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Impact of single risk factor changes on long term outcomes and cost in a type 2 diabetes modeling study contrasting projections with UKPDS 68 versus UKPDS 82 risk equations

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Introduction

The magnitude by which risk factors impact on projected outcomes of disease simulation models is closely related to the applied risk equations that consider these risk factors for the estimation of complication risk and mortality.

The degree to which treatment related risk factor (RF) changes alter long-term clinical and cost outcomes in the IMS-CORE-Diabetes-Model (CDM) (1,2) was reported in earlier publications (3, 4). These studies presented the long-term clinical and cost outcomes associated with changes in HbA1c, blood pressure and lipids. Since the time of their publication the CDM has undergone a series of updates including the integration of UKPDS-68 (UK68) (5) and UKPDS-82 (UK82) (6) risk equations (RE).

Hence, an update of the analysis is required to inform the relationship between treatment effect on risk factors and related outcome changes in the present CDM version 8.5.

Objectives

The objective of this study was to assess the isolated impact of single risk factors on lifetime benefits and costs, thereby opposing results from CDM projections utilizing UK68-RE vs. UK82-RE.

Methods

The CDM version 8.5+ was applied to project the lifetime benefi¬ts (life years (LYs), quality adjusted life years (QALYs)) and total lifetime costs (TLC (£GBP)) associated with baseline RF changes for HbA1c, body-mass-index (BMI), systolic blood pressure (SBP), total cholesterol (T-Chol), high-density- lipoprotein (HDL) and low-density-lipoprotein (LDL). An intermediate risk type-2 diabetes cohort (Table 1) was projected over lifetime to explore the sensitivity of discounted and undiscounted LYs, QALYs and TLC corresponding to a two-step RF change (treatment related RF reduction and increase) versus no effect in the base case analysis (A1c+/-2%, SBP+/-20 mmHg, BMI+/-2 Kg/m2, T_CHOL +/- 20 mg/dl, HDL+/-10 mg/dl, LDL+/-20 mg/dl).

Time trajectories for RFs beyond the 1st year treatment effect were assumed according to the CDM default settings; i.e. two random effect models based on UKPDS data were applied to describe the progression of HbA1c and SBP (5), progression patterns aligned to Framingham data were assumed for HDL and LDL (7) and no parameter level change over time assigned to BMI.

The interrelation of lipid parameters (T- Chol, HDL and LDL) was ignored to explore the single parameter effects changes (i.e. T- Chol was held constant for all changes of HDL and LDL). Further, the impact of treatment changes on triglycerides (TG) was not explored in this analysis since TG are not included in UK82-RE nor UK68-RE.

A disutilitiy of -0.0038 (8) was applied to each unit increase in BMI above 25 Kg/m2.

Future benefits and costs were discounted at 3.5%.

Table 1) Baseline characteristics of intermediate risk cohort

Demographics	
Start age	55 years
Duration of Diabetes	5 years
Prop. Male	50%
Risk factors	
HbA1c	8%
SBP	140 mmHg
T-CHOL	250 mg/dl
HDL	50 mg/dl
LDL	170 mg/dl
TG	150 mg/dl
BMI	30 Kg/m2
Baseline CVD Complications	
Prop. MI	0.06
Prop. angina	0.014
Prop. PVD	0.014
Prop. stroke	0.02
Prop. HF	0.027

MI=myocardial infarction, PVD=peripheral vascular disease, HF=heart failure

Figure 1) Variations in discounted and undiscounted LE and QALE per unit RF change

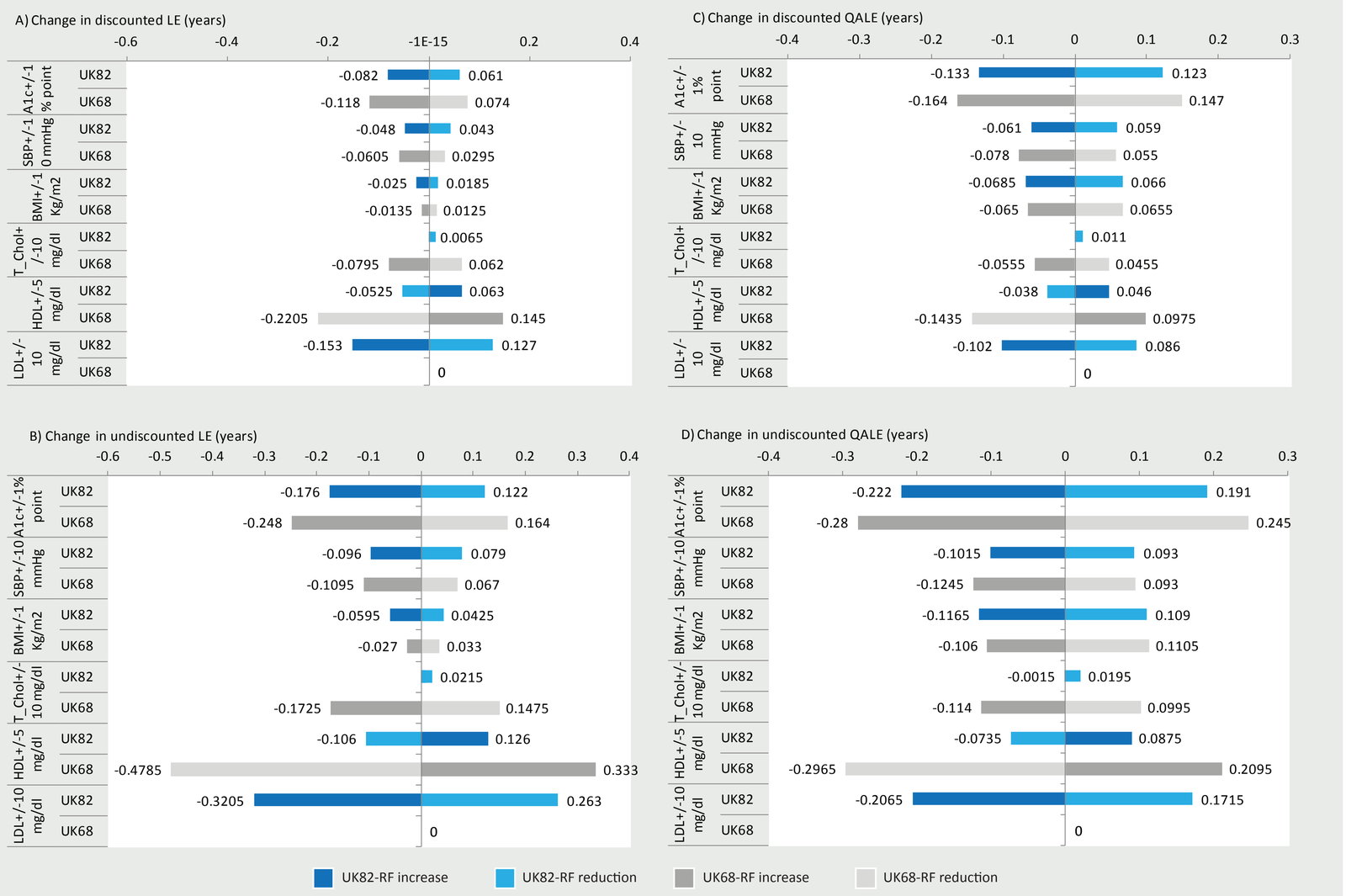


Table 2) Results from base case and sensitivity analyses from CDM projections utilizing UK82-RE and UK68-RE

Base Case		UK82	UK68
	LE (disc)	13.76	14.28
	QALE (disc)	9.35	9.54
	LE (undisc)	20.94	22.26
	QALE (undisc)	13.87	14.41
		£15'415	£21'633

Sensitivity analyses		UK82 RED	UK82 INC	UK68 RED	UK68 INC
A1c +/- 2%	LE (disc)	13.83	13.68	14.35	14.16
	QALE (disc)	9.47	9.21	9.69	9.38
	LE (undisc)	21.06	20.76	22.42	22.01
	QALE (undisc)	14.06	13.65	14.65	14.13
SBP +/- 20mmHg	LE (disc)	13.85	13.67	14.34	14.16
	QALE (disc)	9.46	9.22	9.65	9.39
	LE (undisc)	21.09	20.74	22.39	22.04
	QALE (undisc)	14.06	13.67	14.59	14.16
BMI +/- 2Kg/m2	LE (disc)	13.80	13.71	14.30	14.25
	QALE (disc)	9.48	9.21	9.67	9.41
	LE (undisc)	21.02	20.82	22.33	22.21
	QALE (undisc)	14.09	13.64	14.63	14.19
T_Chol +/- 20mg/dl	LE (disc)	13.79	13.78	14.40	14.12
	QALE (disc)	9.37	9.35	9.63	9.43
	LE (undisc)	20.98	20.95	22.56	21.92
	QALE (undisc)	13.91	13.87	14.61	14.18
HDL +/- 10mg/dl	LE (disc)	13.66	13.89	13.84	14.57
	QALE (disc)	9.27	9.44	9.25	9.74
	LE (undisc)	20.72	21.29	21.30	22.93
	QALE (undisc)	13.73	14.05	13.81	14.83
LDL +/- 20mg/dl	LE (disc)	14.02	13.46	14.28	14.28
	QALE (disc)	9.52	9.14	9.54	9.54
	LE (undisc)	21.46	20.29	22.26	22.26
	QALE (undisc)	14.22	13.46	14.41	14.41

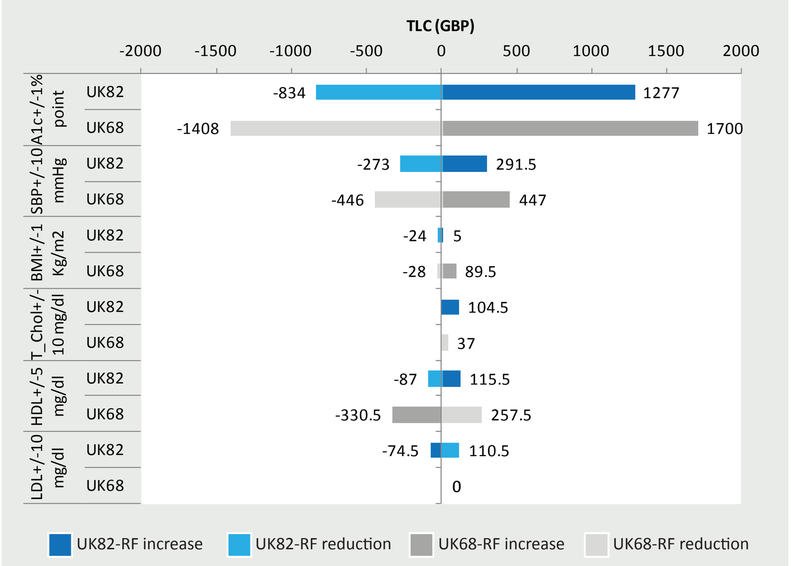
TLC (disc)	UK82 RED	UK82 INC	UK68 RED	UK68 INC
A1c +/- 2%	£14'581	£16'692	£20'225	£23'333
SBP +/- 20mmHg	£14'869	£15'998	£20'741	£22'527
BMI +/- 2Kg/m2	£15'425	£15'367	£21'577	£21'812
T_Chol +/- 20mg/dl	£15'646	£15'241	£20'972	£22'148
HDL +/- 10mg/dl	£15'636	£15'266	£21'633	£21'633
LDL +/- 20mg/dl	£15'448	£15'624	£21'707	£21'636

disc=discounted, undisc=undiscounted, RED=reduction of parameter, INC= increase of parameter

Results

Results from base case - (no parameter effect) and all sensitivity analyses (parameter reduction and increase) from CDM projections utilizing UK82-RE and UK68-RE are presented in Table 2. Figure 1 presents the variations in discounted and undiscounted LE and QALE per unit RF change (HbA1c+/-1%, SBP+/-10 mmHg, BMI+/-1 Kg/m2, T-Chol +/- 10 mg/dl, HDL+/-5 mg/dl, LDL+/-10 mg/dl). Respective changes in TLC are presented in Figure 2.

Figure 2) Variations in discounted TLC per unit RF change



Conclusions

This modeling study provides evidence that treatment related variations of risk factor levels across a range of assumptions are associated with substantial changes in lifetime benefits and costs.

Projections with UK68-RE demonstrated that unit variations of HbA1c, SBP, T-Chol and HDL translate into larger changes of benefits (LE and QALE) vs. those obtained in UK82-RE projections. Conversely, the impact of treatment effects on BMI were larger in UK82-RE vs. UK68-RE projections. The small impact of T-Chol effects on outcomes in UK82 projections is expected since the parameter is not regarded in these equations. Likewise, LDL is not included in UK68-RE.

TLC were predominantly impacted by changes in HbA1c and SBP with is likely attributable to the degree by which these parameters affect the risk of microvascular complications.

Exploring the impact of risk factor changes on long term outcomes is an important study to inform the dynamics of disease simulation models with regard to the implemented RE but also to enable comparison to other models in cross-validations.

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