Evaluating the Effects of the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model Risk Factor Progression Equations on Cost-Utility Outcomes in Type 2 Diabetes: Analyses Using the PRIME Diabetes Model

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Background and Aims

The United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS OM) and the risk equations that drive it remain widely used in the economic modeling of type 2 diabetes mellitus. Two versions of the UKPDS OM have been developed and published to-date (OM1 and OM2).[1,2] The UKPDS OM2 was based on substantially longer follow-up, was derived from more events, and captured more complications and covariates than UKPDS OM1.

The original UKPDS OM1 publication included panel regression equations governing the progression of glycated hemoglobin (HbA1c), systolic blood pressure (SBP), and total cholesterol to high-density lipoprotein (HDL) cholesterol ratio, and a logistic regression equation governing smoking status.[1]

The risk factor progression equations underpinning the UKPDS OM2 were published in 2021, based on 24 years of follow-up and up to 65,252 person-years of data.[3] The UKPDS OM2 risk equations covered 13 risk factors: HbA1c, systolic blood pressure, LDL cholesterol, HDL cholesterol, body mass index, micro- or macro-albuminuria, creatinine, heart rate, white blood cell count, hemoglobin, estimated glomerular filter rate, atrial fibrillation and peripheral vascular disease.[3]

The PRIME Diabetes Model is a patient-level, discrete-time, event simulation model that combines published risk equations and Monte Carlo methods to evaluate risk of mortality and diabetes-related complications based on patient characteristics, risk factors, and complication history.[4]

The objective of the present study was to evaluate differences in the performance of the OM1 and OM2 risk factor trajectory equations for HbA1c and SBP in economic evaluations conducted using the PRIME Diabetes Model.

Methods

In addition to the existing UKPDS OM1 risk equations for HbA1c and SBP, the UKPDS OM2 risk equations were incorporated into the PRIME Diabetes Model using the published functional forms and coefficient values (Table 1).

Figure 1: Progression of glycated hemoglobin based on the UKPDS Outcomes Model 1 and 2 risk equations

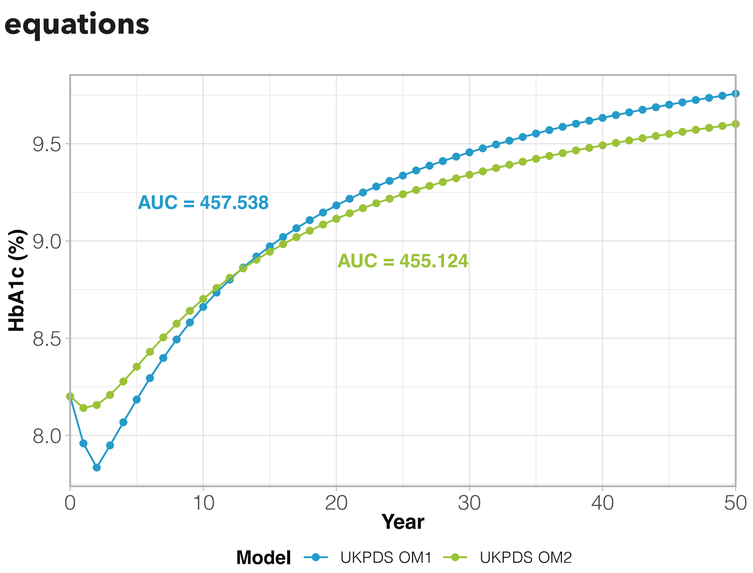
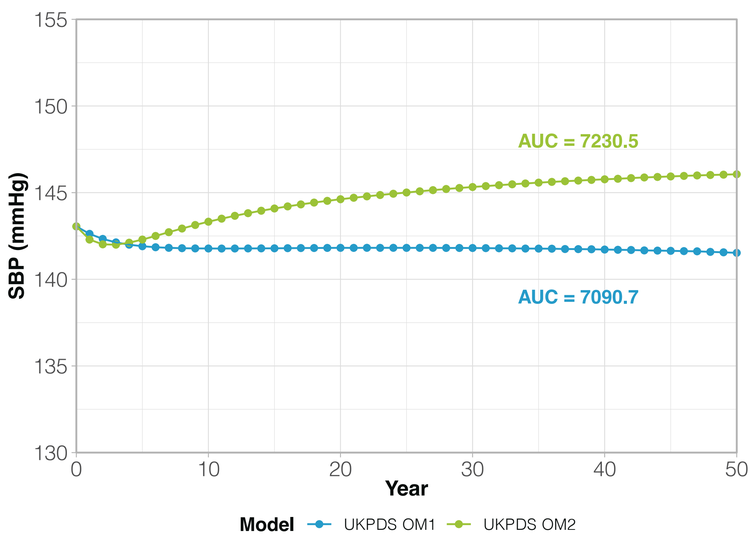


Table 1: Characteristics of the UKPDS OM1 and UKPDS OM2 glycated hemoglobin (HbA1c) and systolic blood pressure (SBP) progression equations, including coefficient values

	UKPDS OM1			UKPDS OM2	
	HbA1c	SBP		HbA1c	SBP
Subjects	3,631	3,592		4,906	4,933
R^2	0.64	0.65		0.603	0.603
Regression type	Panel	Panel		Panel	Panel
Parameter	**HbA1c coefficient (SE)**	**SBP coefficient (SE)**	**Parameter**	**HbA1c coefficient (SE)**	**SBP coefficient (SE)**
α	−0.024 (0.017)	0.030 (0.014)	Constant	1.419 (0.041)	29.007 (0.597)
ln (year)	0.144 (0.009)	0.039 (0.008)	ln (year since diagnosis)	0.141 (0.007)	0.570 (0.064)
Parameter in previous year	0.759 (0.004)	0.717 (0.004)	Parameter in previous year	0.724 (0.005)	0.669 (0.005)
Baseline parameter value	0.085 (0.004)	0.127 (0.004)	Baseline parameter value	0.081 (0.007)	0.118 (0.005)
Year 2	−0.333 (0.050)	–	Female	0.054 (0.012)	0.684 (0.142)
			African Caribbean	0.066 (0.026)	–
			Asian-Indian	0.046 (0.020)	-1.393 (0.224)

The performance of the risk equations from the two UKPDS OM versions was evaluated in the UKPDS baseline cohort, with sensitivity analyses being conducted across a range of mean baseline HbA1c and SBP values. The effects of the analysis time horizon were also investigated in sensitivity analyses.

Figure 2: Progression of systolic blood pressure based on the UKPDS Outcomes Model 1 and 2 risk equations



Differences in area under the curve (AUC) between the UKPDS OM1 and OM2 risk equations were calculated using natural spline interpolation as implemented in the MESS package in R version 4.1.[5]

Downstream complication event incidence, and economic outcomes were compared. Base case analyses were conducted over a 50-year time horizon, with and without discounting, and were run with 100,000 simulated patients per arm.

Table 2: Undiscounted effectiveness outcomes expressed in equal value life years, life expectancy, and quality-adjusted life expectancy with the UKPDS OM1 and UKPDS OM2 HbA1c progression equations

	UKPDS OM 1	UKPDS OM 2	Difference
Equal value life years	35.043	35.112	**+0.068**
Life expectancy (years)	41.179	41.260	**+0.080**
Quality-adjusted life expectancy (QALYs)	30.717	30.775	**+0.057**

Results

The difference in AUC between the HbA1c progression curves was 0.5% over the full duration of the simulation, while the difference in AUC between the SBP curves was larger, at 2.0% (Figures 1 and 2).

The UKPDS OM2 HbA1c risk equation resulted in a modest increase in undiscounted life expectancy versus the corresponding UKPDS OM1 equation (increasing from 41.179 to 41.260 years), with the difference driven by higher HbA1c initially, but lower HbA1c later in the simulation (Table 2).

Differences in complication incidence between the HbA1c equations were modest; the largest incremental cumulative incidence of any modeled complication was 0.4% (stroke and amputation) over the 50-year time horizon. Differences between the SBP risk equations were more pronounced, particularly with regard to microvascular complication incidence, with neuropathy and macular edema incidence 0.8% and 1.6% higher, respectively, with the UKPDS OM2 risk equations versus UKPDS OM1.

Conclusions

The analyses showed that using risk equations from the UKPDS OM2 has a modest effect on modeled clinical and economic outcomes relative to equations from the UKPDS OM1, although the effects of using the SBP equation were more pronounced than the HbA1c equation. Further research would be required to characterize the interactions with discounting, and establish whether these differences would be likely to affect decision making.

References

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Presented at **ISPOR Europe 2022** • Poster EE137 • Vienna, Austria • November 6–9, 2022