Time in range as alternative to HbA1c change in the IQVIA Core Diabetes Model

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Background

- Clinical trials have become shorter, and sometimes do not allow to measure hemoglobin A1c (HbA1c) changes.
- Continuous glucose monitoring devices measure glycemic control with time in range (TIR) of 70-180 mg/dL. Currently, risk equations predicting cardiovascular outcomes based on TIR are not available. However, there are in literature several studies relating TIR change to HbA1c change.
- The IQVIA Core Diabetes Model (CDM) [1,2] is a widely published and validated [3] lifetime cost-effectiveness simulation model that assesses health and economic outcomes in patients with type 1 or type 2 diabetes (T1D or T2D).
- In CDM v10.0, a TIR-to-HbA1c change approach was implemented, as an alternative to the standard approach, the treatment effect on HbA1c.

Objectives

- The aim of this study was to develop an adequate algorithm to convert TIR change into HbA1c change, and to validate the implementation of this approach in CDM v10.0.

Methods

- We performed a target literature search on publications that presented both TIR and HbA1c changes in T1D and T2D randomized trials, and we compared them with available conversion algorithms. From the available data, we developed a conversion table for TIR-to-HbA1c change.
- This conversion table was implemented in CDM v10.0, to convert TIR changes into HbA1c changes and offering this alternative approach.
- To assess this new approach, we performed lifelong analyses in 2 hypothetical cohorts with T1D, cohort A and cohort B, differing in baseline HbA1c values (8% vs 9%, respectively), keeping all other parameters the same: mean age 36.9 years, mean diabetes duration 18 years, proportion of males 39.1%, and BMI 26.6 kg/m^2 (Table 1).
- Six hypothetical scenarios were included in the analyses, 3 scenarios applying a change in baseline HbA1c (0.0, 0.4, and 0.69 %-point decrease), and 3 scenarios applying the equivalent TIR change (0.0, 10, and 20% increase), as presented in Table 2.
- Life years (LY) and quality-adjusted LY (QALY) were compared.

Table 1 – CDM Cohort inputs

Parameter	Values	
	Cohort A	Cohort B
HbA1c	8%	9%
Start age	36.9 years	
Duration of diabetes	18 years	
Proportion male	39.1%	
SBP	122.6 mmHg	
DBP	75.8 mmHg	
Total cholesterol	180.1 mg/dL	
HDL	61.6 mg/dL	
LDL	100 mg/dL	
Triglycerides	93.3 mg/dL	
BMI	26.6 kg/m^2	
eGFR	97.8 mL/min/1.73m^2	

Table 2 – Scenarios tested

Conventional approach		Alternative approach	
Scenario	HbA1c change	Scenario	TIR change
Treatment A	0.0 %-points	Treatment A	0.0 %
Treatment B	-0.40 %-points	Treatment B	+10 %
Treatment C	-0.69 %-points	Treatment C	+20 %

HbA1c: hemoglobin A1c, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, BMI: Body mass index, eGFR: Estimated glomerular filtration rate

Table 3 – CDM approach for conversion of TIR change to HbA1c change

Conversion of TIR to HbA1c change in CDM v10.0									
TIR Change (%)	-20	-15	-10	-5	0	5	10	15	20
HbA1c change (%-points)	0.45	0.31	0.16	0.02	0	-0.26	-0.4	-0.54	-0.69

Results

- Following the literature search, we concluded the TIR-to-HbA1c change presented by Beck et al 2017 [4] to be the most appropriate conversion for both T1D and T2D (Table 3).
- Although Beck et al was focused on T1D, our literature search on T2D did not show that the TIR-to-HbA1c change relation was different in this type of diabetes.
- When using both the conventional and the alternative approach, the predicted LY and QALY were the same for all scenarios and both cohorts (Table 4).
- Predicted LY and QALY were higher in cohort A than in cohort B, as this cohort has a lower baseline HbA1c.
- For the same reason, all treatments show higher incremental LY and QALY in cohort B compared to cohort A, both for the conventional and the alternative approaches.
- The predicted incremental LY and QALY with treatment C were not the double of the predicted LY and QALY with treatment B, even though the TIR effect was doubled.
- This is expected as the conversion algorithm is not linear (Table 3).

Table 4 – Predicted life years and quality adjusted life years

	Conventional approach		Alternative approach	
	Cohort A	Cohort B	Cohort A	Cohort B
Treatment A: no effect				
LY	28.18	26.85	28.18	26.85
QALY	19.15	17.68	19.15	17.68
Treatment B: 0.4 %-point HbA1c decrease (10% TIR increase)				
LY	28.61	27.46	28.61	27.46
QALY	19.66	18.31	19.66	18.31
Treatment C: 0.69 %-point HbA1c decrease (20% TIR increase)				
LY	28.93	27.82	28.93	27.82
QALY	20.04	18.72	20.04	18.72
Treatment B vs Treatment A				
Incremental LY	0.42	0.61	0.42	0.61
Incremental QALY	0.51	0.63	0.51	0.63
Treatment C vs Treatment B				
Incremental LY	0.32	0.37	0.32	0.37
Incremental QALY	0.38	0.41	0.38	0.41

Conclusions

When using both the conventional and the alternative approaches, the predicted results were the same, confirming the correct implementation of the alternative approach.

The initial 10% increase in TIR is more important than further increases. The treatment impact is higher in less controlled populations.

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