Estimating cardiovascular risk and all-cause mortality in individuals with type 2 diabetes using the UKPDS Outcomes Model

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Background and aims: Type 2 diabetes (T2D) cardiovascular (CV) risk calculators predominantly target individuals without CV disease. We evaluated model estimated CV risks in EXSCEL (EXenatide Study of Cardiovascular Event Lowering) participants with T2D, 73.1% of whom had established atherosclerotic CV disease.
Materials and methods: We compared estimated myocardial infarction (MI), stroke, CV death and all-cause mortality (ACM) event rates, obtained using the UKPDS Outcomes Model v2 (OM2), with those observed in EXSCEL. Risk factors included: sex, ethnicity, age, diabetes duration, atrial fibrillation, albuminuria; baseline plus annual measures of smoking, HDL and LDL-cholesterol, weight, systolic blood pressure (SBP), HbA_{1c}, heart rate, white cell count, haemoglobin, estimated glomerular filtration rate; and prior history of ischemic heart disease, heart failure, amputation, blindness, kidney failure, stroke, MI or diabetic foot ulcer.
Results: EXSCEL participants were 38% Female, 76% White Caucasian, with baseline mean (SD) age 62 (9) years, SBP 135 (17) mmHg, HbA_{1c} 8.1 (1.0) % and median (IQR) diabetes duration 11 (6 - 17) years. Of 14752 participants, 1744 (11.8%) experienced ≥1 major CV event over median 3.2 years follow-up with death from any cause occurring in 1091 participants. Estimated event rates were similar to those observed for CV death (6.3% *vs.* 4.9%), ≥1 MI events (5.9% *vs.* 6.6%) and ≥1 stroke event (2.7% *vs.* 2.7%) but OM2 did not identify the ACM risk reduction seen with once-weekly exenatide (Table). Discrimination was fair for MI, stroke and CV death (C-statistic >0.6), and good for ACM (C-statistic >0.7).
Conclusion: The UKPDS Outcomes Model v2 provides similar three-year estimates for MI and stroke event rates in EXSCEL participants to those seen in the trial, but overestimates risks of CV death and ACM. It also underestimates the ACM relative risk reduction seen with once-weekly exenatide, compared with placebo.

Observed and Simulated Event Rates (N, %) in EXSCEL

	Once-weekly exenatide		Placebo		Observed Hazard Ratio (95% CI)	Simulated Relative Risk	C-statistic
	Observed (n=7,356)	Simulated (n=7,356)	Observed (n=7,396)	Simulated (n=7,396)			
Myocardial infarction	483 (6.6%)	431 (5.8%)	493 (6.7%)	438 (5.9%)	0.97 (0.85 – 1.10)	0.98	0.61
Stroke	187 (2.5%)	199 (2.7%)	218 (2.9%)	207 (2.8%)	0.85 (0.70 – 1.03)	0.96	0.66
Cardiovascular death	340 (4.6%)	469 (6.2%)	383 (5.2%)	469 (6.3%)	0.88 (0.76 – 1.02)	0.97	0.69
All-cause mortality	507 (6.9%)	878 (11.9%)	584 (7.9%)	898 (12.1%)	0.86 (0.77– 0.97)	0.98	0.71

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Disclosure: **R.L. Coleman:** None.