

## National Estimates of Healthcare Utilization by Individuals with Hepatitis C Virus Infection in the United States

James W. Galbraith<sup>1</sup>, John P. Donnelly<sup>1</sup>, Ricardo Franco<sup>2</sup>, Turner Overton<sup>2</sup>, Joel B. Rodgers<sup>1</sup>, Henry E. Wang<sup>1</sup>

<sup>1</sup>Department of Emergency Medicine, University of Alabama at Birmingham, AL, USA

<sup>2</sup>Department of Medicine, Division of Infectious Disease, University of Alabama at Birmingham, AL, USA

Corresponding Author: James W. Galbraith M.D. University of Alabama at Birmingham, OHB 251, 619 19<sup>th</sup> Street South, Birmingham, AL 35249, Email: jgalbraith@uabmc.edu

**Summary:** Individuals with HCV infection were large users of outpatient, ED and inpatient health services in the US. We highlight the sizable population of HCV-infected patients that could benefit from linkage to care and novel antiviral treatments.

Accepted Manuscript

**ABSTRACT**

**BACKGROUND:** Hepatitis C virus (HCV) infection is a major public health problem in the United States (US). While prior studies have evaluated HCV-related healthcare burden, these studies examined a single treatment setting and did not account for the growing "baby boomer" population (individuals born 1945-1965).

**METHODS:** Data from the National Ambulatory Medical Care Survey (NAMCS), the National Hospital Ambulatory Medical Care Survey (NHAMCS), and the Nationwide Inpatient Sample (NIS) were analyzed. We sought to characterize healthcare utilization by individuals infected with HCV in the US, examining adult ( $\geq 18$  years) outpatient, ED and inpatient visits among individuals with HCV diagnosis for the period 2001-2010. Key subgroups included persons born before 1945 (older), between 1945 and 1965 (baby boomer), and after 1965 (younger).

**RESULTS:** Individuals with HCV infection were responsible for over 2.3 million outpatient, 73,000 ED, and 475,000 inpatient visits annually. Persons in the baby boomer cohort accounted for 72.5%, 67.6%, and 70.7% of care episodes in these settings, respectively. While the number of outpatient visits remained stable during the study period, inpatient admissions among HCV-infected baby boomers increased by over 60%. Inpatient stays totaled 2.8 million days and cost over \$15 billion annually. Non-whites, uninsured individuals, and individuals receiving publicly funded health insurance were disproportionately affected in all healthcare settings.

**CONCLUSIONS:** Individuals with HCV infection are large users of outpatient, ED, and inpatient health services. Resource use is highest and increasing in the "baby boomer" generation. These observations illuminate the public health burden of HCV infection in the US.

## INTRODUCTION

Hepatitis C virus (HCV) infection poses a major and growing public health problem. An estimated 3.2 million Americans are currently living with chronic HCV infection.[1] HCV infection is particularly prevalent in the “baby boomer” population (those born between 1945 and 1965). Prior studies estimate that 3.3% of baby boomers are HCV-antibody positive, and this birth cohort accounts for up to 75% of all United States (US) HCV infections.[2] Additionally, 43-85% of baby boomers are unaware of their HCV infection status.[3-5] Chronic HCV infection remains the leading cause of chronic liver disease, hepatocellular carcinoma, and liver transplantation.[6] In 2007, mortality from HCV eclipsed that of the Human Immunodeficiency virus (HIV) in the US and is expected to rise over the coming decades.[7]

While much is known about the disease course of individuals with HCV infection, little is known about their collective impact upon the US healthcare system. Prior studies of HCV healthcare utilization have been limited to single centers or treatment settings.[8, 9] Because the chronic nature of HCV may result in healthcare utilization in outpatient, Emergency Department (ED) and inpatient settings, efforts to estimate the national healthcare burden of HCV must account for all three treatment arenas. Few studies describe the comparative rates or patterns of healthcare utilization by HCV individuals in these settings. This information is particularly important given HCV primarily affect the “baby boomer” generation.[10]

Our objective was to determine the characteristics of the outpatient, ED and inpatient healthcare utilization by persons with HCV infection in the US.

## METHODS

### *Study Design and Setting*

We analyzed data from the National Ambulatory Medical Care Survey (NAMCS), the National Hospital Ambulatory Medical Care Survey (NHAMCS), and the Nationwide Inpatient Sample (NIS). The study was approved by the Institutional Review Board of the University of Alabama at Birmingham.

### *Data Sources*

We obtained outpatient data from the NAMCS and the NHAMCS for outpatient departments (NHAMCS-OPD). Operated by the National Center for Health Statistics, the NAMCS is a national survey examining visits to physicians' offices. The NAMCS samples geographic areas, physicians within these areas, and patient visits within practices in order to produce nationally representative samples annually.[11] The NHAMCS is a national probability sample characterizing ED (NHAMCS-ED) and outpatient clinic (NHAMCS-OPD) visits at hospitals across the US. ENREF\_2 Using a four-stage probability design, NHAMCS-ED samples geographically defined areas, hospitals within these areas, emergency service areas within the EDs of the hospitals, and patient visits to the emergency services areas.[12] ENREF\_7 ENREF\_8 NHAMCS-OPD uses a similar design, sampling geographic areas, hospitals within these areas, clinics within outpatient departments, and visits to the clinics.[12]

For an assigned four-week period, NAMCS and NHAMCS systematically select all patients from selected facilities. The National Center for Health Statistics (NCHS) works with each hospital and clinic to abstract clinical data from selected charts. For this study, we used NAMCS and NHAMCS public-use data for the ten-year period 2001-2010. Visits were classified as outpatient if presenting to a physician's office or outpatient clinic (NAMCS or NHAMCS-OPD), consistent with prior efforts utilizing these data sources.[13]

We obtained inpatient data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality. NIS is a comprehensive database of sampled inpatient hospital stays from across the US. The 2010 NIS includes 1,051 hospitals in 45 states, which comprise over 96% of the US population.[14] Each year, data is collected on approximately 8 million inpatient hospital stays.[14]

### *Selection of Participants*

We studied adult ( $\geq 18$  years) patients with a diagnosis of HCV infection. We defined the population as individuals with outpatient, ED or inpatient diagnoses consistent with HCV infection. While the outpatient and ED data contained up to three diagnoses, the inpatient data included up to 25 diagnoses. International Classification of Diseases, 9th Revision(ICD-9) diagnosis codes for HCV included 70.41, 70.44, 70.51, 70.54, 70.70, 70.71, V02.62. We stratified all HCV individuals into three birth cohorts: “older”(individuals born before 1945), “baby boomer” (those born between 1945 and 1965), and “younger” (those born after 1965). We additionally classified visits and discharges as involving a liver-related complication if they had diagnoses of chronic liver disease or cirrhosis (ICD-9: 571), liver abscess and sequelae of chronic liver disease (572), other disorders of the liver (573), ascites (789.5), esophageal varices (456.00-456.21), hepatocellular carcinoma (155.0 and 155.2), or hepatorenal syndrome (674.8).[13]

### *Demographics and Clinical Characteristics*

For each visit and discharge, we identified patient characteristics (year of encounter, race, ethnicity, sex, insurance status, geographic region, population setting, and median household income for patient’s ZIP code (NIS only)) and primary diagnosis. We also identified the total charge and length of stay for inpatient hospitalizations. Because of missing values for sex (1.6% of outpatient visits, 0.8% of ED visits, and 0.2% of inpatient discharges) and race (18.1% of outpatient visits, 10.5% of ED visits, and 23.5% of inpatient discharges), we used imputed variables provided by the respective data sets.[11, 12]\_ENREF\_3 We classified insurance as Medicare, Medicaid, Private, Self-pay or other insurance, using the hierarchy recommended by NAMCS and NHAMCS.[11, 12]\_ENREF\_3 We

also categorized insurance as Private, Public (Medicare/Medicaid), and self-pay. We defined geographic region by census region. Data pertaining to ethnicity (NAMCS and NHAMCS) and household income (NIS) were not available for 2001 or 2002.

### *Data Analysis*

We reported descriptive statistics, utilizing sampling design and weight variables to calculate nationally weighted estimates and corresponding 95% confidence intervals. Because the NCHS considers estimates with greater than 30% relative standard error or based upon less than 30 raw observations to be unreliable, we collapsed subcategories accordingly. For variance and 95% confidence interval calculations, we used ultimate cluster design (single stage sampling), utilizing stratum and primary sampling unit identifiers provided with the NAMCS and NHAMCS data sets.[11, 12, 15]\_ENREF\_4 We used a similar approach for NIS data, making use of discharge weight and sampling variables.

We assessed differences in characteristics using chi-square tests of association corrected for the complex sampling design. We determined temporal trends in HCV encounters by including year as a continuous variable in logistic regression models. To obtain more precise variance estimates, we used two-year temporal intervals for NAMCS and NHAMCS. Means and confidence intervals were reported for continuous measures, with the exception of charge data. Due to the highly skewed distribution, medians and interquartile ranges (IQRs) were reported for inpatient charges. We used the Consumer Price Index for inpatient services and adjusted to the value of the US dollar in 2010 for all inpatient charge calculations, assessing trends by calculating the percent change over the study period.[16] All analyses were conducted using Stata v.12.1 (Stata Corporation, College Station, Texas).

## RESULTS

### *Characteristics of Outpatient Visits*

Among 824 million annual adult outpatient visits from 2001-2010, individuals with HCV infection accounted for 2.29 million (0.28%; 95% CI 0.22-0.34). Baby boomers accounted for almost three-fourths of outpatient visits by HCV-infected individuals. (Table 1) Compared to non-HCV baby boomer visits, HCV-infected visits were disproportionately male (69.9% vs 40.0%;  $p < 0.001$ ), black (29.5% vs 11.4%;  $p < 0.001$ ), and insured by Medicaid (25.9% vs 7.0%;  $p < 0.001$ ). (Table 2) Over the 10-year study period, there was no change in the percentage of outpatient visits for HCV (trend  $p$ -value 0.182). (Figure 1) Liver-related complications occurred in 3.5%, 7.6% and 10.0% of the younger, baby boomer and older cohorts, respectively.

### *Characteristics of Emergency Department Visits*

Among 90 million annual adult ED visits, individuals with HCV infection accounted for 72,138 (0.08%; CI 0.07-0.10). Baby boomers accounted for 67.7% of ED visits by HCV-infected persons. (Table 1) Compared to non-HCV baby boomer visits, HCV-infected ED visits were disproportionately male (62.1% vs 46.9%;  $p < 0.001$ ), of Hispanic ethnicity (19.4% vs 10.6%;  $p = 0.011$ ), and insured by Medicaid (42.1% vs 16.8%;  $p < 0.001$ ). (Table 2) There were no trends in the percentage of ED visits for HCV among baby boomers (trend  $p$ -value 0.519). (Figure 1) The proportion of visits with a liver-related complication was smallest for the younger cohort (5.2%).

For the others, the proportion was elevated, with 16.6% of the baby boomer cohort and 26.3% of the older cohort having a complication.

### *Characteristics of Inpatient Discharges*

Among 31.8 million annual adult inpatient discharges, HCV-infected persons accounted for 475,224 (1.5%; CI 1.4-1.5). The baby boomer cohort accounted for 70.7% of inpatient discharges among HCV-infected persons. (Table 1) Inpatient discharge for HCV increased by 60% for the baby boomer cohort, rising from 2.6 % in 2001 to 4.2% in 2010 (trend p-value <0.001). (Figure 2A) Compared to non-HCV baby boomer discharges, those with HCV infection were disproportionately male (66.1% vs 47.1%; p<0.001), insured by Medicaid (35.1% vs 16.0%; p<0.001) and residents in the lowest median household income quartile (39.8% vs 29.9%; p<0.001). (Table 2) The proportion of discharges with a liver-related complication was smallest for the younger cohort (13.6%; CI 12.8-14.3) and elevated for the others, with 34.5% (CI 33.7-35.3) of the baby boomer and 40.5% (CI 39.5-41.4) of the older cohort having a complication.

For the younger cohort, median charges differed between non-HCV discharges (\$12,559; IQR 7,777-21,973) and those with HCV (\$15,832; 8,763-31,394). For the baby boomer cohort, median charges were similar between non-HCV (\$21,540; 11,696-41,509) and HCV (\$22,364; 11,920-44,619). The greatest difference in median charge was observed for the older cohort, with non-HCV (\$23,484; 12,627-45,053) substantially lower than HCV (\$28,873; 15,385-56,315). There were modest increases in median inpatient charge for HCV-infected discharges in the baby boomer and older cohorts. (Figure 3) However, these increases were smaller than those observed for non-HCV discharges.

### *Diagnosis Subgroup Analysis*

Between 2001 and 2010, there were large increases in the percentage of all baby boomer cohort discharges with HCV and a liver-related complication (Figure 2B; trend  $p < 0.001$ ) and HCV with no liver-related complication (Figure 2C; trend  $p < 0.001$ ). The percentage of liver-related complications among HCV discharges increased for the baby boomer and younger cohorts, but decreased for the older cohort. (Figure 2D) The percentage of non-HCV discharges having a liver-related complication increased from 2001 to 2010 for all age groups. (Figure 2E)

Among all adult inpatient discharges, charges and length of stay were greatest for discharges with a liver-related complication, regardless of HCV status. (Table 3) Annual inpatient charges among HCV-infected persons with a liver-related complication totaled \$463 million for the younger cohort, \$5.8 billion for the baby boomer cohort and \$1.3 billion for the older cohort. Temporal trends in charges did not vary substantially by diagnosis group. (Supplementary Figure 1) Discharges with HCV and no liver-related complication were disproportionately black, underinsured, from the Northeast Census region, composed of residents from ZIP codes in the lowest quartile for household income, and admitted with a primary diagnosis of mental disorder. (Table 3) We observed similar patterns for ambulatory medical care visits in the outpatient or ED setting. (Supplementary Table 1)

## DISCUSSION

This analysis provides current national perspectives of the burden of HCV infection upon the US healthcare system. Individuals with HCV infection were large users of healthcare resources; incurring over 2.3 million outpatient, 73,000 ED, and 475,000 inpatient hospital stays annually. Our findings highlight the challenges of and opportunities for improved care of individuals with HCV infection.

As expected, our study affirmed the disproportionate use of healthcare resources by HCV-infected baby boomer cohort, accounting for approximately 1.7 million outpatient visits, 49,000 ED visits, and 336,000 inpatient discharges annually. However, there were other important observations that highlight the challenges of providing healthcare to this subset. For example, while the rates of outpatient and ED visits by HCV baby boomer cohort remained stable from 2001-2010, the corresponding rates of inpatient discharge increased by over 60%. Compared with outpatient and ED settings, a larger percentage of discharges involved a liver-related complication. Among the baby boomer cohort, discharges with a liver complication were a substantial economic burden, totaling nearly \$6 billion annually. At the current rate, in 10 years, HCV baby boomers may account for up to 912,000 annual hospitalizations, with acuity likely to increase given the underlying progressive liver disease and high comorbidity burden among these patients.[17]

The increase in inpatient discharges relative to outpatient visits is also potentially worrisome. While not indicated by our data, these findings may signal the inability of these individuals to access outpatient care and treatment to prevent the progression of HCV-related liver disease. These observations could also represent the results of delayed HCV detection, with individuals not presenting for care until after developing symptomatic end stage liver disease or other severe sequelae. We also identified a very low percentage of HCV-related visits in rural settings; while potentially suggesting regional disparities in HCV prevalence, these findings may also indicate a lack of suitable HCV care resources outside of metropolitan areas.

Striking differences were noted between HCV inpatient discharges with and without liver-related complications. HCV inpatient discharges without a liver-related diagnosis were disproportionately black and underinsured, and with a primary ICD-9 code diagnosis of mental disorder. From 2001 to 2010, this group revealed a significant and steady rise in proportion to all hospital discharges for the younger and baby boomer cohorts. These findings highlight the burden of mental health disorders, which includes substance abuse and psychiatric illnesses, within this HCV-infected population. This suggests that efforts to successfully link and treat this population might require significant resources to stabilize both drug and alcohol addiction and psychiatric illness.

Across all settings, compared with HCV-seronegative patients, HCV individuals were predominantly Medicaid or Medicare beneficiaries. Furthermore, the percentage of individuals with private insurance in the baby boomer cohort was below 50% for all settings. These findings underscore that the increasing burden of funding HCV care will fall upon public resources. Inadequate health insurance coverage and poor access to regular health care have been extensively described as barriers to HCV screening and treatment. Stepanova, et al. revealed that a high proportion of persons infected with HCV have no insurance (38%) or have publicly funded health insurance (28%). [18] Uninsured HCV-positive individuals in the same study were more likely to use the hospital emergency room than any other type of health care. Efforts to reduce the impact of HCV must consider expansion of HCV screening and early treatment among the uninsured and medically underserved. Additionally, the explosion of new directly acting antiviral medications for the treatment of HCV will be useless without access for this large under-insured and uninsured cohort. [19]

Prior studies examining HCV healthcare burden have limitations. Tsui, et al. examined the NAMCS and NHAMCS-OPD data from 1997 through 2005 and reported a high proportion of HCV related outpatient visits by the baby boomer cohort and disproportionate growth among non-whites and Medicaid recipients. [8] Moorman, et al. assessed the clinical impact of chronic HCV infection through a prospective cohort study from four participating health systems, confirming the prominence of this condition among baby boomers. [9] Grant, et al. also used national inpatient data to characterize healthcare resource utilization by HCV individuals. [13] However, their study was limited to 1994-2001, while our study included 2001-2010 and reflects the most current estimates. We also included ED and outpatient encounters provided by NHAMCS. Our study extends upon these prior efforts, confirming increases

in HCV-related healthcare burden among baby boomers. Most alarming is the increase in inpatient utilization, suggesting that the progression of HCV-related liver disease will create an increasing healthcare burden over the coming decades.

The findings of our study highlight the urgency of expanding HCV detection and initial care nationally. HCV screening is inexpensive and reliable, with evolving treatment strategies making HCV an imminently curable disease. Recent advances in HCV treatment with direct-acting antivirals (DAAs) have transformed the care of this previously incurable disease.[20-22] Coordinated screening efforts are paramount in order to detect the disease at its earliest stages, maximizing opportunities for early treatment and prevention of major health sequelae.[23-25] Early detection and treatment are viable and essential strategies for reducing HCV mortality and healthcare burden. Given the known healthcare utilization disparities and those observed in our study, limiting HCV screening and treatment to traditional settings will fall short of current needs and increasing rates of HCV-related cirrhosis and hepatocellular carcinoma. Ongoing health care reform changes must expand opportunities for HCV screening and treatment to all persons, regardless of insurance status, to achieve success similar to that seen with HIV through the Ryan White Care Act.

We recognize the limitations of the current analysis. NAMCS, NHAMCS and NIS are retrospective, probability-sampled data sets. Recent studies have questioned the validity of the ambulatory medical care surveys.[26, 27] However, the methodologies of NAMCS and NHAMCS are rigorous, and the data sets have been widely used in similar analyses for over 15 years.[28, 29] NAMCS, NHAMCS, and NIS data sets only include visits to non-federally employed office-based practices and non-institutional general and short-stay hospitals (excluding Federal, military, and VA hospitals). Given these known limitations, the large HCV burden identified in this study likely underestimates the true US burden. Furthermore, because a significant percentage of HCV infections remain undiagnosed, our findings will underestimate the true burden of HCV infection in the US. The current analysis provides the best data available regarding the national impact of HCV.

While we were able to characterize collective outpatient, ED and inpatient utilization by HCV-infected individuals, we were not able to determine the care or outcomes of individual persons. NAMCS, NHAMCS, and NIS data

represent visits and discharges, not unique individuals. Therefore, we could not control for or determine patterns of readmission. Because of the limited number of diagnoses collected by each data set, we may have under-detected the number of healthcare encounters, particularly in the outpatient and ED settings. Our study describes the number of healthcare visits by HCV-infected individuals, but does not indicate the prevalence of the disease in the US populations. Furthermore, we did not analyze comorbid diseases, which may have led to increased healthcare visits by HCV-infected individuals.

In conclusion, individuals with HCV infection were large users of outpatient, ED and inpatient health services in the US, with resource use highest and increasing in the baby boomer cohort. These observations illuminate the public health burden of HCV infection in the US.

Accepted Manuscript

**Conflict of Interest Disclosures:**

Dr. Franco reports grant support paid to the institution from Vertex and the Centers for Disease Control and Prevention. Dr. Overton reports grant support paid to the institution from Vertex, BMS, Gilead Sciences, and AbbVie.

**Funding/Support:**

Dr. Wang received support from grant R01-NR012726 from the National Institute for Nursing Research. Dr. Galbraith receives support from contract CDC-PS10-10138 from the Centers for Disease Control and Prevention. Mr. Donnelly is currently supported by grant 2 T32 HS013852 from the Agency for Healthcare Research and Quality, Rockville, MD, USA. Members of the funding organizations outlined had no role in the design, analysis, or presentation of the results.

**Acknowledgements:**

Co-author Henry Wang, who is independent of any commercial funder, certifies that he “had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis.”

## References

1. Armstrong GL, Wasley A, Simard EP, et al. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med* **2006**; 144: 705-14.
2. Smith BD, Morgan RL, Beckett GA, et al. Hepatitis C virus testing of persons born during 1945-1965: recommendations from the Centers for Disease Control and Prevention. *Ann Intern Med* **2012**; 157: 817-22.
3. Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition Examination Survey 2001-2008. *Hepatology* **2012**; 55: 1652-61.
4. Spradling PR, Rupp L, Moorman AC, 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: 1047-55.
5. Younossi ZM, Stepanova M, Afendy M, et al. Knowledge about infection is the only predictor of treatment in patients with chronic hepatitis C. *J Viral Hepat* **2013**; 20: 550-5.
6. Davis GL, Albright JE, Cook SF, Rosenberg DM. Projecting future complications of chronic hepatitis C in the United States. *Liver Transpl* **2003**; 9: 331-8.

7. Ly KN, Xing J, Klevens RM, et al. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. *Ann Intern Med* **2012**; 156: 271-8.
8. Tsui JI, Maselli J, Gonzales R. Sociodemographic trends in national ambulatory care visits for hepatitis C virus infection. *Dig Dis Sci* **2009**; 54: 2694-8.
9. Moorman AC, Gordon SC, Rupp LB, et al. Baseline characteristics and mortality among people in care for chronic viral hepatitis: the chronic hepatitis cohort study. *Clin Infect Dis* **2013**; 56: 40-50.
10. Klevens RM, Hu DJ, Jiles R, Holmberg SD. Evolving epidemiology of hepatitis C virus in the United States. *Clin Infect Dis* **2012**; 55 Suppl 1: S3-9.
11. NCHS. National Center for Health Statistics, Centers for Disease Control and Prevention. Dataset documentation: National Ambulatory Medical Care Survey. (Accessed May 31, 2012 at [ftp://ftp.cdc.gov/pub/Health\\_Statistics/NCHS/Dataset\\_Documentation/NAMCS/](ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS/)).
12. NCHS. National Center for Health Statistics, Centers for Disease Control and Prevention. Dataset documentation: National Hospital Ambulatory Medical Care Survey. (Accessed May 31, 2012 at [ftp://ftp.cdc.gov/pub/Health\\_Statistics/NCHS/Dataset\\_Documentation/NHAMCS/](ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHAMCS/)).

13. Grant WC, Jhaveri RR, McHutchison JG, et al. Trends in health care resource use for hepatitis C virus infection in the United States. *Hepatology* **2005**; 42: 1406-13.
14. HCUP. Nationwide Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). 2001-2010. Agency for Healthcare Research and Quality, Rockville, MD. (Accessed on March 22, 2013 at [www.hcup-us.ahrq.gov/nisoverview.jsp](http://www.hcup-us.ahrq.gov/nisoverview.jsp)).
15. NCHS. National Center for Health Statistics, Centers for Disease Control and Prevention, NHAMCS estimation procedures. (Accessed May 31, 2012, at [http://www.cdc.gov/nchs/ahcd/ahcd\\_estimation\\_procedures.htm#nhamcs\\_procedures](http://www.cdc.gov/nchs/ahcd/ahcd_estimation_procedures.htm#nhamcs_procedures)).
16. BLS. Consumer Price Index (CPI). Bureau of Labor Statistics (BLS). United States Department of Labor. (Accessed on March 22, 2013 at <http://www.bls.gov/cpi/#data>).
17. Louie KS, St Laurent S, Forssen UM, et al. The high comorbidity burden of the hepatitis C virus infected population in the United States. *BMC Infect Dis* **2012**; 12: 86.
18. Stepanova M, Kanwal F, El-Serag HB, Younossi ZM. Insurance status and treatment candidacy of hepatitis C patients: analysis of population-based data from the United States. *Hepatology* **2011**; 53: 737-45.

19. Kiser JJ, Flexner C. Direct-acting antiviral agents for hepatitis C virus infection. *Annu Rev Pharmacol Toxicol* **2013**; 53: 427-49.
20. Asselah T, Marcellin P. Direct acting antivirals for the treatment of chronic hepatitis C: one pill a day for tomorrow. *Liver Int* **2012**; 32 Suppl 1: 88-102.
21. Jacobson IM, McHutchison JG, Dusheiko G, et al. Telaprevir for previously untreated chronic hepatitis C virus infection. *N Engl J Med* **2011**; 364: 2405-16.
22. Poordad F, McCone J, Jr., Bacon BR, et al. Boceprevir for untreated chronic HCV genotype 1 infection. *N Engl J Med* **2011**; 364: 1195-206.
23. Smith BD, Jorgensen C, Zibbell JE, Beckett GA. Centers for Disease Control and Prevention initiatives to prevent hepatitis C virus infection: a selective update. *Clin Infect Dis* **2012**; 55 Suppl 1: S49-53.
24. Ward JW, Valdiserri RO, Koh HK. Hepatitis C virus prevention, care, and treatment: from policy to practice. *Clin Infect Dis* **2012**; 55 Suppl 1: S58-63.
25. USHHS. Combating the Silent Epidemic of Viral Hepatitis (2011). United States Department Of Health And Human Services. 2012.

26. Green SM. Congruence of Disposition After Emergency Department Intubation in the National Hospital Ambulatory Medical Care Survey. *Ann Emerg Med* **2012**.
27. Cooper RJ. NHAMCS: does it hold up to scrutiny? *Ann Emerg Med* **2012**; 60: 722-5.
28. McCaig LF, Burt CW. Understanding and interpreting the National Hospital Ambulatory Medical Care Survey: key questions and answers. *Ann Emerg Med* **2012**; 60: 716-21 e1.
29. McCaig LF, Burt CW, Schappert SM, et al. NHAMCS: Does It Hold Up to Scrutiny? *Ann Emerg Med* **2013**; 62: 549-51.

Accepted Manuscript

**TABLE 1**

Annual healthcare encounters for persons with hepatitis C infection stratified by age cohort and setting, 2001-2010.

	Outpatient Visits (1)		ED Visits (2)		Inpatient Discharges (3)	
	No HCV	HCV	No HCV	HCV	No HCV	HCV
	N (1000s) % (95% CI)	N (1000s) % (95% CI)	N (1000s) % (95% CI)	N (1000s) % (95% CI)	N (1000s) % (95% CI)	N (1000s) % (95% CI)
All Adults	824,347	2,290	89,880	72	31,788	475
Younger (Born After 1965)‡	216,157 26.2 (25.4-27.0)	330 14.4 (10.5-19.4)	41,171 45.8 (45.1-46.5)	15 20.4 (14.9-27.3)	8,318 26.2 (25.7-26.6)	76 16.0 (15.3-16.6)
Baby Boomer (Born 1945-1965)	308,137 37.4 (36.9-37.9)	1,659 72.5 (67.2-77.2)	28,503 31.7 (31.3-32.1)	49 67.6 (59.7-74.7)	8,683 27.3 (27.1-27.6)	336 70.7 (70.3-71.2)
Older (Born Before 1945)	300,052 36.4 (35.4-37.4)	301 13.2 (8.1-20.8)	20,206 22.5 (21.9-23.1)	9* 12.0 (NA)	14,787 46.5 (46.0-47.1)	63 13.3 (12.8-13.9)

All percentages reported are column percentages.

‡Includes adults aged  $\geq 18$  years.

\*Fewer than 30 raw observations. The NCHS considers estimates based on  $< 30$  raw observations to be unreliable.

(1) Data from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Care Survey for Outpatient Departments (NHAMCS-OPD). (2) Data from the National Hospital Ambulatory Medical Care Survey for Emergency Departments (NHAMCS-ED). (3) Data from the Nationwide Inpatient Sample (NIS).

CI=confidence interval; NA=not applicable; OPD=outpatient department; ED=emergency department.

Accepted Manuscript

**TABLE 2**

Characteristics of baby boomer individuals (born 1945-1965) with hepatitis C infection, 2001-2010.

Variable	Percentage of Outpatient HCV Visits (95% CI) (1)	Percentage of ED HCV Visits (95% CI) (2)	Percentage of Inpatient HCV Discharges (95% CI) (3)
	Annual N = 1,659,199	Annual N = 48,791	Annual N = 336,070
Sex			
Male	69.9 (64.4-74.9)	62.1 (53.9-69.7)	66.1 (65.6-66.6)
Female	30.1 (25.1-35.6)	37.9 (30.3-46.1)	33.9 (33.4-34.4)
Race			
White	65.4 (57.6-72.4)	65.0 (56.0-73.1)	57.0 (55.0-59.0)
Black	29.5 (22.3-37.9)	30.8 (23.0-39.9)	25.6 (24.0-27.3)
Other	5.1 (2.8-9.1)	4.2 (NA)*	17.4 (15.9-18.9)#
Ethnicity			
Hispanic	16.6 (11.3-23.7)†	19.4 (11.9-29.9)†	13.0 (11.7-14.5)
Non-Hispanic	83.4 (76.3-88.7)†	80.6 (70.1-88.1)†	87.0 (85.5-88.3)
Region			
Northeast	19.4 (14.0-26.1)	27.0 (18.0-38.3)	24.9 (22.1-27.8)
Midwest	16.8 (10.3-26.4)	14.3 (NA)*	16.4 (14.7-18.3)
South	38.6 (29.1-49.2)	36.3 (24.6-50.0)	35.9 (32.9-38.9)
West	25.2 (15.8-37.6)	22.4 (14.5-33.1)	22.9 (20.8-25.1)
Population Setting <sup>o</sup>			
Metropolitan Statistical Area (MSA) or Urban	90.7 (84.9-94.4)	95.2 (87.1-98.3)	92.4 (91.6-93.2)
Non-MSA or Rural	9.3 (5.6-15.1)	4.8 (NA)*	7.6 (6.8-8.4)
Payor Type			
Medicare	13.0 (9.3-18.0)	11.2 (NA)*	26.5 (25.9-27.2)
Medicaid	25.9 (20.5-32.3)	42.1 (32.6-52.2)	35.1 (33.8-36.5)
Private Insurance	47.5 (38.3-56.8)	25.5 (18.1-34.6)	21.7 (20.7-22.8)
Self-Pay	6.4 (4.1-9.9)	16.2 (NA)*	9.7 (8.9-10.5)
Other	7.2 (4.1-12.3)	5.0 (NA)*	7.0 (6.0-8.0)
Broad Insurance Type			
Private	51.1 (41.9-60.3)	26.8 (19.0-36.4)	23.4 (22.3-24.5)
Public (Medicaid/Medicare)	41.9 (34.3-50.0)	56.1 (45.7-66.0)	66.3 (65.1-67.4)
Self-Pay	6.9 (4.4-10.7)	17.1 (NA)*	10.4 (9.5-11.3)

Median Household Income for Zip Code (Quartile)			
\$1-\$38,999	-	-	39.8 (37.8-41.8)†
\$39,000-\$47,999	-	-	25.7 (24.7-26.8)†
\$48,000-\$62,999	-	-	20.7 (19.7-21.6)†
\$63,000 and Above	-	-	13.9 (12.8-15.0)†
Primary Diagnosis (ICD-9 CM Category)			
Infectious and Parasitic Diseases	58.3 (50.9-65.4)	14.1 (9.6-20.1)	9.1 (8.8-9.4)
Mental Disorders	5.4 (2.7-10.6)	11.8 (7.4-18.4)	13.7 (12.7-14.7)
Respiratory System	2.6 (NA)*	6.6 (NA)*	8.2 (8.0-8.4)
Digestive System	3.8 (2.2-6.4)	11.1 (NA)*	20.0 (19.6-20.5)
Symptoms, Signs, Ill-Defined Conditions, and Other	30.0 (24.3-36.4)	56.4 (47.5-65.0)	49.0 (48.3-49.7)

Includes adults aged  $\geq 18$  years. Results stratified by care setting. All percentages reported are column percentages.

\*Estimates based on fewer than 30 raw observations. The NCHS considers estimates based on  $< 30$  raw observations to be unreliable.

†Data available for 2003-2010 only.

°MSA designation available only for Outpatient and ED data, Inpatient discharge data uses urban and rural classification.

#Includes individuals identified as Hispanic.

(1) Data from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Care Survey for Outpatient Departments (NHAMCS-OPD). (2) Data from the National Hospital Ambulatory Medical Care Survey for Emergency Departments (NHAMCS-ED). (3) Data from the Nationwide Inpatient Sample (NIS).

HCV=hepatitis C virus; CI=confidence interval; MSA=metropolitan statistical area; CM=clinical modification; ED=Emergency Department.

**Table 3**

Characteristics of adult inpatient discharges by diagnosis group, 2001-2010.

<b>Variable</b>	<b>Non-HCV and Non-Liver- Related % (95% CI)</b>	<b>Non-HCV and Liver-Related % (95% CI)</b>	<b>HCV and Non-Liver- Related % (95% CI)</b>	<b>HCV and Liver-Related % (95% CI)</b>
	Annual N = 30,948,144	Annual N = 840,329	Annual N = 323,332	Annual N = 151,891
Median Charge (2010 \$) (IQR)	19,064 (10,383-37,560)	26,395 (14,164-52,045)	20,201 (10,747-40,784)	25,899 (13,865-51,187)
Mean Length of Stay (Days) (95% CI)	4.7 (4.7-4.8)	6.8 (6.7-6.9)	5.9 (5.8-6.0)	6.4 (6.3-6.5)
Mean Age (Years) (95% CI)	57.0 (56.7-57.2)	57.8 (57.6-58.0)	49.2 (48.9-49.4)	53.6 (53.4-53.8)
Sex				
Male	38.6 (38.3-38.9)	51.6 (51.3-51.9)	60.2 (59.6-60.8)	66.5 (66.0-67.0)
Female	61.4 (61.1-61.7)	48.4 (48.1-48.7)	39.8 (39.2-40.4)	33.5 (33.0-34.0)
Race				
White	70.0 (68.7-71.3)	68.1 (66.6-69.5)	56.7 (54.6-58.8)	59.2 (57.4-61.1)
Black	13.7 (12.9-14.5)	12.1 (11.3-12.9)	26.9 (25.2-28.6)	15.9 (14.8-17.0)
Other#	16.3 (15.4-17.4)	19.9 (18.6-21.2)	16.4 (14.9-18.1)	24.9 (23.2-26.7)
Ethnicity				
Hispanic	10.6 (9.7-11.5)	13.5 (12.4-14.7)	11.6 (10.3-13.2)	18.8 (17.2-20.6)
Non-Hispanic	89.4 (88.5-90.3)	86.5 (85.3-87.6)	88.4 (86.8-89.7)	81.2 (79.4-82.8)
Region				
Northeast	20.1 (18.7-21.5)	18.5 (17.0-20.0)	27.7 (24.8-30.9)	20.8 (18.1-23.8)
Midwest	23.5 (22.3-24.8)	21.8 (20.5-23.2)	16.1 (14.4-18.0)	15.6 (13.9-17.4)
South	38.3 (36.6-40.1)	38.5 (36.6-40.4)	35.4 (32.2-38.8)	37.3 (34.5-40.1)
West	18.0 (16.9-19.3)	21.2 (19.7-22.7)	20.7 (18.8-22.9)	26.4 (24.0-28.9)
Population Setting				
Urban	86.0 (85.1-86.8)	88.1 (87.2-88.9)	92.3 (91.4-93.1)	92.3 (91.5-93.1)
Rural	14.0 (13.2-14.9)	11.9 (11.1-12.8)	7.7 (6.9-8.6)	7.7 (6.9-8.5)
Payor Type				
Medicare	46.2 (45.7-46.8)	44.0 (43.4-44.6)	29.9 (29.1-30.7)	33.2 (32.5-34.0)
Medicaid	14.7 (14.2-15.2)	15.7 (15.1-16.2)	34.7 (33.3-36.1)	31.3 (30.3-32.3)
Private Insurance	31.0 (30.4-31.6)	28.9 (28.2-29.5)	18.0 (17.1-19.0)	21.0 (20.0-22.0)
Self-Pay	5.0 (4.7-5.3)	7.7 (7.3-8.1)	10.7 (9.7-11.7)	8.5 (7.8-9.3)
Other	3.1 (2.9-3.4)	3.8 (3.5-4.2)	6.7 (5.8-7.8)	6.0 (5.1-7.0)
Broad Insurance Type				

Private	32.0 (31.4-32.6)	30.0 (29.3-30.7)	19.3 (18.4-20.4)	22.3 (21.3-23.4)
Public (Medicaid/Medicare)	62.9 (62.3-63.4)	62.0 (61.4-62.7)	69.2 (68.1-70.3)	68.6 (67.6-69.7)
Self-Pay	5.2 (4.8-5.5)	8.0 (7.5-8.4)	11.5 (10.4-12.6)	9.1 (8.3-9.9)
Median Household Income for Zip Code (Quartile) †				
\$1-\$38,999	28.6 (27.5-29.8)	29.0 (27.7-30.2)	40.7 (38.6-42.8)	36.4 (34.5-38.2)
\$39,000-\$47,999	26.3 (25.4-27.1)	26.0 (25.2-26.9)	25.1 (24.0-26.2)	26.2 (25.1-27.2)
\$48,000-\$62,999	23.6 (22.9-24.4)	23.8 (23.0-24.5)	20.1 (19.1-21.0)	22.0 (21.0-23.0)
\$63,000 and Above	21.5 (20.1-22.9)	21.2 (19.8-22.7)	14.2 (13.1-15.3)	15.5 (14.3-16.8)
Primary Diagnosis (ICD-9 CM Category)				
Infectious and Parasitic Diseases	2.8 (2.8-2.8)	5.3 (5.3-5.4)	6.8 (6.5-7.1)	13.3 (12.9-13.7)
Mental Disorders	5.1 (4.8-5.3)	5.5 (5.2-5.8)	19.1 (17.6-20.7)	4.8 (4.5-5.2)
Respiratory System	8.8 (8.7-8.9)	5.9 (5.9-6.0)	8.8 (8.6-9.0)	5.8 (5.6-5.9)
Digestive System	9.1 (9.0-9.2)	33.5 (33.2-33.8)	9.1 (8.8-9.4)	38.9 (38.3-39.5)
Symptoms, Signs, Ill-Defined Conditions, and Other	74.2 (73.9-74.5)	49.8 (49.4-50.1)	56.2 (55.1-57.4)	37.2 (36.7-37.7)

Includes adults aged  $\geq 18$  years. All percentages reported are column percentages. Liver-related complication defined as chronic liver disease or cirrhosis, liver abscess and sequelae of chronic liver disease, other disorders of the liver, ascites, esophageal varices, hepatocellular carcinoma, or hepatorenal syndrome.

†Data available for 2003-2010 only.

#Includes individuals identified as Hispanic.

Data from the Nationwide Inpatient Sample (NIS).

HCV=hepatitis C virus; IQR=interquartile range; CI=confidence interval; CM=clinical modification.

**FIGURE 1**

Trends in hepatitis C outpatient and Emergency Department visit by age cohort, 2001-2010.

**Figure 1 Legend:** Outpatient data from the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS-OPD). Emergency Department data from NHAMCS-ED. 95% confidence interval estimates unavailable due to small numbers in some two-year intervals. No significant change in the HCV rate for outpatient and Emergency Department visits in any age group.

**FIGURE 2**

Inpatient discharge trends by age cohort and diagnosis group, 2001-2010.

**Figure 2 Legend:** Data from Nationwide Inpatient Sample (NIS). Error bars represent 95% confidence interval limits. Liver-related complication defined as chronic liver disease or cirrhosis, liver abscess and sequelae of chronic liver disease, other disorders of the liver, ascites, esophageal varices, hepatocellular carcinoma, or hepatorenal syndrome.

Percent change from 2001 to 2010 and test for linear trend:

A) younger 149.1% (p < 0.001); baby boomer 60.7% (p < 0.001); older 23.1% (p < 0.001)

B) younger 200.8% (p < 0.001); baby boomer 84.4% (p < 0.001); older 8.1% (p = 0.215)

C) younger 141.3% (p < 0.001); baby boomer 49.0% (p < 0.001); older 35.3% (p < 0.001)

D) younger 20.8% (p < 0.001); baby boomer 14.8% (p < 0.001); older -12.2% (p < 0.001)

E) younger 146.2% (p < 0.001); baby boomer 74.2% (p < 0.001); older 44.1% (p < 0.001)

HCV=hepatitis C virus.

### FIGURE 3

Trends in inpatient charges by age cohort and HCV status, 2001-2010

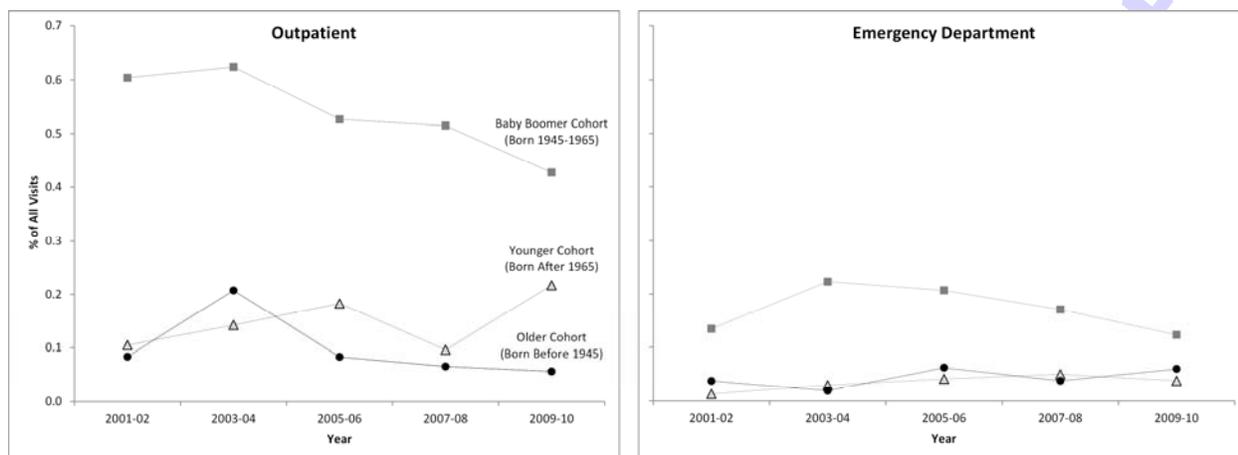
**Figure 3 Legend:** Data from Nationwide Inpatient Sample (NIS). Inpatient charges inflation-adjusted to 2010 dollars using the Consumer Price Index for inpatient services. Median charge calculated with appropriate survey design weights applied.

Percent change in median charge from 2001 to 2010:

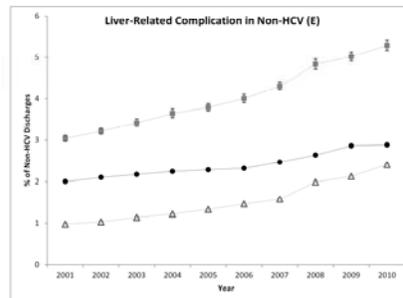
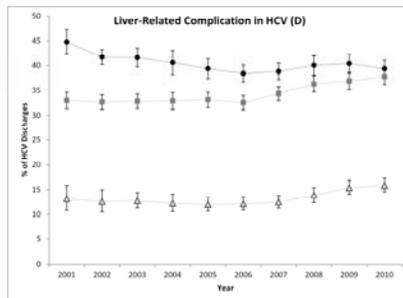
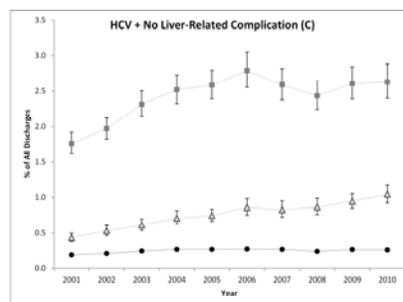
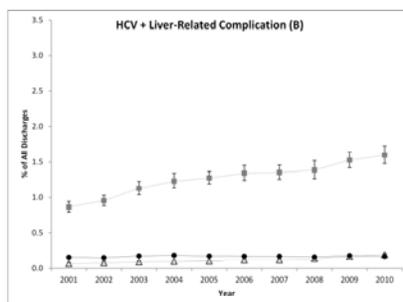
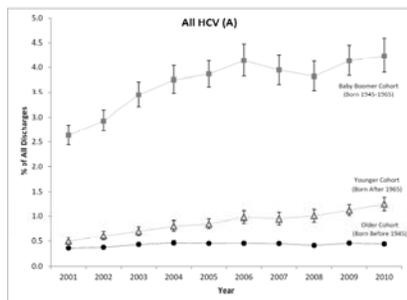
A) younger 27.6%; baby boomer 43.3%; older 16.7%

B) younger 7.3%; baby boomer 19.2%; older 19.2%

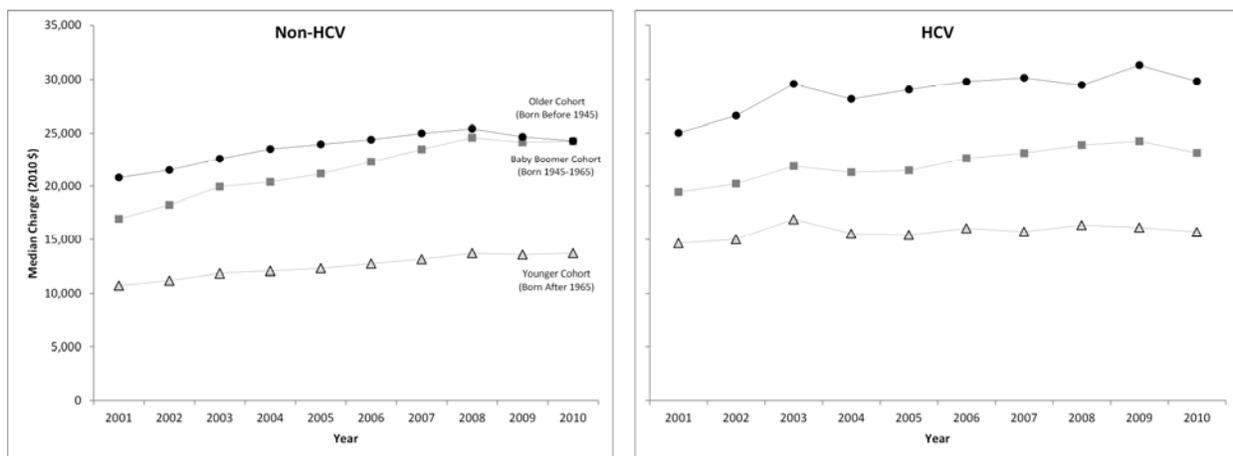
HCV=hepatitis C virus



Accepted Manuscript



Accepted Manuscript



Accepted Manuscript