

# UNDERSTANDING THE INTER-RELATIONSHIP BETWEEN IMPROVED GLYCAEMIC CONTROL, HYPOGLYCAEMIA AND WEIGHT CHANGE WITHIN A TYPE 1 DIABETIC POPULATION

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## Introduction

- Guidelines for the management of type 1 diabetes mellitus (T1DM) advocate treatment regimens that reduce the frequency of hypoglycaemic episodes, while maintaining blood glucose levels as near normal as is feasible.
- Therapy-related consequences of treatment, such as weight gain and hypoglycaemia can act as a barrier to attaining optimal glycaemic control and can therefore influence the incidence of vascular complications. Furthermore, hypoglycaemia and weight gain can have a significant impact upon a patient's quality of life.
- Consequently, changes in HbA1c, weight and the frequency of hypoglycaemia are important determinants of the cost effectiveness of blood glucose lowering therapies in diabetes.
- The objective of this study was to quantify the individual and combined contribution of changes in hypoglycaemia, weight and glycosylated haemoglobin (HbA1c) to predicted quality-adjusted life years (QALYs) in a T1DM population.

**Table 1: Baseline characteristics of the simulated patient cohort**

Variable	Value	Source
Current Age (years)	33.3	3
Proportion female	0.47	3
Duration diabetes (years)	12.1	3
Height (meters)	1.75	1
Proportion AC	0.04	3
Proportion smokers	0.2	6
HbA1c (%)	8.16	6
Total-cholesterol (mmol/l)	4.68	6
HDL Cholesterol (mmol/l)	1.32	6
SBP (mmHg)	115.79	6
BMI (kg/m <sup>2</sup> )	25.79	6
UAE (mg/24hr)	53	6
Number of HSHE	35.5	7
Probability of SHE	1	7

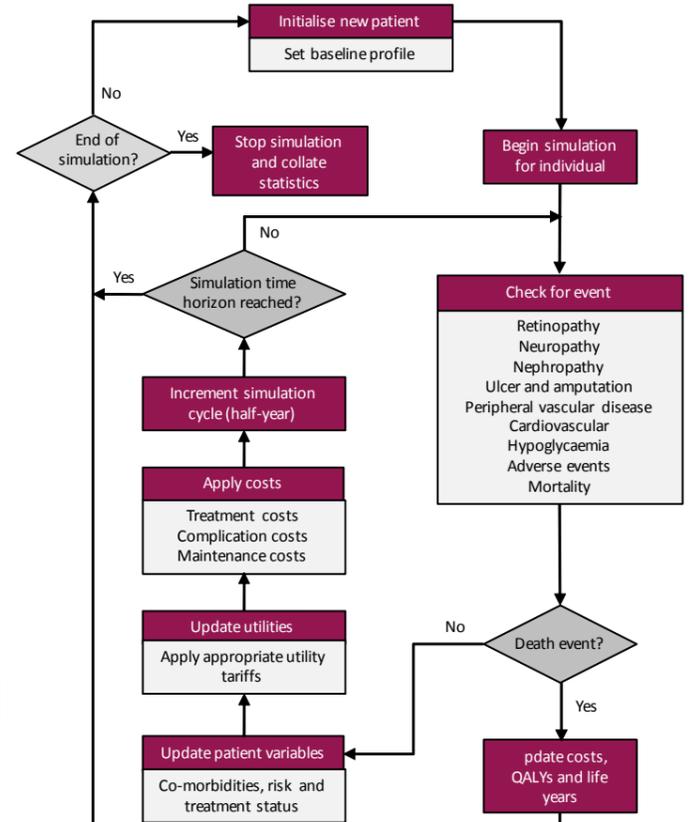
## Results

- Running the baseline cohort profile through the model resulted in a mean predicted life expectancy to an age of 63.6, with a total of 16.8 and 10.5 undiscounted and discounted QALYs respectively.
- Achieving and maintaining a 1% reduction in HbA1c was associated with an estimated gain of 1.37 QALYs per patient.
- A 3kg weight loss and 30% reduction in frequency of symptomatic hypoglycaemic episodes produced a combined QALY gain of 0.59 (70% attributable to weight loss), whereas the reverse gave a QALY decrement of 1.27 (89% attributable to weight gain).
- The relationship between changes in weight and the rate of hypoglycaemia on changes in QALYs are presented in Figure 2 (undiscounted) and Figure 3 (discounted).

**Table 2: Utility values applied in the model**

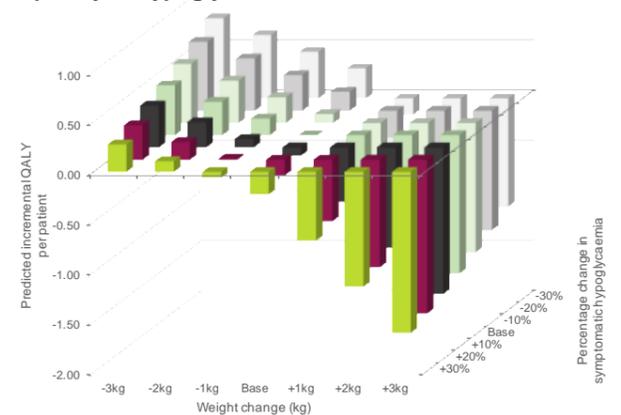
Health state or event	Utility	Source
Baseline T1DM without complications	0.785	8
Cardiovascular disease	-0.065	8
Background diabetic retinopathy	-0.04	8
Proliferative diabetic retinopathy <sup>††</sup>	-0.07	8
Severe vision loss	-0.074	8
Macular edema	-0.04	8
Macro-albuminuria	-0.017	9
Dialysis <sup>†</sup>	-0.164	8
Renal transplant	-0.076	8
Deep foot infection <sup>*</sup>	-0.17	8
Foot ulcer with critical ischaemia <sup>*</sup>	-0.17	8
Minor amputation <sup>**</sup>	-0.063	8
Major amputation	-0.28	8
Severe hypoglycaemic episode	-0.047	10
Non-severe hypoglycaemic episode	-0.014	10
BMI (per unit decrease)	0.017	11
BMI (per unit increase)	-0.047	11

**Figure 1: Flow diagram of patient simulation process in the Cardiff Type 1 Diabetes Model**

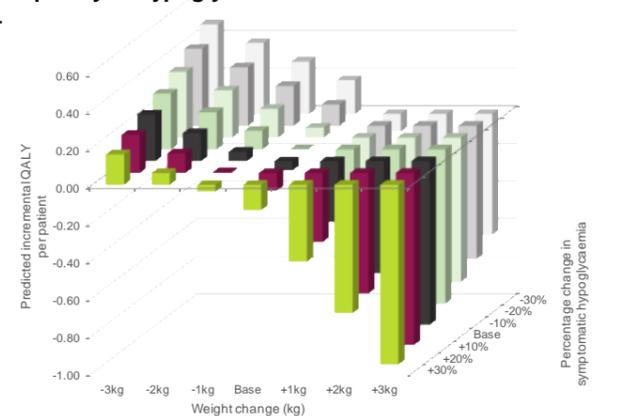


Retinopathy and macular edema includes background diabetic retinopathy, peripheral diabetic retinopathy, severe vision loss, and macular edema. Nephropathy includes micro-albuminuria, macro-albuminuria with impaired glomerular filtration rate, macro-albuminuria, end-stage renal disease, dialysis and renal transplant. Neuropathy includes diabetic peripheral neuropathy and ulcer and amputation events which include uncomplicated ulcer, deep foot infection, foot ulcer and critical

**Figure 2: The predicted change in undiscounted QALYs associated with increases/decrease in patient weight and frequency of hypoglycaemia**



**Figure 3: The predicted change in discounted QALYs associated with increases/decrease in patient weight and frequency of hypoglycaemia**



## Conclusions

- The beneficial effects of improved glycaemic control on QALYs, achieved through the avoidance of diabetes related complications, may be offset by characteristic treatment-specific adverse effects, such as weight gain and frequency of hypoglycaemia.
- The comparative weight and hypoglycaemic profiles of available therapies are therefore key to both their cost-effectiveness and effectiveness in clinical practice.

## Methods

- The Cardiff Type 1 Diabetes Model is a fixed-time-increment stochastic simulation designed to evaluate the impact of therapeutic changes in a cohort of patients with T1DM.
- The model is predominantly based on data from the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) studies to model microvascular complications and the Swedish National Diabetes Registry for cardiovascular complications. Figure 1 shows the model's flow diagram.
- The model is designed to simulate a cohort of up to 10,000 individuals over a period of up to 60 years and was initialised with a population consistent with the EDIC study-type population: age 33.3 years, 47% female, with baseline BMI 25.8 kg/m<sup>2</sup>, HbA1c 8.2% and duration of diabetes 12.1 years (see Table 1).
- Baseline hypoglycaemia rates and utility decrements associated with macro- and microvascular complications, hypoglycaemia and weight change were sourced from the published literature (Table 2).
- The model was used to firstly evaluate the benefit (measured by a change in predicted QALYs) associated with a 1% improvement in HbA1c. Subsequently, the following treatment related changes were applied to the baseline cohort profile: non-severe hypoglycaemic episodes (NSHE) rates were modified by  $\pm 10\%$ ,  $\pm 20\%$  or  $\pm 30\%$ ; weight was then modified by  $\pm 1\text{kg}$ ,  $\pm 2\text{kg}$  or  $\pm 3\text{kg}$ . These changes were evaluated singularly and in combination.
- All changes were applied over the first 6 months with total and incremental QALYs evaluated over a 60-year horizon, discounted at 3.5% annually.

## References

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