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***Fleur Levrat-Guillen is an Abbott shareholder**

Internal, External, and Cross-Validation of the DEDUCE Model a Cost-Utility Tool Using Patient-Level Microsimulation to Evaluate Sensor-Based Glucose Monitoring Systems in Type 1 and Type 2 Diabetes

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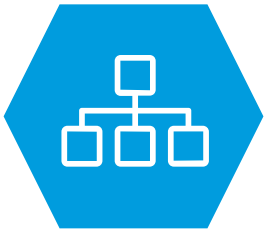
Abbreviations: DEDUCE = DEtermination of Diabetes Utilities, Costs, and Effects.

Agenda

Background

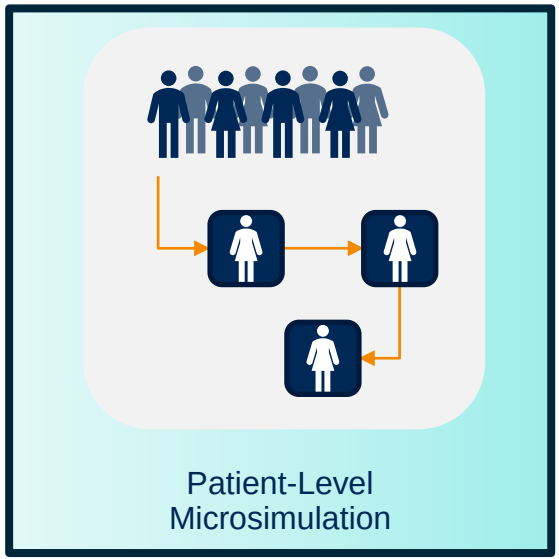


Model Structure & Risk Engines

Key Validation Work

Diabetes models use surrogate endpoints to predict complications and mortality[1]

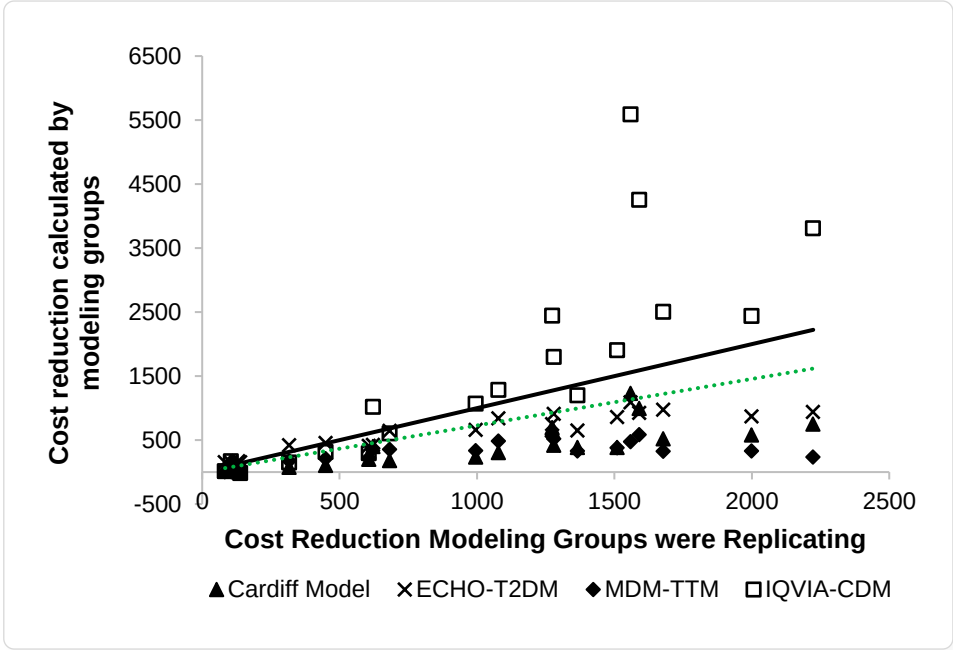
Clinically important endpoints[2]	Surrogate endpoints[2]
Mortality	HbA1c
Health-Related Quality of Life	Postprandial glycaemia
Macrovascular complications	Fasting plasma glucose
Myocardial infarction	BMI
Coronary heart disease	TIR
Cerebral stroke	
Cardiovascular death	
Peripheral vascular disease	
Microvascular complications	
Blindness	
End-stage renal disease	
Foot ulceration	



Abbreviations: BMI = body mass index; HbA1c = glycated haemoglobin; LDL = low-density lipoprotein; LYG = life-years gained; QALYs = quality-adjusted life years; TIR = time-in-range.
References: 1. Palmer AJ, Si L, Tew M, et al. *Value Health*. 2018;21(6):724-731. [2]Wieczorek A, et al. (2008). *Rev Diabet Stud* 5 (3): 128-135.

Background on Diabetes Modelling

- Systematic comparison of diabetes models has revealed[1]:
  - Varying accuracy and transparency
  - Low agreement
- Incidence of events predicted using risk engines
  - Derived from long-term, large-scale studies, with extensive validation
  - Commonly built on older results from the UKPDS study



Abbreviations: UKPDS = UK Prospective Diabetes Study. **References:** 1. Palmer AJ, Si L, Tew M, et al. *Value Health*. 2018;21(6):724-731.

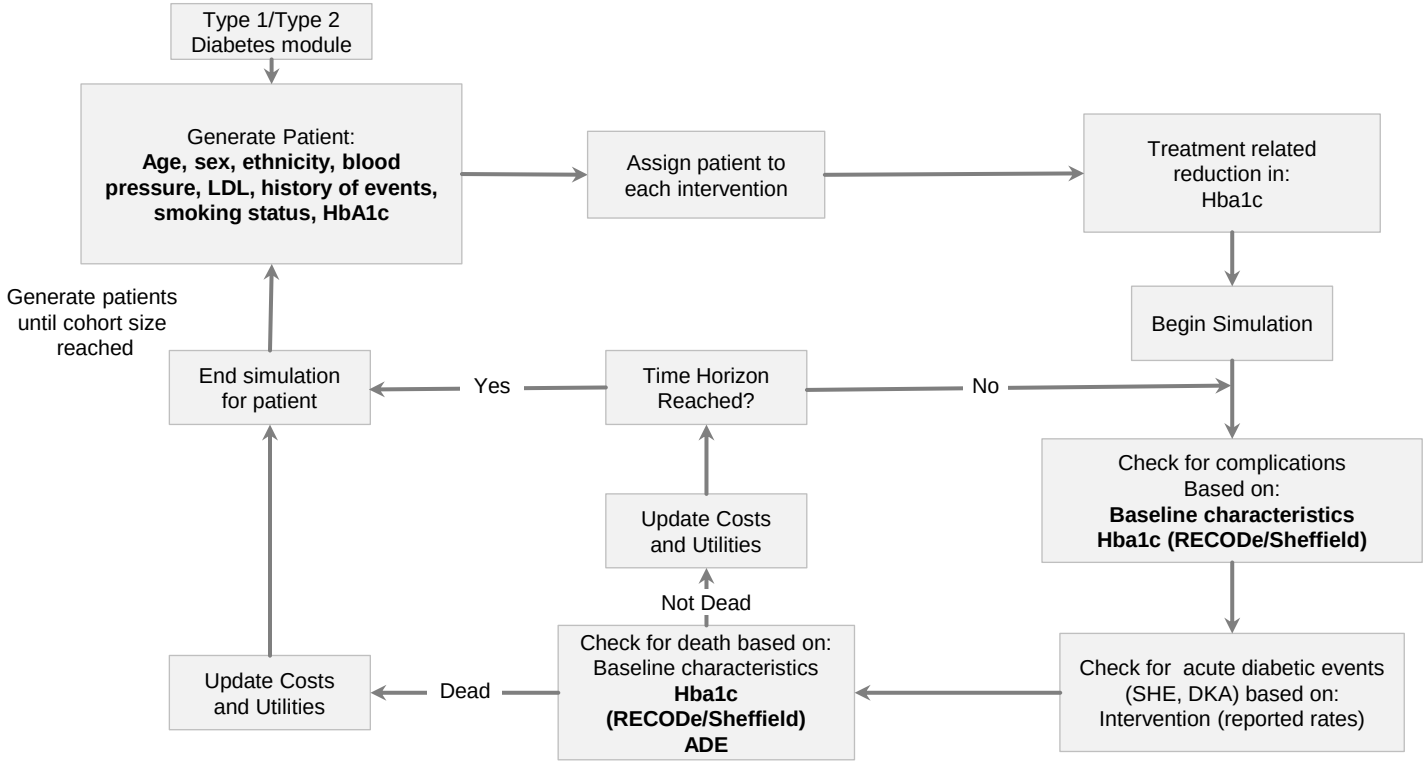
Project Objective

- Engagement with a variety of external stakeholders revealed an opportunity to develop a model with:
  - Transparency
  - Updated risk equations
  - Flexibility

The updated model will be used to answer the primary research objective:

To generate and validate a transparent diabetes cost-utility model for predicting economic and health outcomes

DEDUCE Model Structure



Abbreviations: ADE = acute diabetic event; DKA = diabetic keto-acidosis; HbA1c = glycated haemoglobin; LDL = low density lipoprotein; SHE = severe hypoglycaemia event

DEDUCE Model Validation

Method	T1DM validated against:	T2DM validated against:
Internal Validation - Risk engine originator	DCCT/EDIC[1]	ACCORD[2]
External Validation - Other diabetes trials	FinnDiane[3], WESDR[4], EURODIAB[5]	Look AHEAD[6], ADVANCE[7], DPPOS[8], ASPEN[9]
Cross-validation - Comparative model predictions	EAGLE[10], IQVIA-CDM[11], Archimedes[12]	IQVIA-CDM[13], Michigan[14] ECHO-T2DM[15], UKPDS-OM1[16], UKPDS RE[17], CDC-RTI[18], CDS[19]

Abbreviations: ACCORD = Action to Control Cardiovascular Risk in Diabetes Study, ADVANCE = Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation trial, ASPEN = Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus, DPPOS = Diabetes Prevention Program Outcomes Study, LOOK-AHEAD = Action for Health in Diabetes trial.

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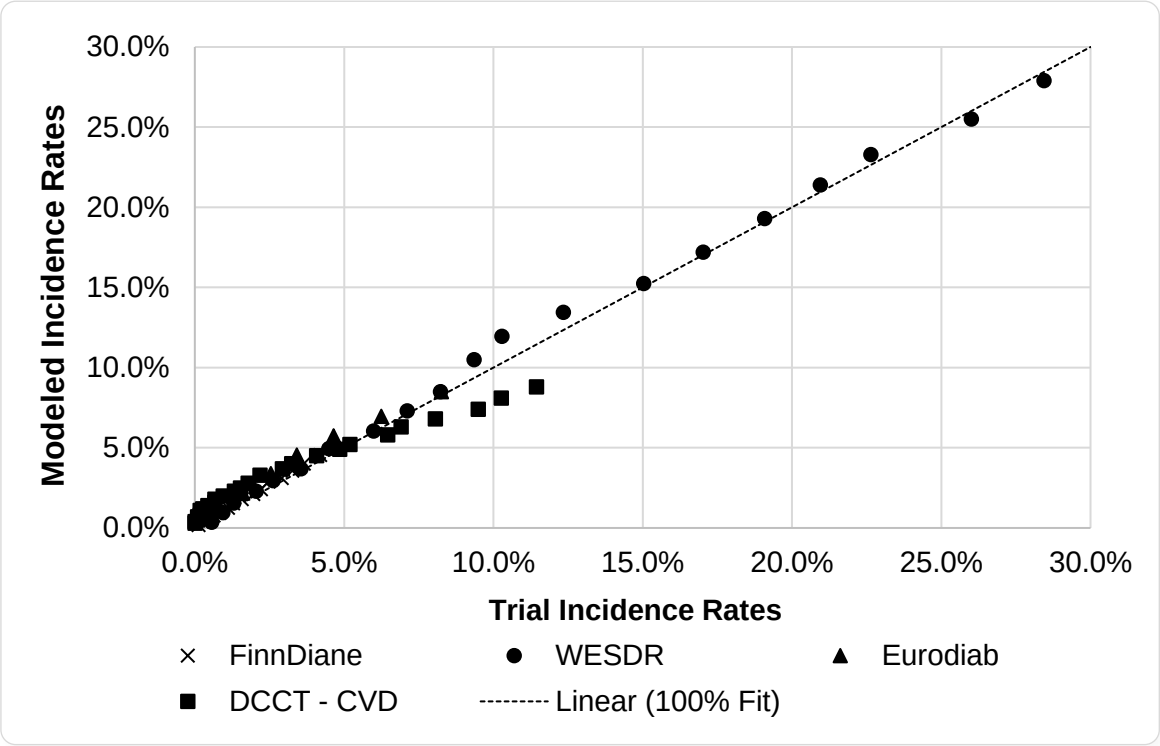
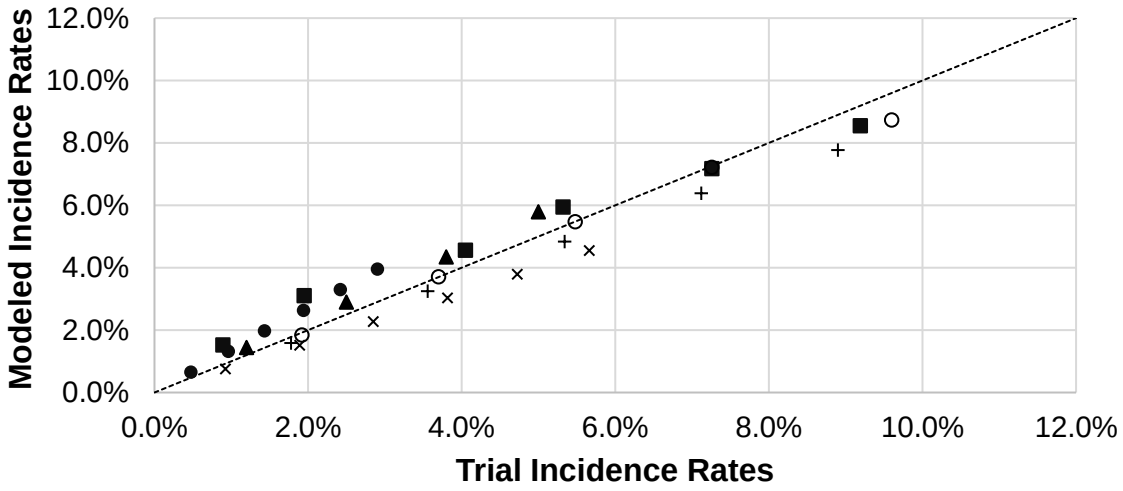
T1DM – Internal/External Macrovascular Outcomes



Study	R^2	MAPE
FinnDiane	0.99	17.5%
WESDR	0.99	7.64%
Eurodiab	0.98	28.9%
DCCT	0.98	68%*
Overall	**0.99**	**14.4%**

Note: Macrovascular events are the composite of: unstable angina + MI + stroke for all trials. *DCCT outcomes were measured from year 10 onwards. **Abbreviations:** CVD = cardiovascular disease, DCCT = Diabetes Control and Complications Trial, Eurodiab = European Diabetes Prospective Complications Study, FinnDiane = Finnish Diabetic Nephropathy trial, MAPE = mean absolute percentage error, WESDR = Wisconsin Epidemiologic Study of Diabetic Retinopathy. **References:** 1. Valentine WJ, et al. 2017 Jul-Aug;20(7):985-991.

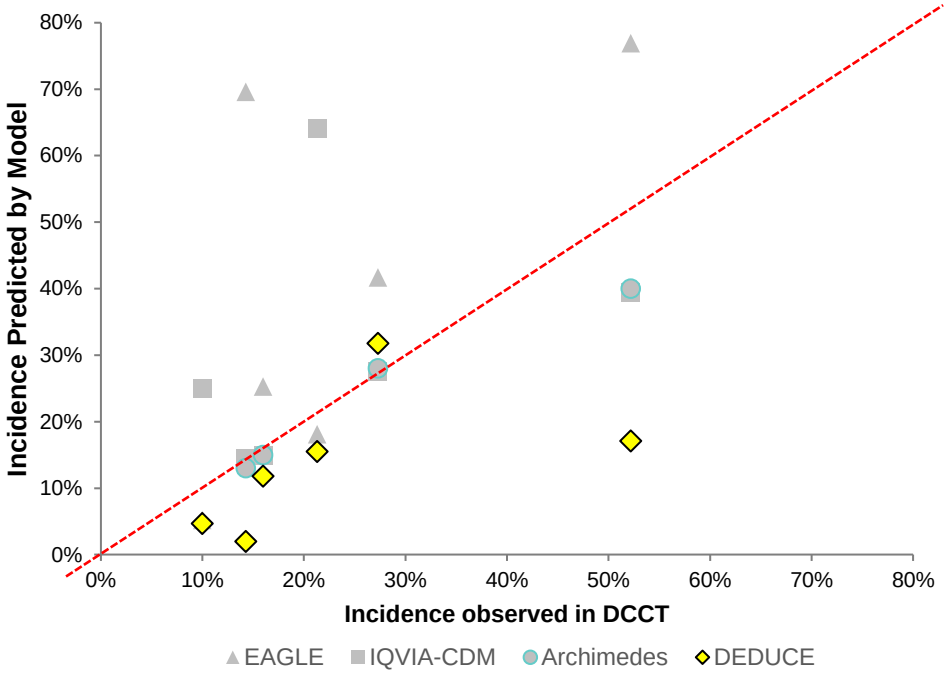
T2DM – Internal/External All-Cause Mortality



Study	R^2	MAPE
ACCORD (Standard)[1]	0.98	27.2%
ADVANCE (Non-intensive)[2]	0.99	2.69%
ADVANCE (Intensive)[2]	0.99	10.3%
ASPEN[3]	0.99	16.8%
DPPOS[4]	0.99	37.1%
LOOK-AHEAD[5]	0.99	19.5%
Overall	**0.94**	**20.0%**

Note: Kaplan-Meier data is used by ACCORD (internal validation dataset), but linear extrapolation applied to other trials to balance figure weighting. **Abbreviations:** ACCORD = Action to Control Cardiovascular Risk in Diabetes Study, ADVANCE = Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation trial; ASPEN = Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus, DPPOS = Diabetes Prevention Program Outcomes Study, LOOK-AHEAD = Action for Health in Diabetes trial, KM = Kaplan-Meier, MAPE = mean absolute percentage error. **References:** [1]ACCORD Study Group, *Am J Cardiol*. 2007 Jun 18;99(12A):21i-33i. [27]ADVANCE Collaborative Group. *Diabet Med.* 2005 Jul;22(7):882-8. [3]Knopp RH, et al. *Diabetes Care.* 2006 Jul;29(7):1478-85. [4]Luchsinger JA, et al. *Diabetes Care.* 2017 Jul;40(7):958-965. [5]Jakicic JM, et al. *Int J Obes (Lond).* 2009 Mar;33(3):305-16.

T1DM – Cross-Validation

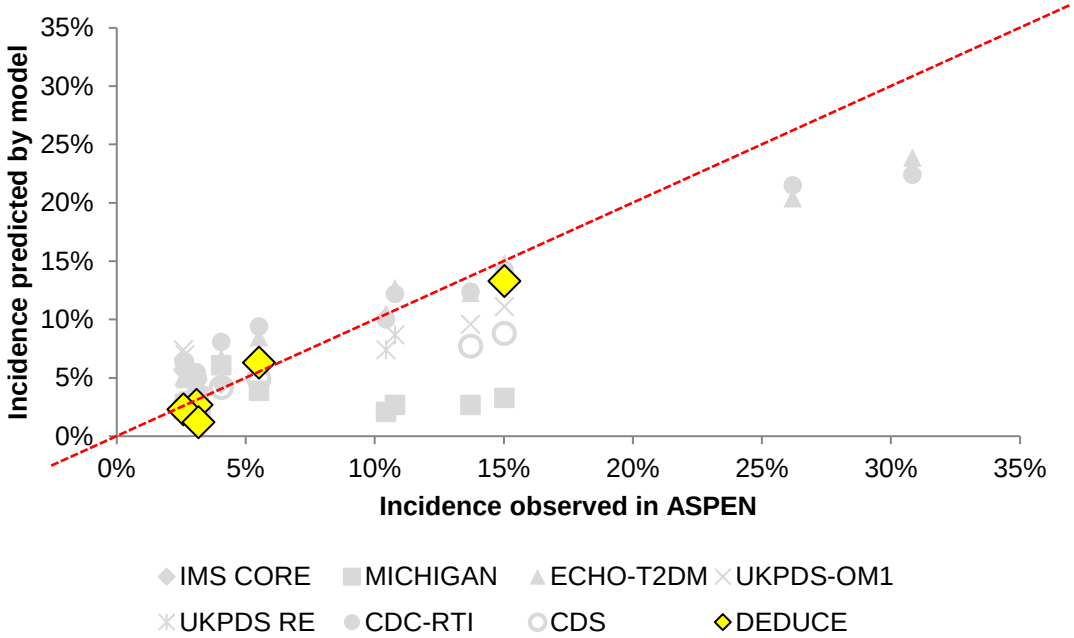


	R^2	MAPE
DEDUCE	0.16	42%
Mount Hood 4 models	0.13 – 0.95	49 - 118%

The DEDUCE model performed within the range of all models from Mount Hood Challenge 4[1]

Notes: Events predicted by DEDUCE include microalbuminuria, background retinopathy, neuropathy for both intensive and non-intensive therapy. **Abbreviations:** DCCT = Diabetes Control and Complications Trial, ESRD = end-stage renal disease, MAPE = mean absolute percentage error, PDR = proliferative diabetic retinopathy. **References:** [1]Mount Hood 4 Modeling Group (2007) *Diabetes Care* 30 (6): 1638-1646.

T2DM – Cross-Validation



	R^2	MAPE
DEDUCE	0.95	25%
Mount Hood 5 models	0.06 – 0.98	24 - 56%

The DEDUCE model performed within the range of all models from Mount Hood Challenge 5[1]

Note: Events predicted by DEDUCE include primary composite endpoints (CV mortality and events), CVD mortality, non-CVD mortality, and both fatal- and non-fatal MI and stroke. **Abbreviations:** ASPEN = Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus, CVD = cardiovascular disease, MI = myocardial infarction, UKPDS = UK Prospective Diabetes Study. [1]Palmer AJ, et al. (2013) *Value Health* 16 (4): 670-685.

Key Takeaways

The DEDUCE model:

Predicts key outcomes

Performs comparably with existing models

Provides an updated risk engine, reflective of modern treatment practices

Is a transparent tool to support value-based decision-making

Thank you!

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