imshealth™
INTELLIGENCE APPLIED.

Contrasting cost effectiveness results derived from the UKPDS 68 and 82 risk equations in Type 2 diabetes

Authors: Phil McEwan [1], Volker Foos [2], and David Grant [3]

1 Centre for Health Economics, Swansea University, United Kingdom; 2 IMS Health, Basel, Switzerland; 3 IMS Health, London, United Kingdom;

Introduction

Accurate estimation of baseline cardiovascular risk is crucial to ensure that economic evaluations of new health technologies for the treatment of type 2 diabetes (T2DM) are robust. Many economic models (such as the IMS CORE Diabetes Model (CDM)) use risk equations (REs) derived from the UKPDS Outcomes model (UKPDS 68 study) (1).

More recently, a new set of REs based on findings from the UKPDS 82 study was published (2) that is based on an extended data set spanning over 20 years of trial data including the 10 year post-trial monitoring period. The updated risk equations appear to have significant advantages as they are based on longer follow up data and reflect a greater statistical power based on up to 89,760 patient-years of data (2).

The CDM has been recently updated to include the UKPDS 82 REs as an option.

While the overall differences between the old- (UKPDS 68) and new (UKPDS 82) set of REs have been extensively described in the original publication of the UKPDS Outcomes model 2 (2), there is considerable interest in how the use of the new REs changes cost effectiveness predictions of contemporary T2DM treatment comparisons versus predictions that are conducted with the older set of (UKPDS 68) REs.

Objectives

The aim of this study was to assess the implications for cost effectiveness (CE) associated with use of UKPDS 82 versus UKPDS 68 REs.

Methods

The IMS CORE Diabetes Model (CDM, version 8.5+) a validated and widely used simulation model (3-5) was initiated with baseline characteristics derived from NHANES (6) (Table 1) to compare dual therapy profiles for metformin + sulfonylurea (M+S) versus metformin + DPP-4 (M+D).

Basal insulin (BI) rescue therapy was applied to both arms at HbA1c threshold levels of 7.5%.

Efficacy data for dual therapy and insulin rescue therapy was sourced from a published systematic review (7); HbA1c and BMI change of -0.8% and 0.199kg/m2 (M+D); -0.79% and 0.707kg/m2 (M+S) and -0.82 and 0.545 kg/m2 (BI), respectively, were applied (Table 2).

Hypoglycemia rates were estimated from odds ratios obtained from the same systematic review (7); 8.22, 1.05 and 5.2 for SU, DPP4 and BI add on therapy to metformin vs. metformin monotherapy, respectively.

The background risk of hypoglycemia with metformin monotherapy was sourced from the UKPDS 73 (8); 0.3 and 1.7 events per 100 patient years for symptomatic and severe episodes, respectively.

Annual treatment costs were expected at $67.6, $2520.0 and $1869.7 for (M+S), (M+D) and (BI), respectively and based on wholesale acquisition cost (WAC) obtained from standard US list prices (2012) (Table 1) .

Static disutilities of -0.0052 (9) and -0.0038 (10) were applied to each symptomatic hypoglycemia event and 1 unit increase in BMI above 25 Kg/m2, respectively.

Lifetime analyses were conducted using UKPDS 82 and UKPDS 68 REs.

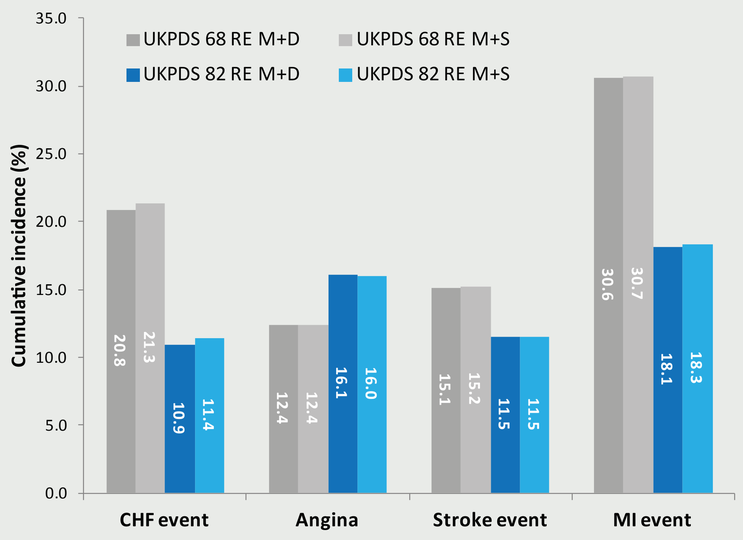
US 2012 costs were used and discounting was applied at 3.0%.

Table 1) Baseline demographics, risk factors and complication of patients in the simulated cohort

Variable	Mean (SD)
Demographics	
Age (years)	56 (9.53)
Sex (% male)	0.56
Duration diabetes (years)	6 (2.35)
BMI (kg/m^2)	32.44 (6.3)
Racial characteristics	
% White	27
% Black	27
% Hispanic	42
% Asian	4
Risk factors	
HbA1c (%)	8.21 (0.54)
SBP (mm Hg)	132.8 (22.89)
Total cholesterol (mg/dl)	209.31 (44.5)
HDL cholesterol (mg/dl)	47.99 (14.12)
Smoker (%)	18

SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; HDL, high density lipoprotein;

Figure 1) Differences in CV end point predictions for CDM projections utilizing UKPDS 68 vs. UKPDS 82 RE



CHF, congestive heart failure; MI, myocardial infarction

Figure 2) Scatter-plot of incremental costs and effectiveness values with UKPDS 68 and UKPDS 82 RE

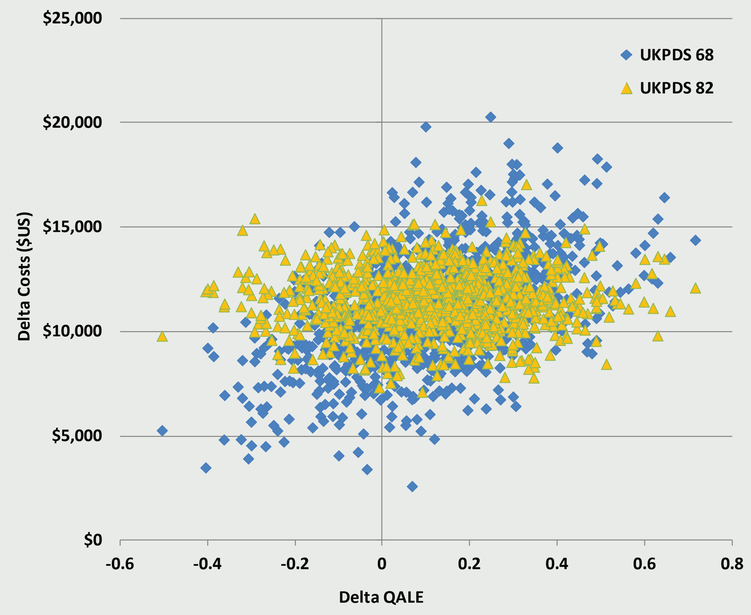


Table 2) Efficacy and safety assumptions and treatment costs for (M+S), (M+D) and (BI)

	(M+S)	(M+D)	(BI)
HbA1c (%)	-0.79%	-0.80%	-0.82%
BMI (kg/m2)	0.707	0.199	0.545
Symptomatic Hypoglycemia	13.974*	1.785*	8.84*
Severe Hypoglycemia	2.466*	0.315*	1.56*
Tx costs ($ USD)	$67	$2,520	$1,869

* Events per 100 patient years; BMI = body mass index

Figure 3) Cost effectiveness acceptability curves with UKPDS 68 and UKPDS 82 RE

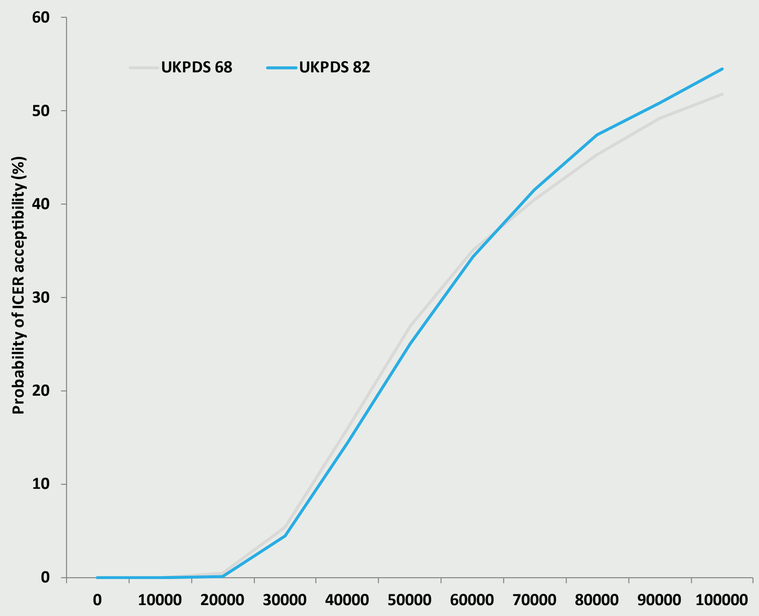


Table 3) Summary costs, benefits and incremental cost effectiveness results for metformin + DPP4 versus metformin + sulfonylurea in CDM projections utilizing UKPDS 68 vs. UMPDS 82 RE

	UKPDS 68 RE applied				UKPDS 82 RE applied			
	Metformin + DPP4		Metformin + SU		Metformin + DPP4		Metformin + SU	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Life expectancy (years)	12.189	0.194	12.089	0.198	11.592	0.182	11.478	0.175
Undiscounted life expectancy (years)	17.123	0.339	16.924	0.338	15.648	0.292	15.459	0.279
Quality-adjusted life expectancy (years)	8.133	0.132	8.018	0.136	7.88	0.128	7.752	0.121
Undiscounted quality-adjusted life expectancy	11.207	0.22	11.015	0.222	10.51	0.2	10.32	0.188
Total costs	$77’274	$1’887	$66’152	$1’912	$59’448	$1’077	$47’884	$1’048
Difference	Mean	95% LCI	95% UCI		Mean	95% LCI	95% UCI	
Δ Life expectancy	0.1	0.083	0.117		0.114	0.099	0.129	
Δ QALE	0.115	0.104	0.127		0.127	0.117	0.138	
Δ Total costs	$11’123	$10’959	$11’287		$11’563	$11’475	$11’652	
Δ Costs/Δ Life expectancy	$111’038	-$14’892	$94’621		$101’493	-$24’436	$33’163	
Δ Costs/Δ QALE	$96’477	-$1’096’113	$423’286		$90’729	-$51’789	$188’800	

Results

Except for ischemic heart disease (IHD) the cumulative incidence of all CV endpoints was reduced using the new set of UKPDS 82 REs with a 48%, 24% and 41% reduction in incidence for CHF, stroke and MI, respectively and a 30% increase for IHD (Figure 1).

Irrespective of the reduction in CV endpoints, overall survival was lower in projections using UKPDS 82 REs with an overall life expectancy (LE) of 12.189 and 12.089 in patients treated with M+D and M+S using UKPDS 68 REs versus 11.592 and 11.478 using UKPDS 82 RE (Table 3).

Quality adjusted life expectancy was 8.133 and 8.018 in patients treated with M+D and M+S using UKPDS 68 REs and 7.880 and 7.752 using UKPDS 82 REs (Table 3).

Total direct costs were estimated at $77,274 and, $66,152 respectively for patients treated with M+D and M+S using UKPDS 68 REs and $59,448 and $47,884 respectively using UKPDS 82 REs.

Incremental differences between REs were less pronounced with incremental QALE estimated at 0.115 (UKPDS 68) and 0.127 (UKPDS 82) and incremental costs estimated at $11,123 (UKPDS 68) and $11,563 (UKPDS 82). This lead to incremental costs per quality adjusted life year (QALY) gained of $96,477 and $90,729 using UKPDS 68 compared to UKPDS 82 REs.

Conclusions

The UKPDS risk equations are widely used in type 2 diabetes cost-effectiveness models.

While the new equations predict appreciable differences in absolute costs and quality adjusted life expectancy the incremental differences were marginal.

Consequently health economic evaluations using the new UKPDS82 equations are appear unlikely to result in significantly different results compared with the UKPDS 68 REs.

As diabetes modelling groups gain experience of working with these new equations their advantages and potential limitation will become better understood. Further validation research using these new equations, particularly from other diabetes modelling groups, is required.

References

[1] Clarke PM et al. Diabetologia 2004; 47(10):1747-59
[2] Hayes AJ et al. Diabetologia 2013; 56(9):1925-33
[3] Palmer et al. Curr Med Res Opin 2004;20:S5–S26.
[4] Palmer et al. Curr Med Res Opin 2004;20:S27–40.
[5] Foos, V et al. Value in Health 2012;15(7)p.A470
[6] NHANES Data. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. 2010
[7] McIntosh B et al. Open Medicine, 2011; 5(1): E35
[8] UKPDS 73, J of Diab and its Complic 20 (2006) 395– 401
[9] Warren et al. Health Technol Assess. 2004 ;8(45): 1-57.
[10] Bagust et al. Health Econ. 2005;14(3):217-30

FOR FURTHER INFORMATION: Please contact Phil McEwan (phil.mcewan@heor.co.uk) or Volker Foos (vfoos@ch.imshealth.com)
IMS HEALTH | 210 PENTONVILLE ROAD, LONDON N1 9JY, UNITED KINGDOM