CONCEPTUALIZATION AND VALIDATION OF A HEALTH ECONOMIC MODEL FOR OSTEOGENESIS IMPERFECTA

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Authors: Tom Edmonds[1], Oliver Darlington[1], Andrew Mumford[1], Ole Henrikson[2], Mark Waker[2], Clive Whitcher[2] , Rafael Pinedo-Villanueva[3]
Affiliations: 1. Initiate Consultancy, London, United Kingdom; 2. Mereo BioPharma, London, United Kingdom; 3. Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, United Kingdom

Background & objectives

Osteogenesis imperfecta (OI) is a rare genetic disorder characterized by bone fragility leading to frequent fractures and skeletal deformities[1]. OI imposes a significant burden on people living with OI with shortened life expectancy and poor health-related quality-of-life (HRQOL)[2], as well as for payers through increased health care resource utilization (HCRU). There is a significant unmet need for treatment options in OI. The objective of this study was to develop and validate a *de novo* health economic model that could be used for future health economic evaluations in OI.

Methods

Model structure

A *de novo* stochastic lifetime discrete event simulation model was developed in Microsoft Excel and used to estimate health outcomes and HCRU in people with OI. Model cycles were incrementally defined by time to next fracture, determined by annual fracture frequency, randomly sampled based on a patient's characteristics, including age, sex, and disease Type (I, III, or IV).

Fracture incidence

Each fracture event was classified by type and severity based on a random sampling with probability relevant to the specific patient's characteristics. Each fracture site & severity have associated probabilities to impact patient mobility and development of thoracic deformities. These probabilities are also impacted by patient specific characteristics (age, gender, disease Type).

Disease progression, HRQOL, and Mortality

The patient's mobility and thoracic deformity status are continually recorded and updated as they progress through treatment. Modelled fracture events increase the likelihood of exacerbating these outcomes. For instance, a severe hip fracture could greatly impair mobility, while a severe spinal fracture could cause thoracic deformity. These cumulative factors influence various aspects of a patient's outcomes. Loss of mobility can result in decreased HRQOL and a heightened risk of mortality[3,4]. Similarly, thoracic deformities may lead to cardiovascular and pulmonary issues, further diminishing HRQOL and increasing mortality risk[2]. Base mortality rates were derived from UK life tables, with hazard ratios applied based on mobility, thoracic deformity, and disease type. Base HRQOL is similarly anchored in UK age-based norms, with adjustments made for mobility and thoracic deformity. Moreover, any accrued fractures cause acute impacts on HRQOL during healing, with a compounding effect if multiple fractures occur simultaneously.

Results

The model predicted life expectancy and fracture incidence in line with published literature describing OI. It predicted overall survival of 77.8, 37.8, and 69.4 in people with Type I, III, and IV OI, in comparison with 73.3, 38.6, and 67.1 in the published literature[5] (+6.0%, -2.0%, +3.4%, respectively). Similarly, fracture incidence was well aligned with published estimates[6], with the R^2 factor (how well does the model account for the variability of observed data) identifying a substantial fit (R^2 = 0.843) for the male population and good fit (R^2 = 0.6872) for the female population.

Figures 1a & 1b present the annual fracture rates in OI patients by age and disaggregated by sex. Published data[6] describing observed fracture rate in real world practice generally decreases with age, before a slight upward trend in people aged >60 years old, most notably in women. The simulated data reflect the trends in fracture rate whilst maintaining a smaller variance than the observed data, owing to the higher sample size of simulated versus observed patients.

Figure 1a: Annual fracture incidence rate* - Female

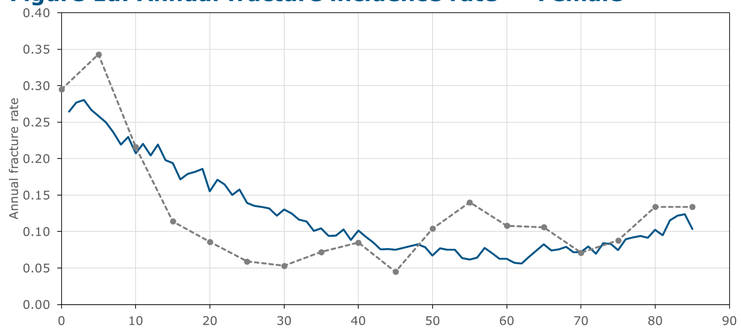
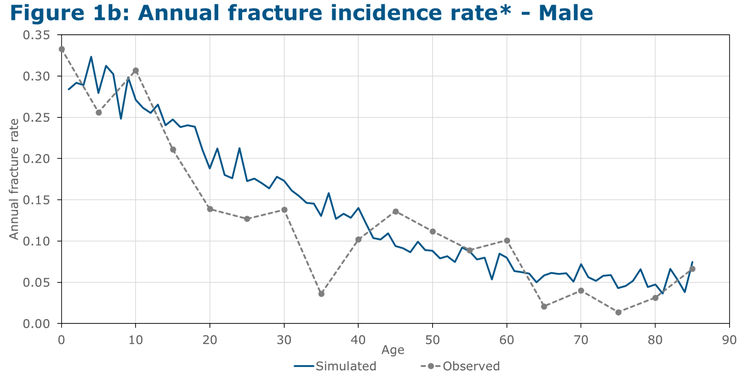


Figure 1b: Annual fracture incidence rate* - Male



The 'Annual fracture incidence rate' presented in **Figure 1a & 1b is calculated as the total number of fractures occurring within the population over a one-year period, divided by the total person-years of observation. This method yields the rate of fractures per person-year, providing insight into the frequency of fractures within the studied population.*

Model Schematic

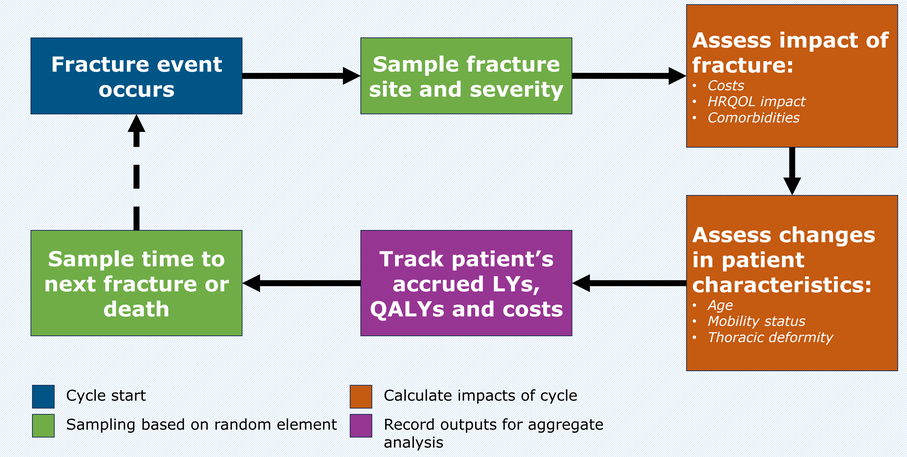
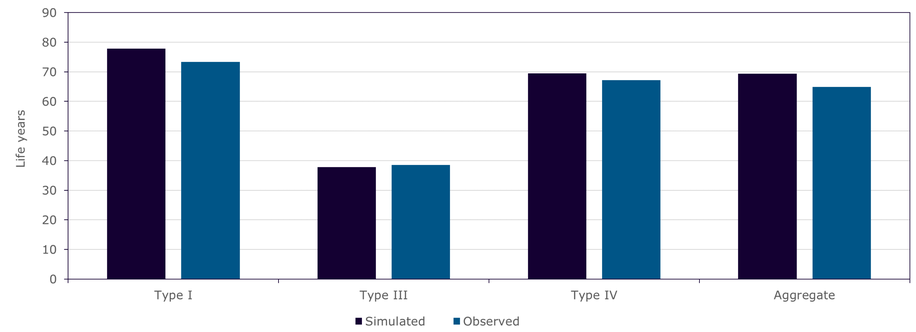


Figure 2 presents the expected life year (LY) gains calculated through simulated means versus observed outcomes from published real world evidence[5] for each individual disease type and as an aggregate. The model predicts patient life expectancy in agreement with previously published estimates, and the small error in LY supports the conceptual link between fractures, mobility, and patient mortality.

Figure 2: Life years gained



Conclusion

These results show that the developed health economic model accurately captures health outcomes in people with OI and aligns well with previously published outcomes with respect to fracture incidence and mortality. The model has the potential to be used for future health economic analyses in OI.

References

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0054_SET_04-24_NPM. April 2024

Presented at ISPOR 2024, 5-8 May, Atlanta, GA, USA

Mereo BioPharma