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The comparison of cardiovascular incidence predictions in Type 1 diabetes utilizing alternative risk prediction models

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Introduction

Cardiovascular disease (CVD) risk prediction models (RPMs) are available for the general population (Framingham) and for type-2-diabetes (T2D) (e.g. UKPDS-68 and 82) but few CVD RPMs based on type 1 diabetes (T1D) populations are available. It is therefore not uncommon that T2D RPMs are applied in modeling analytics to predict scenarios in T1D populations.

However, cardiovascular damage in T1D may be even more substantial than in T2D. Recent epidemiological studies have shown that T1D is associated with as much as a 10 fold increased risk CVD compared to the general population (1-2). CVD differs between individuals with T1DM and T2DM not only because it presents at a younger age but also since women are affected at rates equal to those in men. Further, CVD risk factors appear to affect the risk differently in T1D versus T2D (3).

Recent debate has focused on the contemporary relevance of established T1D models suggesting that new models are required that apply T1D specific data that reflects current epidemiology and treatment practice to support the projections of long-term health and economic impacts of alternative interventions and policies.

For this reason the IMS Core Diabetes Model (CDM), a lifetime simulation model designed to assess the health outcomes and economic consequences of interventions in T1DM or T2DM (4-5), has recently been upgraded to include contemporary epidemiological evidence specific to T1D populations (CDM version 9.0) to assess the risk of micro and macrovascular complications. Among those upgrades, two additional T1D specific RPMs for CVD were included based on data from the Epidemiology-of-Diabetes-Interventions-and Complications-study (EDIC-RPM) (6) and a novel RPM from the Pittsburgh-Epidemiology-of-Diabetes-Complications-Study (PEDC-RPM) (7). In addition, a recently published 5 year risk equation based on T1D registry data from the Swedish-National-Diabetes-Register (SNDR) (8) was added to CDM version 9.5.

Objective

The objective of this study was to contrast model predictions for CVD incidence utilizing three T1D RPMs (EDIC, PEDC and SNDR) and compare those to 30 year published CVD incidence from the EDIC study.

Figure 1 – Cumulative incidence of CVD end points over 30 of T1D duration

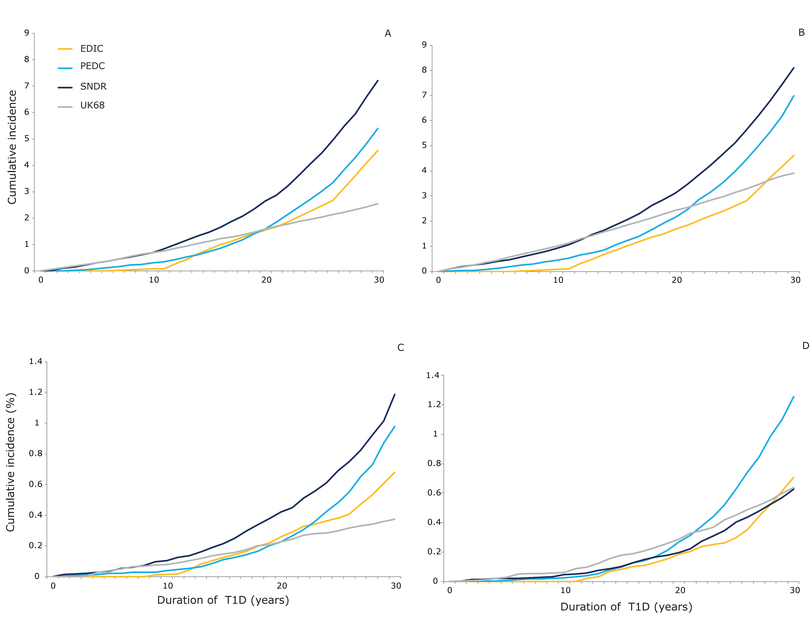


Table 1 – Baseline Characteristics of newly diseased DCCT individuals

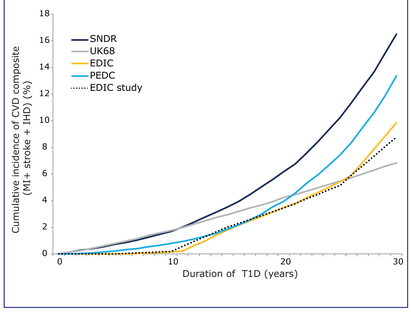
Age (years)	21
Duration of T1D (years)	0
Cigarette smoking (%)	18.5
HbA1c (%)	7
SBP (mm Hg)	114
BMI (Kg/m2)	23.4
HDL (mg/dl)	50.8
LDL (mg/dl)	110
Total Cholesterol (mg/dl)	177
Triglycerides (mg/dl)	80.8

Results

When EDIC -RPMs were applied, the 30-year cumulative incidence of CVD for a newly diagnosed T1D individual was projected at 4.56%, 0.68%, 4.61% and 0.71% for MI, stroke, IHD and HF, respectively. This compared to 5.40%, 0.98%, 6.98% and 1.25% utilizing PEDC -RPM and 5.29%, 0.91%, 6.59% and 7.22%, 1.19%, 8.10% and 0.63% utilizing SNDR-RPM (Figure 2). Finally, the application of the T2D specific model (UK-68 RPM) CVD incidence was projected at 2.55%, 0.37%, 3.91% and 0.64%.

The total composite cumulative incidence of predicted CVD was 9.85%, 13.36% and 16.50% for EDIC-RPM, PEDC-RPM and SNDR-RPM respectively, which compares to 8.70% CVD incidence observed during the EDIC study. In comparison, the T2D specific UK-68 RPM yielded a composite incidence of 6.83%.

Figure 2 – Cumulative incidence of CVD composite end point



Methods

This study used version 9.5 of the IMS CDM model.

Baseline demographics and risk factors were aligned to newly diseased DCCT patient profiles (age 21 years, duration of diabetes =0 years, HbA1c = 7%, systolic-blood-pressure = 114 mmHg, body-mass-index = 23.4 Kg/m2, high-density-lipoprotein 50.8 mg/dl, low density protein = 110.3 mg/dl and total-cholesterol = 177 mg/dl) was projected over 30 years (Table 1).

The CDM was projected over the first 30 years of T1D duration to assess the incidence of myocardial-infarction (MI), stroke, heart-failure (HF) and ischemic-heart-disease (IHD) utilizing three alternative T1D RPMs for CVD:

- T1D specific EDIC-RPM
- T1D specific PEDC-RPM
- T1D specific SNDR-RPM
- In order to allow comparison to respective model predictions obtained with T2D CVD RPMs, one additional analysis was conducted utilizing equations from the UKPDS 68 study (UK-68 RPM) (9)

Time trajectories of risk factors (HbA1c, lipids, SBP etc.) were aligned to observations during DCCT and the observational follow up of the study (EDIC).

Total CVD was assessed as the sum of MI, IHD and stroke incidence to match the EDIC CVD composite end point. This was defined as an event including any of the following components: nonfatal myocardial infarction or stroke, cardiovascular death, confirmed angina, or revascularization (angioplasty, stent, or bypass), all adjudicated, or silent MI on an ECG read centrally.

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Conclusion

- As expected, the CDM reproduced the published EDIC CVD incidence when using the EDIC-RPM approach.
- The higher CVD incidence estimated via PEDC-RPM and SNDR-RPM may be reflective of equations derived from routine clinical practice.
  - While patients in the intensively treated DCCT arm were fairly well controlled within the interventional clinical trial program in early stages of the disease, the population included in the PEDC observational study has been shown to be epidemiologically representative of T1D cases in the general US population which are likely to receive a less stringent glucose control.
  - Likewise, the SNDR-RPM is derived from observational data including Swedish hospital and outpatient records.
- The T2D UK68-RPM yielded the lowest CVD incidence in line with clinical expectations.
- This study demonstrated the gap between modeled projections of cardiovascular incidence in T1D that arises from the utilization of equations based on either clinical or real-world data.

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