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ABSTRACT

Background

Canadian immigrants from countries where the hepatitis B virus (HBV) and hepatitis C virus (HCV) are endemic may be at higher risk of liver-related disease than Canadian-born residents. This study compared HBV- and HCV-related hospitalizations in Canadian immigrants (arriving from 1980 to 2013) and long-term residents (Canadian-born population and pre-1980 immigrants) and aimed to describe the burden of disease in both groups.

Methods

Based on the 2004/2005-to-2013/2014 hospital Discharge Abstract Database linked to the 1980-to-2013 Longitudinal Immigration Database, this descriptive cross-sectional study examined the distribution of HBV- and HCV-related hospitalizations, lengths of stay, comorbidities, and sequelae incurred by immigrants and long-term residents in Canada. With a linkage rate of 85%, 5,854,949 immigrants were included in the study. Proportions of HBV- and HCV-related hospitalizations attributable to immigrants were calculated.

Results

By birth country risk level, 22% of HBV-related hospital events among recent immigrants, and 20% of those related to HCV, were among people from high-risk countries. Proportionally, fewer immigrants had comorbidities than long-term residents. The top two hospital-related sequelae in both groups were cirrhosis and ascites, and liver cancer. While immigrants made up 16% of the Canadian population, they incurred 37% of HBV-related hospitalizations and 9% of HCV-related hospitalizations, giving ratios of hepatitis-related hospitalizations relative to the population share of 2.3 (95% confidence interval [CI]: 2.2 to 2.5) and 0.5 (95% CI: 0.5 to 0.6) respectively. These ratios were higher among seniors, at 4.4 (95% CI: 3.9 to 4.9) and 2.3 (95% CI: 1.9 to 2.6), respectively.

Interpretation

Immigrants can require hospitalization for hepatitis in Canada, especially for HBV. These results may inform health screening for HBV or HCV in the Canadian immigration context.

Keywords

global health, health policy, infectious diseases, public health, statistics, and research methods

AUTHORS

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What is already known on this subject?

- Since viral hepatitis is an important global public health problem, there are international commitments that have prioritized the elimination of hepatitis.
- Chronic viral hepatitis can lead to significant morbidity and mortality, but early detection through screening can help mitigate the risk of clinical deterioration.
- Canada receives over 350,000 immigrants each year, with the numbers expected to grow.
- Patterns of migration have changed over time.
- For admissibility purposes, Canadian immigrants are medically screened for selected diseases to mitigate impacts on Canadian health and social services.

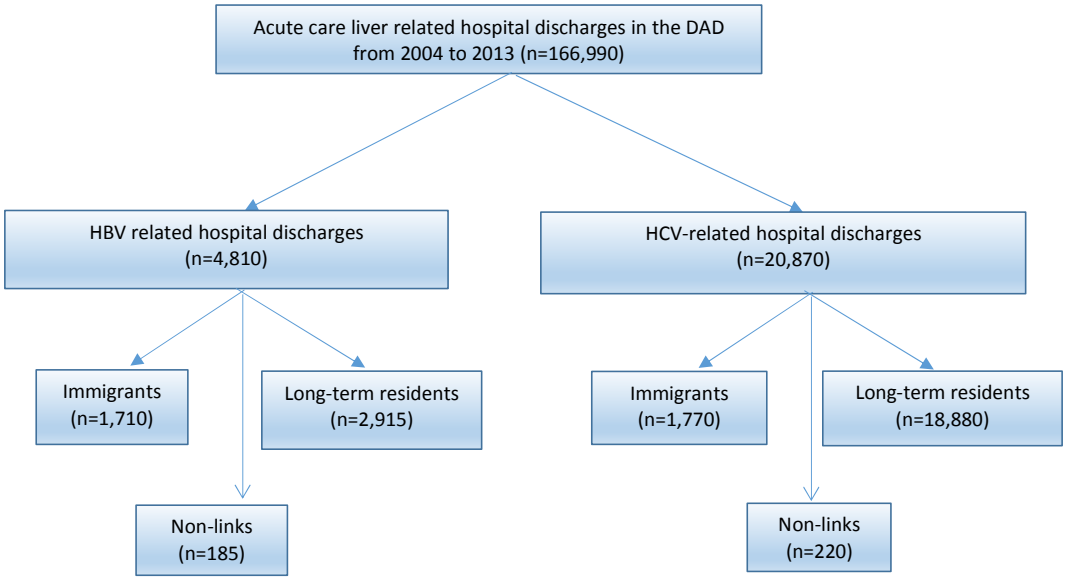
What does this study add?

- This is the first Canadian study at the national level (outside of Quebec) to examine HBV- and HCV-related hospitalizations using high-quality linked data that characterized these hospitalizations among immigrants compared with long-term Canadian residents.
- The findings from this study add to the understanding of the role of immigration on the burden of HBV- and HCV-related hospital care in Canada.
- These results show that recent immigrants contribute to HBV- and HCV-related hospitalizations in Canada, and that the HBV contribution to hospitalizations is particularly noted among seniors.
- Developing and bolstering screening programs would help to identify those at risk of disease progression at earlier stages to prevent HBV- and HCV-related complications.

International commitments from the World Health Organization and the United Nations have prioritized the elimination of hepatitis.[1-3] Worldwide, 1% of the global population is infected with the hepatitis B virus (HBV) or hepatitis C virus (HCV).[4] The prevalence of HCV is highest in African and Asian countries,[5] while that of HBV is highest in Sub-Saharan Africa; Oceania; and parts of Central Asia, East Asia and Southeast Asia.[6] In Canada, an estimated 112,000 individuals are infected with HBV, and 220,000 with HCV.[7,8] Improving people's awareness of their hepatitis status allows them to be better equipped to seek earlier care,[9] and knowledge of their HBV or HCV status could improve the treatment and care of chronic viral hepatitis. Of those infected with HBV or HCV, more than half are unaware of their infection.[7,8] Chronic viral hepatitis can lead to significant morbidity and mortality,[7] and it is estimated that 75% to 85% of HCV-infected individuals develop chronic disease.[7] By contrast, the progression of HBV infection is age dependent, with 80% to 90% of HBV-infected infants developing chronic disease compared with 20% to 30% of HBV-infected adults.[10] These infections are responsible for 80% of hepatocellular carcinoma cases[11] and are major contributors to health care burden. In Canada, HCV is a leading cause for liver transplants among 35- to 59-year-olds.[12,13] Because of long asymptomatic latency periods, chronic HBV- and HCV-associated and liver-related sequelae are related to the duration of infection[4,14] and are often associated with older age. Immigrants from countries where HBV and HCV are endemic, while unaware, may be at a higher risk of infection and future liver-related hospitalization.[15–17]

Currently, Canada receives over 350,000 immigrants each year, with the numbers expected to grow. Patterns of migration have changed over time, with Asia and Africa now major source regions for immigrants to Canada.[18] For admissibility purposes, Canada medically screens immigrants for selected diseases to mitigate the impacts on Canadian health and social services.[19] Over the last several decades, immigration medical screening for HBV and HCV has included a medical history, questions on prior diagnosis and risk behaviour. Published studies show that there are various approaches to HBV and HCV screening to initiate care and mitigate the risk of clinical deterioration (e.g., HCV screening in immigrants from countries with a higher prevalence or screening by age-based cohorts and referrals if positive).[20–22] This descriptive study aims to characterize HBV- and HCV-related hospitalizations among immigrants compared with long-term Canadian residents.

Figure 1
Flow chart on classification of hepatitis B- and hepatitis C-related events from acute care liver-related hospitalization for immigrants and long-term residents,[1] Canada (excluding Quebec and the territories), 2004/2005 to 2013/2014



1 Immigrants are defined as immigrants who arrived from 1980 to 2013, and long-term residents refer to Canadian-born people and pre-1980 immigrants.
Notes: DAD = Discharge Abstract Database; HBV = hepatitis B virus; HCV = hepatitis C virus.
Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

Methods and data

Design and data sources

In this cross-sectional study, records from the hospital Discharge Abstract Database (DAD) were linked to the Immigrant Landing File (ILF) data at Statistics Canada, using previously described methods.[23] Essentially, the Immigrant Landing File (ILF) data were linked to the DAD via a central depository called the Derived Record Depository (DRD) within the Social Data Linkage Environment (SDLE) at Statistics Canada. The DRD is a national dynamic relational database containing only basic personal identifiers, and was created by linking selected Statistics Canada source index files, including tax,birth and death data, to produce a list of unique individuals. The linkage was approved by Statistics Canada's Executive Management Board,[24] and the use and privacy of the data are governed by the Directive on Microdata Linkage.[25]

The DAD, from which the study population was constructed, contains demographic, administrative and clinical data for all acute care and some psychiatric, chronic rehabilitation, and day surgery discharges for all provinces excluding Quebec.[26] Hospital discharges occurring between April 1, 1994, and March 31, 2015, were eligible for linkage in the present study (n=77,925,269 hospital discharge records). The linkage used a deterministic approach (linkage rate of 85%, n=66,246,909).[27]

The Longitudinal Immigration Database (IMDB), a research database representing unduplicated immigrant records derived from the ILF, was used to add recent immigrant status and other immigration-related characteristics to the DAD. At the time of this study, the latest available version of the ILF database contained immigration landing data up to the end of the 2013 calendar year. The ILF/IMDB contains administrative information for all individuals who have landed in Canada since 1980.[28] In the present study, landing records between 1980 and 2013 were eligible for linkage (n=6,896,592 immigrants). Probabilistic methods were used to link the ILF/IMDB to the DRD (linkage rate of 85%, n=5,854, 949).

Outcomes

From the overall data linkage described above, the primary events observed in this study were HBV- or HCV-related hospital discharges occurring between April 1, 2004, and March 31, 2014. Hospital data from 2004 onward were used, since prior to 2004 HCV infection was not captured by all provinces in the International Classification of Diseases (ICD) coding. To characterize hospitalizations in immigrants, the final linked datasets were aligned, and thus information between April 1, 2004, and March 31, 2014, was included.

Stratification variables

Age at hospitalization, derived as the difference between the DAD hospitalization year and the IMDB birth year, was grouped. Province of hospitalization from the DAD was grouped into regions: Atlantic (New Brunswick, Nova Scotia, Newfoundland and Labrador, and Prince Edward Island), Ontario, Prairies (Manitoba, Saskatchewan and Alberta) and

British Columbia. Data from Quebec and the territories were not included in the analysis. Landing year and immigration class obtained from the IMDB were grouped. An individual's birth country risk level was based on published HBV[29] and HCV[30] prevalence rates[31–33](Appendix A).[29–34] Countries not assigned a risk level for HBV or HCV were coded as missing.

Statistical analysis

A two-step approach was adopted to identify HBV- and HCV-related hospitalizations.[15] First, acute care hospital discharges with a primary diagnosis of a liver condition, related complications or liver transplantation were identified (Appendix B). Second, all additional diagnostic fields in each hospital record were scanned hierarchically for selected ICD-10 codes to classify these liver-related hospitalizations as being HBV- or HCV-positive (Appendix C). Sequelae and selected comorbidities of HBV or HCV were also identified (Appendix C). Among these hospitalizations, those linked to IMDB immigrants were classified as occurring among immigrants, and those that were not linked to the IMDB, but linked to the DRD, were classified as occurring among long-term residents (i.e., Canadian-born individuals and pre-1980 immigrants).

The distribution of HBV- or HCV-related hospital events was tabulated by selected characteristics for events and individuals for immigrants and long-term residents, separately. The distribution of major comorbidity and sequelae was examined. The distribution of HBV- or HCV-related hospital events was tabulated by selected characteristics for events and individuals

Table 1-1

Distribution of hepatitis B-related hospitalizations among immigrants[1] by selected characteristics, Canada (excluding Quebec and the territories), 2004/2005 to 2013/2014

	HBV-related hospitalizations						
	People		Events		Average per	Length of stay (days)	
	Number	%	Number	%	person	Mean	Median
Overall	1,175	100	1,710	100	1.5	10	6
Age at hospitalization							
0 to 24	25	2	30	1	1.2	7	4
25 to 34	65	6	80	5	1.2	16	6
35 to 44	135	11	180	11	1.3	10	6
45 to 64	595	51	910	53	1.5	9	6
65 and older	360	31	510	30	1.4	11	6
Sex							
Male	870	74	1,290	75	1.5	9	6
Female	305	26	420	25	1.4	12	6
Region by submitting province							
Atlantic and Ontario[2]	675	57	960	56	1.2	10	6
Prairies	200	17	295	17	1.5	11	6
British Columbia	300	26	455	27	1.5	9	6

1 Immigrants are defined as immigrants who arrived from 1980 to 2013.

2 Figures for the Atlantic provinces and Ontario for HBV are grouped together for recent immigrants because of a small sample size.

Note: HBV = hepatitis B virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

Table 1-2

Distribution of hepatitis B-related hospitalizations among long-term residents[1] by selected characteristics, Canada (excluding Quebec and the territories), 2004/2005 to 2013/2014

	HBV-related hospitalizations						
	People		Events		Average per	Length of stay (days)	
	Number	%	Number	%	person	Mean	Median
Overall	2,035	100	2,915	100	1.4	10	6
Age at hospitalization							
0 to 24	40	2	45	2	1.1	5	3
25 to 34	90	4	115	4	1.3	7	4
35 to 44	255	13	365	13	1.4	9	6
45 to 64	1,090	54	1,610	55	1.5	11	6
65 and older	560	28	775	27	1.4	11	7
Sex							
Male	1,490	73	2,210	76	1.5	10	6
Female	545	27	705	24	1.3	11	7
Region by submitting province							
Atlantic	60	3	85	3	1.4	13	7
Ontario	1,115	55	1,535	53	1.4	9	6
Prairies	385	19	585	20	1.5	12	6
British Columbia	475	23	710	24	1.5	11	6

1 Long-term residents refer to Canadian-born people and pre-1980 immigrants.

Note: HBV = hepatitis B virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

Table 1-3

Distribution of hepatitis C-related hospitalizations among immigrants[1] by selected characteristics, Canada (excluding Quebec and the territories), 2004/2005 to 2013/2014

	HCV-related hospitalizations						
	People		Events		Average per person	Length of stay (days)	
	Number	%	Number	%		Mean	Median
Overall	955	100	1,770	100	1.9	11	6
Age at hospitalization							
0 to 34[2]	25	3	35	2	1.4	7	5
35 to 44	75	8	110	6	1.5	9	6
45 to 64	490	51	960	54	2.0	12	6
65 and older	365	38	665	38	1.8	10	6
Sex							
Male	560	59	1,015	57	1.8	10	6
Female	395	41	750	42	1.9	11	7
Region by submitting province							
Atlantic and Ontario[2]	640	67	1,210	68	1.4	10.9	6
Prairies	145	15	265	15	1.8	13	6
British Columbia	165	17	295	17	1.8	11	6

1 Immigrants are defined as immigrants who arrived from 1980 to 2013.

2 Figures for the Atlantic provinces and Ontario and those aged 0 to 34 for HCV, are grouped together for recent immigrants because of a small sample size.

Note: HCV = hepatitis C virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

Table 1-4

Distribution of hepatitis C-related hospitalizations among long-term residents[1] by selected characteristics, Canada (excluding Quebec and the territories), 2004/2005 to 2013/2014

	HCV-related hospitalizations						
	People		Events		Average per person	Length of stay (days)	
	Number	%	Number	%		Mean	Median
Overall	9,980	100	18,880	100	1.9	11	6
Age at hospitalization							
0 to 24	50	1	65	0	1.3	6.6	4
25 to 34	270	3	345	2	1.3	7.5	5
35 to 44	1,000	10	1,715	9	1.7	9.7	6
45 to 64	7,190	72	14,195	75	2.0	10.9	6
65 and older	1,470	15	2,560	14	1.7	12.9	7
Sex							
Male	6,980	70	13,340	71	1.9	10.6	6
Female	3,000	30	5,535	29	1.8	12.0	6
Region by submitting province							
Atlantic	415	4	735	4	1.8	12.0	7
Ontario	4,845	49	8,515	45	1.8	10.3	6
Prairies	2,425	24	5,240	28	2.2	12.2	6
British Columbia	2,290	23	4,390	23	1.9	10.8	6

1 Long-term residents refer to Canadian-born people and pre-1980 immigrants.

Note: HCV = hepatitis C virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

for immigrants and long-term residents, separately. Counts were rounded up to the nearest 5 in accordance with Statistics Canada policy. To measure the burden of HBV- and HCV-related hospitalizations among immigrants compared with long-term residents, the mean and median of total days in hospital were calculated by selected individual characteristics. The total of days in the hospital was calculated by the difference between the admission date and the discharge date.

The relative distribution of HBV- and HCV-related hospitalizations in immigrants was calculated as the ratio of hepatitis-related hospitalizations relative to the immigrants' population share. This ratio was constructed as the percentage of HBV- and HCV-related hospitalizations occurring among immigrants over the estimated percentage of immigrants in the Canadian population, with the latter obtained from the 2011 National Household Survey (NHS).[35] A ratio of more than 1 suggests that the relative burden of hospitalizations in immigrants was disproportionately more than its population share. Confidence intervals for the ratios were derived using a large sample approximation, and the variance estimates for the ratios are based on the Taylor linearization method,[36] with the assumption that the numerators and denominators of the ratios are uncorrelated. Since potentially high-risk institutional populations in Canada were excluded in the Canadian-born population obtained from the 2011 NHS, but were included in the immigrant IMDB-linked data, a sensitivity analysis that

Table 2

Distribution of hepatitis B- and hepatitis C-related hospitalizations among immigrants[1] by selected immigrant-related characteristics, Canada (excluding Quebec and the territories), 2004/2005 to 2013/2014

	HBV-related hospitalizations							HCV-related hospitalizations						
	Immigrants							Immigrants						
	People		Events		Average	Length of stay (days)		People		Events		Average	Length of stay (days)	
	Number	%	Number	%	per person	Mean	Median	Number	%	Number	%	per person	Mean	Median
Overall	1,175	100	1,710	100	1.5	10	6	955	100	1,770	100	1.9	11	6
Landing year														
1980 to 1982	105	9	170	10	1.6	11	6	80	8	155	9	1.9	12	6
1983 to 1992	415	35	580	34	1.4	10	6	345	36	645	36	1.9	10	6
1993 to 2002	445	38	665	39	1.5	10	6	350	37	675	38	1.9	11	6
2003 to 2013	210	18	300	18	1.4	10	6	175	18	300	17	1.7	10	6
Birth country risk level[2]														
Low	135	11	190	11	1.4	12	7	360	38	605	34	1.7	10	6
Medium	750	64	1,070	63	1.4	10	6	260	27	480	27	1.8	10	6
High	250	21	370	22	1.5	10	6	160	17	350	20	2.2	12	6
Missing	45	4	80	5	1.8	11	7	170	18	330	19	1.9	12	6
Immigrant class														
Economic—principal applicants	290	25	430	25	1.5	10	6	150	16	280	16	1.9	11	6
Economic—spouse or children	125	11	155	9	1.2	9	5	75	8	135	8	1.8	12	6
Family	440	37	610	36	1.4	10	6	445	47	815	46	1.8	10	6
Refugee[3]	255	22	395	23	1.5	10	6	230	24	430	24	1.9	10	6
Others, unknown or missing	65	6	120	7	1.8	10	5	55	6	105	6	1.9	12	5

1 Immigrants are defined as immigrants who arrived from 1980 to 2013, and long-term residents refer to Canadian-born people and pre-1980 immigrants.

2 Classifications for HBV: low <2%, moderate 2% to 8%, and high >8% (Schweitzer et al., 2015); HCV: low <0.8%, moderate 0.8% to 2.9%, and high >2.9% (Polaris Observatory HCV Collaborator, 2017). See Appendix C for complete list.

3 Refugee class includes resettled refugees and in-Canada asylum seekers.

Notes: HBV = hepatitis B virus; HCV = hepatitis C virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

increased the proportion of immigrants aged 65 years and older was conducted.

Ethics approval

Research studies conducted at Statistics Canada do not require submission to an ethics board for approval. The record linkage was approved by Statistics Canada's Executive Management Board[24] and the data use is governed by the Directive on Microdata Linkage—public good, confidentiality and disclosure risk are assessed as part of this process.[25] Participants' privacy during record linkage and use of the linked files is ensured by Statistics Canada. Access to the unique identifying information (e.g., names) was limited to employees directly involved in linking the databases. They did not access the complete data files with information on individuals' characteristics.

Results

Hepatitis B virus and hepatitis C virus acute care hospital events in Canada: Overall comparisons

Approximately 166,990 acute care hospital discharges (or 0.5%) between April 1, 2004, and March 31, 2014, were liver related (Figure 1). Among them, 4,810 (2.9%) were HBV related, and 20,870 (12.5%) were HCV related. After the non-links were removed, 37% (n=1,710) of HBV-related hospitalizations and 9% (n=1,770) of HCV-related hospitalizations were among immigrants (Figure 1). Although the total number of HCV events was more than four times higher than that for HBV, the numbers of HBV- and HCV-related hospitalizations among immigrants were similar (Figure 1). On average, each immigrant HBV patient was hospitalized 1.5 times over the follow-up period, similar to long-term residents (1.4 times), and this increased with age (Table 1). For HCV, the corresponding figure was 1.9 times for both immigrants and long-term residents. For both immigrants and long-term residents, HBV and HCV hospitalizations occurred predominantly within the 45 to 64 age group, and admissions occurred more commonly among males (Table 1). The overall mean length of stay for HBV- and HCV-related hospitalizations was 10 and 11 days, respectively. For HBV, immigrant females stayed longer on average than their male counterparts (12 vs. 9 days). For HCV, the mean hospital stays increased with age, especially among long-term residents.

Hepatitis B virus and hepatitis C virus acute care hospital events in Canada: Immigrant-specific comparisons

Among immigrants, 22% of HBV-related hospital events and 20% of those related to HCV were among those born in high-risk countries (Table 2). The highest proportion of HBV-related hospitalizations was among those from medium-risk countries (63%), and that of HCV-related hospitalizations from low-risk countries (34%). By immigration category, the highest proportion occurred among family class immigrants for both HBV (36%) and HCV (46%), followed by economic class principal applicants for HBV (25%) and by refugees for HCV

Table 3

Distribution of comorbidity and sequelae[1] of hepatitis B- and hepatitis C-related hospitalizations for immigrants and long-term residents,[2] Canada (excluding Quebec and the territories), 2004/2005 to 2013/2014

	HBV-related hospitalizations				HCV-related hospitalizations			
	Immigrants		Long-term residents		Immigrants		Long-term residents	
	People (n=1,175)	%	People (n=2,035)	%	People (n=955)	%	People (n=9,980)	%
Comorbidity								
Cardiovascular disease	220	19	360	18	210	22	1,365	14
Type 2 diabetes	190	16	360	18	280	29	1,685	17
Alcohol-related conditions[1]	60	5	425	21	125	13	3,920	39
HIV	X	X	50	2	0	0	115	1
% of at least one comorbidity	245	21	760	37	385	40	5,150	52
Sequelae								
Primary liver cancer	615	52	645	32	335	35	1,955	20
Cirrhosis and ascites	520	44	1,085	53	640	67	6,830	68
Hepatic failure	185	16	390	19	225	24	2,360	24
Variceal hemorrhage	85	7	135	7	125	13	1,040	10
Peritonitis	50	4	110	5	50	5	760	8
Liver transplantation	20	2	45	2	35	4	365	4
% of at least one sequela	965	82	1,580	78	880	92	8,530	85

x number suppressed to meet the confidentiality requirements of the Statistics Act.

1 See Appendix C.

2 Immigrants are defined as immigrants who arrived from 1980 to 2013, and long-term residents refer to Canadian-born people and pre-1980 immigrants.

Notes: HBV = hepatitis B virus; HCV = hepatitis C virus. HIV = Human immunodeficiency virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

(24%). Person-oriented results demonstrated similar findings. Among immigrants, for both HBV and HCV, minimal differences in mean hospital stay were observed by birth country risk level or immigrant class.

Comorbidity and sequelae distributions

Among those hospitalized for HBV and HCV, immigrants were less likely to have a comorbidity than long-term residents (Table 3). For immigrants with either HBV- or HCV-related hospitalization, the leading comorbid conditions were cardiovascular disease and type 2 diabetes, while alcohol-related conditions were more prevalent among long-term residents, especially those hospitalized with HCV-related conditions.

More than three-quarters of patients hospitalized for HBV and HCV had specific liver-related sequelae (Table 3). For HBV, the top sequelae among immigrants were primary liver cancer, at 52%, followed by cirrhosis and ascites, at 44%. That order was reversed among long-term residents, with cirrhosis and ascites at 53%, followed by liver cancer, at 32%. For HCV, the top sequelae were cirrhosis and ascites for both immigrants (67%) and long-term residents (68%), followed by primary liver cancer (35%) among immigrants and hepatic failure (24%) among long-term residents.

Hospitalizations related to hepatitis B virus and hepatitis C virus attributable to immigrants

Approximately 37% of HBV-related hospital events and 9% of those related to HCV occurred among immigrants, who represented 16% of the Canadian population (Table 4). This resulted in a ratio of 2.3 for HBV-related hospital events and 0.5 for HCV-related hospital events for immigrants. These ratios differed by age group, varying from 1.3 (for those aged 35 to 44 years) to 4.4 (for those aged 65 years and older) for HBV. In contrast, for HCV, ratios by age group never rose above 1, except for those aged 65 years and older (ratio of 2.3). A sensitivity analysis identified that the ratio for HCV among immigrants aged 65 years and older remained above 1 (1.9) when the population share for immigrants was increased from 9% (the proportion of immigrants who were aged 65 years and older in the 2011 NHS)[35] to 11%.

Interpretation

This descriptive cross-sectional study of HBV- and HCV-related hospitalizations in Canada (excluding Quebec and the territories) demonstrates the usefulness of linking large administrative datasets to understand the extent to which immigrants experience serious health outcomes. This study focused on hospitalizations; while these events underrepresent the full spectrum of hepatitis, they are considered to be the most costly component of health care.[37]

Among immigrants, the highest proportions of HBV and HCV hospitalizations were among those from medium-risk and low-risk hepatitis countries, probably because of the high volume of immigrants arriving from countries such as China, India and the Philippines, a dominant trend in recent years.[38] The distributions of comorbidities and sequelae of HBV- and HCV-related hospitalizations were similar between immigrants and long-term residents, except for the higher proportion of alcohol-related conditions among the latter.

Our results corroborate those from other studies showing that, overall, immigrants are disproportionately represented among HBV patients[39] in Canada but less so for HCV.[40] As expected from an infection with a long subclinical phase, the proportion

of hepatitis-related hospitalizations—especially for HCV—increased with age,[38] and more than 40% occurred among immigrants who landed before 1993. In general, HCV is acquired at an older age than HBV.[4,10] Given the age and mechanism[41] of acquisition, and the differences in disease expression related to comorbidities, HCV hospitalizations are expected to be higher in older age groups.[42] This study found a higher distribution of HCV-related hospitalizations among immigrants relative to long-term residents in the group aged 65 years and older. This result may be because of an age-related cohort effect in which a lower burden of HCV among long-term residents in older age groups is associated with fewer hospitalizations as compared with younger long-term residents (i.e., born after 1950). This changes the ratio when compared with immigrants. This effect may be because of lower exposure to risk factors related to adverse outcomes (e.g., alcohol consumption) in the older long-term residents when compared with younger long-term residents. The higher alcohol-related comorbidity among long-term residents with HBV or HCV may account for the higher cirrhotic rate.[12] A longer follow-up period may identify a higher ratio overall for HCV in immigrants.[43] When HCV is managed at an early stage of the disease, it has a very high five-year survival rate (90% or more).[14, 44] As direct-acting antivirals become more accessible worldwide—especially in Canada's main source countries—the epidemiologic picture may shift since newer direct-acting antivirals have a prolonged sustained virologic response rate.

Currently, the absence of a national standard for hepatitis testing practices can explain some of the regional differences in the distribution of hepatitis cases in relation to where immigrants reside. As well, all immigrants are medically screened upon entry to mitigate the impact on health and social services.[19] Immigrants who could pose an excessive demand on these services may have failed the health admissibility criteria. Therefore, it is possible that immigrants who had advanced-stage hepatitis-related disease upon their application would not be admitted to Canada and would not be included in this study. The introduction of worldwide HBV vaccination at birth, coupled with the significant decreases in the cost for HCV treatment and the availability of inexpensive HBV treatment, will likely decrease future hospitalization rates for immigrants with known viral hepatitis. In addition, in 2018, changes were made to Canada's medical admissibility criteria[45] to better align with Canadian values on the inclusion of people with disabilities, while protecting publicly funded health and social services. These adjustments may lead to changes in immigrants' admissibility, which could influence the epidemiology of HBV and HCV in Canada, as well as future hospitalization rates. One way to mitigate the impact on morbidity and future hospitalization rates would be to enhance HBV and HCV screening for early detection and treatment,[15,20,21,42] and implement a routine childhood HBV vaccination program. Hepatitis screening can improve the integration of individuals into health care systems as they relate to viral hepatitis,[46] where clients are provided contacts to ensure continuity of care.[47] To mitigate future hepatitis disease burden, initiatives such as testing, preventative measures (e.g., vaccination), public health education, early access to well tolerated and highly curative antiviral treatment (e.g., for HCV), disease counselling, and the provision of contacts for care have been proposed. Earlier identification and curative treatment could be cost-effective and beneficial for individuals.[48-50]

Table 4-1

Estimated relative burden ratio of hepatitis B-related hospitalizations, overall and by selected characteristics, for immigrants,[1] Canada (excluding Quebec and the territories)

	% of HBV hospital events attributable to immigrants (1980 to 2013)				Relative burden ratio attributable to immigrants		
	HBV hospitalizations				HBV		
	Hospitalized individuals			Estimated % of immigrant population		95% confidence interval	
Characteristics	Total	Immigrants	% immigrants[2]	(1981 to 2011)[3]	Ratio	from	to
Overall	3,210	1,175	37.0	16	2.3	2.2	2.5
Age at hospitalization							
0 to 24	65	25	40.0	11	3.6	2.0	5.2
25 to 34	155	65	41.0	23	1.8	1.3	2.3
35 to 44	390	135	33.0	26	1.3	1.0	1.5
45 to 64	1,685	595	36.1	18	2.0	1.8	2.2
65 and older	920	360	39.7	9	4.4	3.9	4.9
Sex							
Male	2,360	870	36.9	16	2.3	2.1	2.5
Female	850	305	37.3	17	2.2	1.9	2.5
Region by submitting province							
Atlantic and Ontario	1,850	675	37.0	17	2.2	1.2	3.1
Prairies[4]	585	200	33.5	10	3.4	2.8	3.9
British Columbia	775	300	39.1	19	2.1	1.8	2.3

1 Immigrants are defined as immigrants who arrived from 1980 to 2013, and long-term. residents refer to Canadian-born people and pre-1980 immigrants.

2 Proportions were derived from unrounded numbers.

3 Data from the 2011 National Household Survey.

4 Prairie provinces include Manitoba, Saskatchewan and Alberta.

Note: HCV = hepatitis C virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

Table 4-2

Estimated relative burden ratio of hepatitis C-related hospitalizations, overall and by selected characteristics, for immigrants,[1] Canada (excluding Quebec and the territories)

	% of HCV hospital events attributable to immigrants (1980 to 2013)				Relative burden ratio attributable to immigrants		
	HCV hospitalizations				HCV		
	Hospitalized individuals					95% confidence interval	
Characteristics	Total	Immigrants	% immigrants[2]	Estimated % of immigrant population (1981 to 2011)[3]	Ratio	from	to
Overall	10,935	955	8.6	16	0.5	0.5	0.6
Age at hospitalization							
0 to 34	345	25	15.1	34	0.4	0.0	1.2
35 to 44	1,075	75	6.0	26	0.2	0.1	0.4
45 to 64	7,680	490	6.3	18	0.4	0.3	0.4
65 and older	1,835	365	20.6	9	2.3	1.9	2.6
Sex							
Male	7,540	560	7.1	16	0.4	0.3	0.5
Female	3,395	395	11.9	17	0.7	0.6	0.8
Region by submitting province							
Atlantic and Ontario	5,900	640	12.4	17	0.7	0.4	1.0
Prairies[4]	2,570	145	4.8	10	0.5	0.2	0.7
British Columbia	2,455	165	6.3	19	0.3	0.2	0.5

1 Immigrants are defined as immigrants who arrived from 1980 to 2013, and long-term. residents refer to Canadian-born people and pre-1980 immigrants.

2 Proportions were derived from unrounded numbers.

3 Data from the 2011 National Household Survey.

4 Prairie provinces include Manitoba, Saskatchewan and Alberta.

Note: HCV = hepatitis C virus.

Sources: Statistics Canada, 1980 to 2013, Longitudinal Immigration Database and Discharge Abstract Database linked database.

Limitations

Overall, immigrants are underrepresented in this study, since those who arrived before 1980 have not been classified as such and are instead identified as long-term residents. However, the incorporation of immigrants before 1980 into the long-term resident group would be unlikely to affect this study's results since migration trends in Canada have changed over the past 100 years. Prior to the 1970s, European countries (i.e., the United Kingdom, Italy, Germany and the Netherlands) accounted for most of the immigrant source countries, with cultural and health risk profiles very similar to Canada's population profile.[35] The scope of this study was observational, therefore longitudinal factors affecting disease progression (e.g., time since diagnosis) were not available. Emigration data were not available, nor was it known whether immigrants still remained in the country; therefore, person-time at risk was not calculated. Also, since population denominators were unknown, it was not possible to perform age standardization. Thus, it is possible that the results could be confounded by age. This study may not reflect all hospitalizations among immigrants nationally since those from Quebec are excluded. The exclusion of data from the territories is unlikely to affect results because of the low immigrant population in this region. Hospitalization represents end-stage or severe disease and not the full disease spectrum, thus the burden of hepatitis is likely underrepresented in this study's findings. Hepatitis-related hospitalizations generally occur after a long subclinical period. More hospitalization events may have been observed if a longer follow-up period was included. In addition, HCV and HBV country risk in this study is assigned using publicly available data, which are an approximation of the real risk level categorization for the timeframe of the study.[29,30,34]

The ratio to calculate HBV- and HCV-related hospitalizations attributable to immigrants could have been overestimated in this study, since institutional high-risk populations in Canada were excluded from the Canadian-born population obtained from the 2011 NHS data but were included in the immigrant IMDB-linked data. However, a sensitivity analysis showed that the ratio for HCV among immigrants who were most at risk, those aged 65 years and older, remained above 1 (1.9). If immigrants are less likely to access preventative and early care, this could lead to an increase in hospitalization rates among immigrants because of increasing severity over time.[16] Furthermore, survivor selection bias, the bias that some immigrant patients might have died because of late detection, may result in an underestimation of the relative prevalence of HBV and HCV detected in immigrants.[51] Additionally, the length of stay results could partially be a result of other factors, such as language proficiency or other barriers to care, resulting in difficulties for immigrants to interact with the health care system.[52,53] As a result, differences between immigrant and long-term residents must be considered when comparing both groups.

Conclusion

This study provides insights into HBV- and HCV-related hospitalizations incurred by immigrants using linked administrative immigration and hospital data. This additional information contributes to better understanding the health of this population. Developing and bolstering screening programs

would help to identify those at risk of disease progression at earlier stages in order to prevent HCV-related complications, since there could be a high five-year survival rate (over 90%) when HCV is managed at an early stage.[16] Existing literature[40,42] points to early detection, awareness and treatment that would have an impact on this population group as it ages and on health services. The use of health education may be one way to increase awareness among those who may be unaware of their infection.[54–56] The findings from this study point to the risks for this subpopulation and call for future studies, especially for HCV. Given that the recently updated IMDB includes immigrants who arrived in Canada from 1952 to 1979, a new linkage of the IMDB to more recent hospital data to extend the follow-up period would help ensure more comprehensive coverage of hospital events, in light of the long subclinical period of HBV and HCV.

Appendix Table A

Hepatitis B and hepatitis C risk levels by birth country[1]

Country	HBV	HCV	Country	HBV	HCV
Afghanistan	L	L	Libya	M	L
Albania	M	…	Lithuania	L	M
Algeria	M	M	Luxembourg	…	M
Angola	H	…	Madagascar	M	L
Argentina	L	M	Malawi	H	…
Australia	L	M	Malaysia	L	M
Austria	L	L	Mali	H	…
Azerbaijan	M	M	Malta	…	L
Bahrain	L	M	Marshall Islands	M	…
Bangladesh	M	…	Mauritania	H	…
Barbados	L	…	Mexico	L	L
Belarus	M	…	Moldova	M	…
Belgium	L	L	Mongolia	H	H
Belize	M	…	Morocco	L	M
Benin	H	…	Mozambique	H	…
Bhutan	M	…	Myanmar	M	…
Bolivia	L	…	Namibia	H	…
Bosnia and Herzegovina	L	…	Nauru	H	…
Brazil	L	M	Nepal	L	…
Brunei Darussalam	M	…	Netherlands	L	L
Bulgaria	M	M	New Zealand	M	M
Burkina Faso	H	M	Nicaragua	L	…
Burundi	H	M	Niger	H	…
Cambodia	M	M	Nigeria	H	M
Cameroon	H	L	Niue	H	…
Canada	L	L	Norway	L	L
Cape Verde	M	…	Oman	M	L
Central African Republic	H	L	Pakistan	M	H
Chad	…	M	Palau	M	…
Chile	L	L	Palestine	L	…
China	M	L	Panama	L	L
Colombia	M	M	Papua New Guinea	H	M
Congo	H	…	Peru	M	L
Costa Rica	L	…	Philippines	M	L
Côte d'Ivoire	H	…	Poland	L	L
Croatia	L	L	Portugal	L	M
Cuba	L	L	Puerto Rico	…	M
Cyprus	M	…	Qatar	L	M
Czech Republic	L	L	Romania	M	M
Denmark	L	L	Russia	M	H
Djibouti	H	…	Rwanda	H	…
Dominican Republic	M	L	Samoa	M	L
Democratic Republic of the Congo	M	…	Saudi Arabia	M	L
Ecuador	M	…	Senegal	H	…
Egypt	L	H	Serbia	L	…
Equatorial Guinea	H	…	Seychelles	L	…
Eritrea	M	…	Sierra Leone	H	…
Estonia	…	M	Singapore	M	…
Ethiopia	M	L	Slovakia	L	L
Federated States of Micronesia	M	…	Slovenia	L	L
Fiji	M	L	Solomon Islands	H	…
Finland	…	L	Somalia	…	M to H[4,5]
France	L	L	South Africa	M	L
Gabon	H	H	South Korea	M	L
Gambia	H	M	South Sudan	H	…
Georgia	M	H	Spain	L	M
Germany	L	L	Sri Lanka	M	…
Ghana	H	M	Sudan	H	…
Greece	L	M	Suriname	M	…
Guadeloupe	…	L	Swaziland	H	…
Guatemala	L	…	Sweden	L	L
Guinea-Bissau	H	…	Switzerland	L	M

… not applicable

1 Immigrant's birth country risk level was based on published HBV and HCV prevalence rates (see refences 29–34). Classifications for HBV: low (L) <2%, moderate (M) 2% to 8%, and high (H) >8% (Schweitzer et al. 2015); HCV: low (L) <0.8%, moderate (M) 0.8% to 2.9%, and high (H) >2.9% (Polaris Observatory HCV Collaborator, 2017).Countries not assigned a risk level for HBV or HCV were coded as missing.

2 Hong Kong HBV reference: Department of Health, Hong Kong, 2016.

3 Taiwan HBV reference: Wait & Chen, 2012.

4 Somalia HCV reference: Chaabna et al., 2011. 5 - Programmed as medium.

Notes: HBV = hepatitis B virus; HCV = hepatitis C virus. L= low; M = moderate; H = high.

Source: See reference 29 to 34.

Appendix Table A

Hepatitis B and hepatitis C risk levels by birth country[1] (continue)

Country	HBV	HCV	Country	HBV	HCV
Haiti	H	…	Syria	M	H
Hong Kong	M[2]	L	Tahiti	M	…
Hungary	L	L	Taiwan	H[3]	M
Iceland	L	L	Tajikistan	M	…
India	L	L	Tanzania	M	…
Indonesia	L	L	Thailand	M	L
Iran	L	L	Togo	H	…
Iraq	L	L	Tonga	H	…
Ireland	L	L	Tunisia	M	M
Israel	L	M	Turkey	M	L
Italy	M	M	Tuvalu	M	…
Jamaica	M	…	Uganda	H	…
Japan	L	L	United Kingdom	L	L
Jordan	L	L	Ukraine	L	…
Kazakhstan	M	M	United Arab Emirates	L	M
Kenya	M	L	United States	L	M
Kiribati	H	…	Uzbekistan	M	H
Kosovo	M	…	Vanuatu	H	…
Kuwait	L	…	Venezuela	L	L
Kyrgyzstan	H	…	Vietnam	H	M
Laos	H	…	Yemen	H	M
Latvia	…	M	Zambia	M	…
Lebanon	L	L	Zimbabwe	H	…
Liberia	H	…	…	…	…

… not applicable

1 Immigrant's birth country risk level was based on published HBV and HCV prevalence rates (see refences 29–34). Classifications for HBV: low (L) <2%, moderate (M) 2% to 8%, and high (H) >8% (Schweitzer et al. 2015); HCV: low (L) <0.8%, moderate (M) 0.8% to 2.9%, and high (H) >2.9% (Polaris Observatory HCV Collaborator, 2017).Countries not assigned a risk level for HBV or HCV were coded as missing.

2 Hong Kong HBV reference: Department of Health, Hong Kong, 2016.

3 Taiwan HBV reference: Wait & Chen, 2012.

4 Somalia HCV reference: Chaabna et al., 2011. 5 - Programmed as medium.

Notes: HBV = hepatitis B virus; HCV = hepatitis C virus. L= low; M = moderate; H = high.

Source: See reference 29 to 34.

Appendix Table B

Diagnosis and procedure codes used to identify hospitalizations for liver-related conditions

Diagnoses/procedures	ICD-10 codes	Procedure codes (CCI)
Viral hepatitis		
Acute hepatitis A	B15	…
Acute hepatitis B	B16	…
Other acute hepatitis	B17	…
Chronic viral hepatitis	B18	…
Unspecified viral hepatitis	B19	…
Malignant neoplasm of liver and intrahepatic bile ducts (liver cancer)	C22	…
Oesophageal varices	I85	…
Gastric varices	I86.4	…
Oesophageal varices without bleeding in diseases classified elsewhere	198.20	…
Oesophageal varices with bleeding in diseases classified elsewhere	I98.3	…
Peritonitis	K65	…
Diseases of the liver		
Alcoholic liver disease	K70	…
Toxic liver disease	K71	…
Hepatic failure, not elsewhere classified	K72	…
Chronic hepatitis, not elsewhere classified	K73	…
Fibrosis and cirrhosis of liver	K74	…
Other inflammatory liver diseases	K75	…
Other diseases of liver	K76	…
Liver disorders in diseases classified elsewhere	K77	…
Postprocedural hepatorenal syndrome	K91.83	…
Unspecified jaundice	R17	…
Ascites	R18	…
Liver transplantation and complications therefrom	T86.4, Z94.4	1.OA.85.^^

Notes: ICD = International Classification of Diseases; CCI = Canadian Classification of Health Interventions.

Sources: Ng E, Myers RP, Manuel D, Sanmartin C. Hospital stays for hepatitis B or C virus infection or primary liver cancer among immigrants: a census-linked population-based cohort study. Canadian Medical Association Journal Open 2016; 4(2): E162-8. DOI: 10.9778/cmajo.20150117.

Appendix Table C

Diagnostic codes for comorbidity and sequelae for hepatitis B and hepatitis C with description

Type	ICD-10 codes
Hepatitis B virus-related conditions	B16, B17.0, B18.0, B18.1, Z22.50
Hepatitis C virus-related conditions	B17.1, B18.2, Z22.51
Comorbidity	
Alcohol-related conditions: conditions 100% attributable to alcohol	
Alcohol-induced pseudo-Cushing's syndrome	E24.4
Mental and behavioural disorders attributed to use of alcohol	F10
Degeneration of nervous system attributed to alcohol	G31.2
Alcoholic polyneuropathy	G62.1
Alcoholic myopathy	G72.1
Alcoholic cardiomyopathy	I42.6
Alcoholic gastritis	K29.2
Alcoholic liver disease	K70
Alcohol-induced acute pancreatitis	K85.2
Alcohol-induced chronic pancreatitis	K86.0
Maternal care for (suspected) damage to fetus from alcohol	O35.4
Fetal alcohol syndrome (dysmorphic)	Q86.0
Finding of alcohol in blood	R78.0
Toxic effects of alcohol	T51
Accidental poisoning by and exposure to alcohol	X45
Intentional self-poisoning by and exposure to alcohol	X65
Poisoning by and exposure to alcohol, undetermined intent	Y15
Cardiovascular disease (selected conditions)	
Central retinal artery occlusion	H34.1
Cerebral infarction	I63
Diabetes Type 2	E08, E11
HIV	B20-B24
Sequelae	
Hepatic failure	K72
Peritonitis	K65
Cirrhosis and ascites	K71.7, K74.6, R18
Primary liver cancer	C22
Liver transplantation	T86.4, Z94.4
Variceal hemorrhage	I85.0, I85.01, I85.11, I98.20, I98.3

Sources: Canadian Institute for Health Information, 2017, *Alcohol harm in Canada: Examining hospitalizations entirely caused by alcohol and strategies to reduce alcohol harm. Government of the United Kingdom> Liver disease: applying All Our Health -Available: https://www.gov.uk/government/publications/liver-disease-applying-all-our-health/liver-disease-applying-all-our-health [Accessed 25 Oct 2020]. Van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ, A Modification of the Elixhauser Comorbidity Measures into a Point System for Hospital Death Using Administrative Data. Medical Care. Vol. 47, No. 6 (Jun., 2009), pp. 626-633. Wilson R, Williams DM. Cirrhosis. Medical Clinics of North America. 2022 May;106(3):437-446. doi: 10.1016/j.mcna.2021.12.001. Epub 2022 Apr 4. PMID: 35491064.*

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