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Authors

Gordon, SC
Hamzeh, FM
Pockros, PJ
et al.

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Hepatitis C virus therapy is associated with lower health care costs not only in noncirrhotic patients but also in patients with end-stage liver disease

S. C. Gordon[*], **F. M. Hamzeh**[†], **P. J. Pockros**[‡], **R. S. Hoop**[†], **A. R. Buikema**[§], **E. J. Korner**[†], and **N. A. Terrault**[¶]

[*]Henry Ford Health System, Detroit, MI, USA

[†]Genentech, South San Francisco, CA, USA

[‡]Scripps Clinic, La Jolla, CA, USA

[§]OptumInsight, Eden Prairie, MN, USA

[¶]University of California at San Francisco, San Francisco, CA, USA

SUMMARY

Background—The effect of anti-viral treatment on downstream costs for hepatitis C virus (HCV)-infected patients is unknown.

Aim—To evaluate follow-up costs in patients with chronic HCV, stratified by liver disease severity.

Methods—Using a US private insurance database, mean all-cause per-patient-per-month (PPPM) US (2010) medical costs were calculated for HCV-infected persons who did and did not receive anti-HCV treatment between January 2002 and August 2010. Analysis was stratified by liver disease severity [noncirrhotic disease (NCD), compensated cirrhosis (CC) or end-stage liver disease (ESLD)] defined by ICD-9 and CPT codes.

Results—A total of 33 309 patients were included (78% NCD, 7% CC and 15% ESLD); 4111 individuals (12%) received anti-HCV treatment during the 2-year baseline period. Mean PPPM follow-up health care costs were significantly lower among treated patients with NCD ($900 vs. $1378 in untreated patients, $P < 0.001$) and ESLD ($3634 vs. $5071, $P < 0.001$) groups but not in the CC group ($1404 vs. $1795, $P < 0.071$; *t*-test). In a multivariable model adjusted for demographic characteristics, comorbidities, index date and geographical region, incremental cost ratios for total health care costs differed significantly ($P < 0.001$) between treated and untreated

Correspondence to: Dr S. C. Gordon, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202, USA. sgordon3@hfhs.org.

Guarantor of the article: Stuart C. Gordon.

Author contributions: Drs Gordon, Pockros and Terrault were involved in the study concept and design; analysis and interpretation of data; drafting of the manuscript; statistical analyses; and critical revision of the manuscript for important intellectual content. Dr Hamzeh, Dr Korner and Mr Hoop were involved in the study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis; obtained funding; technical or material support; and study supervision. Ms Buikema was involved in the study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis; and technical support. All authors have reviewed and approved the final version of the manuscript.

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patients in the NCD and ESLD groups but not in the CC group. From this model, mean PPPM total health care costs between treated and untreated patients were $885 and $1370 in the NCD, $1369 and $1802 in the CC, and $3547 and $5137 in the ESLD groups, respectively.

Conclusions—Anti-HCV therapy was associated with lower follow-up US health care costs, and these savings were independent of baseline patient comorbidities and stage of disease.

INTRODUCTION

Most patients with chronic hepatitis C virus (HCV) infection in the United States were born between 1945 and 1964 and acquired HCV between 1960 and 1980.[1] As a result, the prevalence of the long-term cirrhotic complications of chronic HCV infection in this cohort, including hepatocellular carcinoma (HCC) and other liver-related morbidity and mortality, is increasing.[2–4] This trend has important implications for the health care system in the United States. HCV infection is the leading indication for liver transplantation and the most common cause of HCC.[5–9] Patients with detectable HCV infection have a significantly increased risk of dying from hepatic and extrahepatic causes, including cardiovascular disease, than patients who are HCV negative.[10–12]

Effective treatment is available for chronic HCV infection, but only a small proportion of patients receive treatment.[13–15] This is due to both underdiagnosis and undertreatment and reflects a lack of awareness on the part of patients, barriers to accessing treatment, and the complexity and tolerability of current treatment.[15–17] The prospect of more effective and better tolerated therapies has led some physicians to recommend treatment deferral.[18] Among those patients who do receive treatment and have advanced fibrosis, achievement of a sustained virological response significantly reduces the cumulative rate of HCC, transplantation and liver-related death.[19–21]

Hepatitis C virus infection increases health care costs,[22–24] and we and others have shown that health care costs increase in a stepwise fashion as HCV-related liver disease progresses.[23, 25] Thus, it seems plausible that treatment of HCV infection may delay or halt disease progression and would be associated with significant reductions in health care costs. However, there are few data that support this assumption. Using a large comprehensive health care database of patients with chronic HCV infection, we evaluated the impact of anti-HCV treatment on health care costs in patients with chronic HCV infection stratified by liver disease severity.

METHODS

In a prior study, we tested the hypothesis that direct medical costs increase with disease severity, and the study provided estimates of those costs.[25] During this study, we also observed that treated patients appeared to have lower costs than untreated patients. Therefore, in the present analysis, we tested the hypothesis that patients who are treated for their HCV infection have lower downstream direct medical costs regardless of demographic characteristics or comorbidities than patients who are not treated.

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Claims data

Deidentified medical and pharmacy claims enrolment information and mortality data were obtained for commercial health plan members enrolled between January 1, 2002, and August 31, 2010, in a large US private insurance database affiliated with OptumInsight (Eden Prairie, MN, USA).[25] The study database included claims for all prescription medications and medical services submitted by providers to constituent health plans for payment.

Data were collected from all available health care sites including physicians' offices, emergency departments and hospitals for all types of services. Claims analyses were based on amounts paid by health plans and patient responsibility amounts; costs paid by other health plans and Medicare were not included. In-patient stays were identified using a combination of AMA site codes, revenue codes and provider specialty codes, which indicated stays in an acute care or long-term care facility. ER visits were identified by a combination of AMA site codes and CPT codes indicating emergency department visits. Office visits and outpatient visits were identified using AMA site codes indicating each type of visit.

Patients included in the analysis were commercial health plan members with chronic HCV infection as evidenced by HCV-specific ICD-9 codes from January 1, 2003, to August 31, 2010. Codes that support the diagnosis of chronic HCV infection were also required for inclusion. The requirement for ≥1 HCV-specific ICD-9 code and ≥1 code on a nondiagnostic claim allowed for the exclusion of patients who only had rule-out codes for HCV infection. The complete list of ICD-9 codes used to identify patients with chronic HCV infection is included in Table 1.

Disease severity groups

Patients were assigned to one of three disease severity categories according to predefined criteria established by a consensus panel of three clinical hepatologists: non-cirrhotic disease (NCD), compensated cirrhosis (CC) or end-stage liver disease (ESLD). Patients included in the NCD cohort had no codes associated with conditions or procedures related to cirrhosis, decompensated cirrhosis, HCC or liver transplantation. Patients included in the CC group were required to have a diagnostic code indicating the presence of cirrhosis, whereas those included in the ESLD group were required to have diagnostic or procedural codes associated with decompensated cirrhosis, HCC or liver transplantation. A complete list of conditions used to assign patients to one of the three disease severity groups is in Table 2.[25]

Patients in each disease severity group were assigned an index date. For patients in the NCD group, the index date was assigned as the date of the first claim with an HCV-related diagnostic code after the patient was continuously enrolled in the health plan for ≥2 years. For patients in the CC group, the index date was assigned as the date of the first claim for cirrhosis; for patients in the ESLD group, the index date was assigned as the date of the first claim for a condition or procedure indicating ESLD. Patients had been observed for ≥2 years before the index date to measure baseline comorbidities and treatment and for ≥30 days after and including the index date to measure outcomes. By definition, patients in the CC group

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had NCD during the baseline period and patients in the ESLD group had either cirrhosis or NCD during the baseline period.

Treatment cohorts

Within each disease severity group, two treatment cohorts were identified: (i) patients treated during the baseline period (treated cohort) and (ii) patients not treated during the baseline period (untreated cohort). To ensure that patients in the treated cohort had completed a treatment regimen during the baseline period, only patients with evidence of treatment in both the baseline and follow-up periods were excluded. Patients in the untreated cohort who received treatment in the follow-up period were retained in the main analysis but excluded as part of a sensitivity analysis.

Outcomes

For each patient, follow-up health care costs were calculated based on health plan – paid amounts reported on all claims submitted for payment during the follow-up period. Indirect costs were not included. Costs were adjusted to 2010 US$ using the annual medical care component of the consumer price index to account for inflation during the study.

Both all-cause and HCV-related costs were measured. Costs were considered HCV related if any HCV-related ICD-9 code or CPT code was listed in a primary or secondary position on the claim (Tables 1 and 2).

Follow-up costs are reported as per-patient-per-month (PPPM, 2010 US$) to adjust for the variable amount of time that patients were enrolled in the health plan following the index date.

Statistical analyses

Analyses were conducted from a health plan perspective. Follow-up health care costs were compared between the treated and untreated cohorts within each disease severity group. Mean differences in all-cause and HCV-related follow-up costs between treated and untreated patients were evaluated by *t*-test. In addition, follow-up costs were modelled using multivariable methods to further adjust for demographics, geographical location and comorbidities. Comorbidity covariates included in the models were those that might influence treatment decisions as determined by clinical hepatologists (SCG, NAT, PJP): Quan-Charlson comorbidity score (a validated comorbidity index that predicts 10-year mortality[26]), HIV/AIDS, cancer (excluding HCC and superficial skin tumours or cancer in situ), alcohol and substance abuse, psychiatric disorders, diabetes, cardiovascular disease and chronic obstructive pulmonary disease (COPD). All comorbidities were identified based on ICD-9 codes reported during the baseline period.

In the multivariable analyses, costs were modelled using a generalised linear model with a log link to account for the highly skewed nature of health care cost data.[27] Adjusted costs were predicted for the treated and untreated cohorts within each disease severity group using a recycled prediction method.[28]

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Because some patients in the untreated cohort received treatment during the follow-up period, a sensitivity analysis was conducted that excluded these patients to determine whether the observed differences in follow-up costs might be attributable to the cost of treatment.

RESULTS

A total of 25 966 with NCD, 2219 with CC and 5124 with ESLD were included in this analysis (Figure 1). Among patients with NCD, 12% (n = 3001) were treated in the baseline period. Among patients with CC and ESLD, 12% (n = 261) and 17% (n = 849), respectively, were treated during the baseline period, before the initial diagnosis of their respective liver disease severity level. Among patients not treated in the baseline period, 13% of patients with NCD (n = 3014), 30% of patients with CC (n = 595) and 12% of patients with ESLD (n = 505) were treated during the follow-up period. The mean duration of follow-up in treated and untreated patients was 773 and 734 days, respectively, among patients with NCD; 609 and 652 days, respectively, among patients with CC; and 646 and 680 days, respectively, among patients with ESLD.

The baseline characteristics of treated and untreated patients in each of the three disease severity groups are in Table 3. Among patients with NCD and ESLD, the mean age was significantly lower ($P < 0.001$) among patients who received anti-HCV treatment compared with untreated patients; however, among patients with CC, the mean age was significantly higher among treated patients ($P = 0.026$). In the NCD group, both the proportion of male patients ($P = 0.006$) and the mean Quan-Charlson comorbidity score ($P < 0.001$) were significantly higher among treated vs. untreated patients. In addition, significantly fewer treated patients with NCD had associated ICD-9 codes for HIV/AIDS ($P < 0.001$), diabetes mellitus ($P < 0.001$), cardiovascular disease ($P < 0.001$) and COPD ($P = 0.007$) compared with untreated patients with NCD.

Of note, a lower proportion of treated patients had associated ICD-9 codes for alcohol/substance abuse compared with untreated patients in both the NCD ($P < 0.001$) and CC groups ($P = 0.047$). In contrast, significantly more treated patients within each of the three disease severity groups had associated ICD-9 codes for psychiatric disease (NCD, $P = 0.002$; CC, $P = 0.024$; ESLD, $P < 0.001$; Table 3).

Unadjusted mean PPPM health care costs

Mean PPPM total health care costs, medical costs and HCV-related health care costs during the follow-up period were highest in patients with ESLD and lowest in patients with NCD (Table 4). Mean PPPM total health care costs were significantly greater in untreated patients both in the NCD group ($P < 0.001$) and the ESLD group ($P < 0.001$) (Table 4). Mean PPPM medical costs were significantly higher among untreated patients in the NCD ($P < 0.001$) and ESLD ($P < 0.001$) groups but not in the CC group ($P = 0.947$). Mean PPPM HCV-related health care costs were also significantly higher among untreated patients in each of the three disease severity groups (NCD, $P < 0.001$; CC, $P = 0.003$; ESLD, $P < 0.001$; Table 4).

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A proportion of patients who were not treated during the baseline period received treatment in the follow-up period (13% of NCD, 30% of CC and 12% of ESLD). To determine if differences in costs during the follow-up period were attributable to follow-up treatment costs, patients receiving treatment in the follow-up period were excluded in a sensitivity analysis, with similar results. Specifically, unadjusted costs were significantly lower among patients who received treatment in the NCD and ESLD groups, with no statistically significant difference in cost between treated and untreated patients in the CC group (data not shown).

Adjusted health care cost models

After adjustment for demographic characteristics, comorbidities, index year, geographical region and treatment, there were statistically significant differences ($P < 0.001$) in incremental total health care costs between treated and untreated patients within the NCD and ESLD groups but not within the CC group ($P = 0.057$) (Table 5, Figure 2).

Patients with NCD who received anti-HCV treatment were estimated to have total health care costs that were approximately 35% lower (cost ratio, 0.646; 95% CI, 0.586–0.712) than that for untreated patients with NCD (Figure 2). Medical costs (cost ratio, 0.713; 95% CI, 0.631–0.806) and HCV-related total costs (cost ratio, 0.380; 95% CI, 0.329–0.439) were also significantly lower in treated than in untreated patients (Figure 2).

Similarly, patients in the ESLD group who received anti-HCV treatment during the baseline period were estimated to have total health care costs that were approximately 30% lower (cost ratio, 0.691; 95% CI, 0.579– 0.824) when compared with that of untreated patients with ESLD during the follow-up period (Table 5). Medical costs (cost ratio, 0.684; 95% CI, 0.564–0.830) and HCV-related total costs (cost ratio, 0.657; 95% CI, 0.522–0.828) were also significantly lower in treated than in untreated patients with ESLD (Table 5, Figure 2).

In contrast, the estimated difference in total health care costs between treated and untreated patients in the CC group was not statistically significant (cost ratio, 0.760; 95% CI, 0.573–1.008; Figure 2). There was also no statistically significant difference in medical costs between treated and untreated patients (cost ratio, 1.043; 95% CI, 0.716–1.518). However, HCV-related costs were significantly lower among treated vs. untreated patients in this group (cost ratio, 0.539; 95% CI, 0.386–0.753; Figure 2).

DISCUSSION

This was an exploratory analysis to assess whether or not HCV treatment might be associated with lower downstream direct medical costs resulting from prescription medications, physician office visits, emergency department use and hospitalisation for patients with chronic HCV infection. In this analysis, we showed that HCV treatment in the baseline period was associated with significant reductions in subsequent all-cause direct health care costs in the follow-up period. Among patients with NCD, all-cause follow-up costs were 35% lower in treated patients than in untreated patients. The reduction in costs was also evident in patients with ESLD, and the magnitude of the reduction (30%) was similar to that in the NCD group. However, although the mean PPPM all-cause health care

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cost was 22% lower in treated patients with CC ($1404) compared with untreated patients with CC ($1795), this difference was not statistically significant ($P = 0.057$). Because it is clinically unlikely that patients with CC would differ from the other groups with respect to costs, we believe that the most likely reason for the lack of a statistically significant difference between treated and untreated patients with CC is the small number of treated patients (261), which reduced the power to detect statistically significant differences between treated and untreated patients.

These results build on previous analyses[25] that showed that all-cause health care costs associated with chronic HCV infection are driven by disease severity. The previous analysis showed that the mean annual all-cause health care costs associated with chronic HCV infection exceeded $24 000 and that the mean annual costs increased in a stepwise fashion and were approximately $17 000, $23 000 and $60 000 for those with NCD, CC and ESLD respectively.[25] A 48-week course of dual peginterferon plus ribavirin would cost approximately $48 000 in US$ 2010, which is approximately $1000 per week, and this would increase by an additional $1100 (US$ 2010) per week if either telaprevir or boceprevir was included in the regimen.[29]

The analysis showed that only 12% of patients with chronic HCV infection received treatment during the baseline period and that altogether approximately 25% of patients received treatment during the baseline or follow-up periods. The nature of a claims database does not allow us to determine how many patients were considered for treatment, how many patients were offered treatment or the specific reasons why treatment was not offered. Regardless, the frequency of treatment was very low, especially given the recognised clinical benefits that can be achieved if treatment is successful.

Comorbidities are common in patients with chronic HCV infection.[30] Indeed, an analysis of data from a cohort of 7411 patients with chronic HCV infection showed that HCV-infected patients had twice the burden of comorbidities compared with uninfected control patients, 99.4% of patients with chronic HCV infection had ≥1 comorbid condition and 52% had 6–15 comorbidities.[31] Many comorbid conditions can complicate or may be contraindications to treatment with peginterferon and ribavirin.[30] Thus, it is not surprising that there were differences in the baseline prevalence of concomitant diseases among those who were and were not treated. It was also not surprising that fewer patients in the NCD group with diagnostic codes for HIV/AIDS, alcohol/substance abuse, diabetes mellitus, cardiovascular disease and COPD received treatment compared with untreated patients. However, the multivariable statistical models were adjusted for the presence of comorbid conditions to ensure that these factors were not driving the differences in costs observed between treated and untreated patients.

It is important to note that the results obtained with *t*-tests and multivariable models were similar (Table 5), which suggests that the covariates in the multivariable model did not account for the differences in total direct medical costs between the treated and untreated groups. However, in an observational study of this type, there are unmeasured confounders.

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This study has limitations that are common in observational studies using administrative claims data. The use of ICD-9 codes rather than liver biopsy to assign patients to disease severity groups may have resulted in misclassification of disease severity. The number of patients with claims for anti-HCV therapy can be determined from the database, but it is not possible to determine whether patients took the medication as prescribed, had adjustments in dosage or had a virological response to treatment. It is also not possible to determine why a medication was prescribed or whether a specific medication was HCV treatment related (e.g. a prescription for an antidepressant for a patient who recently started anti-HCV treatment). In conclusion, in this exploratory analysis, anti-HCV therapy during the baseline period was associated with lower all-cause direct medical costs during the follow-up period in patients with NCD and ESLD. These results suggest that increasing the proportion of patients who receive treatment may be beneficial. Further studies are required to confirm these findings and extend them to include regimens that include direct-acting antiviral agents. The potential availability of more potent and less toxic anti-viral regimens should enable larger numbers of infected individuals to undergo treatment, with the prospect of lower downstream health care costs.

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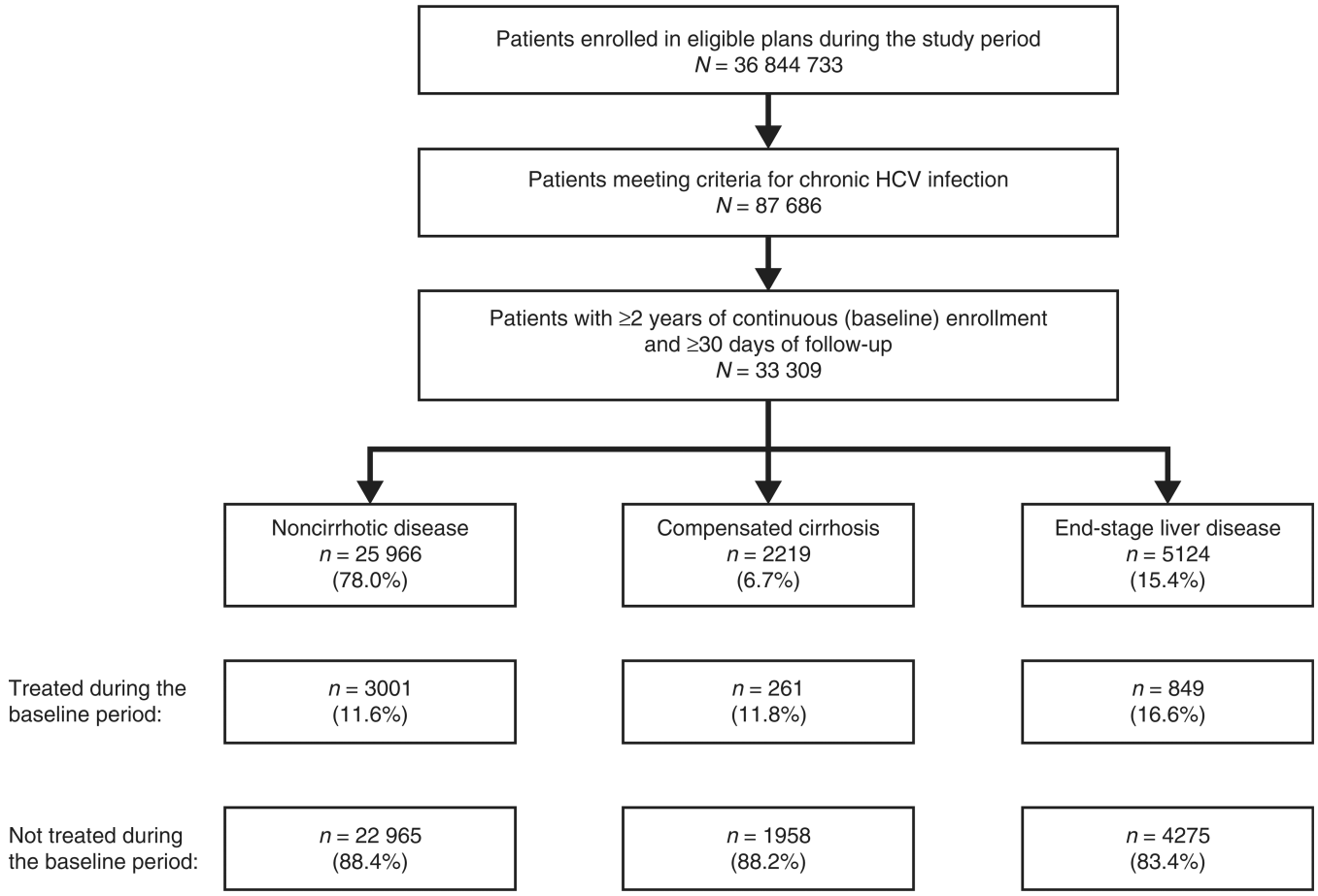

Figure 1.

US patients (*n* = 33 309) included in the analysis, by liver disease severity, for the period January 1, 2002, to August 31, 2010. Patients treated during both baseline and follow-up were excluded (1916 patients with noncirrhotic disease, 166 patients with compensated cirrhosis and 353 patients with end-stage liver disease). HCV, hepatitis C virus.

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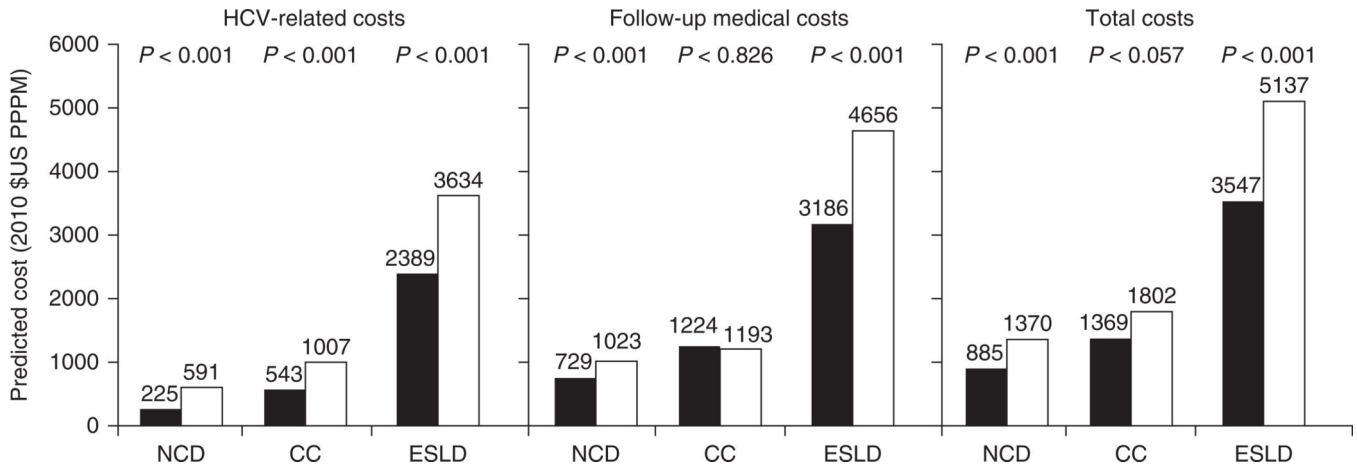

Figure 2.

Predicted total costs [per-patient-per-month (PPPM), 2010 US$] by baseline treatment in patients with noncirrhotic disease (NCD), compensated cirrhosis (CC) and end-stage liver disease (ESLD). Covariates adjusted for in the analysis included age, sex, geographical region, index year, baseline comorbidities and baseline treatment for hepatitis C virus infection. ▪, treated; □, untreated.

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Table 1

HCV diagnostic codes used to identify patients with chronic HCV infection*

Inclusion criteria (one of the following)	Description (ICD-9-CM code)
Single claim with one of these chronic HCV diagnosis codes	Chronic hepatitis C with hepatic coma (070.44) Chronic hepatitis C without mention of hepatic coma (070.54)
Two claims with one of these unspecified HCV diagnosis codes on separate dates of service	Hepatitis C carrier (V02.62) Unspecified viral hepatitis C without hepatic coma (070.70) Unspecified viral hepatitis C with hepatic coma (070.71)
Two claims with one of these acute and unspecified HCV diagnosis codes spaced ≥6 months apart	Acute hepatitis C with hepatic coma (070.41) Acute hepatitis C without mention of hepatic coma (070.51) Hepatitis C carrier (V02.62) Unspecified viral hepatitis C without hepatic coma (070.70) Unspecified viral hepatitis C with hepatic coma (070.71)

HCV, hepatitis C virus

*From January 1, 2003, to August 31, 2010.

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Table 2

Conditions or procedures used to assign patients to liver disease severity groups*

Noncirrhotic disease	Compensated Cirrhosis	End-stage liver disease
No listed conditions or procedures	Cirrhosis	Liver transplant
		Hepatocellular carcinoma
		Liver failure, including hepatorenal syndrome
		Hepatic encephalopathy
		Portal hypertension
		Oesophageal varices
		Other gastrointestinal haemorrhage
		Ascites
		Other sequelae of chronic liver disease
		Abdominal paracentesis procedures
		Shunts and catheter procedures
		Treatment of varices
		Portal decompression procedures

Patients were assigned to the highest level severity category for which they had a qualifying condition or procedure.

*Assignment to a liver disease severity group was based on diagnosis or procedure codes.

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Table 3

Patient and treatment characteristics by disease severity

	NCD (*n* = 25 966)			CC (*n* = 2219)			ESLD (*n* = 5124)		
	Treated (*n* = 3001)	**Not treated (*n* = 22 965)**	***P***	**Treated (*n* = 261)**	**Not treated (*n* = 1958)**	***P***	**Treated (*n* = 849)**	**Not treated (*n* = 4275)**	***P***
Mean age ± s.d. (years)	48.6 ± 7.8	49.8 ± 9.1	<0.001	52.61 ± 7.1	51.6 ± 8.2	0.026	52.2 ± 6.9	53.2 ± 9.1	<0.001
Age category, *n* (%)									
18–34 years	156 (5.2)	1338 (5.8)	<0.001	3 (1.2)	64 (3.3)	0.106	11 (1.3)	112 (2.6)	<0.001
35–44 years	591 (19.7)	3769 (16.4)		30 (11.5)	236 (12.1)		84 (9.9)	451 (10.6)	
45–54 years	1653 (55.1)	11 308 (49.2)		123 (47.1)	1001 (51.1)		450 (53.0)	1906 (44.6)	
55–64 years	564 (18.8)	5802 (25.3)		96 (36.8)	588 (30.0)		271 (31.9)	1457 (34.1)	
≥65 years	37 (1.2)	748 (3.3)		9 (3.5)	69 (3.5)		33 (3.89)	349 (8.2)	
Sex, *n* (%)									
Male	1882 (62.7)	13 799 (60.1)	0.006	173 (66.3)	1275 (65.1)	0.710	568 (66.9)	2812 (65.8)	0.528
Female	1119 (37.3)	9166 (39.9)		88 (33.7)	683 (34.9)		281 (33.1)	1463 (34.2)	
Mean follow-up ± s.d. (days)	773 ± 651	734 ±615		609 ± 544	652 ± 560		646 ± 552	680 ± 591	
Mean Charlson comorbidity score ± s.d.	1.2 ± 1.3	1.0 ± 1.6	<0.001	1.6 ± 1.6	1.6 ± 1.6	0.606	1.8 ± 1.8	1.8 ± 2.1	0.800
Medical conditions, *n* (%)									
HIV/AIDS	62 (2.1)	722 (3.1)	0.001	9 (3.5)	59 (3.0)	0.702	22 (2.6)	125 (2.9)	0.596
Cancer*	95 (3.2)	891 (3.9)	0.054	11 (4.2)	85 (4.3)	0.925	69 (8.1)	364 (8.5)	0.711
Alcohol/substance Abuse†	125 (4.2)	1491 (6.5)	<0.001	14 (5.4)	177 (9.0)	0.047	85 (10.0)	518 (12.1)	0.082
Psychiatric	699 (23.3)	4787 (20.8)	0.002	74 (28.4)	433 (22.1)	0.024	257 (30.3)	971 (22.7)	<0.001
Diabetes	307 (10.2)	3071 (13.4)	<0.001	56 (21.5)	402 (20.5)	0.729	179 (21.1)	981 (23.0)	0.236
Cardiovascular Disease	1146 (38.2)	10 569 (46.0)	<0.001	147 (56.3)	1085 (55.4)	0.782	514 (60.5)	2659 (62.2)	0.364
COPD	118 (3.9)	1161 (5.1)	0.007	11 (4.2)	135 (6.9)	0.101	64 (7.5)	373 (8.7)	0.258
Treatment, *n* (%)									
Dual therapy (with ribavirin)									
Pegylated Interferon	2886 (95.7)			546 (91.8)			459 (90.9)		
Nonpegylated Interferon	34 (1.1)			21 (3.5)			14 (2.8)		
Monotherapy									

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	NCD (*n* = 25 966)			CC (*n* = 2219)			ESLD (*n* = 5124)		
	Treated (*n* = 3001)	**Not treated (*n* = 22 965)**	***P***	**Treated (*n* = 261)**	**Not treated (*n* = 1958)**	***P***	**Treated (*n* = 849)**	**Not treated (*n* = 4275)**	***P***
Pegylated Interferon	46 (1.5)			15 (2.5)			21 (4.2)		
Nonpegylated Interferon	7 (0.2)			2 (0.3)			3 (0.6)		
Ribavirin	41 (1.4)			11 (1.9)			8 (1.6)		

CC, compensated cirrhosis; COPD, chronic obstructive pulmonary disease; ESLD, end-stage liver disease; NCD, noncirrhotic disease.

*Excluding hepatocellular carcinoma, superficial skin tumours and cancer *in situ*.

†Excluding tobacco use.

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Table 4

Mean follow-up all-cause PPPM costs (2010 US$) by treatment history and liver disease severity

	NCD (*n* = 25 966)			CC (*n* = 2219)			ESLD (*n* = 5124)		
	Treated (*n* = 3001)	Not treated (*n* = 22 965)	*P**	Treated (*n* = 261)	Not treated (*n* = 1958)	*P**	Treated (*n* = 849)	Not treated (*n* = 4275)	*P**
Total health care Costs	900.46 (3231.74)	1378.29 (4059.36)	<0.001	1404.42 (3049.46)	1794.90 (4618.80)	0.071	3633.89 (8825.98)	5070.88 (12 545.62)	<0.001
Medical costs	722.23 (3093.42)	1043.14 (3908.14)	<0.001	1214.97 (2932.36)	1201.13 (4539.14)	0.947	3253.78 (8675.48)	4594.17 (12 455.94)	<0.001
Total HCV-related health care costs	246.84 (1638.32)	593.05 (2463.48)	<0.001	574.96 (2081.37)	1002.78 (2810.74)	0.003	2395.10 (7858.05)	3585.26 (11 714.93)	<0.001

CC, compensated cirrhosis; ESLD, end-stage liver disease; HCV, hepatitis C virus; NCD, noncirrhotic disease; PPPM, per-patient-per-month.

* Using *t*-test.

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Table 5

Treated PPPM minus untreated PPPM

	NCD	CC	ESLD
t-test	$478 ($P < 0.001$)	$390 ($P = 0.141$)	$1437 ($P < 0.001$)
GLM model 2	$485 ($P < 0.001$)	$432 ($P = 0.057$)	$1589 ($P < 0.001$)

CC, compensated cirrhosis; ESLD, end-stage liver disease; GLM, general linear model; NCD, noncirrhotic disease; PPPM, per-patient-per-month.