Long-term validation of the CORE diabetes model in Type 1 and Type 2 diabetes

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Background and Aim

• The CORE Diabetes Model (CDM) is an extensively validated simulation model designed for use in both for type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) studies [1-2].
• Validation to external published studies is an ongoing and important part of demonstrating model credibility; importantly, many of these studies have a relatively short period of follow-up.
• The CDM is widely used to estimate long-term clinical outcomes in diabetes patients, therefore the aim of this study was to validate the CDM to contemporary outcomes data; particularly those with a 20-30 year horizon.

Methods

• The CDM is a lifetime simulation model designed to assess the health outcomes and economic consequences of interventions in T1DM or T2DM.
• The model structure comprises of 17 interdependent sub-modules that simulate the complications of diabetes (angiopathy, myocardial infarction (MI), congestive heart failure, stroke, peripheral vascular disease, diabetic retinopathy, nephropathy, cataract, hyperglycaemia, electrolytes, lactate acidosis, nephropathy, end-stage renal disease, neuropathy, foot ulcer, amputation, pulmonary edema and depression) in addition to all-cause mortality.
• The model is a fixed-time increment (annual) stochastic simulation with each sub-module using time, state, and diabetes-type dependent probabilities. Monte Carlo simulations are performed at the individual patient level using tracker variables to accommodate complex interactions between individual complication sub-modules.
• A total of 96 validation endpoints were simulated across 9 pivotal type 1 and type 2 outcomes studies (Table 1a and 1b).
• Results were stratified by duration of study follow-up (long-term defined as > 15 years follow-up); for long-term results simulation cohorts representing baseline DCT and UKPDS cohorts were generated and intensive and conventional treatment arms were defined in the CDM.
• Predicted versus observed macrovascular and microvascular complications and all cause mortality were assessed using the coefficient of determination (R2) goodness of fit measure.

Results

• Across all validation studies predicted events from the CDM are contrasted with observed study events (Table 1 and 1b) producing an R2 statistic of 0.90 (Figure 1).
• In T1DM, validating to 30-year outcomes data resulted in an R2 of 0.67; for long-term 20-year validation to UKPDS in T2DM an R2 of 0.98 was obtained; Figure 2.
• In the T2DM validation studies, model output showed a noteworthy lack of fit when predicting cardiovascular mortality for ACCORD and VADT.
• The ratio of observed to predicted events are summarised in boxplots shown in Figure 3 for studies with duration of follow-up of 5 years, >5 and 10 years and >10 years. Overall variability in the ratio of observed to expected events increased with study follow-up; SO=0, 0.5, 0.8 respectively).
• For validation studies with duration of follow-up ≤5 years the CDM achieved R2 values of 0.9 and 0.88 for T1DM and T2DM respectively.

Conclusion

• Projecting the long-term clinical consequences associated with alternative therapeutic options is an essential part of health technology assessments.
• This study supports the CDM as a credible tool for predicting both the absolute number of clinical events and projecting the future treatment consequences associated with managing patients with diabetes.
• Where long term (>20 years) data exist, for example DCT and UKPDS, this study demonstrates the CDM is capable of reproducing consistent event rates with those observed in the respective trials.
• With increasing incidence and prevalence of diabetes worldwide this is of particular importance for healthcare decision-makers for whom the robust evaluation of alternative healthcare policies and therapeutic options is essential.

References


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