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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, Swedish National Diabetes Registry and the ADVANCE risk equations

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Introduction

The degree to which treatment related changes in risk factors (RF) impact on long-term clinical and cost outcomes in the IMS CORE Diabetes Model (CDM) (1,2) was reported in earlier publications (3-5). Those studies presented the long-term clinical and cost outcomes associated with changes in HbA1c, blood pressure, body mass index (BMI) and lipids across previous versions of the model.

The CDM has recently been updated to include a number of contemporary cardiovascular risk prediction models, among those the risk equations (REs) from the UKPDS 82 study (UK82) (6), REs from the Swedish National Diabetes Registry (S-NDR) (7) and the ADVANCE Risk Engine (ADV) (8). Those equations may be alternatively applied to substitute the default set of UKPDS-68 REs (UK68) (9) which are most commonly used in CDM projections.

The magnitude by which these new equations translate risk factor changes into outcome effects is likely to be different; therefore an update of the analysis is required to inform this relationship across all newly implemented REs in the CDM.

Objectives

The objective of this study was to assess the isolated impact of single risk factors on lifetime benefits and costs in CDM projections using four alternative sets of REs; UK68, UK82 , S-NDR and ADV.

Methods

The CDM version 9.0 was applied to project the discounted (3%) lifetime benefits (life years (LYs), quality adjusted life years (QALYs)) and total lifetime costs (TLC ($US)) associated with baseline RF changes for HbA1c, 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 for a three-step treatment change (reduction, no effect, increase) of individual RFs (A1c+/-2%, SBP+/-20 mmHg, BMI+/-2 Kg/m2, T_CHOL +/- 20 mg/dl, HDL+/-10 mg/dl, LDL+/-20 mg/dl). To assess the impact of each RF in isolation, other RFs were kept at the base case assumption (no treatment effect) in each sensitivity analysis.

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 (9), progression patterns aligned to Framingham data were assumed for HDL and LDL (10) 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 since TG are not considered in any of the applied REs in this analysis.

Lifetime analyses were conducted using UK68, UK82, S-NDR and ADV Res and a disutilitiy of -0.0038 (11) was applied to each unit increase in BMI above 25 Kg/m2.

Table 1: Baseline characteristics

Variable		Mean
Demographics	Start age	55 years
	Duration of Diabetes	5 years
	Prop. Male	50%
Risk factors	HbA1c	8%
	SBP	140 mmHg
	Total cholesterol	250 mg/dl
	HDL	50 mg/dl
	LDL	170 mg/dl
	Triglycerides	150 mg/dl
	BMI	30 Kg/m2
Baseline CVD complications	Prop. MI	6.00%
	Prop. Angina	1.40%
	Prop. PVD	1.40%
	Prop. Stroke	2.00%
	Prop. HF	2.70%

BMI, body mass index; HDL, high density lipoprotein; HF, heart failure; LDL, low density lipoprotein; PVD, peripheral vascular disease; SBP, systolic blood pressure.

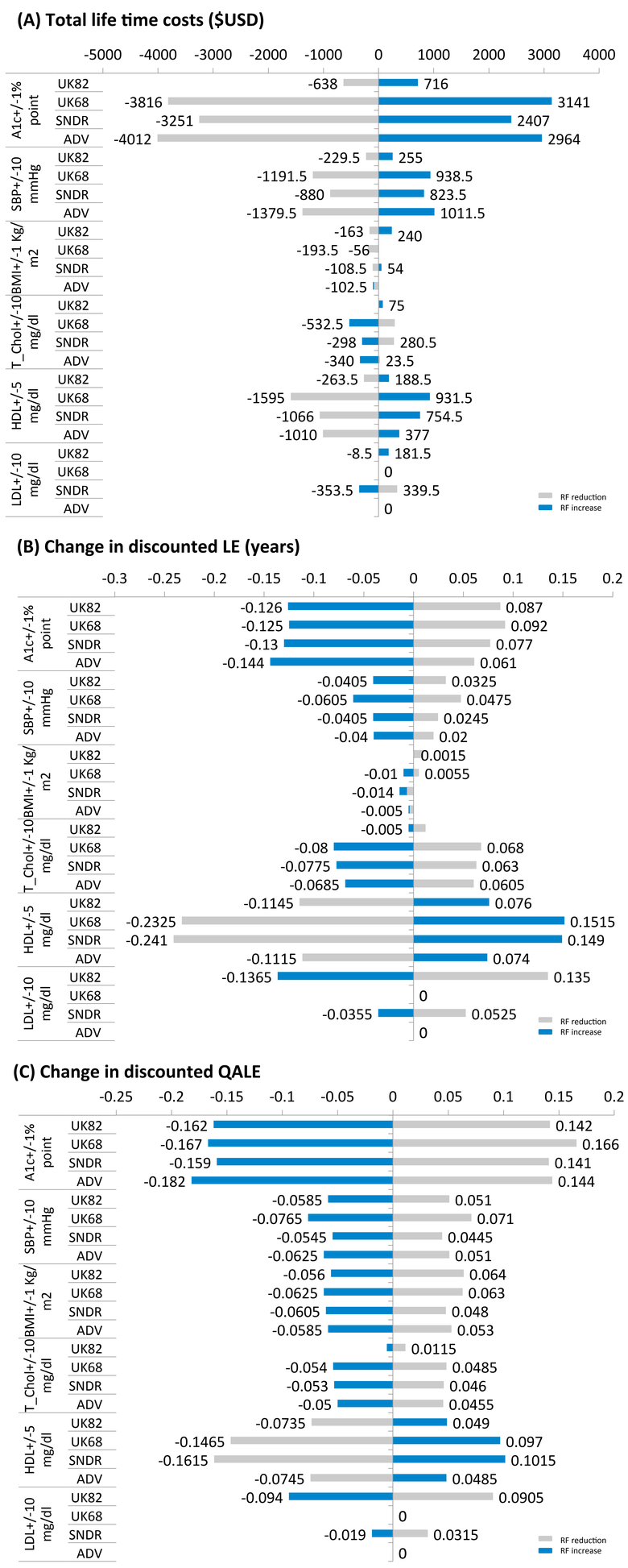
Table 2: Base case and sensitivity analysis results

Base Case		UK68	UK82	S-NDR	ADV
	LE	15.098	14.826	13.135	14.513
	QALE	10.019	9.945	8.537	9.672
	TLC	$71,881	$35,571	$61,559	$67,631

Sensitivity Analysis		RED	INC	RED	INC	RED	INC	RED	INC
HbA1c +/-2%	LE	15.190	14.973	14.913	14.7	13.212	13.005	14.574	14.369
	QALE	10.185	9.852	10.087	9.783	8.678	8.378	9.816	9.490
	TLC	$68,065	$75,022	$34,933	$36,287	$58,308	$63,966	$63,619	$70,595
SBP+/-20 mmHg	LE	15.193	14.977	14.891	14.745	13.184	13.054	14.553	14.433
	QALE	10.161	9.866	10.047	9.828	8.626	8.428	9.774	9.547
	TLC	$69,498	$73,758	$35,112	$36,081	$59,799	$63,206	$64,872	$69,654
BMI+/-2 Kg/ m2	LE	15.109	15.078	14.846	14.829	13.122	13.107	14.505	14.503
	QALE	10.145	9.894	10.073	9.833	8.633	8.416	9.778	9.555
	TLC	$71,494	$71,769	$35,245	$36,051	$61,342	$61,667	$67,464	$67,426
T-chol+/-20 mg/dl	LE	15.234	14.938	14.850	14.816	13.261	12.980	14.634	14.376
	QALE	10.116	9.911	9.968	9.934	8.629	8.431	9.763	9.572
	TLC	$72,473	$70,816	$35,588	$35,721	$62,120	$60,963	$67,678	$66,951
HDL+/-10 mg/dl	LE	14.633	15.401	14.597	14.978	12.653	13.433	14.290	14.661
	QALE	9.726	10.213	9.798	10.043	8.214	8.740	9.523	9.769
	TLC	$68,691	$73,744	$35,044	$35,948	$59,427	$63,068	$65,611	$68,385
LDL+/-20 mg/dl	LE	15.098	15.098	15.096	14.553	13.24	13.064	14.513	14.513
	QALE	10.019	10.019	10.126	9.757	8.600	8.499	9.672	9.672
	TLC	$71,881	$71,881	$35,554	$35,934	$62,238	$60,852	$67,631	$67,631

BMI, body mass index; HDL, high density lipoprotein; INC, increase in parameter value; LDL, low density lipoprotein; LE, life expectancy; QALE, quality-adjusted life expectancy; RED, reduction in parameter value; SBP, systolic blood pressure; T-chol, total cholesterol; TLC, total lifetime cost.

Figure 1: Sensitivity analysis



Results

Results from the four base case analyses (utilizing UK68, UK82, S-NDR and ADV REs) in which no parameter effect was assumed and all sensitivity analyses (parameter reduction and increase) are presented in Table 2.

Overall LE varied from 13.14 (S-NDR) to 15.098 (UK68) with QALE ranging from 8.537 (S-NDR) to 10.019 (UK68). TLC were lowest for UK82 ($35,571) and highest with UK68 ($71,881).

Figure 1 presents the variations in discounted TLC, LE and QALE from base case per unit RF change (AbA1c+/-1%, SBP+/-10 mmHg, BMI+/-1 Kg/m2, T-Chol +/- 10 mg/dl, HDL+/-5 mg/dl, LDL+/-10 mg/dl).

Across risk equations total lifetime costs were typically most sensitive to changes in HbA1c; a noteworthy exception to this was the UK82.

Change in life expectancy was most influenced by changes in HDL for UK68 and S-NDR equations with changes in QALE driven largely by HbA1c (similar across all risk equations).

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.

The impact of unit changes in HbA1c, SBP, and BMI on discounted LE and QALE appears to be comparable across all REs whereas changes in HDL have a stronger effect in projections utilizing UK68 and S-NDR REs.

The small impact of T-chol effects on outcomes in UK82 projections is expected since the parameter is not regarded in these equations. For the remaining REs, T-chol changes demonstrated a comparable effect on LE and QALE.

Likewise, LDL is not considered in UK68 and ADV REs and the related outcome effect is zero. Further LDL changes appear to have a stronger outcome effect in with UK82 vs. S-NDR REs.

TLC were predominantly impacted by changes in HbA1c and SBP which 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 directions of a disease simulations model with regard to its implemented RE but also for comparison to other models in cross-validations.

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