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Research

Health care costs associated with chronic hepatitis C virus infection in Ontario, Canada: a retrospective cohort study

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Abstract

Background: High-quality estimates of health care costs are required to understand the burden of illness and to inform economic models. We estimated the costs associated with hepatitis C virus (HCV) infection from the public payer perspective in Ontario, Canada.

Methods: In this population-based retrospective cohort study, we identified patients aged 18–105 years diagnosed with chronic HCV infection in Ontario from 2003 to 2014 using linked administrative data. We allocated the time from diagnosis until death or the end of follow-up (Dec. 31, 2016) to 9 mutually exclusive health states using validated algorithms: no cirrhosis, no cirrhosis (RNA negative) (i.e., cured HCV infection), compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, both decompensated cirrhosis and hepatocellular carcinoma, liver transplantation, terminal (liver-related) and terminal (non–liver-related). We estimated direct medical costs (in 2018 Canadian dollars) per 30 days per health state and used regression models to identify predictors of the costs.

Results: We identified 48 239 patients with chronic hepatitis C, of whom 30 763 (63.8%) were men and 35 891 (74.4%) were aged 30–59 years at diagnosis. The mean 30-day costs were $798 (95% confidence interval [CI] $780–$816) (*n* = 43 568) for no cirrhosis, $661 (95% CI $630–$692) (*n* = 6422) for no cirrhosis (RNA negative), $1487 (95% CI $1375–$1599) (*n* = 4970) for compensated cirrhosis, $3659 (95% CI $3279–$4039) (*n* = 3151) for decompensated cirrhosis, $4238 (95% CI $3480–$4996) (*n* = 550) for hepatocellular carcinoma, $8753 (95% CI $7130–$10 377) (*n* = 485) for both decompensated cirrhosis and hepatocellular carcinoma, $4539 (95% CI $3746–$5333) (*n* = 372) for liver transplantation, $11 202 (95% CI $10 645–$11 760) (*n* = 3201) for terminal (liver-related) and $8801 (95% CI $8331–$9271) (*n* = 5278) for terminal (non–liver-related) health states. Comorbidity was the most significant predictor of total costs for all health states.

Interpretation: Our findings suggest that the financial burden of HCV infection is substantially higher than previously estimated in Canada. Our comprehensive, up-to-date cost estimates for clinically defined health states of HCV infection should be useful for future economic evaluations related to this disorder.

Like other developed countries, Canada agreed to meet the World Health Organization targets to reduce new cases of hepatitis C virus (HCV) infection by 90% and to treat 80% of eligible cases by 2030.[1–3] Screening detects cases before symptoms develop and allows early treatment, thus potentially reducing disease burden.[4,5] Recently, direct-acting antivirals have transformed HCV infection treatment, offering high cure rates with improved tolerability over interferon-based treatments.[6]

The high costs of direct-acting antivirals initially restricted access in many jurisdictions, including Canada.[7] However, time-limited agreements negotiated between Canadian provincial drug plans and pharmaceutical manufacturers allowed governments of most provinces to fully cover direct-acting antiviral treatment for all eligible patients with chronic HCV infection in 2018 and 2019.[8,9] Economic evaluations are essential in such negotiations. Given that the current agreements may expire in 2–3 years and renegotiations will begin, accurate, up-to-date cost estimates for economic evaluations are critical for effective policy-making.[10] Furthermore, estimates of the cost of illness are important for priority setting and forecasting.

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Current costs associated with HCV infection are poorly understood. In a 2010 Canadian study, Krajden and colleagues[11] used a 3-phase approach (initial, late, predeath), which does not provide enough information for appropriately detailed economic evaluations. The aim of this work was to estimate health care costs for HCV infection health states across the clinical course of illness from diagnosis to death, and to identify predictors of those costs.

Methods

Study design and setting

We conducted a population-based retrospective analysis using administrative health data for a cohort of patients with HCV infection in Ontario, Canada. We used a health state approach, in which the natural history of disease is represented by a set of mutually exclusive and exhaustive clinical categories called health states. We defined health states using clinical events (e.g., development of hepatocellular carcinoma or liver transplantation), with a person in only 1 health state at a given time. Thus, the health state approach produces estimates that can be directly used for economic evaluation.

Patient selection

Cohort selection was based on HCV antibody and HCV RNA test results recorded in the Public Health Ontario laboratory database from Jan. 1, 2003, to Dec. 31, 2014. Public Health Ontario laboratory data were previously linked to administrative databases held at ICES using a combination of deterministic and probabilistic linkage.[12] We included patients aged 18–105 years with a confirmed diagnosis of chronic hepatitis C. The index date for cohort entry was the date of the first positive HCV antibody or RNA test result between 2003 and 2014.

Patients without a valid Ontario Health Insurance Plan (OHIP) number at index date and for 1 year before index date were excluded. Other exclusion criteria were missing age or sex, past infection (a negative RNA test result recorded within 12 mo of a positive antibody test result, with no record of a positive RNA test result within the previous 12 mo), acute infection (a negative RNA test result recorded within 12 mo of a positive RNA test result, with no Ontario Drug Benefit claims for HCV infection therapy within these 12 mo) and coinfection with HIV or hepatitis B virus.

Health states

We characterized the natural history of HCV infection using a set of relevant health states based on the literature:[3,4,13–15] no cirrhosis, no cirrhosis and RNA negative (i.e., cured HCV infection), compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, both decompensated cirrhosis and hepatocellular carcinoma, liver transplantation, and 2 health states that included the 6-month period before death for patients who died, terminal (liver-related) and terminal (non–liver-related).

We defined health states from diagnostic, procedure and death codes in the administrative data, using validated algorithms whenever possible.[16] When this was not possible, we defined health states based on the literature or by consensus of the investigators. Health state definitions are given in Table 1 and Appendix 1, Supplemental Tables S1–S4 (available at www.cmajopen.ca/content/9/1/E167/suppl/DC1).

We identified the sequence of states experienced by each patient from index date to Dec. 31, 2016 or until death, loss of OHIP eligibility or age 106 years, whichever occurred first. Once allocated to a health state, patients remained in that state until they met the criteria for entry into another health state or the end of follow-up.

Data sources and costing methods

Our study was set in a jurisdiction with publicly paid health insurance for physician and hospital services (> 97% of Ontarians are covered by OHIP[17,18]). We took the public payer perspective and included all costs paid by the Ontario Ministry of Health. All costs were adjusted to 2018 Canadian dollars with the use of the Statistics Canada Consumer Price Index for health and personal care for Ontario.[19]

We obtained patient demographic data, including age, sex, residence and neighborhood income quintile, and data on

Table 1: Health state definitions and entry criteria

Health state	Entry criterion/criteria
No cirrhosis	First date of confirmed diagnosis of chronic hepatitis C with positive HCV RNA or HCV antibody test result recorded*
No cirrhosis (RNA negative)	Patient receives negative RNA test result and has no liver disease (CC, DC or HCC)
Compensated cirrhosis	Patient is diagnosed with cirrhosis, or 5 yr before day patient is diagnosed with DC†
Decompensated cirrhosis	Patient is diagnosed with DC‡
Hepatocellular carcinoma	Patient is diagnosed with HCC§
Both decompensated cirrhosis and hepatocellular carcinoma	Patient is diagnosed with HCC while already having DC diagnosis, or is diagnosed with DC while already having HCC diagnosis
Liver transplantation	Patient receives LT during observation period
Terminal, liver-related	6 mo before day of death in patient with advanced liver disease (DC, HCC or LT)
Terminal, non–liver-related	6 mo before day of death in patient without advanced liver disease

Note: CC = compensated cirrhosis, DC = decompensated cirrhosis, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, LR = liver-related, LT = liver transplantation, NLR = non–liver-related.
*See Appendix 1, Supplemental Table S1 for detailed cases definition.
†See Appendix 1, Supplemental Table S2 for detailed cases definition.
‡See Appendix 1, Supplemental Table S3 for detailed cases definition.
§See Appendix 1, Supplemental Table S4 for detailed cases definition.

resource use from administrative databases.[20] We estimated costs for health care resources using standard methods for Ontario administrative data.[20] Detailed data sources and costing methods are described in Appendix 1.

Statistical analysis

We estimated mean health care costs per 30 days and their 95% confidence intervals (CIs) by cost category and health state. We used 3 γ regression models with log-link to identify predictors associated with health care costs per 30 days for health states with no advanced liver disease (no cirrhosis, no cirrhosis [RNA negative], compensated cirrhosis), advanced liver disease (decompensated cirrhosis, hepatocellular carcinoma, both decompensated cirrhosis and hepatocellular carcinoma, liver transplantation) and terminal disease (liver-related and non–liver-related).[21] We used generalized estimating equations to account for within-patient correlation of longitudinal observations. For each model, we incorporated age, sex, income quintile, comorbidity (Johns Hopkins Aggregated Diagnosis Groups score accrued in the 2 yr before the index date), immigrant status (yes/no) and prior treatment (yes/no) as predictors. Patients with missing covariate information were excluded from the regression models. SAS statistical software (SAS Institute) was used for the analyses.

To assess the effects of direct-acting antivirals on overall costs, we performed a sensitivity analysis using data only since 2012, when first-generation direct-acting antivirals became available in Ontario.[22]

Ethics approval

The use of data in this project was authorized under section 45 of Ontario's *Personal Health Information Protection Act*, which does not require review by a research ethics board.

Results

Of the 94 014 patients identified with a positive HCV antibody or RNA test result, 45 775 were excluded: 4679 had past infection, 1259 had acute infection, 22 895 were diagnosed before 2003, and 16 942 had no OHIP number, had coinfection with HIV or hepatitis B virus, or were outside the age limits. There were thus 48 239 patients with chronic hepatitis C who met our criteria.

The cohort's demographic and clinical characteristics at index date (date of diagnosis) are presented in Table 2. About three-quarters of patients (35 891 [74.4%]) were 30–59 years of age, and 30 763 (63.8%) were men. Most were nonimmigrants (43 315 [89.8%]) and resided in urban (43 007 [89.2%]) and low-income (quintiles 1 and 2) (27 718 [57.5%]) neighbourhoods. Of the 29 922 patients (62.0%) who had HCV genotype recorded, 19 572 (65.4%) were infected with genotype 1. At diagnosis, 43 568 patients (90.3%) were noncirrhotic, and 2414 (5.0%) had compensated cirrhosis.

During follow-up, patients moved between health states when they met the entry criteria. For example, of the

Table 2: Baseline characteristics of patients with chronic hepatitis C virus infection

Characteristic	No. (%) of patients *n* = 48 239
Age group, yr	
18–24	2951 (6.1)
25–29	3438 (7.1)
30–34	3959 (8.2)
35–39	4874 (10.1)
40–44	6535 (13.5)
45–49	8007 (16.6)
50–54	7641 (15.8)
55–59	4875 (10.1)
60–64	2266 (4.7)
65–69	1248 (2.6)
70–74	847 (1.8)
75–79	776 (1.6)
80–84	504 (1.0)
85–105	318 (0.7)
Sex	
Male	30 763 (63.8)
Female	17 476 (36.2)
Residence	
Rural	5087 (10.5)
Urban	43 007 (89.2)
Missing	145 (0.3)
Income quintile	
Q1 (lowest)	16 957 (35.2)
Q2	10 761 (22.3)
Q3	8222 (17.0)
Q4	6777 (14.0)
Q5 (highest)	5030 (10.4)
Missing	492 (1.0)
Immigrant	4924 (10.2)
Hepatitis C virus genotype	
G1	19 572 (40.6)
G2	3468 (7.2)
G3	5898 (12.2)
G4	501 (1.0)
G5	41 (0.1)
G6	152 (0.3)
Mixed	290 (0.6)
Missing	18 317 (38.0)
Health state at diagnosis	
No cirrhosis	43 568 (90.3)
Compensated cirrhosis	2414 (5.0)
Decompensated cirrhosis	859 (1.8)
Hepatocellular carcinoma	79 (0.2)
Both decompensated cirrhosis and hepatocellular carcinoma	27 (0.1)
Liver transplantation	108 (0.2)
Terminal, liver-related	504 (1.0)
Terminal, non–liver-related	680 (1.4)
Comorbidity, Aggregated Diagnosis Groups score	
0	1287 (2.7)
1–3	14 321 (29.7)
4–7	20 017 (41.5)
8–10	8037 (16.7)
≥ 11	4577 (9.5)

43 568 patients who entered the no cirrhosis state at diagnosis, 6422 (14.7%) moved into the no cirrhosis (RNA negative) health state, and 2556 (5.9%) moved into the cirrhosis health state. The health state membership of all patients, at diagnosis and during follow-up, is shown in Figure 1. Appendix 1, Supplemental Figure S1 illustrates the conceptual transition.

Our analysis of costs included 43 568 cases of no cirrhosis, 6422 cases of no cirrhosis (RNA negative), 4970 cases of compensated cirrhosis, 3151 cases of decompensated cirrhosis, 550 cases of hepatocellular carcinoma, 485 cases of both decompensated cirrhosis and hepatocellular carcinoma, 372 cases of liver transplantation, 3201 cases of terminal (liver-related) and 5278 cases of terminal (non–liver-related) that contributed observation time to each of those health states. The average number of days in each health state was 2434 for no cirrhosis, 1919 for no cirrhosis (RNA negative), 1247 for compensated cirrhosis and 1146 for decompensated cirrhosis. The average duration of hepatocellular carcinoma was 565 days and of both decompensated cirrhosis and hepatocellular carcinoma, 524 days. The average time since liver transplantation was 1480 days.

Health care costs

The average total health care costs per 30 days increased with disease progression, from $798 during the no cirrhosis state to $11 202 during the terminal (liver-related) state (Table 3). The average total health care costs per 30 days in the advanced liver disease health states were high, at $3659 for decompensated cirrhosis, $4238 for hepatocellular carcinoma, and $8753 for both decompensated cirrhosis and hepatocellular carcinoma. The lowest average total health care cost per 30 days was $661 for those who achieved viral clearance (no cirrhosis [RNA negative]). The weighted average total health care cost per 30 days among all patients was $2184.

Outpatient visits accounted for 16%–30% of total costs throughout the trajectory of HCV infection. Acute inpatient care accounted for more than 60% of costs during terminal states, compared to 15% and 22% of costs during the 2 non-cirrhotic states. Outpatient prescription drugs represented 23% of costs during the no cirrhosis state and 32% of costs in the no cirrhosis (RNA negative) state, versus 14% of costs in both the decompensated cirrhosis state and the hepatocellular carcinoma state.

Our sensitivity analysis of costs from 2012 onward showed that the average total 30-day costs were $1037 for no cirrhosis, $737 for no cirrhosis (RNA negative), $2732 for compensated cirrhosis, $4292 for decompensated cirrhosis, $4670 for hepatocellular carcinoma, $8137 for both decompensated cirrhosis and hepatocellular carcinoma, $6539 for liver transplantation, $10 460 for terminal (liver-related) and $7787 for terminal (non–liver-related) health states (Appendix 1, Supplemental Table S5). These costs were similar to the costs for

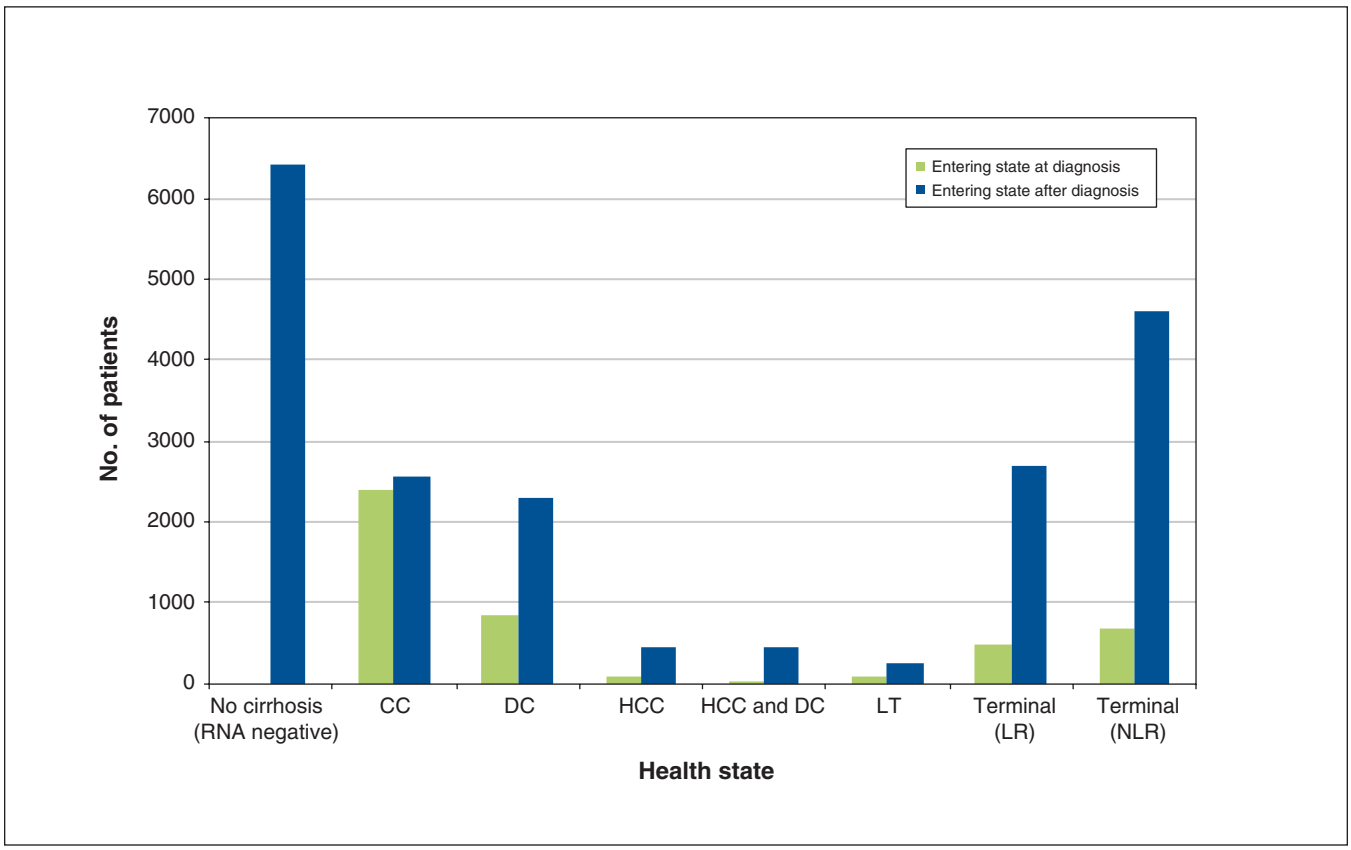

Figure 1: Overall health state membership for Ontario patients with chronic hepatitis C, 2003–2016. Not shown are the 43 568 patients who entered the health state "no cirrhosis" at diagnosis. Note: CC = compensated cirrhosis, DC = decompensated cirrhosis, HCC = hepatocellular carcinoma, LR = liver-related, LT = liver transplantation, NLR = non–liver-related.

Table 3: Mean health care costs per 30 days (2018 Canadian dollars) among patients with chronic hepatitis C virus infection according to cost category and health state

Cost category	Health state; mean cost per 30 d (95% CI), $				
	No cirrhosis	No cirrhosis (RNA negative)	Compensated cirrhosis	Decompensated cirrhosis	Hepatocellular carcinoma
Outpatient visits	51 (50–52)	44 (42–46)	86 (79–93)	198 (181–215)	303 (256–349)
Physician services	160 (157–162)	151 (147–155)	243 (227–260)	599 (442–755)	834 (711–957)
Emergency department visits	31 (30–31)	23 (21–24)	54 (45–63)	163 (137–189)	130 (61–200)
Same-day surgery	12 (12–13)	15 (14–17)	37 (33–42)	69 (58–80)	36 (28–44)
Acute inpatient care	175 (165–185)	98 (86–110)	470 (390–551)	1750 (1529–1971)	1907 (1317–2497)
Outpatient prescription medications	187 (184–191)	215 (204–225)	390 (348–431)	507 (457–556)	609 (448–770)
Home care	23 (22–25)	15 (12–18)	40 (35–45)	100 (89–110)	123 (96–151)
Continuing care	23 (18–27)	7 (1–12)	30 (16–45)	57 (37–76)	33 (0–69)
Long-term care	23 (21–25)	4 (2–7)	27 (19–35)	42 (31–53)	51 (18–85)
Other services	114 (107–121)	89 (72–107)	109 (92–127)	175 (125–224)	212 (102–223)
Total cost	798 (780–816)	661 (630–692)	1487 (1375–1599)	3659 (3279–4039)	4238 (3480–4996)
	Both decompensated cirrhosis and hepatocellular carcinoma	Liver transplantation	Terminal, liver-related	Terminal, non–liver-related	
Outpatient visits	544 (443–646)	325 (276–374)	518 (482–553)	358 (331–386)	
Physician services	1891 (1422–2361)	651 (534–768)	1401 (1327–1475)	1076 (1004–1148)	
Emergency department visits	163 (124–202)	80 (67–93)	305 (290–319)	199 (188–210)	
Same-day surgery	89 (45–133)	96 (31–161)	47 (42–52)	28 (23–33)	
Acute inpatient care	4966 (3880–6052)	1932 (1369–2496)	7564 (7090–8039)	5408 (5016–5800)	
Outpatient prescription medications	683 (526–839)	701 (604–798)	318 (280–357)	332 (310–355)	
Home care	215 (163–266)	130 (94–167)	366 (342–389)	293 (271–316)	
Continuing care	14 (0–29)	102 (0–220)	337 (280–394)	356 (302–410)	
Long-term care	25 (1–49)	45 (11–78)	107 (87–127)	241 (217–265)	
Other services	164 (91–237)	477 (332–621)	240 (196–284)	509 (457–561)	
Total cost	8753 (7130–10 377)	4539 (3746–5333)	11 202 (10 645–11 760)	8801 (8331–9271)	

Note: CI = confidence interval.

all years of the study, except that costs for the early stages were higher. Outpatient drug costs increased to 27% and 39% of total costs for the 2 noncirrhotic states. The mean total cost for compensated cirrhosis was almost twice as high in these later years as in the primary analysis. Outpatient drug costs were almost 3 times as high and represented 41% of total costs.

Predictors of health care costs

The regression models are described in Appendix 1, Supplemental Table S6. When other predictors were held constant, costs decreased significantly with increasing age in the nonadvanced liver disease states and increased with increasing age in the terminal states, but age had no significant effect in the advanced liver disease states (Table 4). Male sex was associated with 7% higher costs than female sex in the nonadvanced liver disease states but had no statistically significant effect in the other states. Patients in higher income quintiles had lower costs during the nonadvanced liver disease states but not in the later health states. Comorbidity was the strongest predictor of total health care costs across all states, with patients with 11 or more Aggregated Diagnosis Groups accruing costs up to threefold higher. In the nonadvanced and advanced disease states, immigrant status was associated with lower costs, and previous treatment for HCV infection was associated with higher costs.

Table 4: Predictors of total health care costs for patients with chronic hepatitis C virus infection

Characteristic	Regression model; relative cost* (95% CI)		
	Nonadvanced liver disease† *n* = 45 539	Advanced liver disease‡ *n* = 3838	Terminal disease§ *n* = 8401
Age, yr			
20	1.38 (1.30–1.47)	0.91 (0.83–1.02)	0.73 (0.65–0.82)
30	1.09 (1.07–1.13)	0.96 (0.91–1.01)	0.87 (0.83–0.91)
40	Reference	Reference	Reference
50	1.04 (1.03–1.06)	1.05 (0.99–1.10)	1.12 (1.08–1.15)
60	1.25 (1.21–1.29)	1.09 (0.98–1.21)	1.21 (1.15–1.28)
70	1.73 (1.64–1.82)	1.14 (0.98–1.33)	1.27 (1.20–1.36)
80	2.73 (2.51–2.98)	1.19 (0.97–1.47)	1.30 (1.20–1.41)
Sex			
Female	Reference	Reference	Reference
Male	1.07 (1.02–1.11)	1.00 (0.90–1.11)	0.94 (0.88–1.00)
Neighbourhood income quintile			
Q1 (lowest)	Reference	Reference	Reference
Q2	0.93 (0.89–0.98)	0.89 (0.77–1.03)	1.07 (1.00–1.15)
Q3	0.87 (0.82–0.93)	0.91 (0.79–1.05)	1.05 (0.97–1.14)
Q4	0.89 (0.84–0.94)	0.92 (0.79–1.07)	1.04 (0.95–1.13)
Q5 (highest)	0.79 (0.74–0.84)	0.84 (0.71–1.00)	0.98 (0.89–1.09)
Measures of comorbidity			
Aggregated Diagnosis Groups score			
0–3	0.64 (0.62–0.68)	1.06 (0.90–1.25)	0.75 (0.69–0.82)
4–7	Reference	Reference	Reference
8–10	1.64 (1.56–1.72)	1.29 (1.13–1.47)	1.48 (1.37–1.59)
≥ 11	3.44 (3.24–3.65)	1.79 (1.58–2.02)	2.10 (1.95–2.25)
Immigrant			
No	Reference	Reference	Reference
Yes	0.62 (0.57–0.67)	0.79 (0.68–0.93)	1.19 (1.06–1.34)
Hepatitis C virus infection treatment			
No	Reference	Reference	Reference
Yes	2.65 (2.56–2.74)	1.78 (1.62–1.97)	1.07 (0.83–1.37)
Health state			
No cirrhosis	1.10 (1.04–1.16)	–	–
No cirrhosis (RNA negative)	Reference	–	–
Compensated cirrhosis	1.53 (1.41–1.66)	–	–
Decompensated cirrhosis	–	Reference	–
Hepatocellular carcinoma	–	1.10 (0.94–1.28)	–
Both decompensated cirrhosis and hepatocellular carcinoma	–	1.69 (1.45–1.97)	–
Liver transplantation	–	1.12 (0.96–1.31)	–
Terminal, non–liver-related	–	–	Reference
Terminal, liver-related	–	–	1.24 (1.17–1.32)

Note: CI = confidence interval.
*Calculated by taking exp (*B*), where *B* is the coefficient in the multiple regression predicting log-transformed cost. Relative cost for any category represents the proportion by which mean cost is increased relative to the referent category, all other variables being held constant.
†Includes health states of no cirrhosis, no cirrhosis (RNA negative) and compensated cirrhosis.
‡Includes health states of decompensated cirrhosis, hepatocellular carcinoma, both decompensated cirrhosis and hepatocellular carcinoma, and liver transplantation.
§Includes health states of terminal (non–liver-related) and terminal (liver-related).

Interpretation

The 2010 Ontario Burden of Infectious Disease Study suggested that HCV infection had the highest health burden of any infectious disease in Ontario in terms of health-adjusted life years.[23] Our findings suggest that the financial burden of HCV infection is also high. Costs increased with severity of disease and were highest at the end of life ($8801 and $11 202 per 30 d for terminal non–liver-related and liver-related health states, respectively). We found that age, sex, immigrant status, previous treatment and especially comorbid illness were important predictors of health care costs. Costs for acute inpatient services were high in all health states and increased with disease progression. Costs for late-stage complications of chronic hepatitis C, including decompensated cirrhosis and liver transplantation, were very high. For example, our mean 30-day cost for decompensated cirrhosis, $3659, is similar to the initial-phase 30-day costs for the 4 most common cancers (breast, colorectal, lung and prostate), $1825–$5236 (2018 Canadian dollars)[24] and is much higher than the average 30-day cost for acute myocardial infarction, $452 (2018 Canadian dollars).[25]

Our findings suggest that the financial burden of HCV infection is substantially higher than previously estimated in Canada. Krajden and colleagues,[11] using data for British Columbia, estimated the total health care costs per 30 days to be $320 (2005 Canadian dollars) for early-stage HCV infection and $904 (2005 Canadian dollars) for late-stage HCV infection (including hepatocellular carcinoma, decompensated cirrhosis and compensated cirrhosis). After adjustment for inflation,[26] our cost estimate for no cirrhosis is almost twice their estimate ($798 v. $386), and our estimates for late-stage disease are at least 37% higher (ranging from $1487 for compensated cirrhosis to $8753 for both decompensated cirrhosis and hepatocellular carcinoma v. $1088). The differences may be due to different costing methods or care patterns, or updated treatments.

In a study in the United States, McAdam-Marx and colleagues[27] estimated the total 30-day health care costs of HCV-related compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma in 2010 to be US$1387, US$3439 and US$4807, respectively. When converted to 2018 Canadian dollars, these costs are congruent with ours ($1852 v. $1487, $4593 v. $3659 and $6420 v. $4238, respectively).[27] In a study in France, the 30-day costs for a hospital stay for HCV-related compensated cirrhosis, decompensated cirrhosis and hepatocellular carcinoma in 2010 were estimated to be €316, €1028 and €1149, respectively ($494, $1608 and $1797, respectively, in 2018 Canadian dollars).[28]

Limitations

Our study has several strengths. Because Ontario has publicly paid health insurance for physician and hospital services, and more than 97% of Ontarians are covered under OHIP,[17,18] we were able to capture use of almost all publicly funded health care services, by resource type. Although our cohort may not have included all asymptomatic patients with chronic HCV infection, it included all diagnosed cases of HCV infection in Ontario from 2003 to 2014. We defined health states in more detail than Krajden and colleagues.[11] Our approach is arguably more clinically meaningful and is more suitable for economic evaluations; most modelling studies[3,4,13] include similarly defined health states.[29]

Limitations of our study include that we excluded patients without valid OHIP numbers, and chronic hepatitis C disproportionately affects socioeconomically marginalized populations,[30] who may not have a permanent address from which to apply for publicly funded health insurance. We could not include costs borne by private health insurers or, more important, out-of-pocket costs paid by patients, many of whom are unable to work because of HCV infection. Patients who are not covered by the Ontario Drug Benefit program must pay for outpatient drugs, including antiviral therapy, out of pocket or through private insurance. Furthermore, our analysis was not able to distinguish between liver-related and non–liver-related costs. Thus, our results may over- or underestimate the economic burden of HCV infection.

Last, owing to data availability, we captured diagnostic information only to December 2014 and follow-up information to December 2016. Thus, our estimates do not fully capture recent screening recommendations and the use of the interferon-free direct-acting antivirals, which were approved for use in Canada in December 2014.[22] Our sensitivity analysis using data as of the approval of first-generation direct-acting antivirals (in 2012) onward[22] indicated that total health care costs for the noncirrhotic and compensated cirrhosis health states were higher during this later era than in earlier years, and outpatient drug costs accounted for higher proportions of total costs. Further analysis will be necessary when more data become available.

Conclusion

Our findings suggest that the financial burden of HCV infection is substantially higher than previously estimated in Canada. Our robust, comprehensive, up-to-date cost estimates for clinically defined health states of HCV infection should be useful for economic evaluations and to estimate the burden of illness for setting priorities, making decisions about reimbursement and forecasting costs. Although our results are most relevant to Ontario, the comprehensiveness of our study should allow analysts in other settings to understand relative costs across disease stages, including end-of-life costs, and the implications of age, sex, and particularly comorbid illness as predictors of total costs. Improving the quality of costing should strengthen the evidence basis of efforts to eliminate HCV infection in Canada and internationally.

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