Mount Hood Diabetes Challenge 2025, Chicago

Type 2 diabetes challenge
Draft 18 March 2025

CIRCULATED FOR COMMENT ONLY
CHALLENGE SUBJECT TO CHANGE

This is being circulated for information and comments only – DO NOT use these instructions for the challenge.

Motivation

The aim of Mt Hood 2025's type 2 diabetes challenge is to examine structural uncertainty and key factors impacting cost-effectiveness estimates of a hypothetical weight-loss intervention. We know from previous challenges (i.e. Mt Hood 2022, Malmo) that structural uncertainty across diabetes models may have important consequences for adopting new interventions and negotiating product prices. We have a great opportunity to examine how model performance could be used to aggregate model outputs and capture structural uncertainty. The type 2 diabetes challenge is split into three parts: (1) Reference Simulation; (2) Model Performance; and (3) Cost-effectiveness of hypothetical weight-loss interventions.

Note that this year's T2DM challenge uses different inputs at each stage, please read the instructions carefully to ensure consistency across groups.

Challenge: Part 1 – Reference Simulation

We ask modelling groups to repeat the reference simulations for a standard patient as reported in the MT Hood model registry. This will enable model simulations to be compared across time and these values will be used to update the model registry: https://www.mthooddiabeteschallenge.com/registry. Previous reference simulations have often assumed that risk factors are held constant over time which is often unrealistic. Since the last Mt Hood challenge several risk factor time path equations have been published (e.g. https://onlinelibrary.wiley.com/doi/10.1111/dme.14656). Hence we ask all modelling groups to run the reference simulations under two scenarios: (i) risk factor values held constant (which was the assumption from the previous challenge); and (ii) allowing them to vary using equations or trajectories that are normally used in your simulation model. Treatment effects will assume to be a constant displacement from the usual time path.

Challenge: Part 2 – Model Performance

We ask modelling groups to estimate total QALYs from a patient population based on the EXSCEL Trial (https://www.nejm.org/doi/full/10.1056/NEJMoa1612917). The trial

population consisted of adults with type 2 diabetes and 70% of enrolled patients had previous cardiovascular events and 30% did not. We will provide the modelling groups with the population (patient-level baseline risk factors), risk factor trajectories, inputs (utility values) and instructions.

The aim of this task is to assess how well models perform in predicting total QALYs across the whole EXSCEL population over the trial follow-up. We will then compare model predictions vs. estimated trial QALYs using mean squared error (MSE). This will serve as a proof of concept of using QALYs to assess model performance from Dakin et al (2025): https://doi.org/10.1177/0272989X241285866).

Finally, the EXSCEL trial compared once-weekly 2 mg exenatide injections (EQW, Bydureon) vs. placebo when added to usual care. However, the modelling groups will not be asked to estimate incremental QALYs but rather estimate QALYs for the whole EXSCEL population.

Challenge: Part 3 – Cost-effectiveness of hypothetical weight-loss interventions

We ask modelling groups to estimate the lifetime cost-effectiveness of an hypothetical weight loss intervention versus usual care from the perspective of the UK healthcare system using the patient population provided in Challenge Part 2. The aim of this task is to examine key areas of structural uncertain across models. We will report a weighted-average across model cost-effectiveness results, using both equal weights and unequal weights – based on model performance in part 2. This builds on previous work examining structural uncertainty from Altunkaya (2024): https://doi.org/10.1016/j.jval.2024.06.010)

Model inputs for Challenge: Part 1 – Reference Simulation

Patient Baseline Characteristics (Challenge: Part 1)

To allow for consistent comparisons across all models, baseline patient characteristics should follow the values as listed in Table 2. Any other baseline patient characteristics that your model may require can be sourced from publicly available literature (but please document this including sources in "Baseline Characteristics" tab in the accompanying Excel spreadsheet).

Table 2: Patient Baseline Characteristics (Challenge: Part 1)

Patient Characteristics	**Type 2 diabetes** [a]		**Type 1 diabetes** [b]	
	Men	**Women**	**Men**	**Women**
Current age	66	66	37	37
Duration of diabetes	8	8	22	22

Current/former smoker	N	N	N	N
Ethnicity	White	White	White	White
HbA1c. %	7.5	7.5	8.1	8.1
Systolic Blood Pressure, mmHg	145	145	127	127
Diastolic Blood Pressure, mmHg	80	80	73	73
Total Cholesterol, mmol/l	5.2	5.2	4.8	4.8
HDL Cholesterol, mmol/l	1.3	1.3	1.6	1.6
LDL Cholesterol, mmol/l	3.0	3.0	2.7	2.7
Triglycerides, mmol/L	2.0	2.0	1.2	1.2
BMI	28	28	25	25
Albumin: creatinine ratio	14.2	14.2		
PVD	N	N	N	N
Micro or macro albuminuria (albuminuria >50)	N	N	N	N
Atrial fibrillation	N	N	N	N
eGFR (ml/min/1.73 m2)	70	70	96	96
WBC (x10^9/l)	7	7		
Heart rate (bpm)	79	79		
Haemoglobin (g/dl)	14	14		
Prior history of macrovascular disease	N	N	N	N
Prior history of microvascular disease	N	N	N	N

Source: [a]ADVANCE—Action in Diabetes and Vascular Disease: patient recruitment and characteristics of the study population at baseline; see Appendix 1 for summary table; [b] Tran-Duy et al 2020 (6)

Utility Values (Challenge: Part 1)

The challenge uses the health utility values from the 2018 Mt Hood Quality of life Challenge for type 2 diabetes and newly added health utility values for type 1 diabetes (Table 1). It will

be adequate to use point estimates and not model second order uncertainty if the model allows it.

If you require additional utility weights for health states not listed, please add utility values you currently use. Please document your sources and assumptions in the "Utility values" tab in the accompanying Excel spreadsheet.

For the challenge, please apply disutility values only to complication events described in the instructions as far as possible. If this is not possible and your model **requires** you to apply additional disutilities for certain health states (e.g. a raised BMI health state which is independent of BMI's effect on complication events) - please report these disutilities here. Please also keep baseline utilities constant across all ages as set out in instruction table 1. Where possible, please do not change baseline utilities by age. However, if your model requires you to do so – please report this in the Excel sheet.

Note: please make sure to avoid confusion with utility/disutility terminology in loading the models and in reporting results. The "Utility/Disutility Values" column in Table 1 reports "utility" only for diabetes without complication (which is positive). The remaining items (all negative) are disutility and are incremental.

Based on the 2018 Mt. Hood challenge conference call on September 5, 2018, two suggestions were made for the Quality of Life challenge, including:

1) The additive quality-of-life (QoL) model is recommended when populating the health utility values into the simulation model. As shown in Table 1 below, if a subject has experienced two different complications belonging to 2 different categories of disease (e.g., stroke [in the category of cerebrovascular disease] and myocardial infarction [in the category of coronary heart disease]), the health utility value will be reduced by 0.219 which is the sum of individual decrement for these 2 complications (i.e., 0.164+0.055). However, if a subject has experienced two or more complications within the same category of disease (e.g., myocardial infarction [in the category of coronary heart disease] and congestive heart failure [in the category of coronary heart disease]), the health utility value will be reduced by 0.108 (the decrement for heart failure) which is the largest decrement of these two complications. If the additive QoL model is not feasible in your model, please document your assumptions how the health utility values are populated in your model.

2) The utility decrement and its 95% confidence interval for renal transplant was assumed to be half of those for hemodialysis.

Table 1. Utility values by categories of diseases/complications (Challenge: Part 1)

Disease category	Complication level provided in Mt. Hood QoL challenge	Type 2 diabetes [a]			Type 1 diabetes *		
		Utility/Disutility Values	Lower 95% CI	Upper 95% CI	Utility/Disutility Values	Lower 95% CI	Upper 95% CI
Baseline utility value	Diabetes without complications	0.785	0.681	0.889	0.900[b]	0.880[b]	0.930[b]
Acute metabolic disorder	Minor hypoglycemia event	-0.014	-0.004	-0.004			
	Major hypoglycemia event	-0.047	-0.012	-0.012	-0.002[c]	-0.004[c]	-0.000[c]
	Major hyperglycemic event				−0.071[d]	-0.116[d]	-0.026[d]
Comorbidity	Excess BMI (each unit above 25 kg/m^2)	-0.006	-0.008	-0.004	-0.005[c]	-0.009[c]	-0.001[c]
Retinopathy	Cataract	-0.016	-0.031	-0.001			
	Moderate non-proliferative background diabetic retinopathy	-0.040	-0.066	-0.014	-0.027[c]	-0.048[c]	-0.005[c]
	Moderate macular edema	-0.040	-0.066	-0.014			
	Vision-threatening diabetic retinopathy	-0.070	-0.099	-0.041			
	Severe vision loss	-0.074	-0.124	-0.025			
Nephropathy	Proteinuria	-0.048	-0.091	-0.005			
	Renal transplant[1]	-0.082	-0.137	-0.027	-0.053[e]	-0.077[e]	-0.029[e]
	Hemodialysis	-0.164	-0.274	-0.054	-0.082[e]	-0.128[e]	-0.036[e]
	Peritoneal dialysis	-0.204	-0.342	-0.066			
Neuropathy	Peripheral vascular disease	-0.061	-0.090	-0.032			

	Neuropathy	-0.084	-0.111	-0.057	-0.236[c]	-0.299[c]	-0.173[c]
	Active ulcer	-0.170	-0.207	-0.133	-0.125[c]	-0.226[c]	-0.023[c]
	Amputation event	-0.280	-0.389	-0.170	-0.117[c]	-0.225[c]	-0.009[c]
Cerebrovascular disease	Stroke	-0.164	-0.222	-0.105	−0.291[b]	−0.475[b]	−0.108[b]
Coronary heart disease	Myocardial infarction	-0.055	-0.067	-0.042			
	Ischemic heart disease	-0.090	-0.126	-0.054	−0.181[b]	−0.331[b]	−0.031[b]
	Heart failure	-0.108	-0.169	-0.048	-0.058[f]	-0.101[f]	-0.015[f]
	Percutaneous revascularization				+0.025[c]	-0.051[c]	0.101[c]
	Coronary revascularization				-0.0787[c]	-0.218[c]	0.060[c]

Source: [a] Beaudet et al. 2014 (1); [b] Solli et al 2010 based on EQ-5D-3L (2); [c] Peasgood et al 2016 based on EQ-5D-3L (3); [d] Hart et al 2003 based on EQ-5D-3L (4); [e] Ahola et al 2010 based on 15D; [f] Coffey et al 2002 based on QWB-SA (5); Abbreviations: QoL, quality of life; CI, confidence interval; T2DM, type 2 diabetes; BMI, body mass index. [1]The utility decrement and its 95% confidence interval for renal transplant was assumed to be the half of those for haemodialysis.

* Compiled by An Tran-Duy (an.tran@unimelb.edu.au) on behalf of the COSMO-T1D modelling group. Note that the 95% CIs were not reported in Hart et al (source: d) and Ahola et al (source: e) and were reconstructed based on t-value, p-value, sample size and/or standard error where relevant.

Challenge Part 1: simulation

Step 1: Run a simulation using the baseline risk factors from Table 2 held constant over a 40-year period for type 2 diabetes and a 70-year period for type 1 diabetes, separately for males and for females

This simulation should match both the 2018 Mt Hood challenge and the reference case simulations which are on the Mt Hood website: (https://www.mthooddiabeteschallenge.com/refsim). Ensure QALYs are **not discounted** for this challenge.

Extract the results and enter input values in a transparent manner in the accompanying Excel workbook in tab labelled "Time paths & Outcomes" (modify the workbook to fit your outcomes if necessary, but please try to preserve the basic structure). Do not forget to include traces (risk factor time paths) for input values of all the above risk factors; rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.), and life-expectancy.

For microsimulation models, please ensure that the number of replications is sufficient to generate stable results. Report how many replications were used.

Step 2: Reference simulation of common treatment effects

Re-run the simulation with four individual interventions (one-at-a-time and then all combined), separately for males and females, that capture initial and permanent reductions in common risk factors from time paths modelled in Step 1. Reductions from these interventions should only be applied to post-baseline cycles and baseline values should remain unchanged.

(i) 0.5%-point reduction in HbA1c;

(ii) 10mm Hg reduction in Systolic Blood Pressure;

(iii) 0.5 mmol/l (19.33 mg/dl) reduction in LDL Cholesterol

(iv) 1-unit reduction in BMI (kg/m2)

(v) All 4 of the interventions above applied simultaneously#

Extract the results and add to the accompanying Excel workbook (in tab labelled "Time paths & Outcomes". Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.) and life expectancy.

Step 3: Estimate incremental QALYs, separately for males and females

Using the "Utility/disutility" values in Table 1 run the baseline simulation and estimate expected QALYs, assuming that decrements apply to the year of the of the event and are similarly applied to each subsequent year. However, if temporary events/states such as hypoglycaemia are modelled, it is likely that these decrements only apply to the year of the event. If so, please document this.

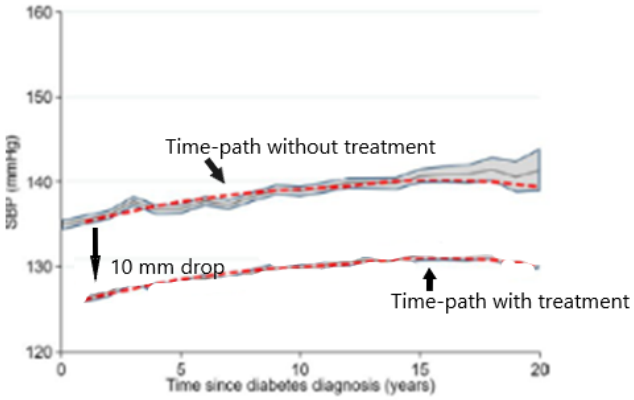
Run each of the four interventions listed in Step 2 to estimate the expected QALYs and calculate the incremental QALYs compared to the baseline (control). Extract the results and add to the accompanying Excel workbook (in tab labelled “Time paths & Outcomes”).

Be sure to report incremental QALYs so that a negative value indicates worse QALYs (not inverting to account for a positive value indicating more disutility)

Step 4: Reference simulation of common treatment effects when risk-factor time-paths are NOT held constant [OPTIONAL]

The simulation in step 1 does not capture the drift that can occur in many risk factors over time eg. the gradual increase in HbA1c. To understand what impact change in risk factors may have on incremental benefits the second component of this challenge is to redo the four simulations outlined in step 2 using the actual risk factor time paths or assumptions regularly used in your model. Please assume that treatment effects are permanent vertical displacements from the trajectories without intervention time-paths.

As an example consider the blood pressure treatment simulation – the treatment will permanently reduce SBP 10 mm Hg below the projected trajectory of SPB without treatment. Similarly, please allow all risk factors that are normally projected in your model to vary. So, when simulating the blood pressure lowering intervention allow HbA1c, LDL, BMI and other risk factors to follow the time-path predicted by your model without any treatment effect.



Extract the results and add to the accompanying Excel workbook (in tab labelled “Time paths & Outcomes”. Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.), QALYs and life expectancy.

Model inputs for Challenge: Part 2 – Model Performance

Patient baseline characteristics (Challenge: Part 2)

To allow for consistent comparison to be made across all models please use the provided baseline patient characteristics. Summary statistics are presented in Table 6. The same population will be used in both *Challenge: Part 1* and *Challenge: Part 2.*

If your model requires other baseline patient characteristics please document values and sources in the "Baseline Characteristics" tab in the Excel sheet. Please note that other patient baseline characteristics must be from publicly available sources

The provided baseline patient characteristics are based on the published patient characteristics from the Exenatide Study of Cardiovascular Event Lowering (EXSCEL) trial. This study assessed the effect of once-weekly 2 mg exenatide injections (EQW, Bydureon) vs. placebo when added to usual care in 14,752 patients with type 2 diabetes with or without previous cardiovascular disease.

Trial paper: https://www.nejm.org/doi/full/10.1056/NEJMoa1612917

Baseline characteristics: https://doi.org/10.1016/j.ahj.2017.02.005

Table 6. Summary of Patient Baseline Characteristics (Challenge: Part 2 and Part 3)

Patient Characteristics	**Type 2 diabetes**	
	Men	**Women**
Current age		
Duration of diabetes		
Current/former smoker		
Ethnicity		
HbA1c. %		
Systolic Blood Pressure, mmHg		
Diastolic Blood Pressure, mmHg		
Total Cholesterol, mmol/l		
HDL Cholesterol, mmol/l		
LDL Cholesterol, mmol/l		
Triglycerides, mmol/L		
BMI		
Albumin: creatinine ratio		
PVD		

Micro or macro albuminuria (albuminuria >50)		
Atrial fibrillation		
eGFR (ml/min/1.73 m2)		
WBC (x10^9/l)		
Heart rate (bpm)		
Haemoglobin (g/dl)		
Prior history of macrovascular disease		
Prior history of microvascular disease		

Utility values (Challenge: Part 2)

Challenge: Part 1 uses health utility values from Dakin et al (2025).(7) Other disutility value not listed in Table 5 should be set to zero. If your model requires additional disutility values and it is not possible to run the model with certain decrements set to zero, then please report the additional complication event(s) and disutility value(s). Unless stated otherwise, subsequent utility decrements are applied the same as in the event the event year.

We recommend using the additive quality of life approach when populating health utility values into the simulation model if a subject has experienced two different complications belonging to 2 different categories of disease (e.g., stroke [in the category of cerebrovascular disease] and myocardial infarction [in the category of coronary heart disease]), the health utility value will be reduced by 0.230 which is the sum of individual decrement for these 2 complications (i.e., 0.165+0.065). However, if a subject has experienced two or more complications within the same category of disease (e.g., myocardial infarction [in the category of coronary heart disease] and congestive heart failure [in the category of coronary heart disease]), the health utility value will be reduced by 0.101 (the decrement for heart failure) which is the largest decrement of these two complications. If the additive QoL model is not feasible in your model, please document your assumptions how the health utility values are populated in your model.

Note: Disutility refers to loss of utility following a complication (negative values). The baseline utility value refers to the starting utility for people with diabetes without yet experiencing complications (positive value).

Table 5. Disutility and utility values by category of diseases/complications (Challenge: Part 2)

Disease category	**Complication level**	**Values (8)**
Baseline utility value	Diabetes without complications	0.807
Coronary heart disease	IHD*	-0.000
	MI: during year of event	-0.065

	MI: in subsequent years	-0.000
	Stroke*	-0.165
	(Congestive) heart failure*	-0.101
Retinopathy	Blindness (in one eye)*	-0.000
Neuropathy	(Diabetic foot) ulcer*	-0.210
	Amputation*	-0.172
Nephropathy	Renal failure*	-0.330

* The same disutility was applied during the year when the event took place and in all subsequent years.

Time path trajectories (Challenge: Part 2)

We provide averaged time path trajectories for high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, systolic blood pressure (SBP), glycated haemoglobin (HbA1c), peripheral artery disease (PVD), atrial fibrillation (AF), bodyweight, albuminuria presence, heart rate, white blood cell count, and estimated glomerular filtration rate (eGFR) for the patient population in *Challenge: Part 2*.

Complication costs (Challenge: Part 2)

In *Challenge: Part 2* we are not concerned with complication costs. Keep default complication cost values.

Instructions for Challenge: Part 2 – Model Performance

Step 1: Input the provided baseline characteristics, risk factor trajectories, and utility/disutility values into your model

Step 2: Run a simulate over 7-years (trial duration)

Step 3: Estimate total (undiscounted) QALYs

Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.) and life expectancy.

Model inputs for Challenge: Part 3 – Cost-effectiveness of hypothetical weight-loss interventions

Utility values (Challenge: Part 3)

Challenge: Part 3 allows modellers to use a more extensive source of health utility values (see Table 7). If your model requires additional disutility values and it is not possible to run the model with certain decrements set to zero, then please report the additional complication event(s) and disutility value(s). Unless stated otherwise, subsequent utility decrements are applied the same as in the event the event year.

We recommend using the additive quality of life approach when populating health utility values into the simulation model if a subject has experienced two different complications belonging to 2 different categories of disease (e.g., stroke [in the category of cerebrovascular disease] and myocardial infarction [in the category of coronary heart disease]), the health utility value will be reduced by 0.230 which is the sum of individual decrement for these 2 complications (i.e., 0.165+0.065). However, if a subject has experienced two or more complications within the same category of disease (e.g., myocardial infarction [in the category of coronary heart disease] and congestive heart failure [in the category of coronary heart disease]), the health utility value will be reduced by 0.101 (the decrement for heart failure) which is the largest decrement of these two complications. If the additive QoL model is not feasible in your model, please document your assumptions how the health utility values are populated in your model.

Note: Disutility refers to loss of utility following a complication (negative values). The baseline utility value refers to the starting utility for people with diabetes without yet experiencing complications (positive value).

Table 7. Disutility and utility values by category of diseases/complications (Challenge: Part 3)

Disease category	Complication level provided in Mt. Hood QoL challenge	Base-case			Source/comment
		Values	Lower 95% CI	Upper 95% CI	
Baseline utility	Diabetes without complication	0.807	0.797	0.817	Alva et al.(8) Default utility inputs within UKPDS-OM2. Fixed-effects models.
Acute metabolic disorder	Minor hypoglycaemic event	-0.014	-0.016	-0.012	Source Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Currie et at. (2006)(10) Assumed standard error is 0.001.
	Major hypoglycaemic event	-0.047	-0.049	-0.042	
Comorbidity	Excess BMI (each unit above 25kg/m^2)	-0.006	-0.008	-0.004	Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Bagust and Beale.(11)
Retinopathy	Cataract	-0.016	-0.031	-0.001	Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Lee et al(12)
	Moderate non-proliferative background diabetic retinopathy	-0.040	-0.066	-0.014	Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Fenwick et al(13)
	Moderate macular edema	-0.040	-0.066	-0.014	

	Vision-threatening diabetic retinopathy	-0.070	-0.099	-0.041	
	Severe vision loss	-0.074	-0.124	-0.025	Source Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Clarke et al.(14).
Nephrology	Proteinuria	-0.048	-0.091	-0.005	Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Bagust and Beale.(11)
	Renal transplant	-0.023	-0.127	+0.081	Beaudet et al. (9) Within this systematic review, these relevant parameters were sourced from Kiberd et al(15). The utility decrement and its 95% confidence interval for renal transplant was calculated using the difference between utility without complication (0.785) and the utility value for renal transplant.
	Hemodialysis	-0.164	-0.274	-0.054	Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Wasserfallen et al(16)
	Peritoneal dialysis	-0.204	-0.342	-0.066	
	Renal failure	-0.330	-0.559	-0.101	Lung et al.(17) Default utility inputs within UKPDS-OM2. 95% CI calculated based on the same standard error in Lung et al for end-stage renal disease utility values

Neuropathy	Peripheral vascular disease	-0.061	-0.090	-0.032	Beaudet et al.(9) Within this systematic review, these relevant parameters were sourced from Bagust and Beale.(11)
	Neuropathy	-0.084	-0.111	-0.057	
	Active ulcer	-0.210	-0.330	-0.090	Lung et al.(17) Default utility inputs within UKPDS-OM2. 95% CI calculated based on the same standard error in Lung et al (2011) for ulcer utility values
	Amputation event	-0.172	-0.260	-0.084	Alva et al.(8) Default utility inputs within UKPDS-OM2. Fixed-effects models.
Cerebrovascular disease	Stroke	-0.165	-0.228	-0.102	
Coronary heart disease	Myocardial infarction (during year of event)	-0.065	-0.079	-0.051	
	Myocardial infarction (in subsequent years)	-0.000	-0.000	-0.000	
	Ischemic heart disease	-0.000	-0.000	-0.000	
	Heart failure	-0.101	-0.164	-0.038	

Patient baseline characteristics (Challenge: Part 3)

The same population in *Challenge: Part 2* will also be used in *Challenge: Part 3* (Table 5). To allow for consistent comparison to be made across all models please use the provided baseline patient characteristics.

If your model requires other baseline patient characteristics be document values and sources in the "Baseline Characteristics" tab in the Excel sheet. Please note that other patient baseline characteristics must be from publicly available sources

Treatment effects, intervention costs, and time path trajectories (Challenge: Part 3)

A hypothetical weight loss intervention for type 2 diabetes costing £3,809 per year of treatment is associated with 1%-point reduction in HbA1c; 1.5-unit reduction in BMI; and 2.5 mmHg reduction in systolic blood pressure. The treatment effect is assumed to be fully captured through conventional risk factors (i.e., no CV-protective effects) and we assume to be perfect adherence/continuation of treatment (Table 8).

It is at the discretion of the modelling group to use published risk factor time path equations or a linear assumption. Note, new risk factor time path equations were estimated based on the EXSCEL trial and TECOS trial (See: https://pubmed.ncbi.nlm.nih.gov/38922488/). Please report what equations or assumptions are used for risk factor progression beyond the treatment effects.

Table 8. Intervention costs (Challenge: Part 3)

Intervention	**Mean effect**	**Duration of treatment effect (years)**	**Mean annual cost (£)**	**Assumption**
Weight-loss intervention (base-case)	1.5-unit reduction in BMI (kg/m2), 1%-point reduction in HbA1c (DCCT), and 2.5-unit reduction in systolic blood pressure (mmHg)	2	3809	Cost of weekly GLP-1RA (NHS Tariff: £73.25) for 52 weeks. Assuming perfect adherence and treatment effect is assumed to be fully captured through conventional risk factors (i.e., no CV-protective effects)
Weight-loss intervention (best-case)	3-unit reduction in BMI (kg/m2), 2%-point reduction in HbA1c (DCCT), and 5-unit reduction in systolic blood pressure (mmHg)	3	3809	Higher efficacy and longer duration. All else remains unchanged from base-case.

Weight-loss intervention (worse-case)	0.5-unit reduction in BMI (kg/m2), 0.5%-point reduction in HbA1c (DCCT), and 1-unit reduction in systolic blood pressure (mmHg)	1	3809	Lower efficacy and shorter duration. All else remains unchanged from base-case.

Complication costs (Challenge: Part 3)

In *Challenge: Part 3* we are concerned with costs, so it is important, where possible, all modelling groups are using the same set of costs. Table 9 shows mean complication costs of diabetic patients obtained from UK literature. Please apply the same set of complication costs for both men and women and for both type 2 and type 1 diabetes individuals.

Please apply costs only to complication events described in the instructions as far as possible. To give example, if your model usually incorporates increased costs from raised BMI increases independently of complication events which occur, please turn this off if possible. If not possible to model costs only for complication events, then please report any additional costs.

Additionally, please keep baseline costs in the absence of complications constant across all ages as set out in instruction. However, if your model requires you to do so – please report this in the excel spreadsheet.

Table 9. Complication costs (£, 2022-23 prices) (Challenge: Part 3)

	Fatal cost	**Non-fatal cost**	**Cost in subsequent years**	**Source**
Ischemic heart disease/Angina	7087	16348	4145	Alva et al. 2015 (18)
Myocardial infarction	3874	11113	3998	Alva et al. 2015 (18)
Heart failure	3298	6597	4994	Alva et al. 2015 (18)
Coronary revascularisation	0	9693	4145	Keng et al. 2021 (19) & Alva 2015 (18)
Stroke	7546	12558	4126	Alva et al. 2015 (18)
Amputation	11472	17693	6221	Alva et al. 2015 (18)
Blindness	0	4959	2576	Alva et al. 2015 (18)
Haemodialysis	0	50626	50626	Davies et al. 2012 (20) as cited in Ramos et al. 2019 (21)

Renal failure / transplant	12014	24027	24027	NHS Blood and Transplant 2009 (22)
Ulcer	0	8262	1252	Kerr et al. 2014 (23)
Peripheral vascular disease	0	5485	1179	Baxter et al. 2016 as cited in Ramos et al. 2019
Cataract operation	0	3078	208	Davies et al. 2012 (20), 2016 (24) as cited in Ramos et al. 2019 (21)
Neuropathy	0	34	34	Davies et al. (24) as cited in Ramos et al. 2019 (21)
Gangrene treatment	0	4313	0	Davies et al. (24) as cited in Ramos et al. 2019 (21)
Retinopathy laser treatment	0	1373	0	Davies et al. 2012 (20) as cited in Ramos et al. 2019 (21)
Peritoneal Dialysis	0	38013	38013	Davies et al. 2012 (20) as cited in Ramos et al. 2019 (21)
Severe hypoglycaemia (req. med. assistance)	0	1716	0	Evans et al. 2017 (25) as cited in Ramos et al. 2019 (21)
Severe hypoglycaemia (req. non med. assistance)	0	0	0	Evans et al. 2017 (25) as cited in Ramos et al. 2019 (21)
Non-severe hypoglycaemia	0	506	0	Evans et al. 2014 (26) as cited in Ramos et al. 2019 (21)
Cost in the absence of complications	2324			Alva et al. 2015 (18)

Instructions for Challenge: Part 3 – simulating cost-effectiveness of hypothetical weight-loss interventions

Step 1: Input the provided baseline characteristics (two treatment groups, hypothetical weight loss intervention, and care as usual), treatment effects, utility/disutility values, costs for complications, and intervention costs (if appropriate) into your model.

Step 2: Run a simulate over 50-years assuming 3.5% discount rate for costs and outcomes. Make sure the assumption about risk factor time path trajectories is noted in the Excel workbook.

Step 3: Estimate total discounted costs and QALYs, incremental costs and QALYs.

Report outcomes and inputs in a transparent manner. Do not forget to include traces (numerical or curves) for input values of all the above risk factors; cumulative rates (or counts) of all major health states in the model (e.g. MI; stroke; renal failure, etc.) and life expectancy.

Step 4: [OPTIONAL] Sensitivity analyses – best/worse case scenarios, weight disutility parameter (use a non-linear approach by Søltoft et al., (2009) see appendix (sources study: https://doi.org/10.1007/s11136-009-9541-8)

Summary of findings

Please complete the Excel spreadsheet including the model characteristics section. Compile a summary of your findings in the accompanying Excel spreadsheet (in tab labelled "Summary"). Please complete the following.

A) Based on your results in Step X, what was your estimation of total QALYs over the trial duration

B) Based on your results in Step X, which scenarios were costs-effective at a £20,000 per QALY threshold?

C) Based on your results in Step 7, report which intervention(s) were costs-effective at a £20,000 per QALY threshold?

D) Provide an overview of what you learnt from this challenge.

Submission

Prior to the meeting, please submit the Excel spreadsheet ("MH CHICAGO CHALLENGE – ICER challenge_GROUP") to Mount Hood at: XXXXX by **XX July 2025.** Please replace GROUP with your modelling group name before submission.

Appendix 1. BMI disutility

Table 3 Multiple linear regression models of HRQoL for men and women (≥18 years of age). The dependent variable is EQ-5D utility values

From: The association of body mass index and health-related quality of life in the general population: data from the 2003 Health Survey of England

Variable	Model 1, men		Model 2, women	
	Coefficient	Robust SE	Coefficient	Robust SE
Age				
18–24	0.0287†	0.0073	0.0055	0.0075
35–44	-0.0028	0.0064	-0.0213†	0.0059
45–54	-0.0081	0.0071	-0.0336†	0.0068
55–64	-0.0430†	0.0077	-0.0425†	0.0072
65–74	-0.0223	0.0089	-0.0619†	0.0092
75–00	-0.0565†	0.0121	-0.0754†	0.0114
BMI[a]				
BMI	0.0990†	0.0265	0.0572‡	0.0183
BMI^2	-0.0032†	0.0009	-0.0018‡	0.0006
BMI^3	0.0000‡	0.0000	0.0000‡	0.0000
GHQ12				
Group 1–3	-0.0727†	0.0056	-0.0695†	0.0050
Group 4+	-0.2507†	0.0117	-0.2192†	0.0090
Age when finished education				
Below 15	-0.0204	0.0103	-0.0202	0.0105
Above 18	0.0234†	0.0049	0.0227†	0.0046
Unfinished	0.0100	0.0107	0.0180‡	0.0090
Non-manual work				
Non-manwork	0.0236†	0.0048	0.0268†	0.0050
Long standing illness				
Type 2 diabetes	-0.0528†	0.0145	-0.0325	0.0183
Heart problems	-0.0486†	0.0084	-0.0278‡	0.0085
Respiratory problems	-0.0242‡	0.0084	-0.0430†	0.0097
Musculoskeletal problems	-0.1721†	0.0078	-0.2014†	0.0074
Cancer	-0.0946†	0.0237	-0.0724†	0.0184
Constant	-0.0228	0.2575	0.4010	0.1786
Observations	5,475		6,445	
df	20		20	
F-value	83.52		114.18	
R^2	0.3952		0.4066	

† $P < 0.001$; ‡ $P < 0.01$

[a] *BMI categories*: continuous variable (BMI), allowing for diminishing effects on the mean (BMI^2) or a non-symmetrical relationship between the BMI and the mean (BMI^3)

Omitted variables represent the 'reference individual'. The reference individual in this study is age 24–34, GHQ-12 score 0, age 15–17 when left school, working with manual work, and has no longstanding illness

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