BMJ open

Clinical Outcomes and Resource Utilization in Chronic Liver Disease – a Temporal Trends Study of Medicare Population

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004318
Article Type:	Research
Date Submitted by the Author:	23-Oct-2013
Complete List of Authors:	Younossi, Zobair; Inova Fairfax Hospital, Medicine and Beatty Center for Integrated Research Zheng, Li; Inova Health Systems, Betty and Guy Beatty Center for Integrated Research Stepanova, Maria; Inova Health Systems, Betty and Guy Beatty Center for Integrated Research Venkatesan, Chapy; Inova Fairfax Hosptial, Medicine Mishra, Alita; Inova Fairfax Hosptial, Medicine
Primary Subject Heading:	Health services research
Secondary Subject Heading:	Gastroenterology and hepatology
Keywords:	Hepatobiliary disease < GASTROENTEROLOGY, Hepatology < INTERNAL MEDICINE, QUALITATIVE RESEARCH

Clinical Outcomes and Resource Utilization in Chronic Liver Disease – a Temporal Trends Study of Medicare Population

Zobair M. Younossi[1,2,] Li Zheng[2], Maria Stepanova[2], Chapy Venkatesan[1], Alita Mishra[1] ,

1. Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, USA.

2. Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, USA

Corresponding author and reprint requests:

Zobair M. Younossi, M.D., M.P.H.

Betty and Guy Beatty Center for Integrated Research

Claude Moore Health Education and Research Building

3300 Gallows Road, Falls Church, VA 22042

PHONE: (703) 776-2540 FAX: (703) 776-4386, E-mail: zobair.younossi@inova.org

Conflict of Interest: There are no conflicts of interest for any of the authors.

Transparency Declaration: The lead author affirms that this study is a complete assessment of the data and no important information has been omitted.

Funding Source: Internal funds only.

Key Words: Chronic liver disease, Medicare, Health Care Resource Utilization

Word count: 3237 (excluding title, abstract, references and tables)

Tables and figures: 6

Supplementary Tables: 2

ABSTRACT

Background: CLD is an important cause of morbidity and mortality. We aimed to describe recent trends in resource utilization and patient outcomes of patients with CLD covered by Medicare in the United States.

Methods: This is a retrospective cohort study of the Medicare claims. We utilized a sample of Medicare claims with a primary diagnosis of CLD based on inpatient (n = 20,943) and outpatient (n = 271,552) from 2005 to 2010. The study outcomes included hospital length of stay (LOS) and inpatient mortality as well as inpatient and outpatient inflation-adjusted charges and payments.

Results: Between 2005 and 2010, there was an annual decrease in LOS of 2.67% accompanied by 0.70% increase in payments and 3.94% increase in charges (all p<0.001) for inpatient CLD patients. Risk-adjusted in-hospital mortality decreased (odds ratio (OR), 0.91, 95% confidence interval (CI), 0.89-0.94), while post-discharge mortality remained stable (OR, 0.99, 95% CI, 0.97-1.02). Average yearly inflation-adjusted payments for outpatient healthcare utilization of CLD was $532 in 2005 and $566 in 2010 (p<0.0001). This change in payment was observed together with significant decrease in beneficiary-paid amount (21.7% to 19.0%, p<0.0001) and a significant increase in yearly Medicare spending (76.1% to 79.0%, p<0.0001). The major predictors of outpatient spending were younger age, Asian race or Hispanic ethnicity, living in California, and more diagnoses, and procedures per claim. The predictors of inpatient spending also included younger age, location, and the number of inpatient procedures.

Conclusions: Length of inpatient stay and inpatient mortality among Medicare beneficiaries with CLD decreased while both inpatient and outpatient spending increased.

Limitations:

- Discharge and admission dates were provided in quarters, making it impossible to assess the exact timing of post-discharge outcomes.
- Mortality was based only on validated deaths, which may result in under-estimated post-discharge mortality.
- Unmeasured confounders may exist in a retrospective cohort study.
- Patients may have sought care outside their Medicare plan which may affect their outcomes

INTRODUCTION

Chronic liver disease (CLD) is a major cause of mortality and morbidity worldwide. [1,2,3,4,5] In the United States, liver-related mortality is the tenth leading cause of death with hepatitis C (HCV) and obesity-related non-alcoholic fatty liver disease (NAFLD) being the major causes of CLD [1-4,6-9].

In patients with chronic liver disease, age is known to be associated with adverse outcomes [7,8,10]. As the U.S. population ages and becomes more obese, the impact of CLD is expected to become more prominent [6,9]. Thus, in the United States, this trend is becoming especially important for the Medicare population. In this context, recent reports by The Institute of Medicine emphasized the need for a national prevention and control strategy for patients with chronic hepatitis [4].

Medicare is a U.S. national government-sponsored health insurance program that guarantees access to healthcare for the U.S. residents of 65 years of age or older, younger individuals with disabilities, those with end-stage renal disease (ESRD) or Lou Gehrig's disease. In Medicare, inpatient hospital care is covered under Part A and outpatient medical services are covered under Part B. In addition to Medicare's payment, enrollees are responsible for a number of out-of-pocket payments including deductibles and coinsurance as well as payment for uncovered services such as long-term, dental, hearing, and vision care; however, a supplemental insurance may be used to cover a certain proportion of the beneficiary-paid amount. To date, Medicare resource utilization related to CLD has not been fully assessed. The recent healthcare reform legislation will be impacting what Medicare spends and how hospitals are reimbursed. The aim

of this study was to assess the recent trends in inpatient and outpatient Medicare spending related to CLD.

METHODS

Data Source: The study analyzes Medicare inpatient and outpatient files from 2005-2010 submitted by outpatient and inpatient providers for reimbursement of treatment and facility costs. For each year, we obtained a 5% random sample of Medicare beneficiaries that were included in the Denominator Files from the Centers for Medicare & Medicaid Services (CMS) in the format of Limited Data Set (LDS) Standard Analytic Files. For the sampled beneficiaries, all inpatient and outpatient claims for all study years were included. This study was provided exempt status by our Internal Review Board.

The inpatient file contains inpatient hospital encounters incurred during the study period. Each record represents a single hospital claim which includes a unique patient identifier, basic demographics, admission type and discharge status, International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes, other conditions related to the Medicare bill that include various claim-related information such as being homeless, unemployed, military, student or over 100 years old, hospital charges, Medicare reimbursement amount, and payment from the patient and another insurance.

In outpatient files, each record represents a unique claim. Of the parameters used for the study, Medicare billing data included a unique patient identifier which was used to link data for each beneficiary across all Medicare files (the last day on the billing statement covered services

rendered to the beneficiary, a list of up to 10 diagnoses and 6 outpatient ICD-9 procedures, total facility charges, Medicare reimbursement amount and payments from patient and other insurance providers).

Finally, the denominator file includes Medicare beneficiary enrollment, demographics and mortality information. No data elements that might permit identification of beneficiaries were left in the CLD files. We obtained institutional review board approval at Inova Fairfax Hospital, and signed a data-use agreement with the CMS.

Study Population

The following ICD-9-CM codes were used to establish the diagnosis of chronic liver disease in both inpatient and outpatient claims: viral hepatitis (070.0, 070.1, 070.20-070.23, 070.30-070.33, 070.41-070.44, 070.49, 070.51-070.54, 070.59, 070.6, 070.70, 070.71, 070.9), primary liver cancer (155.0), liver disorders of iron and copper metabolism (275.0, 275.01-275.03, 275.09, 275.1), esophageal varices with or without bleeding (456.0, 456.1, 456.20, 456.21), peritonitis (567.2), chronic liver disease and cirrhosis (571.0-571.3, 571.40-571.42, 571.49, 571.5, 571.6, 571.8, 571.9), sequelae of chronic liver disease such as hepatic coma, portal hypertension, and hepatorenal syndrome (572.2-572.4, 572.8), other chronic disorders of liver and biliary tract (573.3, 573.5, 573.8, 576.1, 576.8), pruritis (698.9), cholestatic jaundice (782.4), hepatomegaly (789.1), ascites (789.5), nonspecific abnormal serum enzyme levels (790.4-790.5), abnormal liver scan/function study (794.8), and indicators of CLD coded as factors and external causes (E947.9, V02.60, V02.61, V02.62, V02.69, V42.7). A claim was included in the study if the principal diagnosis for that claim was CLD-related. A patient might have had more than one

claim per year. In such case, claims with the principal diagnosis other than CLD were not included even if that patient had established diagnosis of CLD according to other claims. As a result, only CLD-related spending was evaluated.

Patient baseline characteristics were derived from Medicare denominator file, which includes age categories at admission, gender, race/ethnicity, end stage renal disease (ESRD) status, residence (Northeast, South, Midwest, West, and California), discharge disposition type, continued care, hospice status, and inpatient death. Comorbidities scores were derived from up to 9 secondary diagnosis codes using Deyo-modification of the Charlson score developed for claims data analysis [11]. The total number of diagnoses and total number of procedures in each record were also included in the analysis. Claims with missing data on any of the study variables were excluded from analysis.

Inpatient Outcomes

Both resource utilization and short-term mortality outcomes were assessed. Resource utilization parameters included length of stay (LOS), hospital charges and total payments. LOS is defined as the number of full days a patient stays in the hospital. Since admission and discharge dates were not provided in the data, LOS was calculated as the total number of days of care in each claim, which included the number of days of care that are chargeable and the number of days of care that are not chargeable to Medicare facility utilization. If a patient was admitted and discharged on the same day, LOS was counted as one day. According to Medicare policy, patients need to pay certain amount of coinsurance for LOS over 60 days, and no coinsurance for LOS 1-60 days. To remove the potential effect of coinsurance on LOS, cases with LOS over 60 days were dismissed from analysis. Total payments for patient services in each claim was calculated as the

sum of Medicare reimbursement amount, primary insurance payment, beneficiary-paid amounts (copay, deductibles and coinsurance). We used total payment as a surrogate for the total payment for patient services for each claim, which was calculated as the sum of Medicare reimbursement amount, primary insurance payment, beneficiary-paid amounts (copay, deductibles and coinsurance). Since the rates that Medicare pays for covered services are negotiated at the beginning of each year by the government agency, the historic average of 3% was selected as an annual coefficient of inflation for adjustment of hospital charges and total payments to the dollars of 2010. The unit of analysis was the encounter for LOS, hospital charge and total payments.

Mortality outcomes were evaluated for each calendar year. In the case of multiple hospitalizations within a calendar year, the most recent claim was designated as the index event. If a patient was hospitalized for CLD in multiple calendar years, he was counted as new patient for each year. In-hospital mortality was defined as an in-hospital record with discharge status of "Dead", regardless of cause or LOS. Post-discharge mortality was defined as a death from any cause after hospital discharge, after excluding patients who died in hospital. The period of follow-up for post-discharge mortality was the end of March of the year following patient's index discharge. We determined post-discharge mortality based on the death date recorded in the Medicare denominator file.

Outpatient Outcomes

Major resource utilization parameters including total charges, total payments, Medicare spending and the proportion of beneficiary-paid amount were calculated. Total per-claim payment was the

sum of Medicare reimbursement amount, primary insurance payment, and the beneficiary-paid amount which included all applicable co-payments, deductibles and coinsurance. If more than one inpatient or outpatient claim was reported for a patient in a given year, then, for that patient in that year, the resource utilization parameters were added up, and the total yearly resource utilization, together with the average proportion of beneficiary-paid amount in percent of total payments, were calculated.

Statistical Analysis

We described the baseline characteristics of the study population by presenting frequencies for categorical variables and mean ± SD for continuous variables. Mean LOS, hospital charge and total payments for each claim were calculated. Unadjusted rates of all-cause in-hospital mortality and post-discharge mortality were estimated. In both analyses, all available clinical and demographic parameters were compared across the study years to identify parameters that changed significantly over time, using chi-square test for binary or categorical parameters (age, gender, race, mortality, etc) and non-parametric Kruskal-Wallis Test for continuous parameters (length of stay, hospital charge, Charlson score, number of diagnosis, number of procedures).

Multivariable regression analyses were used to assess the independent associations of patient clinic-demographics characteristics with resource utilization. LOS, provider or hospital charge, and total payments were found to be skewed to the right in a non-normal distribution and therefore were analyzed using generalized linear model (GLM) with a gamma error distribution and a log-link function. Association between a risk factor and the outcome was analyzed with the independent-sample *t* test, which was used to compare the means of outcome for those with and

those without the risk factor. The adjusted relationship between risk factors and each outcome were estimated using coefficients from these models, which were exponentiated to yield a percentage change in the outcomes associated with each risk factor. Initially, all available demographic parameters, location and resource utilization were tested in the multiple regression model as potential predictors for the outcomes, but then only predictors with p-values of 0.05 or less were left.

Multivariate logistic regression analysis was performed on in-hospital mortality and post-discharge mortality to determine the independent effect of factors known to influence prognosis. The association between a risk factor and death was analyzed with the χ^2 test, which was used to compare the risk-adjusted rate of mortality among those with and those without the risk factor. Odds ratio was used to estimate the adjusted association between each predictor and mortality. Significance tests and confidence internals (CIs) were based on 95% confidence level. Differences were considered significant at the $P<.05$ level

RESULTS

Demographics and outcomes for inpatients with CLD (Table 1 and 2)

The analysis included 20,943 hospitalizations with a principal diagnosis of CLD during 2005-2010 for a total of 14,774 patients. The annual number of claims ranged from minimum of 4,020 in 2005 to maximum of 4,333 in 2007. The annual percent of re-hospitalizations was about 29%. The most common primary diagnoses were hepatic encephalopathy (21.6%), non-alcoholic cirrhosis of liver (15.7%), alcoholic cirrhosis of liver (13.0%), and primary liver cancer (6.4%).

During the study period, the observed in-hospital mortality decreased from 11.75% to 8.73% ($p < 0.001$), post-discharge mortality increased from 34.7% to 35.8% ($p = 0.036$), number of diagnoses per claim increased from 7.90 to 8.60 ($p < 0.001$), and Charlson score increased (1.35 to 1.43; $p< 0.001$). The proportion of patients discharged to home decreased, while the proportion discharged to hospice or continued care increased.

The number of admissions, diagnoses and procedures were independently associated with increased risk for in-hospital mortality. Independent predictors of post-discharge mortality were discharge disposition, number of admissions, Charlson score, gender and LOS during hospitalization. Age appeared to be a stronger predictor of post-discharge mortality than in-hospital mortality. Furthermore, there were regional and racial variations in post-discharge mortality using the standard reference categories (Table 3).

Inpatient spending for Medicare beneficiaries with CLD

The proportion of CLD-related inpatient spending in the total inpatient spending for Medicare beneficiaries increased from 0.63% in 2005 to 0.81% in 2010. Hospital charges increased from $34,398 to $43,354 per claim ($p< 0.001$), total payments increased from $11,786 to $12,773 per claim ($p < 0.001$), average LOS decreased from 6.11 days to 5.96 days ($p = 0.002$). Independent predictors of increases in hospital charges included number of diagnoses and procedures, LOS and dying during the hospitalization. Independent predictors of increases in estimated costs were similar. Independent predictors of LOS increases were race, ESRD, disposition other than to home, number of diagnoses, and number of procedures (Table 4).

Demographics and outcomes for outpatients with CLD (Table 1):

A total of 271,552 CLD-related outpatient claims for 137,347 unique Medicare beneficiaries with CLD were included for the study period. The number of patients with at least one claim related to their CLD ranged from the minimum of 21,578 in 2008 to the maximum of 23,946 in 2005, representing approximately 430,000-480,000 Medicare beneficiaries with CLD nationwide. The average number of claims per patient did not change during the study period. The most prevalent primary diagnoses on outpatient claims were non-alcoholic cirrhosis of liver (11.5%), abnormal liver scan (10.4%), chronic hepatitis C without mention of hepatic coma (8.8%), other diagnosis of chronic liver disease (5.6%), liver disorders of iron metabolism (5.4%), nonspecific elevation of levels of transaminases (5.4%), and other nonspecific abnormal liver enzymes (5.2%). Similar to findings with the inpatient population, the proportion of patients who were less than 65 years old increased. This was primarily driven by increases in the proportion of patients who were Medicare eligible because of disability.

Outpatient spending for Medicare beneficiaries with CLD (Table 5 and Table 6)

The proportion of CLD-related outpatient spending in the total outpatient spending for Medicare beneficiaries decreased from 0.44% in 2005 to 0.37% in 2010. The average number of claims per year did not change during the study period. Average total payment, average payment by Medicare, average charge, and Medicare's responsibility increased over time ($p < 0.001$ for all). However, the average payment by patients and beneficiary-paid amount decreased over time ($p < 0.001$ for all). After multivariate analysis, total payments actually decreased over the study period. The average number of diagnoses per claim, procedures per claim, and the presence of ESRD were independently associated with total payments. Being in the youngest age group (less

than 65 years old) was the most important predictor of payments. Also, there were racial and geographic variations in payments – being Asian or Hispanic were strong predictors of total payments. A Midwest location was inversely related to payment whereas location in California was strongly related to higher payment. In terms of proportion of beneficiary-paid amount, independent predictors were similar to payments except the presence of ESRD was not associated.

DISCUSSION

This is the first study to report inpatient and outpatient clinical outcomes and Medicare resource utilization for patients with CLD. The majority of CLD primary diagnoses were hepatic encephalopathy and cirrhosis. Interestingly, the Medicare population with ESRD and younger than 65 are becoming a larger portion of this cohort, Although the observed increase in the number of diagnoses per claim and Charlson index may be due to the CLD population becoming more complex with more comorbidities and related conditions, prior reports suggest that such changes might also be explained by the documentation and coding practices [12].

Our data showed that both in-hospital mortality and length of stay decreased. The potential reasons for a decrease in inpatient mortality include improvements in quality, efficiency of care delivery and increasing use of hospice services [13] while the decrease in the length of stay may also be due to changes in payment arrangements and discharge practices. Oddly, the presence of ESRD appeared to be “protective” against in-hospital mortality perhaps because the patients are younger and receive closer care for their ESRD. We believe that understanding these variations

in post-discharge mortality may provide guidance to policy makers for appropriate resource allocation.[14]

After adjusting for inflation, hospitalizations charges and total payments to Medicare increased ($p<0.0001$). As expected, independent predictors of charges, payments, and LOS were similar. Of note, minorities experienced higher charges, payments, and LOS and could be another target for better allocation of resources. The fact that patients who were discharged to extended care facilities or who died were independently associated with higher resource utilization, is consistent with the notion that patients who are at highest risk for mortality consume the greatest portion of the health care resources. [15,16] It has been previously reported that Hispanic patients with CLD (especially NAFLD) are at higher risk for adverse outcome such as cirrhosis and HCC which this study also corroborates as Hispanic ethnicity is independently associated with resource utilization.[6,9].

In the outpatient Medicare population, cirrhosis, abnormal liver imaging, and chronic hepatitis C being the most common diagnoses. Once again, the proportion of patients younger than 65 years old and disability eligible increased. As charges, payments from Medicare and proportion of Medicare's responsibility increased, the beneficiary-paid amount and estimated payments decreased. Racial and geographic variations in payment were again observed. Our study also showed that younger age was the most important independent predictor of Medicare spending. This is probably due to the fact that younger patients with CLD who qualify for Medicare may be sicker. [17,18]

There were some limitations to our study. The exact dates were not available for the year 2005-2009, making it impossible to assess the timing of post-discharge outcomes. Second, we may have under-estimated post-discharge mortality. This may be due to the LDS denominator files for each calendar year are based on information known to CMS in March of the year following hospitalizations so that some patients without date of death may have been dead but treated as alive. However, 96% of death dates were validated making the impact of the "un-validated death date" on mortality very small. The restricted mortality data we had access to did not allow to account for variability in the length of post-discharge follow-up in a survival analysis. Because this was a retrospective cohort study, there were unmeasured confounders for which we could not adjust for, such as the availability of healthcare providers in patient's place of residence, history of major interventions, marital and socioeconomic status, history of substance abuse or psychiatric conditions, metabolic disorders, as well as the results of physical examination and physical activity which may be especially important for appreciating health status of the elderly population. We also couldn't determine whether patients sought care outside their Medicare plan which potentially may have changed outcomes.[19]

In conclusion, CLD is a common disease entity with important patient and financial outcomes for the Medicare population. Although in-hospital mortality and LOS are decreasing, mortality after discharge remains stable. Also, outpatient spending by Medicare is increasing. Our study of chronic hepatitis C in the Medicare beneficiaries showed similar results. [20] Independent demographic and clinical predictors which we identified for payment and clinical outcomes can be used to target resource allocation for prevention. This last point is especially important as the Affordable Care Act (ACA) has begun, ensuring insurance coverage is available to all and

patients with pre-existing conditions are not excluded nor do they suffer from lapse in coverage. [21] It will be imperative to track the impact of the ACA on the long-term outcomes of patients living with CLD especially when one reviews the patients most likely to have CLD are also the patients most likely to be uninsured. Hispanics are the second most prevalent group to be uninsured, especially the young Hispanic male who is working. [22] In this study, younger Hispanic males were more likely to have CLD than any other group. Therefore, efforts should be directed to ensure this group becomes knowledgable about the importance and availability of insurance as well as healthy living.

Author Roles:

-Zobair M. Younossi-study design, data and results interpretation and clinical interpretation, writing, reviewer

-Li Zheng-data development, statistical analysis and interpretation for inpatient data, writing, reviewer

-Maria Stepanova-data development, statistical analysis and interpretation for outpatient, writing, reviewer

-Chapy Venkatesan-study design, results interpretation and clinical interpretation, writing, reviewer

-Alita Mishra-study design, results interpretation and clinical interpretation, writing, reviewer

Competing Interests: None

Data Sharing: Our data source, Medicare, does not allow sharing of data.

REFERENCES

1 Gravitz L. Introduction: a smouldering public-health crisis. *Nature* 2011;474(7350):S2–4.

2 Chak E, Tala AH, Sherman KE, et al. Hepatitis C virus infection in the USA: an estimate of true prevalence. *Liver Int.* 2011;31:1090-1101.

3 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 Feb 21;156(4):271-8.

4 Institute of Medicine. Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C. Washington, DC: The National Academies Press; 2010.

5 Thomas DL, Seeff LB. Natural history of hepatitis C. *Clin Liver Dis.* 2005;9:383-98,vi.

6 Lazo M, Hernaez R, Bonekamp S, et al. Non-alcoholic fatty liver disease and mortality among US adults: prospective cohort study. *BMJ.* 2011 Nov 18;343:d6891.

7 Pradat P, Voirin N, Tillmann HL, et al. Progression to cirrhosis in hepatitis C patients: an age-dependent process. *Liver Int.* 2007;27(3):335–9.

8 Singer ME, Younossi ZM. Cost-effectiveness of screening for hepatitis C virus in asymptomatic, average risk adults: has the time come? *Am. J. Med.* 2001;111:614-621.

9 Koebnick C, Getahun D, Reynolds K, et al. Trends in nonalcoholic fatty liver disease-related hospitalizations in US children, adolescents, and young adults. *J Pediatr Gastroenterol Nutr.* 2009 May;48(5):597-603. doi: 10.1097/MPG.0b013e318192d224.

10 Bruno S, Zuin M, Crosignani A, et al. Predicting mortality risk in patients with compensated HCV-induced cirrhosis: a long-term prospective study. *Am J Gastroenterology.* 2009;104(5):1147–58.

11 Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with *ICD-9-CM* administrative databases. *J Clin Epidemiol.* 1992;45 (6) 613- 61

12 Lindenauer PK, Lagu T, Shieh MS, et al. Association of diagnostic coding with trends in hospitalizations and mortality of patients with pneumonia, 2003-2009. *JAMA*. 2012 Apr 4;307(13):1405-13.

13 Yong-Fang K, Goodwin J. Impact of Hospitalists on Length of Stay in the Medicare Population: Variation by Hospital and Patient Characteristics. *J Am Geriatr Soc.* 2010; 58(9): 1649–1657.

14 Newhouse JP, Garber AM. Geographic Variation in Medicare Services. *N Engl J Med* 2013. 368(16): 1465-1468.

15 Pyenson B, Fitch K, Iwasaki K. Consequences of Hepatitis C Virus (HCV): Costs of a Baby Boomer Epidemic of Liver Disease. New York, NY: Milliman, Inc; May 18, 2009. [Internet, cited 2013 Mar 12]. Available from: http://publications.milliman.com/research/health-rr/pdfs/consequences-hepatitis-c-virus-RR05-18-09.pdf

16 Wong JB, McQuillan GM, McHutchison JG, et al. Estimating future hepatitis C morbidity, mortality, and costs in the United States. *Am J Public Health* 2000;90(10):1562–9.

17 Coughlin TA, Waidmann TA, Phadera L.Among dual eligibles, identifying the highest-cost individuals could help in crafting more targeted and effective responses. *Health Aff* (Millwood). 2012 May;31(5):1083-91. doi: 10.1377/hlthaff.2011.0729. Epub 2012 Apr 18.

18 Bubolz T, Emerson C, Skinner J. State spending on dual eligibles under age 65 shows variations, evidence of cost shifting from Medicaid to Medicare. *Health Aff* (Millwood). 2012 May;31(5):939-47. doi: 10.1377/hlthaff.2011.0921.

19 Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005 Nov; 43(11):1073-1077.

20 Younossi ZM, Stepanova M, Mishra A, et al. The impact of chronic hepatitis C on resource utilization and in-patient mortality for Medicare beneficiaries between 2005 and 2010. *AP&T* 2013 Aug. doi:10.1111/apt.12485

21 Medicare Payment Advisory Group. Medicare and Health Care Spending. June 2012. Obtained from the world wide web at: http://www.medpac.gov/documents/Jun12DataBookEntireReport.pdf. Last accessed on 8 Oct 2013.

22 Centers for Medicare and Medicaid Services. Audience Segmentation for the Emerging Health Care Marketplace. March 22, 2013. Obtained from the world wide web at http://www.marketplace.cms.gov. Last accessed on 8 Oct 2013.

Table 1. Clinico-demographic characteristics of Medicare beneficiaries who sought inpatient and outpatient care in 2005-2010.

Characteristics	Inpatient	P-value *	Outpatient	P-value *
No. of patients	14,774		137,347	
No. of hospitalizations	20,943		271,552	
Percent of re-hospitalizations	29.46		NA	
Number of diagnoses, mean (SD)	8.24 (1.58)	<0.0001	2.26 (1.72)	<0.0001
Number of procedures, mean (SD)	1.68 (1.78)	0.1184	0.001 (0.07)	0.0465
Charlson score, mean (SD)	1.44 (1.75)	<0.0001	0.95 (1.23)	<0.0001
Age				
<65	38.84	<0.0001	32.78	<.0001
65-69	17.88	<0.0001	21.46	0.6715
70-74	14.99	0.0004	16.96	0.0003
75-79	11.56	<0.0001	13.31	<.0001
80-84	9.29	0.0454	9.18	<.0001
85 and over	7.45	0.2001	6.30	0.2088
Race				
White	80.00	0.0025	81.53	<.0001
Black	10.71	0.0911	10.44	<.0001
Hispanic	4.61	0.0718	2.71	0.2113
Other	4.67	0.1445	2.62	0.0092
Male gender	55.09	0.5655	44.93	0.7866
ESRD	6.40	<0.0001	2.54	0.4234
Discharge status				
Home	51.90	<0.0001	NA	NA
Continued care	36.70	<0.0001	NA	NA
Hospice	4.75	<0.0001	NA	NA
Died	6.65	<0.0001	NA	NA
Region				
Northeast	19.83	0.2126	20.66	0.5634
South	40.58	0.4086	35.01	0.0256
Midwest	22.28	0.0138	26.11	0.1438
West	8.31	0.3719	9.25	0.2413
California	9.00	<0.0001	8.97	0.0006

* p-value represents the difference in the parameter between the study years
NA - not applicable

Table 2. Resource utilization and mortality outcomes for Medicare beneficiaries with CLD who sought inpatient care in 2005-2010.

	2005	2006	2007	2009	2010	p
Length of stay						
Mean (SD)	6.11 (5.75)	6.21 (6.23)	6.06 (5.71)	5.83 (5.71)	5.96 (5.79)	0.0017
Median(IQR)	4 (3, 8)	4 (3, 7)	4 (3, 7)	4 (2, 7)	4 (3, 7)	
Hospital charge						
Mean (SD)	34,398 (55,946)	37,544 (67,000)	36,200 (52,282)	40,636 (63,727)	43,354 (70,128)	<0.0001
Median(IQR)	19,199 (10,804, 36,364)	20,059 (11,050, 39,295)	21,741 (12,032, 40,061)	22,735 (12,291, 43,633)	24,266 (13,768, 44,974)	
Estimated cost						
Mean (SD)	11,786 (15,413)	12,039 (1,5893)	12,029 (24,037)	12,447 (16,006)	12,773 (17,359)	<0.0001
Median(IQR)	8,411 (7,295, 10,771)	8,413 (7,283, 10,698)	8,490 (7,255, 10,849)	9,459 (6,134, 12,252)	9,665 (6,147, 12,698)	
In-hospital mortality rate, %	11.75	9.94	8.17	8.75	8.73	0.0001
Post-discharge mortality rate, %	34.68	31.26	34.89	34.84	35.79	0.0363

Table 3. Predictors of in-hospital mortality and overall post-discharge mortality in Medicare beneficiaries hospitalized for CLD in 2005-2010*.

Predictors	In-hospital Mortality		Post-discharge Mortality†	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age				
65-69	Ref		Ref	
<65	0.85 (0.72, 1.00)	0.0537	0.79 (0.70, 0.89)	0.0001
70-74	1.03 (0.85, 1.25)	0.7882	1.08 (0.94, 1.25)	0.2628
75-79	1.25 (1.03, 1.53)	0.0267	1.27 (1.10, 1.48)	0.0012
80-84	0.89 (0.70, 1.12)	0.3045	1.24 (1.06, 1.45)	0.0063
85 and over	1.00 (0.79, 1.27)	0.9967	1.52 (1.30, 1.79)	<0.0001
Gender				
Female	Ref		Ref	
Male	1.26 (1.12, 1.41)	0.0001	1.34 (1.24, 1.46)	<0.0001
Race				
White	Ref		Ref	
Black	1.15 (0.96, 1.38)	0.1204	0.83 (0.72, 0.95)	0.0073
Hispanic	0.77 (0.56, 1.06)	0.1101	0.92 (0.75, 1.13)	0.4287
Other	1.30 (1.00, 1.67)	0.0482	0.84 (0.68, 1.02)	0.0834
ESRD				
No	Ref		Ref	
Yes	0.69 (0.54, 0.89)	0.0034	0.96 (0.81, 1.13)	0.6072
Number of admissions				
1	Ref		Ref	
≥2	1.58 (1.39-1.79)	<0.0001	1.66 (1.51-1.83)	<0.0001
Discharge destination				
Home	N/A		Ref	
Continued care	N/A		2.43 (2.23, 2.65)	<0.0001
Hospice	N/A		49.22 (37.13, 65.25)	<0.0001
Region				
Northeast	Ref		Ref	
South	0.87 (0.75, 1.01)	0.0613	1.20 (1.08, 1.35)	0.0012
Midwest	0.70 (0.59, 0.83)	<0.0001	1.01 (0.89, 1.15)	0.8582
West	0.80 (0.63, 1.01)	0.0639	1.24 (1.05, 1.46)	0.0130
California	0.86 (0.69, 1.08)	0.1951	1.22 (1.04, 1.45)	0.0169
Calendar Year	0.91 (0.89, 0.94)	<0.0001	0.99 (0.97, 1.02)	0.4909
Number of diagnosis	1.22 (1.16, 1.28)	<0.0001	1.05 (1.02, 1.08)	0.0007
Number of procedures	1.32 (1.28, 1.37)	<0.0001	0.99 (0.96, 1.01)	0.3812
Charlson score	1.03 (0.99, 1.06)	0.1151	1.23 (1.20, 1.26)	<0.0001
LOS	1.01 (1.00, 1.02)	0.1244	1.01 (1.00, 1.02)	0.0039

* Data in 2008 were excluded from analysis due to missing information on patient's residence region.

Table 4. Predictors of LOS, hospital charge and total payment of hospitalizations of Medicare beneficiaries for CLD in 2005-2010*.

Predictors	LOS Increase		Hospital Charge Increase†		Estimated Cost Increase†	
	% (95% CI) †	P-value	% (95% CI) ‡	P-value	% (95% CI) ‡	P-value
Age						
65-69	Ref		Ref		Ref	
<65	0.07 (-2.47, 2.61)	0.9557	**-2.64 (-4.92, -0.36)**	**0.0233**	**5.09 (3.11, 7.06)**	**<0.0001**
70-74	-0.99 (-4.07, 2.09)	0.5293	**-4.71 (-7.48, -1.94)**	**0.0009**	**-6.08 (-8.48, -3.68)**	**<0.0001**
75-79	2.36 (-0.97, 5.69)	0.1649	**-3.05 (-6.05, -0.06)**	**0.0456**	**-8.15 (-10.74, -5.55)**	**<0.0001**
80-84	2.85 (-0.72, 6.42)	0.1181	**-3.22 (-6.44, -0.01)**	**0.0496**	**-11.91 (-14.70, -9.13)**	**<0.0001**
85 and over	1.14 (-2.73, 5.00)	0.5635	-2.45 (-5.94, 1.03)	0.1673	**-14.17 (-17.19, -11.16)**	**<0.0001**
Gender						
Female	Ref		Ref		Ref	
Male	**-4.05 (-5.85, -2.26)**	**<0.0001**	**1.69 (0.07, 3.31)**	**0.0407**	**4.65 (3.25, 6.06)**	**<0.0001**
Race						
White	Ref		Ref		Ref	
Black	**11.72 (8.80, 14.64)**	**<0.0001**	**4.86(2.23, 7.48)**	**0.0003**	**2.66 (0.38, 4.93)**	**0.0220**
Hispanic	**9.71 (5.47, 13.95)**	**<0.0001**	**11.04 (7.23, 14.85)**	**<0.0001**	**9.54 (6.23, 12.85)**	**<0.0001**
Other	1.29 (-2.98, 5.56)	0.5536	**3.98 (0.15, 7.81)**	**0.0417**	**8.17 (4.85, 11.49)**	**<0.0001**
ESRD						
No	Ref		Ref		Ref	
Yes	**3.84 (0.06, 7.62)**	**0.0467**	**-5.45 (-8.87, -2.04)**	**0.0017**	-1.07 (-4.03, 1.89)	0.4780
Discharge destination						
Home	Ref		Ref		Ref	
Continued care	**37.32 (35.36, 39.29)**	**<0.0001**	0.46 (-1.34, 2.26)	0.6148	**-11.70 (-13.27, -10.13)**	**<0.0001**
Hospice	**35.98 (31.70, 40.25)**	**<0.0001**	-0.08 (-3.96, 3.79)	0.9662	**-7.56 (-10.91, -4.22)**	**<0.0001**
Died	**25.86 (22.14, 29.58)**	**<0.0001**	**5.58 (2.23, 8.92)**	**0.0011**	1.54 (-1.36, 4.44)	0.2978
Region						
Northeast	Ref		Ref		Ref	
South	**-3.03 (-5.45, -0.60)**	**0.0143**	**-17.34 (-19.52, -15.16)**	**<0.0001**	**-17.88 (-19.77, -15.99)**	**<0.0001**
Midwest	**-11.51 (-14.23, -8.78)**	**<0.0001**	**-23.31 (-25.76, -20.86)**	**<0.0001**	**-10.75 (-12.87, -8.62)**	**<0.0001**
West	**-9.95 (-13.62, -6.28)**	**<0.0001**	**-13.54 (-16.83, -10.24)**	**<0.0001**	**-6.08 (-8.94, -3.22)**	**<0.0001**
California	**-6.23 (-9.81, -2.66)**	**0.0006**	**43.90 (40.68, 47.13)**	**<0.0001**	**8.62 (5.83, 11.42)**	**<0.0001**
Calendar Year	**-2.67 (-3.15, -2.18)**	**<0.0001**	**3.94 (3.50, 4.38)**	**<0.0001**	**0.70 (0.32, 1.08)**	**0.0003**
Number of diagnosis	**9.07 (8.49, 9.65)**	**<0.0001**	**2.97 (2.44, 3.50)**	**<0.0001**	-0.28 (-0.75, 0.19)	0.2389
Number of procedures	**18.08 (17.56, 18.59)**	**<0.0001**	**19.95 (19.44, 20.47)**	**<0.0001**	**13.96 (13.51, 14.40)**	**<0.0001**
Charlson score	**-0.85 (-1.37, -0.33)**	**<0.0015**	-0.36 (-0.84, 0.12)	0.1394	0.77 (0.35, 1.18)	0.0003
LOS	N/A	N/A	**8.55 (8.36, 8.74)**	**<0.0001**	**4.22 (4.08, 4.36)**	**<0.0001**

* Data in 2008 were excluded from multivariate analysis due to missing information on region.

† Hospital charge and cost were adjusted to the 2010 dollars using annual inflation rate of 3%.

‡ For categorical variable, this represents the predicted percentage of increase in outcome for one level of the predictor compared to the reference level, while holding all other variables constant; for continuous variable, this represents the predicted percentage of increase in outcome for each unit increase in that variable, while holding all other variables constant. A negative increase represents a decrease.

Table 5. Resource utilization for Medicare beneficiaries with CLD who sought outpatient care in 2005-2010 (median (IQR)).

	2005	2006	2007	2008	2009	2010	p
Average number of claims per year	1.98 ± 2.68	2.01 ± 2.72	1.98 ± 2.62	1.97 ± 2.50	1.96 ± 2.47	1.96 ± 2.40	0.0569
Average total payment, $	151.2 (72.3-529.1)	163.9 (77.6-567.0)	167.0 (80.2-562.0)	154.5 (78.2-552.2)	159.0 (81.4-568.3)	158.5 (83.0-565.2)	<.0001
Average payment by patient, $	45.5 (0.0-162.5)	41.2 (0.0-158.6)	40.5 (0.0-158.4)	38.6 (0.0-142.2)	37.6 (0.0-126.14)	36.6 (0.0-123.8)	<.0001
Average payment by Medicare, $	113.7 (53.8-336.5)	122.5 (58.0-373.1)	124.4 (58.9-371.3)	117.3 (56.9-369.4)	120.9 (57.9-409.4)	120.3 (56.6-408.9)	<.0001
Average charge, $	725.3 (241.1-2371.9)	787.6 (260.0-2624.4)	823.9 (277.4-2784.0)	803.3 (283.7-2716.2)	848.7 (290.6-2886.4)	885.8 (312.9-2952.5)	<.0001
Beneficiary-paid amounts, %	20.0 (0-41.7)	20.0 (0.0-37.2)	20.0 (0.0-37.2)	19.9 (0.0-35.4)	19.4 (0.0-29.1)	19.7 (0.0-29.7)	<.0001
Medicare's responsibility, %	78.6 (55.9-100)	79.1 (61.6-100)	79.3 (61.8-100)	79.9 (63.8-100)	80.0 (68.1-100)	80.0 (68.0-100)	<.0001

Table 6. Independent predictors of outpatient spending for Medicare beneficiaries with CLD.

Predictors	Estimated costs increase, % (95% CI)
Calendar year	-1.56 (-2.00 - -1.12)
Age <65	+68.76 (+49.80 - +90.12)
Age 65-69	+37.05 (+32.03 - +42.26)
Age 70-74	+32.88 (+27.87 - +38.08)
Age 75-79	+23.40 (+18.59 - +28.40)
Age 80-84	+16.68 (+11.82 - +21.75)
Male	+10.27 (+8.44 - +12.12)
Black	+1.56 (-1.21 - +4.42)
Hispanic	+15.35 (+9.55 - +21.45)
Asian	+32.05 (+24.30 - +40.27)
Disability	-4.75 (-15.05 - +6.80)
ESRD	+7.84 (+1.33 - +14.77)
Location: Midwest	-3.82 (-6.12 - -1.46)
Location: South w/o California	-2.25 (-4.46 - +0.02)
Location: West	+10.48 (+6.94 - +14.14)
Location: California	+15.43 (+11.65 - +19.34)
Average number of diagnoses per claim, per dx	+29.31 (+28.64 - +29.98)
Number of outpatient procedures, per procedure	+18.09 (+13.63 - +22.72)

† The increase is in comparison to the reference value. A negative increase represents a decrease.

Supplementary Table 1. Clinical characteristics of hospitalizations of Medicare beneficiaries for liver disease by discharge year

Characteristics	2005-2010	2005	2006	2007	2009	2010	P-value
No. of patients	14,774	2,852	2,959	3,071	2,938	2,954	
No. of hospitalizations	20,943	4,020	4,120	4,333	4,168	4,302	
Age							
<65	38.84	36.59	36.84	39.74	39.59	41.21	<0.0001
65-69	17.88	16.27	16.46	18.28	18.93	19.32	<0.0001
70-74	14.99	15.82	16.65	14.12	15.28	13.20	0.0004
75-79	11.56	14.00	13.30	11.40	9.79	9.46	<0.0001
80-84	9.29	9.70	9.49	9.69	8.95	8.62	0.0454
85 and over	7.45	7.61	7.26	6.76	7.46	8.18	0.2001
Race							
White	80.00	80.80	81.33	79.62	79.80	78.54	0.0025
Black	10.71	10.50	9.85	11.08	10.68	11.41	0.0911
Hispanic	4.61	4.30	4.47	4.52	4.53	5.20	0.0718
Other	4.67	4.40	4.34	4.78	4.99	4.83	0.1445
Male gender	55.09	54.30	55.75	54.81	55.33	55.25	0.5655
ESRD	6.40	3.86	5.87	6.85	8.21	7.07	<0.0001
Discharge status							
Home	51.90	52.69	54.49	52.87	50.31	49.26	<0.0001
Continued care	36.70	35.25	34.32	36.46	37.93	39.38	<0.0001
Hospice	4.75	3.73	4.05	4.87	5.61	5.39	<0.0001
Died	6.65	8.33	7.14	5.79	6.14	5.97	<0.0001
Region							
Northeast	19.83	20.10	19.59	18.95	19.05	21.46	0.2126
South	40.58	40.95	40.29	41.45	39.88	40.33	0.4086
Midwest	22.28	22.66	23.59	21.79	23.37	20.11	0.0138
West	8.31	8.46	7.99	9.07	8.13	7.90	0.3719
California	9.00	7.84	8.54	8.75	9.57	10.20	<0.0001

*Hospital charge and reimbursement were adjusted to the 2010 dollar using a coefficient of annual inflation of 3%.

Supplementary table 2. Demographics of Medicare beneficiaries with CLD who sought outpatient care in 2005-2010.

	2005	2006	2007	2008	2009	2010	p
Number of patients	23,946	23,331	22,840	21,578	22,540	23,112	
Number of claims	47,460	46,871	45,307	42,408	44,167	45,339	
Age:							
<65 years, %	30.95	31.02	32.41	33.56	34.29	34.71	<.0001
65-69 years, %	21.57	21.44	21.26	21.13	21.64	21.69	0.6715
70-74 years, %	17.84	17.25	16.85	16.87	16.52	16.39	0.0003
75-79 years, %	14.44	14.11	13.83	12.64	12.26	12.40	<.0001
80-84 years, %	9.19	9.86	9.37	9.30	8.78	8.58	<.0001
>=85 years, %	6.00	6.32	6.29	6.51	6.52	6.22	0.2088
Male, %	44.65	44.67	45.00	44.99	45.07	45.22	0.7866
Race/ethnicity:							
White, %	82.00	82.55	81.98	77.83	80.78	80.54	<.0001
Black, %	10.15	9.72	10.19	12.58	10.94	11.07	<.0001
Other race, %	2.90	2.69	2.58	2.99	2.52	2.37	0.0092
Asian, %	1.70	1.69	1.89	2.57	2.19	2.29	<.0001
Hispanic, %	2.57	2.68	2.63	2.71	2.75	2.94	0.2113
Native American, %	0.69	0.67	0.73	1.32	0.82	0.79	0.0361
Medicare eligibility:							
aged, %	68.37	68.35	66.80	66.12	64.95	64.62	<.0001
aged+ESRD, %	0.68	0.63	0.80	0.73	0.76	0.67	0.2818
disabled, %	29.11	29.21	30.52	31.31	32.42	32.96	<.0001
disabled+ESRD, %	1.04	1.06	1.17	1.08	1.11	1.08	0.8106
ESRD, %	0.80	0.74	0.71	0.77	0.75	0.67	0.6873
Location:							
Northeast, %	20.64	20.47	20.42	19.74	20.94	20.89	0.5634
Midwest, %	26.1	26.48	26.36	23.42	25.48	26.27	0.0256
South w/o California, %	35.28	35.53	34.96	34.82	34.95	34.34	0.1438
West, %	9.27	8.92	9.32	10.49	9.43	9.23	0.2413
California, %	8.71	8.6	8.93	11.54	9.2	9.27	0.0006

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-9
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-9*
Bias	9	Describe any efforts to address potential sources of bias	9-10
Study size	10	Explain how the study size was arrived at	6-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	9-10
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	10-11
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-13
		(*b*) Report category boundaries when continuous variables were categorized	10-12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-14
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Clinical Outcomes and Resource Utilization in Medicare Patients with Chronic Liver Disease: A Historical Cohort Study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004318.R1
Article Type:	Research
Date Submitted by the Author:	07-Apr-2014
Complete List of Authors:	Younossi, Zobair; Inova Fairfax Hospital, Medicine and Beatty Center for Integrated Research Zheng, Li; Inova Health Systems, Betty and Guy Beatty Center for Integrated Research Stepanova, Maria; Inova Health Systems, Betty and Guy Beatty Center for Integrated Research Venkatesan, Chapy; Inova Fairfax Hosptial, Medicine Mishra, Alita; Inova Fairfax Hosptial, Medicine
Primary Subject Heading:	Health services research
Secondary Subject Heading:	Gastroenterology and hepatology
Keywords:	Hepatobiliary disease < GASTROENTEROLOGY, Hepatology < INTERNAL MEDICINE, QUALITATIVE RESEARCH

Clinical Outcomes and Resource Utilization in Medicare Patients with Chronic Liver Disease: A Historical Cohort Study

Zobair M. Younossi[1,2,] Li Zheng[2], Maria Stepanova[2], Chapy Venkatesan[1], Alita Mishra[1]

1. Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, USA.

2. Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, USA

Corresponding author and reprint requests:
Zobair M. Younossi, M.D., M.P.H.
Betty and Guy Beatty Center for Integrated Research
Claude Moore Health Education and Research Building
3300 Gallows Road, Falls Church, VA 22042
PHONE: (703) 776-2540 FAX: (703) 776-4386, E-mail: zobair.younossi@inova.org

Transparency Declaration: The lead author affirms that this study is a complete assessment of the data and no important information has been omitted.

Word count: 3399 (excluding title, abstract, references and tables)
Abstract: 297
Tables and figures: 6

ABSTRACT

Objectives: The aim of this study is to assess recent trends in health resource utilization and patient outcomes of Medicare beneficiaries with chronic liver disease (CLD).

Setting: Liver-related mortality is the tenth leading cause of death in the United States, and hepatitis C (HCV) and obesity-related non-alcoholic fatty liver disease (NAFLD) were the major causes of CLD. As the U.S. population ages and becomes more obese, the impact of CLD is expected to become more prominent for the Medicare population.

Participants: This is a retrospective cohort study of the Medicare beneficiaries with a diagnosis of CLD based on inpatient (N=21,576; 14,977 unique patients) and outpatient (N=515,990; 244,196 patients) claims from 2005 to 2010.

Primary and secondary outcome measures: The study outcomes included hospital length of stay (LOS) and inpatient mortality as well as inpatient and outpatient inflation-adjusted payments.

Results: Between 2005 and 2010, there was an annual decrease in LOS of 3.17% for CLD related hospitalizations. Risk-adjusted in-hospital mortality decreased (odds ratio (OR), 0.90, 95% confidence interval, 0.87-0.94), while short-term post-discharge mortality remained stable (1.00, 0.98-1.03). Inpatient per-claim payment increased from $11,769 in 2005 to $12,347 in 2010 (p=0.0006). Similarly, average yearly payments for outpatient care increased from $366 to $404 (p<0.0001). This change in payment was observed together with a consistent decrease in the proportion of beneficiary-paid amount (25.4% to 20.0%, p<0.0001) as opposed to Medicare-paid amount (73.1% to 80.0%, p<0.0001). The major predictors of higher outpatient payments were younger age, Asian race or Hispanic ethnicity, living in California, and having more diagnoses and outpatient procedures per claim. The predictors of inpatient spending also

included younger age, location, and the number of inpatient procedures. **Conclusions:** Length of inpatient stay and inpatient mortality among Medicare beneficiaries with CLD decreases, while both inpatient and outpatient spending increases.

Strengths and limitations of this study:

Strengths include:

- First study assessing recent trend in health resource utilization by Medicare beneficiaries with chronic liver disease.
- Using a representative sample of the national Medicare population.
- Include both inpatient and outpatient claims.
- Identified demographic and clinical factors associated with resource utilization and short term mortality.

Limitations include:

- Exact service dates were not available, making it impossible to conduct survival analysis to account for variability in length of post-discharge follow-up.
- Post-discharge mortality may be underestimated due to some un-validated death dates.
- Unmeasured confounders may exist in a retrospective cohort study.
- Could not determine whether patients sought care outside Medicare.

INTRODUCTION

Chronic liver disease (CLD) is a major cause of mortality and morbidity worldwide. [1,2,3,4,5] In the United States, liver-related mortality is the tenth leading cause of death with hepatitis C (HCV) and obesity-related non-alcoholic fatty liver disease (NAFLD) being the major causes of CLD [1-4,6-9].

Medicare is a U.S. national government-sponsored health insurance program that guarantees access to healthcare for the U.S. residents of 65 years of age or older, younger individuals with disabilities, those with end-stage renal disease (ESRD) or Lou Gehrig's disease. In addition to Medicare's payment, enrollees are responsible for a number of out-of-pocket payments including deductibles and coinsurance as well as payment for uncovered services; however, a supplemental insurance may be used to cover a certain proportion of the beneficiary-paid amount. In 2010, Medicare made up 23% of all personal healthcare spending in the United States [10].

In patients with chronic liver disease, age is known to be associated with adverse outcomes [7-8]. As the U.S. population ages and becomes more obese, the impact of CLD is expected to become more prominent for the Medicare population [6,9]. The cohort of baby boomers (Americans born between 1946 and 1964) also has a large proportion of HCV infection and is currently approaching the age of eligibility for Medicare, adding towards the growing burden of CLD. In this context, recent reports by The Institute of Medicine emphasized the need for a national prevention and control strategy for patients with viral hepatitis-associated CLD [4].

To date, Medicare resource utilization related to CLD has not been fully assessed. The recent healthcare reform legislation will be impacting what Medicare spends and how hospitals are reimbursed. The aim of this study was to assess recent trends in inpatient and outpatient Medicare spending related to CLD.

METHODS

Data Source: This is a retrospective cohort study of the Medicare claims. We analyzed Medicare inpatient and outpatient files from 2005-2010 submitted by outpatient and inpatient providers for reimbursement of treatment and facility costs. For each year, we obtained a 5% random sample of Medicare beneficiaries that were included in the Denominator Files provided to us by the Centers for Medicare & Medicaid Services (CMS) in the format of Limited Data Set (LDS) Standard Analytic Files. Each year, for the sampled beneficiaries, all inpatient and outpatient claims for the study years were included.

The inpatient file contains inpatient hospital encounters incurred during the study period. Each record represents a single hospital claim which includes a unique patient identifier, basic demographics, admission type and discharge status, International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes, other conditions related to the Medicare bill that include various claim-related information such as being homeless, unemployed, military, student, or over 100 years old, as well as hospital charges, Medicare reimbursement amount, and payment from the patient and another insurance.

In outpatient files, each record represents a single outpatient claim. Of the parameters used for the study, Medicare billing data included a unique patient identifier which was used to link data for each beneficiary across all Medicare files, the last day on the billing statement covered services rendered to the beneficiary, a list of up to 10 diagnoses and 6 outpatient ICD-9 procedures, total facility charges, Medicare reimbursement amount and payments from patient and other insurance providers.

The denominator file includes Medicare beneficiary enrollment, demographics (age, gender, ethnicity, the region of residence), and short-term mortality information. No data elements that might permit identification of beneficiaries were left in the CLD files.

We obtained institutional review board approval at Inova Fairfax Hospital, and signed a data-use agreement with the CMS.

Study Population

The following ICD-9-CM codes were used to establish the diagnosis of chronic liver disease in both inpatient and outpatient claims: viral hepatitis (070.0, 070.1, 070.20-070.23, 070.30-070.33, 070.41-070.44, 070.49, 070.51-070.54, 070.59, 070.6, 070.70, 070.71, 070.9), liver disorders of iron and copper metabolism (275.0, 275.01-275.03, 275.09, 275.1), esophageal varices with or without bleeding (456.0, 456.1, 456.20, 456.21), chronic liver disease and cirrhosis (571.0-571.3, 571.40-571.42, 571.49, 571.5, 571.6, 571.8, 571.9), sequelae of chronic liver disease such as hepatic coma, portal hypertension, and hepatorenal syndrome (572.2-572.4, 572.8), other chronic disorders of liver and biliary tract (573.3, 573.5, 573.8, 576.1, 576.8), cholestatic jaundice

(782.4), hepatomegaly (789.1), ascites (789.5), abnormal liver scan/function study (794.8), and indicators of CLD coded as factors and external causes (E947.9, V02.60, V02.61, V02.62, V02.69, V42.7). For inpatient visits, a claim was included in the study only if the principal diagnosis for that claim was CLD-related. Outpatient analysis included claims related CLD identified from either principle or secondary diagnoses.

Patient baseline characteristics were derived from Medicare denominator file, which includes age categories at admission, gender, race/ethnicity, end stage renal disease (ESRD) status, residence (Northeast, South, Midwest, West, and California), discharge disposition type, continued care, hospice status, and inpatient death. Comorbidities scores were derived from up to 9 secondary diagnosis codes using Deyo-modification of the Charlson score developed for claims data analysis [11]. The total number of diagnoses and total number of procedures in each record were also included in the analysis (might exceed 10 diagnoses or 6 procedures that were given explicitly).

Inpatient Outcomes

Both resource utilization and short-term mortality outcomes were assessed. Resource utilization parameters included length of stay and total payments as well as the proportion of Medicare spending and of beneficiary-paid amount. Total payments for patient services in each claim were calculated as the sum of Medicare reimbursement amount, primary insurance payment, beneficiary-paid amounts (copay, deductibles and coinsurance). The annual percent changes of Consumer Price Indexes (CPI) for Medical care were used to adjust the annual payments, to the dollars of 2010.

Length of stay (LOS) is defined as the number of full days a patient stays in the hospital. Since admission and discharge dates were not provided in the data, LOS was calculated as the total number of days of care in each claim, which included the number of days of care that are chargeable and the number of days of care that are not chargeable to Medicare facility utilization. If a patient was admitted and discharged on the same day, LOS was counted as one day. According to Medicare policy, patients need to pay certain amount of coinsurance for LOS over 60 days, and no coinsurance for LOS 1-60 days. To remove the potential effect of coinsurance on LOS, cases with LOS over 60 days were dismissed from analysis.

Short-term mortality outcomes were evaluated for each calendar year. In the case of multiple hospitalizations within a calendar year, the most recent claim was designated as the index event. If a patient was hospitalized for CLD in multiple calendar years, he was counted as new patient for each year. In-hospital mortality was defined as an in-hospital record with discharge status of "Dead", regardless of cause or LOS. Short-term post-discharge mortality was defined as a death from any cause after hospital discharge, after excluding patients who died in hospital. We determined short-term post-discharge mortality based on the death date recorded in the Medicare denominator file. The period of follow-up for short-term post-discharge mortality was the end of March of the year following patient's index discharge.

Outpatient Outcomes

The resource utilization parameters included total payments, Medicare spending and the proportion of beneficiary-paid amount. Total per-claim payment was the sum of Medicare reimbursement amount, primary insurance payment, and the beneficiary-paid amount which

included all applicable co-payments, deductibles and coinsurance. If more than one outpatient claim was reported for a patient in a given year, then, for that patient in that year, the resource utilization parameters were added up, and the total yearly resource utilization, together with the average proportion of beneficiary-paid amount in percent of total payments, was calculated.

Statistical Analysis

We described the baseline characteristics of the study population by presenting frequencies for categorical variables and mean ± SD for continuous variables. Mean LOS, hospital charge and total payments for each claim were calculated. Unadjusted rates of all-cause in-hospital mortality and post-discharge mortality were estimated. In both analyses, all available clinical and demographic parameters were compared across the study years to identify parameters that changed significantly over time, using chi-square test for binary or categorical parameters (age, gender, race, mortality, etc) and non-parametric Kruskal-Wallis Test for continuous parameters (length of stay, hospital charge, Charlson score, number of diagnosis, number of procedures).

Multivariable regression analyses were run to assess the independent association of inpatient and outpatient resource utilization and patients' clinico-demographics characteristics that were used as potential predictors. LOS and total payments were found to be skewed to the right in a non-normal distribution and therefore were analyzed using generalized linear model (GLM) with a gamma error distribution and a log-link function. The adjusted relationship between predictors and resource utilization were estimated using beta coefficients from these models, which were exponentiated to yield a percentage change in the outcomes associated with each predictor. .

Multivariate logistic regression analysis was performed on in-hospital mortality and short-term post-discharge mortality. The association between a mortality predictor and an outcome was analyzed with the χ^2 test, which was used to compare the risk-adjusted rate of mortality among those with and those without the risk factor. Odds ratio was used to estimate the adjusted association between each predictor and mortality. Significance tests and confidence internals (CIs) were based on a two-sided 95% confidence level.

RESULTS

Demographics and outcomes for inpatients with CLD (Table 1 and 2, Supplementary Table 1)

The analysis included 21,576 hospitalizations with a principal diagnosis of CLD during 2005-2010 for a total of 14,977 patients. The annual number of claims ranged from minimum of 3,475 in 2008 to maximum of 3,698 in 2005. The annual percent of re-hospitalizations was about 23%. The most common primary diagnoses were hepatic encephalopathy (25.10%), non-alcoholic cirrhosis of liver (18.01%), alcoholic cirrhosis of liver (15.16%), and sclerosing cholangitis (6.17%).

During the study period, the observed in-hospital mortality decreased from 11.81% to 8.38% ($p < 0.001$), post-discharge mortality decreased from 36.37% to 33.82% ($p = 0.0099$), the average number of diagnoses per claim increased from 7.92 to 8.64 ($p < 0.001$), and Charlson score increased (1.31 to 1.36; $p< 0.001$). The proportion of patients discharged to home decreased, while the proportion discharged to hospice or continued care increased.

The number of admissions, diagnoses and procedures and male gender were independently associated with increased risk for in-hospital mortality. Independent predictors of short-term post-discharge mortality were discharge disposition, number of admissions, Charlson score, gender and LOS during hospitalization. Age appeared to be a stronger predictor of post-discharge mortality than in-hospital mortality. The adjusted in-hospital mortality rate decreased between 2005 and 2010, while the adjusted post-discharge mortality rate remained stable. Furthermore, there were regional and racial variations in post-discharge mortality using the standard reference categories (Table 3).

Inpatient spending for Medicare beneficiaries with CLD

The proportion of CLD-related inpatient spending in the total inpatient spending for Medicare beneficiaries increased from 7.70% in 2005 to 8.84% in 2008 and decreased to 7.66% in 2010. Total payments increased from $11,769 to $12,347 per claim ($p < 0.001$), average LOS decreased from 6.02 days to 5.74 days ($p < 0.001$). Independent predictors of increases in LOS included black or Hispanic race/ethnicity, number of diagnoses and procedures, died in hospital or disposition other than to home. . Independent predictors of increases in total payments were similar. The adjusted total payments also increased with LOS and across the study years (Table 4).

Demographics and outcomes for outpatients with CLD (Table 1, Supplementary Table 2):

A total of 515,990 CLD-related outpatient claims for 244,196 unique Medicare beneficiaries with CLD were included for the study period. Of those, 42.5% were the claims with CLD as a primary diagnosis.

The number of patients with at least one CLD claim ranged from the minimum of 38,485 in 2008 to the maximum of 44,546 in 2010, representing approximately 770,000-890,000 Medicare beneficiaries with CLD nationwide. The most prevalent CLD diagnosis on outpatient claims was non-alcoholic cirrhosis of liver (ICD-9 code 571.5) that was present on 14.0% outpatient claims in patients with CLD. The most prevalent primary diagnoses on claims where CLD was a secondary diagnosis were abdominal pain (789.00), type II diabetes mellitus without mention of complication (250.00), and end-stage renal disease (585.6) each present 3.3% of claims with CLD.

Similarly to the inpatient population, the proportion of patients who were less than 65 years old increased from 30.5% in 2005 to 34.3% in 2010 ($p<0.0001$). Ethnic profile of a Medicare beneficiary with CLD also shifted towards a lower proportion of Caucasians: from 81.94% to 80.58% ($p<0.0001$). The proportion of patients living in the South region also slightly increased, while the gender distribution of Medicare beneficiaries with CLD did not change with 45.8%-46.5% of patients being male (Table 1).

Outpatient spending for Medicare beneficiaries with CLD (Table 5 and Table 6)

The proportion of total outpatient spending for claims with CLD in the total outpatient spending for Medicare beneficiaries decreased from 1.38% in 2005 to 1.34% in 2010. The average number of claims per patient per year did not change during the study period remaining at the level of approximately 2.10-2.12 claims per year ($p=0.56$). Per-patient yearly total payment as well as yearly payment by Medicare and the proportion of Medicare's responsibility all increased over

time (all p<0.0001). At the same time, the average payment by a patient and the proportion of a beneficiary-paid amount decreased between 2005 and 2010 (both p<0.001) (Table 5).

In multivariate analysis, total payments have been found to be decreasing over the study period by -1.66% (95% CI = -1.98% to -1.34%) per calendar year. The average number of diagnoses per claim and the number of outpatient procedures per year were both independently associated with total payments (Table 6). However, after ESRD, being in the youngest age group (less than 65 years old) was the most important predictor of payments (+50.2% (+46.3-54.3%)), likely due to the disability-related Medicare eligibility requirements for such patients. Also, there were racial and geographic variations in payments; in particular, being Asian or Hispanic were independent predictors of higher total payments in comparison to the reference Caucasians, while being African-American was associated with lower payments (Table 6). Finally, the reference Northeast location was associated with the lowest payments in comparison to all other locations (Table 6).

DISCUSSION

This is the first study to report inpatient and outpatient clinical outcomes and Medicare resource utilization for patients with CLD. The majority of CLD primary diagnoses on inpatient claims were hepatic encephalopathy and cirrhosis. Interestingly, the Medicare population with ESRD and younger than 65 are becoming a larger portion of this cohort, Although the observed increase in the number of diagnoses per claim and Charlson index may be due to the CLD population becoming more complex with more comorbidities and related conditions, prior reports suggest that such changes might also be explained by the documentation and coding practices [12].

The risk-adjusted analysis showed that both in-hospital mortality and length of stay decreased. The potential reasons for a decrease in inpatient mortality include improvements in quality, efficiency of care delivery and increasing use of hospice services [13, 14] while the decrease in the length of stay may also be due to changes in payment arrangements and discharge practices. In fact, it is possible the recent focus on "hospital efficiency" has moved a number of CLD patients who were previously cared for in the inpatient setting, to the outpatient arena. This may have resulted in a decrease in inpatient LOS or even mortality but an increase in disease severity in the outpatient setting.

After adjusting for inflation, total payments to hospitals for inpatient services significantly increased. As expected, independent predictors of payments and LOS were similar. Of note, minorities experienced higher payments and LOS and could be another target for better allocation of resources. The fact that discharges to extended care facilities and inpatient deaths were associated with higher inpatient resource utilization is consistent with the notion that patients who are at highest risk for mortality consume the greatest portion of the health care resources [15,16]. It has been previously reported that Hispanic patients with CLD (especially NAFLD) are at higher risk for adverse outcome such as cirrhosis and HCC which this study also corroborates as Hispanic ethnicity is independently associated with resource utilization [6,9].

In the outpatient Medicare population, chronic hepatitis C cirrhosis, abnormal liver imaging, and NAFLD were the most common CLD diagnoses with approximately half of claims with the diagnosis of CLD had one listed as a primary diagnosis. Once again, the proportion of patients

younger than 65 years old and disability eligible increased. As payments from Medicare and proportion of Medicare's responsibility increased, the beneficiary-paid amount decreased. Racial and geographic variations in payment were again observed. Our study also showed that younger age was the most important independent predictor of Medicare spending. This is consistent with the fact that younger patients with CLD who qualify for Medicare can only be enrolled due to their disability or other chronic condition such as ESRD [17,18]. Furthermore, we expect that the rate of patients with HCV will continue to increase as a result of the CDC's current guidelines which recommend screening all patients ages 45-65 regardless of risk factors for hepatitis C [19]. The HCV screening will help to identify cases earlier and with the new more effective treatments, these treatments can possibly lead to a cure, which may, over time, lead to a substantial decrease in the number of patients with advanced liver disease [20,21,22].

There were some limitations to our study. The exact dates were not available for the year 2005-2009, making it impossible to assess the exact timing of post-discharge outcomes. Second, we may have under-estimated post-discharge mortality. This may be due to the LDS denominator files for each calendar year are based on information known to CMS in March of the year following hospitalizations so that some patients without date of death may have been dead but treated as alive. However, 96% of death dates were validated suggesting that the impact of the "un-validated death date" on mortality can be small. The restricted mortality data we had access to did not allow to account for variability in the length of post-discharge follow-up in a survival analysis. Because this was a retrospective cohort study, there were unmeasured confounders for which we could not adjust for, such as the availability of healthcare providers in patient's place of residence, history of other chronic diseases and major interventions, marital and

socioeconomic status, history of substance abuse or psychiatric conditions, metabolic disorders, as well as the results of physical examination and physical activity which may be especially important for appreciating health status of the elderly population. We also could not determine whether patients sought care outside their Medicare plan which potentially may have changed outcomes [23].

In conclusion, CLD is a common disease entity with important patient and financial outcomes for the Medicare population. Although in-hospital mortality and LOS are decreasing, mortality after discharge remains stable. Also, both inpatient and outpatient spending by Medicare is [24]. Independent demographic and clinical predictors which we identified for payment and clinical outcomes can be used to target resource allocation for prevention. This last point is especially important as the Affordable Care Act (ACA) has begun, ensuring insurance coverage is available to all and patients with pre-existing conditions are not excluded nor do they suffer from lapse in coverage [25]. It will be imperative to track the impact of the ACA on the long-term outcomes of patients living with CLD especially when one reviews the patients most likely to have CLD are also the patients most likely to be uninsured. Hispanics are the second most prevalent group to be uninsured, especially the young Hispanic male who is working [26]. In this study, younger Hispanic males were more likely to have CLD than any other group. Therefore, efforts should be directed to ensure this group becomes knowledgeable about the importance and availability of insurance as well as healthy living. Finally, the results are pertinent as the cohort of baby boomers are increasingly eligible for Medicare. Furthermore, the epidemic of obesity will continue to fuel the increasing prevalence of NAFLD and related cirrhosis. As the population of patients with HCV and NAFLD become increasingly eligible for Medicare, the future burden of

CLD on Medicare, the most important source of health care insurance coverage in the U.S. will become even more important.

Funding Source: Internal funds only.

Contributorship Statement: All authors made substantive intellectual contributions to this manuscript and their roles are defined at end of manuscript**.**

Conflict of Interest: There are no conflicts of interest for any of the authors.

Data Sharing Statement: Our data source, Medicare, does not allow sharing of data.

REFERENCES

1. Gravitz L. Introduction: a smouldering public-health crisis. Nature 2011;474(7350):S2–4.

2. Chak E, Tala AH, Sherman KE, et al. Hepatitis C virus infection in the USA: an estimate of true prevalence. Liver Int. 2011;31:1090-1101.

3. 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 Feb 21;156(4):271-8.

4. Institute of Medicine. Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C. Washington, DC: The National Academies Press;2010.

5. Thomas DL, Seeff LB. Natural history of hepatitis C. Clin Liver Dis. 2005;9:383-98, vi.

6. Lazo M, Hernaez R, Bonekamp S et al. Non-alcoholic fatty liver disease and mortality among US adults: prospective cohort study. BMJ. 2011 Nov 18;343:d6891.

7. Pradat P, Voirin N, Tillmann HL, et al. Progression to cirrhosis in hepatitis C patients: an age-dependent process. Liver Int. 2007;27(3):335–9.

8. Singer ME, Younossi ZM. Cost-effectiveness of screening for hepatitis C virus in asymptomatic, average risk adults: has the time come? Am. J. Med. 2001;111:614-621.

9. Koebnick C, Getahun D, Reynolds K, et al. Trends in nonalcoholic fatty liver disease-related hospitalizations in US children, adolescents, and young adults. J Pediatr Gastroenterol Nutr. 2009 May;48(5):597-603. doi: 10.1097/MPG.0b013e318192d224.

10. Health Care Spending and the Medicare Program. Published by Medicare Payment Advisory Commission, Washington DC. June 2012.

11. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with *ICD-9-CM* administrative databases. *J Clin Epidemiol* 1992;45 (6) 613- 61

12. Lindenauer PK, Lagu T, Shieh MS, et al. Association of diagnostic coding with trends in hospitalizations and mortality of patients with pneumonia, 2003-2009. JAMA. 2012 Apr 4;307(13):1405-13.

13. Yong-Fang K, Goodwin J. Impact of Hospitalists on Length of Stay in the Medicare Population: Variation by Hospital and Patient Characteristics. J Am Geriatr Soc. 2010; 58(9): 1649–1657.

14. Newhouse JP, Garber AM. Geographic Variation in Medicare Services. N Engl J Med 2013. 368(16): 14651468.

15. Pyenson B, Fitch K, Iwasaki K. Consequences of Hepatitis C Virus (HCV): Costs of a Baby Boomer Epidemic of Liver Disease. New York, NY: Milliman, Inc; May 18, 2009. [Internet, cited 2013 Mar 12]. Available from: http://publications.milliman.com/research/health-rr/pdfs/consequences-hepatitis-c-virus-RR05-18-09.pdf

16. Wong JB, McQuillan GM, McHutchison JG et al. Estimating future hepatitis C morbidity, mortality, and costs in the United States. Am J Public Health 2000;90(10):1562–9.

17. Coughlin TA, Waidmann TA, Phadera L.Among dual eligibles, identifying the highest-cost individuals could help in crafting more targeted and effective responses. Health Aff (Millwood). 2012 May;31(5):1083-91. doi: 10.1377/hlthaff.2011.0729. Epub 2012 Apr 18.

18. Bubolz T, Emerson C, Skinner J.State spending on dual eligibles under age 65 shows variations, evidence of cost shifting from Medicaid to Medicare. Health Aff (Millwood). 2012 May;31(5):939-47. doi: 10.1377/hlthaff.2011.0921.

19. Centers for Disease Control. Testing recommendations for chronic Hepatitic C. Obtained from the world wide web at: http://www.cd.gov/Hepatitis/guidelinsC.htm. Last accessed on 3 April 2014.

20. Deuffic-Burban S, Mathurin P, Rosa I, et al. Impact of emerging hepatitis C treatment on future needs for liver transplantation Dig Liver Dis. 2014 Feb;46(2):157-63. doi: 10.1016/j.dld.2013.08.137. Epub 2013 Oct 10.

21. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. EJ. N Engl J Med. 2013 May 16;368(20):1878-87. doi: 10.1056/NEJMoa1214853. Epub 2013 Apr 23.

22. Jacobson IM, Gordon SC, Kowdley KV, et al. ; POSITRON Study; FUSION Study. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013 May 16;368(20):1867-77. doi: 10.1056/NEJMoa1214854. Epub 2013 Apr 23.

23. Quan et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005 Nov; 43(11):1073-1077.

24. Younossi ZM, Stepanova M, Mishra A, et al. The impact of chronic hepatitis C on resource utilization and in-patient mortality for Medicare beneficiaries between 2005 and 2010. AP&T. 2013 Aug. doi:10.1111/apt.12485

25. Medicare Payment Advisory Group. Medicare and Health Care Spending. June 2012. Obtained from the world wide web at:

http://www.medpac.gov/documents/Jun12DataBookEntireReport.pdf. Last accessed on 8 Oct 2013.

26. Centers for Medicare and Medicaid Services. Audience Segmentation for the Emerging Health Care Marketplace. March 22, 2013. Obtained from the world wide web at http://www.marketplace.cms.gov. Last accessed on 8 Oct 2013.

Table 1. Clinico-demographic characteristics of Medicare beneficiaries who sought inpatient and outpatient care in 2005-2010.

	Inpatient			Outpatient		
Characteristics	2005	2010	p*	2005	2010	p*
No. of patients	2,582	2,458		39,885	44,546	
No. of claims	3,698	3,680		83,866	94,309	
Percent of re-hospitalizations, %	24.20	25.83	0.0653	NA	NA	
Number of diagnoses	7.92 +/- 1.73	8.64 +/- 1.31	<.0001	3.55 ± 2.11	4.32 ± 2.39	<0.0001
Number of procedures	1.59 +/- 1.75	1.67 +/- 1.79	0.2554	0.01 ± 0.16	0.01 ± 0.18	NS
Charlson score	1.31 +/- 1.58	1.36 +/- 1.67	<.0001	1.25 ± 1.46	1.43 ± 1.50	<0.0001
Age						
<65, %	38.18	42.47	<.0001	30.48	34.33	<.0001
65-69, %	15.87	19.62	<.0001	20.65	21.46	0.0055
70-74, %	16.01	12.64	<.0001	17.66	16.52	0.0006
75-79, %	13.28	8.89	<.0001	15.03	12.35	<.0001
80-84, %	9.19	8.40	0.0166	9.70	8.88	<.0001
85 and over, %	7.46	7.99	0.1107	6.49	6.47	NS
Race						
White, %	81.18	79.24	0.0162	81.85	80.58	<.0001
Black, %	10.25	10.84	0.2218	10.68	11.71	<.0001
Hispanic, %	4.57	5.33	0.1124	2.48	2.70	NS
Other, %	4.00	4.59	0.0428	2.71	2.09	<.0001
Male gender, %	53.95	54.35	0.0836	45.75	46.04	NS
End-stage renal disease, %	3.49	6.11	<.0001	3.48	3.52	NS
Discharge status						
Home, %	52.52	49.57	<.0001	NA	NA	NA
Continued care, %	36.78	39.78	<.0001	NA	NA	NA
Hospice, %	4.25	5.08	<.0001	NA	NA	NA
Died, %	6.46	5.57	<.0001	NA	NA	NA
Region						
Northeast, %	16.88	21.17	0.1323	19.96	19.25	0.0045
South, %	34.86	39.44	<.0001	26.26	25.45	0.0002
Midwest, %	18.85	23.25	0.0044	36.50	37.69	0.0007
West, %	7.23	8.31	0.0025	8.98	8.83	NS
California, %	7.77	9.49	<.0001	8.29	8.78	<.0001

NA - not applicable
* p-value indicates the significance of change over the study years; NS - not significant

Table 2. Resource utilization and mortality outcomes for Medicare beneficiaries with CLD who sought inpatient care in 2005-2010.

	2005	2006	2007	2008	2009	2010	p
Length of stay, days Mean (SD) Median(IQR)	6.02 +/- 5.61 4 (3, 7)	5.92 +/- 5.65 4 (3, 7)	5.86 +/- 5.40 4 (3, 7)	5.78 +/- 5.54 4 (3, 7)	5.61 +/- 5.45 4 (2, 7)	5.74 +/- 5.57 4 (3, 7)	0.0001
Payment by patient, $ Mean +/- SD Median(IQR)	650 +/- 782 1,096 (0-1,096)	649 +/- 695 1,100 (0-1,100)	650 +/- 762 1,098 (0-1,098)	661 +/- 796 1,093 (0-1,093)	661 +/- 802 1,104 (0-1,104)	626 +/- 758 1,100 (0-1,100)	<.0001
Payment by patient, % Mean +/- SD Median(IQR)	7.70 +/- 9.20 7.66 (0-13.36)	7.64 +/- 8.77 7.55 (0-13.38)	8.54 +/- 12.67 7.32 (0-13.59)	8.84 +/- 13.33 7.38 (0-13.71)	8.18 +/- 10.16 6.20 (0-13.80)	7.66 +/- 9.48 4.38 (0-12.75)	0.0507
Payment by Medicare , $ Mean +/- SD Median(IQR)	10,542 +/- 14,023 7,952 (6,581- 9,962)	10,435 +/- 13,085 7,909 (6,568- 9,938)	9,817 +/- 11,768 7,667 (6,268- 9,638)	10,159 +/- 14,975 7,743 (5,749- 10,129)	9,956 +/- 12,547 7,789 (4,996- 10,572)	10,765 +/- 13,779 8,482 (5,194- 11,326)	<.0001
Payment by Medicare, % Mean +/- SD Median(IQR)	89.52 +/- 17.71 91.29 (86.34- 100.00)	89.88 +/- 16.90 91.41 (86.26- 100.00)	87.65 +/- 21.65 91.01 (85.79- 100.00)	87.20 +/- 22.28 91.18 (85.10- 100.00)	88.10 +/- 20.23 92..29 (84.21- 100.00)	89.04 +/- 19.16 93.75 (85.12- 100.00)	0.0011
Total payment, $ of 2010 Mean +/- SD Median(IQR)	11,769 +/- 15,864 8,596 (7,485-10,748)	11,623 +/- 14,745 85,22 (7,448-10,516)	11,652 +/- 25,393 8,382 (7,187-10,486)	11,711 +/- 18,912 8,584 (6,623-11,013)	11,916 +/- 16,045 9,173 (5,985-11,779)	12,347 +/- 17,641 9,478 (5,932-12,192)	0.0006
In-hospital mortality rate, %	8.38	8.89	8.14	8.71	9.86	11.81	<.0001
Short-term post-discharge mortality, % *	36.37	34.21	34.12	35.00	30.91	33.82	0.0099

*Patients were followed up to March of the year following the hospitalization.

Table 3. Predictors of in-hospital mortality and overall post-discharge mortality in Medicare beneficiaries hospitalized for CLD in 2005-2010.*

Predictors	In-hospital Mortality OR (95% CI)	Post-discharge Mortality** OR (95% CI)
Age		
65-69	Ref	Ref
<65	0.83 (0.69, 0.99)	0.83 (0.72, 0.94)
70-74	1.06 (0.85, 1.31)	1.16 (0.99, 1.35)
75-79	1.28 (1.03, 1.60)	1.33 (1.13, 1.56)
80-84	0.91 (0.71, 1.18)	1.23 (1.04, 1.46)
85 and over	0.92 (0.70, 1.21)	1.51 (1.27, 1.80)
Gender		
Female	Ref	Ref
Male	1.27 (1.11, 1.44)	1.34 (1.22, 1.46)
Race		
White	Ref	Ref
Black	1.18 (0.96, 1.44)	0.81 (0.70, 0.95)
Hispanic	0.74 (0.52, 1.04)	0.91 (0.73, 1.13)
Other	1.11 (0.82, 1.51)	0.79 (0.63, 0.99)
ESRD		
No	Ref	Ref
Yes	0.73 (0.55, 0.98)	1.14 (0.93, 1.40)
Number of admissions		
1	Ref	Ref
≥2	1.50 (1.31, 1.73)	1.62 (1.46, 1.80)
Discharge destination		
Home	N/A	Ref
Continued care	N/A	2.51 (2.29, 2.76)
Hospice	N/A	44.98 (33.01,61.28)
Region		
Northeast	Ref	Ref
South	0.95 (0.81, 1.13)	1.27 (1.12, 1.43)
Midwest	0.79 (0.65, 0.96)	1.10 (0.96, 1.26)
West	0.84 (0.65, 1.10)	1.33 (1.11, 1.60)
California	0.95 (0.74, 1.22)	1.23 (1.02, 1.47)
Calendar Year	0.90 (0.87, 0.94)	1.00 (0.98, 1.03)
Number of diagnosis	1.24 (1.17, 1.32)	1.06 (1.03, 1.09)
Number of procedures	1.36 (1.31, 1.41)	0.98 (0.96, 1.01)
Charlson score	1.01 (0.98, 1.05)	1.24 (1.21, 1.28)
LOS	1.01 (1.00, 1.02)	1.02 (1.01, 1.03)

* Data in 2008 were excluded from analysis due to missing information on patient's residence region.
** Patients were followed up to March of the year following the hospitalization

Table 4. Predictors of LOS, hospital charge and total payment of hospitalizations of Medicare beneficiaries for CLD in 2005-2010*.

Predictors	LOS Increase % (95% CI)	Total Payment Increase % (95% CI)
Age		
65-69	Ref	Ref
<65	-0.77 (-3.45, 1.90)	-2.00 (-4.44, 0.43)
70-74	-3.44 (-6.72, -0.16)	-5.23 (-8.22, -2.24)
75-79	-0.16 (-3.73, 3.41)	-3.94 (-7.20, -0.69)
80-84	1.03 (-2.83, 4.89)	-3.21 (-6.73, 0.31)
85 and over	-0.77 (-3.45, 1.90)	-0.37(-4.16, 3.42)
Gender		
Female	Ref	Ref
Male	-4.63 (-6.53, -2.72)	1.11 (-0.63, 2.85)
Race		
White	Ref	Ref
Black	9.57 (6.42, 12.73)	4.82 (1.94, 7.70)
Hispanic	11.36 (6.92, 5.80)	12.67 (8.62, 16.71)
Other	1.90 (-2.76, 6.55)	1.58 (-2.66, 5.82)
ESRD		
No	Ref	Ref
Yes	2.23 (-2.19, 6.65)	-5.86 (-9.90, -1.82)
Discharge destination		
Home	Ref	Ref
Continued care	35.39 (33.31, 37.46)	0.53 (-1.39, 2.45)
Hospice	37.42 (32.67, 42.17)	-1.42 (-5.77, 2.94)
Died	25.95 (21.96, 29.94)	8.07 (4.44, 1.69)
Region		
Northeast	Ref	Ref
South	-4.36 (-6.94, -1.79)	-16.68 (-19.03, -14.33)
Midwest	-12.18 (-15.08, -9.28)	-23.40 (-26.05, -20.75)
West	-13.82 (-17.71, -9.94)	-12.59 (-16.12, -9.05)
California	-9.23 (-13.02, -5.44)	42.62 (39.16, 46.08)
Calendar Year	-3.17 (-3.68, -2.66)	3.08 (2.61, 3.54)
Number of diagnosis	9.34 (8.70, 9.98)	3.72 (3.13, 4.30)
Number of procedures	17.70 (17.15, 18.25)	19.51 (18.95, 20.07)
Charlson score	-1.36 (-1.96, -0.77)	-0.47 (-1.01, 0.08)
LOS	N/A	9.02 (8.80, 9.24)

* Data in 2008 were excluded from multivariate analysis due to missing information on region.

Table 5. Resource utilization for Medicare beneficiaries with CLD who sought outpatient care in 2005-2010 (median (IQR)).

	2005	2006	2007	2008	2009	2010	p
Yearly number of claims per patient (mean ± SD)	2.10 +/- 2.92	2.11 +/- 2.94	2.11 +/- 2.94	2.12 +/- 3.02	2.12 +/- 2.91	2.12 +/- 2.85	<0.0001
Total yearly payment, $	366.2 (111.9-888.1)	387.5 (113.8-901.6)	397.1 (114.7-903.0)	386.2 (113.3-924.3)	408.8 (117.8-940.8)	404.0 (119.5-929.7)	<.0001
Yearly payment by patient, $	104.8 (10.9-307.7)	108.1 (13.0-277.3)	111.2 (15.5-271.7)	104.0 (16.0-256.2)	98.9 (20.3-204.4)	95.5 (22.0-202.2)	<.0001
Yearly payment by patient, %	25.4 (3.7-44.2)	24.5 (7.0-38.4)	24.8 (9.5-38.3)	22.8 (8.9-36.2)	20.0 (10.5-27.5)	20.0 (11.6-27.4)	<.0001
Yearly payment by Medicare, $	237.1 (78.4-554.9)	260.7 (83.6-592.7)	266.9 (85.6-604.0)	263.9 (83.8-629.4)	299.5 (89.4-695.0)	300.00 (90.6-684.7)	<.0001
Yearly payment by Medicare, %	73.1 (55.0-92.7)	74.2 (61.1-90.2)	74.1 (61.4-88.2)	75.9 (63.8-88.4)	80.0 (70.4-87.3)	80.0 (70.7-86.6)	<.0001

Table 6. Independent predictors of outpatient spending for Medicare beneficiaries with CLD.

Predictors	Payment increase, % (95% CI) †
Calendar year	-1.66 (-1.98 - -1.34)
Age <65	+50.24 (+46.30 - +54.27)
Age 65-69	+33.89 (+30.27 - +37.62)
Age 70-74	+29.15 (+25.57 - +32.83)
Age 75-79	+22.80 (+19.29 - +26.41)
Age 80-84	+13.86 (+10.39 - +17.44)
Age 85+	Reference
Male	+3.75 (+2.48 - +5.04)
Caucasian	Reference
Black	-5.21 (-7.10 - -3.29)
Hispanic	+8.74 (+4.55 - +13.10)
Asian	+12.22 (+7.19 - +17.49)
ESRD	+120.67 (+113.32 - +128.27)
Location: Northeast	Reference
Location: Midwest	+8.56 (+6.60 - +10.56)
Location: South	+6.18 (+4.38 - +8.00)
Location: West	+20.99 (+18.04 - +24.01)
Location: California	+9.07 (+6.34 - +11.86)
The number of diagnoses per claim, per dx	+25.45 (+25.11 - +25.80)
The number of outpatient procedures, per procedure	+31.04 (+26.60 - +35.64)

† The increase is in comparison to the reference value. A negative increase represents a decrease.

Clinical Outcomes and Resource Utilization in Chronic Liver Disease – a Temporal Trends Study of Medicare Population

Zobair M. Younossi[1,2], Li Zheng[2], Maria Stepanova[2], Chapy Venkatesan[1], Alita Mishra[1]

1. Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, USA.

2. Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, USA

Corresponding author and reprint requests:
Zobair M. Younossi, M.D., M.P.H.
Betty and Guy Beatty Center for Integrated Research
Claude Moore Health Education and Research Building
3300 Gallows Road, Falls Church, VA 22042
PHONE: (703) 776-2540 FAX: (703) 776-4386, E-mail: zobair.younossi@inova.org

Conflict of Interest: There are no conflicts of interest for any of the authors.

Corresponding Author Statement: The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive license (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ editions and any other BMJPGL products and sublicenses such use and exploit all subsidiary rights, as set out in our license.

Transparency Declaration: The lead author affirms that this study is a complete assessment of the data and no important information has been omitted.

Funding Source: Internal funds only.

Word count: ~~3223~~ 3399 (excluding title, abstract, references and tables)
Abstract: ~~243~~297
Tables and figures: 6

Formatted: Line spacing: single

Formatted: Line spacing: single

Formatted: Highlight

Formatted: Font: Bold

ABSTRACT

Objectives: The aim of this study is to assess recent trends in health resource utilization and patient outcomes of Medicare beneficiaries with chronic liver disease (CLD). **Setting:** Liver-related mortality is the tenth leading cause of death in the United States, and hepatitis C (HCV) and obesity-related non-alcoholic fatty liver disease (NAFLD) were the major causes of CLD. As the U.S. population ages and becomes more obese, the impact of CLD is expected to become more prominent for the Medicare population. **Participants:** This is a retrospective cohort study of the Medicare beneficiaries with a diagnosis of CLD based on inpatient (N=21,576; 14,977 unique patients) and outpatient (N=515,990; 244,196 patients) claims from 2005 to 2010. **Primary and secondary outcomes measures:** The study outcomes included hospital length of stay (LOS) and inpatient mortality as well as inpatient and outpatient inflation-adjusted payments. **Results:** Between 2005 and 2010, there was an annual decrease in LOS of 3.17% for CLD related hospitalizations . Risk-adjusted in-hospital mortality decreased (odds ratio (OR), 0.90, 95% confidence interval , 0.87-0.94), while short-term post-discharge mortality remained stable (1.00, 0.98-1.03). Inpatient per-claim payment increased from $11,769 in 2005 to $12,347 in 2010 (p=0.0006). . Similarly, average yearly payments for outpatient care increased from $366 to $404 (p<0.0001). This change in payment was observed together with a consistent decrease in the proportion of beneficiary-paid amount (25.4% to 20.0%, p<0.0001) as opposed to Medicare-paid amount (73.1% to 80.0%, p<0.0001). The major predictors of higher outpatient payments were younger age, Asian race or Hispanic ethnicity, living in California, and having more diagnoses, and outpatient procedures per claim. The predictors of inpatient spending also included younger age, location, and the number of inpatient procedures. **Conclusions:** Length of

inpatient stay and inpatient mortality among Medicare beneficiaries with CLD decreases, ~~d~~ while both inpatient and outpatient spending increases.

Strengths and limitations of this study:

Strengths include:

- First study assessing recent trend in health resource utilization by Medicare beneficiaries with chronic liver disease.
- Using a representative sample of the national Medicare population.
- Include both inpatient and outpatient claims.
- Identified demographic and clinical factors associated with resource utilization and short term mortality.

Limitations include:

- Exact service dates were not available, making it impossible to conduct survival analysis to account for variability in length of post-discharge follow-up.
- Post-discharge mortality may be underestimated due to some un-validated death dates.
- Unmeasured confounders may exist in a retrospective cohort study.
- Could not determine whether patients sought care outside Medicare.

INTRODUCTION

Chronic liver disease (CLD) is a major cause of mortality and morbidity worldwide. [1,2,3,4,5] In the United States, liver-related mortality is the tenth leading cause of death with hepatitis C (HCV) and obesity-related non-alcoholic fatty liver disease (NAFLD) being the major causes of CLD [1-4,6-9].

~~In patients with chronic liver disease, age is known to be associated with adverse outcomes [7,8,10]. As the U.S. population ages and becomes more obese, the impact of CLD is expected to become more prominent [6,9]. Thus, in the United States, this trend is becoming especially important for the Medicare population. In this context, recent reports by The Institute of Medicine emphasized the need for a national prevention and control strategy for patients with chronic hepatitis [4].~~

Medicare is a U.S. national government-sponsored health insurance program that guarantees access to healthcare for the U.S. residents of 65 years of age or older, younger individuals with disabilities, those with end-stage renal disease (ESRD) or Lou Gehrig's disease. ~~In Medicare, inpatient hospital care is covered under Part A and outpatient medical services are covered under Part B.~~ In addition to Medicare's payment, enrollees are responsible for a number of out-of-pocket payments including deductibles and coinsurance as well as payment for uncovered services ~~such as long-term, dental, hearing, and vision care~~; however, a supplemental insurance may be used to cover a certain proportion of the beneficiary-paid amount. In 2010, Medicare made up 23% of all personal healthcare spending in the United States [10].

In patients with chronic liver disease, age is known to be associated with adverse outcomes [7-8]. As the U.S. population ages and becomes more obese, the impact of CLD is expected to become more prominent for the Medicare population [6,9]. The cohort of baby boomers (Americans born between 1946 and 1964) also has a large proportion of HCV infection and is currently approaching the age of eligibility for Medicare, adding towards the growing burden of CLD. In this context, recent reports by The Institute of Medicine emphasized the need for a national prevention and control strategy for patients with viral hepatitis-associated CLD [4].

To date, Medicare resource utilization related to CLD has not been fully assessed. The recent healthcare reform legislation will be impacting what Medicare spends and how hospitals are reimbursed. The aim of this study was to assess ~~the~~ recent trends in inpatient and outpatient Medicare spending related to CLD.

METHODS

Data Source: This is a retrospective cohort study of the Medicare claims. We analyzed Medicare inpatient and outpatient files from 2005-2010 submitted by outpatient and inpatient providers for reimbursement of treatment and facility costs. For each year, we obtained a 5% random sample of Medicare beneficiaries that were included in the Denominator Files provided to us by~~from~~ the Centers for Medicare & Medicaid Services (CMS) in the format of Limited Data Set (LDS) Standard Analytic Files. ~~For~~ Each year, for the sampled beneficiaries, all inpatient and outpatient claims for ~~all~~ the study years were included. ~~This study was provided exempt status by our Internal Review Board.~~

The inpatient file contains inpatient hospital encounters incurred during the study period. Each record represents a single hospital claim which includes a unique patient identifier, basic demographics, admission type and discharge status, International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes, other conditions related to the Medicare bill that include various claim-related information such as being homeless, unemployed, military, student, or over 100 years old, as well as hospital charges, Medicare reimbursement amount, and payment from the patient and another insurance.

In outpatient files, each record represents a ~~unique~~ single outpatient claim. Of the parameters used for the study, Medicare billing data included a unique patient identifier which was used to link data for each beneficiary across all Medicare files, ~~(~~the last day on the billing statement covered services rendered to the beneficiary, a list of up to 10 diagnoses and 6 outpatient ICD-9 procedures, total facility charges, Medicare reimbursement amount and payments from patient and other insurance providers~~)~~.

~~Finally, t~~The denominator file includes Medicare beneficiary enrollment, demographics (age, gender, ethnicity, the region of residence), and short-term mortality information. No data elements that might permit identification of beneficiaries were left in the CLD files.

~~-~~We obtained institutional review board approval at Inova Fairfax Hospital, and signed a data-use agreement with the CMS.

Study Population

The following ICD-9-CM codes were used to establish the diagnosis of chronic liver disease in both inpatient and outpatient claims: viral hepatitis (070.0, 070.1, 070.20-070.23, 070.30-070.33, 070.41-070.44, 070.49, 070.51-070.54, 070.59, 070.6, 070.70, 070.71, 070.9), ~~primary liver cancer (155.0),~~ liver disorders of iron and copper metabolism (275.0, 275.01-275.03, 275.09, 275.1), esophageal varices with or without bleeding (456.0, 456.1, 456.20, 456.21), ~~peritonitis (567.2),~~ chronic liver disease and cirrhosis (571.0-571.3, 571.40-571.42, 571.49, 571.5, 571.6, 571.8, 571.9), sequelae of chronic liver disease such as hepatic coma, portal hypertension, and hepatorenal syndrome (572.2-572.4, 572.8), other chronic disorders of liver and biliary tract (573.3, 573.5, 573.8, 576.1, 576.8), ~~pruritis (698.9),~~ cholestatic jaundice (782.4), hepatomegaly (789.1), ascites (789.5), ~~nonspecific abnormal serum enzyme levels (790.4-790.5),~~ abnormal liver scan/function study (794.8), and indicators of CLD coded as factors and external causes (E947.9, V02.60, V02.61, V02.62, V02.69, V42.7). For inpatient visits, a~~A~~ claim was included in the study only if the principal diagnosis for that claim was CLD-related. Outpatient analysis included claims related CLD identified from either principle or secondary diagnoses.

~~A patient might have had more than one claim per year. In such case, claims with the principal diagnosis other than CLD were not included even if that patient had established diagnosis of CLD according to other claims. As a result, only CLD related spending was evaluated.~~

Patient baseline characteristics were derived from Medicare denominator file, which includes age categories at admission, gender, race/ethnicity, end stage renal disease (ESRD) status, residence (Northeast, South, Midwest, West, and California), discharge disposition type, continued care, hospice status, and inpatient death. Comorbidities scores were derived from up to 9 secondary diagnosis codes using Deyo-modification of the Charlson score developed for claims data analysis [11]. The total number of diagnoses and total number of procedures in each record were

also included in the analysis (might exceed 10 diagnoses or 6 procedures that were given explicitly). ~~Claims with missing data on any of the study variables were excluded from analysis.~~

Inpatient Outcomes

Both resource utilization and short-term mortality outcomes were assessed. Resource utilization parameters included length of stay ~~(LOS), hospital charges~~ and total payments as well as the proportion of~~,~~ Medicare spending and ~~the proportion~~ of beneficiary-paid amount. Total payments for patient services in each claim were calculated as the sum of Medicare reimbursement amount, primary insurance payment, beneficiary-paid amounts (copay, deductibles and coinsurance). The annual percent changes of Consumer Price Indexes (CPI) for Medical care were used to adjust the annual payments, to the dollars of 2010.

Length of stay (LOS)~~OS~~ is defined as the number of full days a patient stays in the hospital. Since admission and discharge dates were not provided in the data, LOS was calculated as the total number of days of care in each claim, which included the number of days of care that are chargeable and the number of days of care that are not chargeable to Medicare facility utilization. If a patient was admitted and discharged on the same day, LOS was counted as one day. According to Medicare policy, patients need to pay certain amount of coinsurance for LOS over 60 days, and no coinsurance for LOS 1-60 days. To remove the potential effect of coinsurance on LOS, cases with LOS over 60 days were dismissed from analysis. ~~Total payments for patient services in each claim wereas calculated as the sum of Medicare reimbursement amount, primary insurance payment, beneficiary paid amounts (copay, deductibles and coinsurance). Since the~~

~~rates that Medicare pays for covered services are negotiated at the beginning of each year by the government agency, the annual percent changes of Consumer Price Indexes (CPI) for Medical care historic average of 3% wereas usedselected as an annual coefficient of inflation to for adjustment of the annual payments. hospital charges and total payments to the dollars of 2010 [ ]. The unit of analysis was the encounter for LOS, hospital charge and total payments.~~

~~Mortality~~ Short-term mortality outcomes were evaluated for each calendar year. In the case of multiple hospitalizations within a calendar year, the most recent claim was designated as the index event. If a patient was hospitalized for CLD in multiple calendar years, he was counted as new patient for each year. In-hospital mortality was defined as an in-hospital record with discharge status of "Dead", regardless of cause or LOS. Short-term p~~P~~ost-discharge mortality was defined as a death from any cause after hospital discharge, after excluding patients who died in hospital. ~~The period of follow-up for post-discharge mortality was the end of March of the year following patient's index discharge.~~ We determined short-term post-discharge mortality based on the death date recorded in the Medicare denominator file. The period of follow-up for short-term post-discharge mortality was the end of March of the year following patient's index discharge.

Outpatient Outcomes

~~Major~~ The resource utilization parameters includ~~ing total charges,~~ed total payments, Medicare spending and the proportion of beneficiary-paid amount~~ were calculated~~. Total per-claim payment was the sum of Medicare reimbursement amount, primary insurance payment, and the

beneficiary-paid amount which included all applicable co-payments, deductibles and coinsurance. If more than one ~~inpatient or~~ outpatient claim was reported for a patient in a given year, then, for that patient in that year, the resource utilization parameters were added up, and the total yearly resource utilization, together with the average proportion of beneficiary-paid amount in percent of total payments, ~~were~~was calculated.

Statistical Analysis

We described the baseline characteristics of the study population by presenting frequencies for categorical variables and mean ± SD for continuous variables. Mean LOS, hospital charge and total payments for each claim were calculated. Unadjusted rates of all-cause in-hospital mortality and post-discharge mortality were estimated. In both analyses, all available clinical and demographic parameters were compared across the study years to identify parameters that changed significantly over time, using chi-square test for binary or categorical parameters (age, gender, race, mortality, etc) and non-parametric Kruskal-Wallis Test for continuous parameters (length of stay, hospital charge, Charlson score, number of diagnosis, number of procedures).

Multivariable regression analyses were run~~used~~ to assess the independent association~~s~~ of inpatient and outpatient resource utilization and patient~~s'~~ clinico-demographics characteristics that were used as potential predictors ~~with resource utilization~~. LOS~~, provider or hospital charge,~~ and total payments were found to be skewed to the right in a non-normal distribution and therefore were analyzed using generalized linear model (GLM) with a gamma error distribution and a log-link function. ~~Association between a risk factor and the outcome was analyzed with the independent sample *t* test, which was used to compare the means of outcome for those with and~~

~~those without the risk factor.~~ The adjusted relationship between ~~risk factors~~predictors and ~~each outcome~~resource utilization were estimated using beta coefficients from these models, which were exponentiated to yield a percentage change in the outcomes associated with each ~~risk factor~~predictor. ~~Initially, all available demographic parameters, location and resource utilization were tested in the multiple regression model as potential predictors for the outcomes, but then only predictors with p-values of 0.05 or less were left~~.

Multivariate logistic regression analysis was performed on in-hospital mortality and short-term post-discharge mortality~~ to determine the independent effect of factors known to influence prognosis~~. The association between a ~~risk factor~~mortality predictor and ~~death~~ an outcome was analyzed with the χ^2 test, which was used to compare the risk-adjusted rate of mortality among those with and those without the risk factor. Odds ratio was used to estimate the adjusted association between each predictor and mortality. Significance tests and confidence internals (CIs) were based on a two-sided 95% confidence level. ~~Differences were considered significant at the $P<.05$ level~~

RESULTS

Demographics and outcomes for inpatients with CLD (Table 1 and 2, Supplementary Table 1)

The analysis included ~~20,943~~21,576 hospitalizations with a principal diagnosis of CLD during 2005-2010 for a total of ~~14,774~~14,977 patients. The annual number of claims ranged from minimum of ~~4,020~~3,475 in 200~~85~~ to maximum of ~~4,333~~3,698 in 2005~~7~~. The annual percent of re-hospitalizations was about 2~~9~~%. The most common primary diagnoses were hepatic

encephalopathy (~~21.6%~~25.10%), non-alcoholic cirrhosis of liver (~~15.7%~~18.01%), alcoholic cirrhosis of liver (~~13.0%~~15.16%), and sclerosing cholangitis (6.17%)~~primary liver cancer (6.4%)~~.

During the study period, the observed in-hospital mortality decreased from 11.81% ~~11.75%~~ to 8.38% ~~to~~ ~~8.73%~~ ($p < 0.001$), post-discharge mortality decreased ~~increased~~ from ~~34.7~~36.37% to ~~35.8%~~33.82% ($p = 0.0099$~~0.036~~), the average number of diagnoses per claim increased from ~~7.90~~7.92 to ~~8.60~~8.64 ($p < 0.001$), and Charlson score increased (~~1.35~~1.31 to ~~1.43~~1.36; $p< 0.001$). The proportion of patients discharged to home decreased, while the proportion discharged to hospice or continued care increased.

The number of admissions, diagnoses and procedures and male gender were independently associated with increased risk for in-hospital mortality. Independent predictors of short-term post-discharge mortality were discharge disposition, number of admissions, Charlson score, gender and LOS during hospitalization. Age appeared to be a stronger predictor of post-discharge mortality than in-hospital mortality. The adjusted in-hospital mortality rate decreased between 2005 and 2010, while the adjusted post-discharge mortality rate remained stable. Furthermore, there were regional and racial variations in post-discharge mortality using the standard reference categories (Table 3).

Inpatient spending for Medicare beneficiaries with CLD

The proportion of CLD-related inpatient spending in the total inpatient spending for Medicare beneficiaries increased from 7.70% ~~0.63%~~ in 2005 to 8.84% in 2008 and decreased to 7.66% ~~0.81%~~ in 2010. ~~Hospital charges increased from $34,398 to $43,354 per claim (p< 0.001), T~~total

payments increased from $~~11,786~~11,769 to $~~12,773~~12,347 per claim ($p < 0.001$), average LOS decreased from ~~6.11~~6.02 days to ~~5.96~~5.74 days ($p < 0.001$~~$p = 0.002$~~). Independent predictors of increases in LOS ~~hospital charges~~ included black or Hispanic race/ethnicity, number of diagnoses and procedures, died in hospital or disposition other than to home. ~~LOS and dying during the hospitalization~~. Independent predictors of increases in ~~estimated costs~~total payments were similar. The adjusted total payments also increased with LOS and across the study years~~. Independent predictors of LOS increases were race, ESRD, disposition other than to home, number of diagnoses, and number of procedures~~ (Table 4).

Demographics and outcomes for outpatients with CLD (Table 1, Supplementary Table 2):

A total of 515,990 CLD-related outpatient claims for 244,196 unique Medicare beneficiaries with CLD were included for the study period. Of those, 42.5% were the claims with CLD as a primary diagnosis.

The number of patients with at least one CLD claim ranged from the minimum of 38,485 in 2008 to the maximum of 44,546 in 2010, representing approximately 770,000-890,000 Medicare beneficiaries with CLD nationwide. The most prevalent CLD diagnosis on outpatient claims was non-alcoholic cirrhosis of liver (ICD-9 code 571.5) that was present on 14.0% outpatient claims in patients with CLD. The most prevalent primary diagnoses on claims where CLD was a secondary diagnosis were abdominal pain (789.00), type II diabetes mellitus without mention of complication (250.00), and end-stage renal disease (585.6) each present 3.3% of claims with CLD.

Similarly to the inpatient population, the proportion of patients who were less than 65 years old increased from 30.5% in 2005 to 34.3% in 2010 (p<0.0001). Ethnic profile of a Medicare beneficiary with CLD also shifted towards a lower proportion of Caucasians: from 81.94% to 80.58% (p<0.0001). The proportion of patients living in the South region also slightly increased, while the gender distribution of Medicare beneficiaries with CLD did not change with 45.8%-46.5% of patients being male (Table 1).

~~A total of 271,552 CLD related outpatient claims for 137,347 unique Medicare beneficiaries with CLD were included for the study period. The number of patients with at least one claim related to their CLD ranged from the minimum of 21,578 in 2008 to the maximum of 23,946 in 2005, representing approximately 430,000-480,000 Medicare beneficiaries with CLD nationwide. The average number of claims per patient did not change during the study period. The most prevalent primary diagnoses on outpatient claims were non-alcoholic cirrhosis of liver (11.5%), abnormal liver scan (10.4%), chronic hepatitis C without mention of hepatic coma (8.8%), other diagnosis of chronic liver disease (5.6%), liver disorders of iron metabolism (5.4%), nonspecific elevation of levels of transaminases (5.4%), and other nonspecific abnormal liver enzymes (5.2%). Similar to findings with the inpatient population, the proportion of patients who were less than 65 years old increased. This was primarily driven by increases in the proportion of patients who were Medicare eligible because of disability.~~

Outpatient spending for Medicare beneficiaries with CLD (Table 5 and Table 6)

The proportion of total outpatient spending for claims with CLD in the total outpatient spending for Medicare beneficiaries decreased from 1.38% in 2005 to 1.34% in 2010. The average number

of claims per patient per year did not change during the study period remaining at the level of approximately 2.10-2.12 claims per year (p=0.56). Per-patient yearly total payment as well as yearly payment by Medicare and the proportion of Medicare's responsibility all increased over time (all p<0.0001). At the same time, the average payment by a patient and the proportion of a beneficiary-paid amount decreased between 2005 and 2010 (both p<0.001) (Table 5).

In multivariate analysis, total payments have been found to be decreasing over the study period by -1.66% (95% CI = -1.98% to -1.34%) per calendar year. The average number of diagnoses per claim and the number of outpatient procedures per year were both independently associated with total payments (Table 6). However, after ESRD, being in the youngest age group (less than 65 years old) was the most important predictor of payments (+50.2% (+46.3-54.3%)), likely due to the disability-related Medicare eligibility requirements for such patients. Also, there were racial and geographic variations in payments; in particular, being Asian or Hispanic were independent predictors of higher total payments in comparison to the reference Caucasians, while being African-American was associated with lower payments (Table 6). Finally, the reference Northeast location was associated with the lowest payments in comparison to all other locations (Table 6).

~~The proportion of CLD-related outpatient spending in the total outpatient spending for Medicare beneficiaries decreased from 0.44% in 2005 to 0.37% in 2010. The average number of claims per year did not change during the study period. Average total payment, average payment by Medicare, average charge, and Medicare's responsibility increased over time (p < 0.001 for all). However, the average payment by patients and beneficiary-paid amount decreased over time (p < 0.001 for all). After multivariate analysis, total payments actually decreased over the study~~

~~period. The average number of diagnoses per claim, procedures per claim, and the presence of ESRD were independently associated with total payments. Being in the youngest age group (less than 65 years old) was the most important predictor of payments. Also, there were racial and geographic variations in payments – being Asian or Hispanic were strong predictors of total payments. A Midwest location was inversely related to payment whereas location in California was strongly related to higher payment. In terms of proportion of beneficiary paid amount, independent predictors were similar to payments except the presence of ESRD was not associated.~~

DISCUSSION

This is the first study to report inpatient and outpatient clinical outcomes and Medicare resource utilization for patients with CLD. The majority of CLD primary diagnoses on inpatient claims were hepatic encephalopathy and cirrhosis. Interestingly, the Medicare population with ESRD and younger than 65 are becoming a larger portion of this cohort, Although the observed increase in the number of diagnoses per claim and Charlson index may be due to the CLD population becoming more complex with more comorbidities and related conditions, prior reports suggest that such changes might also be explained by the documentation and coding practices [12].

~~Our data~~The risk-adjusted analysis showed that both in-hospital mortality and length of stay decreased. The potential reasons for a decrease in inpatient mortality include improvements in quality, efficiency of care delivery and increasing use of hospice services [13, 14] while the decrease in the length of stay may also be due to changes in payment arrangements and discharge

practices. In fact, it is possible the recent focus on "hospital efficiency" has moved a number of CLD patients who were previously cared for in the inpatient setting, to the outpatient arena. This may have resulted in a decrease in inpatient LOS or even mortality but an increase in disease severity in the outpatient setting.

~~Oddly, the presence of ESRD appeared to be "protective" against in hospital mortality perhaps because the patients are younger and receive closer care for their ESRD. We believe that understanding these variations in post discharge mortality may provide guidance to policy makers for appropriate resource allocation [14].~~

After adjusting for inflation, ~~hospitalizations charges and~~ total payments to hospitals~~Medicare~~ for inpatient services significantly increased ~~(p<0.0001)~~. As expected, independent predictors of ~~charges,~~ payments~~,~~ and LOS were similar. Of note, minorities experienced higher ~~charges,~~ payments~~,~~ and LOS and could be another target for better allocation of resources. The fact that ~~patients who were~~ discharge~~d~~ to extended care facilities and inpatient deaths ~~or who died were~~were ~~independently~~ associated with higher inpatient resource utilization~~,~~ is consistent with the notion that patients who are at highest risk for mortality consume the greatest portion of the health care resources~~.~~ [15,16]. It has been previously reported that Hispanic patients with CLD (especially NAFLD) are at higher risk for adverse outcome such as cirrhosis and HCC which this study also corroborates as Hispanic ethnicity is independently associated with resource utilization ~~,~~[6,9].

In the outpatient Medicare population, chronic hepatitis C cirrhosis, abnormal liver imaging, and NAFLD ~~and chronic hepatitis C were~~being the most common CLD diagnoses with ~~, and only~~

approximately half of claims with the diagnosis of CLD had one listed as a primary diagnosis. Once again, the proportion of patients younger than 65 years old and disability eligible increased. As ~~charges,~~ payments from Medicare and proportion of Medicare's responsibility increased, the beneficiary-paid amount decreased~~and estimated payments decreased~~. Racial and geographic variations in payment were again observed. Our study also showed that younger age was the most important independent predictor of Medicare spending. This is consistent with ~~probably due to~~ the fact that younger patients with CLD who qualify for Medicare can only be enrolled due to their disability or other chronic condition such as ESRD~~may be sicker.~~ [17,18]. Furthermore, we expect that the rate of patients with HCV will continue to increase as a result of the CDC's current guidelines which recommend screening all patients ages 45-65 regardless of risk factors for hepatitis C [19]. The HCV screening will help to identify cases earlier and with the new more effective treatments, these treatments can possibly lead to a cure, which may, over time, lead to a substantial decrease in the number of patients with advanced liver disease [20,21,22].

Formatted: Adjust space between Latin and Asian text, Adjust space between Asian text and numbers, Tab stops: Not at 2.58"

There were some limitations to our study. The exact dates were not available for the year 2005-2009, making it impossible to assess the exact timing of post-discharge outcomes. Second, we may have under-estimated post-discharge mortality. This may be due to the LDS denominator files for each calendar year are based on information known to CMS in March of the year following hospitalizations so that some patients without date of death may have been dead but treated as alive. However, 96% of death dates were validated suggesting that~~making~~ the impact of the "un-validated death date" on mortality can be ~~very~~ small. The restricted mortality data we had access to did not allow to account for variability in the length of post-discharge follow-up in

a survival analysis. Because this was a retrospective cohort study, there were unmeasured confounders for which we could not adjust for, such as the availability of healthcare providers in patient's place of residence, history of other chronic diseases and major interventions, marital and socioeconomic status, history of substance abuse or psychiatric conditions, metabolic disorders, as well as the results of physical examination and physical activity which may be especially important for appreciating health status of the elderly population. We also could notdn't determine whether patients sought care outside their Medicare plan which potentially may have changed outcomes. [1923].

In conclusion, CLD is a common disease entity with important patient and financial outcomes for the Medicare population. Although in-hospital mortality and LOS are decreasing, mortality after discharge remains stable. Also, both inpatient and outpatient spending by Medicare is increasing. Our study of chronic hepatitis C in the Medicare beneficiaries showed similar results. [2420]. Independent demographic and clinical predictors which we identified for payment and clinical outcomes can be used to target resource allocation for prevention. This last point is especially important as the Affordable Care Act (ACA) has begun, ensuring insurance coverage is available to all and patients with pre-existing conditions are not excluded nor do they suffer from lapse in coverage. [2521]. It will be imperative to track the impact of the ACA on the long-term outcomes of patients living with CLD especially when one reviews the patients most likely to have CLD are also the patients most likely to be uninsured. Hispanics are the second most prevalent group to be uninsured, especially the young Hispanic male who is working. [2622]. In this study, younger Hispanic males were more likely to have CLD than any other group. Therefore, efforts should be directed to ensure this group becomes knowledgable about the

importance and availability of insurance as well as healthy living. Finally, the results are pertinent as the cohort of baby boomers are increasingly eligible for Medicare. Furthermore, the epidemic of obesity will continue to fuel the increasing prevalence of NAFLD and related cirrhosis. As the population of patients with HCV and NAFLD become increasingly eligible for Medicare, the future burden of CLD on Medicare, the most important source of health care insurance coverage in the U.S. will become even more important.

REFERENCES

1. Gravitz L. Introduction: a smouldering public-health crisis. Nature 2011;474(7350):S2–4.

2. Chak E, Tala AH, Sherman KE, et al. Hepatitis C virus infection in the USA: an estimate of true prevalence. Liver Int. 2011;31:1090-1101.

3. Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW, Holmberg SD.The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. Ann Intern Med. 2012 Feb 21;156(4):271-8.

4. Institute of Medicine. Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C. Washington, DC: The National Academies Press;2010.

5.Thomas DL, Seeff LB. Natural history of hepatitis C. Clin Liver Dis. 2005;9:383-98, vi.

6. Lazo M, Hernaez R, Bonekamp S, Kamel IR, Brancati FL, Guallar E, Clark JM. Non-alcoholic fatty liver disease and mortality among US adults: prospective cohort study. BMJ. 2011 Nov 18;343:d6891.

7. Pradat P, Voirin N, Tillmann HL, Chevallier M, Trépo C. Progression to cirrhosis in hepatitis C patients: an age-dependent process. Liver Int. 2007;27(3):335–9.

8. Singer ME, Younossi ZM. Cost-effectiveness of screening for hepatitis C virus in asymptomatic, average risk adults: has the time come? Am. J. Med. 2001;111:614-621.

9. Koebnick C, Getahun D, Reynolds K, Coleman KJ, Porter AH, Lawrence JM, Punyanitya M, Quinn VP, Jacobsen SJ. Trends in nonalcoholic fatty liver disease-related hospitalizations in US children, adolescents, and young adults.J Pediatr Gastroenterol Nutr. 2009 May;48(5):597-603. doi: 10.1097/MPG.0b013e318192d224.

10. Health Care Spending and the Medicare Program. Published by Medicare Payment Advisory Commission, Washington DC. June 2012.

11. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with *ICD-9-CM* administrative databases. *J Clin Epidemiol* 1992;45 (6) 613- 61

12. Lindenauer PK, Lagu T, Shieh MS, Pekow PS, Rothberg MB. Association of diagnostic coding with trends in hospitalizations and mortality of patients with pneumonia, 2003-2009. JAMA. 2012 Apr 4;307(13):1405-13.

13. Yong-Fang K, Goodwin J. Impact of Hospitalists on Length of Stay in the Medicare Population: Variation by Hospital and Patient Characteristics. J Am Geriatr Soc. 2010; 58(9): 1649–1657.

14. Newhouse JP, Garber AM. Geographic Variation in Medicare Services. N Engl J Med 2013. 368(16): 14651468.

15. Pyenson B, Fitch K, Iwasaki K. Consequences of Hepatitis C Virus (HCV): Costs of a Baby Boomer Epidemic of Liver Disease. New York, NY: Milliman, Inc; May 18, 2009. [Internet,

cited 2013 Mar 12]. Available from: http://publications.milliman.com/research/health-rr/pdfs/consequences-hepatitis-c-virus-RR05-18-09.pdf

16. Wong JB, McQuillan GM, McHutchison JG, Poynard T. Estimating future hepatitis C morbidity, mortality, and costs in the United States. Am J Public Health 2000;90(10):1562–9.

17. Coughlin TA, Waidmann TA, Phadera L.Among dual eligibles, identifying the highest-cost individuals could help in crafting more targeted and effective responses. Health Aff (Millwood). 2012 May;31(5):1083-91. doi: 10.1377/hlthaff.2011.0729. Epub 2012 Apr 18.

18. Bubolz T, Emerson C, Skinner J.State spending on dual eligibles under age 65 shows variations, evidence of cost shifting from Medicaid to Medicare. Health Aff (Millwood). 2012 May;31(5):939-47. doi: 10.1377/hlthaff.2011.0921.

19. Centers for Disease Control. Testing recommendations for chronic Hepatitic C. Obtained from the world wide web at: http://www.cd.gov/Hepatitis/guidelinsC.htm. Last accessed on 3 April 2014.

20. Deuffic-Burban S, Mathurin P, Rosa I, Bouvier AM, Cannesson A, Mourad A, Canva V, Louvet A, Deltenre P, Boleslawski E, Truant S, Pruvot FR, Dharancy S. Impact of emerging hepatitis C treatment on future needs for liver transplantation Dig Liver Dis. 2014 Feb;46(2):157-63. doi: 10.1016/j.dld.2013.08.137. Epub 2013 Oct 10.

21. Sofosbuvir for previously untreated chronic hepatitis C infection. Lawitz E, Mangia A, Wyles D, Rodriguez-Torres M, Hassanein T, Gordon SC, Schultz M, Davis MN, Kayali Z, Reddy KR, Jacobson IM, Kowdley KV, Nyberg L, Subramanian GM, Hyland RH, Arterburn S, Jiang D, McNally J, Brainard D, Symonds WT, McHutchison JG, Sheikh AM, Younossi Z, Gane EJ. N Engl J Med. 2013 May 16;368(20):1878-87. doi: 10.1056/NEJMoa1214853. Epub 2013 Apr 23.

22. Jacobson IM, Gordon SC, Kowdley KV, Yoshida EM, Rodriguez-Torres M, Sulkowski MS, Shiffman ML, Lawitz E, Everson G, Bennett M, Schiff E, Al-Assi MT, Subramanian GM, An D, Lin M, McNally J, Brainard D, Symonds WT, McHutchison JG, Patel K, Feld J, Pianko S, Nelson DR; POSITRON Study; FUSION Study. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013 May 16;368(20):1867-77. doi: 10.1056/NEJMoa1214854. Epub 2013 Apr 23.

~~19~~23. Quan et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005 Nov; 43(11):1073-1077.

~~20~~24. Younossi ZM, Stepanova M, Mishra A, Venkatesan C,– Henry L,– Hunt S. The impact of chronic hepatitis C on resource utilization and in-patient mortality for Medicare beneficiaries between 2005 and 2010. AP&T. 2013 Aug. doi:10.1111/apt.12485

~~21~~25. Medicare Payment Advisory Group. Medicare and Health Care Spending. June 2012. Obtained from the world wide web at: http://www.medpac.gov/documents/Jun12DataBookEntireReport.pdf. Last accessed on 8 Oct 2013.

~~22~~26. Centers for Medicare and Medicaid Services. Audience Segmentation for the Emerging Health Care Marketplace. March 22, 2013. Obtained from the world wide web at http://www.marketplace.cms.gov.– Last accessed on 8 Oct 2013.

Table 1. Clinico-demographic characteristics of Medicare beneficiaries who sought inpatient and outpatient care in 2005-2010.

Characteristics	Inpatient	P-value *	Outpatient	P-value *
No. of patients	14,774		137,347	
No. of hospitalizations	20,943		271,552	
Percent of re-hospitalizations	29.46		NA	
Number of diagnoses, mean (SD)	8.24 (1.58)	<0.0001	2.26 (1.72)	<0.0001
Number of procedures, mean (SD)	1.68 (1.78)	0.1184	0.001 (0.07)	0.0465
Charlson score, mean (SD)	1.44 (1.75)	<0.0001	0.95 (1.23)	<0.0001
Age				
—<65	38.84	<0.0001	32.78	<.0001
—65-69	17.88	<0.0001	21.46	0.6715
—70-74	14.99	0.0004	16.96	0.0003
—75-79	11.56	<0.0001	13.31	<.0001
—80-84	9.29	0.0454	9.18	<.0001
—85 and over	7.45	0.2001	6.30	0.2088
Race				
—White	80.00	0.0025	81.53	<.0001
—Black	10.71	0.0911	10.44	<.0001
—Hispanic	4.61	0.0718	2.71	0.2113
—Other	4.67	0.1445	2.62	0.0092
Male gender	55.09	0.5655	44.93	0.7866
ESRD	6.40	<0.0001	2.54	0.4234
Discharge status				
—Home	51.90	<0.0001	NA	NA
—Continued care	36.70	<0.0001	NA	NA
—Hospice	4.75	<0.0001	NA	NA
—Died	6.65	<0.0001	NA	NA
Region				
—Northeast	19.83	0.2126	20.66	0.5634
—South	40.58	0.4086	35.01	0.0256
—Midwest	22.28	0.0138	26.11	0.1438
—West	8.31	0.3719	9.25	0.2413
—California	9.00	<0.0001	8.97	0.0006

* p-value represents the difference in the parameter between the study years
NA - not applicable

Table 2. Resource utilization and mortality outcomes for Medicare beneficiaries with CLD who sought inpatient care in 2005-2010.

	2005	2006	2007	2009	2010	p
Length of stay						
— Mean (SD)	6.11 (5.75)	6.21 (6.23)	6.06 (5.71)	5.83 (5.71)	5.96 (5.79)	0.0017
— Median(IQR)	4 (3, 8)	4 (3, 7)	4 (3, 7)	4 (2, 7)	4 (3, 7)	
Hospital charge						
— Mean (SD)	34,398 (55,946)	37,544 (67,000)	36,200 (52,282)	40,636 (63,727)	43,354 (70,128)	<0.0001
— Median(IQR)	19,199 (10,804, 36,364)	20,059 (11,050, 39,295)	21,741 (12,032, 40,061)	22,735 (12,291, 43,633)	24,266 (13,768, 44,974)	
Estimated cost						
— Mean (SD)	11,786 (15,413)	12,039 (1,5893)	12,029 (24,037)	12,447 (16,006)	12,773 (17,359)	<0.0001
— Median(IQR)	8,411 (7,295, 10,771)	8,413 (7,283, 10,698)	8,490 (7,255, 10,849)	9,459 (6,134, 12,252)	9,665 (6,147, 12,698)	
In-hospital mortality rate, %	11.75	9.94	8.17	8.75	8.73	0.0001
Post-discharge mortality rate, %	34.68	31.26	34.89	34.84	35.79	0.0363

Table 3. Predictors of in-hospital mortality and overall post-discharge mortality in Medicare beneficiaries hospitalized for CLD in 2005-2010*.

Predictors	In-hospital Mortality		Post-discharge Mortality†	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age				
65-69	Ref		Ref	
<65	0.85 (0.72, 1.00)	0.0537	0.79 (0.70, 0.89)	0.0001
70-74	1.03 (0.85, 1.25)	0.7882	1.08 (0.94, 1.25)	0.2628
75-79	1.25 (1.03, 1.53)	0.0267	1.27 (1.10, 1.48)	0.0012
80-84	0.89 (0.70, 1.12)	0.3045	1.24 (1.06, 1.45)	0.0063
85 and over	1.00 (0.79, 1.27)	0.9967	1.52 (1.30, 1.79)	<0.0001
Gender				
Female	Ref		Ref	
Male	1.26 (1.12, 1.41)	0.0001	1.34 (1.24, 1.46)	<0.0001
Race				
White	Ref		Ref	
Black	1.15 (0.96, 1.38)	0.1204	0.83 (0.72, 0.95)	0.0073
Hispanic	0.77 (0.56, 1.06)	0.1101	0.92 (0.75, 1.13)	0.4287
Other	1.30 (1.00, 1.67)	0.0482	0.84 (0.68, 1.02)	0.0834
ESRD				
No	Ref		Ref	
Yes	0.69 (0.54, 0.89)	0.0034	0.96 (0.81, 1.13)	0.6072
Number of admissions				
1	Ref		Ref	
≥2	1.58 (1.39-1.79)	<0.0001	1.66 (1.51-1.83)	<0.0001
Discharge destination				
Home	N/A		Ref	
Continued care	N/A		2.43 (2.23, 2.65)	<0.0001
Hospice	N/A		49.22 (37.13, 65.25)	<0.0001
Region				
Northeast	Ref		Ref	
South	0.87 (0.75, 1.01)	0.0613	1.20 (1.08, 1.35)	0.0012
Midwest	0.70 (0.59, 0.83)	<0.0001	1.01 (0.89, 1.15)	0.8582
West	0.80 (0.63, 1.01)	0.0639	1.24 (1.05, 1.46)	0.0130
California	0.86 (0.69, 1.08)	0.1951	1.22 (1.04, 1.45)	0.0169
Calendar Year	0.91 (0.89, 0.94)	<0.0001	0.99 (0.97, 1.02)	0.4909
Number of diagnosis	1.22 (1.16, 1.28)	<0.0001	1.05 (1.02, 1.08)	0.0007
Number of procedures	1.32 (1.28, 1.37)	<0.0001	0.99 (0.96, 1.01)	0.3812
Charlson score	1.03 (0.99, 1.06)	0.1151	1.23 (1.20, 1.26)	<0.0001
LOS	1.01 (1.00, 1.02)	0.1244	1.01 (1.00, 1.02)	0.0039

* Data in 2008 were excluded from analysis due to missing information on patient's residence region.

Table 4. Predictors of LOS, hospital charge and total payment of hospitalizations of Medicare beneficiaries for CLD in 2005-2010*.

Predictors	LOS Increase		Hospital Charge Increase†		Estimated Cost Increase†	
	% (95% CI) ‡	P-value	% (95% CI) ‡	P-value	% (95% CI) ‡	P-value
Age						
— 65-69	Ref		Ref		Ref	
—<65	0.07 (-2.47, 2.61)	0.9557	**-2.64 (-4.92, -0.36)**	**0.0233**	**5.09 (3.11, 7.06)**	**<0.0001**
— 70-74	-0.99 (-4.07, 2.09)	0.5293	**-4.71 (-7.48, -1.94)**	**0.0009**	**-6.08 (-8.48, -3.68)**	**<0.0001**
— 75-79	2.36 (-0.97, 5.69)	0.1649	**-3.05 (-6.05, -0.06)**	**0.0456**	**-8.15 (-10.74, -5.55)**	**<0.0001**
— 80-84	2.85 (-0.72, 6.42)	0.1181	**-3.22 (-6.44, -0.01)**	**0.0496**	**-11.91 (-14.70, -9.13)**	**<0.0001**
— 85 and over	1.14 (-2.73, 5.00)	0.5635	-2.45 (-5.94, 1.03)	0.1673	**-14.17 (-17.19, -11.16)**	**<0.0001**
Gender						
— Female	Ref		Ref		Ref	
— Male	**-4.05 (-5.85, -2.26)**	**<0.0001**	**1.69 (0.07, 3.31)**	**0.0407**	**4.65 (3.25, 6.06)**	**<0.0001**
Race						
— White	Ref		Ref		Ref	
— Black	**11.72 (8.80, 14.64)**	**<0.0001**	**4.86(2.23, 7.48)**	**0.0003**	**2.66 (0.38, 4.93)**	**0.0220**
— Hispanic	**9.71 (5.47, 13.95)**	**<0.0001**	**11.04 (7.23, 14.85)**	**<0.0001**	**9.54 (6.23, 12.85)**	**<0.0001**
— Other	1.29 (-2.98, 5.56)	0.5536	**3.98 (0.15, 7.81)**	**0.0417**	**8.17 (4.85, 11.49)**	**<0.0001**
ESRD						
— No	Ref		Ref		Ref	
— Yes	**3.84 (0.06, 7.62)**	**0.0467**	**-5.45 (-8.87, -2.04)**	**0.0017**	-1.07 (-4.03, 1.89)	0.4780
Discharge destination						
— Home	Ref		Ref		Ref	
— Continued care	**37.32 (35.36, 39.29)**	**<0.0001**	0.46 (-1.34, 2.26)	0.6148	**-11.70 (-13.27, -10.13)**	**<0.0001**
— Hospice	**35.98 (31.70, 40.25)**	**<0.0001**	-0.08 (-3.96, 3.79)	0.9662	**-7.56 (-10.91, -4.22)**	**<0.0001**
— Died	**25.86 (22.14, 29.58)**	**<0.0001**	**5.58 (2.23, 8.92)**	**0.0011**	1.54 (-1.36, 4.44)	0.2978
Region						
— Northeast	Ref		Ref		Ref	
— South	**-3.03 (-5.45, -0.60)**	**0.0143**	**-17.34 (-19.52, -15.16)**	**<0.0001**	**-17.88 (-19.77, -15.99)**	**<0.0001**
— Midwest	**-11.51 (-14.23, -8.78)**	**<0.0001**	**-23.31 (-25.76, -20.86)**	**<0.0001**	**-10.75 (-12.87, -8.62)**	**<0.0001**
— West	**-9.95 (-13.62, -6.28)**	**<0.0001**	**-13.54 (-16.83, -10.24)**	**<0.0001**	**-6.08 (8.94, -3.22)**	**<0.0001**
— California	**-6.23 (-9.81, -2.66)**	**0.0006**	**43.90 (40.68, 47.13)**	**<0.0001**	**8.62 (5.83, 11.42)**	**<0.0001**
Calendar Year	**-2.67 (-3.15, -2.18)**	**<0.0001**	**3.94 (3.50, 4.38)**	**<0.0001**	**0.70 (0.32, 1.08)**	**0.0003**
Number of diagnosis	**9.07 (8.49, 9.65)**	**<0.0001**	**2.97 (2.44, 3.50)**	**<0.0001**	-0.28 (-0.75, 0.19)	0.2389
Number of procedures	**18.08 (17.56, 18.59)**	**<0.0001**	**19.95 (19.44, 20.47)**	**<0.0001**	**13.96 (13.51, 14.40)**	**<0.0001**
Charlson score	**-0.85 (-1.37, -0.33)**	**<0.0015**	-0.36 (-0.84, 0.12)	0.1394	0.77 (0.35, 1.18)	0.0003
LOS	N/A	N/A	**8.55 (8.36, 8.74)**	**<0.0001**	**4.22 (4.08, 4.36)**	**<0.0001**

* Data in 2008 were excluded from multivariate analysis due to missing information on region.

† Hospital charge and cost were adjusted to the 2010 dollars using annual inflation rate of 3%.

‡ For categorical variable, this represents the predicted percentage of increase in outcome for one level of the predictor compared to the reference level, while holding all other variables constant; for continuous variable, this represents the predicted percentage of increase in outcome for each unit increase in that variable, while holding all other variables constant. A negative increase represents a decrease.

Table 5. Resource utilization for Medicare beneficiaries with CLD who sought outpatient care in 2005-2010 (median (IQR)).

	2005	2006	2007	2008	2009	2010	p
Average number of claims per year	1.98 ± 2.68	2.01 ± 2.72	1.98 ± 2.62	1.97 ± 2.50	1.96 ± 2.47	1.96 ± 2.40	0.0569
Average total payment, $	151.2 (72.3-529.1)	163.9 (77.6-567.0)	167.0 (80.2-562.0)	154.5 (78.2-552.2)	159.0 (81.4-568.3)	158.5 (83.0-565.2)	<.0001
Average payment by patient, $	45.5 (0.0-162.5)	41.2 (0.0-158.6)	40.5 (0.0-158.4)	38.6 (0.0-142.2)	37.6 (0.0-126.14)	36.6 (0.0-123.8)	<.0001
Average payment by Medicare, $	113.7 (53.8-336.5)	122.5 (58.0-373.1)	124.4 (58.9-371.3)	117.3 (56.9-369.4)	120.9 (57.9-409.4)	120.3 (56.6-408.9)	<.0001
Average charge, $	725.3 (241.1-2371.9)	787.6 (260.0-2624.4)	823.9 (277.4-2784.0)	803.3 (283.7-2716.2)	848.7 (290.6-2886.4)	885.8 (312.9-2952.5)	<.0001
Beneficiary-paid amounts, %	20.0 (0-41.7)	20.0 (0.0-37.2)	20.0 (0.0-37.2)	19.9 (0.0-35.4)	19.4 (0.0-29.1)	19.7 (0.0-29.7)	<.0001
Medicare's responsibility, %	78.6 (55.9-100)	79.1 (61.6-100)	79.3 (61.8-100)	79.9 (63.8-100)	80.0 (68.1-100)	80.0 (68.0-100)	<.0001

Table 6. Independent predictors of outpatient spending for Medicare beneficiaries with CLD.

Predictors	Estimated costs increase, % (95% CI)
Calendar year	-1.56 (-2.00 - -1.12)
Age <65	+68.76 (+49.80 - +90.12)
Age 65-69	+37.05 (+32.03 - +42.26)
Age 70-74	+32.88 (+27.87 - +38.08)
Age 75-79	+23.40 (+18.59 - +28.40)
Age 80-84	+16.68 (+11.82 - +21.75)
Male	+10.27 (+8.44 - +12.12)
Black	+1.56 (-1.21 - +4.42)
Hispanic	+15.35 (+9.55 - +21.45)
Asian	+32.05 (+24.30 - +40.27)
Disability	-4.75 (-15.05 - +6.80)
ESRD	+7.84 (+1.33 - +14.77)
Location: Midwest	-3.82 (-6.12 - -1.46)
Location: South w/o California	-2.25 (-4.46 - +0.02)
Location: West	+10.48 (+6.94 - +14.14)
Location: California	+15.43 (+11.65 - +19.34)
Average number of diagnoses per claim, per dx	+29.31 (+28.64 - +29.98)
Number of outpatient procedures, per procedure	+18.09 (+13.63 - +22.72)

† The increase is in comparison to the reference value. A negative increase represents a decrease.

Table 1. Clinico-demographic characteristics of Medicare beneficiaries who sought inpatient and outpatient care in 2005-2010.

	Inpatient			Outpatient		
Characteristics	2005	2010	p*	2005	2010	p*
No. of patients	2,582	2,458		39,885	44,546	
No. of claims	3,698	3,680		83,866	94,309	
Percent of re-hospitalizations, %	24.20	25.83	0.0653	NA	NA	
Number of diagnoses	7.92 +/- 1.73	8.64 +/- 1.31	<.0001	3.55 ± 2.11	4.32 ± 2.39	<0.0001
Number of– procedures	1.59 +/- 1.75	1.67 +/- 1.79	0.2554	0.01 ± 0.16	0.01 ± 0.18	NS
Charlson score	1.31 +/- 1.58	1.36 +/- 1.67	<.0001	1.25 ± 1.46	1.43 ± 1.50	<0.0001
Age						
<65, %	38.18	42.47	<.0001	30.48	34.33	<.0001
65-69, %	15.87	19.62	<.0001	20.65	21.46	0.0055
70-74, %	16.01	12.64	<.0001	17.66	16.52	0.0006
75-79, %	13.28	8.89	<.0001	15.03	12.35	<.0001
80-84, %	9.19	8.40	0.0166	9.70	8.88	<.0001
85 and over, %	7.46	7.99	0.1107	6.49	6.47	NS
Race						
White, %	81.18	79.24	0.0162	81.85	80.58	<.0001
Black, %	10.25	10.84	0.2218	10.68	11.71	<.0001
Hispanic, %	4.57	5.33	0.1124	2.48	2.70	NS
Other, %	4.00	4.59	0.0428	2.71	2.09	<.0001
Male gender, %	53.95	54.35	0.0836	45.75	46.04	NS
End-stage renal disease, %	3.49	6.11	<.0001	3.48	3.52	NS
Discharge status						
Home, %	52.52	49.57	<.0001	NA	NA	NA
Continued care, %	36.78	39.78	<.0001	NA	NA	NA
Hospice, %	4.25	5.08	<.0001	NA	NA	NA
Died, %	6.46	5.57	<.0001	NA	NA	NA
Region						
Northeast, %	16.88	21.17	0.1323	19.96	19.25	0.0045
South, %	34.86	39.44	<.0001	26.26	25.45	0.0002
Midwest, %	18.85	23.25	0.0044	36.50	37.69	0.0007
West, %	7.23	8.31	0.0025	8.98	8.83	NS
California, %	7.77	9.49	<.0001	8.29	8.78	<.0001

NA - not applicable
* p-value indicates the significance of change over the study years; NS - not significant

Table 2. Resource utilization and mortality outcomes for Medicare beneficiaries with CLD who sought inpatient care in 2005-2010.

	2005	2006	2007	2008	2009	2010	p
Length of stay, days	6.02 +/- 5.61	5.92 +/- 5.65	5.86 +/- 5.40	5.78 +/- 5.54	5.61 +/- 5.45	5.74 +/- 5.57	0.0001
– – Mean (SD)	4 (3, 7)	4 (3, 7)	4 (3, 7)	4 (3, 7)	4 (2, 7)	4 (3, 7)	
– – Median(IQR)							
Payment by patient, $	650 +/- 782	649 +/- 695	650 +/- 762	661 +/- 796	661 +/- 802	626 +/- 758	<.0001
– – Mean– +/- SD							
– – Median(IQR)	1,096 (0-1,096)	1,100 (0-1,100)	1,098 (0-1,098)	1,093 (0-1,093)	1,104 (0-1,104)	1,100 (0-1,100)	
Payment by patient, %	7.70 +/- 9.20	7.64 +/- 8.77	8.54 +/- 12.67	8.84 +/- 13.33	8.18 +/- 10.16	7.66 +/- 9.48	0.0507
– – Mean– +/- SD							
– – Median(IQR)	7.66– (0-13.36)	7.55– (0-13.38)	7.32– (0-13.59)	7.38– (0-13.71)	6.20– (0-13.80)	4.38– (0-12.75)	
Payment by Medicare , $	10,542 +/- 14,023	10,435 +/- 13,085	9,817 +/- 11,768	10,159 +/- 14,975	9,956 +/- 12,547	10,765 +/- 13,779	<.0001
– – Mean– +/- SD							
– – Median(IQR)	7,952 (6,581- 9,962)	7,909 (6,568- 9,938)	7,667 (6,268- 9,638)	7,743 (5,749- 10,129)	7,789 (4,996- 10,572)	8,482 (5,194- 11,326)	
Payment by Medicare, %	89.52 +/- 17.71	89.88 +/- 16.90	87.65 +/- 21.65	87.20 +/- 22.28	88.10 +/- 20.23	89.04 +/- 19.16	0.0011
– – Mean– +/- SD							
– – Median(IQR)	91.29 (86.34- 100.00)	91.41 (86.26- 100.00)	91.01 (85.79- 100.00)	91.18 (85.10- 100.00)	92..29 (84.21- 100.00)	93.75 (85.12- 100.00)	
Total payment, $ of 2010	11,769 +/- 15,864	11,623 +/- 14,745	11,652 +/- 25,393	11,711 +/- 18,912	11,916 +/- 16,045	12,347 +/- 17,641	0.0006
– – Mean– +/- SD							
– – Median(IQR)	8,596 (7,485-10,748)	85,22 (7,448-10,516)	8,382 (7,187-10,486)	8,584 (6,623-11,013)	9,173 (5,985-11,779)	9,478 (5,932-12,192)	
In-hospital mortality rate, %	8.38	8.89	8.14	8.71	9.86	11.81	<.0001
Short-term pPost-discharge mortality ~~rate~~, % *	36.37	34.21	34.12	35.00	30.91	33.82	0.0099

*Patients were followed up to March of the year following the hospitalization.

Table 3. Predictors of in-hospital mortality and overall post-discharge mortality in Medicare beneficiaries hospitalized for CLD in 2005-2010.*

Predictors	In-hospital Mortality OR (95% CI)	Post-discharge Mortality** OR (95% CI)
Age		
– – 65-69	Ref	Ref
– – <65	0.83 (0.69, 0.99)	0.83 (0.72, 0.94)
– – 70-74	1.06 (0.85, 1.31)	1.16 (0.99, 1.35)
– – 75-79	1.28 (1.03, 1.60)	1.33 (1.13, 1.56)
– – 80-84	0.91 (0.71, 1.18)	1.23 (1.04, 1.46)
– – 85 and over	0.92 (0.70, 1.21)	1.51 (1.27, 1.80)
Gender		
– – Female	Ref	Ref
– – Male	1.27 (1.11, 1.44)	1.34 (1.22, 1.46)
Race		
– – White	Ref	Ref
– – Black	1.18 (0.96, 1.44)	0.81 (0.70, 0.95)
– – Hispanic	0.74 (0.52, 1.04)	0.91 (0.73, 1.13)
– – Other	1.11 (0.82, 1.51)	0.79 (0.63, 0.99)
ESRD		
– – No	Ref	Ref
– – Yes	0.73 (0.55, 0.98)	1.14 (0.93, 1.40)
Number of admissions		
– – 1	Ref	Ref
– – ≥2	1.50 (1.31, 1.73)	1.62 (1.46, 1.80)
Discharge destination		
– – Home	N/A	Ref
– – Continued care	N/A	2.51 (2.29, 2.76)
– – Hospice	N/A	44.98 (33.01,61.28)
Region		
– – Northeast	Ref	Ref
– – South	0.95 (0.81, 1.13)	1.27 (1.12, 1.43)
– – Midwest	0.79 (0.65, 0.96)	1.10 (0.96, 1.26)
– – West	0.84 (0.65, 1.10)	1.33 (1.11, 1.60)
– – California	0.95 (0.74, 1.22)	1.23 (1.02, 1.47)
Calendar Year	0.90 (0.87, 0.94)	1.00 (0.98, 1.03)
Number of diagnosis	1.24 (1.17, 1.32)	1.06 (1.03, 1.09)
Number of– procedures	1.36 (1.31, 1.41)	0.98 (0.96, 1.01)
Charlson score	1.01 (0.98, 1.05)	1.24 (1.21, 1.28)
LOS	1.01 (1.00, 1.02)	1.02 (1.01, 1.03)

* Data in 2008 were excluded from analysis due to missing information on patient's residence region.
** Patients were followed up to March of the year following the hospitalization

Table 4. Predictors of LOS, hospital charge and total payment of hospitalizations of Medicare beneficiaries for CLD in 2005-2010*.

Predictors	LOS Increase % (95% CI)	Total Payment Increase % (95% CI)
Age		
65-69	Ref	Ref
<65	-0.77 (-3.45, 1.90)	-2.00 (-4.44, 0.43)
70-74	-3.44 (-6.72, -0.16)	-5.23 (-8.22, -2.24)
75-79	-0.16 (-3.73, 3.41)	-3.94 (-7.20, -0.69)
80-84	1.03 (-2.83, 4.89)	-3.21 (-6.73, 0.31)
85 and over	-0.77 (-3.45, 1.90)	-0.37(-4.16, 3.42)
Gender		
Female	Ref	Ref
Male	-4.63 (-6.53, -2.72)	1.11 (-0.63, 2.85)
Race		
White	Ref	Ref
Black	9.57 (6.42, 12.73)	4.82 (1.94, 7.70)
Hispanic	11.36 (6.92, 5.80)	12.67 (8.62, 16.71)
Other	1.90 (-2.76, 6.55)	1.58 (-2.66, 5.82)
ESRD		
No	Ref	Ref
Yes	2.23 (-2.19, 6.65)	-5.86 (-9.90, -1.82)
Discharge destination		
Home	Ref	Ref
Continued care	35.39 (33.31, 37.46)	0.53 (-1.39, 2.45)
Hospice	37.42 (32.67, 42.17)	-1.42 (-5.77, 2.94)
Died	25.95 (21.96, 29.94)	8.07 (4.44, 1.69)
Region		
Northeast	Ref	Ref
South	-4.36 (-6.94, -1.79)	-16.68 (-19.03, -14.33)
Midwest	-12.18 (-15.08, -9.28)	-23.40 (-26.05, -20.75)
West	-13.82 (-17.71, -9.94)	-12.59 (-16.12, -9.05)
California	-9.23 (-13.02, -5.44)	42.62 (39.16, 46.08)
Calendar Year	-3.17 (-3.68, -2.66)	3.08 (2.61, 3.54)
Number of diagnosis	9.34 (8.70, 9.98)	3.72 (3.13, 4.30)
Number of procedures	17.70 (17.15, 18.25)	19.51 (18.95, 20.07)
Charlson score	-1.36 (-1.96, -0.77)	-0.47 (-1.01, 0.08)
LOS	N/A	9.02 (8.80, 9.24)

* Data in 2008 were excluded from multivariate analysis due to missing information on region.

Table 5. Resource utilization for Medicare beneficiaries with CLD who sought outpatient care in 2005-2010 (median (IQR)).

	2005	2006	2007	2008	2009	2010	p
Yearly number of claims per patient (mean ± SD)	2.10 +/- 2.92	2.11 +/- 2.94	2.11 +/- 2.94	2.12 +/- 3.02	2.12 +/- 2.91	2.12 +/- 2.85	<0.0001
Total yearly payment, $	366.2 (111.9-888.1)	387.5 (113.8-901.6)	397.1 (114.7-903.0)	386.2 (113.3-924.3)	408.8 (117.8-940.8)	404.0 (119.5-929.7)	<.0001
Yearly payment by patient, $	104.8 (10.9-307.7)	108.1 (13.0-277.3)	111.2 (15.5-271.7)	104.0 (16.0-256.2)	98.9 (20.3-204.4)	95.5 (22.0-202.2)	<.0001
Yearly payment by patient, %	25.4 (3.7-44.2)	24.5 (7.0-38.4)	24.8 (9.5-38.3)	22.8 (8.9-36.2)	20.0 (10.5-27.5)	20.0 (11.6-27.4)	<.0001
Yearly payment by Medicare, $	237.1 (78.4-554.9)	260.7 (83.6-592.7)	266.9 (85.6-604.0)	263.9 (83.8-629.4)	299.5 (89.4-695.0)	300.00 (90.6-684.7)	<.0001
Yearly payment by Medicare, %	73.1 (55.0-92.7)	74.2 (61.1-90.2)	74.1 (61.4-88.2)	75.9 (63.8-88.4)	80.0 (70.4-87.3)	80.0 (70.7-86.6)	<.0001

Table 6. Independent predictors of outpatient spending for Medicare beneficiaries with CLD.

Predictors	Payment increase, % (95% CI) †
Calendar year	-1.66 (-1.98 - -1.34)
Age <65	+50.24 (+46.30 - +54.27)
Age 65-69	+33.89 (+30.27 - +37.62)
Age 70-74	+29.15 (+25.57 - +32.83)
Age 75-79	+22.80 (+19.29 - +26.41)
Age 80-84	+13.86 (+10.39 - +17.44)
Age 85+	Reference
Male	+3.75 (+2.48 - +5.04)
Caucasian	Reference
Black	-5.21 (-7.10 - -3.29)
Hispanic	+8.74 (+4.55 - +13.10)
Asian	+12.22 (+7.19 - +17.49)
ESRD	+120.67 (+113.32 - +128.27)
Location: Northeast	Reference
Location: Midwest	+8.56 (+6.60 - +10.56)
Location: South	+6.18 (+4.38 - +8.00)
Location: West	+20.99 (+18.04 - +24.01)
Location: California	+9.07 (+6.34 - +11.86)
The number of diagnoses per claim, per dx	+25.45 (+25.11 - +25.80)
The number of outpatient procedures, per procedure	+31.04 (+26.60 - +35.64)

† The increase is in comparison to the reference value. A negative increase represents a decrease.

Supplementary Table 1. Clinical characteristics of hospitalizations of Medicare beneficiaries for liver disease by discharge year

Characteristics	2005	2006	2007	2008	2009	2010	P-value
No. of patients	2,582	2,444	2,560	2,482	2,451	2,458	
No. of hospitalizations	3,698	3,494	3,677	3,475	3,552	3,680	
Age							
<65	38.18	38.44	41.39	39.48	40.65	42.47	<.0001
65-69	15.87	16.49	18.14	17.38	19.14	19.62	<.0001
70-74	16.01	16.20	13.82	14.73	15.34	12.64	<.0001
75-79	13.28	12.68	11.15	12.52	9.66	8.89	<.0001
80-84	9.19	9.27	9.03	8.03	8.14	8.40	0.0166
85 and over	7.46	6.93	6.47	7.86	7.07	7.99	0.1107
Race							
White	81.18	81.37	79.93	79.88	80.69	79.24	0.0162
Black	10.25	9.50	10.44	10.50	9.57	10.84	0.2218
Hispanic	4.57	4.95	5.25	5.09	4.95	5.33	0.1124
Other	4.00	4.18	4.38	4.52	4.79	4.59	0.0428
Male gender	53.95	56.01	54.31	46.99	54.42	54.35	0.0836
ESRD	3.49	4.06	5.41	6.91	6.64	6.11	<.0001
Discharge status							
Home	53.57	55.58	53.85	51.77	50.82	49.57	<.0001
Continued care	35.02	33.92	35.68	38.10	38.18	39.78	<.0001
Hospice	3.16	3.61	4.41	4.32	4.90	5.08	<.0001
Died	8.25	6.90	6.06	5.81	6.11	5.57	<.0001
Region							
Northeast	19.36	19.23	18.33	N/A	18.89	21.17	0.1323
Midwest	22.47	22.55	21.16	N/A	23.25	20.05	<.0001
West	8.49	7.90	9.19	N/A	8.31	7.91	0.0044
California	7.57	8.56	8.76	N/A	9.49	10.46	0.0025
South	40.72	40.84	41.56	N/A	39.44	40.05	<.0001
Number of diagnoses Mean +/SD	7.92 +/- 1.73	7.98 +/- 1.70	8.27 +/- 1.46	8.34 +/- 1.45	8.49 +/- 1.38	8.64 +/- 1.31	<.0001
Number of procedures Mean +/SD	1.59 +/- 1.75	1.61 +/- 1.74	1.62 +/- 1.76	1.61 +/- 1.75	1.58 +/- 1.78	1.67 +/- 1.79	0.2554
Charlson Score Mean +/SD	1.31 +/- 1.58	1.35 +/- 1.63	1.47 +/- 1.72	1.26 +/- 1.57	1.33 +/- 1.63	1.36 +/- 1.67	<.0001

Supplementary Table 2. Clinical characteristics of hospitalizations of Medicare beneficiaries for liver disease by discharge year

Characteristics	2005	2006	2007	2008	2009	2010	P-value
No. of patients	39885	39605	39693	38485	41982	44546	
No. of claims	83866	83422	83728	81735	88930	94309	
CLD as a primary DX, %	46.94	45.78	43.93	41.51	39.63	38.15	<.0001
Age							
<65	30.48	30.61	31.67	33.22	33.43	34.33	<.0001
65-69	20.65	20.54	20.69	20.6	21.08	21.46	0.0055
70-74	17.66	17.36	17.11	17.03	17.22	16.52	0.0006
75-79	15.03	14.72	14.28	13.19	12.71	12.35	<.0001
80-84	9.7	10.23	9.76	9.47	9.06	8.88	<.0001
85 and over	6.49	6.53	6.49	6.5	6.5	6.47	0.9995
Race							
White	81.85	81.94	81.67	77.76	80.84	80.58	<.0001
Black	10.68	10.56	10.94	13.41	11.45	11.71	<.0001
Hispanic	2.48	2.56	2.43	2.78	2.6	2.7	0.1731
Other	2.71	2.54	2.43	2.37	2.23	2.09	<.0001
Male gender	45.75	45.89	45.84	46.49	45.83	46.04	0.3652
ESRD	3.48	3.55	3.71	3.56	3.51	3.52	0.5772
Region							
Northeast	19.96	20.05	20.16	18.97	19.51	19.25	0.0045
Midwest	26.26	26.4	25.66	23.58	25.5	25.45	0.0002
South	36.5	36.61	36.7	37.59	37.44	37.69	0.0007
West	8.98	8.63	9.01	9.18	8.87	8.83	0.4301
California	8.29	8.31	8.47	10.68	8.68	8.78	<.0001
Mean number of diagnoses per claim, Mean +/SD	3.55 ± 2.11	3.69 ± 2.15	3.8 ± 3 2.22	3.95 ± 2.27	4.15 ± 2.33	4.32 ± 2.39	<0.0001
Total number of procedures per year, Mean +/SD	0.01 ± 0.16	0.01 ± 0.17	0.01 ± 0.20	0.01 ± 0.17	0.01 ± 0.18	0.01 ± 0.18	0.9532
Mean Charlson Score per claim, Mean +/SD	1.25 ± 1.46	1.30 ± 1.48	1.35 ± 1.50	1.39 ± 1.48	1.41 ± 1.51	1.43 ± h 1.50	<0.0001

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-8*
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	5-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-11
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-12
		(*b*) Report category boundaries when continuous variables were categorized	9-12
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.