The Clinical Burden of Fractures in Osteogenesis Imperfecta: A Systematic Review

CO237

Samantha Prince[1], Colin Song[2], Matthew Carter[2], Ogün Sazova[1], James Clancy[1], and Clive Whitcher[1]
1. Mereo BioPharma Plc., London, United Kingdom; 2. Wickenstones Ltd., Oxford, United Kingdom

Background & objectives

- Osteogenesis imperfecta (OI), or brittle bone disease, is a rare genetic condition (with a ~1 in 10,000–20,000 prevalence[1]).
- The condition is characterised by low bone mass, and bone fragility, leading to a heightened risk of fractures, bone deformities, and growth deficiencies.[2]
- OI is genetically and phenotypically diverse and often classified by clinical severity.[3] The condition is managed using a multidisciplinary approach, with most pharmacological treatments used off-label,[4] resulting in a large unmet need.
- Although a core symptom, there is limited understanding of the fracture burden in OI across life stages.

Methods

- A systematic review was performed in March 2024.
- Inclusion criteria are outlined in Table 1.
- Searches were conducted in: MEDLINE, Embase, Cochrane CENTRAL, PsycINFO, ClinicalTrials.gov, ICTRP, and CPCIS-S.
- Conference proceedings were searched by hand: Care4BrittleBone, Osteogenesis Imperfecta congress, International Conference on Children's Bone Health, European Calcified Tissue Society, International Osteoporosis Foundation, and The American Society for Bone and Mineral Research
- Bibliographies of all included studies were searched.
- Reports were double-screened, with data extracted and verified by separate researchers.

Table 1: Inclusion criteria

Population
- People with OI (>10 study participants)

Outcomes
- Characteristics of first fractures
- Fracture frequency
- Fracture locations
- Fracture healing time
- Downstream events of fractures

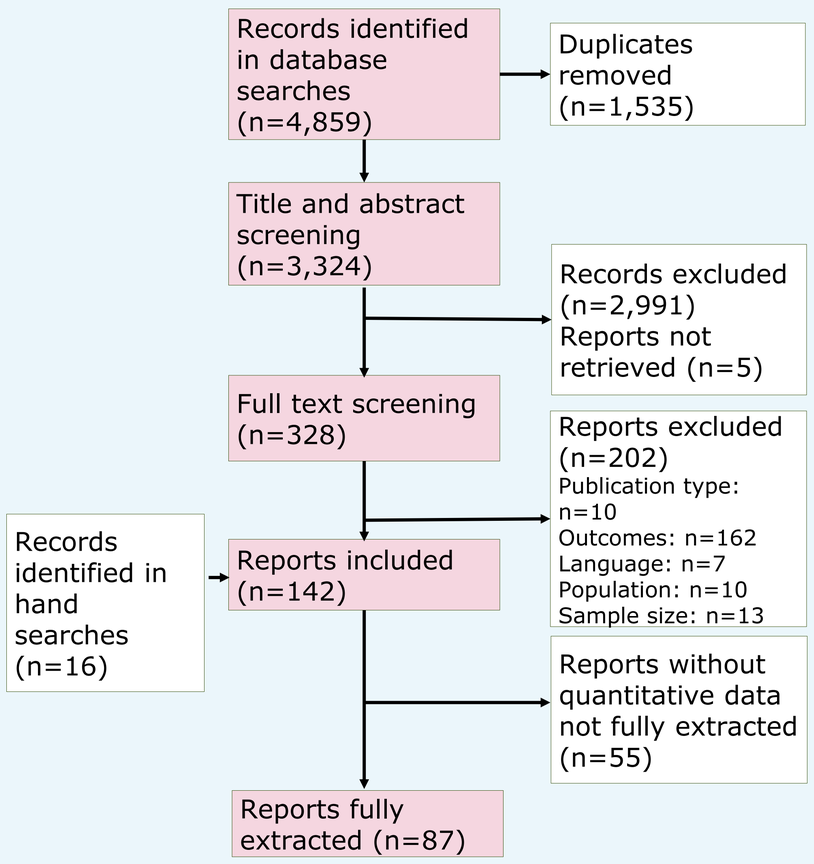
Study design
- Cohort studies
- Patient surveys
- Randomised controlled trials

Publication type
- Manuscripts
- Conference proceedings

Date
- Conference proceedings: 2021–present
- Full-text manuscripts: 2000–present

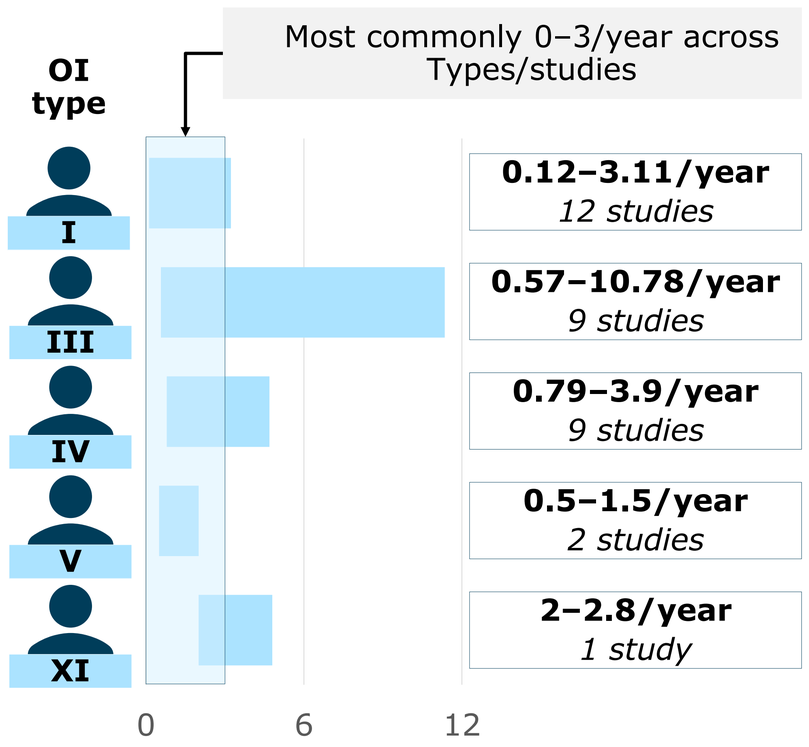
Results

Figure 1: PRISMA flow diagram



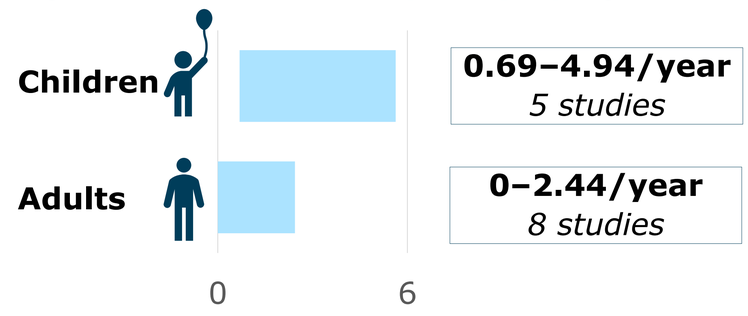
Abbreviations: PRISMA, PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Figure 2: Average fracture frequency by OI Type



Abbreviations: OI, osteogenesis imperfecta.

Figures 3: Fracture frequency by age



Average age of first fracture

Average age of first fractures varied significantly but occurred most at 0–4 years across Types/studies. Averages ranged:
- **Type I:** 1.4–6.7 years *(4 studies)*
- **Type III:** 0.1–0.63 years *(2 studies)*
- **Type IV:** 1–11.5 years *(2 studies)*
- **Type V:** 1.13–2 years *(2 studies)*
- **Type XI:** 0.1 years *(1 study)*

Data points for age at first fracture are at risk of being skewed due to incomplete medical records, particularly in instances with late referrals.

- 87 reports were included (Figure 1).

Age and frequency of fractures

- Average age of first fracture in identified reports ranged 0–11.5 years.
- First fractures were most reported early in life (0–3 years).
- Age of first fracture varied substantially by study.
- Average fracture rates were 0–10.78 fractures per year, most commonly 0–4 fractures per year.
- Average fracture frequency differed by OI type but also varied substantially within types (Figure 2).
- Fracture frequency tended to be lower in adults than children but remained high throughout life (Figure 3).

Fracture locations

- Long bone (0.04–8 per year on average) and vertebral fractures (0–1.8 per year on average) were most frequent; with other fracture locations (0.12–2.3 per year on average) also being common.

Fracture healing time

- Fracture healing time was reported by four studies and ranged from 6 to 8 weeks.

Downstream events

- Three studies described downstream signs, symptoms and events of fractures for people with OI, finding that:
  - Most (73–97%) people with OI reported limitations to daily living activities due to fracture pain.
  - Fracture rate and pain were positively and significantly correlated.
  - Fractures often (13.2%; 26 of 197 total fractures) occurred at the same anatomical site as previous fractures, compared to the rate of recurrent fractures in children without OI (1.7–2.7%).

Limitations

- This review prioritised breadth over comparability, hence caution should be applied when considering results across subgroups.
- Few studies directly compared fracture characteristics across groups, meaning confounders have not been considered.
- Many included studies were retrospective and relied on hospital records, which may be incomplete or inaccurate. This can affect data reliability and introduce bias. Age at first fracture may be skewed by late referrals and fracture rates may be underestimated where individuals did not seek care.

Conclusion

- People with OI fracture frequently throughout life.
- Fracture frequency in OI is much higher compared with the overall population, who fracture at a rate of 0.036 fractures per person per year*.[5]
- Fracture rates are highly variable and can be high regardless of age or type, however younger age and more severe OI type are associated with more frequent fractures.
- Gaps in the literature highlight the importance of further research, such as through initiatives like the SATURN programme,[6] which aims to generate a core dataset for OI, and a large longitudinal study initiated by Brittle Bone Disorders Consortium.[7]

References

1. Orphanet. 2021. Accessed on 28 October 2025 via https://www.orpha.net/en/disease/detail/216804.
2. Deguchi et al., 2021. 10.3390/medicina57050464.
3. Sillence et al., 2024. 10.1007/s00223-024-01248-7.
4. Westerheim et al., 2024. 10.1186/s13023-024-03345-0.
5. Donaldson et al., 2008. 10.1136/jech.2006.056622.
6. Sangiorgi et al., 2024. 10.1186/s13023-024-03185-y.
7. Brittle Bone Disorders Consortium. 2025. Accessed on 10 September 2025 via https://bbd.rarediseasesnetwork.org/research-study/7701.

Footnote: *Based on UK population statistics

0377_SET_10-25_NPM

Mereo BioPharma