Achievement of hepatitis C cascade of care milestones: a population-level analysis in Alberta, Canada

Conar R. O'Neil¹ · Emily Buss² · Sabrina Plitt^{2,3} · Mariam Osman^{2,4} · Carla S. Coffin⁵ · Carmen L. Charlton^{6,7} · Stephen Shafran¹

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Abstract

Objectives Despite highly effective directly acting antiviral (DAA) therapy for hepatitis C virus (HCV), many patients do not receive treatment. We characterized the achievement of cascade of care milestones within 2 years of diagnosis among the Alberta population and evaluated variables associated with engagement at each stage.

Methods All Albertans with a first-time positive HCV antibody between 2009 and 2014 were included in this retrospective study. We determined which patients received follow-up testing (HCV RNA and HCV genotype), referral to hepatitis specialty care, and antiviral prescription, and achieved SVR within 2 years of diagnosis. Factors associated with achieving cascade milestones were identified by multivariable logistic regression analysis.

Results Of 6154 patients with HCV antibody and complete follow-up, 4238 (68.9%) had HCV RNA testing, 2360 (38.3%) had HCV genotyping, 2096 (34.1%) were assessed by a specialist, 711 (11.6%) were prescribed treatment and 207 (3.4%) achieved SVR within 2 years of diagnosis. Independent variables associated with reduced likelihood of achieving cascade milestones were Indigenous heritage (adjusted odds ratio (AOR) 0.53 (0.41–0.68) for HCV RNA testing), unstable housing (AOR 0.50 (0.32–0.79) for specialist assessment) and alcohol misuse (AOR 0.61 (0.38–0.99) for antiviral prescription). Men, older patients, patients with a higher income and patients with more advanced liver disease were more likely to achieve cascade of care milestones.

Conclusion At each stage of patient engagement, opportunities for improvement were identified. Understanding the local cascade of care and factors associated with achieving cascade milestones will help prioritize initiatives to facilitate access to DAA therapy in Alberta.

Résumé

Objectifs Malgré la grande efficacité des traitements antiviraux à action directe (AAD) contre le virus de l'hépatite C (VHC), de nombreux patients ne sont pas traités. Nous avons caractérisé l'atteinte des étapes critiques de la cascade des soins dans les deux ans qui suivent le diagnostic dans la population de l'Alberta et évalué les variables associées à la participation à chaque étape.

Conar R. O'Neil and Emily Buss contributed equally to this work.

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✉ Conar R. O'Neil
conar@ualberta.ca

¹ Division of Infectious Diseases, Department of Medicine, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada

² School of Public Health, University of Alberta, Edmonton, Alberta, Canada

³ Centre for Communicable Disease and Infection Control, Public Health Agency of Canada, Ottawa, Ontario, Canada

⁴ Alberta Health, Edmonton, Alberta, Canada

⁵ Calgary Liver Unit, Division of Gastroenterology and Hepatology, University of Calgary Cumming School of Medicine, Calgary, Alberta, Canada

⁶ Provincial Laboratory for Public Health, Edmonton, Alberta, Canada

⁷ Division of Diagnostic and Applied Microbiology, Department of Laboratory Medicine and Pathology, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada

Méthode Tous les Albertains chez qui des anticorps anti-VHC ont été détectés pour la première fois entre 2009 et 2014 ont été inclus dans cette étude rétrospective. Nous avons déterminé quels patients ont subi un dépistage de suivi (ARN du VHC et génotype du VHC), lesquels ont été dirigés vers des soins spécialisés pour l'hépatite, lesquels se sont fait prescrire des antiviraux et lesquels ont présenté une réponse virale soutenue (RVS) dans un délai de deux ans du diagnostic. Les facteurs associés à l'atteinte des étapes critiques de la cascade ont été cernés au moyen d'une analyse de régression logistique multivariée.

Résultats Sur les 6 154 patients ayant des anticorps anti-VHC et ayant fait l'objet d'un suivi, 4 238 (68,9 %) ont subi un dépistage de l'ARN du VHC, 2 360 (38,3 %) ont subi un dépistage du génotype du VHC, 2 096 (34,1 %) ont été vus par un spécialiste, 711 (11,6 %) se sont fait prescrire un traitement, et 207 (3,4 %) ont présenté une RVS moins de deux ans après leur diagnostic. Les variables indépendantes associées à la probabilité réduite d'atteindre les étapes critiques de la cascade étaient l'ascendance autochtone [rapport de cotes ajusté (RCa) 0,53 (0,41-0,68) pour le dépistage de l'ARN du VHC], la précarité du logement [RCa 0,50 (0,32-0,79) pour l'évaluation par un spécialiste] et l'abus d'alcool [RCa 0,61 (0,38-0,99) pour la prescription d'antiviraux]. Les hommes, les patients âgés, les patients ayant un revenu élevé et les patients ayant une maladie hépatique à un stade avancé ont été les plus susceptibles d'atteindre les étapes critiques de la cascade des soins.

Conclusion Il y a matière à amélioration à chaque étape de la participation des patients. L'étude de la cascade des soins locale et des facteurs associés à l'atteinte des étapes critiques de cette cascade permettrait de définir les initiatives les mieux à même de faciliter l'accès aux traitements par AAD en Alberta.

Keywords Hepatitis C · Vulnerable populations · Delivery of health care · Canada

Mots-clés Hépatite C · Populations vulnérables · Prestations des soins de santé · Canada

Introduction

An estimated 1% of the Canadian population has been exposed to the hepatitis C virus (HCV) with approximately 75% developing chronic infection characterized by persistent detection of HCV RNA in serum (Micallef et al. 2006; Trubnikov et al. 2014). Chronic hepatitis C is associated with significant morbidity and mortality and a lifetime cost to the Canadian health system of \$64,000 per chronic infection (Myers et al. 2014). Furthermore, the disease burden is disproportionately borne by vulnerable populations, including people who inject drugs and Indigenous peoples (Chen and Krahn 2015; Ha et al. 2016). HCV treatment is associated with a significant reduction in mortality and morbidity; however, at present only a very small proportion of patients receive treatment (Iversen et al. 2017; Janjua et al. 2016; Simmons et al. 2015; Simmons et al. 2018; Yehia et al. 2014).

The landscape of HCV treatment has changed dramatically since the introduction of directly acting antiviral (DAA) therapy. A variety of treatment options are now available, all of which have minimal side effects, short (8–12-week) duration and efficacy of greater than 95% regardless of HCV genotype, degree of underlying liver disease, HIV co-infection or presence of active injection drug use (Falade-Nwulia et al. 2017; AASLD/IDSA 2015; European Association for Study of Liver 2015). Furthermore, there is emerging evidence that expansion of HCV treatment can reduce population-level HCV transmission, so-called 'treatment as prevention' (Grebely et al. 2013; Hagan et al. 2013; Hajarizadeh et al. 2016). Based on the success of DAAs, the World Health

Organization (WHO) announced a target of HCV elimination by 2030, which they define as a 90% reduction in HCV incidence (WHO 2016). In order to achieve this goal, an estimated 80% of eligible patients will need to be treated.

The province of Alberta removed fibrosis restriction for access to HCV treatment in April 2018, allowing patients to access treatment earlier after diagnosis. In anticipation of expanded access to HCV treatment in Alberta, our objective was to describe the state of HCV care and treatment in Alberta from 2009 until 2016. We aimed to characterize achievement of HCV cascade of care indicators from diagnosis to sustained virologic response (SVR) within a 2-year follow-up period for all newly diagnosed patients. Our secondary objective was to identify independent predictors of achieving cascade of care milestones.

Methods

All patients with a newly identified positive HCV antibody between January 1, 2009 and December 31, 2014 and a valid Alberta personal health care number (PHN) were included in this retrospective cohort study. All patients were assessed for a 2-year period following their HCV antibody testing to determine if HCV RNA and HCV genotyping was performed, if the patient was assessed by a hepatitis specialist and if HCV antiviral therapy was prescribed with successful achievement of SVR. This study was approved by the Health Research Ethics Board at the University of Alberta.

Study population

Newly positive HCV antibody results were identified through the Alberta Provincial Laboratory for Public Health (ProvLab) Laboratory Information System (LIS). HCV testing (HCV antibody, HCV RNA and HCV genotyping) in Alberta is centralized to ProvLab and thus these records are representative of the Alberta population with the exception of a minority of patients tested privately (e.g., for insurance purposes) or under federal jurisdiction (e.g., federal penitentiary system). All newly positive HCV antibody results identified at ProvLab are reported to the Provincial Public Health Department (Alberta Health) for follow-up. Public health nurses contact patients and provide education on HCV and harm reduction as well as complete the Notifiable Disease Report (NDR). HCV risk factors, Indigenous heritage, and immigration status are recorded on the NDR and then compiled in the Communicable Disease Reporting System (CDRS).

Database generation

Basic demographic information as well as HCV RNA and HCV genotype were obtained from the ProvLab LIS. Geographic area and income quintile were derived from postal code. Geographic area was based on local planning aggregates, which include the total population and population density as previously described (Passi et al. 2017). Estimated income was determined from pooled 2011 Alberta census estimates and divided into quintiles for both rural and urban postal codes. Quintile 1 represented the lowest incomes, ranging from \$8978 to \$24,287 in rural postal codes and \$1554 to \$29,373 in urban postal codes. Quintile 5 captured the highest median incomes, ranging from \$41,050 to \$67,577 in rural postal codes and \$48,124 to \$122,760 in urban postal codes.

Other demographic information, including immigration history, Indigenous heritage, hepatitis B or HIV co-infection, and risk factor data, were obtained from the CDRS. Indigenous heritage was self-reported and includes people of Inuit, Métis, and First Nations heritage. Risk factor information was self-reported and included unstable housing, history of incarceration, history of alcohol misuse and history of injection drug use. The aspartate aminotransferase (AST) to platelet ratio index (APRI) was used as a surrogate for advanced fibrosis or cirrhosis. An APRI threshold of ≥ 1.0 is 76% sensitive and 72% specific for cirrhosis (Lin et al. 2011). AST and platelet values were obtained from provincial databases (University of Alberta Hospital LIS, Calgary Lab Services and DynaLIFE®). If multiple values were available, the closest to the date of HCV antibody testing was used. HCV treatment information was obtained from the Pharmacy Integration Network (PIN), a provincial repository of all medication prescriptions in Alberta. The minority of patients who received HCV treatment as part of a clinical trial are not captured in

this database. The Alberta Vital Statistics database was used to identify patients who died within 2 years of HCV antibody testing.

Evaluation of cascade milestones

Patients with any positive HCV RNA, including a single measurement, were considered to have chronic hepatitis C for the purposes of this analysis. During the study period, HCV genotype required submission of a second blood sample. Assessment by an HCV care provider was defined as having an AST or complete blood count (CBC) ordered by an HCV care provider within 2 years of a positive HCV antibody result or if the patient was prescribed HCV treatment. An HCV care provider was defined as a hepatologist, an infectious disease specialist known to treat HCV, or an internist or family physician known to treat HCV. Non-specialist HCV care providers were identified through known contacts of the authors and cross-referenced with the list of prescribing providers for HCV treatment obtained from the PIN database. We defined SVR as a negative HCV RNA at least 16 weeks following the last dispensed antiviral. This definition assumes antivirals were dispensed on at most a monthly basis, the standard of care during our study period.

Statistical analysis

Statistical analyses were performed using STATA 15 (StataCorp. 2017. College Station, TX, USA). Patients achieving cascade of care milestones are described as a proportion of total HCV antibody positive patients and as a proportion of patients achieving the preceding step in the cascade. Patients who died prior to 2 years of follow-up were included in the cohort for the purposes of descriptive statistics but excluded from cascade of care analysis and multivariable logistic regression. Simple and multivariable logistic regression was performed to identify independent factors associated with progression to HCV cascade of care milestones. Simple logistic regression was used to investigate significance ($p < 0.05$) of individual variables. Variables that were significant in simple logistic regression or were of particular clinical significance were retained in the multivariable model. Final regression models were assessed by Hosmer–Lemeshow goodness of fit tests.

Results

New case description

We identified 10,601 patients with a positive HCV antibody, of whom 6292 had a valid PHN, were confirmed to be newly positive and were thus included in our study population (Table 1 and Supplementary Table 1). The remaining patients

Table 1 Baseline characteristics of patients with positive hepatitis C antibody ($n = 6292$)

Characteristic	Number of patients (%)
Gender ($n = 6260$)	
Male	3985 (63.7%)
Birth cohort ($n = 6288$)	
Pre-1950	535 (8.5%)
1950–1959	1931 (30.7%)
1960–1969	1584 (25.2%)
1970–1979	1145 (18.2%)
1980 and later	1093 (17.4%)
Geographic area ($n = 6283$)	
Rural remote	165 (2.6%)
Rural	1021 (16.3%)
Urban	743 (11.8%)
Metropolitan (Edmonton or Calgary)	4354 (69.3%)
Income quintile ($n = 6227$)	
Quintile 1 (lowest)	1907 (30.6%)
Quintile 2	1223 (19.6%)
Quintile 3	1649 (26.5%)
Quintile 4	788 (12.7%)
Quintile 5 (highest)	660 (10.6%)
HCV acquired outside of Canada ($n = 6176$)	
Any	756 (12.2%)
South Asia	259 (4.2%)
Southeast or East Asia	198 (3.2%)
Europe	110 (1.8%)
Africa	74 (1.2%)
Other	115 (1.9%)
Indigenous heritage ($n = 3876$)	816 (21.1%)
Social determinants ($n = 5244$)	
Unstably housed	463 (8.8%)
History of incarceration	454 (8.7%)
Alcohol misuse	730 (13.9%)
History of injection drug use ^a	1937 (36.9%)
Co-infections ($n = 6292$)	
Chronic hepatitis B	69 (1.1%)
HIV	134 (2.1%)
APRI score ≥ 1 ($n = 4247$)	1490 (35.1%)
HCV genotype ($n = 2347$)	
Genotype 1	1480 (63.1%)
Genotype 2	251 (10.7%)
Genotype 3	542 (23.1%)
Genotype 4	50 (2.1%)
Genotype 5, 6 or mixed	24 (1.0%)

HCV hepatitis C virus, HIV human immunodeficiency virus, APRI aspartate aminotransferase to platelet ratio index

^a Inclusive of past or current injection drug use

were either found to have been previously diagnosed ($n = 2865$) or had no PHN associated with their laboratory result

($n = 1444$). Of patients included in the study population, 63.7% of patients were male with a median age at diagnosis of 48 (interquartile range 37–56). Most patients (69.3%) resided in Edmonton or Calgary and just over half (50.3%) had an income in the lowest two quintiles. 12.2% of patients reported acquiring HCV outside of Canada. Of 3876 patients with available data, 816 (21.1%) self-identified as having Indigenous heritage. A minority of patients reported being unstably housed (8.8%) or having a history of incarceration (8.7%). 13.9% reported alcohol misuse while 36.9% reported a history of injection drug use. Hepatitis B and HIV co-infection were rare at 1.1% and 2.1%, respectively. 35.1% of patients had an APRI score ≥ 1.0 , suggestive of advanced fibrosis or cirrhosis. 138 patients (2.2%) died within 2 years of diagnosis and were thus excluded from subsequent analysis.

Cascade of care milestones

Of the 6154 HCV antibody-positive patients examined, 4238 (68.9%) had HCV RNA testing, 2360 (38.3%) had HCV genotyping, 2096 (34.1%) were assessed by an HCV specialist, 711 (11.6%) were prescribed HCV treatment and 207 (3.4%) achieved SVR within 2 years of diagnosis (Fig. 1 and Supplementary Table 1). Of patients who had HCV RNA testing, 76.5% (3244) were positive. Of viremic patients, 72.7% (2360) had HCV genotyping. Of these patients, 88.8% (2096) were assessed by HCV specialist. Of those assessed by a specialist, 33.9% (711) were prescribed HCV treatment, and of these, 29.1% (207) achieved SVR (Fig. 1). The proportion of patients with HCV RNA testing varied by year of diagnosis: increasing from diagnosis in 2009 to 2010, decreasing from 2012 to 2013 and increasing from 2013 to 2014 (Fig. 2). The proportion of patients receiving specialist assessment decreased from diagnosis years 2010 to 2012 and the proportion of patients receiving antiviral prescription increased from 2013 to 2014. The proportion of patients achieving SVR decreased from 2012 to 2013 but increased for those diagnosed in 2014.

Of HCV-treated patients, 56.8% (404) were prescribed pegIFN (pegylated interferon) plus RBV (ribavirin), 17.0% (121) were prescribed a DAA plus pegIFN with or without RBV, and 26.2% (186) were prescribed pegIFN-free, DAA-based therapy with or without RBV. 12.0% (85) of patients received more than one course of HCV treatment during the follow-up period. Of HCV-treated patients who did not achieve SVR within the 2-year follow-up period, 133/504 (26.4%) achieved SVR by the end of the overall study period (December 2016). Thus, 5.4% (340/6292) of the overall cohort achieved SVR by the end of the study period.

Fig. 1 Achievement of hepatitis C cascade of care milestones within 2 years of diagnosis in Alberta (2009–2016). *HCV* hepatitis C virus, *RNA* ribonucleic acid, *SVR* sustained virologic response. Percentages are presented as a proportion of total HCV antibody positive patients

(above each bar) and as a proportion of patients achieving the preceding step in the cascade (between bars). HCV genotyping is presented as a proportion of those who were HCV RNA positive (between bars)

Multivariable logistic regression analysis (Table 2)

Patients diagnosed later in the study period were less likely to have HCV RNA testing (adjusted odds ratio (AOR) 0.52 (0.36–0.75) for 2013 and AOR 0.65 (0.44–0.95) for 2014; both compared to 2009) and specialist assessment (AOR 0.54 (0.34–0.88) for 2014) but were more likely to have been prescribed treatment (AOR 2.08 (1.24–3.52)) and achieve SVR (AOR 7.85 (2.76–22.29)). Men were significantly more likely to have had a specialist assessment (AOR 1.51 (1.14–2.00)) but gender was not a predictor of achieving other cascade of care milestones. Older patients were more likely to have HCV RNA testing (AOR 1.42 (1.01–1.99) for the 1950–59 birth cohort compared to 1980 or later birth cohort),

specialist assessment (AOR 1.87 (1.22–2.87) for the 1950–59 birth cohort) and antiviral prescription (AOR 4.10 (2.13–7.91) for the 1950–59 birth cohort). Birth cohort did not predict achievement of SVR. Patients with a higher income were more likely to have HCV RNA testing (AOR 2.15 (1.43–3.23) for quintile 4 compared to quintile 1), specialist assessment (AOR 2.11 (1.34–3.32) for quintile 4 and AOR 1.64 (1.01–2.66) for quintile 5) and to achieve SVR (AOR 3.74 (1.44–9.69) for quintile 4). Patients with advanced fibrosis or cirrhosis (APRI score ≥ 1.0) were more likely to have a specialist assessment (AOR 1.38 (1.04–1.83)) and to have been prescribed treatment (AOR 1.44 (1.05–1.96)). Indigenous patients were half as likely to have HCV RNA testing (AOR 0.53 (0.41–0.68)) and were less likely to achieve other

Fig. 2 Proportion of patients achieving hepatitis C cascade of care milestones by year of diagnosis in Alberta (2009–2016). *HCV* hepatitis C virus, *RNA* ribonucleic acid, *SVR* sustained virologic response

Table 2 Multivariable logistic regression for variables associated with achieving hepatitis C cascade of care milestones within 2 years of diagnosis in Alberta (2009–2016)

	HCV RNA testing (<i>n</i> = 2130) AOR (95% CI)	Hepatitis specialist assessment (<i>n</i> = 1364) AOR (95% CI)	Antiviral prescription (<i>n</i> = 1027) AOR (95% CI)	SVR (<i>n</i> = 235) AOR (95% CI)
Year of diagnosis (ref = 2009)				
2010	1.20 (0.79–1.80)	1.06 (0.66–1.68)	1.08 (0.69–1.70)	1.22 (0.49–3.04)
2011	1.23 (0.83–1.83)	0.71 (0.45–1.11)	0.86 (0.53–1.40)	0.94 (0.33–2.67)
2012	1.07 (0.71–1.59)	0.70 (0.44–1.11)	1.16 (0.66–2.02)	1.93 (0.62–5.98)
2013	0.52** (0.36–0.75)	0.66 (0.41–1.06)	1.21 (0.71–2.06)	Omitted [†]
2014	0.65* (0.44–0.95)	0.54* (0.34–0.88)	2.08** (1.24–3.52)	7.85** (2.76–22.29)
Gender				
Male	1.07 (0.85–1.35)	1.51** (1.14–2.00)	1.10 (0.79–1.53)	1.22 (0.59–2.50)
Birth cohort (ref = 1980 or later)				
1970–1979	0.95 (0.67–1.33)	0.66 (0.42–1.02)	2.63* (1.27–5.48)	0.86 (0.18–4.11)
1960–1969	1.18 (0.85–1.65)	1.02 (0.67–1.55)	3.34** (1.72–6.48)	0.39 (0.09–1.65)
1950–1959	1.42* (1.01–1.99)	1.87** (1.22–2.87)	4.10** (2.13–7.91)	0.50 (0.12–2.03)
Pre-1950	1.35 (0.81–2.26)	1.09 (0.61–1.96)	1.76 (0.76–4.10)	0.62 (0.10–3.83)
Geographic area (ref = rural remote)				
Rural	1.00 (0.55–1.79)	1.52 (0.71–3.23)	0.96 (0.36–2.57)	0.36 (0.04–3.20)
Urban	1.09 (0.58–2.05)	1.23 (0.56–2.68)	1.86 (0.69–5.04)	0.48 (0.06–4.05)
Metropolitan	1.22 (0.69–2.15)	1.53 (0.75–3.14)	1.25 (0.49–3.17)	0.70 (0.09–5.28)
Income quintile (ref = quintile 1)				
Quintile 2	1.06 (0.79–1.42)	1.17 (0.81–1.69)	1.19 (0.76–1.86)	1.32 (0.48–3.67)
Quintile 3	1.18 (0.88–1.59)	1.37 (0.96–1.95)	1.22 (0.80–1.88)	1.57 (0.61–4.04)
Quintile 4	2.15** (1.42–3.23)	2.11** (1.34–3.32)	1.60* (1.01–2.55)	3.74** (1.44–9.69)
Quintile 5 (highest)	1.03 (0.71–1.50)	1.64* (1.01–2.66)	1.50 (0.87–2.57)	2.30 (0.70–7.55)
APRI score (ref < 1.0)				
≥ 1.0	1.09 (0.86–1.37)	1.38* (1.04–1.83)	1.44* (1.05–1.96)	1.39 (0.71–2.73)
HCV acquired outside of Canada	3.28 (0.42–25.71)	0.97 (0.24–3.97)	0.53 (0.06–4.76)	Omitted [†]
Indigenous heritage	0.53** (0.41–0.68)	0.74 (0.53–1.04)	0.65 (0.41–1.04)	0.53 (0.18–1.54)
Social determinants				
Unstably housed	0.75 (0.53–1.07)	0.50** (0.32–0.79)	0.47 (0.20–1.07)	0.41 (0.06–2.79)
History of incarceration	0.93 (0.66–1.30)	0.93 (0.59–1.46)	0.81 (0.44–1.50)	0.60 (0.15–2.44)
Alcohol misuse	0.81 (0.61–1.07)	0.79 (0.55–1.14)	0.61* (0.38–0.99)	0.76 (0.25–2.33)
Person who injects drugs	0.89 (0.72–1.11)	0.91 (0.70–1.20)	0.83 (0.61–1.13)	0.94 (0.48–1.84)
Co-infections				
Chronic hepatitis B	1.81 (0.49–6.68)	0.62 (0.13–2.87)	Omitted [†]	Omitted [†]
HIV	1.28 (0.74–2.21)	7.96** (2.70–23.47)	0.15 (0.02–1.14)	Omitted [†]
HCV genotype (ref = genotype 1)				
Genotype 2			3.14** (2.01–4.90)	3.98** (1.62–9.76)
Genotype 3			2.54** (1.75–3.68)	2.87** (1.34–6.17)
Genotype 4, 5, 6 or mixed			0.64 (0.07–5.47)	Omitted [†]

Number of variables included in models lower than total number of individuals reaching cascade milestones due to missing data

HCV hepatitis C virus, RNA ribonucleic acid, AOR adjusted odds ratio, CI confidence interval, SVR sustained virologic response, APRI aspartate aminotransferase to platelet ratio index, HIV human immunodeficiency virus

* $p < 0.05$, ** $p < 0.01$. [†] Not calculated due to zero cell count or co-linearity

cascade milestones within the follow-up period, although this did not reach statistical significance. Patients reporting unstable housing were significantly less likely to have a specialist assessment (AOR 0.50 (0.32–0.79)) and patients reporting alcohol misuse were less likely to be prescribed treatment (AOR 0.61 (0.38–0.99)). A history of injection drug use was not a statistically significant predictor of achieving cascade of care milestones.

Discussion

In our large population-based cohort, we identified substantial gaps in the HCV cascade of care in Alberta. Only two thirds of patients were tested for HCV viremia, only one third was assessed by an HCV care provider and very few achieved SVR within 2 years of diagnosis. We found that Indigenous people, women, people who are unstably housed and people with the lowest income were less likely to achieve cascade of care milestones.

Similar rates of HCV RNA testing, specialist referral, and treatment initiation have been observed in other population-based studies conducted prior to the introduction of DAAs (Iversen et al. 2017; Janjua et al. 2016; Maier et al. 2016; Simmons et al. 2018; Yehia et al. 2014). A British Columbia study showed only 74% of people testing anti-HCV positive had HCV RNA testing, and only 16% received treatment (Janjua et al. 2016). In England, the rates of HCV RNA testing and treatment initiation were 77% and 21%, respectively (Simmons et al. 2018). A similar study of over 200,000 American veterans demonstrated a comparable rate of HCV treatment initiation (Maier et al. 2016). Accessing HCV care can be particularly challenging for people who inject drugs (PWID). Iversen et al. (2017) showed that among 43,000 PWIDs in Australia who tested anti-HCV positive, only 46% had HCV RNA testing and only 8% initiated treatment (Iversen et al. 2017).

We identified a significant gap between HCV antibody detection and follow-up measurement of HCV RNA. This was particularly apparent among Indigenous peoples. This gap could be addressed in a number of ways. Reflexive HCV RNA testing for all patients with newly positive HCV antibody would eliminate this step in the cascade entirely. When this was implemented as part of a comprehensive HCV pathway in one American study, 100% of patients had HCV RNA testing and 70% of viremic patients were retained in care (Jonas et al. 2016). Further, a variety of point-of-care tests, such as finger stick HCV viral load testing, have been evaluated (Coats and Dillon 2015; Lamoury et al. 2018). Point-of-care testing can be particularly helpful in high-risk groups and in settings where laboratory testing may not be readily available, such as many Indigenous communities.

One component of the HCV cascade of care not addressed by our investigation was the prevalence of undiagnosed HCV. Previous Canadian analyses estimate the rate of undiagnosed HCV to be 21–44% (Remis 2007; Trubnikov et al. 2014). If we conservatively estimate that the 6292 patients diagnosed with HCV infection represent 75% of HCV cases in Alberta, then there would be 8389 new HCV infections during our study period, with only 8.5% being prescribed antiviral treatment. Patients with undiagnosed HCV are at risk of progressive liver disease and are a reservoir for ongoing transmission. In order to meet the WHO goals for HCV elimination, expanding access to HCV treatment must be coupled with expanded hepatitis screening and public health capacity.

Our study has several limitations. First, 13.6% of patients with positive HCV antibody had no recorded PHN and therefore could not be confirmed to be new cases or linked to the analytic database. Patients tested anonymously and non-Alberta residents may account for some of this difference. Second, our estimate of specialist assessment is derived from an indirect measure utilizing submitting physician on laboratory records and is thus subject to possible bias. Third, HCV risk factors collected through the NDR forms are likely underreported. In an earlier national study, injection drug use was the most common risk factor for HCV transmission in Canada accounting for 61% of infections, compared to 36.9% in our study (Public Health Agency of Canada 2009). Fourth, our study restricted the follow-up period to 2 years following diagnosis as we considered this to be an achievable clinical goal and allowed us to examine trends over time in a straightforward manner. However, we acknowledge that some patients who were not engaged in care in a timely manner may not have had sufficient time to complete treatment and document SVR, especially if they received prolonged interferon treatment. Because of this, our results may be lower than those from other HCV cascade care of analyses which allowed for longer follow-up. Finally, the landscape of HCV care and access to DAAs underwent considerable change during our study period and thus caution is advised in extrapolating our findings to other settings. Our study includes an era of transition in HCV care from IFN-based treatment to IFN-free DAA-based treatment, for which access was restricted to patients with at least moderate liver fibrosis. First-generation DAAs were approved in Canada in 2011, though interferon-free therapy was not widely available until 2015–2016. During that time in Alberta, access to treatment was restricted to patients with certain comorbidities (for example, greater than F2 fibrosis, HIV co-infection, extrahepatic manifestations). A later year of diagnosis was associated with decreased likelihood of specialist assessment, but increased likelihood of antiviral initiation and SVR. This may reflect an increase in referrals to specialists (due to DAA availability), thus delaying timely assessment. However, once patients were assessed they were more likely to receive DAA-based therapy and therefore achieve SVR.

Conclusion

We identified key factors associated with failure to achieve cascade of care milestones. In particular, Indigenous persons were less likely to receive appropriate follow-up testing; young people, women, and those who were unstably housed were less likely to have seen a hepatitis specialist, and patients reporting alcohol misuse were less likely to be prescribed antiviral therapy. Improved understanding of the local cascades of care will allow us to prioritize initiatives as access to DAA therapy in Alberta is expanded. Furthermore, cascade of care analyses provide a framework to evaluate delivery of HCV care over time and within subgroups in order to monitor the impact of new screening and linkage to care initiatives.

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Compliance with ethical standards

Conflict of interest CSC reports grants from Glaxo-Smith-Kline, Gilead Sciences, Arbutus Biopharma, Bristol-Myers Squibb, Merck, Janssen Inc., Springbank Pharmaceuticals and Transgene; advisory board membership for Merck, Gilead and Glaxo-Smith-Kline; and CTPC committee membership for Springbank Pharmaceuticals. CLC reports grants from Merck. SS reports grants from AbbVie, Bristol-Myers Squibb, Janssen Inc. and Merck. There are no other competing interests.

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