EPH65

Epidemiology and Healthcare Resource Utilization of Osteogenesis Imperfecta in Ontario, Canada

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Background

- Osteogenesis Imperfecta (OI) is a group of rare heritable disorders of connective tissue resulting in bone fragility, decreased bone mass, with susceptibility to fracture from minimal trauma, as well as bone deformity and growth deficiency.[1,2]
- While the prevalence of OI has been estimated to be 1:10,000-20,000 patients worldwide[3], there is minimal evidence on the epidemiology and burden of illness (BOI) of OI in Canada.
  - Ontario represents ~40% of the Canadian population, resulting in real-world data from the province being widely used for epidemiological and BOI studies in Canada.

Aim: To use real-world data to estimate the prevalence of OI and describe clinical characteristics, healthcare resource utilization (HCRU), and direct healthcare costs of patients with OI in Ontario, Canada.

Methods

- A retrospective observational study was conducted using administrative health data in Ontario, Canada held by a not-for-profit health research corporation, ICES.
  - ICES captures data related to HCRU within Ontario's publicly-funded healthcare system, including diagnostic (ICD-10-CA), procedural (CCI), and billing (OHIP) codes. Private claims are not captured.
- Patients with 2 ICD-10-CA codes for OI (Q78) in hospital abstracts >30 days apart, from January 1, 2008, to December 31, 2021, were indexed into the **Prevalence cohort** on their first OI code.
  - Sensitivity analysis using only one ICD-10-CA code was conducted for prevalence.
- Patients >105 years of age or a non-Ontario resident at index, or missing key demographics were excluded.
- Patients with ≥1 year of follow-up were further included in the **BOI cohort**.
- The control group for the BOI cohort was identified from individuals in Ontario without a record of an ICD-10-CA OI code, matched on index date, age at index date, sex, and geographic location of residence using Local Health Integration Networks (LHIN).
- A minimum 1-year lookback period, up to 3-years, was used to identify baseline characteristics prior to the OI index date.
- A minimum 1-year follow-up period, up to 3-years, following and including index date was used to evaluate clinical outcomes (i.e., fractures, complications, interventions), HCRU and direct healthcare costs in the BOI cohort.
  - Complications, interventions, and fractures were identified using ICD-10-CA, CCI, and OHIP codes across inpatient and outpatient settings.
  - For fractures, codes must have been separated by at least one day to be counted as a new fracture, to avoid double-counting.

Analysis

- Descriptive statistics were summarized for all outcome variables.
- Mean differences (MD) in HCRU and direct healthcare costs between BOI cohort and controls was evaluated using generalized linear models with generalized estimating equations (GEE) methodology to account for the matched design.

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Results

Prevalence

- The **Prevalence cohort** included 565 patients, with a median (IQR) age of 14 (5, 37) years, and 48% were male.
- Between 2008 to 2016, the prevalence of OI increased from 2.0 to 3.8 per 100,000.
- From 2017 to 2021, the prevalence of OI was stable at 3.9 per 100,000.
  - However, when utilizing one ICD-10-CA OI code, the prevalence was higher ranging from 10.6 to 11.8 per 100,000 throughout this period.
- Prevalence was lower among older age groups, with the highest rates found among young children (**Table 1**).
  - Specifically, in 2021, prevalence was 27.7 per 100,000 among children under 2 and ranged from 10.1 to 14.0 per 100,000 among children aged 2 to under 18.
  - Among adults, the prevalence of OI remained at or below 2.4 per 100,000.

Table 1. Prevalence of OI* by Age Groups

Prevalence per 100,000								
Age	**All Age Groups**	**<2**	**2 to <7**	**7 to <12**	**12 to <18**	**18 to <26**	**26 to 64**	**65+**
2017	3.9	26.3	13.2	11.4	9.9	2.4	2.0	0.5
2018	3.9	26.8	13.9	11.8	10.3	2.3	1.9	0.6
2019	3.9	28.1	14.2	12.3	10.1	2.4	1.9	0.5
2020	3.9	27.2	14.2	12.4	10.1	2.5	1.9	0.5
2021	3.9	27.7	14.0	12.3	10.1	2.4	1.8	0.5

**Note: OI is based on case definition (two ICD-10-CA diagnosis codes indicating OI (Q78) in hospital abstracts more than 30 days apart)*

Clinical Outcomes

- The **BOI cohort** included 469 patients, with a median (IQR) age of 15 (8, 43) years, and 50% were male; the mean (SD) follow-up duration for patients was 2.9 years (0.3).
- During the total follow-up period, commonly reported complications, in inpatient and outpatient settings, were related to cardiovascular disease (52%), pneumonia (31%), hearing loss (18%) and cardiopulmonary disease (14%).
  - Cardiovascular disease (<18=32%, ≥18= 79%), pneumonia (<18=19%, ≥18=47%), and cardiopulmonary disease (<18=7%, ≥18=22%) were primarily driven by adult OI patient population, whereas hearing loss (<18 =18%, ≥18 =19%) occurred with similar frequency across age groups.

Fractures

- In Year 1 (n=469), Year 2 (n=469) and Year 3 (n=451) of follow-up, OI patients had a fracture rate of 1.23, 0.51 and 0.37 per person, respectively.
- In comparison, during this time, fracture rates for controls (n=1,873) remained stable at 0.03 per person per year.
- Higher fracture rates were found among children (i.e., 1.35 per person in Year 1) than adults (i.e., 1.08 per person in Year 1) across all three years of follow-up (**Table 2**).
- Most common fractures during follow-up among OI patients were related to femur and/or tibia.
- Furthermore, 67% of OI patients reported undergoing interventions for fracture repair, including fixation techniques, reconstructive surgery, and application of casts.
  - Interventions for fracture repair were slightly greater among the pediatric population (<18=72%, ≥18=60%).

Table 2: Fracture Rate and Number of Patients with At least One Fracture During Follow-up Period, Among OI Patients in BOI Cohort, by Age Groups

Fractures During Follow-up Period, Among BOI Cohort								
Age	**All Age Groups**		**Under 18**		**18-64**		**65+**	
	Year 1 (N=469)	**Total Follow-up Period[1] (N=469)**	**Year 1 (N=266)**	**Total Follow-up Period (N=266)**	**Year 1 (N=181)**	**Total Follow-up Period (N=181)**	**Year 1 (N=22)**	**Total Follow-up Period (N=22)**
Fracture Rate[2], Mean (SD)	1.2 (1.4)	0.7 (0.9)	1.3 (1.4)	0.8 (0.9)	1.1 (1.3)	0.6 (0.8)	1.1 (1.1)	0.6 (0.7)
Number of Patients with At least 1 Fracture (%)[3]	281 (60%)	236 (50%)	173 (65%)	*135-143 (51%-54%)	*91-99 (50%-55%)	*82-90 (45%-50%)	*9-17 (41%-77%)	*7-15 (32%-68%)

Abbreviations: SD=Standard Deviation

[1] Total follow-up period (i.e., minimum 1 year, maximum 3 years) may differ for patients. All 469 OI patients have 2 years of follow-up, but only 451 OI patients have 3 years of follow-up.

[2] Fracture rate (per person per year) is calculated for each patient as the ratio of total number of fracture events per patient during the follow-up period, divided by the length of follow-up period

[3] Year 1 presents the number of patients with at least 1 fracture during Year 1, while total follow-up period presents the average number of patients with at least 1 fracture over the length of the follow-up period (i.e., 2 fractures in Year 1, 1 fracture in Year 2, 1 fracture in Year 3 = 1.3 fractures per year).

**N values <6 have been masked; secondary suppression is also used to avoid back calculation*

HCRU and Direct Healthcare Costs

- Overall, HCRU (i.e., specialist visits, GP visits, ED visits and inpatient hospitalizations) and direct healthcare costs were significantly greater for OI patients compared to controls for all follow-up years (p<0.001) (**Table 3, Figure 1**).
  - In general, this pattern was also consistent across age groups (p<0.001) (**Table 4, Figure 1**).
- HCRU among OI patients during the total follow-up period:
  - Pediatric patients were attended to by orthopedic surgeons (<18 years = 43.6%) more than adult patients (18-64 years = *12%-14%; 65+ years = *5%-23%).
  - On average, the number of GP visits (<18 years = 8 (SD=9); 18-64 years = 32 (SD=46); 65+ years = 37 (SD=28)), specialist visits (<18 years = 24 (SD=25); 18-64 years = 36 (SD=45); 65+ years = 40 (SD=47)) and inpatient hospitalizations (<18 years = 1.6 (SD=1.9); 18-64 years = 1.8 (SD=2.3); 65+ years = 2.2 (SD=1.5)) increased with age.
  - Adult patients aged 18 to 64 years, on average, had more ED visits than both pediatric and senior patients (<18 years = 4.1 (SD=4.7); 18-64 years = 6.1 (SD=15.1); 65+ years = 4.3 (SD=4.2))
- The mean total costs to the healthcare system for an OI patient ranged from $26,881 in Year 1 to $10,674 in Year 3 (**Figure 1**)
- During total follow-up period, the mean total costs were greater in OI patients aged 18 to 64 ($74,542) and those 65 and older ($70,472) compared to the pediatric population ($32,613)
  - This trend was consistent for physician billing (<18 years = $6,429; 18-64 years = $11,088; 65+ years = $10,434), GP billing (<18 years = $334; 18-64 years = $1,268; 65+ years = $1,633), specialist billing (<18 years = $1,666; 18-64 years = $2,675; 65+ years = $2,797), ED visits (<18 years = $1,146; 18-64 years = $2,180; 65+ years = $2,006), and inpatient hospitalizations(<18 years = $12,629; 18-64 years = $26,915; 65+ years = $17,267).

Table 3: Comparison of Mean Difference in Healthcare Resource Utilization Categories Between OI Patients in BOI Cohort and Control Group, Follow-up Period (Year 1, 2, 3, Total), All Age Groups

Comparison of BOI Cohort vs Control Group, Total Follow-up Period and by Year 1, 2, 3, All Age Groups								
Healthcare Resource Utilization (HCRU) Categories	**Year 1**				**Year 2**			
	MD	**95%**	**CI**	**P-value**	**MD**	**95%**	**CI**	**P-value**
Specialists Visits	13.7	11.6	15.9	<.0001	5.9	4.9	7.0	<.0001
GP Visits	5.7	4.2	7.3	<.0001	3.2	1.9	4.4	<.0001
ED Visits	1.9	1.4	2.4	<.0001	1.1	0.8	1.3	<.0001
Inpatient Hospitalizations	1.0	0.9	1.1	<.0001	0.4	0.3	0.4	<.0001
Healthcare Resource Utilization (HCRU) Categories	**Year 3**				**Total Follow-up Period**			
	MD	**95%**	**CI**	**P-value**	**MD**	**95%**	**CI**	**P-value**
Specialists Visits	4.8	3.9	5.7	<.0001	24.2	21	27.5	<.0001
GP Visits	2.5	1.8	3.1	<.0001	11.2	8.3	14.1	<.0001
ED Visits	0.9	0.7	1.1	<.0001	3.8	2.9	4.7	<.0001
Inpatient Hospitalizations	0.3	0.2	0.3	<.0001	1.6	1.4	1.8	<.0001

Abbreviations: GP = General Practitioner, ED = Emergency Department, MD = Mean Difference

Table 4: Comparison of Mean Difference in Healthcare Resource Utilization Categories Between OI Patients in BOI Cohort and Control Group, Total Follow-up Period, by Age Groups

Comparison of BOI Cohort vs Control Group, Total Follow-up Period, by Age Groups												
Healthcare Resource Utilization (HCRU) Categories	**<18**				**18-64**				**65+**			
	MD	**95%**	**CI**	**P-value**	**MD**	**95%**	**CI**	**P-value**	**MD**	**95%**	**CI**	**P-value**
Specialists Visits	20.0	17.0	23.0	<.0001	29.9	23.3	36.5	<.0001	28.3	9.6	47	0.0031
GP Visits	2.7	1.6	3.8	<.0001	22.2	15.5	28.9	<.0001	22.9	10.7	35.1	0.0002
ED Visits	3.1	2.6	3.7	<.0001	4.9	2.7	7.1	<.0001	3.3	1.6	5.0	0.0001
Inpatient Hospitalizations	1.5	1.3	1.8	<.0001	1.7	1.3	2.0	<.0001	1.8	1.2	2.5	<.0001

Abbreviations: GP = General Practitioner, ED = Emergency Department, MD = Mean Difference

Figure 1.1: Mean Total Direct Healthcare Costs* in Canadian Dollars for BOI cohort, Follow-up Period (Year 1, 2, 3, Total), by Age Groups**

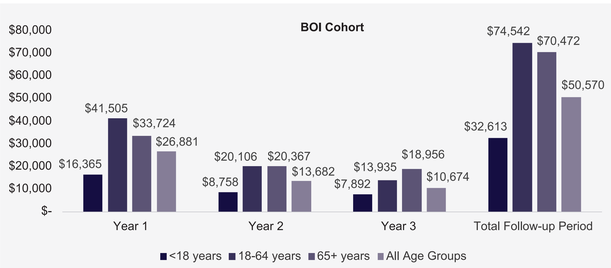
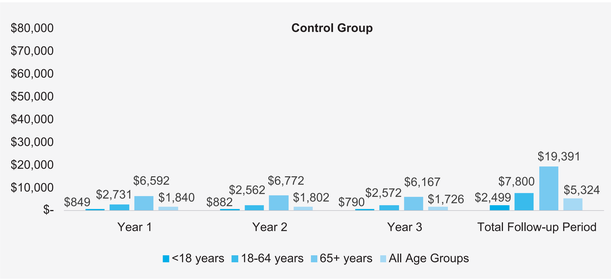


Figure 1.2: Mean Total Direct Healthcare Costs in Canadian Dollars for Control Group, Follow-up Period (Year 1, 2, 3, Total) by Age Groups



Note: Mean total direct healthcare costs will be automatically higher in Year 1 in OI patients, as they needed to visit the ED or hospital to index
**Mean difference between mean total direct healthcare costs between BOI cohort and control group in Year 1, Year 2, Year 3, and total follow-up period for all age groups, <18 years, 18-64 years and 65+ years was significant (p-value < 0.0001).*
*** A weighted methodology was utilized to calculate the hospitals cost4. All costs were standardized to 2021 Canadian dollars.*

Conclusions

- This study estimates OI prevalence in Ontario at almost 4 cases per 100,000, with fractures most prevalent among young children.
- Due to the limited capture of diagnoses in administrative health data, prevalence of OI and fracture rates are likely underestimated.
- Patients with OI experience significant complications, namely fractures, and with no approved treatments available this poses significant burden to patients and the healthcare system.

Limitations

- Due to the nature of the data, this study was not able to capture privately covered treatments and interventions OI patients may have received.
- Reliance on medical codes may have resulted in underestimation of some outcomes due to under-reporting, miscoding, or lack of specificity, particularly in outpatient settings.
- Results among small sample sizes (i.e., 65+ years) should be interpreted with caution.
- As the study period overlapped with COVID-19 pandemic, HCRU and costs may be underestimated due to changes in healthcare access[5].

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