Mount Hood 2025 Challenges

(Type 2 Diabetes)

Motivation and Overview:

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 (e.g. Mt Hood 2022, Malmo) that structural uncertainty across diabetes models can have important consequences for adopting new interventions and negotiating product prices. In this challenge, we have a great opportunity to examine how model performance could be used to aggregate model outputs and capture structural uncertainty.

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

The type 2 diabetes challenge consist of two parts:

1. Assessing Model Performance in Estimating Quality-Adjusted Life Years (QALYs) Challenge

The modelling groups are asked to estimate total QALYs and costs from a patient population based on the Exenatide Study of Cardiovascular Event Lowering (EXSCEL) trial (https://www.nejm.org/doi/full/10.1056/NEJMoa1612917). This trial assessed the effect of once-weekly 2 mg exenatide injections (EQW, Bydureon) vs. placebo when added to usual care in 14,752 adult patients with type 2 diabetes with or without previous cardiovascular disease. The modelling groups are provided with baseline population characteristics, risk factor trajectories, inputs (utility values and costs), and instructions for running the simulations (e.g., time horizons, discount rates, etc.).

The aim of this challenge is to assess how well models perform in predicting total QALYs across the EXSCEL trial population over the trial follow-up. This will serve as a proof of concept of using QALYs to assess model performance from Dakin et al. (2025). [1]

2. Estimating the Cost-effectiveness of Hypothetical Weight-loss Interventions Challenge

The modelling groups are asked to estimate the lifetime cost-effectiveness of a hypothetical weight loss intervention versus usual care from the perspective of the UK healthcare system using the baseline characteristics provided in Part 1. The aim of this task is to explore possibilities of using multiple models to reduce structural uncertainty and improve decision certainty. We will report a weighted-average across model cost-effectiveness results, using both equal weights and unequal weights – based on model performance in part 1. This builds on work examining structural uncertainty from Altunkaya (2024): https://doi.org/10.1016/j.jval.2024.06.010.

Model inputs for Challenge Part 1: Assessing Model Performance in Estimating Quality-Adjusted Life Years (QALYs)

Patient baseline characteristics

To allow for consistent comparison to be made across all models please use the provided baseline patient characteristics (Tab: *Challenge Part 1 Population*). Summary statistics are presented in Table 1. Note same baseline patient characteristics is used for both parts of the challenge

If your model requires other baseline patient characteristics, please document values and sources in the "*Challenge Part 1 Additional Var*" tab in the Excel sheet. Please note that other patient baseline characteristics must be from publicly available sources.

We will provide groups with baseline patient characteristics to ensure consistency with the approach used by Dakin et al. (2025).[1]

- For groups using a cohort-level simulation model, please refer to Table 1 for baseline characteristics.
- For groups using patient-level simulation models, please use the patient-level dataset provided.

The dataset (n=1,000) was generated using publicly available means, standard deviations, and proportions reported from the EXSCEL trial, along with assumptions made by Dakin et al. (2025).

Disclaimer 1: The dataset **does not** contain real patient-level level data, nor can patient-level information be identified from it. It should be considered as a synthetic dataset derived from summary-level data.

Disclaimer 2: The dataset does not preserve correlations between demographic characteristics, risk factors, and pre-existing comorbidities. As a result, the representativeness of our synthetic patients may differ from real patients. The impact of not preserving correlations is underexplored, and discussions are ongoing to investigate this further as part of a future Mt Hood challenge.

Disclaimer 3: A sample size of 1,000 was chosen to reduce computational burden while still well approximating the original population distribution. However, this introduces sampling error (Bias: 0.18; MAE; 0.43, RMSE: 0.37 for baseline characteristics), which will also be acknowledged as a limitation of this challenge.

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

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

Dakin et al. (2025): https://pubmed.ncbi.nlm.nih.gov/39474832/

Table 1. Summary of Synthetic Patient Baseline Characteristics (used in both parts of the challenge)

Patient Characteristics	**Mean/Proportion (SD)**
Current age (Years)	62.46 (9.57)
Female	0.39 (0.49)
Trial follow-up (Years)	3.28 (1.30)
Duration of diabetes (Years)	12.56 (7.94)
Current/former smoker (proportion)	0.51 (0.50)
Race – White (proportion)	0.92 (0.28)
Race – Black (proportion)	0.06 (0.23)
Race – Asian (proportion)	0.03 (0.16)
HbA1c, %	8.15 (1.00)
Systolic Blood Pressure, mmHg	134.99 (16.82)
HDL Cholesterol, mmol/l	1.13 (0.32)
LDL Cholesterol, mmol/l	2.48 (0.92)
Height, m	1.68 (0.10)
Weight, kg	93.29 (21.55)
BMI, kg/m^2	32.79 (6.39)
PVD (proportion)	0.20 (0.40)
Presence of macro or micro albuminuria (proportion)	0.21 (0.41)
Atrial fibrillation (proportion)	0.07 (0.26)
eGFR, ml/min/1.73 m^2	78.87 (23.48)
WBC, x10^9/l	7.46 (0.71)
Heart rate, bpm	73.05 (10.72)

Haemoglobin, g/dl	13.86 (1.32)
Prior history of IHD (proportion)	0.07 (0.26)
Prior history of MI (proportion)	0.31 (0.46)
Prior history of Stroke (proportion)	0.14 (0.35)
Prior history of HF (proportion)	0.16 (0.37)
Prior history of Amputation (proportion)	0.04 (0.19)
Prior history of Blindness (proportion)	0.01 (0.09)
Prior history of Renal Failure (proportion)	0.00 (0.00)
Prior history of Ulceration (proportion)	0.04 (0.19)

Source: Mentz (2017)[2], Holman (2017) [3], Dakin (2025) [1]. Abbreviations: HbA1c – Glycated Haemoglobin, HDL – High-Density Lipoprotein, LDL – Low-Density Lipoprotein, PVD – Peripheral Vascular Disease, MI – Myocardial Infarction, HF – Heart Failure, IHD – Ischaemic Heart Disease, WBC – White Blood Cell count, eGFR – Estimated Glomerular Filtration Rate, bpm – Beats Per Minute, SD – standard deviation.

Utility values

For part 1 of the challenge, please use the health utility values reported in Table 2, which were used in Dakin et al (2025).[1] 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) in "*Challenge Part 1 Utilities*" tab. Unless stated otherwise, the same utility decrement is applied in both the event year and subsequent years.

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

Disease category	Complication	Values [4]
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.
Note: values are applied irrespective of age and sex.

Time path trajectories

We provide 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 1 Population*" tab.

- For groups using a cohort-level simulation model, please refer to Table 3 for average risk factor time path trajectories.
- For groups using patient-level simulation models, please use the patient-level dataset provided.

Table 3. Average Risk Factor Time Path Trajectories for Cohort Models

Year of simulation	Year 1; Mean (SD)	Year 2; Mean (SD)	Year 3; Mean (SD)	Year 4; Mean (SD)
HbA1c, %	7.70 (1.23)	7.82 (1.34)	7.90 (1.11)	7.882 (0.99)
HDL Cholesterol, mmol/l	1.14 (0.29)	1.142 (0.28)	1.136 (0.27)	1.12 (0.25)
LDL Cholesterol, mmol/l	2.39 (0.87)	2.38 (0.84)	2.32 (0.76)	2.40 (0.68)
Systolic Blood Pressure, mmHg	133.32 (15.08)	132.89 (15.35)	133.71 (12.27)	134.39 (10.87)
Weight, kg	91.78 (21.38)	91.41 (20.80)	90.60 (20.71)	91.02 (20.01)
Current/former smoker	0.39 (0.49)	0.30 (0.46)	0.26 (0.44)	0.24 (0.42)
Presence of macro or micro albuminuria	0.24 (0.43)	0.24 (0.43)	0.28 (0.45)	0.31 (0.46)
Peripheral artery disease	0.19 (0.39)	0.20 (0.40)	0.20 (0.40)	0.21 (0.41)
Atrial fibrillation	0.09 (0.29)	0.09 (0.29)	0.09 (0.29)	0.10 (0.29)
Heart rate	75.31 (9.79)	74.49 (9.27)	74.74 (8.18)	74.34 (7.36)
White blood cell count	7.53 (0.53)	7.56 (0.43)	7.60 (0.41)	7.61 (0.38)
Estimated glomerular filtration rate (eGFR)	76.94 (22.07)	75.19 (22.00)	72.69 (20.49)	69.91 (18.21)

Source: Mentz (2017)[2], Holman (2017) [3], Dakin (2025) [1]. Abbreviations: HbA1c – Glycated Haemoglobin, HDL – High-Density Lipoprotein, LDL – Low-Density Lipoprotein, PVD – Peripheral Vascular Disease, MI – Myocardial Infarction, HF – Heart Failure, IHD – Ischaemic Heart Disease, WBC – White Blood Cell count, eGFR – Estimated Glomerular Filtration Rate, bpm – Beats Per Minute, SD – standard deviation.

For model requiring other baseline patient characteristics, please assume constant (Last Value Carried Forward) trajectories.

Complication costs

Table 4 shows mean complication costs of type 2 diabetes patients obtained from the UK literature. Please apply the same set of complication costs for both men and women across all ages.

Please apply costs only to complication events described in the instructions as far as possible to ensure consistency across modelling groups. To give an 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 tab "*Challenge Part 1 & 2 Costs*".

Table 4. Complication costs (£, 2022-23 prices) (Challenge: Part 3)

Complication	Fatal cost	Non-fatal cost	Cost in subsequent years	Source
Ischemic heart disease/Angina	7087	16348	4145	Alva et al. 2015 [5]
Myocardial infarction	3874	11113	3998	Alva et al. 2015 [5]
Heart failure	3298	6597	4994	Alva et al. 2015 [5]
Coronary revascularisation	0	9693	4145	Keng et al. 2021 [6] & Alva 2015 [5]
Stroke	7546	12558	4126	Alva et al. 2015 [5]
Amputation	11472	17693	6221	Alva et al. 2015 [5]
Blindness	0	4959	2576	Alva et al. 2015 [5]
Haemodialysis	0	50626	50626	Davies et al. 2012 [7] as cited in Ramos et al. 2019 [8]
Renal failure / transplant	12014	24027	24027	NHS Blood and Transplant 2009 [9]

Ulcer	0	8262	1252	Kerr et al. 2014 [10]
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 [7], 2016 [11] as cited in Ramos et al. 2019 [8]
Neuropathy	0	34	34	Davies et al. [11] as cited in Ramos et al. 2019 [8]
Gangrene treatment	0	4313	0	Davies et al. [11] as cited in Ramos et al. 2019 [8]
Retinopathy laser treatment	0	1373	0	Davies et al. 2012 [7] as cited in Ramos et al. 2019 [8]
Peritoneal Dialysis	0	38013	38013	Davies et al. 2012 [7] as cited in Ramos et al. 2019 [8]
Severe hypoglycaemia (req. med. assistance)	0	1716	0	Evans et al. 2017 [12] as cited in Ramos et al. 2019 [8]
Severe hypoglycaemia (req. non med. assistance)	0	0	0	Evans et al. 2017 [12] as cited in

				Ramos et al. 2019 [8]
Non-severe hypoglycaemia	0	506	0	Evans et al. 2014 [13] as cited in Ramos et al. 2019 [8]
Cost in the absence of complications	2324			Alva et al. 2015 [5]

Note: values are applied irrespective of age and sex.

Instructions for Challenge Part 1: Assessing Model Performance in Estimating Quality-Adjusted Life Years (QALYs)

Step 1: Input the provided baseline characteristics (Table 1 for cohort-level models), risk factor trajectories (Table 3 for cohort-level models), utility/disutility values (Table 2), and complication costs (table 4) into your model.

*If your model only allows drift assumptions, and not specific values, over time, then calculate the average risk factor growth rate for each risk factor instead and record the assumption within the specific risk factor tab.

Step 2: Run a simulation of the 1,000 synthetic patients firstly over a **3-year** time horizon* with no discount rate (0%) and 100,000 internal loops*

*Note that we define internal loops (or Monte-Carlo trials) as the number of times the same patient is simulated through the risk equations to reduce first order uncertainty (also known as stochastic variability or Monte-Carlo error).

Step 3: Run the same simulation of the 1,000 synthetic patients now over a **4-year** time horizon with no discount rate (0%) and 100,000 internal loops.

Step 3: To estimate the total (undiscounted) QALYs over the mean trial follow-up duration (3.28 years). You will need to deduce the 4th year total estimate from the 3rd year total estimate, then multiple the difference by 0.28 and add this onto the 3rd year total estimate*. Note models with cycle lengths other than 1 year will need to alter this approach appropriately.

*For example, assume the estimate at the 4-year time horizon is 2.0 QALYS and at the 3-year time horizon it is 1.8 QALYs, the analyst would simply take the difference between the time horizons (2.0 QALYs - 1.8 QALYs = 0.2 QALYs), multiple this difference by 0.28 (0.22*0.28=0.056), then add this onto the 3rd year estimate (1.8+0.056= 1.856 QALYs)

Step 4: Please input results into *"Challenge Part 1 Results".* For cohort-level models, we ask groups to report results in the "*Total Estimates*" table. For patient-level models, we ask the groups to report results in the "*Patient-level Estimates*". Note the workbook is set up to calculate performance metrics. Please also include any deviations or assumptions to run your simulation in the text box.

Model inputs for Challenge Part 2: Estimating the Cost-effectiveness of Hypothetical Weight-loss Interventions

Patient baseline characteristics

To allow for consistent comparison to be made across all models we use the same baseline patient characteristics as in part 1 of the challenge. Please see "*Challenge Part 2 Baseline Pop*" tab.

- For groups using a cohort-level simulation model, please refer to Table 1 for baseline characteristics.
- For groups using patient-level simulation models, please use the patient-level dataset provided.

However, instead of simply having one group, we assume there are two treatment groups with the identical baseline characteristics used in part 1 of the challenge.

If your model requires other baseline patient characteristics, please ensure you have documented the values and sources in the "*Challenge Part 2 Additional Var*" tab in the Excel sheet. Note this should be consistent with the characteristics used in part 1. Please again note that these other patient baseline characteristics must be from publicly available sources.

Treatment effects and intervention costs

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 over a 2-year duration of treatment (Table 8).

Note that, we have already applied these treatment effects to the synthetic cohort in the Excel workbook for you (see Excel workbook).

Table 4. Hypothetical Weight-loss Intervention Costs

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 units), and 2.5-unit reduction in systolic blood pressure (mmHg)	2	7618	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 units), and 5-unit reduction in systolic blood pressure (mmHg)	3	11427	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 units), and 1-unit reduction in systolic blood pressure (mmHg)	1	3809	Lower efficacy and shorter duration. All else remains unchanged from base-case.

Source: Marso et al. (2016)[14]. Note: Treatment effects are approximately based on 1mg once-weekly Semaglutide. Abbreviations: HbA1c – Glycated Haemoglobin, BMI – Body Mass Index, DCCT units – Diabetes Control and Complications Trial units, mmgHg – millimetres of mercury, GLP-1RA – Glucagon-Like Peptide-1 Receptor Agonists.

Time path trajectories

We provide the completed time path trajectories for each synthetic patient in the Excel workbook. We use newly estimated risk factor time path equations from Gao et al. (2024). [15] The source study provides trajectories for the following 7 continuous risk factors: high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, systolic blood pressure (SBP), glycated haemoglobin (HbA1c), haemoglobin, heart rate, BMI. If you require other risk factors not provided, then please use the following linear assumptions relative to the previous value:

- Triglycerides: -0.35 % drift per year (i.e. $TG_t = 0.9965*TG_{t-1}$)
- Total cholesterol: -0.50% drift per year (i.e. $TC_t = 0.9950*TC_{t-1}$)
- FPG: +0.04% drift per year (i.e. $FPG_t = 1.0004*FPG_{t-1}$).

Where FPG_t , TG_t , and TC_t denote the value at year t, and FPG_{t-1}, TG_{t-1}, TC_{t-1} denote the value at year t–1. The drift is applied multiplicatively to the previous year's value. TG and TC drift assumptions based on Davis et al. (2001): https://pubmed.ncbi.nlm.nih.gov/11423497/. FPG drift is assumed to be the mean HbA1c drift in our control group.

If we have not provided you with a linear assumption for a risk factor within your model, then please make your own clinically plausible assumption and report this in the "*Challenge Part 2 Additional Var*" tab.

Gao et al. (2024): https://pubmed.ncbi.nlm.nih.gov/38922488/).

Complication costs

To allow for consistent comparison to be made across all models please use the same complication costs as in part 1 of the challenge (Tab: *Challenge Part 1 & 2 Costs*).

Please apply costs only to complication events described in the instructions as far as possible. To give an 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.

Utility values

A more extensive source of health utility values may be used to estimate the cost-effectiveness of the hypothetical interventions (Table 5). 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) in the "*Challenge Part 1 & 2 Costs*" tab. 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

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.[4] 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.[16] Within this systematic review, these relevant parameters were sourced from Currie et at. (2006)[17] 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.[16] Within this systematic review, these relevant parameters were sourced from Bagust and Beale.[18]
Retinopathy	Cataract	-0.016	-0.031	-0.001	Beaudet et al.[16] Within this systematic review, these relevant parameters were sourced from Lee et al[19]
	Moderate non-proliferative background diabetic retinopathy	-0.040	-0.066	-0.014	Beaudet et al.[16] Within this systematic review, these relevant parameters were sourced from Fenwick et al[20]
	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.[16] Within this systematic review, these relevant parameters were sourced from Clarke et al.[21].
Nephrology	Proteinuria	-0.048	-0.091	-0.005	Beaudet et al.[16]

					Within this systematic review, these relevant parameters were sourced from Bagust and Beale.[18]
	Renal transplant	-0.023	-0.127	+0.081	Beaudet et al. [16] Within this systematic review, these relevant parameters were sourced from Kiberd et al[22]. 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.[16]
	Peritoneal dialysis	-0.204	-0.342	-0.066	Within this systematic review, these relevant parameters were sourced from Wasserfallen et al[23]
	Renal failure	-0.330	-0.559	-0.101	Lung et al.[24] 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.[16]
	Neuropathy	-0.084	-0.111	-0.057	Within this systematic review, these relevant parameters were sourced from Bagust and Beale.[18]
	Active ulcer	-0.210	-0.330	-0.090	Lung et al.[24] 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.[4] 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	

Note: values are applied irrespective of age and sex.

Instructions for Challenge Part 2: Estimating the Cost-effectiveness of Hypothetical Weight-loss Interventions

Step 1: We use the **same** baseline characteristics and complication costs (table 4) in part 1 of the challenge. Please navigate to *"Challenge Part 2 Baseline Pop"* in the Excel workbook. This patient cohort is the identical baseline characteristics used in part 1 duplicated into 2 treatment groups.

Step 2: Next, use the risk factor progression tabs in the workbook (Smoking, LDL, HDL, PVD, AF, Albuminuria, eGFR, Haemoglobin, white blood cell count, heart rate, BMI, HbA1c, systolic blood pressure) to input the risk factor data*. Note, continuous variables have been estimated using Gao et al (2024) equations. Binary variables are assumed to stay constant over the time horizon (Last Value Carried Forward). Simulated eGFR predictions have also been estimated using Gao et al (2024) equations.

If you do not have a particular risk factor, please report this in the *"Challenge Part 2 Additional Var"* tab in the Excel spreadsheet. If you require other risk factors not provided, then please use the following linear assumptions:

- Triglycerides: -0.35 % drift per year (i.e. $TG_t = 0.9965*TG_{t-1}$)
- Total cholesterol: -0.50% drift per year (i.e. $TC_t = 0.9950*TC_{t-1}$)
- FPG: +0.04% drift per year (i.e. $FPG_t = 1.0004*FPG_{t-1}$).

Where FPG_t , TG_t , and TC_t denote the value at year t, and FPG_{t-1}, TG_{t-1}, TC_{t-1} denote the value at year t–1. The drift is applied multiplicatively to the previous year's value. TG and TC drift assumptions based on Davis et al. (2001): https://pubmed.ncbi.nlm.nih.gov/11423497/. FPG drift is assumed to be the mean HbA1c drift in our control group.

If we have not provided you with a linear assumption for a risk factor within your model, then please make your own clinically plausible assumption and report this in the returned Excel spreadsheet.

*Note, if you are using a **cohort-level model** you will need to take the mean risk factor trajectory for treatment and control groups, respectively.

Step 3: Please input the disutility/utility and cost values into your model. We have tried to provide a range of complications and risk factors, however, if a required variable is missing, then report please report the variable, chosen value, and source in the respective cost or disutility tab in the Excel workbook.

Step 4: Set up your model to run 2,000 synthetic patients (1,000 whom receive the treatment reported in Table 4, and 1,000 whom do not). We assume that the treatment effects are averaged over the treatment window. Note the treatment effects have

already been applied to HbA1c, BMI, and SBP (& indirectly to eGFR) and can be found in the respective Excel tabs.

Step 5: Run the model with 2,000 synthetic patients over a **50-year time horizon** with a **3.5% discount rate** and **10,000 internal loops**. Note that we define internal loops (or Monte-Carlo trials) as the number of times the same patient is simulated through the risk equations to reduce first order uncertainty (also known as stochastic variability or Monte-Carlo error). Also note, discounting starts from simulation Year 1.

Step 6: Report outcomes (Total Life Years, QALYs, Costs, number of MI, Stroke, Heart Failure, Renal Failure, CV Death, and Death) in the "*Challenge Part 2 Results*" tab.

Submission:

Prior to the meeting, please submit the Excel spreadsheet ("Mt Hood T2D CHALLENGE – CHICAGO_GROUP") to Mount Hood at: mthood2016@gmail.com **by 15 June 2025.** Please replace GROUP with your modelling group name before submission.

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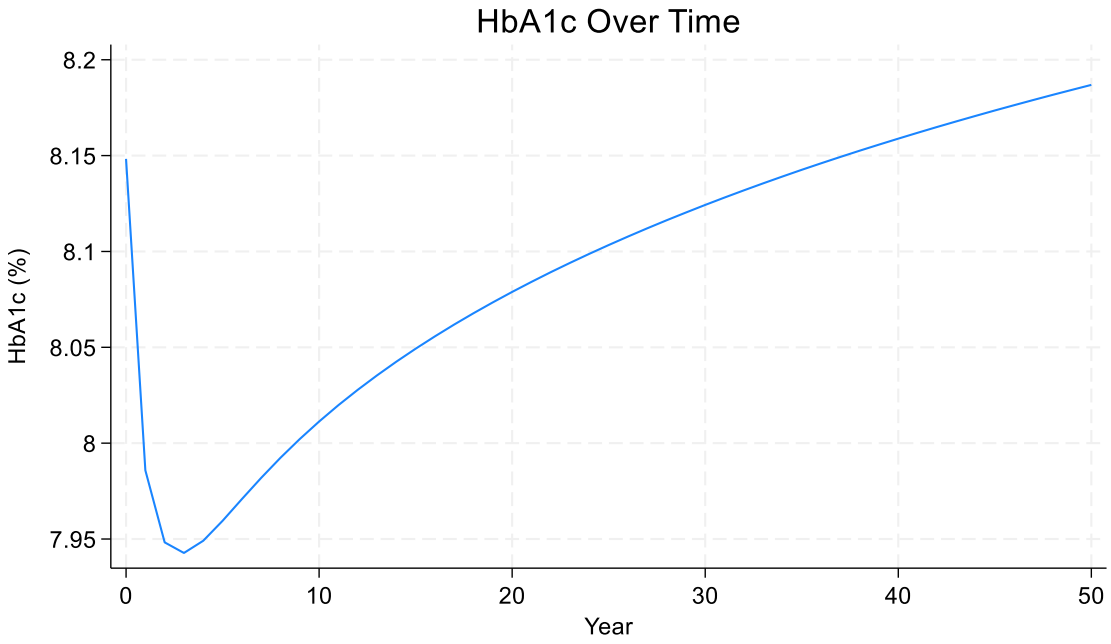
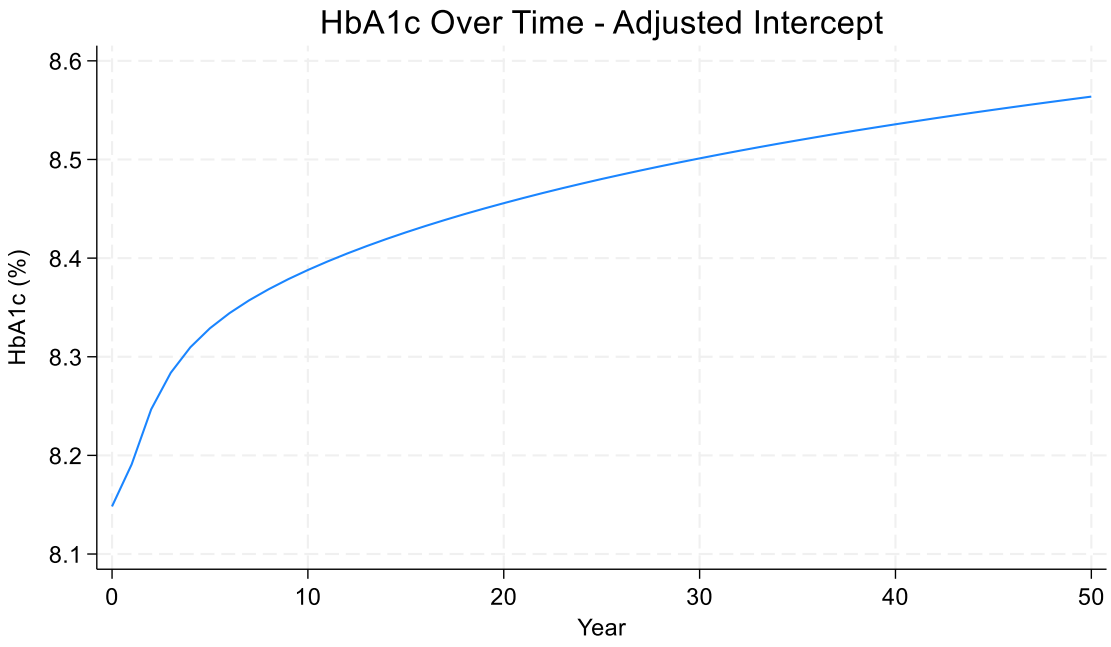
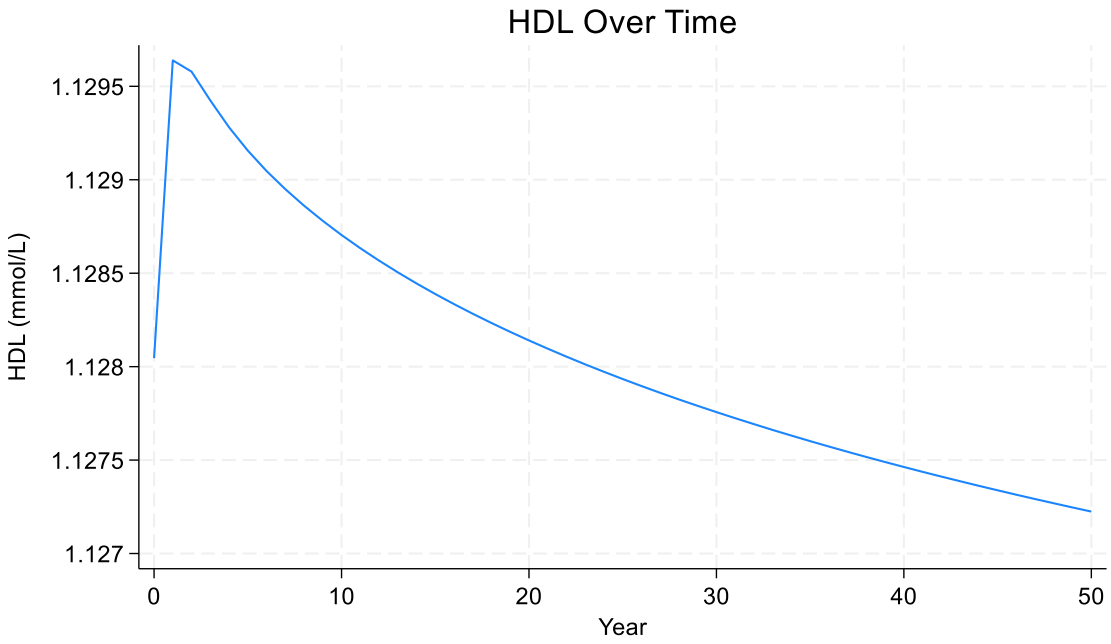
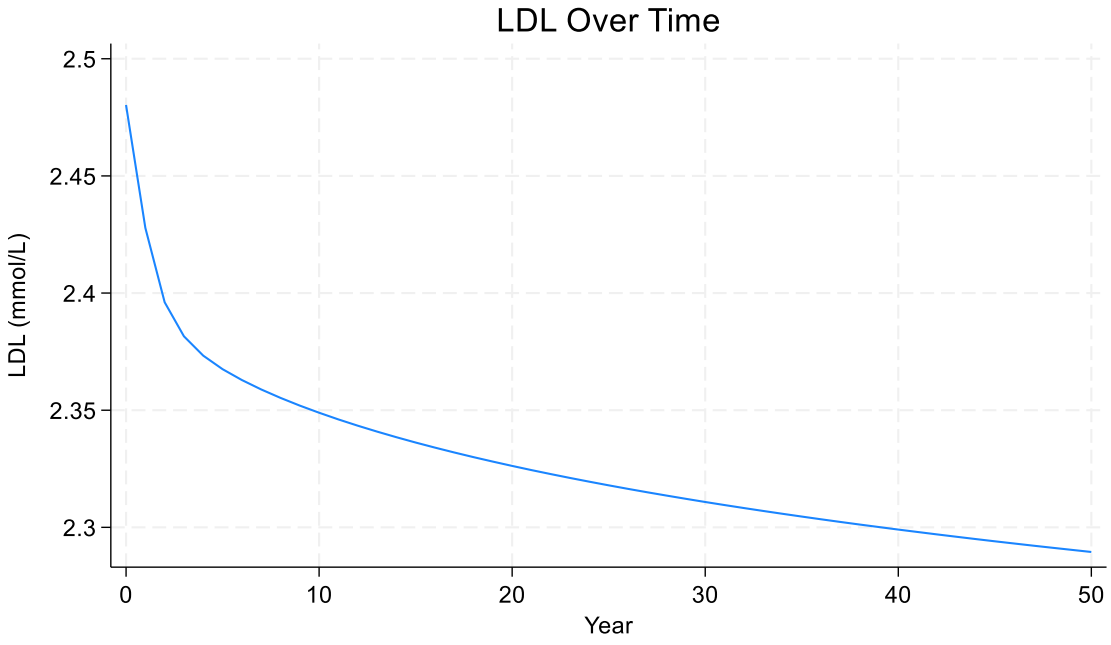
Appendix

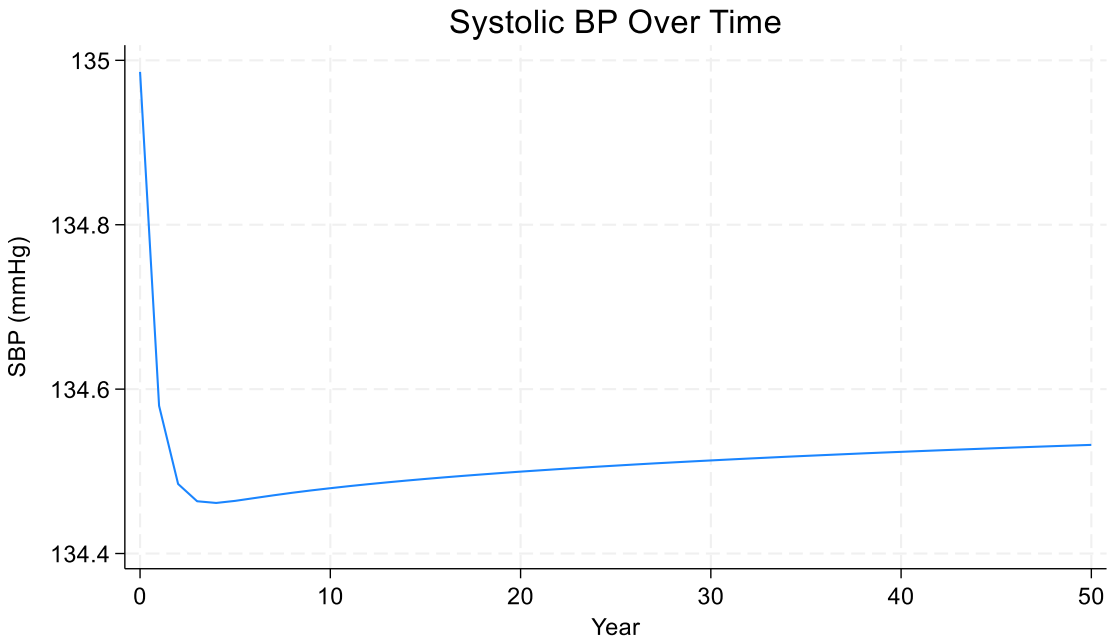
Continuous Time Paths: Some baseline values fall outside the sample used to estimate the original autoregressive equations, leading to sharp increases or decreases in predicted values for certain risk factors in early simulation years. Intercepts can be calibrated, as demonstrated for HbA1c, to better reflect disease progression without treatment. However, we opted to preserve the original equation predictions and not calibrate. x

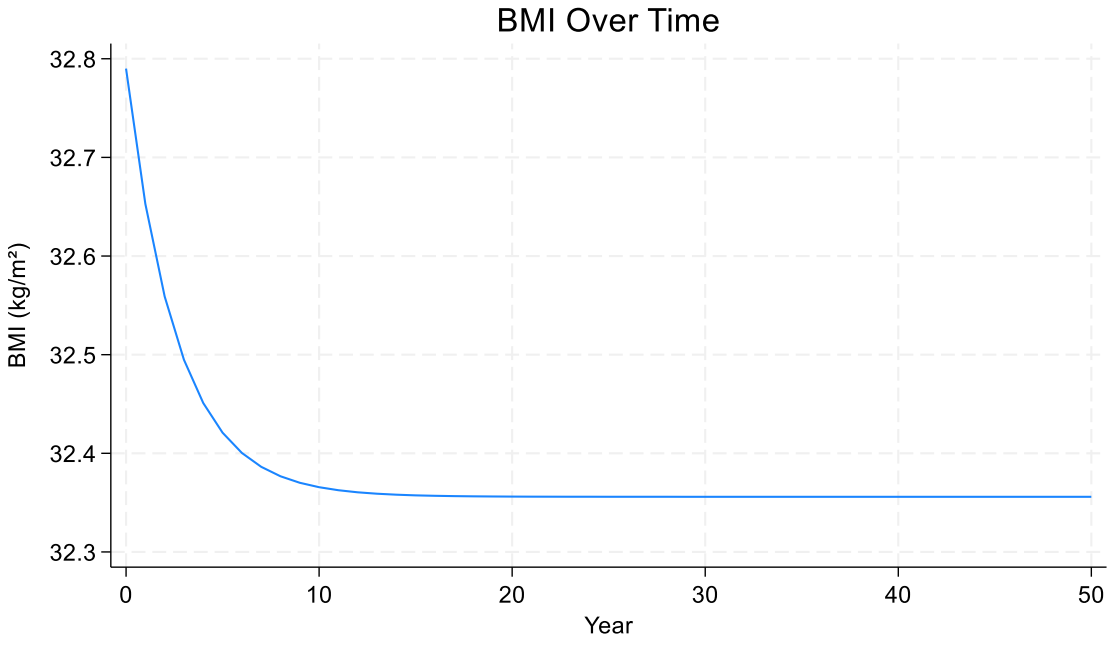


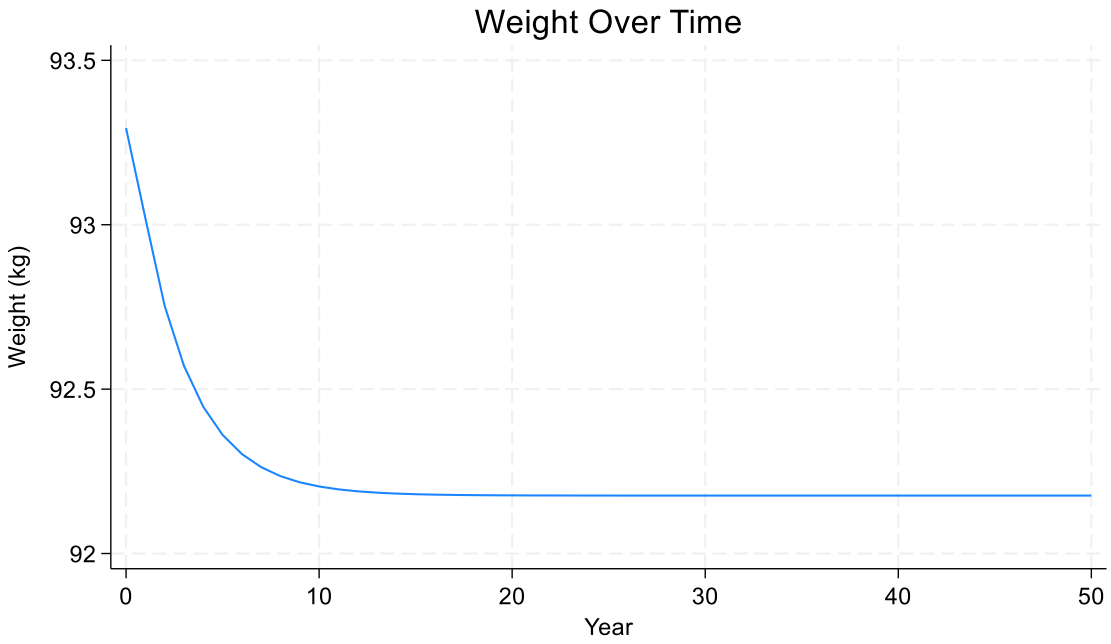


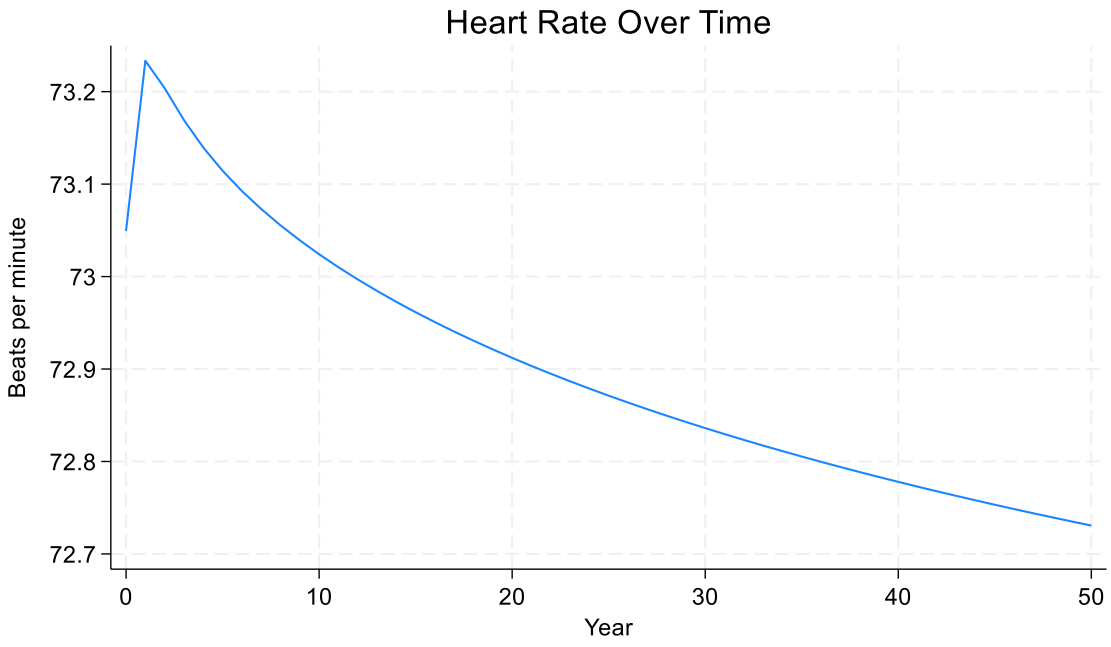

HDL Over Time
HDL (mmol/L)
1.1295
1.129
1.1285
1.128
1.1275
1.127
0
10
20
30
40
50
Year

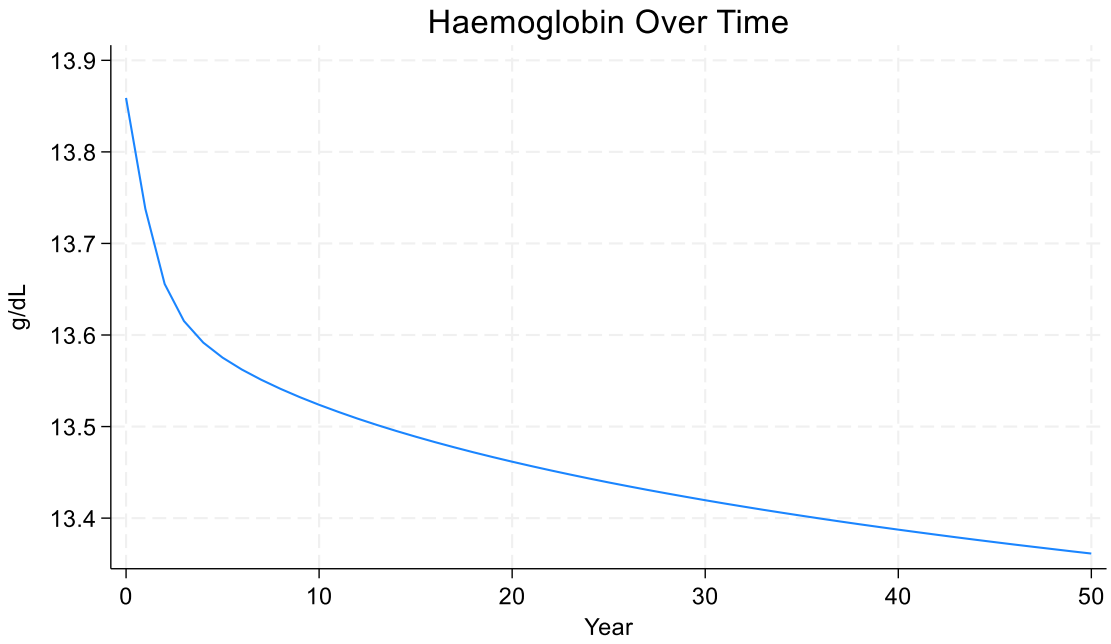

LDL Over Time
LDL (mmol/L)
2.5
2.45
2.4
2.35
2.3
0
10
20
30
40
50
Year

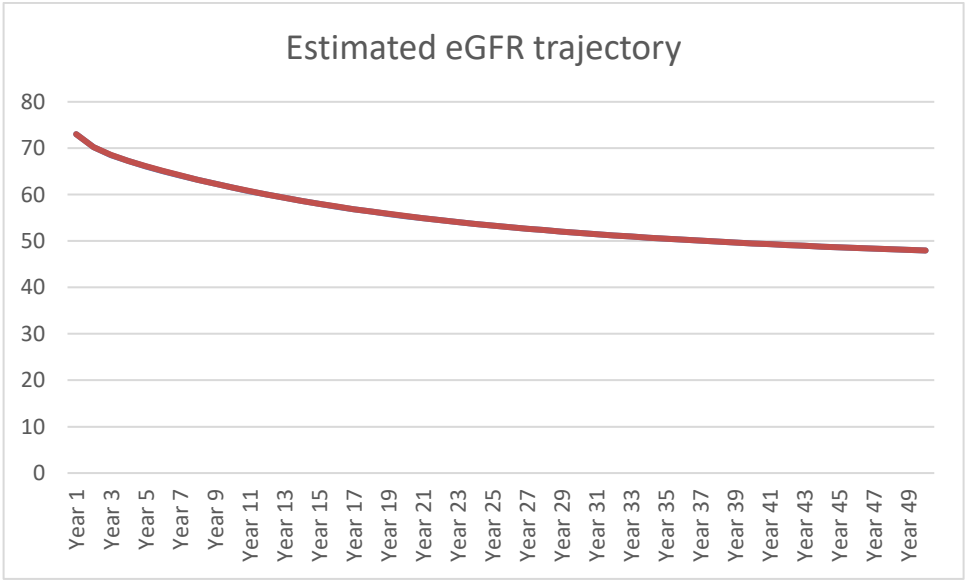

Systolic BP Over Time
SBP (mmHg)
135
134.8
134.6
134.4
0
10
20
30
40
50
Year


BMI Over Time
BMI (kg/m²)
32.8
32.7
32.6
32.5
32.4
32.3
0
10
20
30
40
50
Year


Weight Over Time
93.5
93
92.5
92
Weight (kg)
0
10
20
30
40
50
Year


Heart Rate Over Time
73.2
73.1
73
72.9
72.8
72.7
Beats per minute
0
10
20
30
40
50
Year


Haemoglobin Over Time
13.9
13.8
13.7
13.6
13.5
13.4
g/dL
0
10
20
30
40
50
Year


Estimated eGFR trajectory
80
70
60
50
40
30
20
10
0
Year 1
Year 3
Year 5
Year 7
Year 9
Year 11
Year 13
Year 15
Year 17
Year 19
Year 21
Year 23
Year 25
Year 27
Year 29
Year 31
Year 33
Year 35
Year 37
Year 39
Year 41
Year 43
Year 45
Year 47
Year 49