Supplementary materials B

Title

The Chronic Kidney Disease Care Model: quantifying management strategies for improving patient outcomes in the United States.

Authors

Andrew H Briggs, DPhil,[1]

0000-0002-0777-1997

Ciaran N Kohli-Lynch, PhD,[2]

0000-0001-5516-1862

Adrian R Levy, PhD,[3,4]

0000-0002-8966-0966

Ziyi Lin, MSc,[1]

0000-0002-3656-3601

Satabdi Chatterjee, PhD,[5]

Bonnie MK Donato, PhD, [5]

0000-0001-5099-2456.

Csaba P Kovesdy, MD.[6]

0000-0002-8204-911X

1. Department of Health Services Research & Policy, London School of Hygiene & Tropical Medicine, London, UK.
2. Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, US.
3. Department of Community Health and Epidemiology, Dalhousie University, Halifax, NS, Canada.
4. Pelican Research Inc, Halifax, NS, Canada.
5. Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, US.
6. Division of Nephrology, University of Tennessee Health Science Center, Memphis TN, US.

Corresponding Author information

Andrew H Briggs, DPhil

Professor of Health Economics

Department of Health Services Research & Policy

London School of Hygiene & Tropical Medicine

London, United Kingdom.

Email:andrew.briggs@lshtm.ac.uk

Phone: +44 (0)207 927 2348

Statistical Methods for Smoothing the Event Probabilities and Costs

1 Overview

This appendix details the statistical methods used to generate continuous estimates for the incidence of heart failure (HF), cardiovascular disease (CVD), and end-stage renal disease (ESRD), and the annual costs for patients with chronic kidney disease (CKD), based on a patient's estimated glomerular filtration rate (eGFR), urine albumin-to-creatinine ratio (UACR), and diabetes status.

The approach treated published data reported by discrete stages from observational studies as a series of sub-studies and used meta-regression to create a predictive function.

2 Data Sources

Data on 5-year cumulative incidence with 95% confidence intervals were taken from the Chronic Renal Insufficiency Cohort (CRIC) study. The data were structured in a cross-tabulated format by eGFR stage (G1/G2, G3a, G3b, G4/G5) and albuminuria stage (A1, A2, A3), separately for patients with and without diabetes (24 data points per event).

Mean and standard deviation of annual costs were obtained from Optum Claims Data, stratified by eGFR stage, diabetes status, and age group (<65, ≥65), for both the first year and subsequent years.

3 Meta-Regression Model Specification

A fixed-effect meta-regression was performed for each clinical event (HF, CVD, and ESRD) using the rma function from the metafor package in R. For each of the 24 subgroups per event, the reported cumulative incidence (p) was converted to the log-odds scale. The annual costs were converted to the log scale to avoid negative values. For each eGFR/albuminuria subgroup, the mean eGFR (in mL/min/1.73m^2) and mean UACR (in mg/g) reported in the CRIC study were used as continuous regressors in the meta-regression models. To model the non-linear relationships, biomarker variables were transformed prior to analysis. Due to its highly right-skewed distribution, UACR was natural log-transformed (lnUACR). We assumed a monotonic relationship between decreasing eGFR and increasing risk/cost. To identify the best functional form, we separately tested the original eGFR, log-eGFR, square root eGFR, and inverse eGFR as predictors. Model fit was compared using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). The inverse of eGFR (inveGFR) generally provided the lowest AIC and BIC and was therefore selected for use in all final models.

The analysis began with a full model that included potential predictors and all two-way and three-way interactions. For the probability models, potential predictors are lnUACR, inveGFR, and baseline diabetes, while for the cost model, they are inveGFR, age group (<65, ≥65), baseline diabetes, and first year or subsequent year. A stepwise backward elimination procedure was then employed, using AIC and BIC to select the best model.

4 Model Coefficients and Visualisations

The tables below present the coefficients, standard errors, and significance levels for the final meta-regression models. The figures compare the model predicted values to the reported values.

Table 1: Meta-Regression Coefficients for 5-Year Log-odds of Cardiovascular Disease

Term	Estimate	Std. Error	z-value	p-value
Intercept	-6.442	0.687	-9.372	< .001
inveGFR	113.030	24.476	4.618	< .001
Diabetes (Yes)	0.762	0.097	7.880	< .001
lnUACR	0.789	0.145	5.454	< .001
inveGFR × lnUACR	-16.530	5.038	-3.281	0.001

Table 2: Meta-Regression Coefficients for 5-Year Log-odds of Heart Failure

Term	Estimate	Std. Error	z-value	p-value
Intercept	-8.131	1.014	-8.020	< .001
inveGFR	126.364	31.132	4.059	< .001
Diabetes (Yes)	1.536	0.608	2.528	0.011
lnUACR	1.012	0.209	4.850	< .001
inveGFR × lnUACR	-19.378	6.327	-3.063	0.002
Diabetes (Yes) × lnUACR	-0.184	0.125	-1.469	0.142

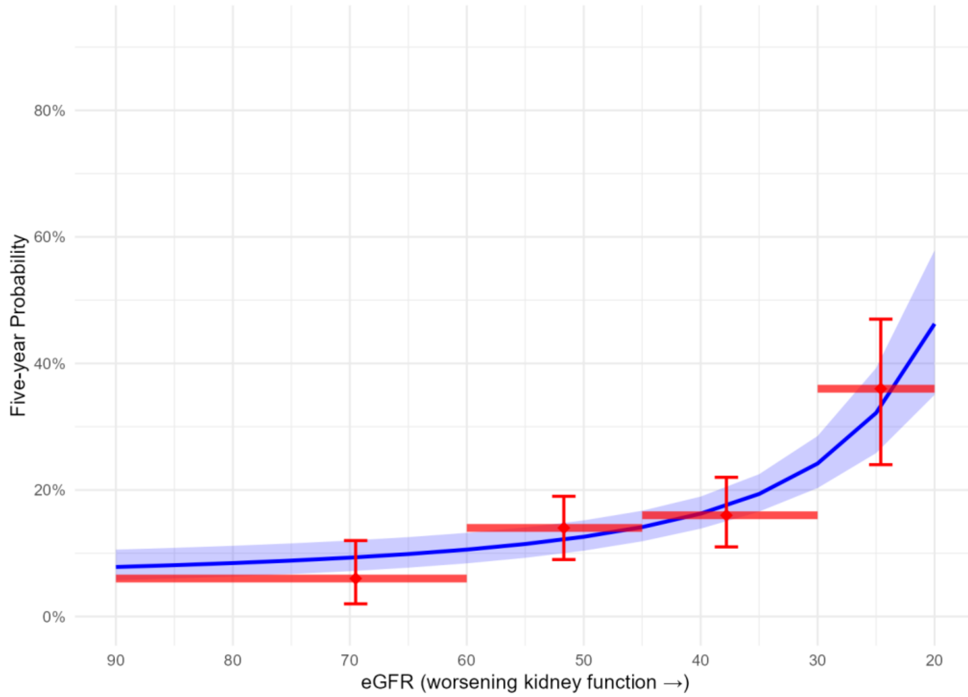
Table 3: Meta-Regression Coefficients for 5-Year Log-odds of End-Stage Renal Disease

Term	Estimate	Std. Error	z-value	p-value
Intercept	-10.257	0.394	-26.061	< .001
inveGFR	96.193	6.113	15.737	< .001
Diabetes (Yes)	0.389	0.106	3.660	< .001
lnUACR	1.228	0.064	19.227	< .001

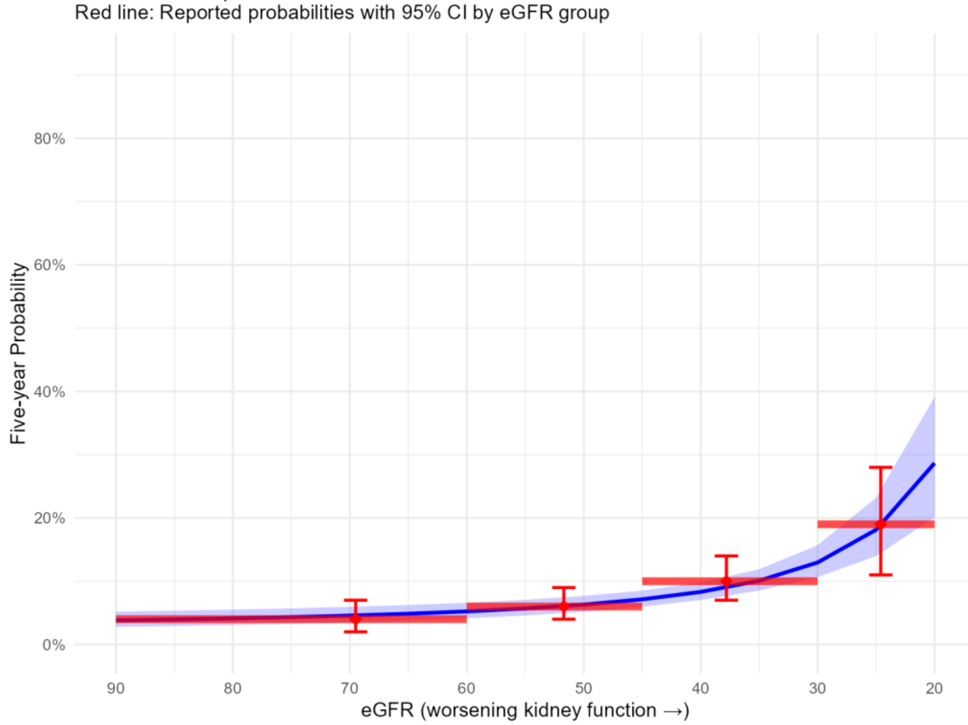
Table 4: Meta-Regression Coefficients for Annual CKD-related Costs (Log Scale)

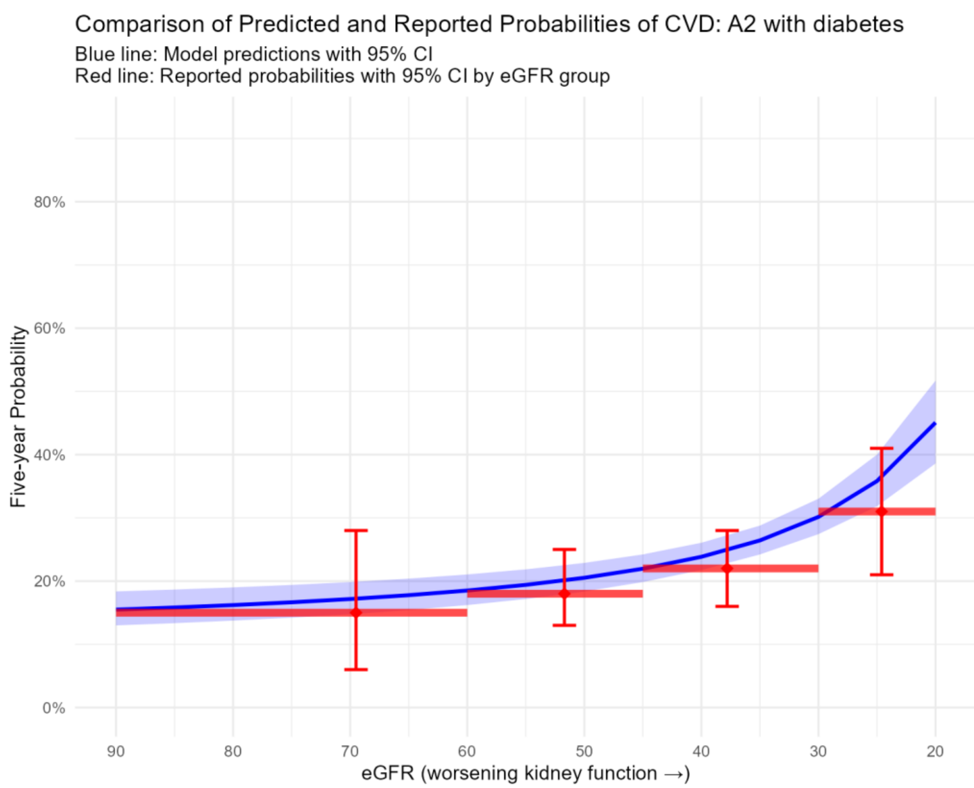
Term	Estimate	Std. Error	z-value	p-value
Intercept	9.050	0.058	155.189	< .001
inveGFR	3.678	2.554	1.440	0.150
Age < 65	-0.024	0.116	-0.204	0.838
Baseline T2D	0.021	0.016	1.336	0.181
Year 1	0.320	0.073	4.367	< .001
inveGFR × Age < 65	1.385	5.145	0.269	0.788
inveGFR × Year 1	0.416	3.204	0.130	0.897
Age < 65 × Baseline T2D	0.074	0.033	2.264	0.024
Age < 65 × Year 1	-0.281	0.149	-1.892	0.058
inveGFR × Age < 65 × Year 1	14.275	6.645	2.148	0.032

Comparison of Predicted and Reported Probabilities of CVD: A1 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group

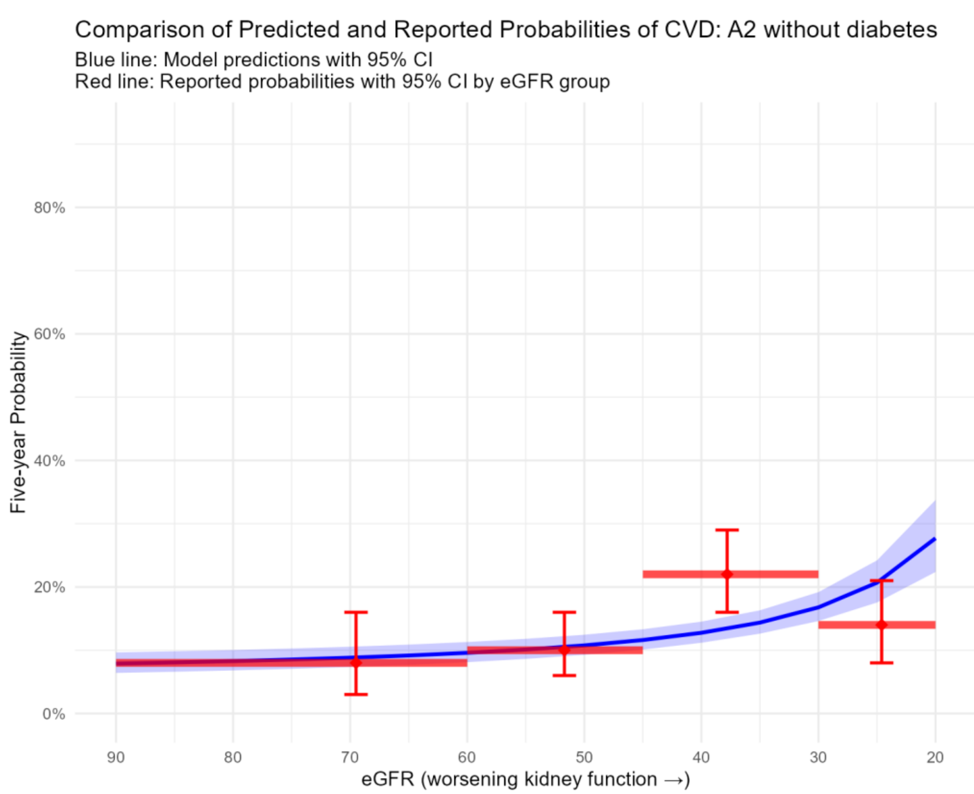


Comparison of Predicted and Reported Probabilities of CVD: A1 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group

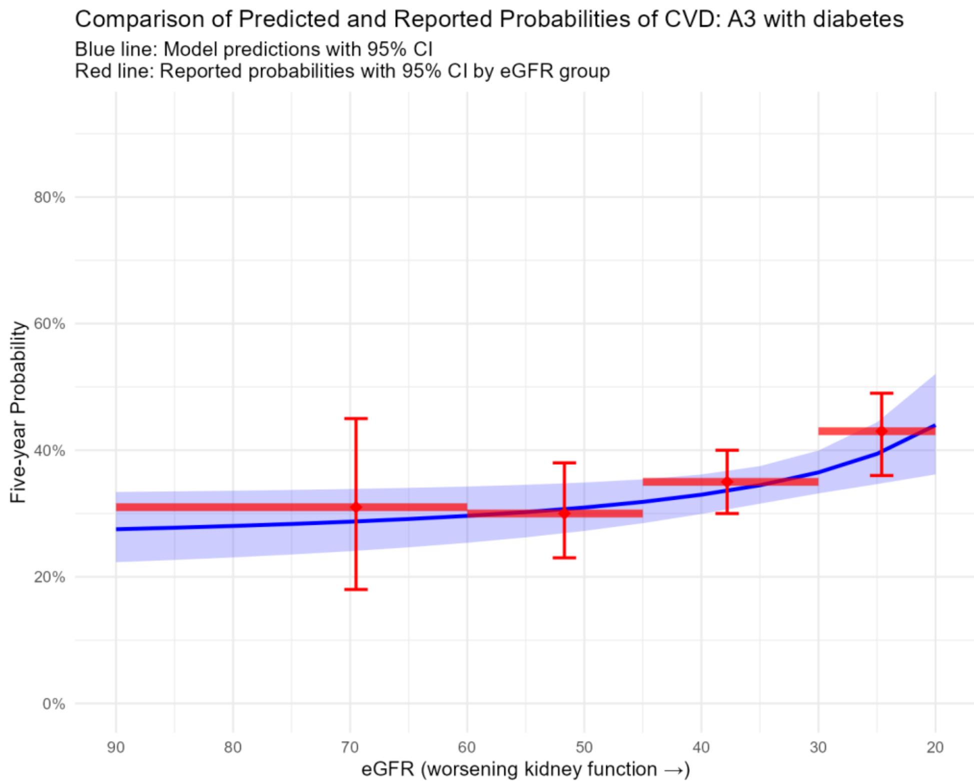


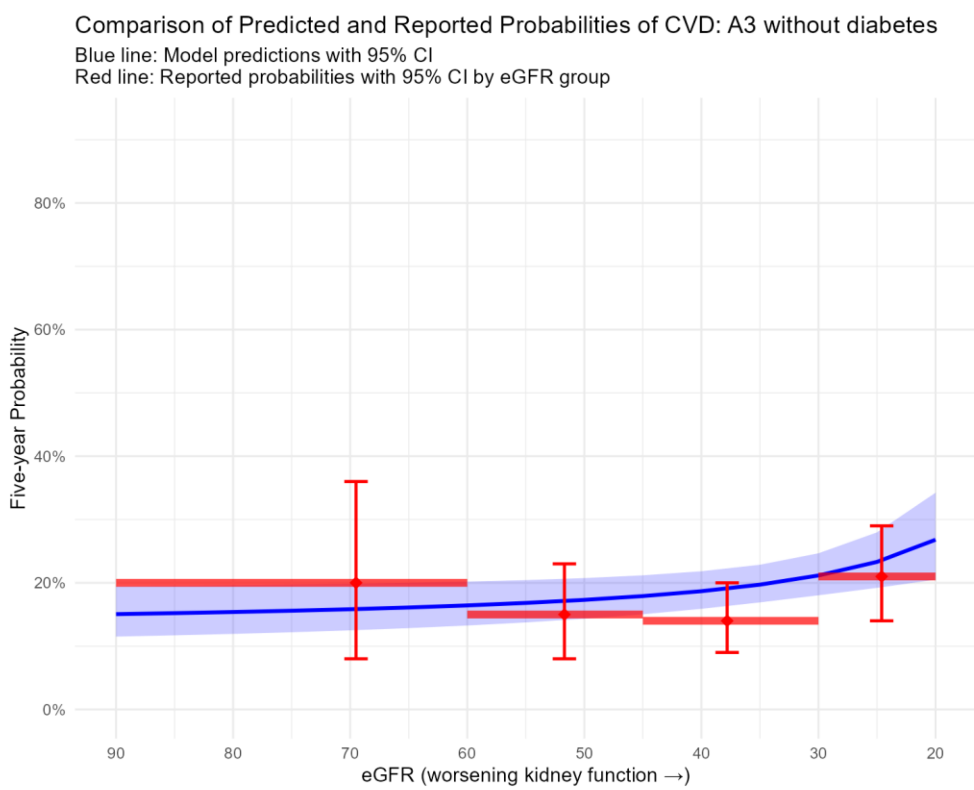


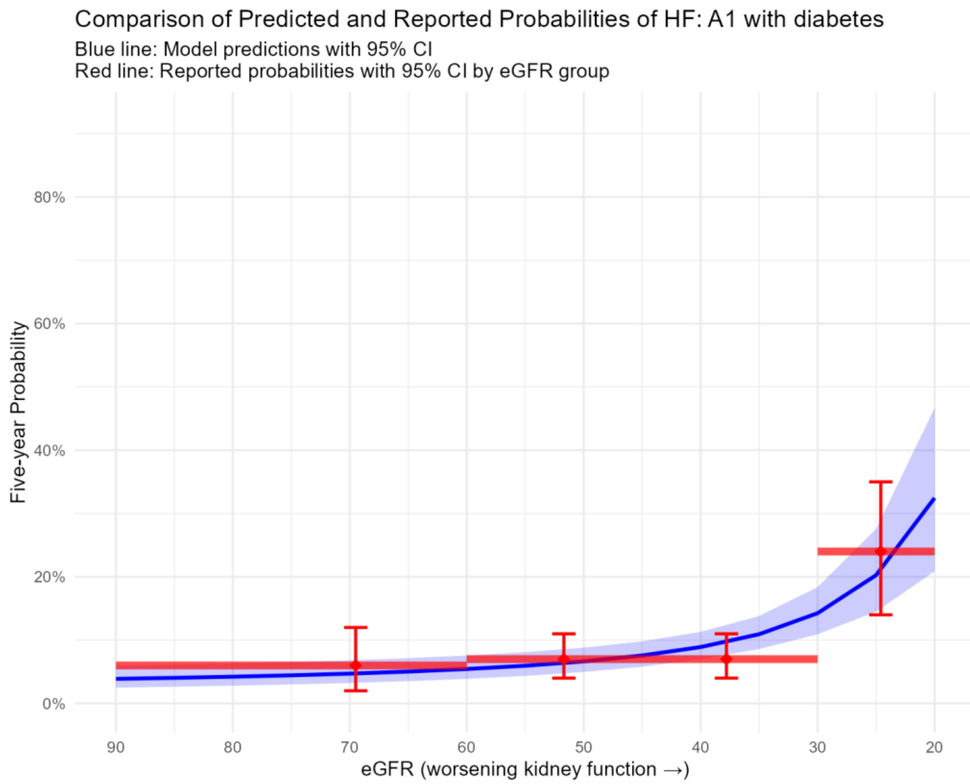
Comparison of Predicted and Reported Probabilities of CVD: A2 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

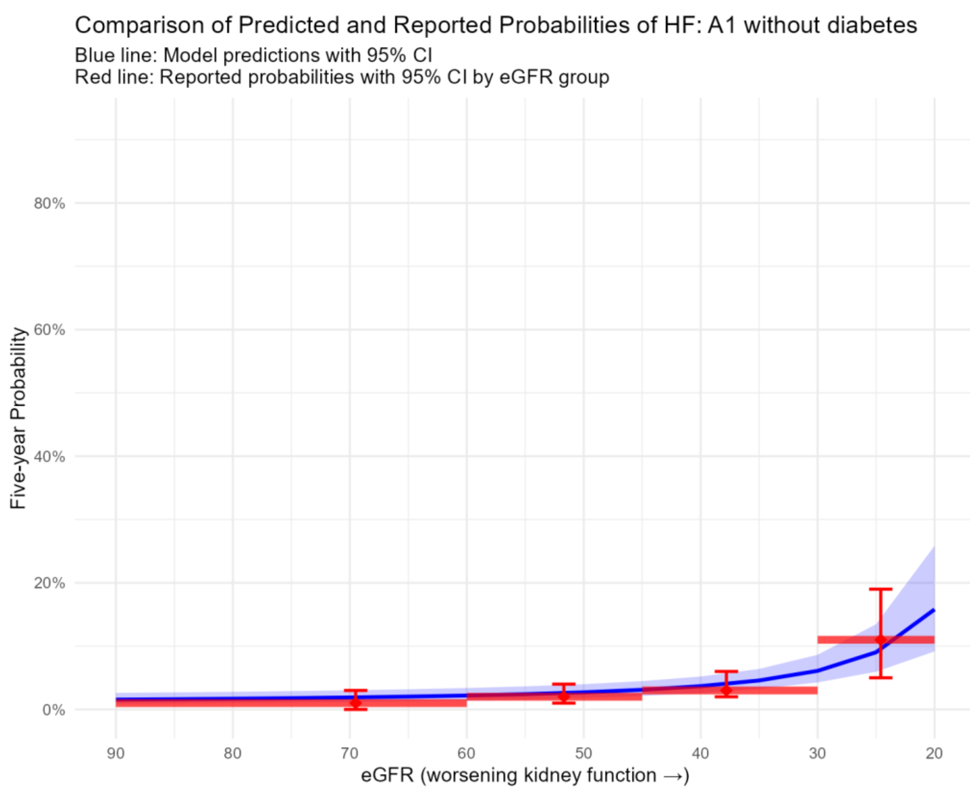


Comparison of Predicted and Reported Probabilities of CVD: A2 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

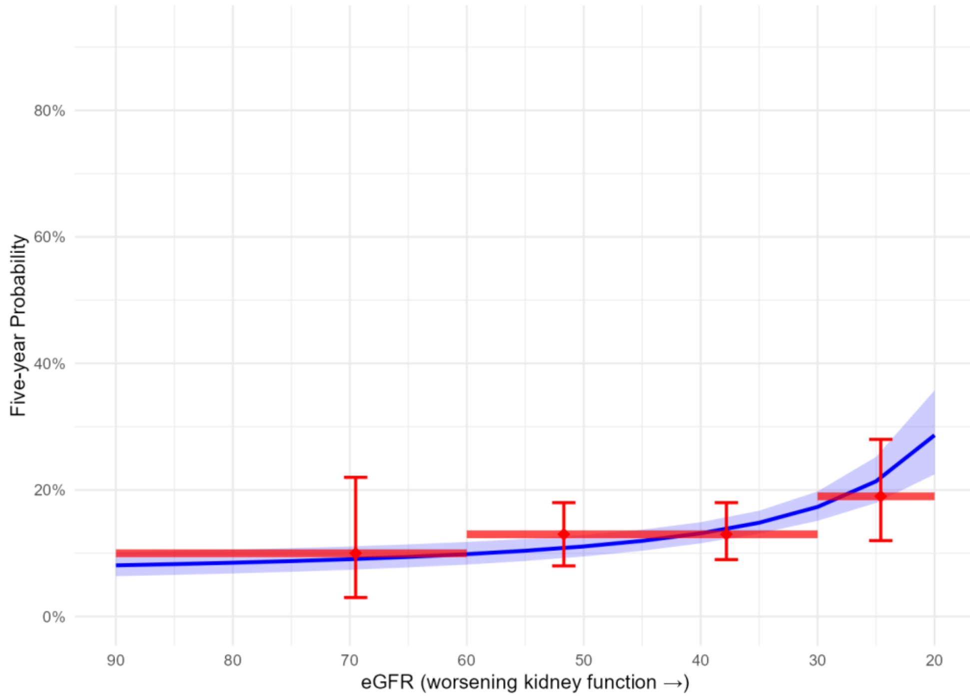

Comparison of Predicted and Reported Probabilities of CVD: A3 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)


Comparison of Predicted and Reported Probabilities of CVD: A3 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

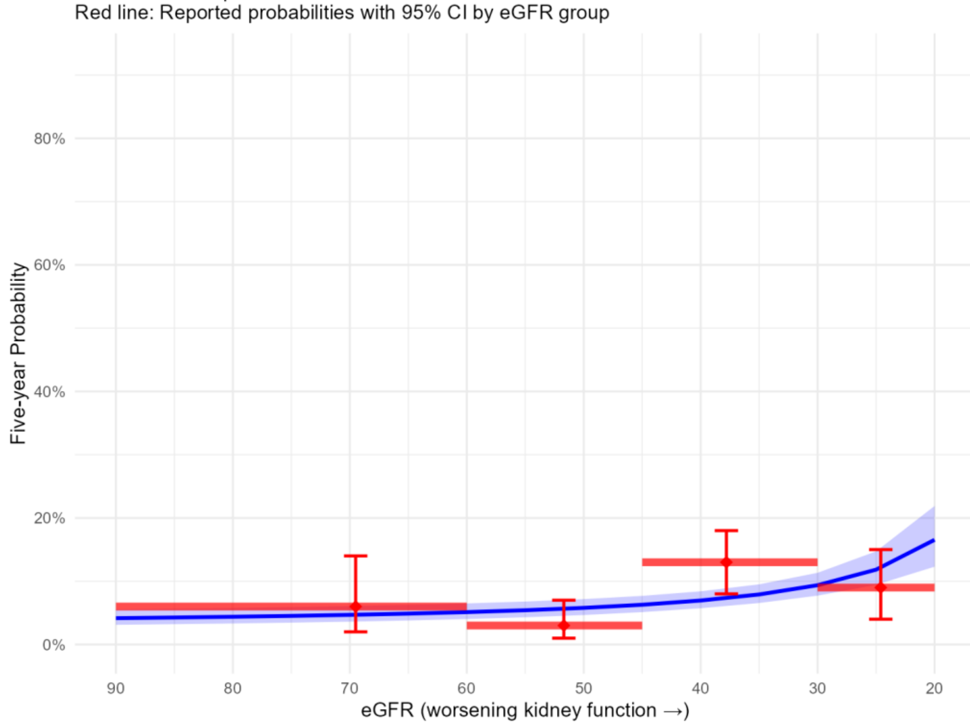

Comparison of Predicted and Reported Probabilities of HF: A1 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

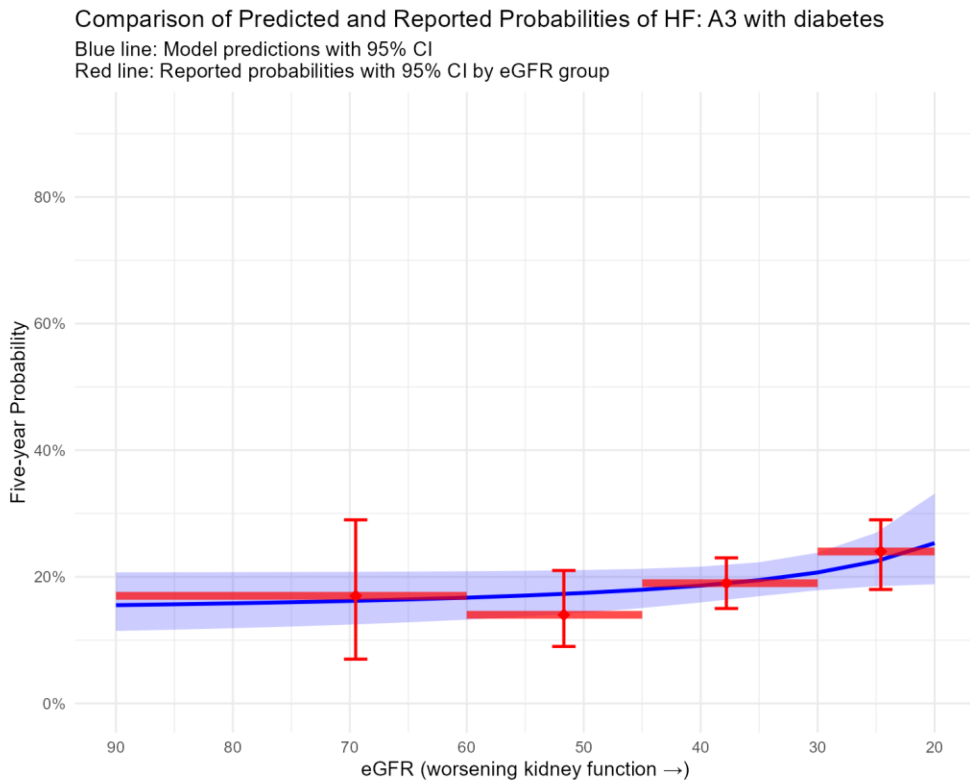

Comparison of Predicted and Reported Probabilities of HF: A1 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

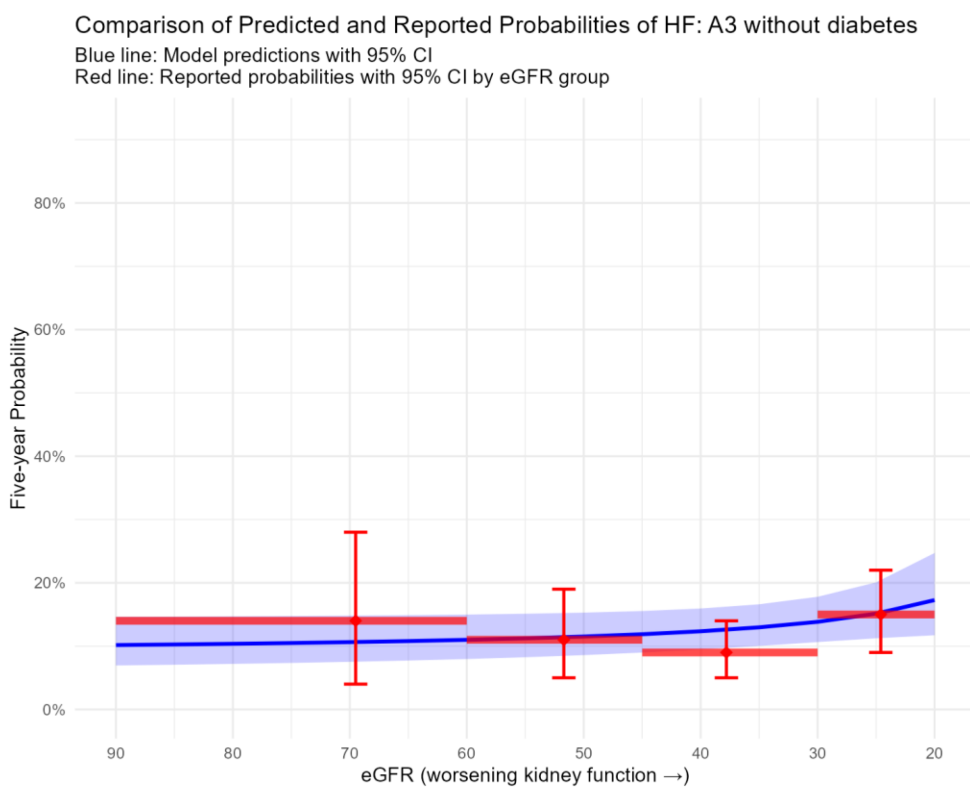
Comparison of Predicted and Reported Probabilities of HF: A2 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group

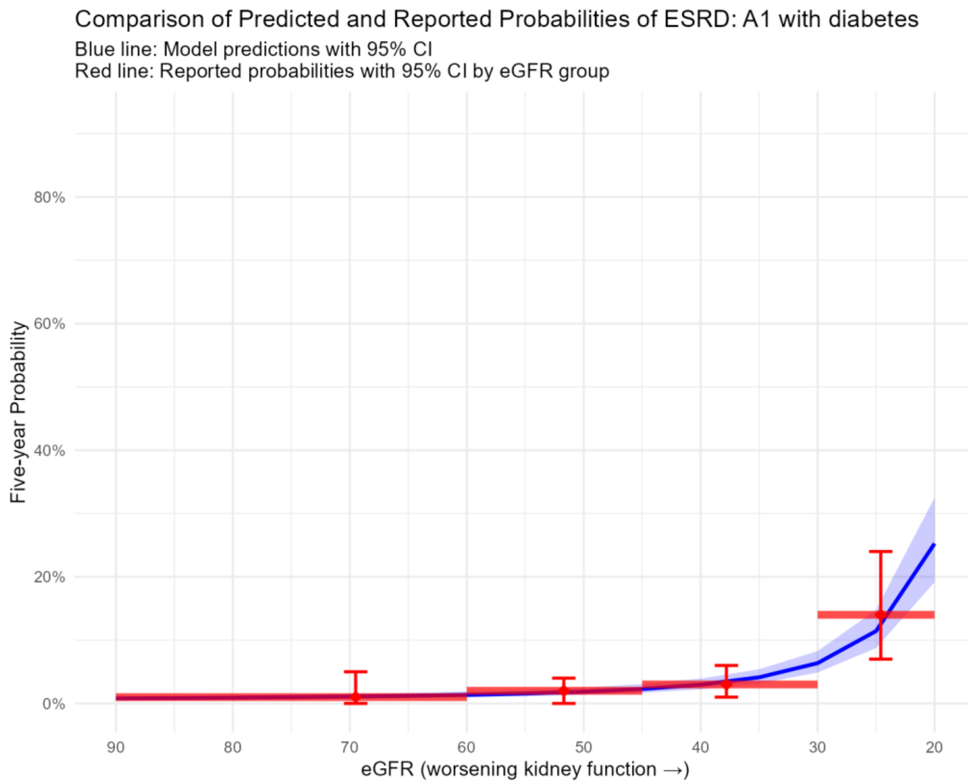


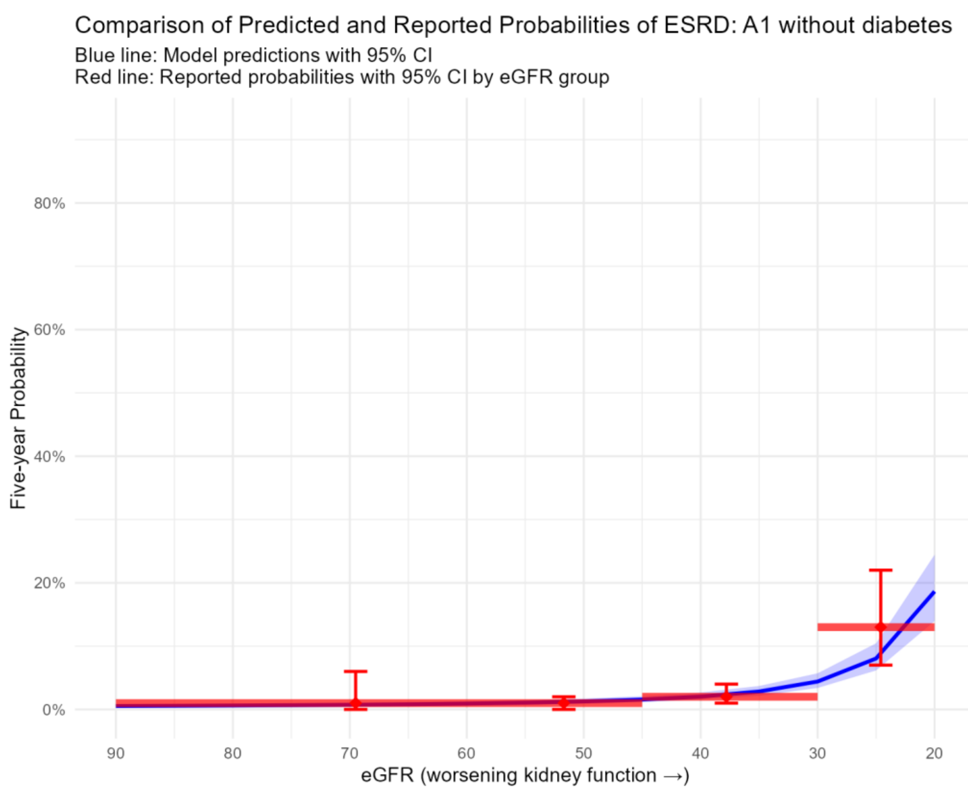
Comparison of Predicted and Reported Probabilities of HF: A2 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group

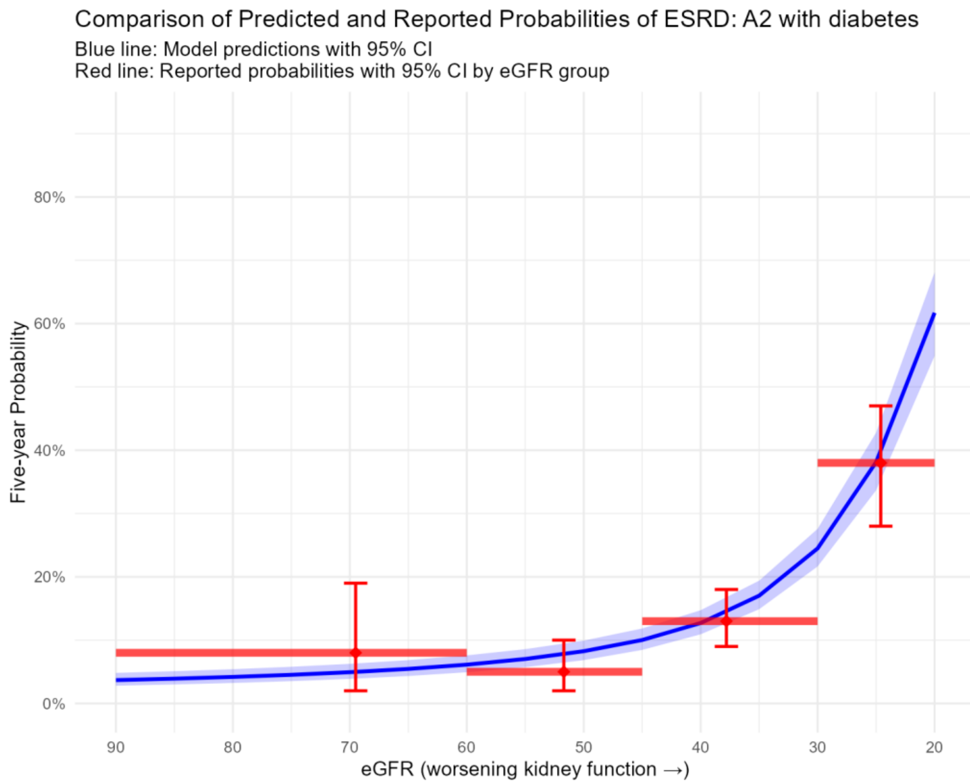


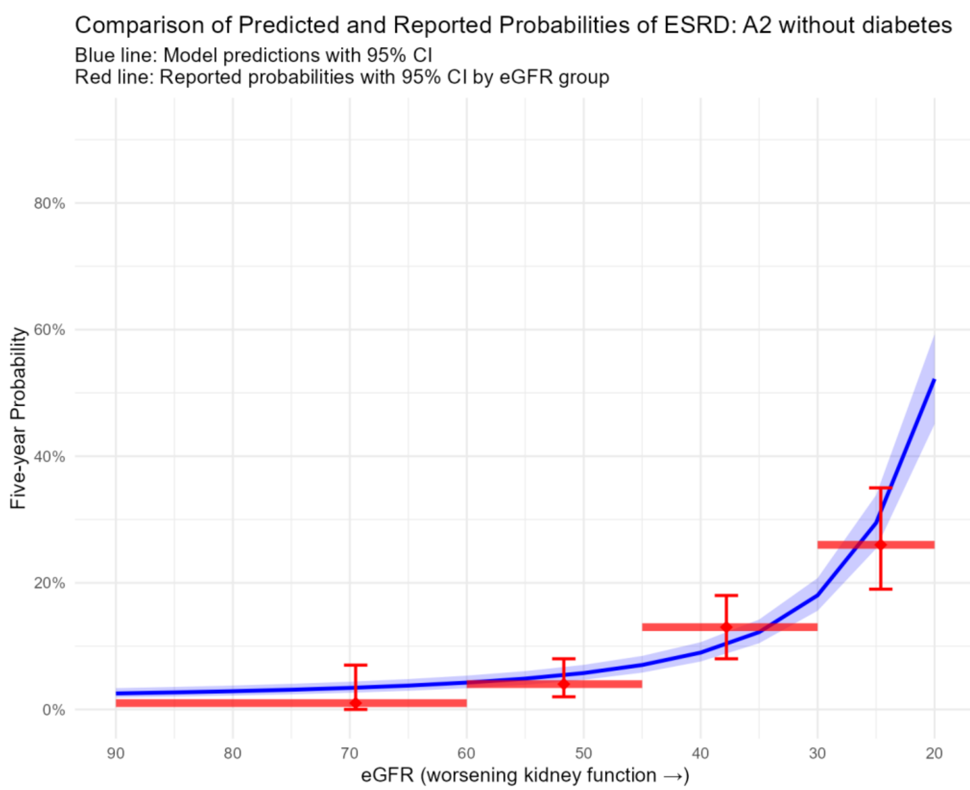

Comparison of Predicted and Reported Probabilities of HF: A3 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
0%
20%
40%
60%
80%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)


Comparison of Predicted and Reported Probabilities of HF: A3 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
0%
20%
40%
60%
80%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

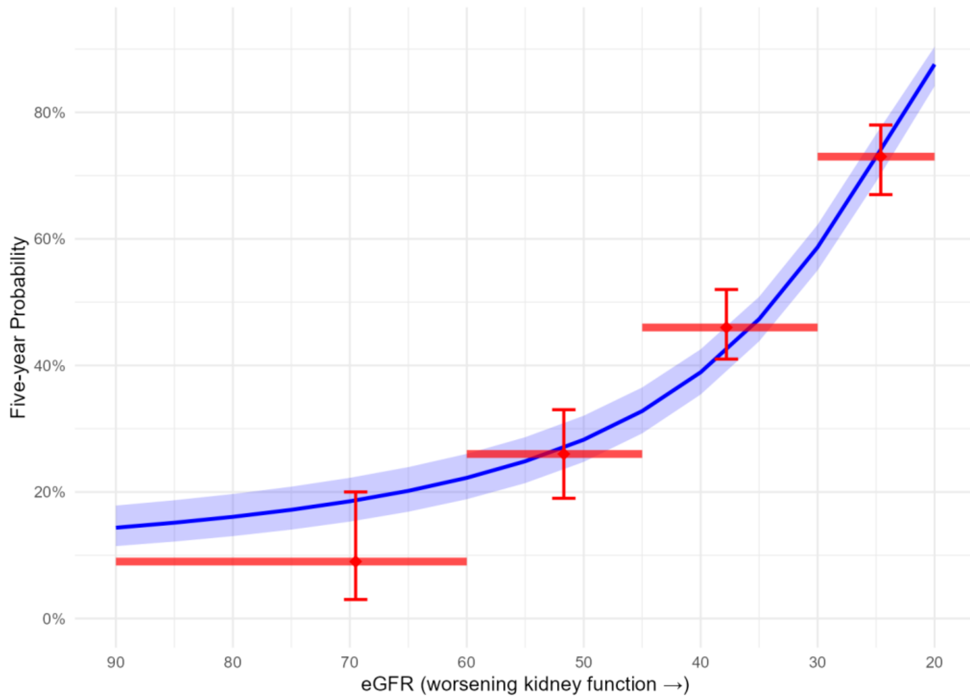

Comparison of Predicted and Reported Probabilities of ESRD: A1 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)


Comparison of Predicted and Reported Probabilities of ESRD: A1 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

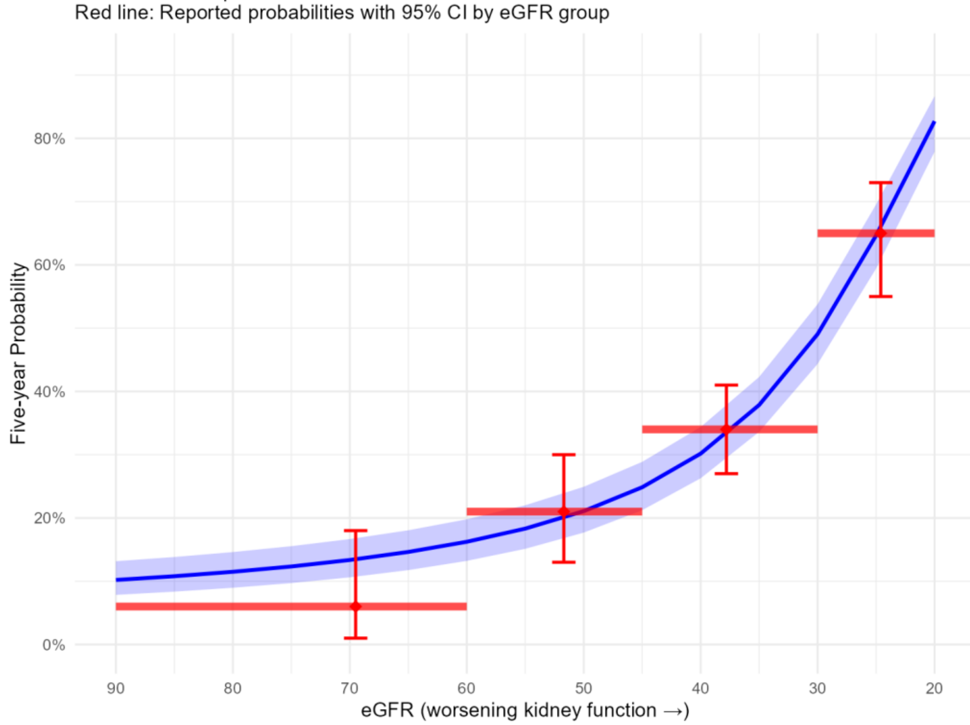

Comparison of Predicted and Reported Probabilities of ESRD: A2 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)


Comparison of Predicted and Reported Probabilities of ESRD: A2 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group
Five-year Probability
80%
60%
40%
20%
0%
90
80
70
60
50
40
30
20
eGFR (worsening kidney function →)

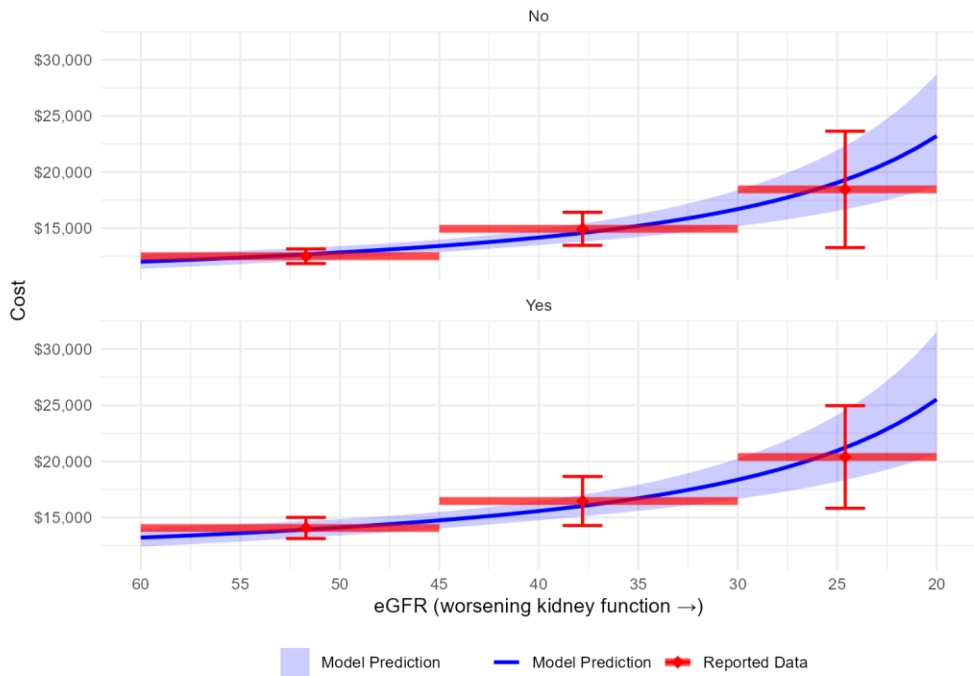
Comparison of Predicted and Reported Probabilities of ESRD: A3 with diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group



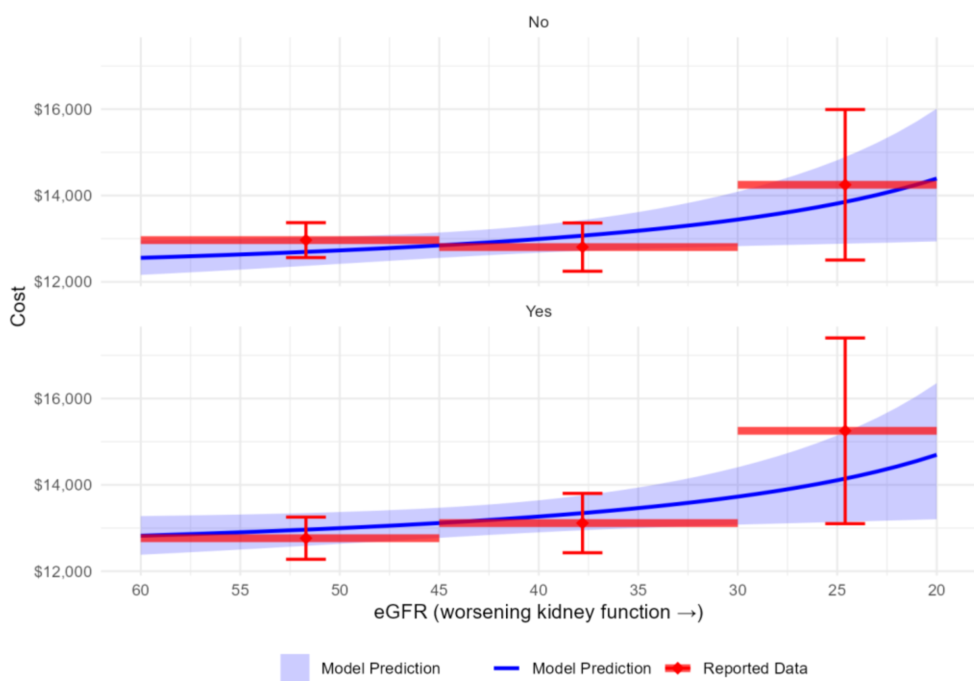
Comparison of Predicted and Reported Probabilities of ESRD: A3 without diabetes
Blue line: Model predictions with 95% CI
Red line: Reported probabilities with 95% CI by eGFR group



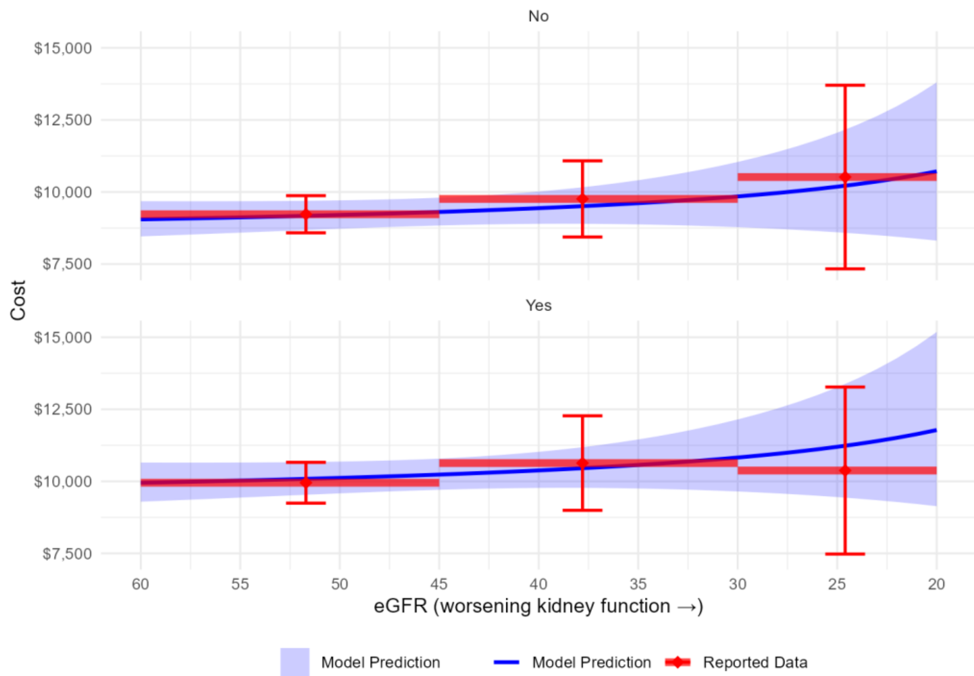
Comparison of Predicted and Reported Year 1 Costs of CKD Patients
Aged < 65 with CKD only
By Diabetes Status at Baseline



Comparison of Predicted and Reported Year 1 Costs of CKD Patients
Aged >= 65 with CKD only
By Diabetes Status at Baseline



Comparison of Predicted and Reported Year 2+ Costs of CKD Patients
Aged < 65 with CKD only
By Diabetes Status at Baseline



Comparison of Predicted and Reported Year 2+ Costs of CKD Patients
Aged >= 65 with CKD only
By Diabetes Status at Baseline