Supplement to:

A novel drug response score more accurately predicts renoprotective drug effects than existing renal risk scores

Content:

Supplement Table 1. Identified renal risk scores that were developed in populations including patients with type 2 diabetes and/or diabetic kidney disease. The risk scores marked grey in the table below are used in the present study.

	Year	Population	Patients, *n*	Events, *n*	Predictors	Outcome
Tangri et al. [S1]	2011	CKD stage 3-5	3449	386	eGFR, age, sex, UACR, albumin, phosphate, bicarbonate, calcium	ESRD
Jardine et al. [S2]	2012	T2D, high renal and/or CV risk	11,140	128	eGFR, retinopathy, sex, UACR, SBP, waist circumference, HbA1c, age at completion formal education	Composite of DSCR to ≥200 µmol/L and ESRD
Bidadkosh et al. [S3]	2017	T2D, advanced CKD	861	60	UACR, sCr, Hb, age, sex, NT-proBNP, hsTNT	Composite of ESRD and 40% eGFR decline
Desai et al. [S4]	2011	T2D, anemia, CKD stage 3-4	995	222	Age, sex, race, BMI, insulin use, eGFR, SUN, UPCR, albumin, prior stroke/PAD/HF, cardiac arrhythmia, Hb, CRP, prior AKI, NT-proBNP, TnT	ESRD
Hoshino et al. [S5]	2015	T1D or T2D, CKD stage 1-5	205	NR	Pathological features based on renal biopsy	ESRD
Johnson et al. [S6]	2008	CKD stage 3-4	9782	323	Age, sex, eGFR, diabetes, anemia, hypertension	ESRD
Landray et al. [S7]	2010	CKD stage 3-5	382	190	Sex, UACR, phosphate, sCr	ESRD

Li et al. [S8]	2016	T2D	604	22	HbA1c, eGFR, proteinuria, VAP-1	ESRD
Schroeder et al. [S9]	2017	CKD stage 3-4	22,460	737	Age, sex, eGFR, Hb, proteinuria, SBP, antihypertensive treatment, diabetes	ESRD
Xie et al. [S10]	2016	CKD stage 3-5 Low socio-economic status	28,779	1730	Age, sex, race, eGFR, dipstick proteinuria	ESRD

T2D, type 2 diabetes; CKD, chronic kidney disease; CV, cardiovascular; DSCR, doubling of serum creatinine; ESRD, end-stage renal disease; UACR, urine albumin: urine creatinine ratio; sCr, serum creatinine; Hb, haemoglobin; NT-proBNP, N-terminal pro-brain natriuretic peptide; hsTNT, high sensitivity troponin T; BMI, body mass index; eGFR, estimated glomerular filtration rate; SUN, serum urea nitrogen; UPCR, urine protein: urine creatinine ratio, PAD; peripheral arterial disease; HF, heart failure; CRP, C-reactive protein; AKI, acute kidney injury; SBP, systolic blood pressure; HbA1c, glycated haemoglobin; VAP-1, vascular adhesion protein 1.

Supplement Table 2A. Characteristics of the populations used to develop the renal risk scores.

	Study	Population	Outcome	Patients, n	Events, n	Median FU, y	Predictors	Validation **
KFRE	Tangri 2011 [S1]	CKD stage 3-5	ESRD after 1, 3 and 5 y	3449	386	2.1	Age, sex, alb, eGFR, ACR, ca, phos, HCO3	External
ADVANCE	Jardine 2012 [S2]	T2D, high renal and/or CV risk	Composite renal outcome after 5 y	11140	128	4.4	Sex, eGFR, retn, ACR, SBP, waist circ, HbA1c, education age	Internal
PRE score	Parving 2012 [S11]	T2D, high renal and/or CV risk	Composite renal outcome / ESRD	4287	ESRD: 110 Comp: 248	2.7	ACR, SBP, HbA1c, Hb, uric acid, TC, BMI, K	External
	Packham 2012 [S12]	T2D, overt proteinuria	Composite renal outcome / ESRD	598	ESRD: 9 Comp: 30	0.8		
	Lewis 2001 [S13]	T2D, overt proteinuria	Composite renal outcome / ESRD	569	ESRD: 101 Comp: 158	2.6		

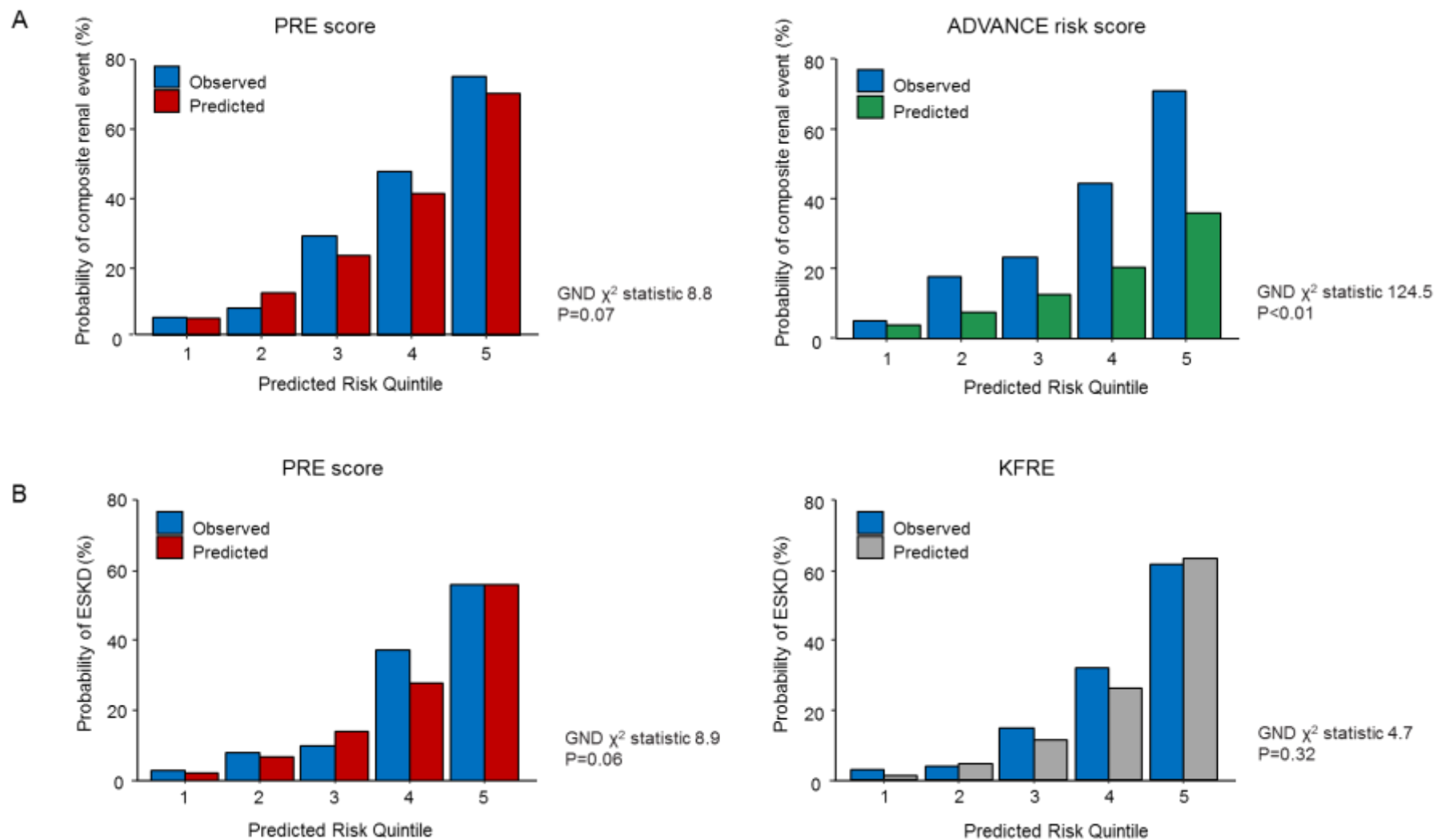* Defined as a doubling of serum creatinine to ≥200 μmol/L or ESRD
** Internally validated scores are tested in the dataset used to develop the risk model. Externally validated scores are additionally tested in a different dataset that is not used for development.

Supplement Table 2B. Characteristics of the RENAAL clinical trial population.

Study	Inclusion criteria	Intervention	Primary outcome	Event rate, *N/n (%)*	Median FU, *y*
RENAAL [S14]	T2D, ACR>300 mg/g sCr 1.3-3.0 mg/dl	Losartan 100 mg/day on top of standard care	Composite of DSCR, ESRD and death	Placebo: 359/762 (47.1) Losartan: 327/751 (43.5)	3.4

CKD, chronic kidney disease; T2D, type 2 diabetes; CV, cardiovascular; ESRD, end-stage kidney disease; FU, follow-up; alb, serum albumin; eGFR, estimated glomerular filtration rate; retn, retinopathy; ACR, urine albumin: urine creatinine ratio; ca, serum calcium; phos, serum phosphate; HCO3. Serum bicarbonate; SBP, systolic blood pressure; waist circ, waist circumference; HbA1c, glycated haemoglobin; education age, age at completion of formal education; Hb, haemoglobin; TC, total cholesterol; BMI, body mass index; K, potassium; sCr, serum creatinine; DSCR, doubling of serum creatinine.

Supplement Figure 1. Observed versus predicted risk for the composite renal outcome of doubling of serum creatinine to ≥200 μmol/L or ESRD based on predictions by the ADVANCE risk score and the PRE score **(A)** and for the separate ESRD endpoint based on predictions by the KFRE and the PRE score **(B)**.

Supplement Figure 2. Receiver operating curves (ROC) for the composite renal endpoint of doubling of serum creatinine to ≥200 μmol/L or ESRD based on predictions by the ADVANCE risk score and the PRE score **(A)** and for the separate ESRD endpoint based on predictions by the KFRE and the PRE score **(B)**.
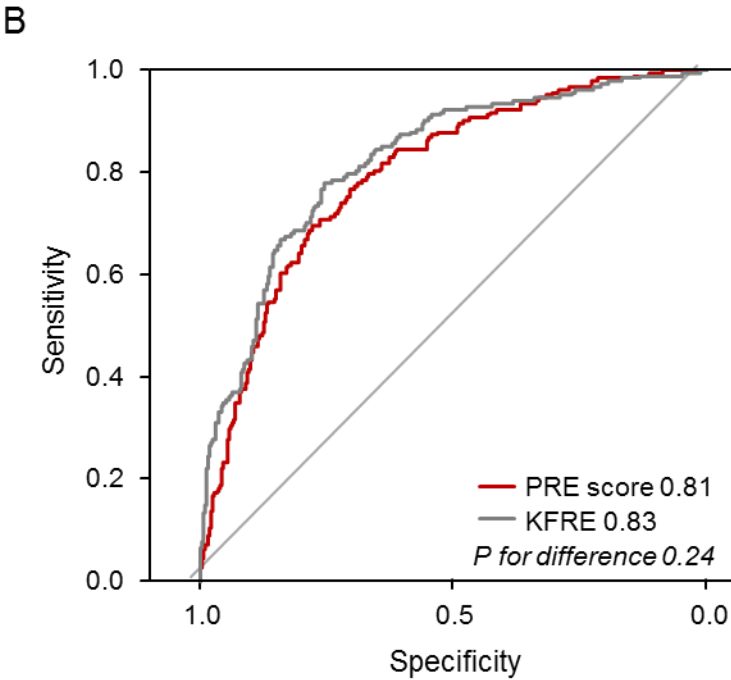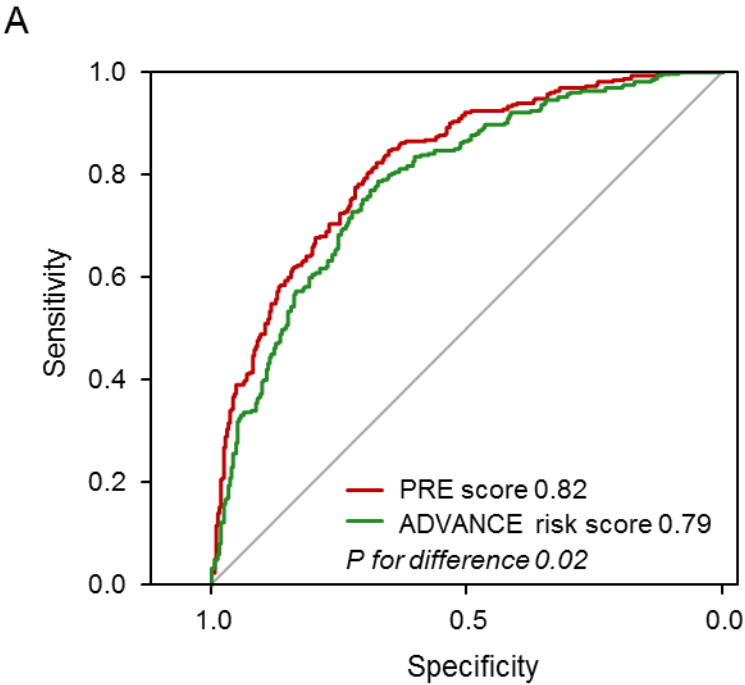
Supplement Figure 3: Regression coefficients (β) of covariates included in the PRE score are consistent in various patient subgroups from the background population used to derive the PRE score
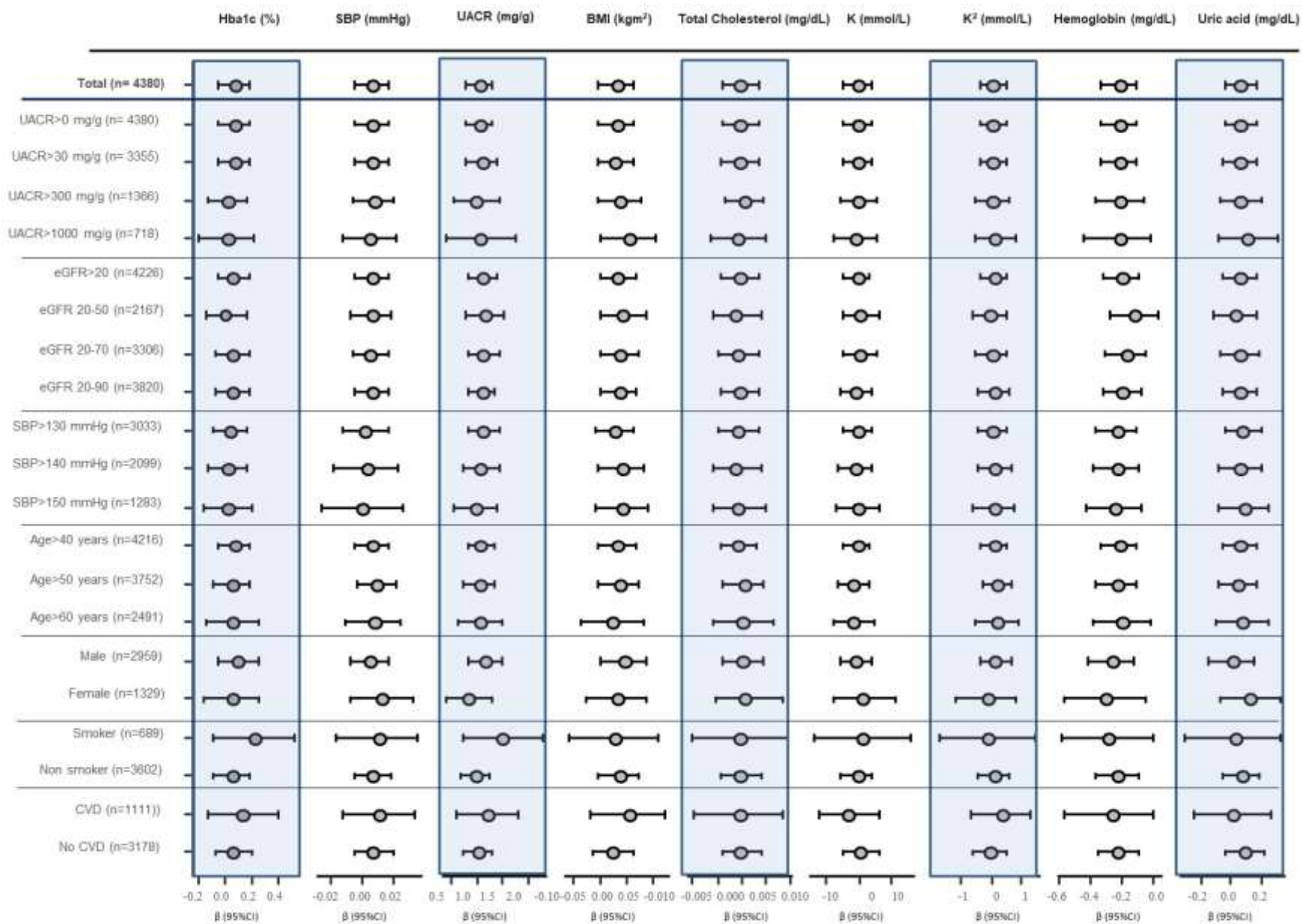
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