The Burden of Hepatitis C to the United States Medicare System in 2009: Descriptive and Economic Characteristics

David B. Rein, Joshua Borton, Danielle K. Lifmann, and John S. Wittenborn

The aim of this work was to estimate and describe the Medicare beneficiaries diagnosed with hepatitis C virus (HCV) in 2009, incremental annual costs by disease stage, incremental total Medicare HCV payments in 2009 using the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data covering the years 2002 to 2009. We weighted the 2009 SEER-Medicare data to create estimates of the number of patients with an HCV diagnosis, used an inverse probability-weighted two-part, probit, and generalized linear model to estimate incremental per patient per month costs, and used simulation to estimate annual 2009 Medicare burden, presented in 2014 dollars. We summarized patient characteristics, diagnoses, and costs from SEER-Medicare files into a person-year panel data set. We estimated there were 407,786 patients with diagnosed HCV in 2009, of whom 61.4% had one or more comorbidities defined by the study. In 2009, 68% of patients were diagnosed with chronic HCV only, 9% with cirrhosis, 12% with decompensated cirrhosis (DCC), 2% with liver cancer, 2% with a history of transplant, and 8% who died. Annual costs for patients with chronic infection only and DCC were higher than the values used in many previous cost-effectiveness studies, and treatment of DCC accounted for 63.9% of total Medicare’s HCV expenditures. Medicare paid $2.7 billion (credible interval: $0.7-$4.6 billion) in incremental costs for HCV in 2009. Conclusions: The costs of HCV to Medicare in 2009 were substantial and expected to increase over the next decade. Annual costs for patients with chronic infection only and DCC were higher than values used in many cost-effectiveness analyses.

Hepatitis C virus (HCV) is the most common blood-borne infection in the United States, with at least 2.7 million chronically infected Americans. Current patients with HCV were primarily infected by behavioral and medical exposures between the 1960s and the early 1990s, and as a result, an estimated 70.1% of those HCV antibody positive were born during the years of 1945-1965. In 2010, the first members of the 1945-1965 birth cohort became eligible for the U.S. Medicare program through the aged (age 65) eligibility pathway, and many more are likely to enter the program over the coming decades.

To date, no paper has attempted to estimate either the per person costs or the aggregate health impact of HCV on the Medicare system, and the number of HCV patients seeking care in Medicare is unknown. This is an important knowledge gap because at least 1 million new chronically infected persons are likely to age into Medicare over the next 10-20 years. Costs for HCV patients in Medicare may be different than in private insurance owing to their age, the high prevalence of other comorbidities, and differences in Medicare reimbursements compared to other payers. Finally, the need to offer treatment to patients before Medicare entry is in dispute.

Abbreviations: CCI, Charlson Comorbidity Index; CI, confidence interval; CLD, chronic liver disease; DCC, decompensated cirrhosis; DME, durable medical equipment; ESLD, end-stage liver disease; ESRD, end-stage renal disease; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IPW, inverse probability weights; PPPM, per patient per month; SEER, Surveillance, Epidemiology, and End Results; SVR, sustained viral response

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Although the potential costs of providing new hepatitis C treatments have been hotly debated since their introduction in the fall of 2013, only two empirical studies have attempted to estimate the medical cost burden of HCV in the United States. Galbraith et al. used national survey data to estimate outpatient, emergency department, and inpatient visits associated with HCV and estimated that inpatient charges alone exceeded $15 billion in 2010. Razavi et al. used a simulation model to combine cost estimates with assumptions about disease prevalence, progression, and health care utilization to estimate an annual HCV burden of $6.5 billion in 2010. However, each study was limited by available data.

Several studies have attempted to estimate the annual or per patient per month (PPPM) costs of HCV services among people in care. Younossi et al (2014) used Medicare claims data to estimate the mean annual yearly chronic liver disease (CLD) costs of in- and outpatient services among beneficiaries with CLD, estimating an inpatient cost of $12,347 per inpatient episode and annual outpatient cost of $404 in 2010. The study used an accounting method to calculate costs (averaging annual per person payments for claims with a diagnostic code for CLD). In contrast, studies that used econometric or quasi-experimental methods to estimate incremental costs of patients with an HCV diagnosis, compared to those without, have consistently reported higher incremental HCV costs.

For example, McAdam-Marx et al. compared the mean annual allowable charges per person for patients with HCV, as compared to a stratified matched cohort of control individuals drawn from commercial managed care data, and reported incremental cost increases ranging from a low of $5,870 for those with HCV and no liver disease to a high of $168,845 for those who received a transplant in that year. Davis et al. used regression methods to estimate incremental annual reimbursed costs (2007 dollars) among patients with HCV contained in a commercial database of approximately 50 million covered lives. That study estimated incremental annual costs of $6,839 for patients with mild HCV, $11,230 for patients with moderate HCV, to $12,481 per year for patients with severe HCV. Gordon et al. also used similar regression methods to estimate the incremental PPPM costs of individuals with HCV in 2010 among privately insured patients. For untreated patients, their PPPM estimates would translate to annual costs of $7,117 for patients without cirrhosis, $12,034 for patients with cirrhosis, and $43,023 for patients with end-stage liver disease (ESLD), assuming 12 months of enrollment.

These higher empirical estimates, especially for the cost of chronic disease, are largely ignored in cost-effectiveness studies, which favor estimates closer to the accounting cost inputs reported by Younossi et al. For example, whereas each of the four empirical studies estimated an annual cost for chronic infection in excess of $5,000, the median chronic cost used in 13 cost-effectiveness studies of U.S. HCV prevention studies that have been published since 2012 was only $457 (Supporting Tables A1 and A2). Of these 13 studies, seven used a cost below $500, four used a cost between $500 and $1,500, and two used a cost between $2,500 and $3,500, with no studies using costs higher than $3,500. If HCV treatment reduces the annual costs of chronic disease, then cost-effectiveness studies using values lower than empirical estimates likely underestimate the potential benefits of HCV prevention and treatment efforts.

This study provides additional evidence about the direct medical costs of HCV observed in the U.S. Medicare system between 2003 and 2009 at the individual and Medicare system level, a time period in which the vast majority of Medicare HCV patients were untreated. We used econometric and quasi-experimental methods to estimate individual unit costs for each HCV disease stage, and then used simulation approaches to combine unit cost estimates with estimates of HCV patients in care in

ARTICLE INFORMATION:
From the NORC at the University of Chicago, Atlanta, GA

ADDRESS CORRESPONDENCE AND REPRINT REQUESTS TO:
David B. Rein, Ph.D.
NORC at the University of Chicago
3520 Piedmont Road Northeast, Suite 225
Atlanta, GA 30305.
E-mail: rein-david@norc.org
2009 in order to estimate the annual burden of HCV disease to the Medicare system in 2009. Our results are intended to provide baseline information about the individual and aggregated costs of HCV before the expansion of treatment, and to support future efforts to simulate the incremental cost impacts of HCV prevention effects within Medicare and elsewhere.

Materials and Methods

DATA

We used the Surveillance, Epidemiology, and End Results (SEER) program’s SEER-Medicare-linked data and Medicare 5% data for patients living in SEER registry areas for the years 2002-2009 to create an analytical data set that summarized information per person per year, which included information from 6,173,194 years of life. We identified individuals who were ever diagnosed with HCV using a previously published algorithm for identification. We then used International Classification of Diseases, Ninth Revision, codes and visit dispositions to categorize HCV patients into six mutually exclusive diagnostic categories: (1) chronic HCV alone; (2) cirrhosis; (3) decompensated cirrhosis (DCC); (4) hepatocellular carcinoma (HCC); (5) transplant and post-transplant; or (6) died with an HCV diagnosis. We created analytical variables indicating whether an individual received an HCV test or had comorbidities of alcohol abuse, diabetes, human immunodeficiency virus (HIV), kidney or renal disease, mental health disorders (other than alcohol or substance abuse), or substance abuse, and an annual Charlson Comorbidity Index (CCI) Score. We chose these comorbidities because they are associated with, but not caused by, HCV and have a high impact on costs. We included kidney disorders to differentiate the high costs of kidney problems from those of HCV. The file also included reporting source (SEER vs. Medicare 5%), age, Medicare eligibility pathway, race/ethnicity, months of enrollment, and annual payments by Medicare (excluding patient copay and payments from other insurers) by Medicare service category. We divided total annual payments for all claims by months of enrollment to obtain an estimate of patient per month costs, which we adjusted for each year by the Consumer Price Index into 2014 dollars.

STATISTICAL ANALYSIS

Descriptive Characteristics of 2009 Medicare Population

We estimated the total number of patients in Medicare and those with HCV in 2009 and their characteristics by applying weights (71.4 for patients from the Medicare 5% file and 3.6 for patients from SEER files) to inflate the data frequencies to the Medicare population. For those with HCV, we estimated the unweighted and weighted frequencies of demographic characteristics, diagnosed comorbidities, eligibility category, HCV diagnostic state, and years of observed HCV diagnosis. We also estimated the mean age, CCI score, and annual Medicare payment amount.

Medicare Cost per Patient per Month by HCV Diagnosis Stage

We estimated Medicare costs PPPM for each HCV diagnosis stage using a regression approach. For each year of observation, we estimated a two-part model, with the first part estimating the probability of incurring any medical costs using probit regression and the second part estimating the dollar value of care, given that at least some care was received using a generalized linear model assuming a gamma distribution with a log link using the “tpm” module in STATA (StataCorp LP, College Station, TX). Estimations of sequential cross-sections were used to avoid heteroscedasticity resulting from repeated measures because the two-part model cannot easily incorporate random effects. Cross-sectional estimates generated from each of the 6 years of observations were summarized using inverse variance weighting.

We used logistic regression, with Medicare weights, to create a propensity score of the probability of ever being diagnosed with HCV in future years based on the variable values observed in the base year (the first year preceding an HCV diagnosis or the first year of eligibility for those without HCV) for each year observed in the data. To adjust for attrition, we created a different propensity score for each year of observation (1 to 6) using base-year covariate information, but with only those observations that had remained in the sample up to that year. Each propensity score model used the variables ever tested for HCV, male, age and age squared, race (African American, Asian, Latino, Native American/Pacific Islander, and white as the reference), eligibility category (disability and end-stage renal disease [ESRD], aged as the reference), file of...
### TABLE 1. Descriptive Characteristics of 2009 SEER-Medicare Data, Uninflated Estimates, and Estimates Weighted to the Medicare Population

|                                | All Patients | Raw Data | Frequency | Percent | Weighted to Medicare | Frequency | Percent |
|--------------------------------|--------------|----------|-----------|---------|----------------------|-----------|---------|
|                                |              |          |           |         |                      |           |         |
| All patients in sample         | 668,717      | 668,717  | 47,146,168| 1.11    |                      | 47,146,168| 0.86    |
| Ever diagnosed with hepatitis C| 7,398        | 7,398    | 407,786   | 0.86    |                      | 407,786   | 0.86    |
| File source                    |              |          |           |         |                      |           |         |
| SEER                           | 100,050      | 100,050  | 6,527,097 | 13.84   |                      | 6,527,097 | 13.84   |
| Medicare 5%                    | 568,667      | 568,667  | 40,619,071| 86.16   |                      | 40,619,071| 86.16   |

### Patients with Diagnoses of Hepatitis C

|                                | Raw Data (n = 7,398) | Weighted to Medicare (n = 407,786) |
|--------------------------------|----------------------|-----------------------------------|
|                                | Frequency | Percent | Frequency | Percent |
| File source                    |           |         |           |         |
| SEER                           | 2,437     | 32.94   | 53,489    | 13.12   |
| Medicare 5%                    | 4,961     | 67.06   | 354,357   | 86.90   |
| Demographics                   |           |         |           |         |
| Male                           | 4,339     | 58.65   | 223,750   | 54.87   |
| Race                           |           |         |           |         |
| Unknown                        | 16        | 0.22    | 1,007     | 0.25    |
| White                          | 4,579     | 61.90   | 257,846   | 63.23   |
| Black                          | 1,459     | 19.72   | 85,418    | 20.95   |
| Other                          | 284       | 3.84    | 12,482    | 3.06    |
| Asian                          | 602       | 8.14    | 25,154    | 6.17    |
| Hispanic                       | 398       | 5.38    | 22,525    | 5.52    |
| Native American                | 63        | 0.85    | 3,414     | 0.84    |
| Birth decade                   |           |         |           |         |
| Before 1915                    | 25        | 0.34    | 1,650     | 0.40    |
| 1915 to 1924                   | 406       | 5.49    | 22,554    | 5.53    |
| 1925 to 1934                   | 1,509     | 20.40   | 77,657    | 19.04   |
| 1935 to 1944                   | 1,993     | 26.94   | 97,707    | 23.96   |
| 1945 to 1954                   | 1,666     | 22.52   | 91,314    | 22.39   |
| 1955 to 1964                   | 1,380     | 18.65   | 87,443    | 21.44   |
| 1965 to 1974                   | 332       | 4.49    | 23,307    | 5.72    |
| 1975 or Later                  | 87        | 1.18    | 6,214     | 1.52    |
| Comorbidities                  |           |         |           |         |
| Alcohol abuse                  | 459       | 6.20    | 25,661    | 6.29    |
| Diabetes                       | 2,882     | 38.96   | 155,236   | 38.07   |
| HIV infection                  | 346       | 4.68    | 21,729    | 5.33    |
| Kidney or other renal disease  | 1,955     | 26.43   | 98,182    | 24.08   |
| Mental health other than alcohol/substance abuse | 976 | 13.19 | 60,079 | 14.73 |
| Substance abuse                | 508       | 6.87    | 31,671    | 7.77    |
| Eligibility                    |           |         |           |         |
| Aged                           | 3,736     | 50.50   | 188,414   | 46.20   |
| Disabled only                  | 3,381     | 45.70   | 201,396   | 49.39   |
| ESRD only                      | 94        | 1.27    | 5,900     | 1.45    |
| ESRD and disabled              | 187       | 2.53    | 12,136    | 2.98    |
| Highest HCV diagnosis          |           |         |           |         |
| Chronic                        | 3,909     | 52.84   | 276,907   | 67.90   |
| Compensated cirrhosis          | 519       | 7.02    | 35,239    | 8.64    |
| DCC                            | 702       | 9.49    | 48,582    | 11.91   |
| HCC                            | 817       | 11.04   | 7,668     | 1.88    |
| Transplant or post-transplant  | 349       | 4.72    | 6,268     | 1.54    |
| Died in 2009                   | 1,102     | 14.90   | 33,182    | 8.14    |
| Years with Diagnosed HCV       |           |         |           |         |
| 1                              | 1,765     | 23.86   | 86,511    | 21.21   |
| 2                              | 1,305     | 17.64   | 66,989    | 16.92   |
| 3                              | 1,074     | 14.52   | 61,175    | 15.00   |
origin (SEER, Medicare 5% as reference), region (18 SEER data collection region codes, California as the reference), CCI Score in the first year of eligibility, the comorbidities of alcohol abuse, diabetes, HIV, kidney or renal disorders, substance abuse, or other mental health disorders if observed in the first year of eligibility, and total Medicare payments in the base year.

The propensity scores were used to create inverse probability weights (IPWs) for each individual in each year of inclusion in the data equal to 1/propensity score for those who were ever diagnosed with HCV, and 1/(1-propensity score) for those who were not. The purpose of IPW weighting is to balance the sample on potentially confounding covariates before the estimation of coefficients.(30) Each weight was then multiplied by the individual’s Medicare weight to avoid confounding from over-representation of SEER file individuals.

### Estimates of Medicare Payment Burden in 2009

We estimated annual (as opposed to monthly) costs per stage per person by simulating 10,000 randomly and normally distributed replicates of each service area PPPM cost for each HCV state across “n” number of months with “n” equal to the average number of months patients in that HCV state were in Medicare in 2009, estimating the mean annual cost per HCV state and its 95% credible interval using the percentile method. To estimate incremental annual Medicare payments in 2009, we assumed that estimates of HCV patients were invariant and multiplied the number of individuals in each HCV state in 2009 by the estimated annual incremental costs for each of those states. For each burden estimate, we present the proportion of simulated replicates in which the burden was the same sign as the mean value.

### Results

#### DESCRIPTIVE CHARACTERISTICS

In 2009, we estimated that there were 407,786 individuals in Medicare who had received an HCV diagnosis in that year or previously, of whom 67.9% had a diagnosis of chronic HCV only, 8.6% were diagnosed with cirrhosis, 11.9% were diagnosed with DCC, 1.9% with HCC, 1.5% with a transplant in that or a preceding year, and 8.1% died in the year with HCV (Table 1). Of those who did not die in 2009, 74.7% were diagnosed with chronic only and 25.3% were in higher states. HCV patients in Medicare had a high frequency of comorbidities: 61.4% had at least one of the comorbidities we defined and 40.3% had a Charlson Score of 1 or higher.

#### MEDICARE COST PER PATIENT

Incremental costs of HCV varied widely across HCV health state and service category (Table 2). Chronic HCV was significantly associated with higher monthly physician carrier and prescription drug costs PPPM, significantly lower hospice and durable medical equipment (DME) costs PPPM, and was not significantly associated with incremental differences in other cost categories. HCV and cirrhosis was associated with significant increases in
prescription drug costs only. HCV and decompensation was associated with significantly higher costs for inpatient, physician carrier, outpatient, home health, and prescription drug costs and was not significantly associated with hospice or DME costs. HCV and HCC was significantly associated with higher costs for all services, except for home health and DME. Costs for HCV with transplant or post-transplant

| Health State and Service Category | Incremental Cost Per Service Category Per Month |
|----------------------------------|-----------------------------------------------|
|                                  | Cost PPPM | Standard Error | CI Low | CI High |
| HCV Dx, No Other Information     | $4.31     | $7.73          | $10.85 | $19.47 |
| Physician/supplier, i.e., carrier claims (Part B) | $162.67 | $30.36         | $103.16 | $222.18 |
| Outpatient                       | $87.95    | $160.54        | $120.88 | $296.77 |
| Home health agency               | $103.93   | $82.17         | $57.12  | $264.98 |
| Hospice                          | $128.62   | $42.41         | $211.74 | $45.50  |
| DME                              | $12.40    | $4.51          | $21.28  | $3.55   |
| Part D (prescription drugs)      | $12.98    | $5.73          | $7.75   | $24.21  |
| Bootstrapped total               | $230.82   | $291.10        | $328.33 | $839.46 |

HCV and cirrhosis

Medical provider analysis and review (MEDPAR), Part A | $92.51 | $52.38 | $10.16 | $195.18 |
Physician/supplier, i.e., carrier claims (Part B) | $70.34 | $54.20 | $35.90 | $176.58 |
Outpatient | $288.38 | $210.71 | $124.62 | $701.38 |
Home health agency | $233.26 | $154.72 | $536.50 | $69.99 |
Hospice | $234.56 | $71.97 | $375.63 | $39.49 |
DME | $11.49 | $11.69 | $34.40 | $11.43 |
Part D (prescription drugs) | $61.78 | $14.23 | $33.88 | $89.67 |
Bootstrapped total | $33.70 | $669.64 | $1,071.34 | $1,218.31 |

HCV and DDC

Medical provider analysis and review (MEDPAR), Part A | $469.27 | $50.84 | $369.63 | $568.91 |
Physician/supplier, i.e., carrier claims (Part B) | $382.30 | $49.83 | $284.64 | $479.96 |
Outpatient | $1,347.81 | $238.23 | $880.88 | $1,814.74 |
Home health agency | $794.05 | $149.95 | $500.16 | $1,087.95 |
Hospice | $63.05 | $14.23 | $33.88 | $89.67 |
DME | $14.85 | $11.69 | $34.40 | $11.43 |
Part D (prescription drugs) | $47.01 | $14.23 | $33.88 | $89.67 |
Bootstrapped total | $2,962.55 | $595.28 | $1,834.20 | $4,163.65 |

HCV and HCC

Medical provider analysis and review (MEDPAR), Part A | $433.98 | $69.27 | $298.22 | $569.75 |
Physician/supplier, i.e., carrier claims (Part B) | $287.84 | $55.55 | $171.92 | $45.83 |
Outpatient | $1,802.23 | $295.13 | $1,223.76 | $2,380.69 |
Home health agency | $304.55 | $200.93 | $89.27 | $698.38 |
Hospice | $217.78 | $55.98 | $108.05 | $327.50 |
DME | $14.85 | $11.69 | $34.40 | $11.43 |
Part D (prescription drugs) | $90.68 | $22.63 | $46.32 | $135.05 |
Bootstrapped total | $3,128.58 | $752.31 | $1,696.42 | $4,665.98 |

HCV and transplant or post-transplant

Total costs: assumed accounting costs | $2,017.65 | $50% | $1,008.82 | $3,026.47 |

HCV and death in that year

Medical provider analysis and review (MEDPAR), Part A | $139.91 | $45.98 | $49.79 | $230.03 |
Physician/supplier, i.e., carrier claims (Part B) | $107.76 | $63.86 | $17.45 | $232.96 |
Outpatient | $566.60 | $199.92 | $948.44 | $164.75 |
Home health agency | $483.14 | $180.02 | $835.97 | $130.30 |
Hospice | $125.15 | $23.91 | $172.02 | $78.29 |
DME | $12.40 | $4.51 | $21.25 | $3.55 |
Part D (prescription drugs) | $58.07 | $14.12 | $85.75 | $30.39 |
Bootstrapped total | $987.69 | $663.87 | $2,040.36 | $151.22 |

Because of small sample size, costs for transplant and post-transplant were estimated as the average sum of claims across all service categories, without econometric estimation (reported in Table 3). The credible interval for this value was assumed to be ± 50%. HCV and death in that year referred to patients that had received a previous diagnosis for HCV and died in that year and does not imply that HCV was the cause of death. Total values estimated as the observed mean, 2.5% and 97.5% percentiles of a bootstrapped array of 10,000 sums based on their coefficient and standard error. This is not equal to the sum of coefficients for each stage. Death with HCV refers to patients who died while diagnosed in one of the HCV states and does not necessarily mean that HCV was the cause of the death.

Abbreviation: Dx, diagnosis,
services were estimated using accounting methods for which we did not estimate confidence intervals (CIs) or statistical significance. Finally, HCV and death in a given year was associated with significantly higher inpatient and physician carrier costs, but, at the same time, significantly associated with lower incremental costs for all other service categories, resulting in net negative incremental costs for patients with HCV who also died in the same year.

These estimated PPPM results were highly sensitive to the inclusion/exclusion of the “ever tested for HCV” variable. All costs across all service categories and health states (with the exception of transplant procedures) were positive, statistically significant, and substantially higher when the ever tested variable was excluded from the calculation of propensity scores (and by extension IPWs) and the subsequent two-part regression models. The exclusion of the diagnostic marker for chronic kidney disease resulted in slightly higher costs across HCV states and changed some values from insignificant to significantly positive. The independent exclusion of all other variables from the model had minimal to no impact on the results. Estimates using a logit regression in the first part of the model instead of the probit led to slightly higher PPPM cost estimates. Specifications that used log-ordinary least squares in the second part of the model resulted in substantially higher costs across all health states, but this functional form also provided an exceedingly poor fit for the actual data points modeled.

**MEDICARE PAYMENT BURDEN**

We estimated a total payment burden of $2.7 billion (range, $0.7-$4.6) in 2009 (2014 dollar equivalent). Chronic HCV with no other diagnosis comprised 67.9% of all cases and accounted for 28.2% of these costs whereas those with cirrhosis (8.6% of HCV cases) accounted for less than 1% of costs. Patients with DCC comprised 11.9% of the HCV population, but generated 63.9% of total costs. Patients with HCC (1.9% of those with HCV) generated 10.1% of costs. The 1.5% of HCV patients who were in transplant or post-transplant stages generated 5.3% of total costs, and, finally, those with HCV who died in 2009 resulted in a cost reduction of 8.0% (Table 3).

**TABLE 3. Estimated Financial Burden of HCV to the U.S. Medicare System in 2009**

| Stage                  | Proportion of Patients | Annual Cost, Per Patient | Annual Cost, Low | Annual Cost, High | Burden | Burden Low | Burden High | P (Burden = 0) |
|------------------------|------------------------|--------------------------|------------------|-------------------|--------|------------|-------------|---------------|
| Chronic                | 276,907               | $2,708                   | $6,376           | $749,775,546      | $254,062,173 | $1,785,462,115 | 0.081*       |
| Cirrhosis              | 35,239                | $348                     | $7,795           | $12,264,934       | $243,621,655 | $274,689,062 | 0.447        |
| DCC                    | 48,582                | $34,976                  | $42,422          | $1,699,185,085    | $341,652,658 | $2,060,936,859 | 0.000†       |
| HCC                    | 7,668                 | $35,011                  | $43,865          | $268,466,029      | $197,526,683 | $336,355,670 | 0.000†       |
| Transplant and post    | 6,268                 | $22,638                  | $41,319          | $141,894,984      | $70,947,492  | $212,842,476 | n/a†         |
| Death with HCV         | 33,182                | $6,412                   | $11,583          | $212,757,011      | $384,357,392 | $20,521,740  | 0.000†       |
| Cumulative burden      | 407,846               | $6,519.20                | $11,351.75       | $2,658,831,566    | $728,085,613 | $4,629,764,442 | 0.004†       |

Chronic refers to patients who received an HCV diagnosis, but no higher diagnostic stage and may include patients with undiagnosed problems associated with higher stages of disease.

*The probability that burden from chronic HCV is less than $0 is less than 10%.

†The probability that the burden from DCC, HCC, or the total burden from HCV is less than $0 is less than 0.01.

‡Transplant and post refers to those with evidence of transplant procedures at any time now or in the past. Because of small sample size, costs for transplant and post-transplant were estimated as the average sum of claims across all service categories, without econometric estimation, and methods used to estimate credible intervals do not apply because the credible interval was assumed. The credible interval for this value was assumed to be ± 50%.

§The probability that burden from death in years with HCV is greater than $0 is less than 0.01. Death with HCV referred to patients that had received a previous diagnosis for HCV and died in that year and does not imply that HCV was the cause of death.

Abbreviation: n/a, not applicable.

**Conclusions**

We estimated that over 400,000 patients were enrolled in Medicare and diagnosed with HCV in 2009 generating over $2.7 billion in incremental HCV costs. The estimated total payment burden of $2.7 billion (range, $0.7-$4.6) in 2009 (2014 dollar equivalent) was used to assess the financial impact of HCV on the Medicare system. Chronic HCV with no other diagnosis comprised 67.9% of all cases and accounted for 28.2% of these costs whereas those with cirrhosis (8.6% of HCV cases) accounted for less than 1% of costs. Patients with DCC comprised 11.9% of the HCV population, but generated 63.9% of total costs. Patients with HCC (1.9% of those with HCV) generated 10.1% of costs. The 1.5% of HCV patients who were in transplant or post-transplant stages generated 5.3% of total costs, and, finally, those with HCV who died in 2009 resulted in a cost reduction of 8.0% (Table 3).

Those with chronic HCV generated positive burden to Medicare in 91.9% of the simulations. Patients with cirrhosis were essentially as likely to generate positive burden (55.3% of the time) as negative (44.7%) burden. Those with DCC and HCC generated positive burden to Medicare in 100% of the simulated replications, and likewise patients with HCV who died in that year resulted in lower costs to Medicare in 100% of the simulated replications.
Medicare payments. Although these 2009 costs represent only approximately 0.5% of Medicare’s total expenditures of $492 billion in 2013, with no changes in policy they are likely to rise precipitously over the next decade given that over 1 million new chronically infected patients enter the Medicare because of age qualification. The patients observed in 2009 were quite sick, with greater than 60% diagnosed with one or more of the comorbidities defined by our study.

We estimated an annual cost of $2,708 per patient with chronic disease (95% Cr.I.: −$918–$6,376), a point estimate meaningfully higher than the values used in all but 2 of the 13 cost-effectiveness studies noted above, yet slightly less than half the median value estimated in previous econometric analyses of administrative data. (8,9,12,17,24,32) In 8% of simulations, the annual incremental cost of chronic disease was less than zero and the range of possible values contained all those used in the 13 cost-effectiveness models above as well as nearly all those estimated in previous empirical studies.

The monthly and annual costs of patients with cirrhosis were indistinguishable from Medicare patients without HCV, a result we cannot explain without additional clinical information on these patients. Speculatively, a diagnosis of cirrhosis in administrative claims may paradoxically indicate a conscientious patient, who frequently receives physician evaluations, and possibly takes good care of themselves in other ways that would result in lower health care costs.

Once patients received a DCC diagnosis, their annual costs increased dramatically to $34,976 (95% Cr.I.: $27,616–$42,422) per year, an annual cost higher than any used in cost-effectiveness studies and nearly equal to the value estimated by Gordon et al. in two previous studies. (9,24) Higher costs of DCC suggest that the cost-effectiveness of treating patients with chronic disease may be more favorable than previously thought. However, because of the high death rate of patients in Medicare, at least some of this benefit is likely to be mitigated by the shorter time horizon in which patients are able to accrue benefits from treatment.

Caution should be used in interpreting patient staging. Patient-state classifications in this study were determined by physician-assigned diagnostic code, and no clinical lab or chart data existed to verify the accuracy of these diagnoses (other than the diagnosis of HCC, which was recorded by the SEER registry). Many patients classified as HCV with no other information may have experienced quite advanced, but undiagnosed, fibrosis progression, cirrhosis, or even early decompensation. Compared to models of the natural history of HCV, cirrhosis appears to be under-represented compared to DCC. (10,33) This is likely, in part, attributable to underdiagnosis of cirrhosis among patients with chronic HCV owing to the lack of a clinical triggering event for cirrhosis and possibly some degree of upcoding of patients with cirrhosis into DCC by providers seeking higher Medicare reimbursement.

Our estimated costs PPPM for chronic HCV and cirrhosis were significantly and substantially reduced by the inclusion of a variable measuring if an individual had ever received an antibody test for HCV. Because people who inject drugs are much more likely to have been tested for HCV than others, we included an HCV testing variable as an innovative control for differences in lifestyle and behavioral risks between those who have injected drugs and others. The same individual factors associated with a lifetime risk of injecting drug use are also associated with other lifestyle, diet, and behavioral health problems that can increase health expenditures. We used the ever tested for HCV variable to control for unmeasured individual factors that can result in both higher risk of injecting drug use that results in HCV infection and also to higher health expenditures from conditions and injuries associated with lifestyle and behavioral health risks. We hypothesized that the use of a proxy variable, such as the HCV testing variables, would enable the statistical model to separate the incremental health expenditures associated with HCV disease from those associated with underlying risk-seeking personalities.

Lower estimated costs from chronic HCV when the ever tested variable is included could support our hypothesis. Alternatively, similar results could be possible if HCV antibody tests were being used to rule out more-expensive diseases or disorders among a sample of patients matched to the case population on other variables. This alternative explanation for the causal impact of ever tested for HCV seems less likely, because when it is included, our model estimates an annual cost for chronic HCV that falls between the lower bound estimated using accounting methods and the higher bound estimated using quasi-experimentally designed econometric estimates that did not use a proxy adjustment of underlying health risks. (7-9) As would be expected for high-severity conditions, the costs of DCC, HCC, and deaths among people with HCV did not change meaningfully when ever tested for HCV was excluded. Including the HCV testing
variable, in part, explains the difference between our this study’s lower cost estimates for chronic HCV and cirrhosis when compared to results obtained using similar econometric methods and administrative data.\textsuperscript{(8,9)}

It is important to note that although a sustained viral response (SVR) does prevent progression to more advanced liver disease among most patients, it is not known, and this study did not test, what affect, if any, an SVR would have on the costs of managing patients with chronic HCV. Whereas previous research has indicated that treatment of HCV is associated with at least some decline in health expenditures among privately insured populations, additional research with a larger, more contemporary data set is needed to assess the impact of treatment on chronic HCV costs in Medicare.\textsuperscript{(9)}

This study is limited by at least several other factors. First, our study relies on administrative diagnosis codes to identify HCV. Our estimates represent the number and costs of Medicare patients who received an HCV diagnosis and exclude the costs of chronically infected Medicare patients who are undiagnosed. In addition, the HCV case identification algorithm chosen for this study relies on the identification of an HCV diagnostic code on two separate occasions in order to rule out false-positive cases.\textsuperscript{(24)} This likely led to some degree of undercounting given that at least some patients with only one HCV diagnosis code were likely chronically infected.

However, for the purpose of this study, which is to estimate the payment burden of HCV to Medicare, the use of administrative payment coding is likely sufficient. Second, our study uses Medicare 5\% data drawn from the SEER registry locations, which are not representative of the national population. Our population size estimates may be inaccurate if HCV diagnoses occur at a differential rate in SEER than in non-SEER areas. Third, because the two-part model has not currently been developed to a point where it can incorporate random effects, we estimated our model on successive cross-sections of data and summarized the results using inverse variance weighting. Finally, although our weighting approach substantially reduced characteristic imbalances, it did not eliminate them, especially with respect to variables such as comorbidities. However, our estimates of PPPM costs were insensitive to the inclusion/exclusion of these variables suggesting that weighting the regressions by IPW was sufficient to control for the possible confounding effects of sample imbalances related to comorbidities.

**IMPLICATIONS**

Medicare paid an estimated $2.7 billion to care for 407,786 patients with diagnosed HCV in 2009. Of those 407,786 patients, 67.9\% were diagnosed with chronic HCV only, 24\% with higher stages of disease, and 8.1\% of these patients died from HCV or other causes during the year. Whereas the costs of chronic HCV were relatively manageable, both the frequency, annual per person costs, and cumulative costs of end-stage disease, especially DCC, were higher than anticipated. Treatment of DCC accounted for 63.9\% of Medicare’s total HCV expenditures. Given both the cost and frequency of ESLD, Medicare may wish to investigate treatment or other strategies to prevent these patients currently diagnosed with chronic HCV from progressing to higher risk and cost diagnoses of cirrhosis, decompensation, and HCC.

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