Variation between Canadian centres in the uptake of treatment for Hepatitis C by patients co-infected with HIV – a cohort study

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Abstract

Background

Uptake of HCV treatment in Canada is low despite its publicly funded health care system. We explored HCV treatment uptake within the Canadian Co-infection Cohort (CCC) to see if some treatment centres were more successful than others at starting co-infected patients on HCV treatment.

Methods

We estimated the variation between centres in HCV treatment uptake using a Weibull time to event model with adjustment for patient characteristics thought likely to influence treatment uptake. We asked the principal investigator at each centre about access to hepatitis related specialists and services and the importance of various criteria when determining whether patients should be treated for HCV.

Results

Among 681 untreated patients in the CCC, 163 patients started HCV treatment over a period of 1827 years (9 per 100 patient years). Even with case mix adjustment, there was still appreciable variation in treatment uptake between centres with mean hazard ratios of 0.42 and 3.6 for the centres least and most likely to start the average co-infected patient on HCV treatment. The most important criteria for principal investigators when determining eligibility for treatment were fibrosis severity, current psychiatric co-morbidities, current alcohol intake, past HCV treatment and a history of re-infection with HCV. However opinions were wide ranging: 8 of the 15 criteria elicited both the responses ‘less important’ and ‘very important’.

Interpretation

The magnitude of centre effects and diverse opinions about the importance of treatment eligibility criteria suggest provider related barriers to HCV treatment uptake are as important as patient related barriers.

Introduction

The burden of hepatitis C virus (HCV) on the Canadian health care system has steadily increased since the 1990s, and is expected to further increase as patients age.[1] Patients co-infected with HCV and HIV have shown 'alarming' annual increases of 30 to 40% in liver-related and all-cause HCV hospitalisations.[1] Curative treatment for HCV is available and cost effective for patients both with and without HIV coinfection,[2;3] greatly reducing progression to end-stage liver disease, decompensation, transplantation, hospitalisation and death. For co-infected patients, effective treatment for HCV also reduces HIV progression and non-liver related mortality.[4;5]

Current HCV treatment is complex, difficult to tolerate, and requires expert supervision. Uptake of HCV treatment in Canada is low despite its publicly funded health care system and 'unacceptably' low among injection drug users, the risk group within which most new infections arise.[6] In a recent survey, 80% of Canadian physicians specialised in HCV said they were not likely to treat active injection drug users.[7] Injection drug users are often considered ineligible for treatment because of poor adherence to care, psychiatric illness, or ongoing drug or alcohol use.[8;9] Even if eligible, patients may be reluctant to start treatment.[10] Patients are less likely to be offered and to accept HCV treatment if older, male, not Caucasian, infected with difficult to treat genotypes, afflicted with psychiatric illness, or if using drugs or alcohol.[11-13] Many studies have evaluated these patient related barriers to treatment,[14;15] which are difficult to overcome. Provider and institutional barriers are also important,[11;16] and perhaps more amenable to intervention. While an experienced provider is clearly important for the uptake of HCV treatment,[11-13] it is not clear what other provider and institutional barriers are involved.

Given that most co-infected patients are current or past injection drug users, this subgroup represents a priority for HCV treatment if transmission risk is to be reduced and

healthcare costs contained. This will require a better understanding of provider and institutional barriers to treatment in a Canadian context. We investigated HCV treatment uptake within the Canadian Co-infection Cohort (CCC) to see if some treatment centres were more successful than others at starting patients on HCV treatment and explored factors that could be associated with between centre differences.

Methods

The CCC is a prospective cohort of adult patients infected with both HIV and HCV.[17] Patients are enrolled at 16 centres across Canada, with centres in university hospitals and community based clinics in both small and large urban areas. Cohort patients complete questionnaires and provide a blood sample at follow up visits scheduled every six months.

We modelled time to HCV treatment uptake in cohort patients not receiving such treatment at or prior to enrolment. We fitted a Weibull time to event model with a normally distributed random intercept for each centre so we could estimate the variation between centres in treatment uptake. In this model, we adjusted for patient characteristics thought likely to influence treatment uptake and then ranked centres according to their success in starting patients on HCV treatment. To allow for differences between centres in case mix, we adjusted for the following covariates: age, gender, ethnicity, genotype; and at cohort entry, duration of HCV infection, use of combination antiretroviral therapy, CD4 cell count, and self-reported homelessness, use of injection drugs, and use of alcohol.[11-13] In two subsequent analyses, additional covariates were added to the model to allow for differences in treatment uptake between provinces (British Colombia, Ontario and Alberta, Quebec and Nova Scotia) or between primary and tertiary care centres. The model was fit in WinBUGS using uninformative prior distributions for each of the model's parameters: normal distributions with large variance for covariate effects;[18] a wide uniform distribution for the standard deviation of centre effects.[19]

In a sensitivity analysis, we added prior information about centre effects. We modelled the probability that patients received HCV treatment at or prior to enrolment using a log binomial model that included the covariates listed above.[20;21] With this model, we estimated the risk in each centre that patients were treated at enrolment relative to the average risk across all centres.

These risk ratios were then used to calculate a mean for the prior distribution for each centre effect, rather than assuming a normal distribution with mean zero.

To explore possible reasons for differences in HCV treatment uptake between centres, we invited the principal investigator at each centre to complete a web based survey (www.surveymonkey.com). We asked questions about access to hepatitis related specialists and services and the importance of various criteria when determining whether patients should be treated for HCV. We calculated associations between the specialists and services available at each centre and the median centre ranks from our model for HCV treatment uptake.

Results

Among the 1119 patients in the cohort (as at 1 July 2012), 100 patients had spontaneously cleared HCV when enrolled, 184 patients started HCV treatment prior to or at enrolment and 154 patients had no additional follow up beyond enrolment. Among the remaining 681 patients, 163 patients started HCV treatment over a period of 1827 patient years (9 patients per 100 years of follow up). Those starting HCV treatment, either at enrolment or later, were more likely to be male, infected with HCV genotype 2 or 3 and on antiretroviral therapy, and were less likely to be of aboriginal ethnicity or to report either crack or cocaine use (Table 1). On average patients starting HCV treatment had been infected with HCV for a shorter duration but had a higher aspartate aminotransferase to platelet ratio index (APRI) score indicating more advanced fibrosis.

In a Weibull model of treatment uptake beyond enrolment, patients of aboriginal ethnicity, infected with HCV for longer or reporting crack or cocaine use were less likely to start HCV treatment, while those with easier to treat genotypes or higher CD4 cell counts at enrolment were more likely to start HCV treatment (Table 2). Even with case mix adjustment, there was still appreciable variation in treatment uptake between centres (estimated between centre variance [σ^2] = 0.9, 95% credible interval [CI] 0.5 to 1.5, without informative centre priors; σ^2 = 0.9, 95% CI 0.5 to 1.5, with informative centre priors). This variation was not reduced by adding additional covariates to the model to allow for any differences either between provinces (σ^2 = 0.9, 95% CI 0.4 to 1.6) or between primary and tertiary care centres (σ^2 = 0.9, 95% CI 0.5 to 1.6).

There was considerable uncertainty about which centres were best at starting the average patient on HCV treatment (Figure 1). Adding prior information about centre effects did not

reduce the uncertainty in this analysis. However Centres 8 and 15 appeared particularly effective at getting patients started on HCV treatment.

The principal investigator in each centre reported access to tests for HCV and HIV, HCV genotyping and liver biopsy and to hepatologists and nephrologists in all or nearly all centres (Table 3). Neither transient elastography (Fibroscan) nor addiction services were always available but tended to be available in centres where patients were more likely to start HCV treatment. The most important criteria for principal investigators when determining eligibility for treatment were (Table 4): fibrosis severity (median score 5 [where 1 = less important, 5 = very important]), current psychiatric co-morbidities (4), current alcohol intake (4), past HCV treatment (4), a history of re-infection with HCV (4), HCV genotype (3.5) and current injection drug use (3.5). However opinions were wide ranging and 8 of the 15 criteria elicited both the responses ‘less important’ and ‘very important’.

Interpretation

There is variation in the uptake of HCV treatment between our cohort centres that cannot be explained by differences in the patients seen at each centre. The centre effects are considerable, relative to the effects of patient characteristics, with mean hazard ratios of 0.42 and 3.6 for the centres least and most likely to start the average co-infected patient on HCV treatment. These between centre differences seem independent of the province or whether treatment takes place in a primary care or tertiary hospital setting. These differences may be related to access to transient elastography, a simple and safe method for liver disease staging, and to addiction services. It is plausible that access to these services promotes treatment uptake given that fibrosis severity and drug and alcohol abuse are seen as important criteria when determining eligibility for treatment. But it is just as plausible that diverse opinions about patient eligibility for treatment are responsible for between centre differences either through centre treatment policies or through individual decision making.

A previous US study has shown that provider differences can be as important as patient differences in explaining variability in HCV treatment uptake, with institutional differences far less important.[11] This suggests that the differences seen here between centres are more likely due to individual decision making rather than access to specialists and services. At the time of our study, regulations governing access to HCV treatment were more restrictive in some provinces than others: in British Columbia, regulations required biopsy-proven fibrosis or abnormal hepatic transaminases; in Alberta and Ontario, regulations required evidence of fibrosis; whereas in Quebec and Nova Scotia, regulations required only the presence of chronic HCV. Hence in our model, we grouped a centre in Alberta with centres in Ontario and a centre in Nova Scotia with centres in Quebec. In theory, the trend away from federal health care administration could

increase disparity between provinces in access to health services.[22;23] The restrictive policies in some provinces have been cited as a barrier to HCV treatment by patients and providers.[24] While we found no evidence of provincial effects in our data, our estimates were not precise enough to rule out such effects.

While it is clear that there are differences between cohort centres in treatment uptake, there is considerable uncertainly when ranking centres according to their success at starting patients on treatment. Including prior information on treatment uptake prior to or at cohort enrolment did not reduce this uncertainty. As a result, our estimates of associations between access to specialists and services and centre rankings are approximate. In any case, access to transient elastography and addiction services could simply be a characteristic of centres where patients are started on treatment, rather than services that will encourage treatment uptake if provided. We did not survey all clinicians working at each centre, and between centre differences could be due, at least in part, to different levels of clinical experience and expertise at each centre. The survey itself was relatively informal and it did not cover all aspects of clinical decision making; therefore its results are exploratory and should be interpreted with caution. Treatment success is ultimately measured by the rate at which patients achieve a sustained viral response after treatment, and not by the rate at which patients start treatment. Nevertheless, a necessary first step to improving treatment success in co-infected patients is to convince patients and providers to attempt treatment.

Effective treatment is now available for HCV and will become even more so when combined with new direct acting antivirals. Increased treatment uptake by co-infected patients is essential to reduce the transmission of HCV and contain future health care costs.[25] Programs designed to increase HCV treatment uptake in injection drug users are being introduced in

Canada,[26] when it is not clear how best to improve the unacceptably low uptake in this key patient population.[7] Patient related barriers to treatment uptake are important but difficult to overcome. Our study suggests provider barriers are as important – the magnitude of centre effects in our study are surprising, as are the diverse opinions held by our principal investigators about the importance of eligibility criteria for treatment. All but two of our principal investigators have had more than 10 years experience in clinical practice. Training and continuing medical education programmes have been recommended to widen the pool of clinicians comfortable treating HCV,[27] but even specialists can be reluctant to treat injection drug users.[7] Qualitative research is needed to explore whether certain patients would receive HCV treatment in some centres but not in others and if so, why that is. Our results also suggest that there is an urgent need for updated HCV treatment and management guidelines for co-infected patients and these guidelines need to be disseminated to and adopted by both primary care givers and specialists.

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Contributors

Study design – JY, MP, JC, MBK; survey design – MP; collected data – MP, JC, CC, JG, MH, SW, MBK; data analysis – JY (guarantor); wrote first draft – JY, MBK; contributed to subsequent drafts – MP, JC, CC, JG, MH, SW; all authors approved the draft submitted for publication.

References

1. Myers RP, Liu M, Shaheen AA. The burden of hepatitis C virus infection is growing: a Canadian population-based study of hospitalizations from 1994 to 2004. *Can J Gastroenterol* 2008;22:381-7.

2. Campos NG, Salomon JA, Servoss JC, Nunes DP, Samet JH, Freedberg KA et al. Cost-effectiveness of treatment for hepatitis C in an urban cohort co-infected with HIV. *Am J Med* 2007;120:272-9.

3. Grishchenko M, Grieve RD, Sweeting MJ, De Angelis D, Thomson BJ, Ryder SD et al. Cost-effectiveness of pegylated interferon and ribavirin for patients with chronic hepatitis C treated in routine clinical practice. *Int J Technol Assess Health Care* 2009;25:171-80.

4. Berenguer J, Alvarez-Pellicer J, Martin PM, Lopez-Aldeguer J, Von Wichmann MA, Quereda C et al. Sustained virological response to interferon plus ribavirin reduces liver-related complications and mortality in patients coinfected with human immunodeficiency virus and hepatitis C virus. *Hepatology* 2009;50:407-13.

5. Berenguer J, Rodriguez E, Miralles P, Von Wichmann MA, Lopez-Aldeguer J, Mallolas J et al. Sustained virological response to interferon plus ribavirin reduces non-liver-related mortality in patients coinfected with HIV and Hepatitis C virus. *Clin Infect Dis* 2012;55:728-36.

6. Grebely J, Raffa J, Lai C, Krajden M, Kerr T, Fischer B et al. Low uptake of treatment for hepatitis C virus infection in a large community-based study of inner city residents. *J Viral Hepat* 2009;16:352-8.

7. Myles A, Mugford GJ, Zhao J, Krahn M, Wang PP. Physicians' attitudes and practice toward treating injection drug users with hepatitis C: results from a national specialist survey in Canada. *Can J Gastroenterol* 2011;25:135-9.

8. Fleming CA, Craven DE, Thornton D, Tumilty S, Nunes D. Hepatitis C virus and human immunodeficiency virus coinfection in an urban population: low eligibility for interferon treatment. *Clin Infect Dis* 2003;36:97-100.

9. Perut V, Labalette C, Sogni P, Ferrand I, Salmon-Ceron D, Vidal-Trecan G. Access to care of patients with chronic hepatitis C virus infection in a university hospital: Is opioid dependence a limiting condition? *Drug Alcohol Depend* 2009;104:78-83.

10. Moirand R, Bilodeau M, Brissette S, Bruneau J. Determinants of antiviral treatment initiation in a hepatitis C-infected population benefiting from universal health care coverage. *Can J Gastroenterol* 2007;21:355-61.

11. Kanwal F, Hoang T, Spiegel BM, Eisen S, Dominitz JA, Gifford A et al. Predictors of treatment in patients with chronic hepatitis C infection - role of patient versus nonpatient factors. *Hepatology* 2007;46:1741-9.

12. Osilla KC, Wagner G, Garnett J, Ghosh-Dastidar B, Witt M, Bhatti L et al. Patient and provider characteristics associated with the decision of HIV coinfected patients to start hepatitis C treatment. *AIDS Patient Care STDS* 2011;25:533-8.

13. Kramer JR, Kanwal F, Richardson P, Giordano TP, Petersen LA, El Serag HB. Importance of patient, provider, and facility predictors of hepatitis C virus treatment in veterans: a national study. *Am J Gastroenterol* 2011;106:483-91.

14. Grebely J, Genoway KA, Raffa JD, Dhadwal G, Rajan T, Showler G et al. Barriers associated with the treatment of hepatitis C virus infection among illicit drug users. *Drug Alcohol Depend* 2008;93:141-7.

15. McLaren M, Garber G, Cooper C. Barriers to hepatitis C virus treatment in a Canadian HIV-hepatitis C virus coinfection tertiary care clinic. *Can J Gastroenterol* 2008;22:133-7.

16. Volk ML. Antiviral therapy for hepatitis C: why are so few patients being treated? *J Antimicrob Chemother* 2010;65:1327-9.

17. Klein MB, Saeed S, Yang H, Cohen J, Conway B, Cooper C et al. Cohort profile: the Canadian HIV-hepatitis C co-infection cohort study. *Int J Epidemiol* 2010;39:1162-9.

18. Gelman A, Carlin JB, Stern HS, Rubin DB. Appendix C: Example of computation in R and Bugs. *Bayesian Data Analysis*, pp 591-609. CRC Press, 2003.

19. Gelman A. Prior distributions for variance parameters in hierarchical models. *Bayesian Anal* 2006;1:515-33.

20. Greenland S. Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. *Am J Epidemiol* 2004;160:301-5.

21. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol* 2005;199-200.

22. Jimenez-Rubio D, Smith PC, van Doorslaer E. Equity in health and health care in a decentralised context: evidence from Canada. *Health Econ* 2008;17:377-92.

23. Zhong H. The impact of decentralization of health care administration on equity in health and health care in Canada. *Int J Health Care Finance Econ* 2010;10:219-37.

24. Tomlinson K. Hep C sufferers endangering health to get treatment. *CBC News* 2010 Mar 3. Available: http://www.cbc.ca/news/canada/british-columbia/story/2010/03/02/bc-hepcbinging.html (accessed 2012 Nov 20).

25. Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, Hickman M. Can antiviral therapy for hepatitis C reduce the prevalence of HCV among injecting drug user populations? A modeling analysis of its prevention utility. *J Hepatol* 2011;54:1137-44.

26. Agence de la Santé et des Services Sociaux de Montréal. *Plan régional de santé publique 2010-2015 - Garder notre monde en santé*. 2011. Available: http://publications.santemontreal.qc.ca/uploads/tx_asssmpublications/978-2-89673-084-1.pdf (accessed 2012 Nov 20).

27. Cox J, Graves L, Marks E, Tremblay C, Stephenson R, Lambert-Lanning A et al. Knowledge, attitudes and behaviours associated with the provision of hepatitis C care by Canadian family physicians. *J Viral Hepat* 2011;18:e332-e340.

Figure 1. Ranking of treatment centres according to their success at initiating HIV-HCV Co-infected patients on HCV therapy.

Bars represent the 95% confidence interval for the rank of each cohort centre after having adjusted for patient case mix. Rank 1 = centre most successful at getting patients started on HCV therapy and Rank 16 = the centre least successful at starting patients on therapy. Letters indicate the provinces in which centres are located grouped according to similar regulations for HCV treatment access during the study period (Q= Quebec and Nova Scotia; B= British Columbia; O= Ontario and Alberta).

Table 1. Characteristics of patients (n=1119) when enrolling in the Canadian Coinfection Cohort – median or proportion.

Characteristics at cohort enrolment	Spontaneous clearance of HCV (n=100)	HCV treatment at or before enrolment (n=184)	No follow up beyond enrolment (n=154)	No HCV treatment during follow up (n=518)	HCV treatment during follow up (n=163)
Age (years)	45	46	45	44	44
Male	0.58	0.78	0.77	0.70	0.82
Aboriginal ethnicity	0.23	0.12	0.17	0.17	0.07
Genotype 1	0.14	0.61	0.57	0.62	0.62
Genotype 2, 3	0.09	0.28	0.21	0.15	0.25
Genotype unknown	0.77	0.08	0.21	0.21	0.10
Hepatitis B	0.06	0.05	0.09	0.07	0.03
On ART	0.81	0.90	0.79	0.78	0.80
CD4 cell count (cells/ul)	370	420	400	360	400
Duration of HCV infection (years)	19	17	19	19	16
APRI	0.33	0.68	0.67	0.61	0.94

End stage liver disease	0.04	0.20	0.08	0.08	0.09
Using crack or cocaine	0.72	0.60	0.82	0.75	0.57
Psychiatric problems	0.58	0.49	0.54	0.48	0.49
Homeless	0.15	0.04	0.19	0.14	0.11
Currently drinking	0.45	0.47	0.59	0.51	0.51

Abbreviations: HCV, hepatitis C; ART, antiretroviral therapy; APRI, aspartate aminotransferase to platelet ratio index.

Table 2. Weibull model for the uptake of hepatitis C (HCV) treatment after enrolment in the Canadian Coinfection Cohort (n=669 [1]).

Covariate at enrolment	Hazard ratio (95% credible interval)	
	Uninformative priors [2]	Informative centre priors [3]
Age (per 10 years)	0.93 (0.75 to 1.1)	0.93 (0.75 to 1.1)
Female	0.61 (0.38 to 0.93)	0.59 (0.37 to 0.91)
Aboriginal ethnicity	0.57 (0.29 to 1.1)	0.56 (0.28 to 1.0)
HCV genotype 2, 3	1.8 (1.2 to 2.6)	1.8 (1.2 to 2.6)
Not on antiretroviral therapy	0.82 (0.54 to 1.2)	0.83 (0.54 to 1.2)
CD4 cell count (per 100 cells/ul)	1.1 (1.0 to 1.1)	1.1 (1.0 to 1.1)
Duration of HCV infection (per 10 years)	0.84 (0.71 to 0.99)	0.83 (0.71 to 0.99)
Using crack or cocaine	0.63 (0.44 to 0.90)	0.61 (0.43 to 0.86)
Psychiatric problems	1.2 (0.86 to 1.6)	1.2 (0.86 to 1.6)
Homeless	0.91 (0.54 to 1.5)	0.93 (0.53 to 1.6)
Currently drinking	0.90 (0.65 to 1.2)	0.89 (0.65 to 1.2)

[1] Of the 681 patients followed beyond enrolment, 12 were omitted from this analysis because their CD4 cell count or the duration of their HCV infection were not known at enrolment.

[2] Estimated centre variance 0.87, 95% credible interval 0.49 to 1.5.

[3] Estimated centre variance 0.90, 95% credible interval 0.49 to 1.5.

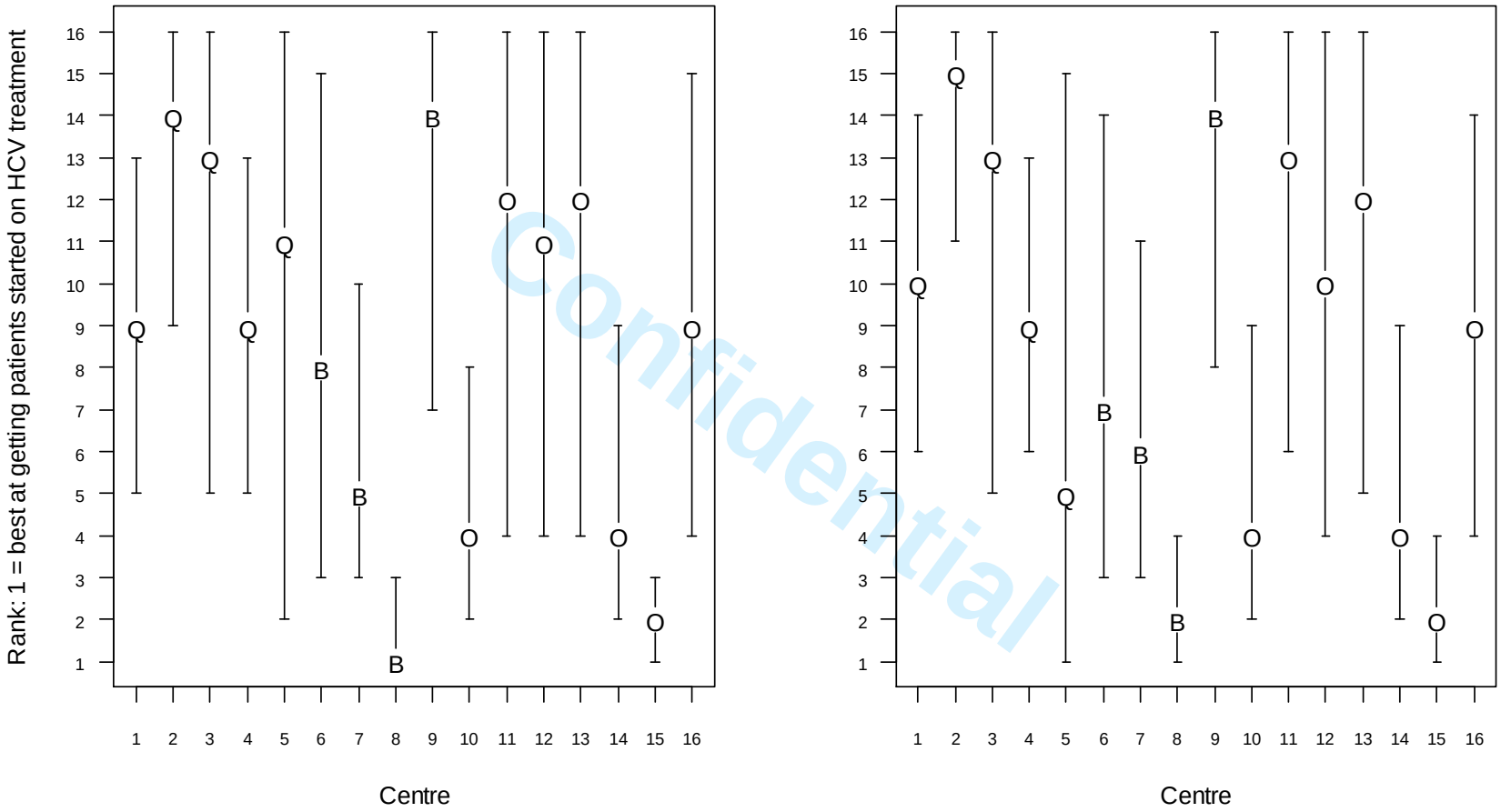
Table 3. Survey of centre principal investigators (n=16): access to specialists and services.

Access to specialist or service	Proportion	Correlation with median centre rank [1]
Qualitative HCV PCR	0.94	1.00
HCV viral load measurement	1.00	NA
HCV genotyping	1.00	NA
Transient elastography (Fibroscan)	0.69	0.56
Liver biopsy	1.00	NA
Hepatologist	1.00	NA
Nephrologist	0.94	0.60
Psychiatrist or psychologist	0.89	0.07
Social worker	0.88	0.29
Clinical pharmacist	0.81	-0.13
Dedicated HCV nurse	0.69	0.02
Industry sponsored nurse or social worker	0.36	0.04
Dedicated HCV social worker	0.25	-0.15
Out-reach team for patients with HCV	0.38	-0.20
Addiction services	0.69	0.44
Methadone or suboxone programme	0.75	0.19

[1] Rank biserial correlation with the median rank success of each centre in starting patients on HCV treatment, such that a positive correlation implies patients are more likely to start treatment. NA: not applicable – a correlation cannot be calculated.

Table 4. Survey of centre principal investigators (n=16): importance of criteria when determining eligibility for hepatitis C (HCV) treatment.

Eligibility criteria for HCV treatment (1 = less important, 5 = very important)	Median	Range
Age	1.0	1.0 to 3.0
Gender	1.0	1.0 to 3.0
HCV genotype	3.5	1.0 to 5.0
Severity of fibrosis	5.0	3.0 to 5.0
Past psychiatric co-morbidities	3.0	1.0 to 5.0
Current psychiatric co-morbidities	4.0	1.0 to 5.0
Current incarceration	3.0	1.0 to 5.0
Past incarceration	1.0	1.0 to 3.0
Past injection drug use	1.0	1.0 to 3.0
Current injection drug use	3.5	1.0 to 5.0
Past alcohol intake	1.0	1.0 to 4.0
Current alcohol intake	4.0	3.0 to 5.0
Past HCV treatment	4.0	1.0 to 5.0
History of re-infection with HCV	4.0	1.0 to 5.0
Potential for re-infection with HCV	3.0	1.0 to 5.0



Province: Q = Quebec and Nova Scotia, B = British Colombia, O = Ontario and Alberta