

SUPPLEMENT

Definition of diabetic kidney disease (DKD) severity

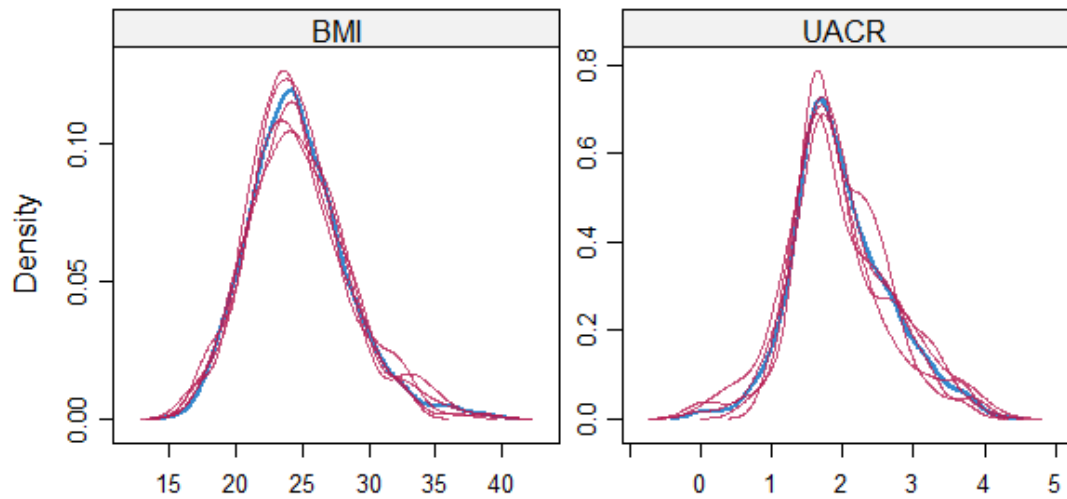
Severity of DKD by eGFR and Albuminuria Categories: KDIGO 2012			UACR categories (mg/g) Description and range		
			Normal to mildly increased	Moderately increased	Severely increased
			< 30	30-300	> 300
eGFR categories (ml/min/1.73m ²) Description and range	Normal or high	≥ 90			
	Mildly decreased	60-89.9			
	Mildly to moderately decreased	45-59.9			
	Moderately to severely decreased	30-44.9			
	Severely decreased	15-29.9			
	Kidney failure	< 15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk

Supplementary Figure 1. Severity of DKD by eGFR and UACR categories.

Multiple imputation

Before multiple imputation, UACR was log-transformed to achieve normality. Using multiple imputation, we generated 5 independently imputed datasets. The density curves below demonstrated the distribution of BMI and UACR in the five imputation datasets were qualitatively similar to those in the observed data (Supplementary Figure 2). The red curve is the density curve of each imputed dataset, and the blue curve is the density curve of the observed data.



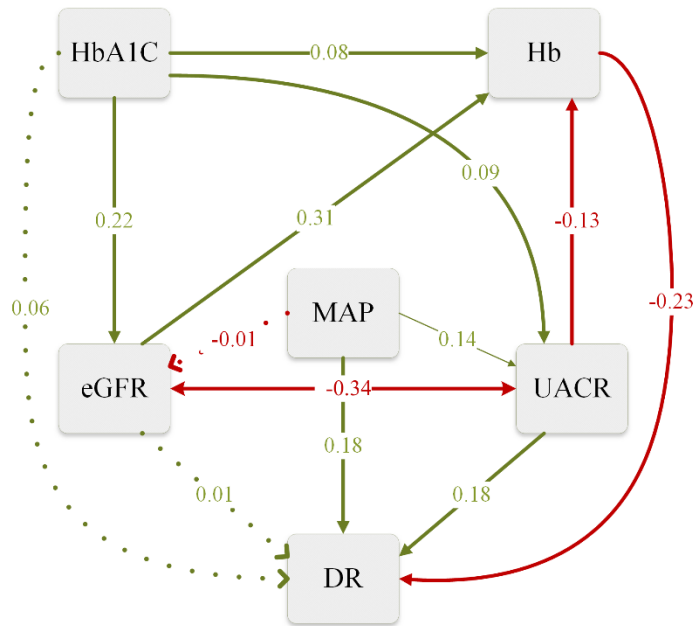
Supplementary Figure 2. Density curves for BMI and UACR.

Path analysis

Supplementary Table 1. Associations between path variables in the original model (model 1).

Variables	Standardized estimate	standard errors	Z-statistic	P-value
DR				
Hb	-0.2302	0.0315	-7.3079	< 0.0001
UACR	0.1809	0.0316	5.7200	< 0.0001
eGFR	0.0058	0.0340	0.1703	0.8647
HbA1c	0.0622	0.0343	1.8130	0.0698
MAP	0.1766	0.0307	5.7574	< 0.0001
Hb	~			
UACR	-0.1285	0.0249	-5.1636	< 0.0001
eGFR	0.3052	0.0246	12.4051	< 0.0001
HbA1c	0.0794	0.0260	3.0532	0.0023
UACR	~			
HbA1c	0.0937	0.0266	3.5295	0.0004
MAP	0.1426	0.0257	5.5441	< 0.0001
eGFR	~			
HbA1c	0.2179	0.0242	9.0062	< 0.0001
MAP	-0.0050	0.0262	-0.1894	0.8497
eGFR ~ UACR	-0.3422	0.0226	-15.1737	< 0.0001

Shown were the dependent variables with their associated independent variables indented beneath them. Standardized estimates expressed this increase in standardized units of measurement. Standardized estimates indicated these changes in standardized units of measurement, facilitating comparisons of the size of the association across different scales of measurement. Abbreviation: DR = diabetic retinopathy (categorical variable); MAP = mean arterial pressure; HbA1c = glycated hemoglobin; eGFR = estimated glomerular filtration rate; UACR = urine albumin-to-creatinine ratio.



Supplementary Figure 3. Path diagram of the original model (model 1). Abbreviation: DR = diabetic retinopathy (categorical variable); MAP = mean arterial pressure; HbA1c = glycated hemoglobin; eGFR = estimated glomerular filtration rate; UACR = urine albumin-to-creatinine ratio. Green arrows indicate significant positive effects and red arrows significant negative effects. One-headed arrows represent a causal effect of one variable on another (i.e., a path). Double-headed arrows link variables with correlated errors. Dashed arrows indicate the path is not significant ($P > 0.05$). The values shown were standardized regression coefficient.

Supplementary Table 2. Associations between path variables in the reduced model (model 2).

Variables	Standardized estimate	standard errors	Z-statistic	P-value
DR				
Hb	-0.2173	0.0311	-6.9788	< 0.0001
UACR	0.1876	0.0300	6.2563	< 0.0001
MAP	0.1762	0.0308	5.7173	< 0.0001
Hb				
UACR	-0.1288	0.0252	-5.1115	< 0.0001
eGFR	0.3055	0.0248	12.3042	< 0.0001
HbA1c	0.0725	0.0263	2.7603	0.0058
UACR				
HbA1c	0.1003	0.0268	3.7368	0.0002
MAP	0.1428	0.0262	5.4598	< 0.0001
eGFR				
HbA1c	0.2179	0.0242	9.0062	< 0.0001
eGFR ~ UACR	-0.3418	0.0227	-15.0659	< 0.0001

Shown were the dependent variables with their associated independent variables indented beneath them. Standardized estimates expressed this increase in standardized units of measurement. Standardized estimates indicated these changes in standardized units of measurement, facilitating comparisons of the size of the association across different scales of measurement. Abbreviation: DR = diabetic retinopathy (categorical variable); MAP = mean arterial pressure; HbA1c = glycated hemoglobin; eGFR = estimated glomerular filtration rate; UACR = urine albumin-to-creatinine ratio.

Supplementary Table 3. Model fit indices for the reduced model in path analysis

Model fit index	Good fit threshold levels	Model fit statistic value
RMSEA	< 0.100	0.031
SRMR	< 0.050	0.003
GFI	> 0.900	0.998
AGFI	> 0.900	0.988
NNFI	> 0.900	0.988
CFI	> 0.900	0.994

Abbreviation: RMSEA = Root Mean Square Error Approximation; SRMR = Standardized Root Mean Square Residual; GFI = Goodness of Fit; AGFI = Adjusted Goodness of Fit; NNFI = Non-normed Fit Index; CFI = Comparative Fit Index.

Supplementary Table 4. Associations of anemia and renal function measures with the risk of DR based on observed data[§] (n = 1070)

Variables	N	NPDR(n=276)			PDR(n=80)		
		n (%)	Adjusted OR (95% CI)*	P-value	n (%)	Adjusted OR (95% CI)*	P-value
Anemia [†]							
-	932	231(24.8)	ref		52(5.6)	ref	
+	138	45(32.6)	1.73(1.09, 2.74)	0.020	28(20.3)	4.01(2.16, 7.44)	< 0.001
DKD severity [‡]							
low/medium	843	205(24.3)	ref		45(5.3)	ref	
high/very high	227	71(31.3)	1.38(0.95, 2.01)	0.089	35(15.4)	2.51(1.44, 4.39)	0.001
eGFR [‡]							
≥ 60	1026	263(25.6)	ref		70(6.8)	ref	
< 60	44	13(29.6)	1.14(0.51, 2.51)	0.752	10(22.7)	2.34(0.90, 6.08)	0.083
UACR [‡]							
≤ 300	855	207(24.2)	ref		45(5.3)	ref	
> 300	215	69(32.1)	1.49(1.02, 2.18)	0.040	35(16.3)	2.78(1.59, 4.85)	< 0.001

Abbreviation: DR = diabetic retinopathy; NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; DKD = diabetic kidney disease; eGFR = estimated glomerular filtration rate; UACR = urine albumin-to-creatinine ratio. * Adjusted for age, sex, duration of diabetes, BMI, HbA1c, hypertension, hyperlipidemia, medication on diabetes. † Additionally adjusted for DKD; ‡ Additionally adjusted for anemia; §These 4 variables were analyzed separately. || Units of variables: eGFR in ml/min/1.73m²; UACR in mg/g.

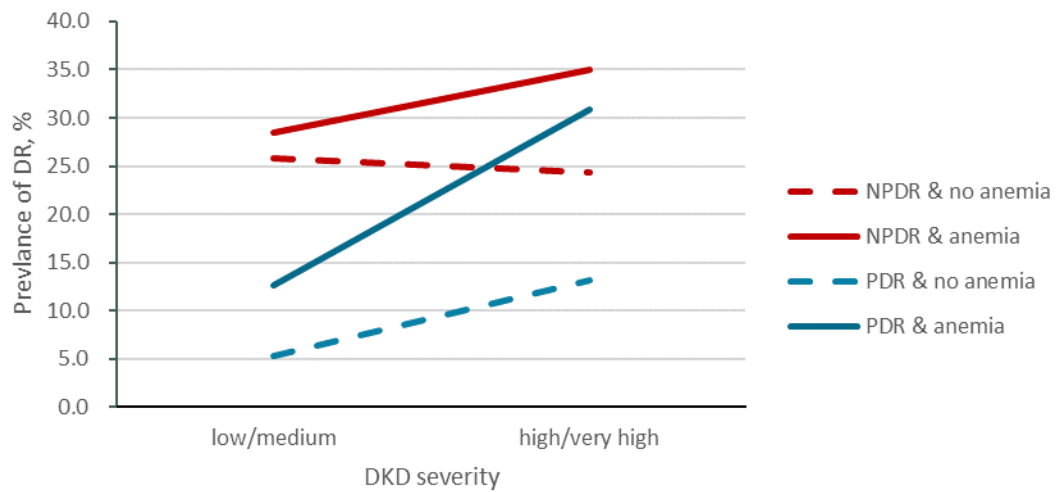
Supplementary Table 5. The joint effects of anemia and renal function indexes with the risk of DR based on observed data without imputation[§] (n = 1070)

Variables [‡]		N	NPDR (n=276)			PDR (n=80)		
			n (%)	Adjusted OR (95% CI)*	P-value [§]	n (%)	Adjusted OR (95% CI)*	P-value [§]
DKD	anemia							
low/medium	-	775	188(24.3)	ref		37(4.8)	ref	
high/very high	-	157	43(27.4)	1.20(0.79, 1.83)	0.393	15(9.6)	2.23(1.14, 4.36)	0.019
low/medium	+	68	17(25.0)	1.28(0.69, 2.38)	0.428	8(11.8)	3.21(1.33, 7.76)	0.010
high/very high	+	70	28(40.0)	3.15(1.66, 5.98)	< 0.001	20(28.6)	12.27(5.62, 26.76)	< 0.001
P for trend					0.001			< 0.001
eGFR	anemia							
≥ 60	-	914	228(25.0)	ref		50(5.5)	ref	
< 60	-	18	3(16.7)	0.65(0.17, 2.49)	0.533	2(11.1)	2.87(0.58, 14.18)	0.195
≥ 60	+	112	35(31.3)	1.70(1.05, 2.76)	0.032	20(17.9)	4.63(2.43, 8.83)	< 0.001
< 60	+	26	10(38.5)	2.80(1.03, 7.61)	0.044	8(30.8)	11.62(3.76, 35.88)	< 0.001
P for trend					0.007			< 0.001
UACR	anemia							
≤ 300	-	785	188(24.0)	ref		37(4.7)	ref	
> 300	-	147	43(29.3)	1.37(0.89, 2.10)	0.149	15(10.2)	2.49(1.27, 4.88)	0.008
≤ 300	+	70	19(27.1)	1.44(0.79, 2.63)	0.229	8(11.4)	3.23(1.34, 7.81)	0.009
> 300	+	68	26(38.2)	3.00(1.56, 5.74)	0.001	20(29.4)	12.42(5.70, 27.07)	< 0.001
P for trend					0.001			< 0.001

Abbreviation: DR = diabetic retinopathy; NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; DKD = diabetic kidney disease; eGFR = estimated glomerular filtration rate; UACR = urine albumin-to-creatinine ratio. * Adjusted for age, sex, duration of diabetes, BMI, HbA1c, hypertension, hyperlipidemia, medication on diabetes. † The 4 variables were analyzed separately. ‡ Units of variables: SCr in μmol/L; BUN in mmol/L; eGFR in ml/min/1.73m²; UACR in mg/g. § All p for multiplicative interaction > 0.05.

Interaction

Using the PDR & no anemia as the imaging reference line, the PDR & anemia is not completely parallel to the PDR & no anemia. When patients with both high risk of DKD and anemia, the prevalence of PDR is greater than the sum of prevalence in patients only with anemia or high DKD risk.



Supplementary Figure 4. Prevalence of DR by DKD severity and anemia. Abbreviation: DR = diabetic retinopathy; NPDR = non-proliferative diabetic retinopathy; PDR = proliferative diabetic retinopathy; DKD = diabetic kidney disease