

SUPPLEMENTARY DATA

Supplementary Table S1. Baseline demographic and clinical characteristics of 300 participants with type 2 diabetes by incident CKD.

	N	No CKD	Incident CKD	P
Number (%)		263 (87.7)	37 (12.3)	
Age (years)	300	65.2±9.2	70.8±7.8	0.001
Gender, % male	300	49.0	59.5	0.29
BMI (kg/m ²)	300	31.3±5.7	30.3±5.3	0.33
Waist circumference (cm)	300	102.7±14.0	101.2±11.2	0.54
Ethnic background (% AC/SE/OE/Asian/Ab/other)	300	68.8/10.3/7.2/3.8/0.4/9.5	59.5/16.2/2.7/0.0/0.0/21.6	0.16
Age at diabetes diagnosis (years)	300	56.1±11.1	60.6±9.9	0.021
Diabetes duration (years)*	300	7.9 [3.0-14.6]	10.0 [2.0-15.5]	0.38
Fasting plasma glucose (mmol/L)†	299	7.2 (5.6-9.2)	6.8 (5.2-8.8)	0.17
HbA _{1c} (%)	300	6.9±1.0	6.9±1.1	0.62
HbA _{1c} (mmol/mol)	300	52±11.1	51±12.0	
Serum total cholesterol (mmol/L)	300	4.4±1.0	3.8±0.9	0.001
Serum HDL-cholesterol (mmol/L)	300	1.30±0.31	1.19±0.34	0.045
Serum triglycerides (mmol/L)†	300	1.5 (0.9-2.3)	1.3 (0.7-2.3)	0.13
Serum uric acid (mmol/L)†	299	0.33 (0.25-0.42)	0.37 (0.30-0.45)	0.003
Serum creatinine (μmol/L)†	300	68 (56-82)	83 (70-99)	<0.001
Urine albumin to creatinine ratio (mg/mmol)†	300	2.6 (0.9-7.6)	2.6 (1.0-6.5)	0.91
eGFR (mL/min/1.73m ²)	300	88.2±11.3	71.7±9.3	<0.001
Systolic blood pressure (mmHg)	300	146±19	151±23	0.14
Diastolic blood pressure (mmHg)	300	80±12	81±14	0.55
Neuropathy (%)	300	73.0	75.7	0.84
PAD (%)	300	17.5	8.1	0.23
CVD (%)	300	3.4	10.8	0.062
IHD (%)	300	18.6	40.5	0.005
Alcohol consumption (standard drinks/day)*	285	0.3 [0.0-1.5]	0.1 [0.0-0.3]	0.43
Smoking status (% never/ex-/current)	300	49.8/43.0/7.2	40.5/59.5/0.0	0.074
Any physical activity (%)	296	95.4	91.9	0.41
Diabetes treatment (%)				
Diet	300	32.7	18.9	0.13
OHA	300	46.8	62.2	0.11
Insulin±OHA	300	20.5	18.9	>0.99
Anti-hypertensive medication (%):	300	74.9	91.9	0.021
Diuretic	300	31.2	40.5	0.26
ACE-I	300	42.6	45.9	0.73

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ARB	300	28.1	51.4	0.007
Beta-blocker	300	19.4	32.4	0.084
Calcium channel blocker	300	24.7	16.2	0.31
Other	300	2.7	8.1	0.11
Lipid-lowering medication (%):	300	72.6	73.0	>0.99
Aspirin use (%)	300	41.1	56.8	0.078
Plasma Biomarkers (peak area ratios)†:				
APOA4	300	1.03 (0.52-2.05)	1.50 (0.76-2.99)	0.002
APOC3	300	0.79 (0.32-1.96)	0.95 (0.28-3.23)	0.37
CD5L	299	2.30 (1.13-4.68)	2.68 (1.23-5.85)	0.23
C1QB	286	0.41 (0.23-0.73)	0.40 (0.22-0.70)	0.71
CFHR2	299	0.89 (0.51-1.54)	1.05 (0.60-1.85)	0.088
IBP3	291	0.97 (0.61-1.54)	0.98 (0.51-1.89)	0.87

Incident CKD was defined as eGFR<60 mL/min/1.73m² at year 4 in individuals eGFR ≥60 mL/min/1.73m² year at baseline. All values are mean±SD (standard deviation) unless labeled otherwise; * Median [IQR – interquartile range]; † Geometric Mean (SD range). BMI, body mass index; AC, Anglo-Celt; SE, southern European; OE, other European; Ab, Aboriginal; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; OHA, oral hypoglycaemic agent; eGFR, estimated glomerular filtration rate by CKD Epidemiology Collaboration equation; PAD, peripheral arterial disease; CVD, cerebrovascular disease; IHD, ischemic heart disease.

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Supplementary Table S2. Baseline demographic and clinical characteristics of 345 participants with type 2 diabetes by rapid eGFR decline $\geq 30\%$.

	N	eGFR decline $<30\%$	eGFR decline $\geq 30\%$	P
		315 (91.3)	30 (8.7)	
Age (years)	345	66.5 $\pm$ 9.4	72.5 $\pm$ 7.1	<0.001
Gender, % male	345	49.8	73.3	0.02
BMI (kg/m ²)	345	31.1 $\pm$ 5.6	29.9 $\pm$ 4.6	0.27
Waist circumference (cm)	345	102.6 $\pm$ 13.8	103.5 $\pm$ 11.0	0.73
Ethnic background (% AC/SE/OE/Asian/Ab/other)	345	66.7/10.5/6.7/3.5/0.3/12.4	46.7//16.7/10.0/0.0/0.0/26.7	0.11
Age at diabetes diagnosis (years)	345	56.8 $\pm$ 11.0	60.2 $\pm$ 9.5	0.10
Diabetes duration (years)*	345	8.4 [3.0-15.0]	14.5 [5.5-17.9]	0.043
Fasting plasma glucose (mmol/L)†	344	7.1 (5.5-9.1)	7.5 (5.3-10.5)	0.44
HbA _{1c} (%)	345	6.9 $\pm$ 1.0	7.2 $\pm$ 1.3	0.25
HbA _{1c} (mmol/mol)	345	52 $\pm$ 10.9	55 $\pm$ 14.2	
Serum total cholesterol (mmol/L)	344	4.4 $\pm$ 1.0	3.8 $\pm$ 0.7	0.002
Serum HDL-cholesterol (mmol/L)	344	1.29 $\pm$ 0.31	1.20 $\pm$ 0.31	0.14
Serum triglycerides (mmol/L)†	344	1.5 (0.9-2.3)	1.5 (0.9-2.6)	0.74
Serum uric acid (mmol/L)†	344	0.34 (0.26-0.44)	0.37 (0.31-0.45)	0.045
Serum creatinine (μ mol/L)†	345	73 (56-97)	97 (67-141)	<0.001
Urine albumin to creatinine ratio (mg/mmol)†	345	2.7 (0.9-8.0)	4.9 (1.2-20.6)	0.006
eGFR (mL/min/1.73m ²)	345	82.1 $\pm$ 17.7	64.6 $\pm$ 22.8	<0.001
eGFR categories (% G1/G2/G3a/G3b/G4)‡	345	40.0/48.9/6.3/3.8/1.0	13.3/53.3/6.7/23.3/3.3	<0.001
CKD stage (% 0/1/2/3)§	345	58.4/31.1/6.0/4.4	43.3/26.7/6.7/23.3	0.004
Systolic blood pressure (mmHg)	345	146 $\pm$ 19	160 $\pm$ 24	<0.001
Diastolic blood pressure (mmHg)	345	79 $\pm$ 11	86 $\pm$ 13	0.005
Neuropathy (%)	345	73.0	80.0	0.52
PAD (%)	345	17.8	13.3	0.80
CVD (%)	345	4.8	13.3	0.072
IHD (%)	345	22.5	56.7	<0.001
Alcohol consumption (standard drinks/day)*	326	0.1 [0.0-1.5]	0.1 [0.1-1.3]	0.92
Smoking status (% never/ex-/current)	345	48.6/45.4/6.0	33.3/63.3/3.3	0.20
Any physical activity (%)	341	94.2	96.7	>0.99
Diabetes treatment (%):				
Diet	345	30.8	13.3	0.057
OHA	345	47.9	60.0	0.25
Insulin $\pm$ OHA	345	21.3	26.7	0.49

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Anti-hypertensive medication (%):	345	78.1	96.7	0.015
Diuretic	345	33.0	53.3	0.043
ACE-I	345	42.5	63.3	0.034
ARB	345	33.3	40.0	0.55
Beta-blocker	345	20.3	43.3	0.010
Calcium channel blocker	345	25.4	33.3	0.39
Other	345	3.8	10.0	0.13
Lipid-lowering medication (%):	345	72.7	86.7	0.13
Statin	344	71.0	86.7	0.086
Fibrate	345	1.9	0.0	>0.99
Other	341	6.4	3.3	>0.99
Aspirin use (%)	345	42.5	56.7	0.18
Plasma Biomarkers (peak area ratios)†:				
APOA4	345	1.12 (0.55-2.29)	1.82 (0.86-3.82)	<0.001
APOC3	345	0.85 (0.32-2.23)	1.05 (0.37-2.95)	0.25
CD5L	344	2.36 (1.17-4.76)	2.53 (1.24-5.15)	0.61
C1QB	328	0.42 (0.23-0.78)	0.35 (0.20-0.62)	0.15
CFHR2	344	0.94 (0.52-1.69)	1.11 (0.64-1.93)	0.14
IBP3	335	0.99 (0.59-1.67)	0.80 (0.48-1.36)	0.036

All values are mean±SD (standard deviation) unless labeled otherwise; * Median [IQR – interquartile range]; † Geometric Mean (SD range); ‡ eGFR categories G1 ≥90, G2 60-89, G3a 45-59, G3b 30-44, G4 15-29 mL/min/1.73m²; § CKD (chronic kidney disease) stage defined by KDIGO 2012 guidelines. BMI, body mass index; AC, Anglo-Celt; SE, southern European; OE, other European; Ab, Aboriginal; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; OHA, oral hypoglycemic agent; eGFR, estimated glomerular filtration rate by CKD Epidemiology Collaboration equation; PAD, peripheral arterial disease; CVD, cerebrovascular disease; IHD, ischemic heart disease.

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Supplementary Table S3. Baseline demographic and clinical characteristics of 345 participants with type 2 diabetes by rapid eGFR decline $\geq 5 \text{ mL/min/1.73m}^2/\text{yr}$.

	N	eGFR decline <5 mL/min/1.73m ² /yr	eGFR decline $\geq 5 \text{ mL/min/1.73m}^2/\text{yr}$	P
Number (%)		317 (91.9)	28 (8.1)	
Age (years)	345	67.0±9.4	67.5±9.3	0.77
Gender, % male	345	50.8	64.3	0.24
BMI (kg/m ²)	345	31.0±5.6	31.3±4.9	0.79
Waist circumference (cm)	345	102.4±13.6	105.9±12.0	0.19
Ethnic background (% AC/SE/OE/Asian/Ab/other)	345	65.3/10.4/7.3/3.5/0.3/13.2	60.7/17.9/3.6/0.0/0.0/17.9	0.63
Age at diabetes diagnosis (years)	345	57.1±11.0	56.6±10.3	0.83
Diabetes duration (years)*	345	8.5 [3.0-15.1]	10.0 [3.5-16.8]	0.33
Fasting plasma glucose (mmol/L)†	344	7.1 (5.5-9.0)	7.8 (5.4-11.3)	0.18
HbA _{1c} (%)	345	6.9±1.0	7.5±1.5	0.003
HbA _{1c} (mmol/mol)	345	52±10.9	59±16.4	
Serum total cholesterol (mmol/L)	344	4.3±1.0	4.1±1.2	0.25
Serum HDL-cholesterol (mmol/L)	344	1.29±0.31	1.17±0.35	0.06
Serum triglycerides (mmol/L)†	344	1.4 (0.9-2.3)	1.6 (0.9-2.8)	0.38
Serum uric acid (mmol/L)†	344	0.34 (0.26-0.44)	0.35 (0.29-0.42)	0.39
Serum creatinine (μmol/L)†	345	75 (56-102)	75 (61-93)	0.99
Urine albumin to creatinine ratio (mg/mmol)†	345	2.8 (0.9-8.3)	4.2 (1.0-17.3)	0.06
eGFR (mL/min/1.73m ²)	345	80.4±19.3	82.6±12.6	0.40
eGFR categories (% G1/G2/G3a/G3b/G4)‡	345	38.2/47.9/6.6/6.0/1.3	32.1/64.3/3.6/0.0/0.0	0.55
CKD stage (% 0/1/2/3)§	345	57.1/30.3/6.3/6.3	57.1/35.7/3.6/3.6	0.91
Systolic blood pressure (mmHg)	345	146±20	153±26	0.07
Diastolic blood pressure (mmHg)	345	79±11	86±13	0.007
Neuropathy (%)	345	73.8	71.4	0.82
PAD (%)	345	18.3	7.1	0.19
CVD (%)	345	5.4	7.1	0.66
IHD (%)	345	23.7	46.4	0.012
Alcohol consumption (standard drinks/day)*	326	0.1 [0.0-1.2]	0.3 [0.1-1.5]	0.30
Smoking status (% never/ex-/current)	345	48.3/45.7/6.0	35.7/60.7/3.6	0.28
Any physical activity (%)	341	93.9	100.0	0.39
Diabetes treatment (%):				
Diet	345	30.6	14.3	0.083
OHA	345	48.6	53.6	0.70

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Insulin±OHA	345	20.8	32.1	0.23
Anti-hypertensive medication (%):	345	78.5	92.9	0.086
Diuretic	345	33.8	46.4	0.21
ACE-I	345	43.2	57.1	0.17
ARB	345	33.8	35.7	0.84
Beta-blocker	345	20.5	42.9	0.015
Calcium channel blocker	345	26.8	17.9	0.37
Other	345	4.1	7.1	0.35
Lipid-lowering medication (%)	345	73.2	82.1	0.37
Aspirin use (%)	345	42.3	60.7	0.074
Plasma Biomarkers (peak area ratios)†:				
APOA4	345	1.16 (0.56-2.43)	1.31 (0.74-2.30)	0.41
APOC3	345	0.86 (0.32-2.26)	0.94 (0.34-2.58)	0.62
CD5L	344	2.37 (1.17-4.80)	2.44 (1.24-4.82)	0.82
C1QB	328	0.42 (0.22-0.78)	0.37 (0.24-0.59)	0.39
CFHR2	344	0.96 (0.53-1.73)	0.91 (0.52-1.60)	0.68
IBP3	335	0.99 (0.59-1.68)	0.77 (0.51-1.16)	0.015

All values are mean±SD (standard deviation) unless labeled otherwise; * Median [IQR – interquartile range]; † Geometric Mean (SD range); ‡ eGFR categories G1 ≥90, G2 60-89, G3a 45-59, G3b 30-44, G4 15-29 mL/min/1.73m²; § CKD (chronic kidney disease) stage defined by KDIGO 2012 guidelines. BMI, body mass index; AC, Anglo-Celt; SE, southern European; OE, other European; Ab, Aboriginal; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; OHA, oral hypoglycaemic agent; eGFR, estimated glomerular filtration rate by CKD Epidemiology Collaboration equation; PAD, peripheral arterial disease; CVD, cerebrovascular disease; IHD, ischemic heart disease.

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Supplementary Table S4. Performance of the clinical and clinical plus biomarkers prediction models for incident CKD.

	Clinical Model (N=300)	Clinical + Biomarkers Model 1 (N=300)	Clinical + Biomarkers Model 2 (N=276)§
Variable	OR (95% CI), <i>P</i>		
Ischaemic heart disease	4.32 (1.64-11.38), 0.003	5.33 (1.93-14.72), 0.001	4.48 (1.54-13.02), 0.006
eGFR (per mL/min/1.73m ²)	0.86 (0.82-0.90), <0.001	0.86 (0.82-0.90), <0.001	0.86 (0.81-0.90), <0.001
Total cholesterol (per mmol/L)	0.54 (0.32-0.92), 0.022	0.59 (0.35-1.00), 0.052	0.60 (0.34-1.06), 0.079
Ln(APOA4)*	NI	2.16 (1.04-4.47), 0.038	2.38 (1.03-5.51), 0.042
Ln(C1QB)*	NI	NI	0.60 (0.26-1.42), 0.246
Ln(CD5L)*	NI	NI	1.13 (0.58-2.18), 0.726
Ln(IBP3)*	NI	NI	0.75 (0.28-1.97), 0.558
Performance Measure			
LRT χ^2 test, <i>P</i>	80.43, <0.001	85.13, <0.001	81.70, <0.001
Δ LRT χ^2 test, <i>P</i>	reference	4.69, 0.03	5.98, 0.20
H-L test χ^2 , <i>P</i>	3.21, 0.07	4.04, 0.85	5.70, 0.68
Sensitivity (%)†	91.9	91.9	94.3
Specificity (%)†	74.1	82.0	78.0
PPV (%)†	33.3	41.9	38.4
NPV (%)†	98.5	98.6	98.9
AUC (95% CI)	0.91 (0.87-0.94)	0.92 (0.88-0.95)	0.92 (0.88-0.95)
Δ AUC, <i>P</i>	reference	0.01, 0.18	0.01, 0.23
Optimism-corrected AUC‡	0.90	0.90	0.90
Calibration intercept‡	-0.07	-0.07	-0.16
Calibration slope‡	0.93	0.91	0.83
NRI (>0) (95% CI):	reference	0.30 (0.25-0.35)	0.41 (0.34-0.47)
NRI _R	reference	0.08 (-0.24-0.40)	0.09 (-0.24-0.42)
NRI _{NR}	reference	0.22 (0.10-0.34)	0.32 (0.20-0.44)
Absolute IDI (%) (95% CI):	reference	1.8 (-1.3-5.1)	2.7 (-1.2-6.7)
IDI _R	reference	1.6 (-1.5-4.8)	2.4 (-1.6-6.3)
IDI _{NR}	reference	0.2 (-0.2-0.7)	0.3 (-0.2-0.9)
Relative IDI (%)	reference	5.8	6.5

Only participants with complete data were included in each model. The most parsimonious clinical model was derived as described in methods, followed by inclusion of biomarkers with significant independent predictive value (clinical + biomarkers model 1), then all significant biomarkers across the four definitions of rapid eGFR decline were forced into the clinical model (clinical + biomarkers model 2). * A 2.72 fold change in mean peak area ratio of APOA4, C1QB, CD5L or IBP3 corresponds to a change of 1 in natural logarithm transformed (APOA4, C1QB, CD5L or IBP3), respectively. † Based on optimal cut-off defined by Youden Index. ‡ Based on internal validation by bootstrap resampling. § The performance of this model was compared to the clinical model applied to the same 276

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individuals. NI = not included. LRT = likelihood ratio test, H-L = Hosmer-Lemeshow, PPV = positive predictive value, NPV = negative predictive value, AUC = area under the curve, IDI = integrated discrimination index, NRI (>0) = category-free/continuous net reclassification index, NRI_R = NRI for rapid decliners, NRI_{NR} = NRI for non-rapid decliners, IDI_R = IDI for rapid decliners, IDI_{NR} = IDI for non-rapid decliners. Rapid and non-rapid refer to the two categories of incident CKD and no CKD.

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Supplementary Table S5. Performance of the clinical and clinical plus biomarkers prediction models for rapid eGFR decline $\geq 30\%$.

	Clinical Model (N=334)	Clinical + Biomarkers Model 1 (N=334)	Clinical + Biomarkers Model 2 (N=316)§
Variable	OR (95% CI), <i>P</i>		
Ischemic heart disease	3.86 (1.60-9.33), 0.003	4.56 (1.77-11.75), 0.002	3.86 (1.42-10.50), 0.008
Diuretic use	2.49 (1.08-5.76), 0.033	2.73 (1.11-6.70), 0.029	2.83 (1.08-7.41), 0.035
Age (per 10 yrs)	2.03 (1.19-3.46), 0.009	1.66 (0.94-2.91), 0.080	1.67 (0.93-3.01), 0.086
Diastolic blood pressure (per 10mm)	1.81 (1.32-2.48), <0.001	1.97 (1.39-2.81), <0.001	2.04 (1.40-2.96), <0.001
Total cholesterol (per mmol/L)	0.57 (0.35-0.92), 0.022	0.58 (0.35-0.96), 0.034	0.57 (0.34-0.98), 0.042
Ln(APOA4)*	NI	4.85 (2.04-11.50), <0.001	4.53 (1.86-11.05), 0.001
Ln(1BP3)*	NI	0.32 (0.13-0.81), 0.015	0.37 (0.13-1.05), 0.062
Ln(C1QB)*	NI	NI	0.71 (0.33-1.57), 0.400
Ln(CD5L)*	NI	NI	0.97 (0.49-1.93), 0.936
Performance Measure			
LRT χ^2 test, <i>P</i>	45.04, <0.001	62.12, <0.001	58.00, <0.001
Δ LRT χ^2 test, <i>P</i>	reference	17.08, <0.001	16.53, 0.002
H-L test χ^2 , <i>P</i>	3.03, 0.93	3.38, 0.91	7.65, 0.47
Sensitivity (%)†	76.7	86.7	85.2
Specificity (%)†	79.6	78.9	79.6
PPV (%)†	27.1	28.9	28.1
NPV (%)†	97.2	98.4	98.3
AUC (95% CI)	0.84 (0.78-0.91)	0.88 (0.82-0.93)	0.88 (0.82-0.94)
Δ AUC, <i>P</i>	reference	0.04, 0.14	0.04, 0.20
Optimism-corrected AUC‡	0.82	0.85	0.84
Calibration intercept‡	-0.19	-0.24	-0.34
Calibration slope‡	0.89	0.84	0.77
NRI (>0) (95% CI):	reference	0.81 (0.68-0.94)	0.80 (0.68-0.92)
NRI _R	reference	0.41 (0.31-0.51)	0.41 (0.06-0.75)
NRI _{NR}	reference	0.40 (0.07-0.73)	0.39 (0.29-0.50)
Absolute IDI (%) (95% CI):	reference	8.1 (1.0-15.1)	9.2 (1.4-16.9)
IDI _R	reference	7.3 (0.3-14.3)	8.4 (0.7-16.1)
IDI _{NR}	reference	0.8 (0.4-1.4)	0.8 (0.1-1.5)
Relative IDI (%)	reference	47.6	53.1

Only participants with complete data were included in each model. The most parsimonious clinical model was derived as described in methods, followed by inclusion of biomarkers with significant independent predictive value (clinical + biomarkers model 1), then all significant biomarkers across the four definitions of

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rapid eGFR decline were forced into the clinical model (clinical + biomarkers model 2). * A 2.72 fold change in mean peak area ratio of APOA4, C1QB, CD5L or IBP3 corresponds to a change of 1 in natural logarithm transformed (APOA4, C1QB, CD5L or IBP3), respectively. † Based on optimal cut-off defined by Youden Index. ‡ Based on internal validation by bootstrap resampling. § The performance of this model was compared to the clinical model applied to the same 316 individuals. NI = not included. LRT = likelihood ratio test, H-L = Hosmer-Lemeshow, PPV = positive predictive value, NPV = negative predictive value, AUC = area under the curve, IDI = integrated discrimination index, NRI (>0) = category-free/continuous net reclassification index, NRI_R = NRI for rapid decliners, NRI_{NR} = NRI for non-rapid decliners, IDI_R = IDI for rapid decliners, IDI_{NR} = IDI for non-rapid decliners. Rapid and non-rapid refer to the two categories of eGFR decline $\geq 30\%$ and $< 30\%$.

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Supplementary Table S6. Performance of the clinical and clinical plus biomarkers prediction models for rapid eGFR decline $\geq 5\text{mL}/\text{min}/1.73\text{m}^2/\text{yr}$.

	Clinical Model (N=335)	Clinical + Biomarkers Model 1 (N=335)	Clinical + Biomarkers Model 2 (N=317)§
Variable	OR (95% CI), <i>P</i>		
Ischaemic heart disease	3.11 (1.35-7.15), 0.006	2.74 (1.18-6.37), 0.019	2.29 (0.89-5.87), 0.084
Diastolic blood pressure (per 10mm)	1.52 (1.13-2.05), 0.008	1.51 (1.12-2.03), 0.007	1.64 (1.19-2.26), 0.003
HbA _{1c} (%)	1.51 (1.09-2.09), 0.014	1.51 (1.09-2.11), 0.014	1.58 (1.10-2.26), 0.012
Ln(IBP3)*	NI	0.38 (0.15-0.95), 0.039	0.27 (0.09-0.85), 0.026
Ln(APOA4)*	NI	NI	1.24 (0.59-2.62), 0.570
Ln(C1QB)*	NI	NI	1.14 (0.49-2.66), 0.759
Ln(CD5L)*	NI	NI	1.01 (0.51-2.00), 0.983
Performance Measure			
LRT χ^2 test, <i>P</i>	19.91, <0.001	24.62, <0.001	27.12, <0.001
Δ LRT χ^2 test, <i>P</i>	reference	4.72, 0.03	6.34, 0.18
H-L test χ^2 , <i>P</i>	5.82, 0.67	9.47, 0.31	8.07, 0.43
Sensitivity (%)†	71.4	85.7	83.3
Specificity (%)†	74.3	64.2	77.5
PPV (%)†	20.2	17.9	23.3
NPV (%)†	96.6	98.0	98.3
AUC (95% CI)	0.76 (0.67-0.85)	0.78 (0.69-0.87)	0.82 (0.74-0.90)
Δ AUC, <i>P</i>	reference	0.02, 0.42	0.03, 0.26
Optimism-corrected AUC‡	0.74	0.75	0.78
Calibration intercept‡	-0.21	-0.26	-0.46
Calibration slope‡	0.90	0.86	0.77
NRI (>0) (95% CI):	reference	0.18 (0.16-0.21)	0.37 (0.32-0.42)
NRI _R	reference	0.14 (-0.22-0.51)	0.25 (-0.14-0.64)
NRI _{NR}	reference	0.04 (-0.07-0.15)	0.12 (0.01-0.23)
Absolute IDI (%) (95% CI):	reference	1.8 (-0.1-3.8)	2.3 (-0.2-4.7)
IDI _R	reference	1.7 (0.2-3.6)	2.1 (-0.3-4.5)
IDI _{NR}	reference	0.1 (-0.2-0.6)	0.2 (-0.3-0.6)
Relative IDI (%)	reference	26.9	28.9

Only participants with complete data were included in each model. The most parsimonious clinical model was derived as described in methods, followed by

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inclusion of biomarkers with significant independent predictive value (clinical + biomarkers model 1), then all significant biomarkers across the four definitions of rapid eGFR decline were forced into the clinical model (clinical + biomarkers model 2). * A 2.72 fold change in mean peak area ratio of APOA4, C1QB, CD5L or IBP3 corresponds to a change of 1 in natural logarithm transformed (APOA4, C1QB, CD5L or IBP3), respectively. † Based on optimal cut-off defined by Youden Index. ‡ Based on internal validation by bootstrap resampling. § The performance of this model was compared to the clinical model applied to the same 317 individuals. NI = not included. LRT = likelihood ratio test, H-L = Hosmer-Lemeshow, PPV = positive predictive value, NPV = negative predictive value, AUC = area under the curve, IDI = integrated discrimination index, NRI (>0) = category-free/continuous net reclassification index, NRI_R = NRI for rapid decliners, NRI_{NR} = NRI for non-rapid decliners, IDI_R = IDI for rapid decliners, IDI_{NR} = IDI for non-rapid decliners. Rapid and non-rapid refer to the two categories of eGFR decline ≥ 5 and < 5 mL/min/1.73m²/yr.

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Supplementary Figure S1. The observed probabilities were plotted against predicted probabilities over deciles of predictions (from Hosmer-Lemeshow goodness-of-fit test) for the clinical model, represented by black-filled circles (•), and the clinical + biomarkers model, represented by the triangles (Δ). A. eGFR trajectory, B. Incident CKD, C. eGFR decline $\geq 30\%$, D. Annual decline $\geq 5\text{mL/min/1.73m}^2/\text{yr}$.

