Manifestations and Comorbid Conditions Among Patients with Osteogenesis Imperfecta (OI): A US Retrospective Claims Database Analysis

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INTRODUCTION

- Osteogenesis imperfecta (OI) is a hereditary, lifelong, systemic connective tissue disorder characterized by bone fragility resulting in recurrent fractures and skeletal deformities[1]
- Patients also suffer from extra-skeletal manifestations and comorbidities including muscle disorders, pain, cardiopulmonary disorders, and more[1]

OBJECTIVES

- This retrospective cohort study assesses clinical manifestations and comorbid conditions beyond fractures among patients with OI.

METHODS

- This retrospective, real-world cohort study used the IQVIA Pharmetrics® Plus database, which contains adjudicated, deidentified, and integrated medical and pharmacy (retail and mail order) claims data for >150 million members from >70 US commercial health plans.
- Individuals with OI inclusion criteria:
  - with at least two ICD-10-CM diagnosis codes of OI (Q78.0x) 30 days apart
  - ≥12 months continuous enrollment (CE) between January 2016 and February 2020 (before COVID-impacted period)
  - Excluded if there is any evidence of clinical trial participation
- Age group, gender, payer type, and CE start year matched individuals in the database without any diagnosis of OI were selected as the comparator group
  - 1:3 exact matching
  - Individuals in the comparator group were required to have ≥12 months CE between January 2016 and February 2020
- Clinical manifestations/comorbidities were identified via ICD-10 diagnosis codes (any position) during continuous enrollment period
- Results were reported overall and by age groups

Results

- In total, 2095 patients with OI were included in the study **(Table 1)**
  - 55.7% female; 87.1% commercially-insured
- The average continuous enrollment duration for OI cohort was 3.4 years and 3.2 for matched comparators.
- The average age for OI cohort was 41.6 and for comparators was 30.6; both group has median age at 28.
- 35.1% of patients with OI or comparators were pediatric (<18 years)

Table 1. Baseline Patient Characteristics (N=2095)

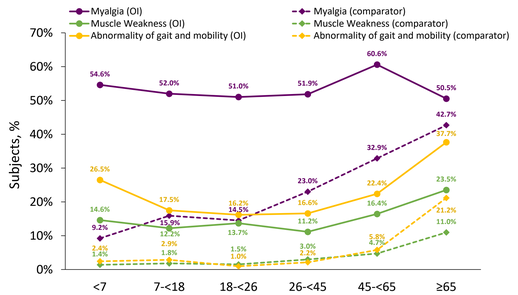
Demographic	OI Cohort (N = 2095)		Comparators (N = 6285)	
Age				
Age (mean, sd)	41.56	151.23	30.63	20.60
Age (median, iqr)	28	13, 48	28	13, 48
Gender (n, %)				
Male	929	44.3%	2787	44.3%
Female	1166	55.7%	3498	55.7%
US Region (n, %)				
Northeast	352	16.8%	1065	16.9%
Midwest	549	26.2%	1595	25.4%
South	834	39.8%	2415	38.4%
West	347	16.6%	1151	18.3%
Region Unknown	13	0.6%	59	0.9%
Region				
Medicare	78	3.7%	234	3.7%
Commercial	1825	87.1%	5475	87.1%
Medicaid	187	8.9%	561	8.9%
Other	5	0.2%	15	0.2%
Continuous Enrollment Period				
Years (mean, SD)	3.40	2.03	3.17	2.09
Years (median, IQR)	2.91	1.51, 5.16	2.42	1.33, 4.75
Year of Index Date (n, %)				
2016	1140	54.4%	4249	67.6%
2017	499	23.8%	859	13.7%
2018	370	17.7%	842	13.4%
2019	86	4.1%	335	5.3%

RESULTS

Muscle/Mobility Disorders

- Muscle or mobility disorders were common among individuals with OI (62.7%) vs comparators (25.5%); Common ones were shown in **Figure 1.**
- Myalgia is the most common muscle or mobility disorders assessed among OI cohort (54.3% overall compared with 22.0% in comparators)

Figure 1: Occurrence of Muscle/Mobility Disorders* by Age



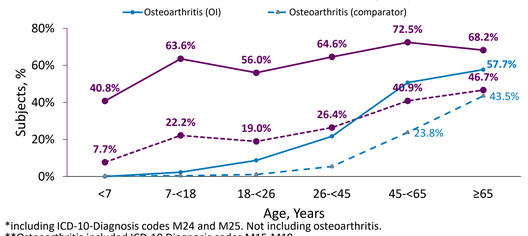
Age, years	< 7	7 - <18	18 - <26	26 - <45	45 - <65	≥65
OI, N (%)	260 (12.4%)	475 (22.7%)	241 (11.5%)	511 (24.4%)	523 (25.0%)	85 (4.1%)
Comparator, N (%)	780 (12.4%)	1,425 (22.7%)	723 (11.5%)	1,533 (24.4%)	1,569 (25.0%)	255 (4.1%)

*Only those disorders with high occurrence are included in the figure. Overall muscle or mobility disorders also included other disorders of myopathy, muscle atrophy, and gout (not in figure)

Joint Disorders

- Overall occurrence of a joint disorder was higher among OI patients (62.5%) than comparators (26.7%) in all age groups; adult OI patients had higher occurrence of osteoarthritis **(Figure 2)**

Figure 2: Occurrence of Joint Disorders*and Osteoarthritis **by Age

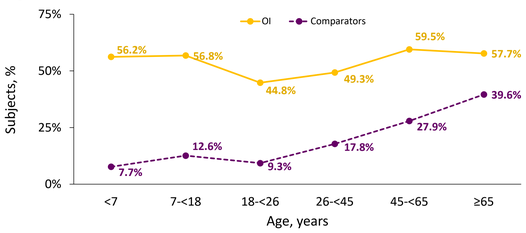


*including ICD-10-Diagnosis codes M24 and M25. Not including osteoarthritis.
**Osteoarthritis included ICD-10 Diagnosis codes M15-M19

Skeletal Deformity

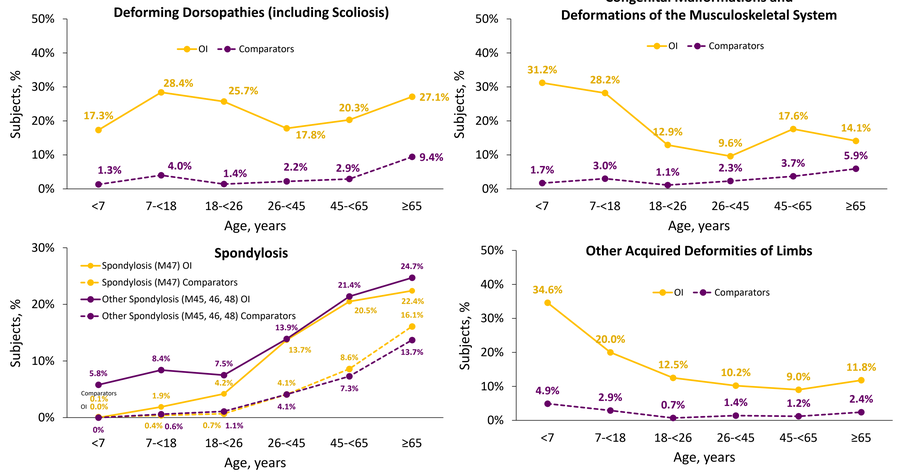
- 54.2% patients with OI and 17.8% comparators had skeletal deformities **(Figure 3A)**
  - Deformities include ICD-10-Diagnosis codes M20-23, M26, M40-43, M45-48, M50, M51, M53, Q65-79, Q77.4 and M95.
- Occurrence of skeletal deformities was higher among patients with OI in all age groups **(Figure 3B)**
- The most common deformities among patients with OI were:
  - ICD10 M21, other acquired deformities of the limbs , 19.1% OI vs 2.7% comparators
  - ICD10 M40-43, deforming dorsopathies, 22.1% OI vs. 2.9% comparators (including ICD10 M41 scoliosis, 16.6% OI vs 1.3%)
  - ICD10 M47, spondylosis, 10.3% OI vs 4.0% comparators; and ICD10 M45, M46 and M48,other spondylosis, 13.2% OI vs 3.6% comparators
  - Both OI and comparators had higher occurrence with older age with higher occurrence in OI patients at all ages ICD10 Q65-79, congenital malformation and deformation of the musculoskeletal system, 15.5% OI vs 2.1% comparators

Figure 3A: Occurrence of Skeletal Deformities



Skeletal Deformity, continued

Figure 3B: Occurrence by Type of Skeletal Deformity



Pain

- Patients with OI had higher occurrence of diagnosed pain starting early on that remained high throughout the rest of life **(Figure 4A)**
- Pain in limbs (M796) or joint (M255) was most common among patients with OI **(Figure 4B)**
- Among patients with OI, pain in limbs occurred at young age and remained high in all age groups; the occurrence of pain in joint, dorsalgia (M54) or chronic pain (G892, G894) increased with age

Figure 4A: All Pain Diagnoses

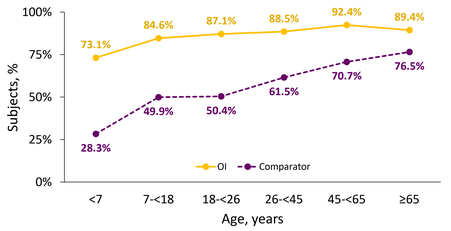
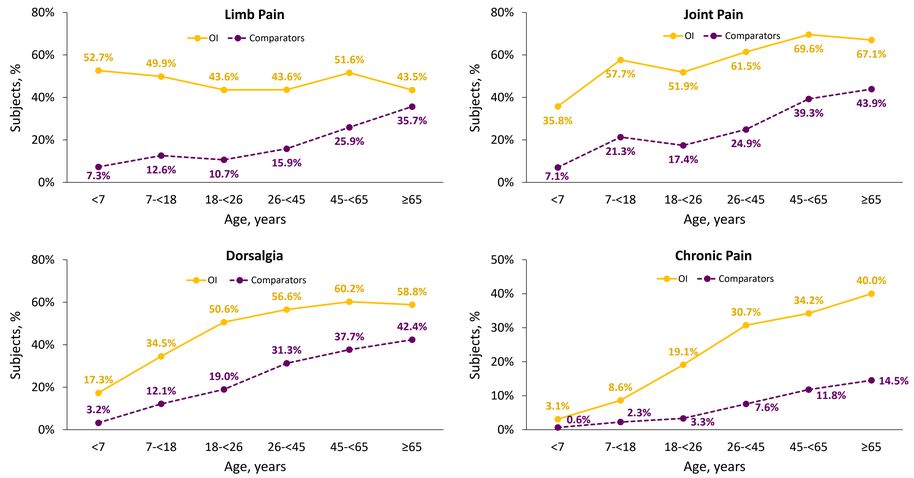


Figure 4B: Occurrence by Type of Pain



Other Manifestations/Comorbidities

- Incidence of cardiovascular/cardiopulmonary disease **(Figure 5)** and respiratory disorders **(Figure 6)** was greater in patients with OI than comparators

Figure 5: Occurrence of Cardiovascular/Cardiopulmonary Disease*

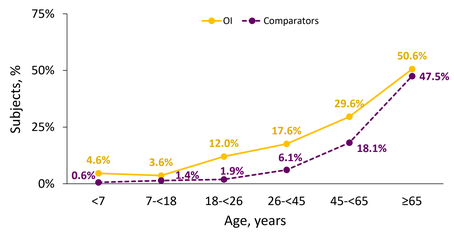
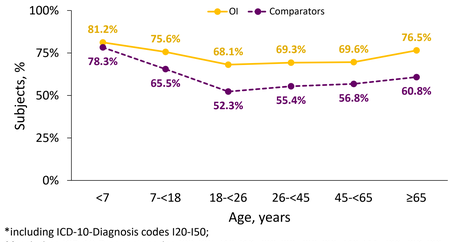


Figure 6: Occurrence of Respiratory Disorders**



*including ICD-10-Diagnosis codes I20-I50;
**including ICD-10-Diagnosis codes J00-J06, J12-J18, J20-J22, J30-J39, J40-J4A, J96, J98-J99.

Other Manifestations/Comorbidities, continued

- 44.8% of patients with OI and 32.6% of comparators had eye issues defined using ICD-10-Diagnosis codes of H00-H59 **(Figure 7)**
  - Patients with OI had blue sclera diagnosis most often before age 7 (14.2%); comparators had no blue sclera
- Overall, 25.1% patients with OI and 10.1% comparators had hearing loss ICD-10-Diagnosis codes of H90-H93 **(Figure 8)**

Figure 7: Occurrence of Eye Issues and Blue Sclera

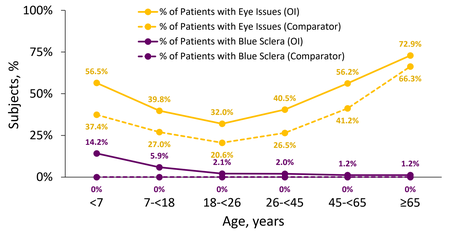
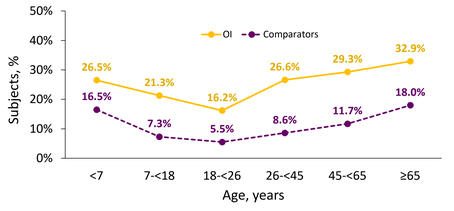


Figure 8: Occurrence of Hearing Loss



- Other common manifestations/comorbidities among patients with OI included:
  - Vitamin D deficiency (23.1% vs 9.3% in comparators)
  - Digestive system disorders (56.0% vs 38.9% in comparators)
  - 4.6% with kidney stone (2.0% in comparators)
- Patients with OI also had higher psychological disorders compared with comparators mostly commonly in anxiety (32.8% vs 19.0%), depression (22.5% vs 13.2%) and sleep disorders (22.2% vs 12.3%)
- Fatigue was diagnosed among 24.4% patients with OI and 15.6% for comparators; OI patients had higher occurrence of fatigue at all ages

LIMITATIONS

- The long-term burden of OI was underestimated due to the limited duration and mostly commercial population
- Payment records are based on diagnostic coding that may be driven by reimbursement concerns and may or may not accurately reflect the true medical condition
- Only used ICD-10 codes to identify OI and subtype information not available

SUMMARY

- The prevalence of skeletal, joint, and mobility complications is high in patients with OI vs age-matched comparators
- In addition, OI imparts systemic complications including cardiac and respiratory disease
- Patients with OI suffer from numerous types of pain including joint, limb, back, and chronic pain

REFERENCES

1. Marini JC, et al. *Nat Rev Dis Primers.* 2017; 3(17052).

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