Fracture rates in 6475 individuals with osteogenesis imperfecta stratified by age, sex and clinical severity

Poster 2119

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BACKGROUND

- Osteogenesis imperfecta (OI) is a rare genetic disorder characterized by bone fragility caused by mutations related to type 1 collagen biosynthesis.
- Fractures are a cardinal manifestation of OI, but fracture incidence across the lifespan is poorly understood.

OBJECTIVE

- To describe fracture rates in individuals living with OI, stratified by clinical severity

METHODS

- Individuals with OI were identified by ICD-9 (756.5) and/or ICD-10 (Q78.0) diagnosis codes in MarketScan claims data (2006-2022) and a 5% random sample of US Medicare Fee-for-Service data (2006-2021).
- Reference population matched 5:1 by data source, age, sex, race, index calendar year, and baseline length of continuous coverage
- Severe OI defined by long-term wheelchair use (identified using durable medical equipment (DME) claims)
- Incident fractures identified using adaptation (rolling 90-day fracture free period) of previously validated algorithm with high specificity (Wright et al. 2019)

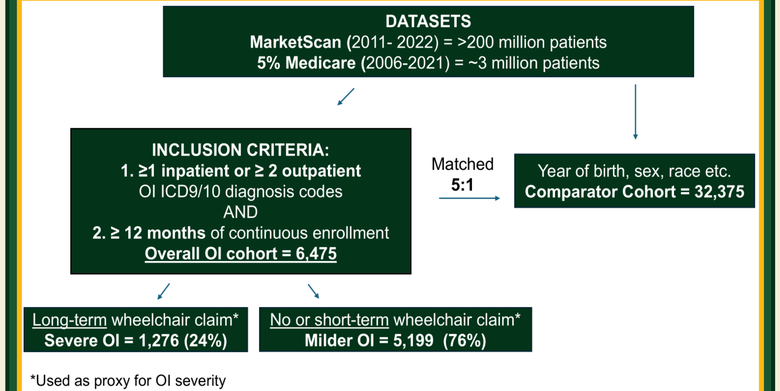
RESULTS

- We included 6,475 individuals with OI **(Figure 1)**
  - Median age was 21.0 years (IQR: 8.0, 43.0) **(Table 1)**
  - Severe OI was present in 24%
  - Median follow-up time was 2.1 years (IQR: 0.9, 4.5) in OI and 2.0 years (IQR: 0.8, 4.3) in the comparator group.
  - OI fracture rate was 129.6 (95% CI: 124.7, 134.6) per 1000 person-years (py) vs 8.0 (95% CI: 7.4, 8.6) in the reference cohort (incidence rate ratio (IRR): 16.2, 95% CI: 15.0, 17.2).
  - Across all ages, the fracture rates were higher in severe vs milder OI (IRR: 238.6, 95% CI: 226.1, 251.7) vs 87.8 (95% CI: 83.2, 92.8) per 1000py **(Figure 2).**
  - In both sexes, fracture rates were highest in childhood and lowest in early adulthood

CONCLUSION

- **We report fracture rates stratified by sex, age and clinical severity in one of the largest datasets ever assembled of US individuals living with osteogenesis imperfecta.**
- These data provide unique and necessary information for the clinical care **of individuals living with OI and for the design of trials for new therapeutics.**

Figure 1: Cohort construction



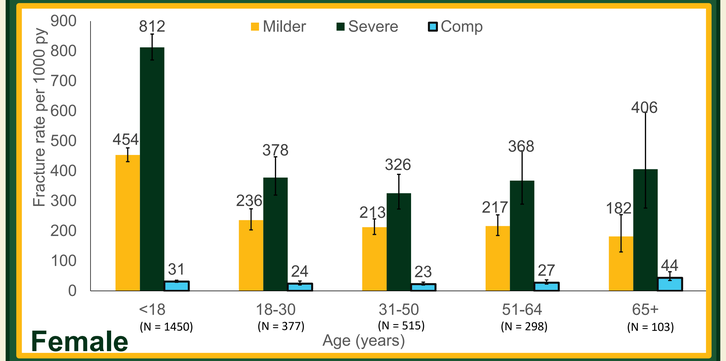
*Used as proxy for OI severity

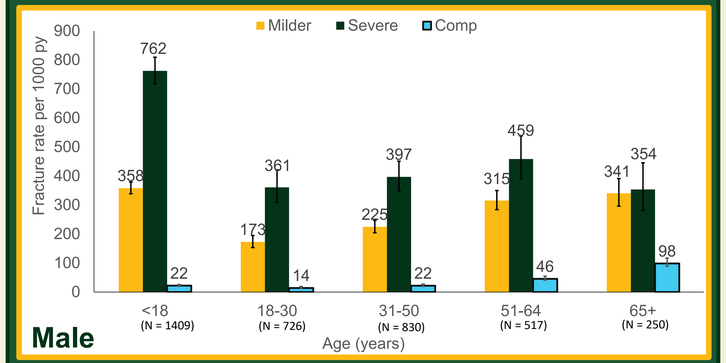
Table 1: Baseline demographics of OI and comparator groups*

Characteristics	All OI N=6,475	Severe OI N=1,276	Milder OI N=5,199	Comparator N=32,375
Median age, years (IQR)	21.0 (8.0, 43.0)	18.0 (8.0, 44.0)	22.0 (8.0, 43.0)	21.0 (8.0, 43.0)
Adults (≥18 years)	55.8%	51.1%	57.0%	55.8%
Female	57.6%	55.3%	58.2%	57.6%
Race/Ethnicity n=2,115				
White	76.6%	76.4%	76.6%	76.6%
Black	23.2%	23.2%	23.2%	23.2%
Asian	<11	0.0%	<11	<11
Other	<11	<11	<11	0.2%
Any anti-fracture medication**	15.2%	20.6%	13.9%	1.1%

OI: Osteogenesis imperfecta. IQR: Interquartile range.
* %, unless otherwise specified; ** Any anti-fracture medication defined as romosozumab, denosumab, bisphosphonates, or parathyroid hormone.

Figure 2 : Follow-up fractures incidence rates in OI vs. comparator patients by sex and age





OI: Osteogenesis imperfecta. Comp: Comparator. PY: Person-years.

ACKNOWLEDGEMENTS This study was supported by Osteogenesis Imperfecta Foundation and NIAMS P30AR072583.

DISCLOSURES *WYL, LF, EEH, YL, FX,SD, and JZ have nothing to disclose. JRC* has received support from AbbVie, Amgen, BMS, Janssen, Lilly, Novartis, Pfizer, Radius, Sanofi, Setpoint, AQTUAL, and UCB. *EO receives support from Amgen, Angitia, and Ultragenyx.*