitis C and all types of liver disease increased during the study period (Exhibit 1). The greatest increases were observed for hepatorenal syndrome and liver transplant. The smallest increase was for cirrhosis of the liver without mention of alcohol.

When we combined the increases in per hospitalization charge and number of hospitalizations (Exhibit 1), we estimated that the total nationwide charges for hospitalizations with hepatitis C as the principal diagnosis increased from \$0.9 billion during 2004–05 (20,963 hospitalizations at \$42,415 per hospitalization) to \$3.5 billion (64,867 hospitalizations at \$53,626 per hospitalization) during 2010–11. This was a relative percent change of 291 percent. Similarly, the estimated nationwide charges from the 663,114 hospitalizations principally caused by advanced liver disease totaled \$69.4 billion during 2010–11 (an average of \$34.7 billion per year), which resulted in a relative percent change of 44 percent when compared with 2004–05.

We calculated the rates of three types of hospitalizations: those for which hepatitis C was the principal diagnosis, those for which advanced liver disease was the principal diagnosis and hepatitis C was a secondary diagnosis, and the first

190%

Increase

The rate of hospitalizations for hepatitis C in the United States rose 190% during the period 2004–11.

EXHIBIT 1
Trends In Rates And Costs Of Hospitalization In Adults In The Nationwide Inpatient Sample For Hepatitis C Or Advanced Liver Disease, 2004-11

Principal diagnosis	2004-05	2006-07	2008-09	2010-11	Relative percent change ^a
HEPATITIS C INFECTION					
Number of hospitalizations	20,963	21,812	52,074	64,867	— ^b
Rate per 100,000 people	4.76	4.85	11.32	13.81**	190
Average per hospitalization charge	\$42,415	\$39,522	\$49,882	\$53,626	26
LIVER TRANSPLANT					
Number of hospitalizations	20,207	16,097	26,598	22,590	— ^b
Rate per 100,000 people	4.59	3.58	5.78	4.81	5
Average per hospitalization charge	\$178,939	\$191,377	\$226,921	\$239,999	34
LIVER CANCER					
Number of hospitalizations	36,572	37,050	44,339	44,071	— ^b
Rate per 100,000 people	8.31	8.24	9.64	9.38**	13
Average per hospitalization charge	\$46,858	\$48,365	\$60,519	\$60,863	30
ESOPHAGEAL AND OTHER VARICEAL BLEEDING					
Number of hospitalizations	8,667	7,953	8,274	8,835	— ^b
Rate per 100,000 people	1.97	1.77	1.80	1.88	-4
Average per hospitalization charge	\$34,344	\$39,454	\$42,929	\$45,392	32
ASCITES					
Number of hospitalizations	213,853	237,592	274,767	311,448	— ^b
Rate per 100,000 people	48.57	52.81	59.74	66.30**	37
Average per hospitalization charge	\$34,347	\$35,951	\$40,209	\$41,252	20
HEPATORENAL SYNDROME					
Number of hospitalizations	2,953	3,010	4,265	6,087	— ^b
Rate per 100,000 people	0.67	0.67	0.93	1.30**	93
Average per hospitalization charge	\$51,654	\$51,791	\$73,207	\$77,254	50
HEPATIC ENCEPHALOPATHY					
Number of hospitalizations	85,465	90,351	85,533	98,150	— ^b
Rates per 100,000 persons	19.41	20.08	18.60	20.90	8
Average per hospitalization charge	\$28,911	\$30,674	\$36,061	\$37,937	31
PORTAL HYPERTENSION					
Number of hospitalizations	5,781	5,080	5,828	10,014	— ^b
Rate per 100,000 people	1.31	1.13	1.27	2.13**	62
Average per hospitalization charge	\$36,275	\$37,316	\$45,536	\$48,205	33
ALCOHOLIC CIRRHOSIS OF LIVER					
Number of hospitalizations	106,532	106,121	99,911	96,385	— ^b
Rate per 100,000 people	24.19	23.59	21.72	20.52**	-15
Average per hospitalization charge	\$42,494	\$45,093	\$52,699	\$52,308	23
CIRRHOSIS OF LIVER WITHOUT MENTION OF ALCOHOL					
Number of hospitalizations	73,264	71,322	63,907	53,861	— ^b
Rate per 100,000 people	16.64	15.85	13.89	11.47**	-31
Average per hospitalization charge	\$46,994	\$45,623	\$56,883	\$55,560	18
OTHER SEQUELAE OF CHRONIC LIVER DISEASE					
Number of hospitalizations	6,662	6,086	10,286	11,673	— ^b
Rate per 100,000 people	1.51	1.35	2.24	2.49**	64
Average per hospitalization charge	\$45,611	\$44,550	\$57,455	\$55,879	23

SOURCE Authors' analysis of data from the Healthcare Cost and Utilization Project. **NOTES** Significance represents the *p* value for the trend. All charges are expressed in 2011 US dollars after inflation was accounted for, using the hospital services component of the Personal Consumption Expenditure index (see Note 26 in text). ^aRelative percent change is calculated as $(\text{rate}_{2010-11} - \text{rate}_{2004-05}) / \text{rate}_{2004-05}$. ^bThe numbers of hospitalizations should not be compared over time because of changes in population sizes. Instead, we compared rates of hospitalizations over time. ***p* < 0.05

two types combined (Exhibit 2). During the study period the most dramatic increase occurred in rates of hospitalization for which the principal diagnosis was hepatitis C, which rose from 5.0 to 14.4 per 100,000 people. The rates of both types of hospitalizations combined also increased, from 29.9 to 34.5 per 100,000 people.

CHARACTERISTICS OF PATIENTS HOSPITALIZED BECAUSE OF HEPATITIS C Exhibit 3 presents the characteristics of patients hospitalized with hepatitis C as the principal diagnosis; all of these patients also had secondary diagnosis codes indicating liver disease. The share of people in the 1945–1964 birth cohort increased during the study period, from 68.7 percent of hospitalized patients in 2004–05 to 77.3 percent in 2010–11. The proportion of males also increased.

The racial and ethnic characteristics of the patient population did not change significantly during the study period: It remained predominantly white (Exhibit 3). The regional distribution did not change either, with patients were more likely to be from the South and West than from the Northeast or the Midwest throughout the study period.

Strong trends were seen among proportions of payer types (Exhibit 3). The proportion of people with Medicare increased from 28.7 percent in 2004–05 to 33.9 percent in 2010–11, while the proportion of those with private insurance declined from 28.6 percent to 22.7 percent.

When we looked at the secondary diagnoses of advanced liver disease among hospitalizations associated with hepatitis C, we found that the proportions of most liver diseases increased significantly (Exhibit 3). However, the proportion of in-hospital deaths remained relatively con-

stant during the study period.

HOSPITALIZATION TRENDS ASSOCIATED WITH HEPATITIS C, HEPATITIS B, AND HIV For comparison, we present hospitalization rates associated with hepatitis C, hepatitis B, and HIV during the study period (Exhibit 4). When we looked at the trends based on the data from three states—California, Florida, and Michigan (data not shown)—we found that they were largely consistent with national trends.

During the study period the annual rate of hospitalizations associated with HIV declined nationally and in all three states. In contrast, the hospitalization rate associated with hepatitis C uniformly increased. The hospitalization rate associated with hepatitis B changed only slightly.

Discussion

The increase in the rate of hospitalizations associated with hepatitis C is striking, with a relative percent change of 190 percent in the period 2004–11. This dramatic increase is part of a larger trend that we observed among hospitalizations with hepatitis C listed as either the principal diagnosis or as one of the secondary diagnoses when liver disease was listed as the principal diagnosis. We also observed increases in hospitalization for advanced liver disease sequelae, particularly hepatorenal syndrome, portal hypertension, ascites, and liver cancer. During the same period, rates of hospitalizations principally for hepatitis B and for alcoholic cirrhosis of the liver, the other two main etiologies for advanced liver disease, were stable or declined.

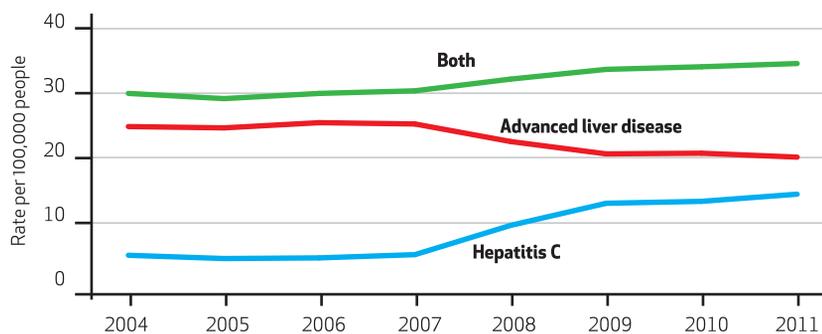
Taken together, our data provide evidence for a rapidly increasing nationwide trend in morbidity attributable to hepatitis C and advanced liver disease related to hepatitis C in the United States. This is consistent with the trends observed during the period 1998–2003.²⁷ These findings suggest that hepatitis C is a public health problem and has been growing in magnitude in recent years.

The increased morbidity related to hepatitis C was associated with large and increasing medical costs. The total charge of hospitalizations principally caused by hepatitis C reached \$3.5 billion in 2010–11 and more than tripled during the study period (291 percent). Increased costs were also observed for diagnoses of advanced liver disease (44 percent).

A recent study also investigated the burden of hepatitis C in the health care system and reported the inpatient burden to be greater than \$15 billion annually.²⁸ This cost estimate included all hospitalizations that listed hepatitis C as a principal or secondary diagnosis. When all hos-

EXHIBIT 2

Rates Of Hospitalization In Adults In The Nationwide Inpatient Sample With Hepatitis C As The Primary Diagnosis Or As A Secondary Diagnosis With Advanced Liver Disease As The Primary Diagnosis, 2004–11



SOURCE Authors' analysis of data from the Healthcare Cost and Utilization Project. **NOTES** "Hepatitis C" indicates hospitalizations for which that was the primary diagnosis. "Advanced liver disease" indicates hospitalizations for which that was the primary diagnosis and hepatitis C was a secondary diagnosis. "Both" indicates "hepatitis C" and "advanced liver disease" combined.

EXHIBIT 3

Characteristics Of Adults In The Nationwide Inpatient Sample Hospitalized With Hepatitis C As The Principal Diagnosis, 2004-11

Characteristic	2004-05 (n=4,299)		2006-07 (n=4,495)		2008-09 (n=10,543)		2010-11 (n=13,230)		p value for trends
	Mean or %	SE	Mean or %	SE	Mean or %	SE	Mean or %	SE	
Age (years)	51.5	(0.3)	52.0	(0.3)	54.1	(0.2)	54.6	(0.2)	<0.0001
Year of birth (%)									
After 1965	13.1	(0.7)	14.3	(0.9)	11.2	(0.5)	13.1	(0.5)	0.25
1945-64	68.7	(1.0)	71.4	(1.1)	76.3	(0.6)	77.3	(0.6)	<0.0001
Before 1945	18.2	(0.9)	14.3	(0.8)	12.5	(0.5)	9.6	(0.4)	<0.0001
Male (%)	60.5	(1.0)	63.5	(1.5)	64.8	(0.7)	64.6	(0.6)	0.0007
Race or ethnicity (%)									
White	62.3	(2.1)	57.8	(1.8)	60.8	(1.5)	59.2	(1.7)	0.42
African American	12.7	(1.0)	14.0	(1.1)	12.8	(0.8)	14.9	(1.1)	0.26
Hispanic	19.0	(1.7)	22.7	(1.9)	19.8	(1.4)	20.8	(1.7)	0.71
Other	6.0	(0.7)	5.5	(0.8)	6.6	(0.6)	5.1	(0.5)	0.60
Health insurance (%)									
Medicare	28.7	(0.9)	27.5	(1.5)	33.3	(0.7)	33.9	(0.7)	<0.0001
Medicaid	28.1	(1.3)	25.5	(1.7)	29.2	(0.9)	29.0	(1.0)	0.21
Private	28.6	(1.4)	23.9	(1.8)	22.9	(1.0)	22.7	(0.9)	0.0007
Other	14.6	(1.0)	23.1	(3.6)	14.5	(0.9)	14.4	(0.8)	0.12
Region (%)									
Northeast	19.0	(3.5)	15.0	(1.9)	17.4	(2.2)	20.7	(2.8)	0.58
Midwest	14.2	(1.6)	14.4	(2.2)	17.8	(2.4)	15.4	(2.6)	0.49
South	38.0	(3.1)	38.9	(4.1)	35.6	(2.8)	39.6	(2.9)	0.93
West	28.8	(3.4)	31.7	(4.1)	29.2	(2.6)	24.3	(2.2)	0.24
Teaching hospital (%)	53.8	(3.3)	56.6	(3.7)	56.9	(2.7)	57.8	(2.8)	0.39
In-hospital death (%)	4.9	(0.4)	4.2	(0.3)	5.3	(0.3)	5.1	(0.2)	0.16
Secondary diagnosis of liver disease (%)									
Liver transplant	5.3	(1.2)	3.6	(1.1)	4.2	(0.7)	3.9	(0.6)	0.32
Liver cancer	4.5	(0.7)	4.5	(0.5)	6.9	(0.6)	8.3	(0.5)	<0.0001
Esophageal and other variceal bleeding	4.7	(0.3)	4.0	(0.3)	5.2	(0.3)	8.3	(0.3)	<0.0001
Ascites	31.3	(1.3)	29.3	(1.2)	39.2	(0.9)	43.3	(0.8)	<0.0001
Hepatorenal syndrome	3.2	(0.3)	2.7	(0.3)	5.4	(0.5)	6.1	(0.3)	<0.0001
Hepatic encephalopathy	2.8	(0.3)	2.4	(0.3)	0.5	(0.1)	0.8	(0.1)	<0.0001
Portal hypertension	12.9	(0.9)	15.2	(0.9)	22.6	(0.8)	26.6	(0.8)	<0.0001
Alcoholic cirrhosis of liver	16.2	(0.8)	20.5	(0.9)	25.0	(0.7)	25.1	(0.6)	<0.0001
Cirrhosis of liver without mention of alcohol	39.4	(1.8)	38.2	(2.2)	46.5	(0.9)	49.7	(0.9)	<0.0001
Other sequelae of chronic liver disease	9.0	(1.3)	7.9	(1.5)	9.0	(0.6)	8.3	(0.4)	0.85

SOURCE Authors' analysis of data from the Healthcare Cost and Utilization Project. **NOTE** SE is standard error.

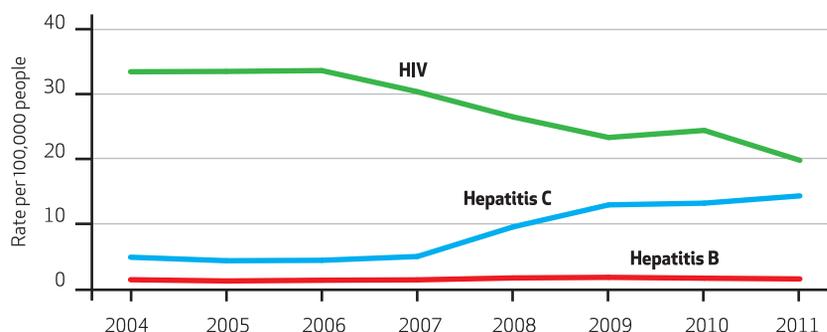
pitalizations that listed hepatitis C as a secondary diagnosis were included, even if the principal diagnosis was unrelated to hepatitis C or liver disease, the resulting cost estimate was much higher than ours.

The most probable explanation of the increasing rates of hospitalizations is that a large cohort of people infected with hepatitis C is aging and developing severe liver disease. This is supported by the patient characteristics shown in Exhibit 3. Most patients were born in the period 1945-65. This result is consistent with those of other studies of hospitalizations related to hepatitis C⁹ and the emerging literature that has been documenting the associated rising mortality rates.⁷

The increasing trend in liver disease could have many different causes, including a large

EXHIBIT 4

Rates Of Hospitalization In Adults In The Nationwide Inpatient Sample With Hepatitis C, Hepatitis B, Or HIV As The Principal Diagnosis, 2004-11



SOURCE Authors' analysis of data from the Healthcare Cost and Utilization Project.

number of hepatitis C infections that have not been diagnosed.¹³ Recent validation studies²⁹ have shown that the ICD-9-CM codes for advanced liver disease that we used in our analysis—particularly the codes for liver transplant, liver cancer, variceal bleeding, and ascites—have high positive predictive values. This gives us confidence that our estimates are reasonable.

However, increased awareness of hepatitis C in the later part of our study period might have led to higher rates of testing for hepatitis C, and more prompt diagnosis of hepatitis C might have led to coding changes that favored listing hepatitis C as the principal cause of a hospitalization related to advanced liver disease. The decline in hospitalization rates characterized by liver disease as the principal diagnosis and hepatitis C as the secondary diagnosis contrasts with the increasing hospitalization rates characterized by hepatitis C as the principal diagnosis. The presence of these two diametrically opposed trends is consistent with changing coding practices.

A more detailed investigation into specific coding practices is beyond the scope of the current study. Nonetheless, when these two types of hospitalizations are combined (Exhibit 2), the overall trend is increasing. This suggests that morbidity related to hepatitis C is on the rise.

The apparent shifting to Medicare for insurance by the aging cohort of people infected with hepatitis C is an important finding for health care policy makers. During the study period, the proportion of hepatitis C hospitalizations paid for by private insurance decreased, and the proportion paid for by Medicare increased by 5 percentage points, from 28.7 percent to 33.9 percent (Exhibit 3). As the baby boomers age, they are more likely to leave health plans provided by their employers and private insurance companies, replacing those plans with Medicare coverage.

With the recent licensure by the Food and Drug Administration of more effective and curative therapies for hepatitis C,^{17,18} especially in the case

of patients who have evidence of advanced liver disease or who had failed with previous treatment,³⁰ the growth in hospitalizations and deaths resulting from chronic hepatitis C can be slowed substantially.³¹ Large health care payers such as Medicare and private insurance companies must consider the costs of providing access to hepatitis C therapies, which could exceed \$84,000 per patient, as well as the benefits of such treatments, which could include forgone ambulatory services and hospital stays associated with advanced and end-stage liver disease sequelae.

Partly because of the expensive hospital visits and procedures that may be associated with hepatitis C and advanced liver disease, many newer-generation pharmaceuticals have largely been found to be cost-effective in recent modeling efforts.^{32,33} The high rates of hospitalization and the morbidity burden associated with hepatitis C, along with the rapidly evolving availability of effective new hepatitis C therapies, are an impetus for national programs of testing and linkage to care. Eventually, initiatives such as the recent Centers for Disease Control and Prevention's screening recommendations³ to identify people born in the period 1945–65 who are infected with hepatitis C may reverse the trend in hospitalizations associated with cirrhosis and end-stage liver disease.

Conclusion

This article has identified increasing trends in hospitalization rates resulting from hepatitis C and advanced liver disease in the period 2004–11. In addition to the rising rates of hospitalization, the average cost of the hospitalizations nationally increased 18–50 percent. Implementation of the recommended screening of people born in the period 1945–65 and of more effective treatment for hepatitis C in the United States has the potential to reverse the rising morbidity and costs from hepatitis C. ■

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

NOTES

1 Denniston MM, Jiles RB, Drobeniuc J, Kleven RM, Ward JW, McQuillan GM, Holmberg SD. Chronic hepatitis C virus infection in the United States, National Health and Nutritional Examination Survey 2003 to 2010. *Ann Intern Med.* 2014;

160(5):293–300.

2 Jafri SM, Gordon SC. Care of the cirrhotic patient. *Infect Dis Clin North Am.* 2012;26(4):979–94.

3 Smith BD, Morgan RL, Beckett GA, Falck-Ytter Y, Holtzman D, Teo CG, et al. Recommendations for the

identification of chronic hepatitis C virus infection among persons born during 1945–1965. *MMWR Recomm Rep.* 2012;61(RR-4):1–32.

4 Moorman AC, Gordon SC, Rupp LB, Spradling PR, Teshale EH, Lu M, et al. Baseline characteristics and

- mortality among people in care for chronic viral hepatitis: the Chronic Hepatitis Cohort Study. *Clin Infect Dis*. 2013;56(1):40–50.
- 5 Rein DB, Wittenborn JS, Weinbaum CM, Sabin M, Smith BD, Lesesne SB. Forecasting the morbidity and mortality associated with prevalent cases of pre-cirrhotic chronic hepatitis C in the United States. *Dig Liver Dis*. 2011;43(1):66–72.
 - 6 Razavi H, ElKhoury AC, Elbasha E, Estes C, Pasini K, Poynard T, et al. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. *Hepatology*. 2013; 57(6):2164–70.
 - 7 Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW, Holmberg SC. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. *Ann Intern Med*. 2012;156(4):271–8.
 - 8 Kim WR. The burden of hepatitis C in the United States. *Hepatology*. 2002;36(5 Suppl 1):S30–4.
 - 9 Sie L, Gatto NM, Bancroft E. Hospitalizations due to hepatitis C in Los Angeles County, 2007–2009: case characteristics and factors associated with mortality. *J Viral Hepat*. 2013;20(9):628–37.
 - 10 Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology*. 2009;49(4): 1335–74.
 - 11 Rosen HR. Clinical practice. Chronic hepatitis C infection. *N Engl J Med*. 2011;364(25):2429–38.
 - 12 Rein DB, Smith BD, Wittenborn JS, Lesesne SB, Wagner LD, Roblin DW, et al. The cost-effectiveness of birth-cohort screening for hepatitis C antibody in U.S. primary care settings. *Ann Intern Med*. 2012;156(4): 263–70.
 - 13 Holmberg SD, Spradling PR, Moorman AC, Denniston MM. Hepatitis C in the United States. *N Engl J Med*. 2013;368(20):1859–61.
 - 14 Volk ML, Tocco R, Saini S, Lok AS. Public health impact of antiviral therapy for hepatitis C in the United States. *Hepatology*. 2009;50(6): 1750–5.
 - 15 Spradling PR, Rupp L, Moorman AC, Lu M, Teshale EH, Gordon SC, et al. Hepatitis B and C virus infection among 1.2 million persons with access to care: factors associated with testing and infection prevalence. *Clin Infect Dis*. 2012;55(8):1047–55.
 - 16 Jacobson IM, Gordon SC, Kowdley KV, Yoshida EM, Rodriguez-Torres M, Sulkowski MS, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. *N Engl J Med*. 2013;368(20): 1867–77.
 - 17 Lawitz E, Poordad FF, Pang PS, Hyland RH, Ding X, Mo H, et al. Sofosbuvir and ledipasvir fixed-dose combination with and without ribavirin in treatment-naïve and previously treated patients with genotype 1 hepatitis C virus infection (LONESTAR): an open-label, randomised, phase 2 trial. *Lancet*. 2014; 383(9916):515–23.
 - 18 Sulkowski MS, Gardiner DF, Rodriguez-Torres M, Reddy KR, Hassanein T, Jacobson I, et al. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. *N Engl J Med*. 2014; 370(3):211–21.
 - 19 Van der Meer AJ, Veldt BJ, Feld JJ, Wedemeyer H, Dufour JF, Lammert F, et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. *JAMA*. 2012; 308(24):2584–93.
 - 20 To access the Appendix, click on the Appendix link in the box to the right of the article online.
 - 21 Healthcare Cost and Utilization Project. National (Nationwide) Inpatient Sample [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; [last modified 2014 Jul 18; cited 2014 Aug 26]. Available from: <http://www.hcup-us.ahrq.gov/nisoverview.jsp>
 - 22 Healthcare Cost and Utilization Project. Introduction to the HCUP Nationwide Inpatient Sample (NIS) 2011 [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Jun [cited 2014 Aug 26]. Available from: http://www.hcup-us.ahrq.gov/db/nation/nis/NIS_Introduction_2011.jsp
 - 23 Healthcare Cost and Utilization Project. Overview of the State Inpatient Databases (SID) [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; [last modified 2014 Jun 27; cited 2014 Aug 26]. Available from: <http://www.hcup-us.ahrq.gov/sidoverview.jsp>
 - 24 Healthcare Cost and Utilization Project. Introduction to the HCUP State Inpatient Databases (SID) [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Aug [cited 2014 Sep 5]. Available from: http://www.hcup-us.ahrq.gov/db/state/siddist/Introduction_to_SID.pdf
 - 25 Healthcare Cost and Utilization Project. Population denominator data for use with the HCUP databases (updated with 2012 population data) [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2013 Mar 8 [cited 2014 Sep 5]. (HCUP Methods Series Report No. 2013-01). Available from: http://www.hcup-us.ahrq.gov/reports/methods/2013_01.pdf
 - 26 Department of Commerce, Bureau of Economic Analysis. National data: personal consumption expenditures [Internet]. Washington (DC): Department of Commerce; 2013. Table 2.4.4U. Available for download from: <http://www.bea.gov/iTable/iTable.cfm?ReqID=12&step=1&acrdn=2#reqid=12&step=1&isuri=1>
 - 27 Nguyen GC, Segev DL, Thuluvath PJ. Nationwide increase in hospitalizations and hepatitis C among inpatients with cirrhosis and sequelae of portal hypertension. *Clin Gastroenterol Hepatol*. 2007;5(9):1092–9.
 - 28 Galbraith JW, Donnelly JP, Franco R, Overton T, Rodgers JB, Wang HE. National estimates of healthcare utilization by individuals with hepatitis C virus infection in the United States. *Clin Infect Dis*. 2014 Jun 9. [Epub ahead of print].
 - 29 Chacra W, Rabin D, Yang JJ, Gordon SC. Development of an algorithm based on ICD-9 codes to identify patients with decompensated cirrhosis. Poster presented at: 64th Annual Meeting of the American Association for the Study of Liver Diseases; 2013 Nov 1–5; Washington, DC.
 - 30 Afdhal N, Reddy KR, Nelson DR, Lawitz E, Gordon SC, Schiff E, et al. Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. *N Engl J Med*. 2014;370(16): 1483–93.
 - 31 Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression. *Gastroenterology*. 2010;138(2): 513–21.
 - 32 Cammà C, Petta S, Enea M, Bruno R, Bronte F, Capursi V, et al. Cost-effectiveness of boceprevir or telaprevir for untreated patients with genotype 1 chronic hepatitis C. *Hepatology*. 2012;56(3):850–60.
 - 33 Hagan LM, Yang Z, Ehteshami M, Schinazi RF. All-oral, interferon-free treatment for chronic hepatitis C: cost-effectiveness analyses. *J Viral Hepat*. 2013;20(12):847–57.