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All documents and other materials will be updated accordingly. In the meantime the remaining content of this Isis Innovation document is still valid.

URLs beginning www.isis-innovation.com/... are automatically redirected to our new domain, www.innovation.ox.ac.uk/...

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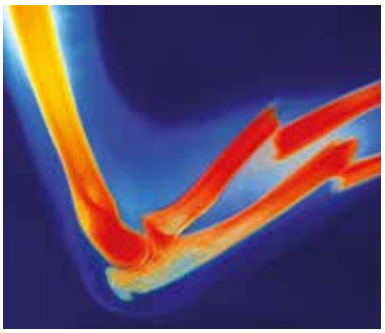
# Type 2 Diabetes Fracture Risk Predictor

Analysis of a large cohort of patients with type 2 diabetes identified key predictors of fracture, and led to the the development of a clinical assessment tool that enables the simple identification of high risk individuals.

### Fracture in type 2 diabetes

People with type 2 diabetes (T2DM) have increased bone mass yet an excess fracture risk, suggesting that predictors in these patients are different to those displaying osteoporosis. We therefore aimed to develop a clinical prediction tool (CPT) that includes T2DM-specific factors (complications, severity, related drugs) for the estimation of absolute hip fracture risk amongst T2DM patients.



*Coloured X-ray of fractured ulna/radius arm bones*

### Predicting Fracture Risk in T2DM

We analysed anonymised data from >100,000 T2DM subjects, sourced from computerised records linked to hospital admissions and pharmacy dispensations for >5 million people in Catalonia, Spain.

### The clinical prediction tool was derived using the following steps:

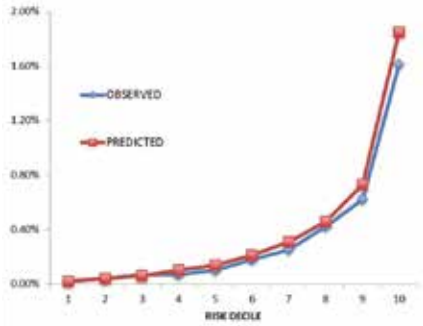
1) Descriptive analysis
2) Multiple imputation of 10 datasets to account for missing information in three variables (body mass index, smoking, and alcohol drinking)
3) Each imputed data set was sampled with replacement 100 bootstraps
4) In each of the resulting 1000 samples a model was fitted using backward stepwise (p exit 0.157)
5) Predictors retained in >70% of the models were considered for the final tool
6) CPT was derived using the resulting coefficients and standard errors following the combination rules by Rubin
7) Harrell's concordance statistic for discrimination was calculated
8) Calibration was examined graphically by comparing observed versus expected fractures by tenths of predicted risk

### A Model with Good Discrimination

2,047 out of 82,306 prevalent T2DM participants fractured their hip during the study period, equivalent to an incidence rate of 3.63/1,000 person-years [95%CI 3.47 to 3.79]. Predictors included in the final model were: age, sex, time since diabetes onset, body mass index, fracture history, cardiovascular disease, osteoarthritis, cataracts, glomerular filtration rate, falls, use of statins and insulin-therapy.

We found that our model showed good discrimination (C = 0,81) and calibration.

### Calibration plot % observed versus % predicted stratified by risk decile




*Our model showed good discrimination when compared to the observed fracture risk in T2DM patients.*

*This CPT could hail a paradigm shift in the clinical management of T2DM, enabling practitioners to predict which of their patients are of increased risk of fracture, and would therefore benefit from additional assessments and/or interventions.*

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