

# Prevalence of Primary Biliary Cholangitis in Canada: First National Study

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## Background

Primary biliary cholangitis (PBC) is a rare, progressive autoimmune liver disease that can result in significant morbidity, need for a liver transplant, and premature mortality.<sup>1,3</sup> Despite available disease treatments, PBC progresses to end-stage liver disease in approximately 10% of patients and is a common reason for liver transplantation in Western countries.<sup>4,6</sup> While consistently increasing, published prevalence estimates of PBC show a large range of 19.1 to 402 cases per million.<sup>7-22</sup> The most recently published Canadian PBC prevalence estimate reported a 2002 prevalence of 227 cases per million using Alberta medical records.<sup>17</sup> Our study sought to provide the first national and regional epidemiological analysis of PBC and PBC liver transplants in Canada.

## Study Objectives

The objectives of this study were to estimate and characterize the prevalent PBC population and associated PBC liver transplant recipients across Canada. Specifically this study will:

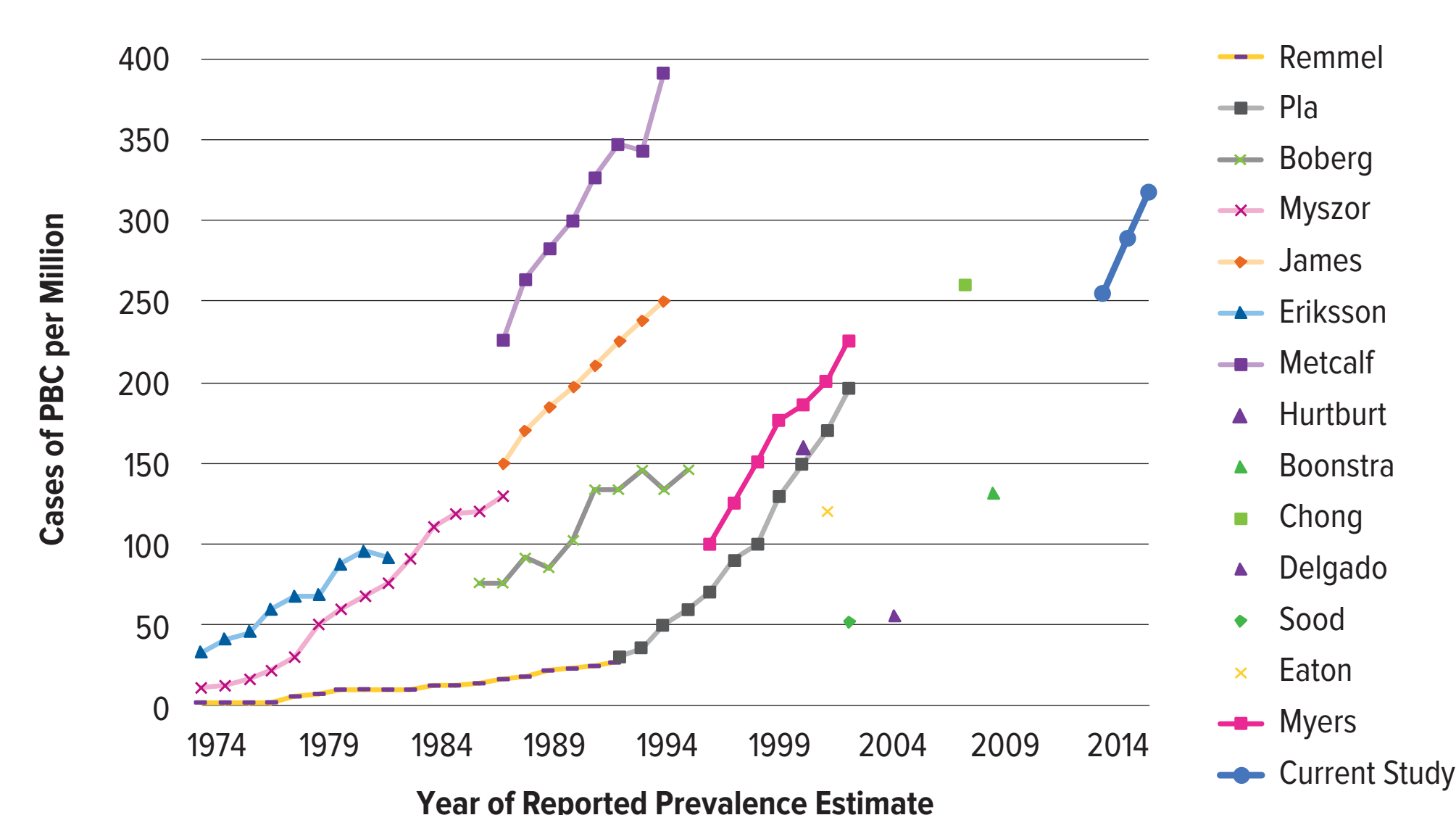
- Estimate the prevalence of PBC
- Describe the PBC patient population
- Estimate the prevalence of PBC liver transplants
- Describe the PBC liver transplant population

## Results

### THE CANADIAN PBC PREVALENCE

In 2015, 11,366 PBC patients were prevalent in Canada, after adjusting by population size to account for the absence of Quebec data (8,739 patients were observed outside of Quebec, while 2,627 patients were estimated to be inside of Quebec). This translates into a prevalence of 318 (95% CI 309-327) cases per million rising from 256 (95% CI 248, 264) cases per million in 2013. Compared to published PBC prevalence estimates from a broad range of countries, this study's prevalence estimates align within the expected range and has a similar increasing annual prevalence slope (Figure 1).

**Figure 1: PBC prevalence of current study alongside published PBC prevalence estimates**



This figure was modified from Boonstra et al., 2012 which carried out a systematic review of published PBC epidemiology studies. The results of the current study are overlaid in the figure.

Of the total PBC population, 78% were female; similarly, 85% were between the ages of 40-79. The PBC population was similar in age distribution to previously published Canadian PBC demographics<sup>17</sup> (Figure 2a). Further, of the top diagnoses recorded in the PBC population's medical records, a majority are associated with liver deterioration (Figure 2b). Of the subset of patients studied to estimate disease severity, 29% (95% CI 26%-32%) were categorized as having late-stage PBC.

## Methods

### DATA SOURCE

Longitudinal patient-level records obtained from the Canadian Institute for Health Information (CIHI) and QuintilesIMS were used for this study (Table 1).

**Table 1: Description of datasets used for this study**

DATA SOURCE	DATABASE	DESCRIPTION
CIHI Databases	Discharge Abstract Database (DAD)	These databases consist of hospital discharge abstracts from all acute care and same-day surgery visits across Canada, the majority of emergency department visits across Canada, and all outpatient clinic visits in Alberta. Demographic, clinical, and admission data were leveraged for this study. Quebec data are not available for study in this dataset.
	National Ambulatory Care Reporting System (NACRS)	This database consists of organ transplantation records submitted by organ procurement facilities and hospitals across Canada. Quebec and British Columbia data are not available for study in this dataset.
	Canadian Organ Replacement Registry (CORR)	This database consists of 76% of dispensed retail pharmacy prescriptions, which are then projected to national coverage. Demographic and prescription data were used for this study.
QuintilesIMS Databases	Longitudinal Prescriptions (LRx)	This database consists of 76% of dispensed retail pharmacy prescriptions, which are then projected to national coverage. Demographic and prescription data were used for this study.

### STUDY DESIGN

#### Estimating the Prevalence of PBC:

To estimate the number of PBC patients in Canada, the DAD and NACRS datasets were used to conduct an observational retrospective cohort study. Cases were indexed between 2007-2015 at their first recorded PBC diagnosis (International Classification of Diseases Version 10-Canadian Edition K74.3). Due to the chronic nature of PBC, patients were considered prevalent until a death code specific to the CIHI databases was observed. The prevalence of PBC diagnosed at outpatient clinics in Alberta was used to account for the outpatient clinic activity in other provinces. While Quebec data from CIHI was not available for study, the national prevalence estimate from the remaining provinces was applied to the 2015 Quebec population count to estimate the Quebec PBC population count.

Ursodeoxycholic acid (UDCA) is a key molecule used in the treatment of PBC. Therefore, our study quantified the number of patients prescribed UDCA using the LRx dataset, as a way of providing validation for the PBC regional prevalence trends. All patients who received UDCA for any diagnosis during 2015 were included in this study.

Statistics Canada regional population counts were used for prevalence estimates.<sup>23</sup> Regional PBC prevalence and UDCA recipient distribution estimates were age-sex standardized to the 2015 Canadian population.

Patients in Alberta were further categorized as late-stage PBC if their medical records included late-stage PBC associated diagnosis. The list of diagnosis codes associated with late-stage PBC were generated using published literature,<sup>1,3</sup> and expert clinical opinion (available upon request). This additional analysis was limited to Alberta as it was the only province with full coverage of outpatient clinics and hospital visits required for a robust determination of late-stage disease.

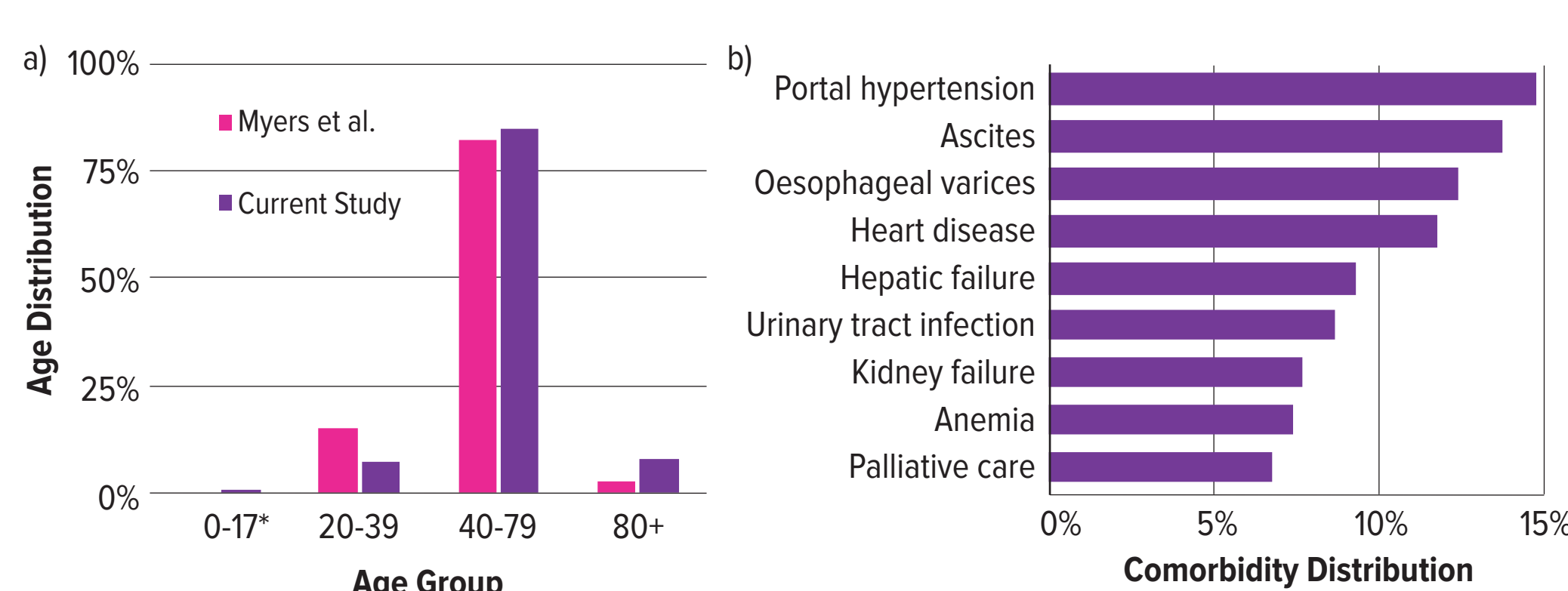
#### Estimating the Prevalence of PBC Liver Transplants:

To estimate the number of PBC liver transplants in Canada, the CORR dataset was used to conduct an observational retrospective cross-sectional study. We included all patients within the selection period, between 2010-2015, who received a liver transplant and had an associated diagnostic reason for the transplant. Within this population, we analyzed records with a PBC diagnosis. A 6-year prevalence of liver transplants was calculated, rather than an annual prevalence, to account for low annual transplant counts and therefore better elucidate regional trends. Statistics Canada 2013 regional population counts were used for prevalence estimates – the selection period's mid-point.<sup>23</sup> Regional prevalence of PBC liver transplant estimates were age-sex standardized to the 2013 Canadian population.

### STATISTICAL ANALYSIS

Descriptive statistics were used to describe population proportions throughout the study. Where confidence intervals are provided, the Wald-type method was used.

**Figure 2: The PBC population's age distribution compared to a previous Canadian PBC study and reported comorbidities**

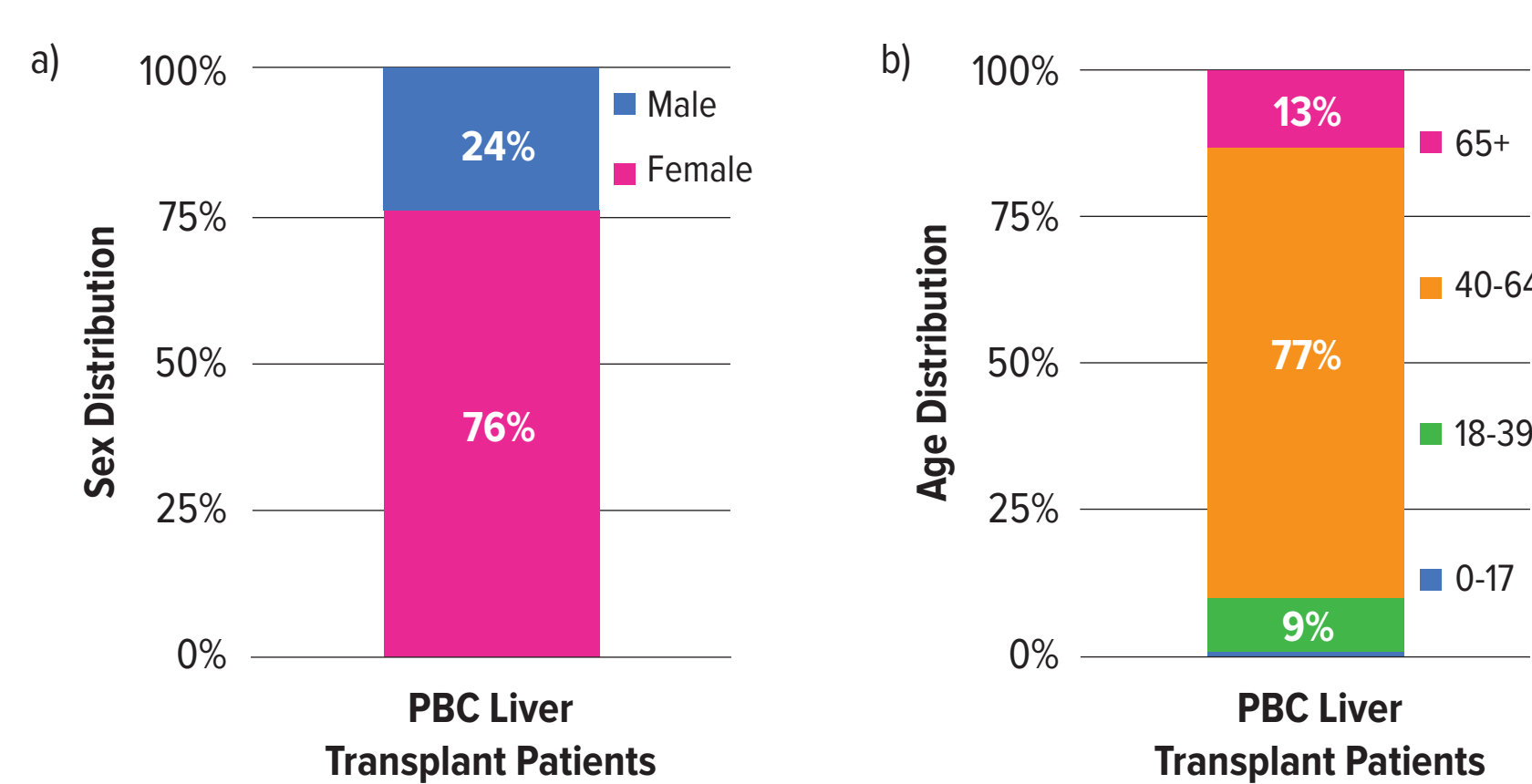


a) Age distribution of PBC prevalent population compared to the most recently published Canadian PBC prevalence study, Myers et al., 2009 b) Distribution of top 10 comorbid conditions in the PBC prevalent population. \*The Myers et al., 2009 study did not assess prevalence in PBC patients aged 0-17.

### CANADIAN PBC LIVER TRANSPLANTS

Of the 1,800 liver transplants records analyzed, 92 (5.1%) were performed due to PBC. Of all liver transplants performed on female patients, 16% were due to PBC, making PBC the most common reason for a female to require a liver transplant. Within the PBC liver transplantation population, 76% were female and 77% were between 40-64 years old (Figure 3).

**Figure 3: Sex and age distributions of the patients who received a liver transplant due to PBC**

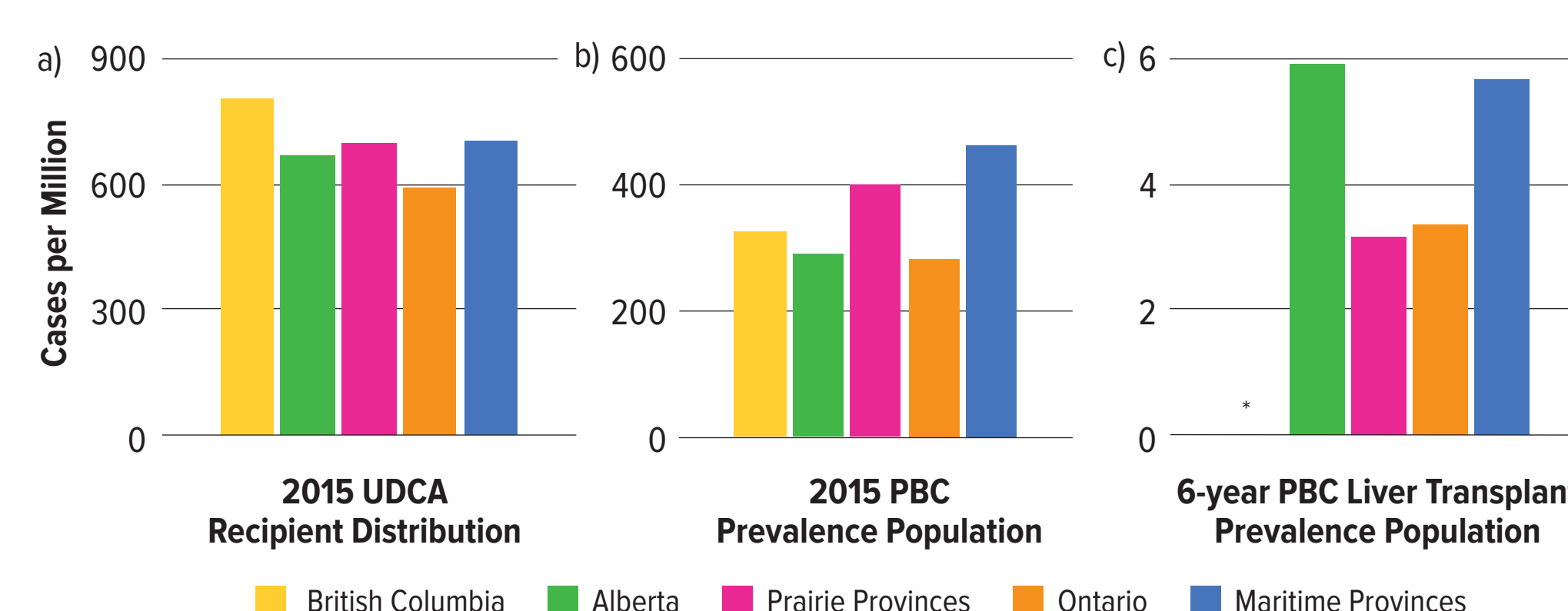


a) Sex distribution of PBC liver transplant patients b) Age distribution of PBC liver transplant patients.

### REGIONAL DISTRIBUTION OF PBC

Regionally, the Maritime Provinces (New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador) have the highest PBC prevalence estimate, which is mirrored by high UDCA recipients and a high 6-year prevalence of PBC liver transplants (Figure 4). The 2015 UDCA recipient counts showed higher than expected rates of use in British Columbia. Similarly, Alberta had a higher than expected 6-year prevalence of liver transplants; however, patients from neighboring Prairie Provinces (Saskatchewan and Manitoba) travel to Alberta for liver transplant procedures and may inflate Alberta's prevalence. As the UDCA prescriptions were used to treat PBC along with other indications, the regional UDCA recipient distribution is higher than the PBC prevalence – ranging between 1.5-2.5 times more UDCA recipients than PBC patients.

**Figure 4: Canadian regional distribution of UDCA recipients\*\*, PBC prevalence, and PBC liver transplants**



a) Distribution of UDCA recipients by Canadian geographic region, b) Prevalence of PBC by Canadian geographic region, c) Prevalence of liver transplants due to PBC by Canadian geographic region. \*Data from British Columbia was not available for study. \*\*All patients who received UDCA for any diagnosis during 2015 were included in this study.

**Table 2: Canadian regional distribution of UDCA recipients\*, PBC prevalent population, and PBC liver transplants**

	BRITISH COLUMBIA	ALBERTA	PRAIRIE PROVINCES	ONTARIO	MARITIME PROVINCES
UDCA Recipients	809 (95% CI 776-842)	669 (95% CI 640-698)	700 (95% CI 661-739)	595 (95% CI 580-610)	703 (95% CI 666-740)
PBC Population	327 (95% CI 302-352)	292 (95% CI 275-309)	399 (95% CI 360-438)	283 (95% CI 269-297)	465 (95% CI 426-504)
PBC Liver Transplants	N/A	5.92 (95% CI 3.71-9.08)	3.17 (95% CI 1.27-6.54)	3.37 (95% CI 2.47-4.50)	5.70 (95% CI 3.19-9.56)

\*All patients who received UDCA for any diagnosis during 2015 were included in this study.

## Conclusion

This study reports the first Canadian national and regional PBC prevalence estimates, demonstrating the burden of PBC in Canada is high and growing. Maritime Provinces have the highest prevalence of PBC in Canada, and given the significant genetic component in PBC's etiology, this observation is possibly due to a founder effect.<sup>23,24</sup>

Even with ubiquitous access to UDCA, PBC is still the number one reason for liver transplants in females, has a high proportion of its patients classified as late-stage, and represents a significant burden on the healthcare system highlighting the need for further treatment options.

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