

Cross-validation of the glycated haemoglobin (HbA1c) Translator: a predictive tool to evaluate the relationship between diabetes complications and associated healthcare costs

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Introduction

- HbA1c testing is used to measure average blood glucose levels over the previous 3 months and is important for the diagnosis and monitoring of diabetes¹
- Among insulin-treated people with diabetes (PwD), improvements in HbA1c level is associated with a delayed incidence of diabetes complications²
- The modified HbA1c Translator is an updated version of a predictive tool developed by Fortwaengler et al.³ to estimate the relationship between HbA1c level changes and the incidence and corresponding cost of diabetes complications
- In accordance with ISPOR-SMDM Modelling Good Research Practices Task Force-7 for Model Transparency and Validation, modified tools for predicting healthcare outcomes should be validated against previously established external models⁴

Study objective

- To cross-validate a modified version of the HbA1c Translator against an established model—the IQVIA Core Diabetes Model (CDM), by comparing model predictions for:
 - Incidences of diabetes complications, before and after a simulated HbA1c reduction (pre-treatment and with-treatment)
 - Cost savings resulting from delayed onset of diabetes complications due to HbA1c level control

Methods

- A total of 10 diabetes complications were included in the validation exercise: angina pectoris (AP), heart failure (HF), myocardial infarction (MI), Stroke, peripheral artery disease (PAD), proliferative retinopathy (PF), severe vision loss (SVL), amputation (Ampu), neuropathy, end-stage renal disease (ESRD)
- Baseline characteristics were aligned between the HbA1c Translator and the CDM to ensure comparability between models with CDM inputs derived from the HbA1c Translator evidence base for type 1 diabetes (T1D) and Isitt et al.⁵ for type 2 diabetes (T2D) (**Table 1**)

Table 1. Baseline characteristic inputs for the CDM

	Mean values
T1D cohort	
Age, years	37.2
HbA1c level (%)	8.50
Diabetes duration, years	21.5
T2D cohort ⁵	
Age, years	64.5
HbA1c level (%)	8.27
Diabetes duration, years	16

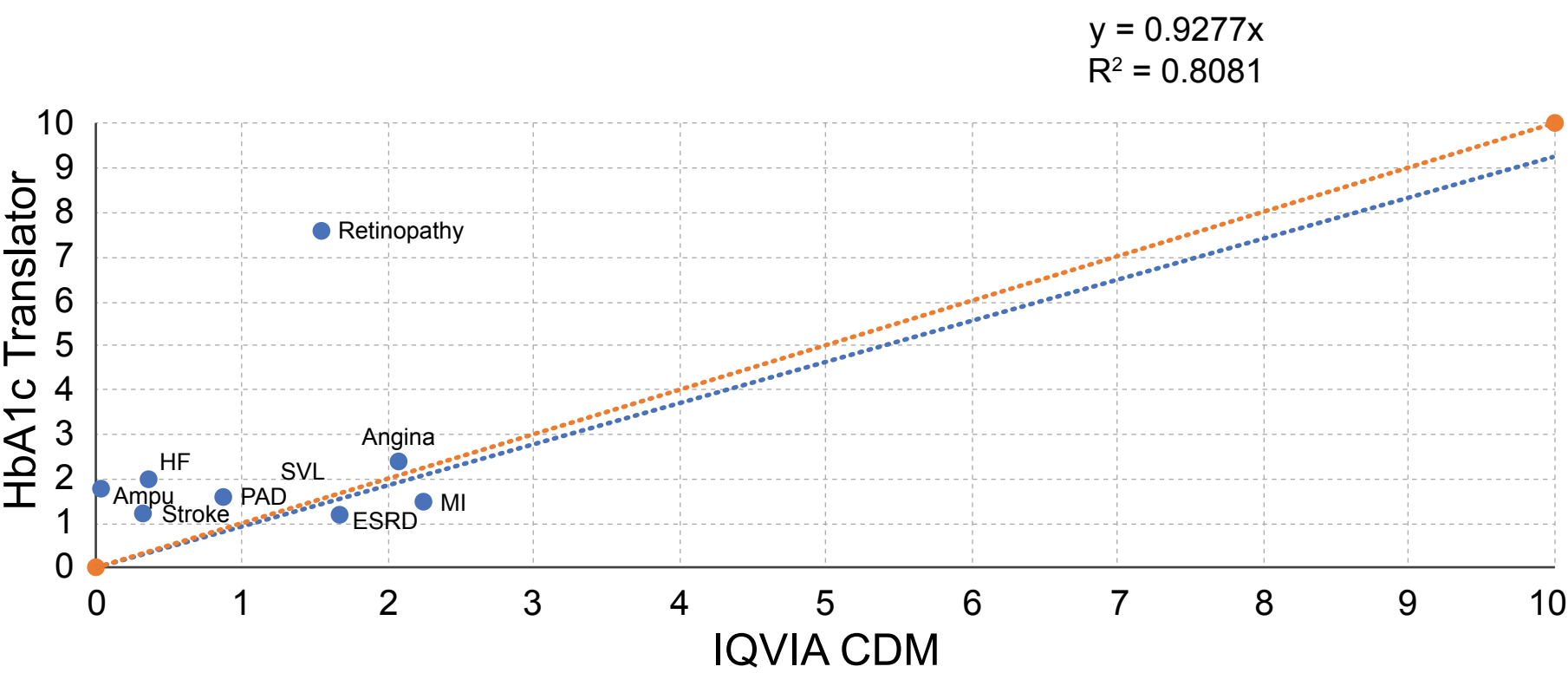
- Cumulative incidences of complications pre-treatment and with-treatment per 100 PwD were generated over a 5-year time period
- Simulations were conducted for T1D and T2D, assuming a hypotheticalal -1% reduction in HbA1c over 5 years vs no reduction
- Concordance between predicted results from the HbA1c Translator and the CDM using ordinary least squares linear regression lines (OLS-LRL) with zero intercepts—slopes above or below 1.0 indicated over- or underestimation by the HbA1c Translator, respectively
- The coefficient of determination (R²) was used to evaluate model fit (with R² closer to 1 being indicative of better linear fit)
- Aligning with the HbA1c Translator, the CDM analysis did not consider diabetes treatment costs or lines of diabetes treatment; for complication costs, Ward et al. 2014, a US study in the cost evidence base, was used⁶

Results

HbA1c Translator vs CDM validation results: T1D

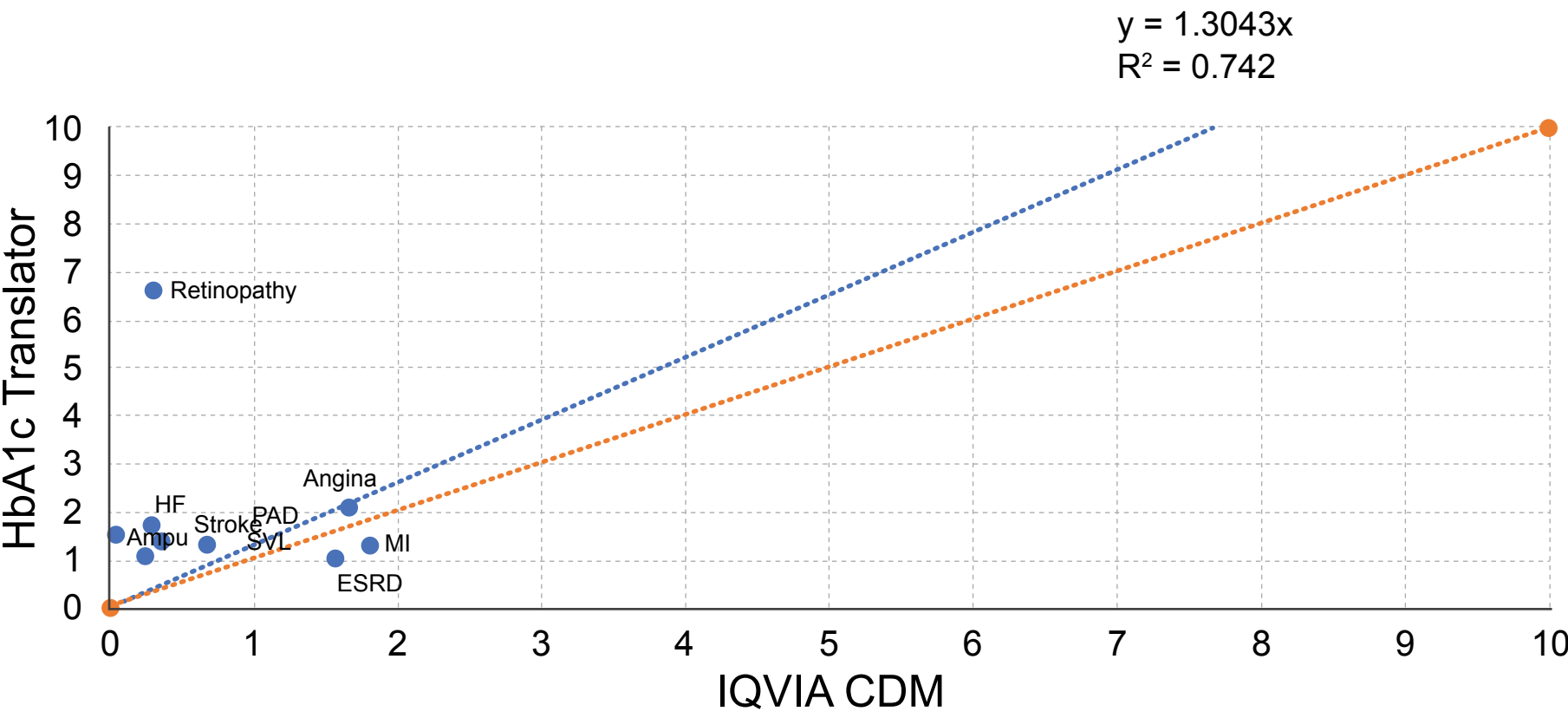
- In the pre-treatment analysis, the HbA1c Translator's predictions of diabetes-related events were closely aligned with the CDM (R²=0.81), showing a slight underestimation of cumulative event rates (OLS-LRL slope of 0.93) (**Figure 1**)

Figure 1. HbA1c Translator vs CDM T1D cumulative incidences: pre-treatment



- When a treatment effect of -1%-points over 5 years was considered, in the with-treatment analysis, the OLS-LRL slope increased to 1.30 (R²=0.74), indicating a moderate overestimation of the incidence of diabetes-related complications by the HbA1c Translator vs the CDM (**Figure 2**)

Figure 2. HbA1c Translator vs CDM T1D cumulative incidences: with-treatment



- The moderate overestimation of cumulative incidences by the HbA1c Translator vs the CDM resulted in a corresponding overestimation of projected cost savings, amounting to an overall additional difference between the models of 217 United States dollar (USD) per PwD over 5 years, primarily driven by an overprediction by the HbA1c Translator of ESRD incidence (**Table 2**)

Table 2. Predicted costs per PwD over a 5-year period: T1D

	HbA1c Translator cost predictions (USD)			CDM cost predictions (USD)			Difference between costs predicted by each model (USD)
	Pre-treatment	With-treatment	Difference	Pre-treatment	With-treatment	Difference	
Heart and stroke complications	4,035	3,476	-559	5,618	5,067	-551	8
Eye complications	226	197	-29	102	63	-38	-9
Foot complications	561	477	-84	368	210	-158	-74
ESRD complications	2,809	2,394	-416	3,483	3,359	-125	291
Total per PwD	7,632	6,543	-1,089	9,571	8,700	-872	217

References

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Results (continued)

HbA1c Translator vs CDM validation results: T2D

- Cumulative incidences predicted by the HbA1c Translator were generally consistent with those projected by the CDM across both pre-treatment and with-treatment scenarios with OLS-LRL slopes of 1.11 (R²=0.86) (**Figure 3**) and 1.22 (R²=0.80) (**Figure 4**) respectively, indicating a moderate overestimation of cumulative incidences by the HbA1c Translator vs the CDM in both analyses

Figure 3. HbA1c Translator vs CDM T2D cumulative incidences: pre-treatment

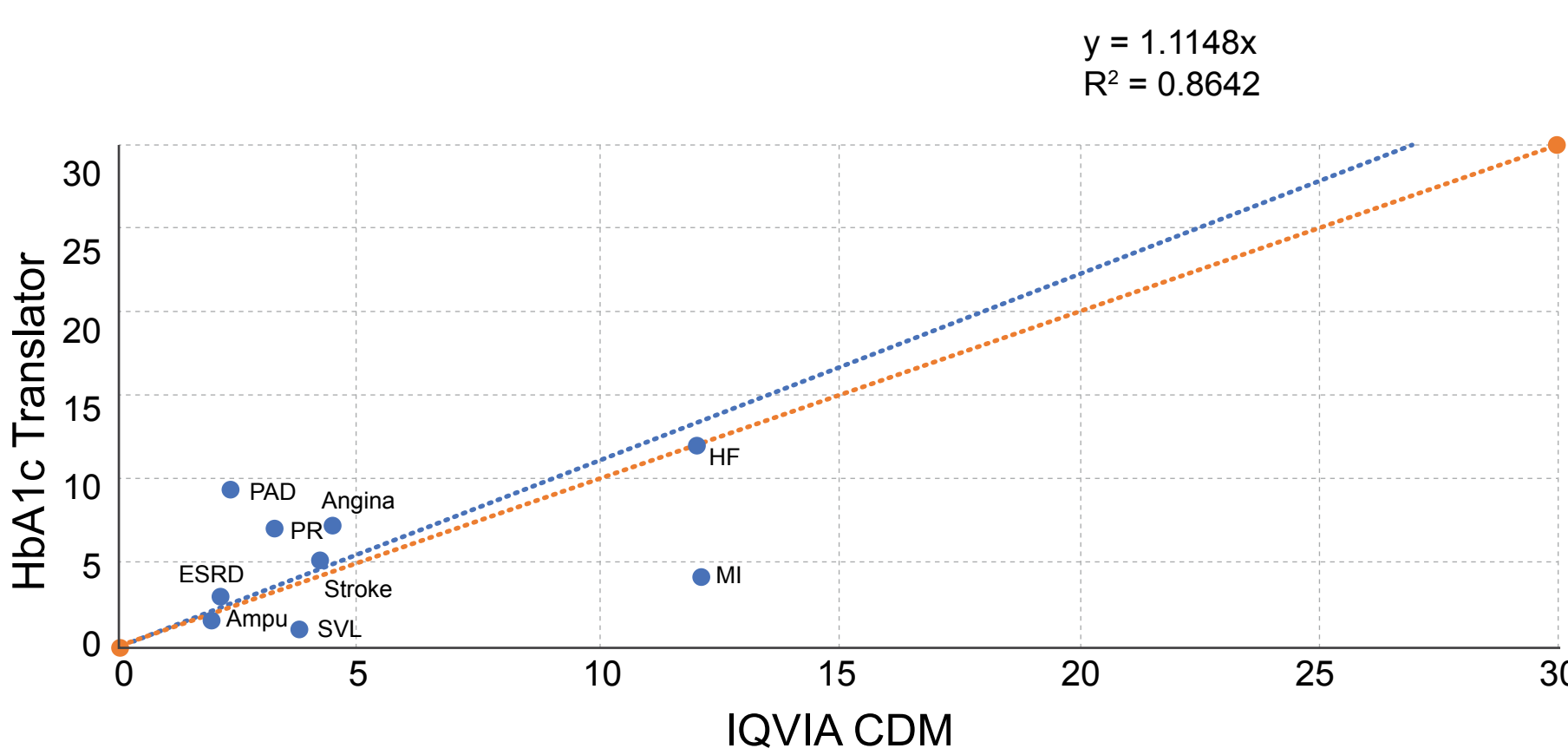
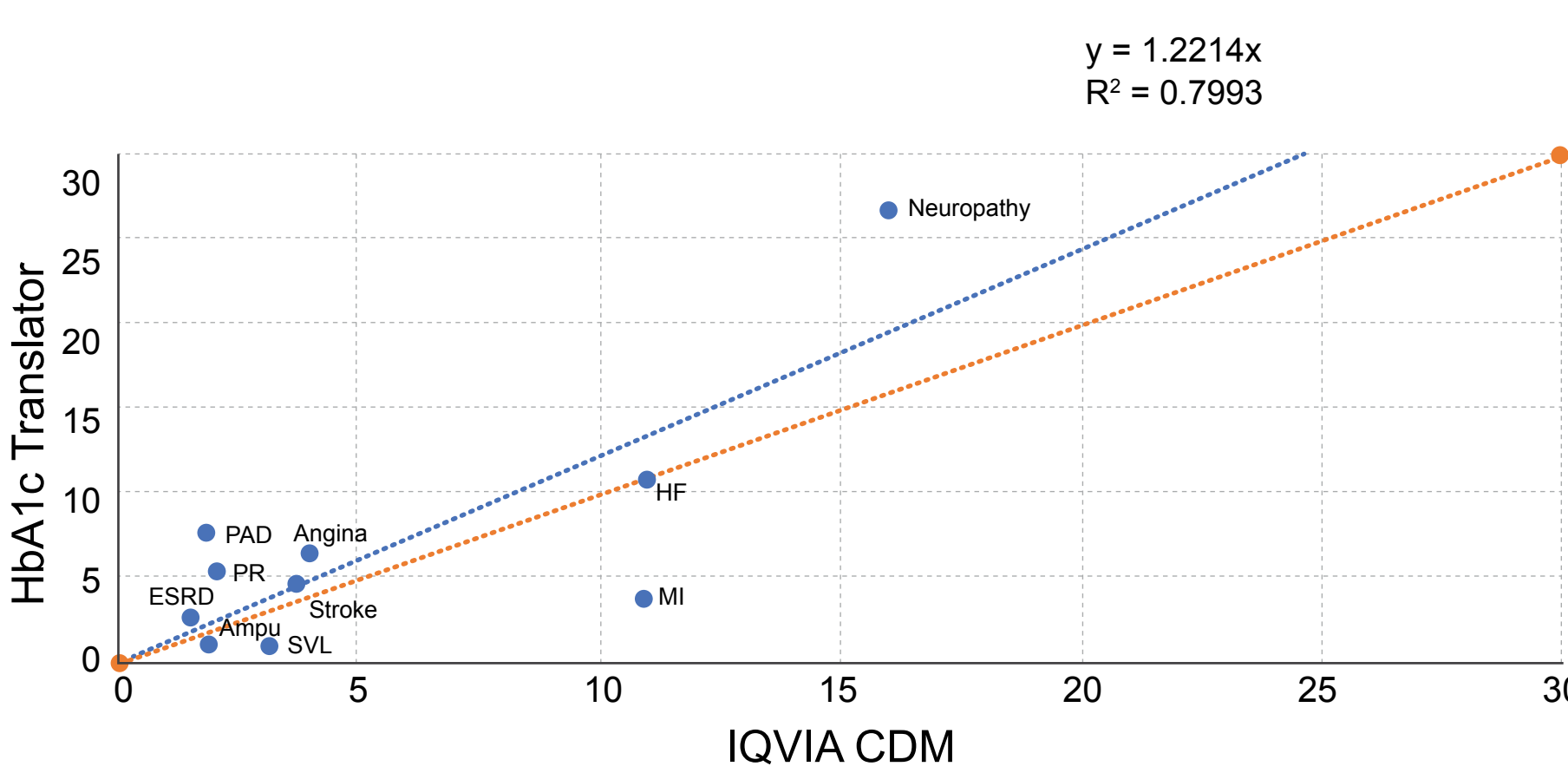


Figure 4. HbA1c Translator vs CDM T2D cumulative incidences: with-treatment



- The moderate overestimation of cumulative diabetes-related incidences with the HbA1c Translator led to a corresponding overestimation of projected cost savings amounting to a difference of 317 USD per PwD over 5 years vs the CDM (**Table 3**)

Table 3. Predicted costs per PwD over a 5-year period: T2D

	HbA1c Translator cost predictions (USD)			CDM cost predictions (USD)			Difference between costs predicted by each model (USD)
	Pre-treatment	With-treatment	Difference	Pre-treatment	With-treatment	Difference	
Heart and stroke complications	15,736	14,194	-1,542	17,767	16,629	-1,138	404
Eye complications	169	130	-39	488	414	-74	-35
Foot complications	1,006	895	-110	1,517	1,398	-119	-9
ESRD complications	6,756	6,201	-555	8,365	7,767	-598	-43
Total per PwD	23,666	21,420	-2,246	28,137	26,208	-1,929	317

Conclusions

- Cross-validation of the modified HbA1c Translator vs the IQVIA CDM demonstrated reliability of results, with a moderate overestimation of predicted incidences and corresponding per-person cost savings in T1D and T2D over the 5-year period analysed

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