Publicly funded, pegylated interferon-alpha treatment in British Columbia: Disparities in treatment patterns for people with hepatitis C

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BACKGROUND: An estimated 60,000 British Columbians are chronically infected with the hepatitis C virus (HCV); 10% to 20% will develop cirrhosis after 20 years and 5% to 10% of these will develop hepatocellular carcinoma. Although treatment may prevent cirrhosis and liver cancer, and improve quality of life, availability is limited.

METHODS: Individuals with HCV genotypes 1, 4, 5 and 6 who underwent baseline HCV-RNA tests between January 1, 2003 and December 31, 2005, and were eligible for publicly funded treatment through PharmaCare were linked to British Columbia's reportable disease database. Patterns in treatment were examined, including age at treatment, sex, location, time to treatment from HCV diagnosis and seasonality of treatment.

RESULTS: When corrected for HCV prevalence, men were more likely to receive treatment than women (RR 1.16, 95% CI 1.02 to 1.31). Patients aged 35 to 54 years and 55 years or older were 3.45 times (95% CI 2.80 to 4.26 times) and 4.49 times (95% CI 3.55 to 5.69 times), respectively, more likely to initiate treatment than 15- to 34-year-olds. Differences were noted between health authorities. Patients in rural health service delivery areas (HSDAs) were 1.25 times (95% CI 1.10 to 1.42 times) more likely to receive treatment than those in urban HSDAs. Patients had an average lapse of four years between HCV diagnosis and receiving treatment. The highest proportion of patients initiated therapy between January and March (36.5%), with the lowest between October and December (less than 14%).

CONCLUSIONS: This data linkage enabled us to identify populations less likely to receive publicly funded treatment. Rural HSDAs have higher rates of therapy initiation; this pattern merits further research but may be a result of integrated prevention and care projects in rural areas. Policy changes to the current PharmaCare funding co-payment schedules could reduce seasonal variability of treatment initiations throughout the year.

Key Words: HCV; Hepatitis C virus; Pegylated interferon; Ribavirin; Therapy; Treatment

It is estimated that more than 170 million people worldwide, including 250,000 Canadians, are chronically infected with the hepatitis C virus (HCV) (1-3). British Columbia (BC) was the first province in Canada to make HCV reportable in 1992 (2). Since then, more than 58,000 people with HCV have been reported in British Columbia. Because 75% of acute HCV cases progress to chronic infection (2), it is estimated that more than 40,000 of the people reported are living with HCV in BC, with an additional 20,000 British Columbians projected to be unaware of their infection (J Buxton, personal communication).
receive the full 24 weeks of treatment funding without further monitoring. The objectives of the present study were to describe the characteristics of this treated population and to determine differences in treatment rates by demographics, location, population density, time to treatment from initial report of HCV and seasonality of treatment initiation.

**METHODS**

**Data source**

Three data sources were used for the present study: the BCCDC Laboratory Information System (BCCDC-LIS), the Integrated Public Health Information System (iPHIS) and the BCCDC PharmaCare Decision Support Database (BCCDC-PDSD). The data stored in the BCCDC-LIS contain more than 95% of the HCV antibody tests and 75% of the HCV-RNA tests conducted in BC, including data on all HCV genotypes since 2001. The BC regional health authorities report newly identified HCV cases within their geographical area into the iPHIS, the BC reportable disease database. The BCCDC epidemiology service collates, analyzes and interprets the data in the iPHIS to identify trends throughout the province.

The BCCDC-PDSD is a drug coverage approval and reporting system for PharmaCare, a BC government prescription drug program. BCCDC-PDSD contains demographic information and laboratory results of patients with HCV genotypes 1, 4, 5 and 6 who are approved to receive PharmaCare coverage of pegylated interferon-α and ribavirin combination therapy; it sends regular updates to PharmaCare so that they may determine whether to continue coverage of therapy for patients. The BCCDC-PDSD contains information on individuals eligible for PharmaCare coverage of HCV treatment only; information on people paying for therapies through other avenues (eg, out-of-pocket or private insurance) are not included. Since June 2003, pegylated interferon-α and ribavirin combination therapy has been available through PharmaCare. To qualify for PharmaCare coverage of HCV treatment in BC, a patient must be anti-HCV reactive, have qualitative HCV-RNA detected and ALT >1.5 times the upper limit of normal on 2 consecutive occasions at least 3 months apart (11). Thus, it is critical that effective antiviral therapies are accessible to this population to prevent progression to end-stage liver disease, where the cost burden to health care systems is the heaviest.

The current standard therapy for HCV is a combination of pegylated interferon-alpha (α) and ribavirin, which became available in BC in 2003. The recommended length of treatment and response depends on HCV genotype: 24 weeks of treatment for genotypes 2 and 3 is 24 weeks, with no renewals. ALT Alanine aminotransferase

**Procedure**

The BCCDC-PDSD was linked with 1992 to 2005 iPHIS data by a Personal Health Number. Data extracted from the iPHIS included date of birth, sex, HCV report date (ie, date the HCV case was first identified and reported in BC) and reporting health service delivery area (HSDA) (ie, residence of the HCV patient at the time of the report). BC has five geographic health authorities divided into 16 HSDAs (Figure 2, Table 1). The BCCDC-PDSD contained date of birth, sex, HCV genotype, and baseline and week 12 HCV-RNA results. The baseline HCV-RNA result represents the test result when approved for treatment, not the first ever HCV-RNA test. If duplicate baseline or 12-week HCV-RNA tests were found, the most recent was used for analysis. The BCCDC-LIS data were used.
TABLE 1
Proportions of individuals with hepatitis C virus (HCV) genotypes 1, 4, 5 and 6 on the British Columbia PharmaCare pegylated interferon-alpha and ribavirin treatment program and estimates of people reported with HCV genotypes 1, 4, 5 and 6 in the Integrated Public Health Information System (iPHIS) from 1992 to 2005, as well as the corresponding RRs

| Characteristic               | Treated, n | Estimated reported*, n | Treated, % | RR  | 95% CI   |
|-----------------------------|------------|------------------------|-----------|-----|----------|
| Sex                         |            |                        |           |     |          |
| Male                        | 788        | 23,045                 | 3.42      | 1.16| 1.02–1.31|
| Female                      | 342        | 11,606                 | 2.95      | 1.00|          |
| Age, years                  |            |                        |           |     |          |
| 15–34                       | 96         | 8748                   | 1.10      | 1.00|          |
| 35–54                       | 811        | 20,851                 | 3.89      | 3.45| 2.80–4.26|
| 55+                         | 223        | 4349                   | 5.13      | 4.49| 3.55–5.69|
| Health Authority            |            |                        |           |     |          |
| Fraser                      | 344        | 10,267                 | 3.35      | 1.00|          |
| East                        | 72         | 2563                   | 2.81      |     |          |
| North                       | 124        | 4171                   | 2.97      |     |          |
| South                       | 148        | 3566                   | 4.15      |     |          |
| Vancouver Island            | 262        | 6545                   | 4.00      | 1.19| 1.01–1.39|
| South                       | 98         | 3169                   | 3.07      |     |          |
| North                       | 63         | 1272                   | 4.95      |     |          |
| Central                     | 101        | 2114                   | 4.78      |     |          |
| Vancouver Coastal           | 285        | 10,180                 | 2.80      | 0.84| 0.72–0.98|
| Richmond                    | 44         | 671                    | 6.56      |     |          |
| North Shore                 | 54         | 1518                   | 3.56      |     |          |
| Coast Garibaldi             |            |                        |           |     |          |
| Interior                    | 169        | 4964                   | 3.40      | 1.02| 0.85–1.22|
| Okanagan                    | 87         | 2348                   | 3.71      |     |          |
| East Kootenay               | 12         | 389                    | 3.09      |     |          |
| Kootenay                    | 20         | 589                    | 3.39      |     |          |
| Boundary                    |            |                        |           |     |          |
| Thompson                    | 50         | 1625                   | 3.08      |     |          |
| Cariboo Shuswap             |            |                        |           |     |          |
| Northern                    | 70         | 1979                   | 3.54      | 1.05| 0.82–1.36|
| Northwest                   | 11         | 493                    | 2.23      |     |          |
| Northeast                   | 7          | 337                    | 2.08      |     |          |
| Northern Interior           | 52         | 1142                   | 4.55      |     |          |
| Population density          |            |                        |           |     |          |
| Urban                       | 814        | 25,977                 | 3.13      | 1.00|          |
| Rural                       | 316        | 7980                   | 3.96      | 1.25| 1.10–1.42|

*Estimates are derived from the percentage of genotypes 1, 4, 5 and 6 in the BC Centre for Disease Control Laboratory Information System and multiplied by the total number of people reported with HCV in the iPHIS (n=54,356) for each characteristic; †Classified as an urban health service delivery area; ‡Values represent P<0.05

RESULTS

One thousand five hundred fifty-two patients in the BCCDC-PDSD with HCV genotypes 1, 4, 5 and 6 were identified in the study period. Of these, 422 were excluded, leaving 1130 patient cases to be included in the study (Table 2 and Figure 3). The mean age was 48 years and more than two-thirds were male. When corrected for HCV prevalence, males were more likely to receive treatment than females (RR 1.16, 95% CI 1.02 to 1.31) (Table 1). More males received treatment than...
patients in every age category except for younger (15 to 29 years) and older (60 to 64 years) age groups (Figure 4).

Compared with patients in the youngest age category of 15 to 34 years, patients aged 35 to 54 years and patients aged 55 years or older were significantly more likely to initiate treatment (RR 3.45 and 4.49, respectively). The mean (± SD) time interval between reporting of HCV and receiving treatment was 4.08±3.20 years; 38% of patients were treated within two years of being reported with HCV and less than 5% waited 10 years or more to receive treatment.

Treatment rates varied among and within each health authority (Table 1). The Fraser Health Authority treated the largest number patients of all the health authorities, but ranked second last when comparing treated cases to reported HCV cases. Patients in the Vancouver Island Health Authority were most likely to receive treatment, while patients in the Vancouver Coastal Health Authority were the least. Although the Vancouver HSDA had the highest number of HCV cases treated of any HSDA, it had the lowest treatment rate when corrected for HCV prevalence (excluding two HSDAs with small numbers and hence unstable rates).

Patients in rural areas were 1.25 times more likely to receive treatment than patients in urban areas (95% CI 1.10 to 1.42). Figure 5 shows the initiation of therapy by quarter and by geographic categories since therapy data became available in 2003.

**DISCUSSION**

We found that males and older individuals were more likely to be treated. Sex differences in alcohol consumption may result in males being more likely to progress to liver disease and require treatment. Older people may exhibit symptoms of liver damage because they have had the disease longer, and thus are more likely to seek health care and receive treatment. In younger age categories (younger than 30 years), we found that more females initiated treatment than males. Studies have
shown that HCV infection rates are higher among young females than males of similar ages (13,15,16) due to risk factors such as needle and equipment sharing, and assistance with injection (17-19). Young females may also experience increased HCV testing because of health care encounters for sexually transmitted disease testing, contraception and/or pregnancy. According to the BCCDC-LIS, more females (57% to 65%) are tested for HCV than males in younger age categories (15 to 29 years). Once infected, females have been shown to be more likely to clear HCV than males, resulting in more males actually needing treatment than females (13).

We found that patients in urban areas were less likely to initiate treatment than in rural areas. The number of HCV cases in urban areas might exceed the treatment capacity available. The BC Medical Association guidelines for the management of HCV lists ongoing drug abuse as a relative contraindication to antiviral therapy. However, many studies have shown that modified treatment strategies for substance dependence have been effective in attaining an SVR (20-25). An overall SVR rate of 65% was achieved by a study examining the treatment of HCV in injection drug users within a directly observed therapy program in BC (25). Because intravenous drug use is currently the most common risk factor for contracting HCV (26), it is possible that large numbers of socially marginalized individuals in urban areas, including Vancouver’s downtown eastside, infected with HCV may be less likely to seek or be offered treatment. A study (27) conducted at a large liver disease clinic in Quebec found that risk factors usually associated with socially marginalized populations such as current intravenous drug use, alcoholic liver damage on biopsy, unstable housing arrangements and mental disorders were negatively associated with treatment initiation. It is interesting to note that although the Richmond HSDA is an urban area, it had the highest treatment rate of any HSDA. This may be because it has a small HCV population, which enables comprehensive follow-up, treatment and support by public health and health care providers.

Northern Interior, North Vancouver Island and Fraser South HSDAs had the highest treatment rates in their respective health authorities. This may be because each contains a hepatitis demonstration site (see Figure 2 for locations) developed in 2001 by BC Hepatitis Services and funded by the BC Ministry of Health to build local capacity and integrate prevention and care of hepatitis. A review of the demonstration sites from 2001 to 2004 found that they successfully integrated prevention, community development, education and support, as well as clinical services (28). Specialized nurses and collaborative teams help patients make treatment decisions and connect patients with health and social service support in a timely manner.

Many patients initiated treatment within two years of HCV diagnosis; these patients may have been tested for HCV because they were exhibiting symptoms of liver damage and therefore commenced treatment soon after HCV diagnosis. PharmaCare implemented the pegylated interferon-α and ribavirin treatment program in June 2003. Some people eligible for HCV treatment before June 2003 are reported to have deferred treatment until the new regimen was available (personal communication, Warren Hill). The trend of reduced treatment uptake in the latter quarters of 2004 and 2005 might be the result of PharmaCare’s deductible-based drug coverage program payment schedule (29). Aside from people on income assistance who receive complete drug coverage, the majority of patients pay their full drug costs until they reach a maximum, income-based deductible; PharmaCare then pays for the remaining drug costs for that calendar year. For example, a patient with a family income of $50,000 would pay $1,500 before PharmaCare covers the remaining treatment costs. Because the treatment coverage for genotypes 1, 4, 5 and 6 is 48 weeks, a patient considering treatment at the end of the calendar year may opt to postpone their treatment until the beginning of the subsequent year to avoid paying the deductible twice. Therefore, patients may endure worsening symptoms and psychological distress while waiting for a more financially favourable time to begin treatment. From the system perspective, the peak in treatment initiation in the early months of each year can put unnecessary stress on the health care system. Other provinces with similar income-based universal drug coverage programs (eg, Quebec and Manitoba) might also be experiencing the same situation, where patients forgo or delay necessary treatments due to financial disincentives created by a system utilizing deductibles. Thus, it is worthwhile for federal and provincial governments to explore alternative drug funding mechanisms that promote equity, access and efficiency. These mechanisms might involve a blend of complete drug coverage for vulnerable populations and universal deductible-based drug coverage for entire populations (30).

There are several limitations to our study. The BCCDC-PDSD only contains data for genotypes 1, 4, 5 and 6; therefore, we cannot make any conclusions for genotypes 2 and 3. Our sample may have been biased by excluding patients without Personal Health Numbers who might be more likely to be homeless, have lower socioeconomic status and poorer access to treatment. Also, people on treatment in correctional facilities would have been identified as an HCV case in the iPHIS but, if treated, would be excluded from the BCCDC-PDSD because they are under federal jurisdiction. The exclusion of privately funded patients may influence the treatment patterns found in our study; for example, employed individuals with private drug plans may be more likely to be male, older or reside in urban areas. Because a liver biopsy is not required for HCV treatment initiation in BC, our findings might not be generalizable to other jurisdictions that have different eligibility criteria for HCV therapy. Our estimation of the proportion of HCV genotypes 1, 4, 5 and 6 from the BCCDC-LIS might have been

**Pegylated-interferon treatment patterns in hepatitis C**

![Graph showing pegylated-interferon treatment patterns in hepatitis C](image-url)
inaccurate and that would have affected our estimation of HCV genotypes reported in the iPHIS and the accuracy of our RR values. However, our study population data was from 2003 to 2005, which falls within the time period (1992 to 2005) used to derive the genotype estimates from the BCCDC-LIS data. Another limitation is our definition of urban and rural; other definitions might have resulted in different results. For example, although the North Shore/Coast Garibaldi HSDA is classified as an urban area, a large portion includes rural coastal mainland further north. The HSDA for cases in the iPHIS is based on the location where it was first reported. Some people may have moved before treatment, especially those with a long lapse between HCV report and treatment initiation dates. Others may have been identified in a rural community but travel to an urban centre for treatment because of a lack of services in their community.

It is important to note that 20% of patients in our linked dataset did not have an HCV-RNA test at week 12; further research is needed to determine if these patients did not initiate treatment or if they dropped out of treatment before their week 12 tests and if so, these people might need more resources and social services support to assist them through the challenges of receiving HCV treatment.

CONCLUSIONS
Our study presented data from a publicly funded treatment program in BC, from 2003 to 2005. Patients who were older, male and who reported their HCV in rural areas were more likely to initiate treatment. Our findings suggest that the demonstration sites in rural areas of BC have higher HCV treatment rates in their surrounding areas. It is worthwhile to consider applying our knowledge of the demonstration sites and expanding these integrated services to other areas of BC. Wider policy implications include revising the current PharmaCare funding guidelines for HCV treatment to achieve a balance of treatment initiations throughout the year.

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