

Estimated 10-year benefit for diabetes complication rates by 1% HbA_{1c} decrements in people with type 2 diabetes and cardiovascular disease

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Background and aims: Randomised controlled trials and meta-analyses of glucose lowering in type 2 diabetes mellitus (T2DM) demonstrate reductions in microvascular outcomes and modest reductions in macrovascular complications. International guidelines recommend individualisation of HbA_{1c} targets; however, few data are available on the potential benefits that different targets might achieve. We have estimated 10-year risks for micro- and macrovascular T2DM complications when targeting HbA_{1c} levels between 10% and 6% to quantify the likely incremental benefits.

Materials and methods: We used UKPDS Outcomes Model v2 (OM2) to estimate 10-year event rates for myocardial infarction (MI), stroke, blindness and amputation for a contemporaneous population with T2DM and cardiovascular disease enrolled in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS). Complete baseline risk factor values for age, sex, ethnicity, systolic BP, HDL, LDL, weight, heart rate, haemoglobin, smoking status, presence of albuminuria, atrial fibrillation and history of micro- and macrovascular events, were available for 5766 of 14724 enrolled patients. Complication rates were estimated with HbA_{1c} levels held constant at 10%, 9%, 8%, 7% and 6% for each individual whilst maintaining their risk factors at their baseline values. Point estimates of event rates (PEER) were compared using ANOVA, and relative risk reductions (RRR) at each 1% HbA_{1c} decrement compared using Tukey pairwise comparisons, with p<0.05 as significant.

Results: Patients were mean (SD) age 66.2 (7.8) years, T2DM duration 10.9 (8.2) years, systolic BP 134 (17) mmHg, LDL 2.3 (0.9) mmol/l, HDL 1.1 (0.3) mmol/l, with 27.5% women, 84.6% White ethnicity and 10.9% current smokers. PEERs decreased significantly for each HbA_{1c} decrement from 10% to 6% for all simulated outcomes; p for trend <0.001 (Table). RRRs increased to a similar extent for each 1% HbA_{1c} decrement, but numerically were greater for micro- than macrovascular complications. RRR estimates when targeting an HbA_{1c} of 7.0% (current guideline target) from a baseline of 10% were 12.9%, 14.8%, 43.1% and 61.8% for MI, stroke, blindness and amputation respectively.

Conclusion: As expected, greater estimated risk reductions were seen with HbA_{1c} lowering for micro- than macrovascular complications. These simulated outcomes provide patients and clinicians a guide to the potential glucose-lowering benefit possible when targeting progressively lower HbA_{1c} values from a baseline of 10%. Running OM2 for individual patients could give personalised risk reduction estimates to help inform diabetes management.

	HbA _{1c} (%)	10.0	9.0	8.0	7.0	6.0
Macrovascular Complications	MI	24.2 (20.7-27.6)	23.0 (19.7-26.3)	21.9 (18.7-25.0)	20.9 (17.8-24.0)	19.9 (16.9-23.1)
	Cumulative RRR	Reference	4.3	8.5	12.9	17.3
	Stroke	14.0 (10.9 - 17.2)	13.3 (10.4-16.1)	12.6 (9.9-15.3)	11.9 (9.3-14.5)	11.3 (8.7-13.8)
	Cumulative RRR	Reference	4.7	8.7	14.8	21.1
Microvascular Complications	Blindness	7.4 (4.4-10.3)	6.3 (3.8-8.9)	5.4 (3.2-7.7)	4.6 (2.7-6.6)	3.9 (2.3-5.7)
	Cumulative RRR	Reference	14.4	28.7	43.1	57.5
	Amputation	5.5 (4.3-7.2)	4.5 (3.6-5.8)	3.72 (2.9-4.8)	3.1 (2.4-3.9)	2.6 (1.9-3.4)
	Cumulative RRR	Reference	21.0	41.6	61.8	81.8

Data presented as PEER (%) with 95% CI; Cumulative RRR are % and compared to an HbA_{1c} of 10% (reference).

Disclosure: S.A. Mostafa: None.