# Appendix to "A BMI-based Cross-classification Approach for the Assessment of Prognostic Factors in Chronic Kidney Disease Progression"

This appendix provides further methodological detail, results, discussion, references, supplementary figures, and supplementary tables for the main paper.

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#### Research in context

### Evidence before this study

Stratification analysis with one attribute is commonly performed in conventional subgroup analyses, but there have been few reports on cross-classification analysis using multiple attributes. As a prognostic factor, body mass index (BMI), which has a non-linear association with kidney outcome, is an ideal attribute for cross classification. We searched the terms "cross-classification", "body mass index" and "chronic kidney disease" on PubMed databases with no language restrictions but found no matching published original research articles.

### Added value of this study

Cross-classification is a method that improves subgroup analysis by adding secondary attributes to the conventional attributes. In medical settings where a variety of individuals are being treated, investigations based on cross-classification that can assess multiple attributes simultaneously can produce results that closely reflect real clinical experiences. Cross-classification is expected to be a useful method in the practice of patient-centered medicine. The BMI-based cross-classification method is based on the ideology of Oriental medicine of treating according to a patient's body size, so it provides a link between Oriental medicine and Western medicine. To the best of our knowledge, this is the first study to conduct a detailed investigation of prognostic factors associated with chronic kidney disease (CKD) progression using BMI-based cross-classification.

### Implications of all available evidence

Although currently used clinical practice guidelines for renal anemia and serum phosphorous have no set target serum hemoglobin and phosphate values according to the cross-classification of sex and BMI, our BMI-based cross-classification showed differences in cut-off values for serum hemoglobin and phosphorous. Evidence of treatment in elderly patients with diabetes is deficient, especially in terms of glucose lowering. Our cross-classification method demonstrated that BMI should be considered in the treatment of elderly diabetic patients with CKD. Decreased urinary potassium excretion has been reported as a risk factor for CKD progression in patients with CKD stages 1–3, but there have been few reports on patients with CKD stages 4–5. In the present study, decreased urinary potassium excretion was detected as a prognostic factor in a "BMI < 25, CKD stages 4–5" cohort. Currently used clinical practice guidelines for CKD patients with hypertension do not consider PP × HR. The present study identified PP × HR, which reflects pulsatile stress as a prognostic predictor for CKD progression. These results indicate that there may be a substantial benefit associated with a change in clinical practice guidelines for CKD patients by using BMI-based cross-classification.

### **Supplementary Results**

### Characteristics of diabetic patients in the subcohort of "BMI < 25, Age ≥ 65"

Relating to diabetic patients in the subcohort of "BMI < 25, Age  $\geq$  65", who showed similar Kaplan—Meier survival curve to those of Non-DM patients, the characteristics at baseline of the subcohorts stratified by age = 65 years in the cohort of "BMI < 25, DM" and that stratified by BMI = 25 kg/m² in the cohort of "Age  $\geq$ 65 years, DM" are shown in Appendix Tables (Appendix Table 4). In the subcohort of "BMI < 25, although their baseline HbA1c (6.54% vs 6.59%) and prognostic factors including eGFR (27.6 vs 27.3 ml/min/1.73m²) were not significantly different with young DM patients, elderly DM patients had lower urinary albumin excretion (UACR: 513.3 vs 921.8 mg/g Cre) and had higher renal survival rate (4 years survival rate: 70.7% vs 56.1%) than young DM patients (Fig. 9B).

### Characteristics of e24hUK in correlation diagrams

As shown in Appendix Fig. 5, an e24hUK was significantly positively correlated with eGFR (r = 0.33, p < 0.0001) and BMI (r = 0.28, p < 0.0001), slightly negatively correlated with age, and slightly positively correlated with SBP.

#### Supplementary analyses

With consideration for accessibility in clinical settings, the prognostic predictors identified in the final Cox regression analyses model were dichotomized using cut-off values determined by time- ROC curves. The prognostic effects of CKD progression were confirmed using the Kaplan–Meier method (Appendix Figs. 7–8) and DOR (Appendix Fig. 9, Appendix Table 8) for all cohorts.

The cut-off values for the total cohort were utilized in the Kaplan–Meier analyses (<u>Appendix Figs. 7–8</u>), while those for the subcohorts were utilized in the DOR analyses (<u>Appendix Fig. 9</u>). Representative cut-off values according to the ROC curve were 10.6 (female, BMI <25), 11.2 (female, BMI ≥25), 11.7 (male, BMI <25), and 12.8 (male, BMI ≥25) for hemoglobin (g/dL) (<u>Appendix Fig. 9C, left side</u>); and 4.0 (female) and 3.5 (male) for phosphorus (mg/dL) (<u>Appendix Fig. 9C, right side</u>).

## Supplementary analyses of PP×HR and e24hUK (representative cut-off values and DOR)

In the total cohort, the cut-off value of PP × HR and e24hUK was 4216 mmHg-bpm (DOR, 2.38) and 36.8 mEq/day (DOR, 1.79), respectively (<u>Appendix Fig. 9A</u>). DOR of PP × HR had a maximum of 3.58 at the cut-off value of 4253 mmHg-bpm in the "BMI < 25, CKD Stage 3" subcohort (<u>Appendix Fig. 9A</u>, <u>left side</u>). The DOR of e24hUK had a maximum of 2.60 at the cut-off value of 36.7 mEq/day in the "BMI < 25, CKD stages 4–5" subcohort (<u>Appendix Fig. 9A</u>, right side).

### **Supplementary Discussion:**

### Primary analyses regarding e24hUK

Although the e24hUK cut-off value of 36.8 mEq/day determined in the present study is similar to that used in previous studies, interpretations should be made cautiously, owing to the small AUC. Nonetheless, e24hUK was identified as a prognostic factor in the "BMI <25, CKD stages 4–5" subcohort (Fig. 15, top right), with a cut-off value of 39.1 mEq/day, which corresponds to 1.53 g/day (Appendix Fig. 9A, right side). Reportedly, a diet rich in fruits and leafy green vegetables is associated with better renal outcomes [1], and the Kidney Disease Outcomes Quality Initiative recommends a dietary potassium intake of 2–4 g/day in patients with CKD stages 3–4 [2]. Decreased urinary potassium excretion has been reported as a risk factor for CKD progression in patients with CKD stages 1–3 [1, 3]; however, reports on patients with CKD stages 4–5 are lacking. As the present study is observational in nature, the results must be interpreted carefully. Nevertheless, there is a possibility that low urinary potassium levels are a marker of poor nutritional status, renal tubular function, or excessive dietary restrictions. The results of the present study indicate that patients with CKD and low urinary potassium excretion should be treated carefully.

### Supplementary analyses

From a clinical point of view, our BMI-based cross-classification analysis demonstrated differences in the appropriate cut-off values for renal prognostic factors. Especially, the difference in the hemoglobin cut-off value between males with BMI ≥25 (12.8 g/dL) and females with BMI <25 (10.6 g/dL) was impressive (Appendix Fig. 9C, left side). Generally, obese patients have high hemoglobin, but it remains unclear whether renal anemia should be treated in obese CKD patients with high hemoglobin. Similarly, the difference in the serum phosphorus cut-off value between males (3.5 mg/dL) and females (4.0 mg/dL) was impressive (Appendix Fig. 9C, right side). Females generally have higher serum phosphorus; thus, it may be necessary to set control targets according to sex. Current clinical practice guidelines for renal anemia [4, 5] and serum phosphorous [6] do not set any targets according to the cross-classification of sex and BMI. Further prospective investigations are expected for the evaluation of hemoglobin and phosphorous in patients with CKD.

### **Supplementary References**

- Dunkler D, Dehghan M, Teo KK, Heinze G, Gao P, Kohl M, Clase CM, Mann JF, Yusuf S, Oberbauer R: Diet and kidney disease in high-risk individuals with type 2 diabetes mellitus. JAMA internal medicine 2013;173:1682-1692.
- 2 KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. Am J Kidney Dis 2012;60:850-886.
- Smyth A, Dunkler D, Gao P, Teo KK, Yusuf S, O'Donnell MJ, Mann JF, Clase CM: The relationship between estimated sodium and potassium excretion and subsequent renal outcomes. Kidney international 2014;86:1205-1212.
- 4 Chapter 1: Diagnosis and evaluation of anemia in CKD. Kidney international supplements 2012;2:288-291.
- 5 Drueke TB, Parfrey PS: Summary of the KDIGO guideline on anemia and comment: reading between the (guide)line(s). Kidney international 2012;82:952-960.
- 6 KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney international Supplement 2009:S1-130.

Recruited 
$$(2007 - 2013)$$
 n = 3,087

Excluded at baseline (n = 121)

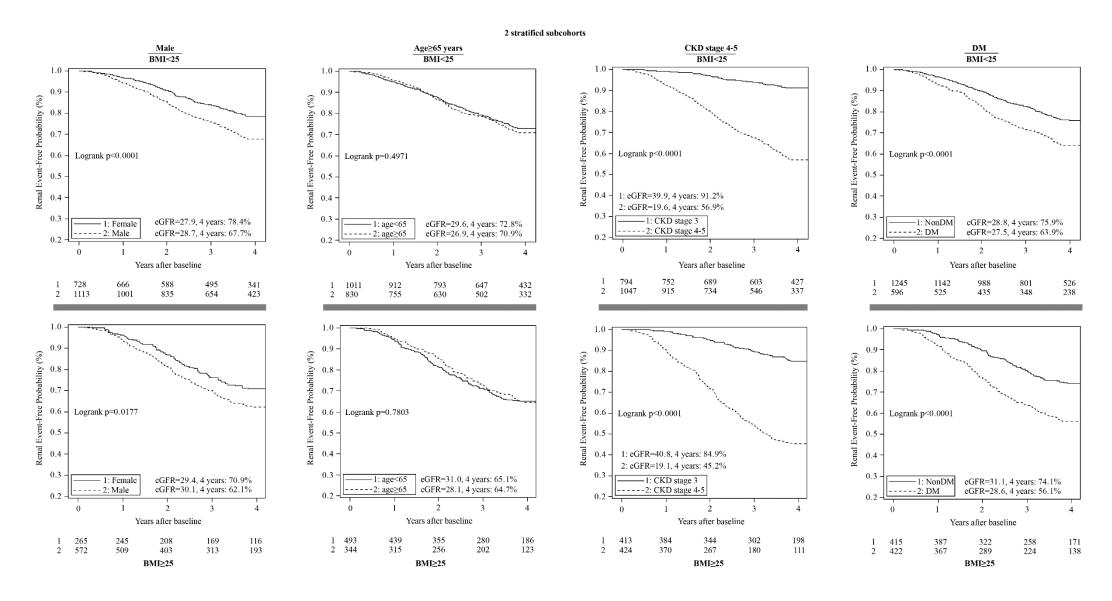
- 59 Withdrew consent
- 27 Fell under the exclusion criteria
- 25 No baseline data available
- 5 Attending-Physician's discretion
- 4 Lost to follow up
- 1 Deceased

Excluded from the present study (n = 288) 288 Without baseline BMI data

Enrolled n = 2,678

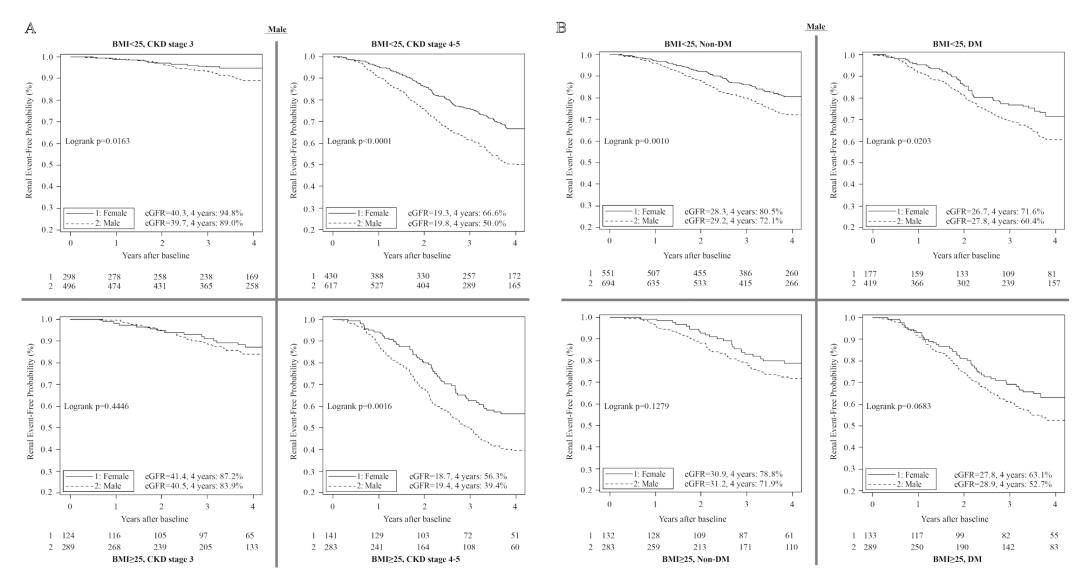
# Appendix Fig. 2: Kaplan–Meier survival curves for renal prognosis stratified by sex, age, CKD stage, and DM in BMI-based two stratified subcohorts (Upper side: BMI < 25 kg/m², Lower side: BMI ≥ 25 kg/m²)

BMI = body mass index. eGFR = estimated glomerular filtration rate. CKD = chronic kidney disease. DM = diabetes mellitus.



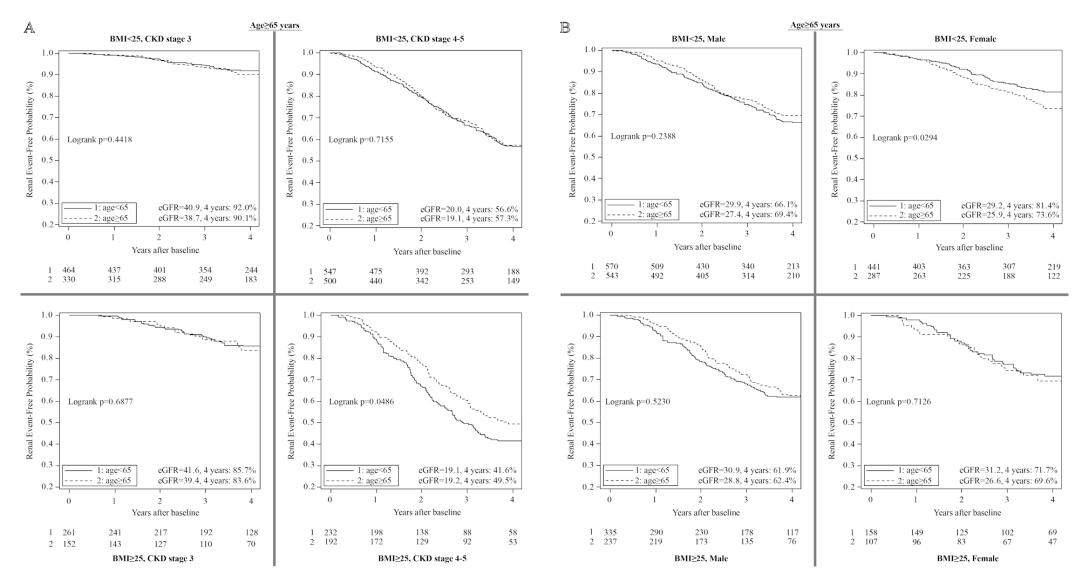
# Appendix Fig. 3A: Kaplan-Meier survival curves for renal prognosis stratified by sex in BMI-based four cross-classified subcohorts

BMI = body mass index. eGFR = estimated glomerular filtration rate. CKD = chronic kidney disease. DM = diabetes mellitus.



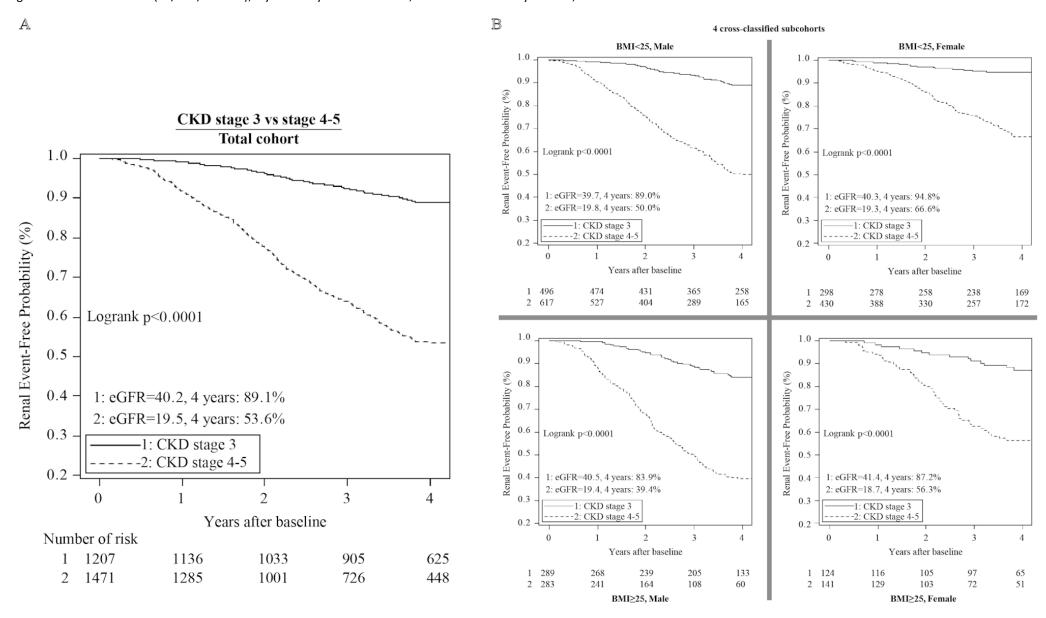
# Appendix Fig. 3B: Kaplan-Meier survival curves for renal prognosis stratified by age in BMI-based four cross-classified subcohorts

BMI = body mass index. eGFR = estimated glomerular filtration rate. CKD = chronic kidney disease.



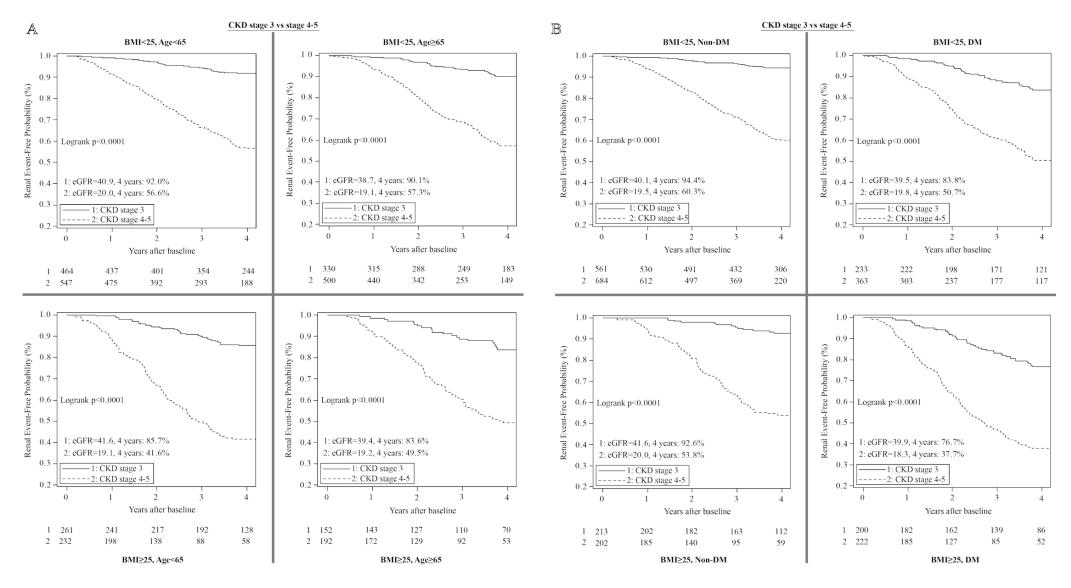
## Appendix Fig. 3C-1: Kaplan-Meier survival curves stratified by CKD stage

Kaplan–Meier survival curves stratified by CKD stage are shown for the total cohort (a) and four BMI-based cross-classified subcohorts (b). BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate; CKD = chronic kidney disease; DM = diabetes mellitus



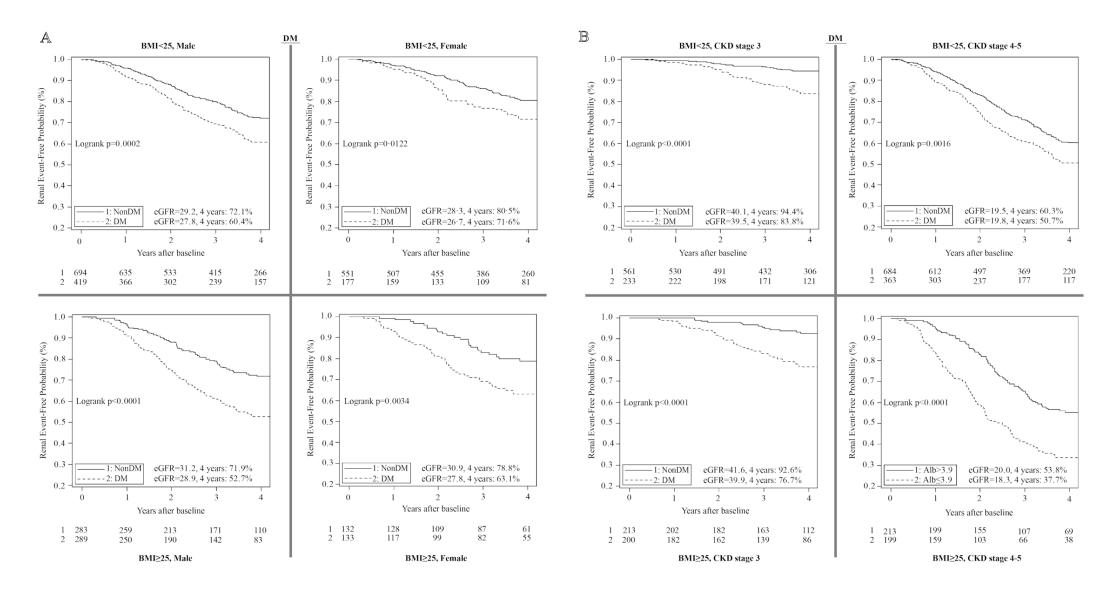
# Appendix Fig. 3C-2: Kaplan-Meier survival curves for renal prognosis stratified by CKD stage in BMI-based four cross-classified subcohorts

BMI = body mass index. eGFR = estimated glomerular filtration rate. CKD = chronic kidney disease. DM = diabetes mellitus.



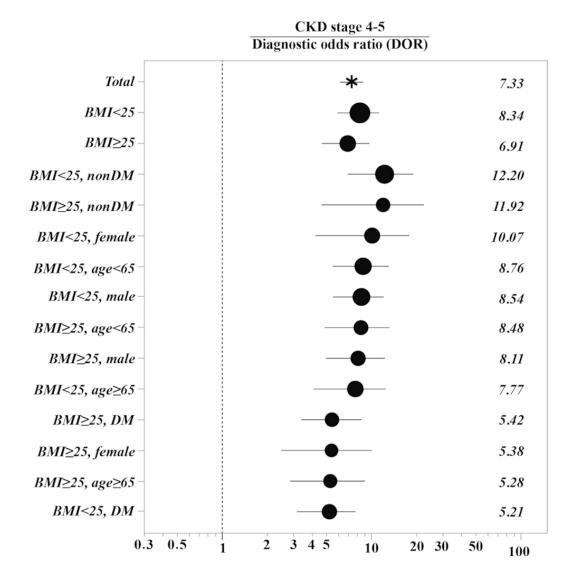
# Appendix Fig. 3D: Kaplan-Meier survival curves for renal prognosis stratified by DM in BMI-based four cross-classified subcohorts

BMI = body mass index. eGFR = estimated glomerular filtration rate. CKD = chronic kidney disease. DM = diabetes mellitus.



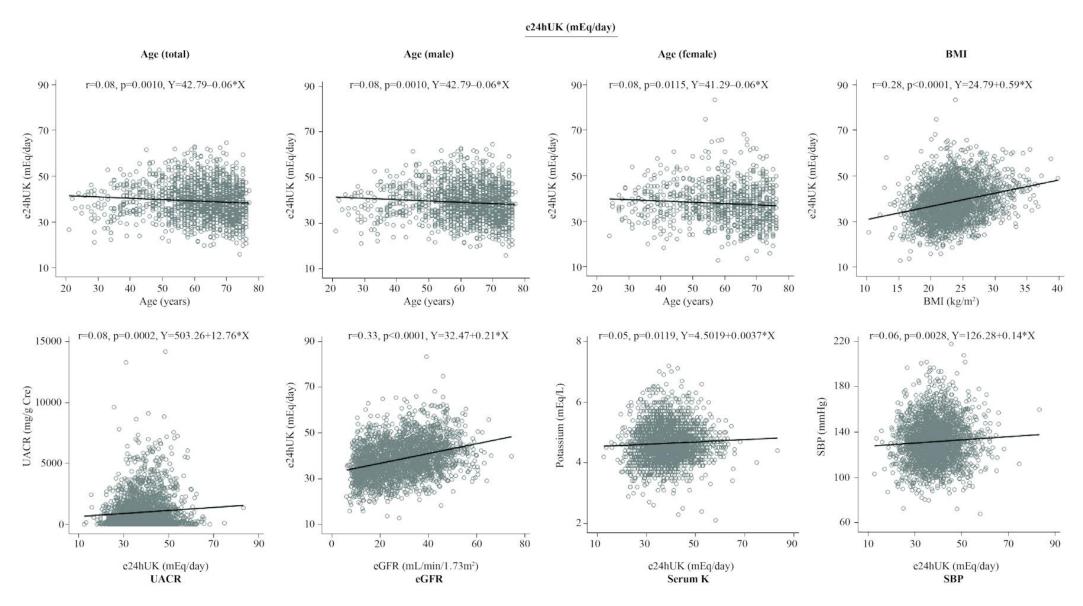
# Appendix Fig. 4: Diagnostic odds ratios of CKD stage 4–5 according to subcohort

A summary of Appendix Table 5 is depicted. Diagnostic odds ratios (DORs) of CKD stage 4–5 for a decline in estimated glomerular filtration rate by  $\geq$  50% from baseline or end-stage renal disease during the follow-up examination period are shown according to subcohort. BMI = body mass index; CKD = chronic kidney disease; DM = diabetes mellitus



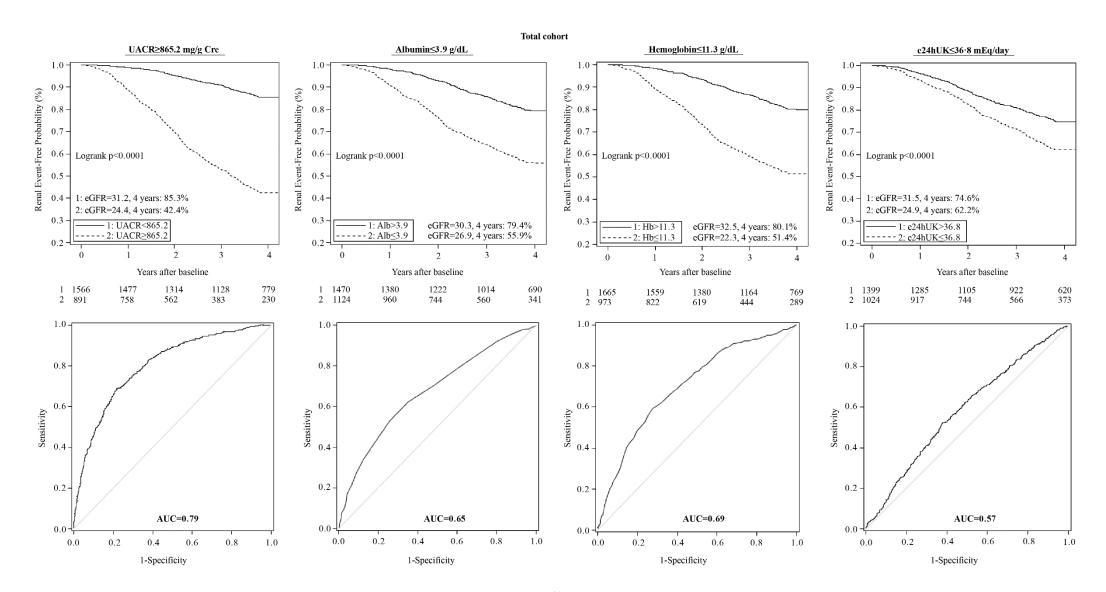
# Appendix Fig. 5: Relationship between the estimated 24-hour urinary potassium excretion (e24hUK) with baseline variables.

The analyses in relation to age were stratified by sex. BMI = body mass index. UACR = urine albumin-to-creatinine ratio. eGFR = estimated glomerular filtration rate. Serum K = serum potassium. SBP = systolic blood pressure.



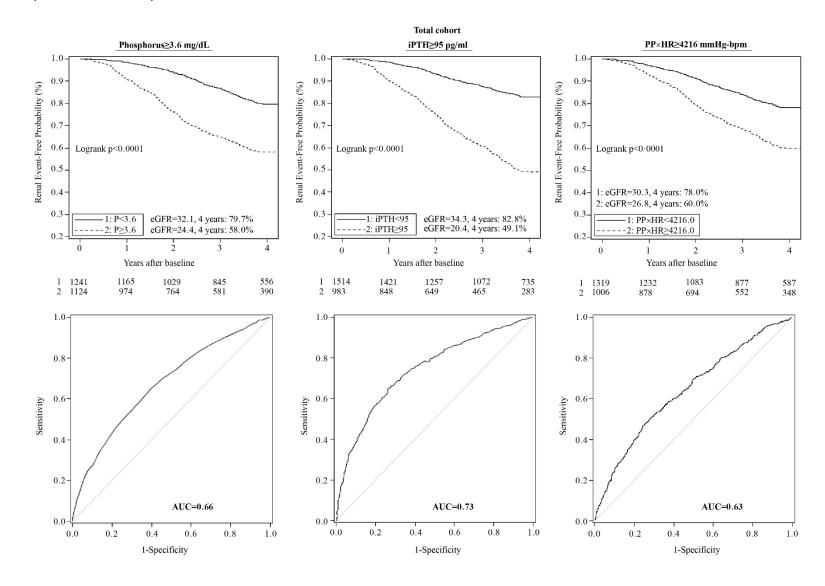
# Appendix Fig. 6A: ROC analyses to identify the optimal cut-off values in the total cohort for predicting renal outcome (Lower side), and Kaplan–Meier survival curves stratified by the cut-off value in the total cohort (Upper side)

Cut-off values in the total cohort for predicting an eGFR decline by ≥ 50% from baseline or ESRD that requires renal replacement therapy during the follow-up examination period were examined by ROC analyses. Area under the ROC curves (AUCs) are described in the bottom of the figures respectively. Kaplan—Meier survival curves were stratified by the cut-off value in the total cohort for identified prognostic factors in multivariate Cox analyses in the total cohort. eGFR = estimated glomerular filtration rate. UACR = urine albumin-to-creatinine ratio. e24hUK = estimated 24-hour urinary potassium excretion.



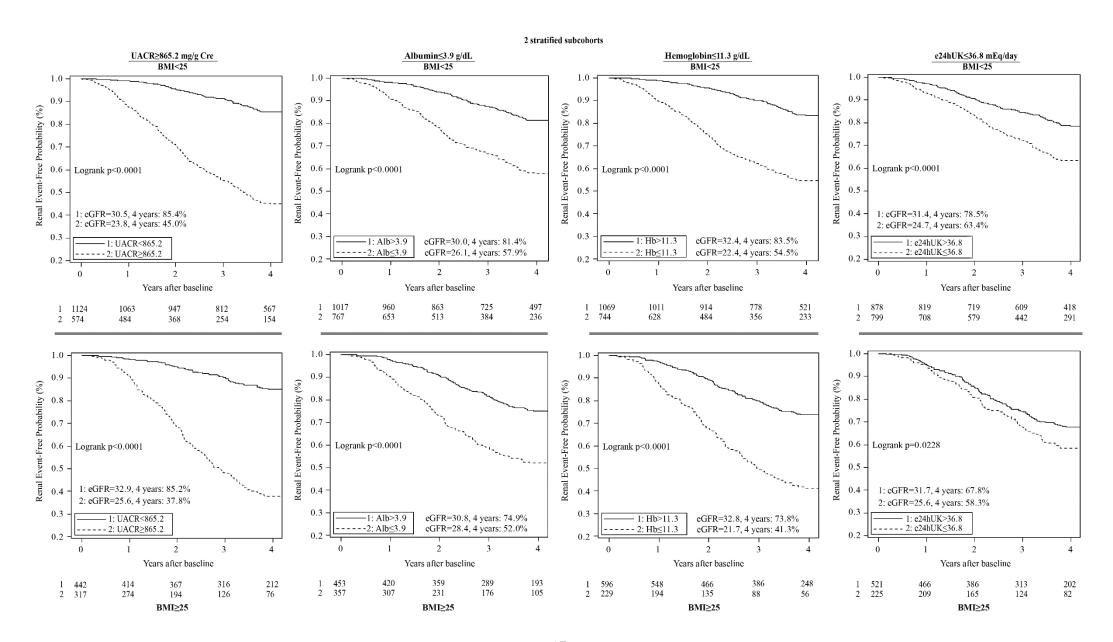
# Appendix Fig. 6B: ROC analyses to identify the optimal cut-off values in the total cohort for predicting renal outcome (Lower side), and Kaplan–Meier survival curves stratified by the cut-off value in the total cohort (Upper side)

Cut-off values in the total cohort for predicting an eGFR decline by ≥ 50% from baseline or ESRD that requires renal replacement therapy during the follow-up examination period were examined by ROC analyses. Area under the ROC curves (AUCs) are described in the bottom of the figures respectively. Kaplan—Meier survival curves were stratified by the cut-off value in the total cohort for identified prognostic factors in multivariate Cox analyses in the total cohort. eGFR = estimated glomerular filtration rate. iPTH = intact parathyroid hormone. PP×HR = pulse pressure × heart rate product.



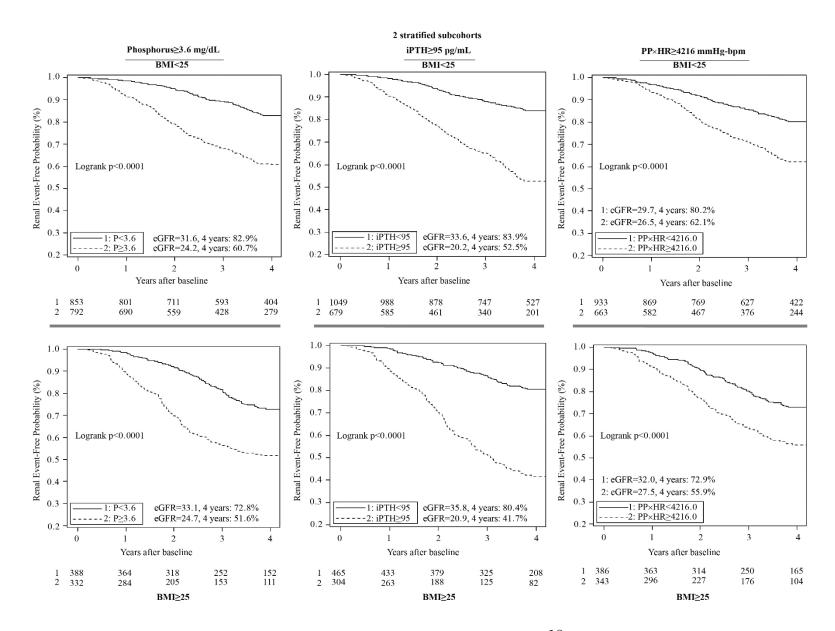
# Appendix Fig. 7A: Kaplan–Meier survival curves for renal prognosis stratified by the cut-off values of renal prognostic factors in the total cohort, in BMI-based two stratified subcohorts (Upper side: BMI < 25 kg/m², Lower side: BMI ≥ 25 kg/m²)

BMI = body mass index. eGFR = estimated glomerular filtration rate. UACR = urine albumin-to-creatinine ratio. e24hUK = estimated 24-hour urinary potassium excretion.



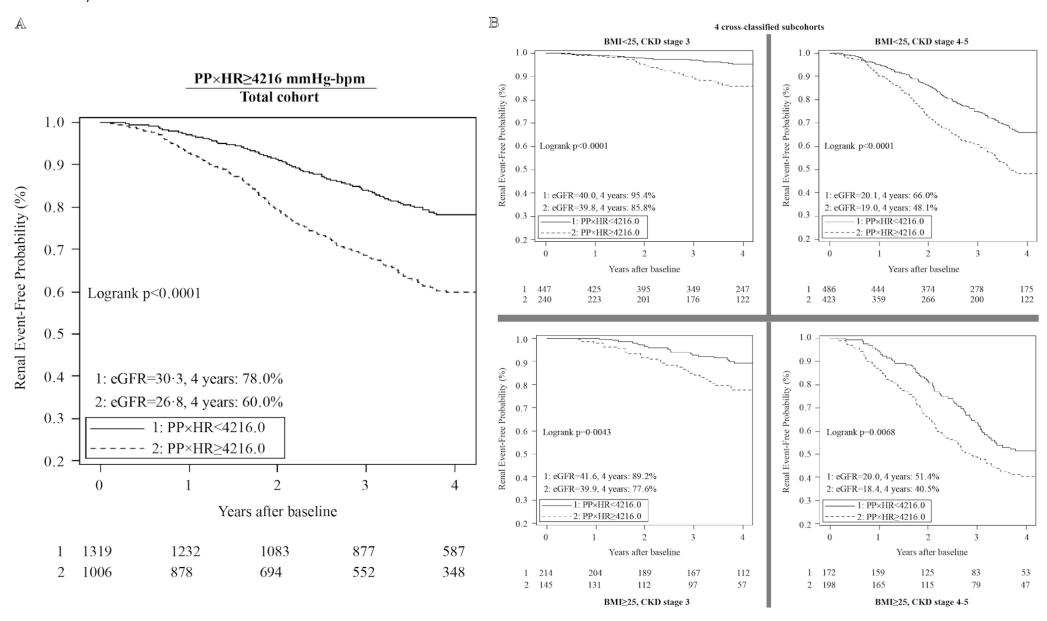
Appendix Fig. 7B: Kaplan—Meier survival curves for renal prognosis stratified by the cut-off values of renal prognostic factors in the total cohort, in BMI-based two stratified subcohorts (Upper side: BMI < 25 kg/m², Lower side: BMI ≥ 25 kg/m²)

BMI = body mass index. eGFR = estimated glomerular filtration rate. iPTH = intact parathyroid hormone. PP × HR = pulse pressure × heart rate product.



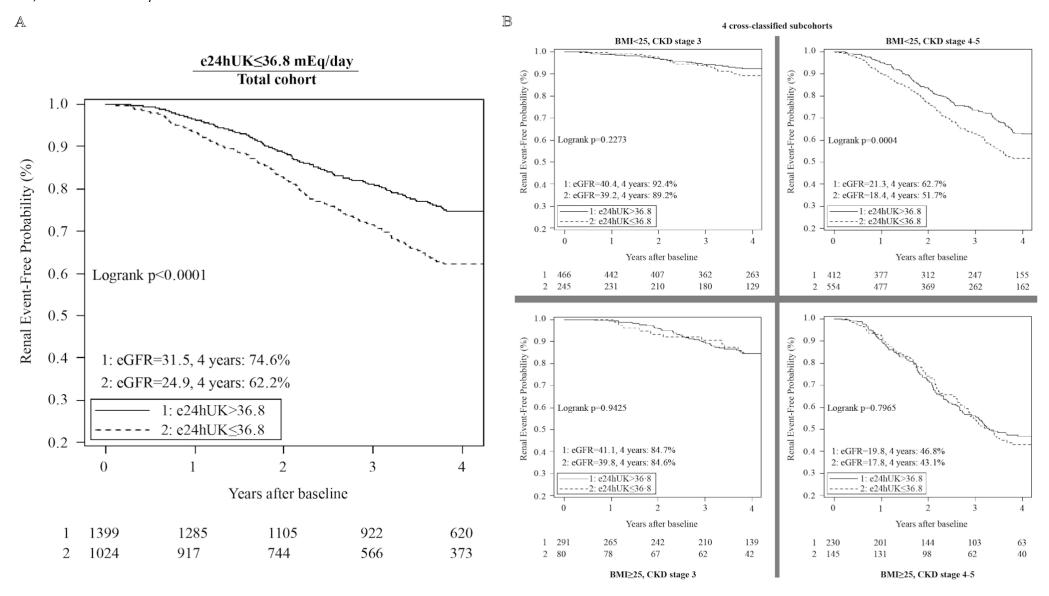
# Appendix Figure 8A: Kaplan-Meier survival curves stratified by the PP × HR cut-off value

Kaplan–Meier survival curves for renal prognosis stratified by the PP × HR cut-off value (determined using the total cohort) are shown for the total cohort (A) and four BMI-based cross-classified subcohorts (B). PP × HR = pulse pressure × heart rate product; BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m<sup>2</sup>); 4 years = 4-year survival rate; CKD = chronic kidney disease



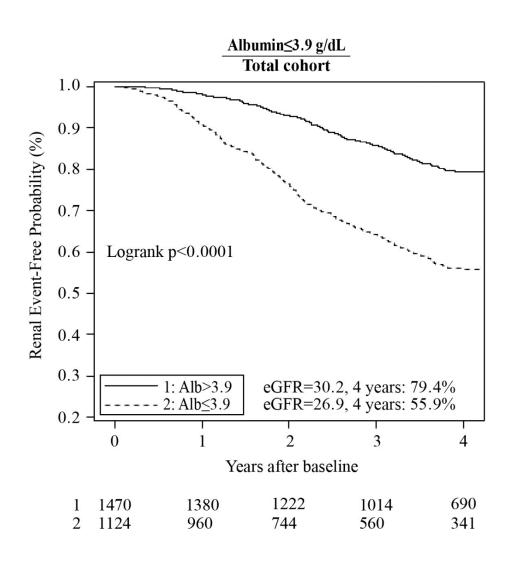
## Appendix Figure 8B: Kaplan-Meier survival curves stratified by the e24hUK cut-off value

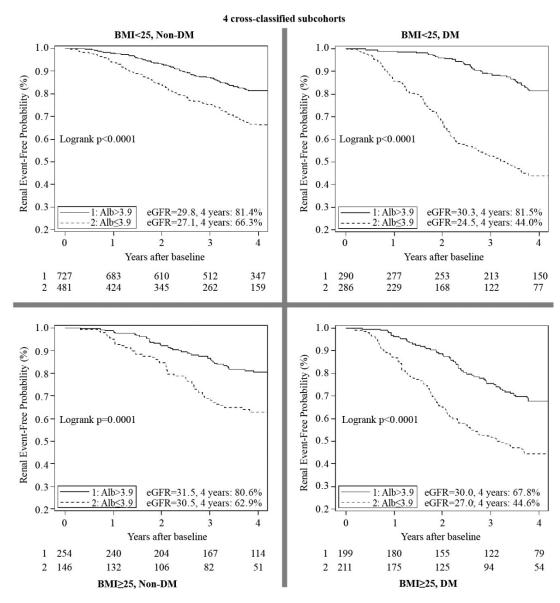
Kaplan—Meier survival curves for renal prognosis stratified by the e24hUK cut-off value (determined using the total cohort) are shown for the total cohort (A) and four BMI-based cross-classified subcohorts (B). e24hUK = estimated 24-hour urinary potassium excretion; BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate; CKD = chronic kidney disease



# Appendix Fig. 8C: Kaplan-Meier survival curves stratified by the serum albumin cut-off value

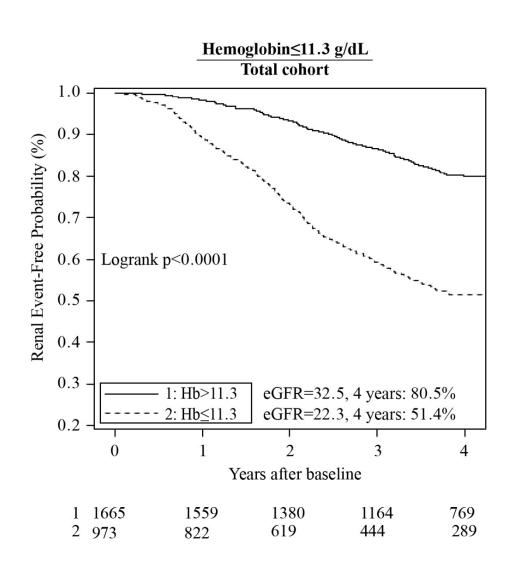
Kaplan—Meier survival curves for renal prognosis stratified by the serum albumin cut-off value (determined using the total cohort) are shown for the total cohort (Left side) and four BMI-based cross-classified subcohorts (Right side). BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate; DM = diabetes mellitus

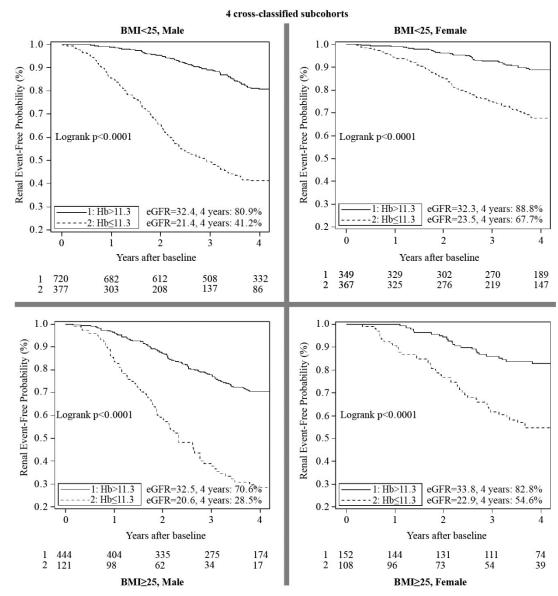




### Appendix Fig. 8D: Kaplan-Meier survival curves stratified by the hemoglobin cut-off value

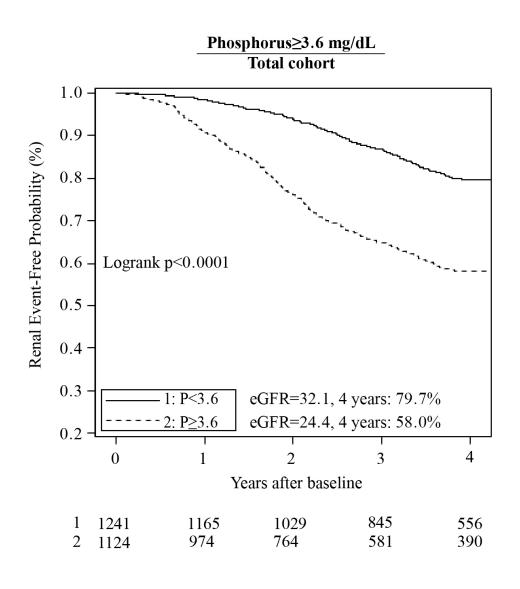
Kaplan—Meier survival curves for renal prognosis stratified by the hemoglobin cut-off value (determined using the total cohort) are shown for the total cohort (Left side) and four BMI-based cross-classified subcohorts (Right side). BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate

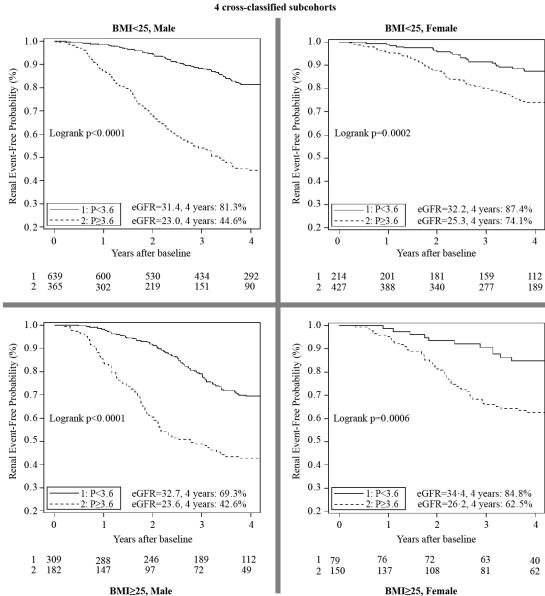




# Appendix Fig. 8E: Kaplan-Meier survival curves stratified by the serum phosphorous cut-off value

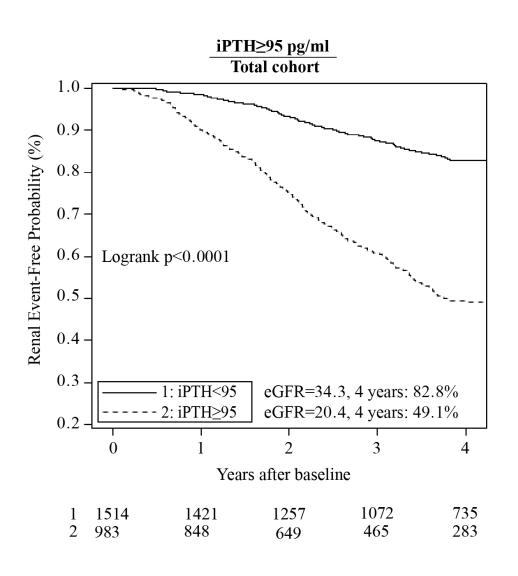
Kaplan—Meier survival curves for renal prognosis stratified by the serum phosphorous cut-off value (determined using the total cohort) are shown for the total cohort (Left side) and four BMI-based cross-classified subcohorts (Right side). BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate

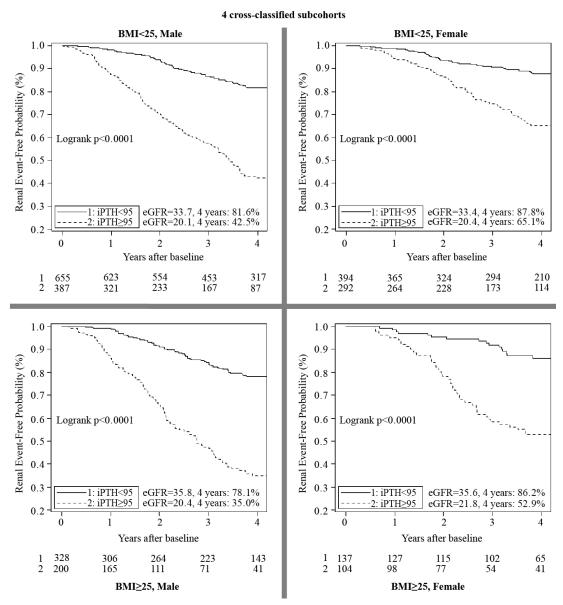




### Appendix Fig. 8F: Kaplan-Meier survival curves stratified by the iPTH cut-off value

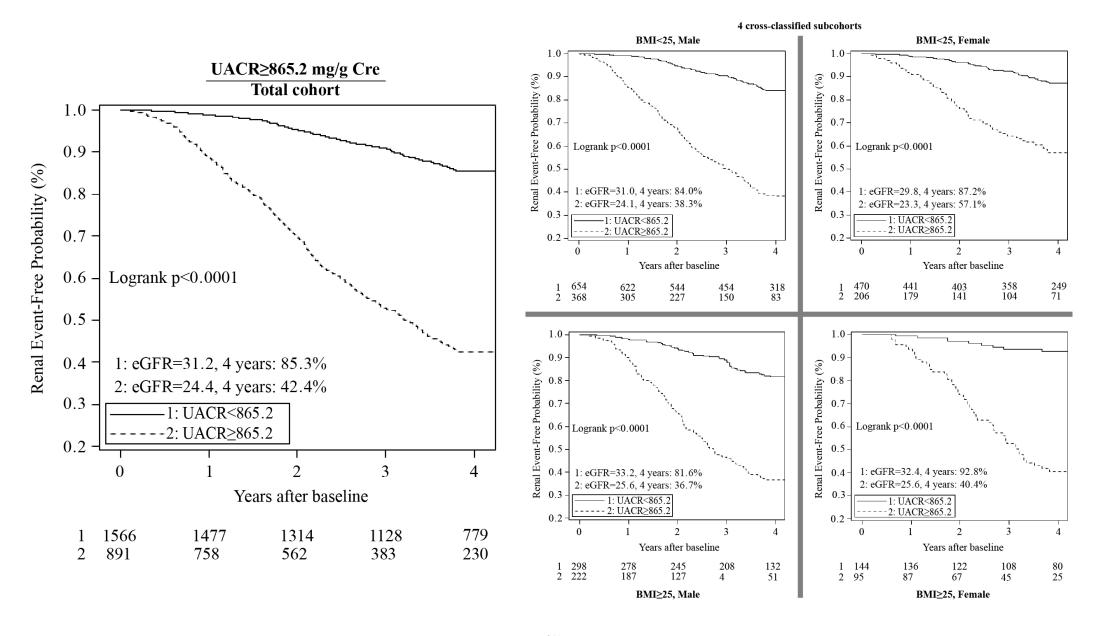
Kaplan—Meier survival curves for renal prognosis stratified by the iPTH cut-off value (determined using the total cohort) are shown for the total cohort (Left side) and four BMI-based four cross-classified subcohorts (Right side). BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate





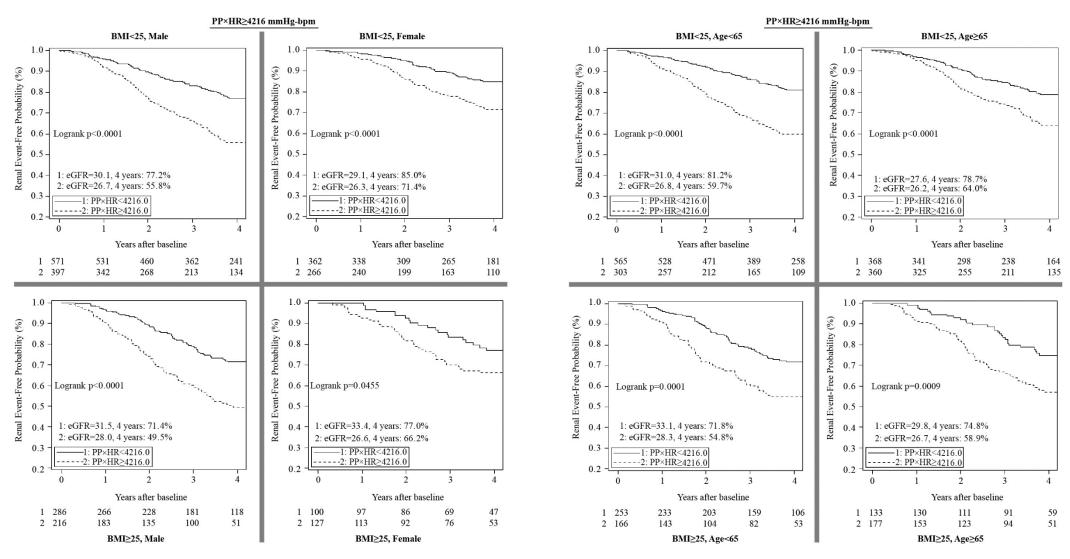
## Appendix Fig. 8G: Kaplan-Meier survival curves stratified by the UACR cut-off value

Kaplan–Meier survival curves for renal prognosis stratified by the UACR cut-off value (determined using the total cohort) for the total cohort (Left side) and four BMI-based four cross-classified subcohorts (Right side). BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate



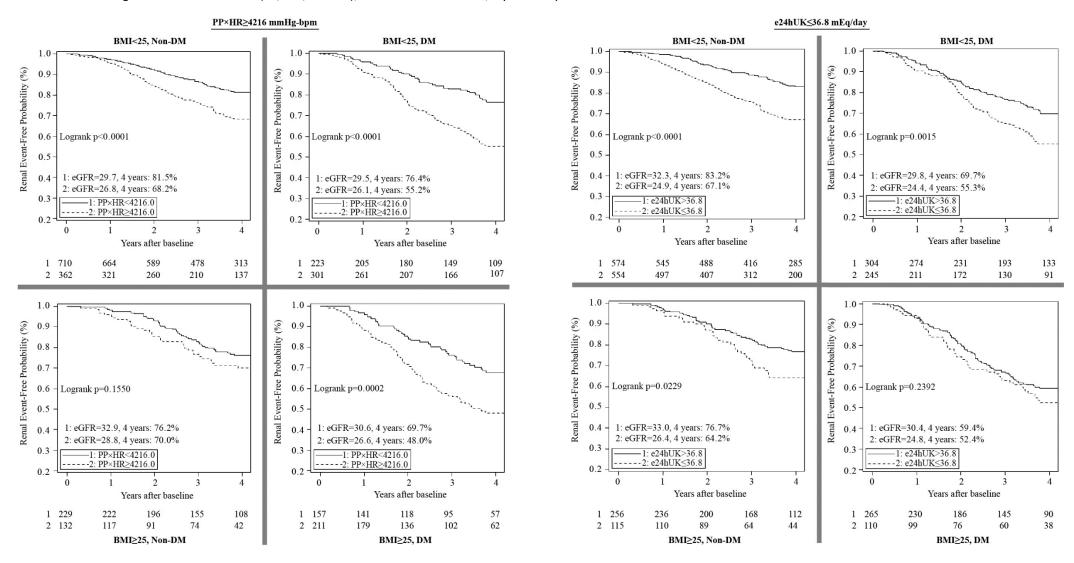
### Appendix Fig. 8H: Kaplan-Meier survival curves stratified by the PP × HR cut-off value

Kaplan—Meier survival curves for renal prognosis stratified by the PP × HR cut-off value (determined using the total cohort) are shown four BMI-based cross-classified subcohorts. PP × HR = pulse pressure × heart rate product; BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m<sup>2</sup>); 4 years = 4-year survival rate



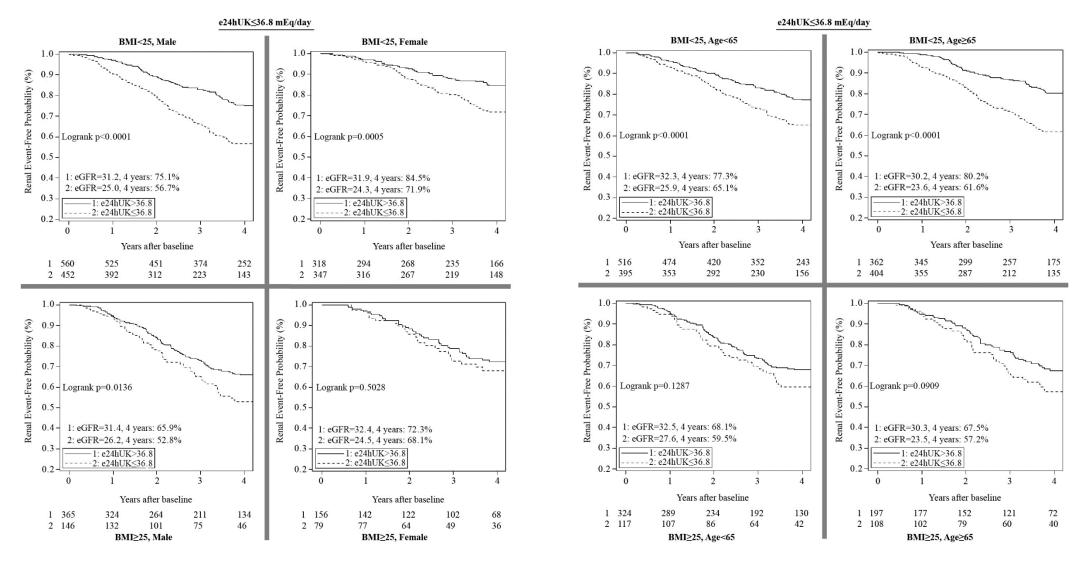
## Appendix Fig. 81: Kaplan–Meier survival curves stratified by the PP × HR cut-off value (Left side) and the e24hUK cut-off value (Right side)

Kaplan—Meier survival curves for renal prognosis stratified by the PP × HR cut-off value (determined using the total cohort) and e24hUK cut-off value (determined using the total cohort) are shown for four BMI-based cross-classified subcohorts. PP × HR = pulse pressure × heart rate product; e24hUK = estimated 24-hour urinary potassium excretion; BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m<sup>2</sup>); DM = diabetes mellitus; 4 years = 4-year survival rate



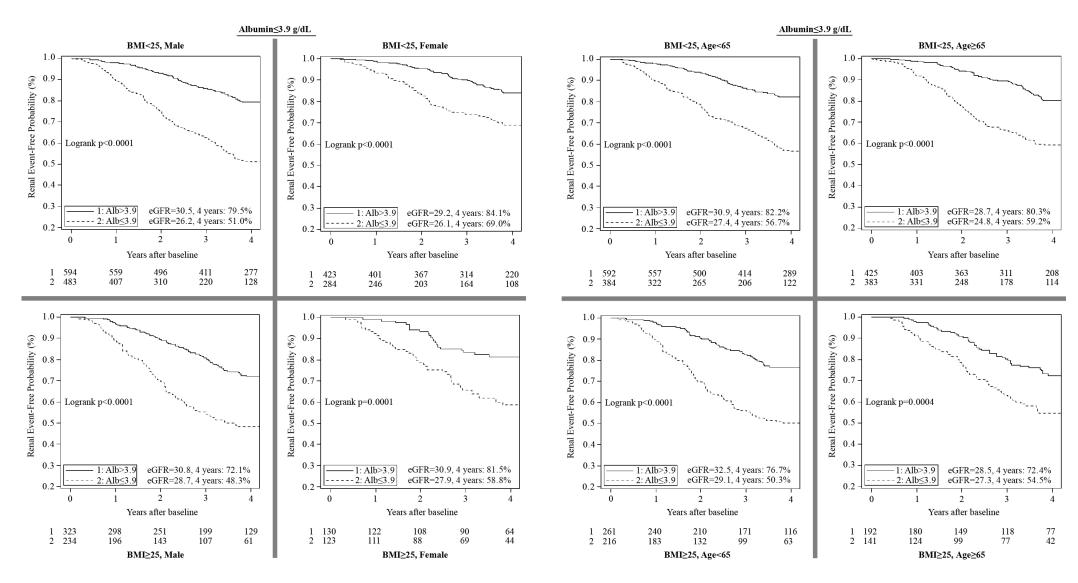
### Appendix Fig. 8J: Kaplan-Meier survival curves stratified by the e24hUK cut-off value

Kaplan—Meier survival curves for renal prognosis stratified by the e24hUK cut-off value (determined using the total cohort) are shown for four BMI-based cross-classified subcohorts. e24hUK = estimated 24-hour urinary potassium excretion; BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate



### Appendix Fig. 8K: Kaplan-Meier survival curves stratified by the serum albumin cut-off value

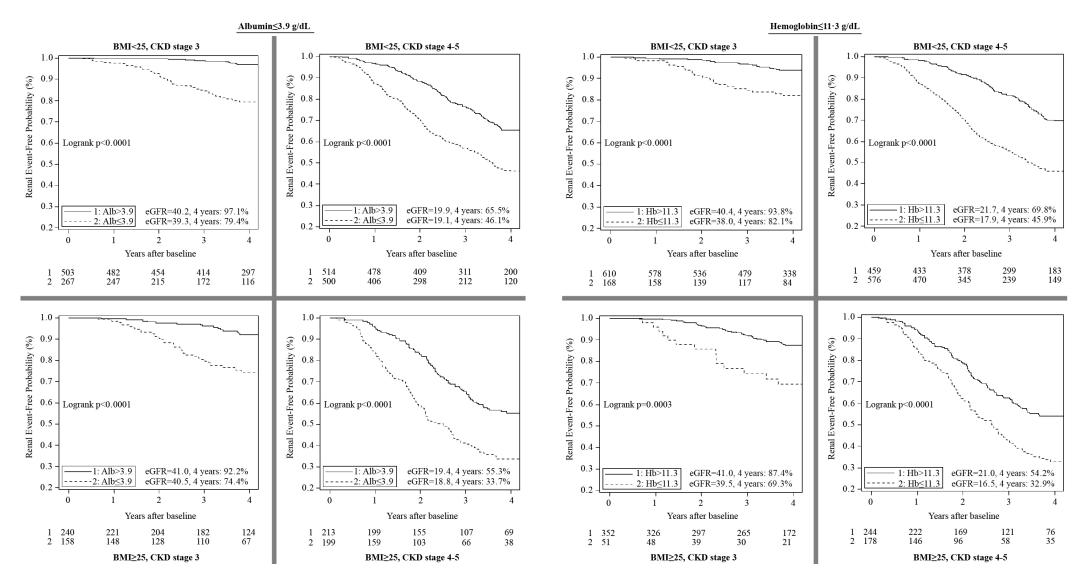
Kaplan—Meier survival curves for renal prognosis stratified by the serum albumin cut-off value (determined using the total cohort) are shown for four BMI-based cross-classified subcohorts. BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); 4 years = 4-year survival rate



# Appendix Fig. 8L: Kaplan–Meier survival curves stratified by the serum albumin cut-off value (Left side) and the hemoglobin cut-off value (Right side)

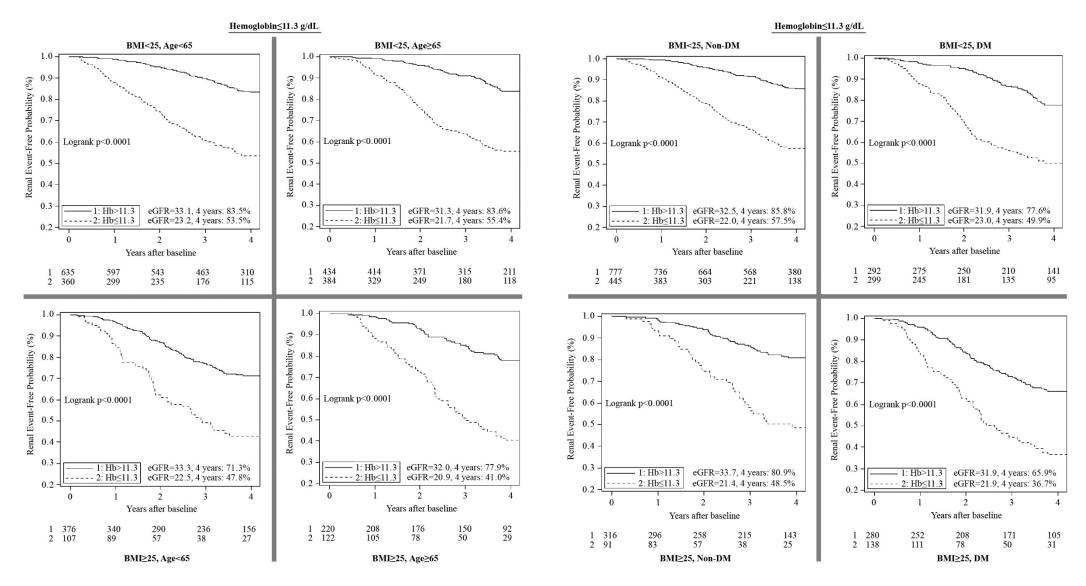
Kaplan—Meier survival curves for renal prognosis stratified by the serum albumin cut-off value (determined using the total cohort) and the hemoglobin cut-off value (determined using the total cohort) are shown for four BMI-based cross-classified subcohorts.

BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m<sup>2</sup>); CKD = chronic kidney disease; 4 years = 4-year survival rate



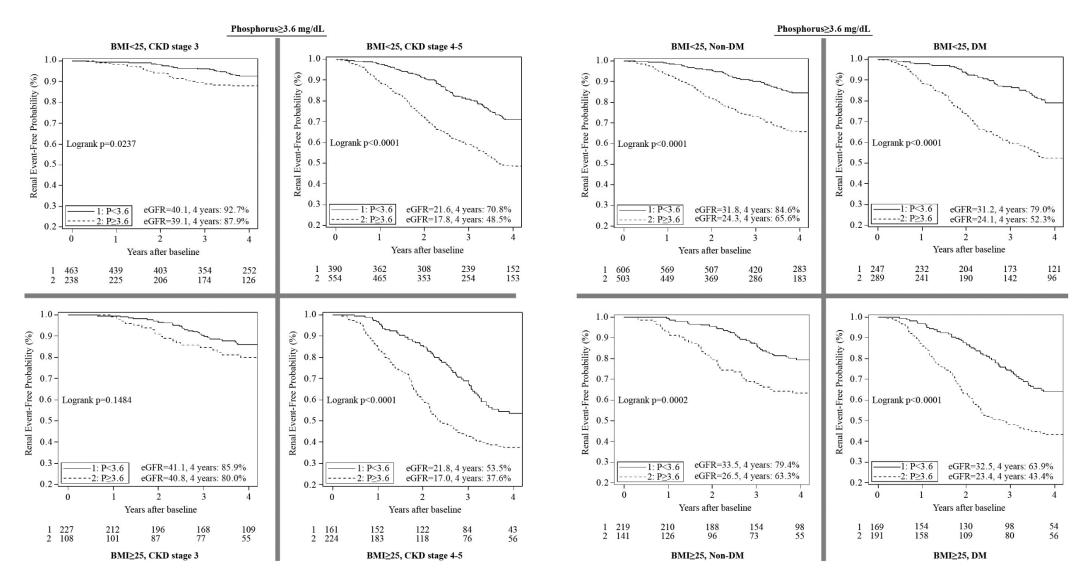
### Appendix Fig. 8M: Kaplan-Meier survival curves stratified by the hemoglobin cut-off value

Kaplan–Meier survival curves for renal prognosis stratified by the hemoglobin cut-off value (determined using the total cohort) are shown four BMI-based cross-classified subcohorts. BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); DM = diabetes mellitus; 4 years = 4-year survival rate



### Appendix Fig. 8N: Kaplan-Meier survival curves stratified by the serum phosphorous cut-off value

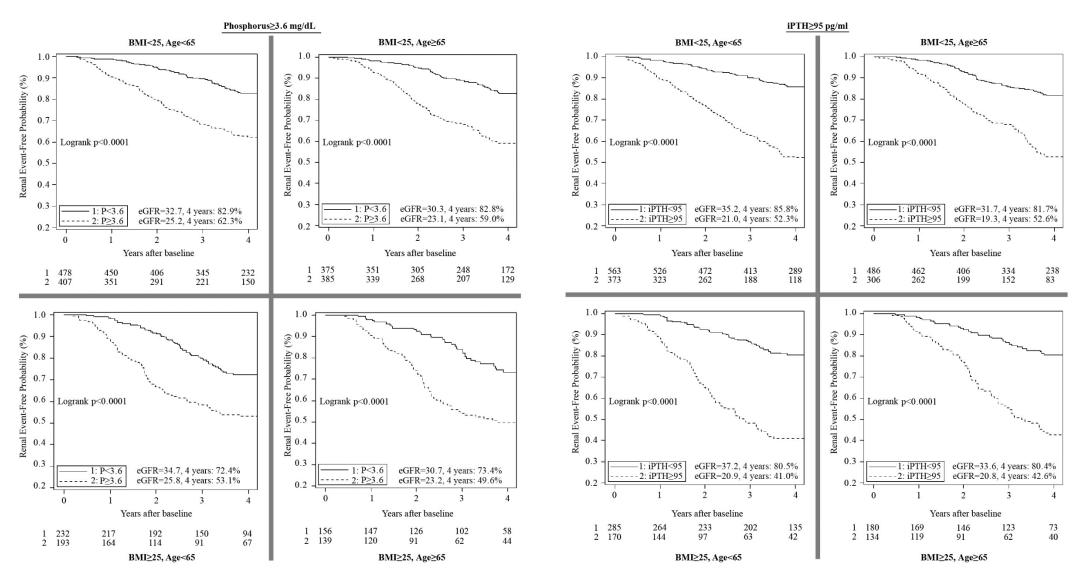
Kaplan—Meier survival curves for renal prognosis stratified by the serum phosphorous cut-off value (determined using the total cohort) are shown for four BMI-based cross-classified subcohorts. BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); CKD = chronic kidney disease; DM = diabetes mellitus; 4 years = 4-year survival rate



# Appendix Fig. 80: Kaplan–Meier survival curves stratified by the serum phosphorous cut-off value (Left side) and the iPTH cut-off value (Right side)

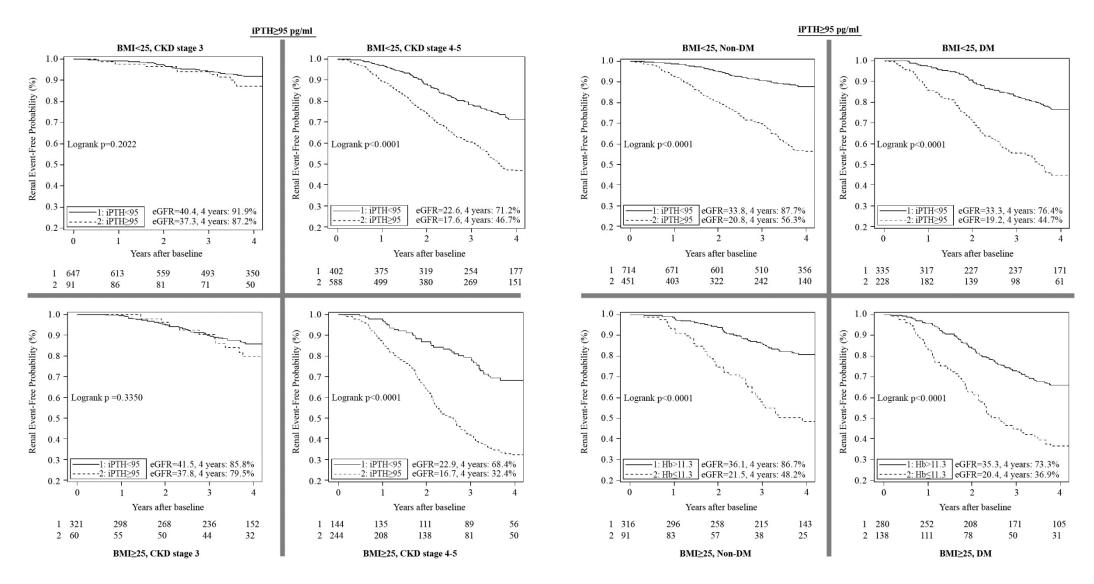
Kaplan—Meier survival curves for renal prognosis stratified by the serum albumin cut-off value (determined using the total cohort) and iPTH cut-off value (determined using the total cohort) are shown for four BMI-based cross-classified subcohorts.

BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m<sup>2</sup>); iPTH = intact parathyroid hormone; 4 years = 4-year survival rate



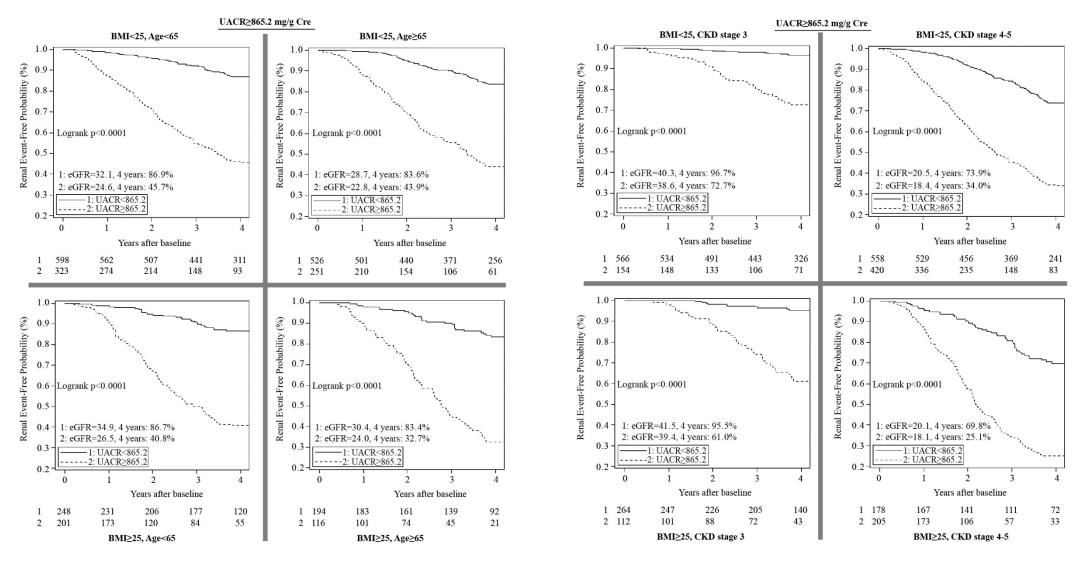
## Appendix Fig. 8P: Kaplan-Meier survival curves stratified by the iPTH cut-off value

Kaplan—Meier survival curves for renal prognosis stratified by the iPTH cut-off value (determined using the total cohort) are shown for four BMI-based cross-classified subcohorts. BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); iPTH = intact parathyroid hormone; CKD = chronic kidney disease; 4 years = 4-year survival rate



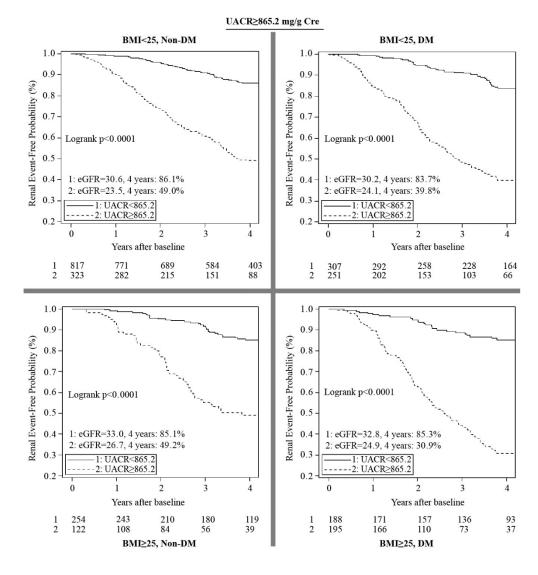
# Appendix Fig. 8Q: Kaplan-Meier survival curves stratified by the UACR cut-off value

Kaplan—Meier survival curves for renal prognosis stratified by the UACR cut-off value (determined using the total cohort) for four BMI-based four cross-classified subcohorts. UACR = urine albumin-to-creatinine ratio; BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); CKD = chronic kidney disease; 4 years = 4-year survival rate



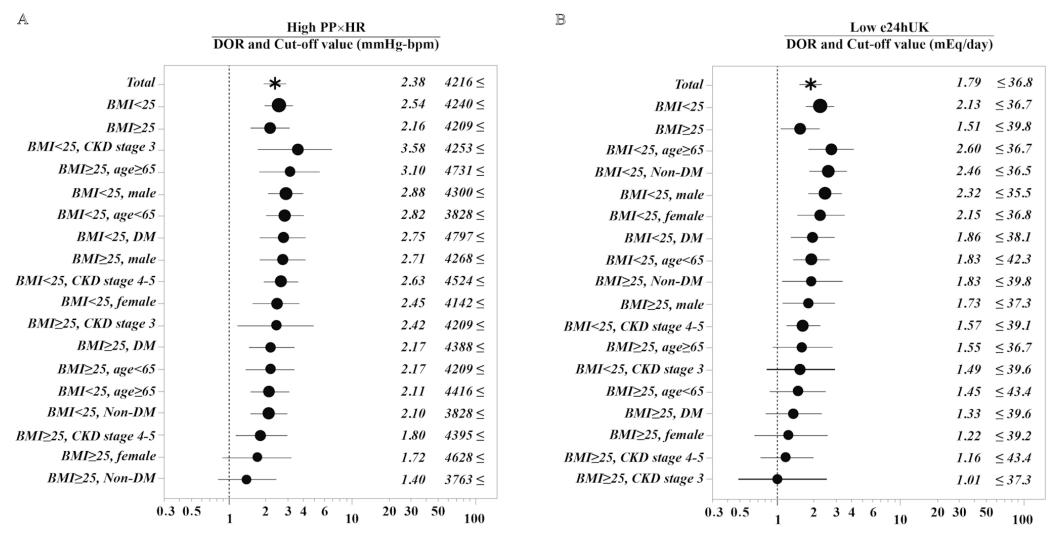
# Appendix Fig. 8R: Kaplan-Meier survival curves stratified by the UACR cut-off value

Kaplan—Meier survival curves for renal prognosis stratified by the UACR cut-off value (determined using the total cohort) for four BMI-based four cross-classified subcohorts. UACR = urine albumin-to-creatinine ratio; BMI = body mass index; eGFR = baseline estimated glomerular filtration rate (ml/min/1.73 m²); DM = diabetes mellitus; 4 years = 4-year survival rate



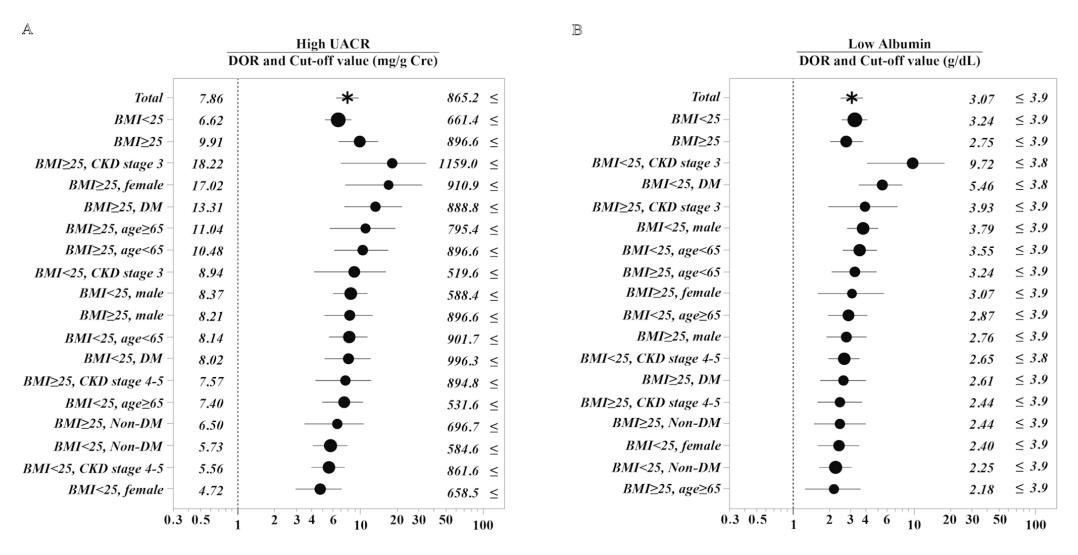
### Appendix Fig. 9A: Diagnostic odds ratios and PP × HR and e24hUK cut-off values according to subcohort

A summary of Appendix Table 8 is depicted. Diagnostic odds ratios (DORs) and cut-off values for a decline in eGFR by  $\geq$  50% from baseline or end-stage renal disease during the follow-up examination period are shown according to subcohort for PP × HR (A) and e24hUK (B). In all cohorts, cut-off values were determined by ROC analyses. The asterisk reflects the DOR for the total cohort. For each subcohort, the DOR is represented by a circle, and the horizontal line crossing the circle represents the 95% confidence interval. Circle size is proportional to the number in each subcohort. BMI = body mass index; CKD = chronic kidney disease; DM = diabetes mellitus; PP × HR = pulse pressure × heart rate product; e24hUK = estimated 24-hour urinary potassium excretion; ROC = receiver operating characteristics



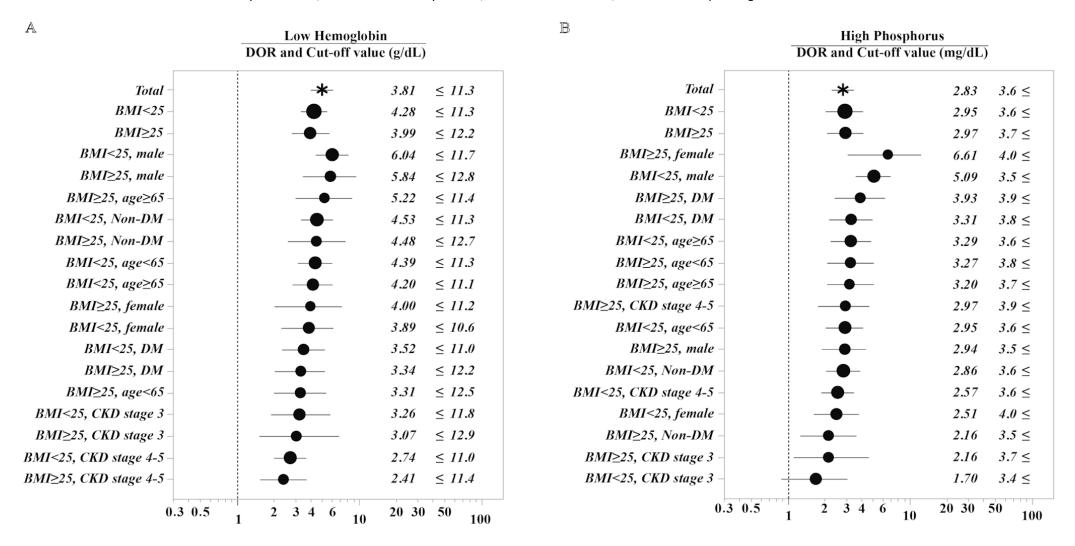
### Appendix Fig. 9B: Diagnostic odds ratios and UACR and serum albumin cut-off values according to subcohort

A summary of <u>Appendix Table 8</u> is depicted. Diagnostic odds ratios (DORs) and cut-off values according to subcohort for a decline in eGFR by ≥ 50% from baseline or end-stage renal disease during the follow-up examination period are shown for UACR (A) and serum albumin (B). For all cohorts, cut-off values were determined by ROC analyses. The asterisk reflects the DOR for the total cohort. For each subcohort, the DOR is represented by a circle, and the horizontal line crossing the circle represents the 95% confidence interval. Circle size is proportional to the number in each subcohort. BMI = body mass index; CKD = chronic kidney disease; DM = diabetes mellitus; UACR = urine albumin-to-creatinine ratio; ROC = receiver operating characteristics



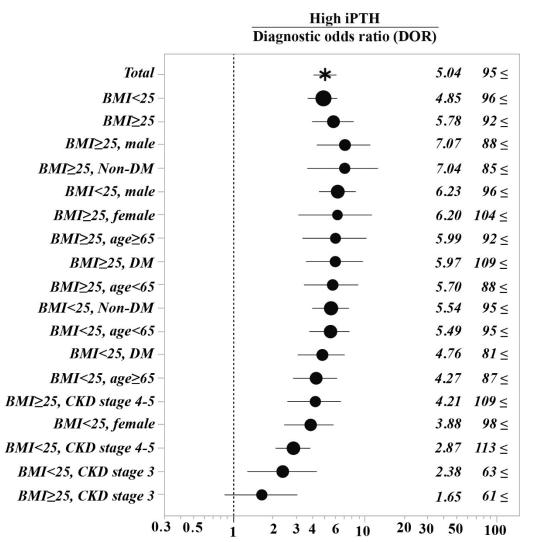
#### Appendix Fig. 9C: Diagnostic odds ratios and hemoglobin and serum phosphorous cut-off values according to subcohort

A summary of Appendix Table 8 is depicted. Diagnostic odds ratios (DORs) and cut-off values according to subcohort for a decline in eGFR by  $\geq$  50% from baseline or end-stage renal disease during the follow-up examination period are shown for hemoglobin (A) and serum phosphorous (B). For all cohorts, cut-off values were determined by ROC analyses. The asterisk reflects the DOR for the total cohort. For each subcohort, the DOR is represented by a circle, and the horizontal line crossing the circle represents the 95% confidence interval. Circle size is proportional to the number in each subcohort. BMI = body mass index; CKD = chronic kidney disease; DM = diabetes mellitus; ROC = receiver operating characteristics



## Appendix Fig. 9D: Diagnostic odds ratios and the iPTH cut-off value according to subcohort

A summary of <u>Appendix Table 8</u> is depicted. Diagnostic odds ratios (DORs) and cut-off values according to subcohort for a decline in eGFR by ≥ 50% from baseline or end-stage renal disease during the follow-up examination period are shown for iPTH. For all cohorts, the cut-off value was determined by ROC analyses. The asterisk reflects the DOR for the total cohort. For each subcohort, the DOR is represented by a circle, and the horizontal line crossing the circle represents the 95% confidence interval. Circle size is proportional to the number in each subcohort. iPTH = intact parathyroid hormone; BMI = body mass index; CKD = chronic kidney disease; DM = diabetes mellitus; ROC = receiver operating characteristics



Appendix Table 1. Baseline patient characteristics of subcohorts stratified by BMI

Veriable	BMI < 18.5	18.5 ≤ BMI < 23	23 ≤ BMI < 25	BMI ≥ 25 < 27.5	27.5 ≤ BMI < 30	30 ≤ BMI	
Variable	(N = 197)	(N = 1090)	(N = 554)	(N = 446)	(N = 241)	(N = 150)	p value
Demographic and Clinical Characteristics							
Age* (y)	57.8 ± 14.1	60.7 ± 11.6	61.6 ± 10.4	61.7 ± 10.1	59.0 ± 11.9	55.9 ± 12.7	<0.0001
Sex* Male	70 (35.5)	659 (60.5)	384 (69.3)	321 (72.0)	155 (64.3)	96 (64.0)	<0.0001
BMI (kg/m²)	17.02 ± 1.43	21.08 ± 1.25	23.95 ± 0.56	26.11 ± 0.70	28.53 ± 0.72	32.36 ± 1.97	<0.0001
SBP (mmHg)	124.9 ± 20.8	129.7 ± 17.7	132.9 ± 18.1	135.1 ± 19.0	136.6 ± 18.4	135.3 ± 18.8	<0.0001
DBP (mmHg)	72.3 ± 11.8	74.9 ± 11.5	77.1 ± 11.7	77.6 ± 12.4	78.4 ± 10.7	79.3 ± 13.3	<0.0001
MBP* (mmHg)	89.8 ± 13.5	93.2 ± 12.3	95.7 ± 12.5	96.8 ± 13.1	97.8 ± 12.0	98.0 ± 14.0	<0.0001
Pp (mmHg)	52.7 ± 15.7	54.8 ± 13.7	55.8 ± 14.0	57.5 ± 15.1	58.2 ± 14.3	56.0 ± 13.3	<0.0001
HR (beats/min)	78.7 ± 14.0	74.9 ± 12.6	76.2 ± 12.6	76.0 ± 12.8	75.8 ± 13.1	76.7 ± 12.6	0.0175
PP × HR* (mmHg-beats/min)	4164.4 ± 1503.2	4093.2 ± 1231.7	4232.9 ± 1256.8	4353.9 ± 1358.9	4447.6 ± 1320.9	4337.3 ± 1148.8	0.0007
Pulse wave velocity (cm/s)	1655.3 ± 405.8	1675.0 ± 579.0	1688.7 ± 355.5	1718.1 ± 435.5	1673.8 ± 385.3	1458.0 ± 287.3	0.2681
Ankle brachial index	1.103 ± 0.141	$1.100 \pm 0.143$	1.120 ± 0.115	1.131 ± 0.124	1.115 ± 0.131	1.096 ± 0.106	0.5142
Primary cause of CKD							
Diabetic nephropathy	23 (11.7)	168 (15.4)	117 (21.1)	120 (26.9)	86 (35.7)	46 (30.7)	<0.0001
Chronic glomerulonephritis	95 (48.2)	523 (48.0)	245 (44.2)	168 (37.7)	79 (32.8)	49 (32.7)	
Nephrosclerosis	29 (14.7)	191 (17.5)	98 (17.7)	101 (22.6)	48 (19.9)	34 (22.7)	
Others	50 (25.4)	208 (19.1)	94 (17.0)	57 (12.8)	28 (11.6)	21 (14.0)	
CKD stage							
3A	8 (4.1)	97 (8.9)	64 (11.6)	61 (13.7)	34 (14.1)	17 (11.3)	0.0018
3B	60 (30.5)	384 (35.2)	181 (32.7)	157 (35.2)	82 (34.0)	62 (41.3)	
4	89 (45.2)	433 (39.7)	226 (40.8)	164 (36.8)	79 (32.8)	56 (37.3)	
5	40 (20.3)	176 (16.1)	83 (15.0)	64 (14.3)	46 (19.1)	15 (10.0)	
Laboratory Findings (Whole blood, Serum, Urine)							
Hemoglobin* (g/dL)	11.13 ± 1.64	11.77 ± 1.71	12.21 ± 1.82	12.43 ± 1.88	12.54 ± 1.95	13.01 ± 2.01	<0.0001
Albumin* (g/dL)	$3.94 \pm 0.44$	3.95 ± 0.44	$4.00 \pm 0.42$	3.96 ± 0.41	$3.93 \pm 0.42$	$3.98 \pm 0.42$	0.2450

		(		(	(		40 0001a
ALT* (IU/L)	13.0 (10.0–19.0)	14.0 (11.0–20.0)	16.0 (11.0–22.0)	17.0 (13.0–23.0)	17.0 (13.0–23.0)	21.0 (14.0–32.0)	<0.0001ª
Uric acid* (mg/dL)	7.10 ± 1.58	7.07 ± 1.55	7.28 ± 1.52	7.18 ± 1.51	7.53 ± 1.64	7.69 ± 1.50	<0.0001
Creatinine (mg/dL)	2.20 ± 0.98	2.15 ± 1.06	2.17 ± 1.07	2.13 ± 1.08	2.24 ± 1.18	2.03 ± 0.90	0.5007
eGFR* (ml/min/1.73m²)	25.82 ± 10.88	28.55 ± 12.09	28.88 ± 12.16	29.99 ± 12.86	29.02 ± 13.21	30.65 ± 12.09	0.0013
Potassium* (mEq/L)	$4.61 \pm 0.71$	4.67 ± 0.57	4.63 ± 0.55	4.62 ± 0.62	4.63 ± 0.56	4.57 ± 0.47	0.3110
Phosphorus* (mg/dL)	3.77 ± 0.81	$3.54 \pm 0.66$	3.47 ± 0.68	$3.48 \pm 0.69$	$3.64 \pm 0.84$	$3.44 \pm 0.60$	<0.0001
iPTH* (pg/mL)	98.5 (59.0–151.0)	79.0 (53.0–124.0)	76.0 (53.0–124.0)	76.0 (52.0–123.0)	82.5 (55.0–130.0)	78.0 (55.0–113.0)	0.0598ª
LDL cholesterol* (mg/dL)	100.8 ± 32.5	106.8 ± 33.4	111.5 ± 33.4	109.1 ± 32.5	110.4 ± 33.3	108.7 ± 32.5	0.0167
HDL cholesterol* (mg/dL)	68.8 ± 23.4	59.2 ± 20.2	51.9 ± 15.0	47.9 ± 13.5	46.9 ± 13.9	46.0 ± 13.7	<0.0001
Triglycerides* (mg/dL)	122.2 ± 66.4	141.4 ± 90.2	170.0 ± 100.0	192.1 ± 132.3	204.3 ± 119.5	223.7 ± 150.7	<0.0001a
Glucose* (mg/dL)	112.7 ± 46.5	115.3 ± 41.1	119.9 ± 40.3	124.3 ± 48.5	128.6 ± 42.9	138.6 ± 57.8	<0.0001
Hemoglobin A1c (NGSP) (%)	5.59 ± 0.75	5.78 ± 0.79	5.95 ± 0.92	$6.10 \pm 0.94$	6.25 ± 1.09	6.45 ± 1.21	<0.0001
UACR* (mg/g Cre)	515.80 (149.50–1137.30)	409.85 (105.70–1218.10)	529.80 (95.10–1295.90)	493.40 (113.35–1545.45)	889.40 (259.90–2132.50)	596.75 (132.70–1556.50)	<0.0001 <sup>a</sup>
e24hUK* (mEq/day)	34.35 ± 7.77	37.26 ± 7.87	39.18 ± 7.98	40.36 ± 7.52	40.95 ± 7.55	43.68 ± 7.23	<0.0001
e24hUNa* (mEq/day)	137.92 ± 42.40	144.31 ± 40.04	151.17 ± 41.10	157.89 ± 45.48	164.67 ± 50.35	179.68 ± 52.69	<0.0001
UCACR* (mg/g Cre)	45.0 ± 56.6	35.9 ± 51.4	36.3 ± 55.0	33.7 ± 43.5	34.1 ± 51.0	40.7 ± 55.0	0.2013
UPCR* (mg/g Cre)	464.5 ± 223.9	408.3 ± 179.1	421.4 ± 152.4	423.2 ± 167.3	421.6 ± 157.2	455.1 ± 168.6	0.0007
<u>Medications</u>							
Antihypertensive medicine Yes	145 (73.6)	949 (87.1)	507 (91.5)	417 (93.5)	231 (95.9)	145 (96.7)	<0.0001
RASI Yes	129 (65.5)	864 (79.3)	469 (84.7)	387 (86.8)	213 (88.4)	141 (94.0)	<0.0001
Ca blocade Yes	79 (40.1)	537 (49.3)	323 (58.3)	292 (65.5)	171 (71.0)	98 (65.3)	<0.0001
Statin Yes	48 (24.4)	394 (36.1)	235 (42.4)	211 (47.3)	119 (49.4)	77 (51.3)	<0.0001
Allopurinol Yes	70 (35.5)	454 (41.7)	277 (50.0)	209 (46.9)	123 (51.0)	84 (56.0)	<0.0001
Insulin Yes	17 (8.6)	109 (10.0)	69 (12.5)	66 (14.8)	43 (17.8)	27 (18.0)	0.0006
ESAs Yes	48 (24.4)	165 (15.1)	63 (11.4)	45 (10.1)	24 (10.0)	11 (7.3)	<0.0001
Active vitamin D Yes	28 (14.2)	99 (9.1)	41 (7.4)	36 (8.1)	14 (5.8)	7 (4.7)	0.0108
Antiplatelet Yes	27 (13.7)	216 (19.8)	125 (22.6)	117 (26.2)	63 (26.1)	30 (20.0)	0.0025
Diuretics* Yes	46 (23.4)	269 (24.7)	167 (30.1)	156 (35.0)	116 (48.1)	76 (50.7)	<0.0001

#### **Comorbidities**

Hypertension* Yes	154 (78.2)	983 (90.3)	521 (94.2)	422 (94.6)	233 (96.7)	147 (98.0)	<0.0001
Hypercholesterolemia Yes	81 (54.7)	535 (61.9)	314 (66.2)	278 (70.2)	154 (72.6)	94 (69.1)	0.0005
Hypertriglyceridemia Yes	68 (43.6)	549 (58.6)	353 (70.6)	330 (78.4)	186 (83.0)	118 (84.3)	<0.0001
Hyperuricemia Yes	148 (76.3)	807 (75.1)	452 (82.0)	353 (80.4)	203 (84.9)	130 (87.2)	0.0001
Hypoalphalipoproteinemia Yes	55 (39.3)	471 (55.3)	285 (62.0)	273 (71.1)	152 (73.4)	99 (73.9)	<0.0001
Diabetes mellitus* Yes	49 (24.9)	330 (30.3)	217 (39.2)	211 (47.3)	131 (54.4)	80 (53.3)	<0.0001

Using the recommended BMI classified according to the WHO expert consultation (2004), the patients were divided into six groups: BMI <  $18.5 \text{ kg/m}^2$ ,  $18.5 \leq \text{BMI} < 25.0 \text{ kg/m}^2$ ,  $25.0 \leq \text{BMI} < 27.5 \text{ kg/m}^2$ ,  $27.5 \leq \text{BMI} < 30.0 \text{ kg/m}^2$ ,  $80.0 \text{ kg/m}^2$ ,

Appendix Table 2A. Baseline patient characteristics of subcohorts stratified by sex and age

Female	Male	a walio	Age < 65	Age ≥ 65	
Variable (N = 993)	(N = 1685)	p value	(N = 1504)	(N = 1174)	p value
Demographic and Clinical Characteristics					
Age* (yrs) $58.9 \pm 12.1$	61.3 ± 11.1	<0.0001	52.8 ± 9.7	70.3 ± 3.2	<0.0001
Sex* Male 0 (0.0)	1685 (100.0)	<0.0001	905 (60.2)	780 (66.4)	0.0009
BMI (kg/m <sup>2</sup> ) $22.86 \pm 4.20$	23.90 ± 3.51	<0.0001	23.64 ± 4.05	23.35 ± 3.48	0.0466
SBP (mmHg) $130.4 \pm 19.3$	132.7 ± 18.2	0.0017	130.3 ± 18.5	133.8 ± 18.6	<0.0001
DBP (mmHg) $75.3 \pm 12.0$	76.7 ± 11.8	0.0041	77.9 ± 11.9	74.0 ± 11.5	<0.0001
MBP* (mmHg) $93.7 \pm 13.1$	95.4 ± 12.6	0.0009	95.3 ± 13.1	94.0 ± 12.5	0.0055
Pp (mmHg) $55.0 \pm 14.6$	56.0 ± 14.0	0.0798	52.4 ± 13.1	59.8 ± 14.6	<0.0001
HR (beats/min) $77.1 \pm 12.4$	75.1 ± 13.0	0.0002	76.5 ± 12.9	74.9 ± 12.7	0.0028
PP × HR* (mmHg-beats/min) 4264.3 ± 1360.5	4188.3 ± 1243.2	0.1697 40	003.4 ± 1211.1	4480.1 ± 1331.1	<0.0001
Pulse wave velocity (cm/s) $1590.5 \pm 361.6$	1710.0 ± 516.0	0.0171	1498.0 ± 289.2	1892.7 ± 563.4	<0.0001
Ankle brachial index $1.104 \pm 0.106$	1.114 ± 0.143	0.4187	1.128 ± 0.112	1.090 ± 0.150	0.0013
Primary cause of CKD					
Diabetic nephropathy 162 (16.3)	398 (23.6)	<0.0001	301 (20.0)	259 (22.1)	<0.0001
Chronic glomerulonephritis 534 (53.8)	625 (37.1)		754 (50.1)	405 (34.5)	
Nephrosclerosis 115 (11.6)	386 (22.9)		219 (14.6)	282 (24.0)	
Others 182 (18.3)	276 (16.4)		230 (15.3)	228 (19.4)	
CKD stage					
3A 105 (10.6)	176 (10.4)	0.0624	201 (13.4)	80 (6.8)	<0.0001
3B 317 (31.9)	609 (36.1)		524 (34.8)	402 (34.2)	
4 394 (39.7)	653 (38.8)		564 (37.5)	483 (41.1)	
5 177 (17.8)	247 (14.7)		215 (14.3)	209 (17.8)	
<u>Laboratory Findings (Whole blood, Serum, Urine)</u>					
Hemoglobin* (g/dL) $11.39 \pm 1.53$	12.46 ± 1.91	<0.0001	12.31 ± 1.86	11.74 ± 1.78	<0.0001
Albumin* (g/dL) $3.97 \pm 0.40$	3.96 ± 0.44	0.4077	3.99 ± 0.44	3.93 ± 0.41	0.0014

ALT* (IU/L)	13.0 (10.0–18.0)	17.0 (12.0–24.0)	<0.0001 <sup>a</sup>	16.0 (12.0–22.0)	15.0 (11.0–21.0)	0.0048 <sup>a</sup>
Uric acid* (mg/dL)	6.90 ± 1.50	7.40 ± 1.55	<0.0001	7.26 ± 1.53	7.15 ± 1.58	0.0595
Creatinine (mg/dL)	1.87 ± 0.91	2.33 ± 1.11	<0.0001	2.14 ± 1.09	2.17 ± 1.02	0.5056
eGFR* (ml/min/1.73m²)	28.27 ± 12.58	29.14 ± 12.11	0.0790	30.04 ± 12.76	27.26 ± 11.48	<0.0001
Potassium* (mEq/L)	$4.60 \pm 0.58$	4.67 ± 0.58	0.0025	4.61 ± 0.58	4.67 ± 0.58	0.0111
Phosphorus* (mg/dL)	3.81 ± 0.65	3.38 ± 0.68	<0.0001	3.54 ± 0.74	$3.54 \pm 0.65$	0.9086
iPTH* (pg/mL)	83.0 (56.0–133.0)	77.0 (52.0–122.0)	0.0018 <sup>a</sup>	79.0 (53.0–129.0)	78.5 (54.0–124.0)	0.7793ª
LDL cholesterol* (mg/dL)	113.9 ± 34.0	105.1 ± 32.4	<0.0001	110.8 ± 33.2	105.1 ± 33.0	<0.0001
HDL cholesterol* (mg/dL)	61.6 ± 19.2	50.2 ± 16.8	<0.0001	56.0 ± 19.3	52.2 ± 17.3	<0.0001
Triglycerides* (mg/dL)	132.0 (95.0–186.0)	140.5 (97.0–210.0)	0.0027 <sup>a</sup>	139.0 (96.0–210.0)	134.0 (97.0–196.0)	0.0824ª
Glucose* (mg/dL)	112.8 ± 39.5	124.5 ± 46.5	<0.0001	117.1 ± 43.9	124.0 ± 44.7	0.0002
Hemoglobin A1c (NGSP) (%)	$5.89 \pm 0.97$	5.95 ± 0.89	0.1322	5.87 ± 0.95	6.01 ± 0.87	0.0002
UACR* (mg/g Cre)	451.00 (113.50–1211.40)	539.80 (123.20–1427.70)	0.0724 <sup>a</sup>	568.70 (167.90–1409.30)	430.20 (76.80–1240.50)	<0.0001a
e24hUK* (mEq/day)	37.73 ± 8.61	39.17 ± 7.64	<0.0001	39.52 ± 7.93	37.53 ± 8.05	<0.0001
e24hUNa* (mEq/day)	146.50 ± 43.54	154.06 ± 44.36	<0.0001	154.82 ± 43.71	146.75 ± 44.42	<0.0001
UCACR* (mg/g Cre)	45.1 ± 62.3	31.2 ± 43.1	<0.0001	35.7 ± 51.3	37.2 ± 51.8	0.4572
UPCR* (mg/g Cre)	466.9 ± 198.7	394.1 ± 150.9	<0.0001	420.0 ± 176.4	422.5 ± 170.5	0.7344
<u>Medications</u>						
Antihypertensive medicine Yes	857 (86.3)	1537 (91.2)	<0.0001	1339 (89.0)	1055 (89.9)	0.4865
RASI Yes	785 (79.1)	1418 (84.2)	0.0008	1256 (83.5)	947 (80.7)	0.0557
Ca blocade Yes	497 (50.1)	1003 (59.5)	<0.0001	756 (50.3)	744 (63.4)	<0.0001
Statin Yes	473 (47.6)	611 (36.3)	<0.0001	608 (40.4)	476 (40.5)	0.9501
Allopurinol Yes	329 (33.1)	888 (52.7)	<0.0001	662 (44.0)	555 (47.3)	0.0929
Insulin Yes	112 (11.3)	219 (13.0)	0.1920	169 (11.2)	162 (13.8)	0.0456
ESAs Yes	168 (16.9)	188 (11.2)	<0.0001	152 (10.1)	204 (17.4)	<0.0001
Active vitamin D Yes	118 (11.9)	107 (6.4)	<0.0001	137 (9.1)	88 (7.5)	0.1354
Antiplatelet Yes	142 (14.3)	436 (25.9)	<0.0001	242 (16.1)	336 (28.6)	<0.0001
Diuretics* Yes	284 (28.6)	546 (32.4)	0.0398	422 (28.1)	408 (34.8)	0.0002

## **Comorbidities**

Hypertension* Yes	892 (89.9)	1568 (93.1)	0.0034	1372 (91.3)	1088 (92.7)	0.2102
Hypercholesterolemia Yes	633 (74.4)	823 (59.7)	<0.0001	835 (67.3)	621 (62.7)	0.0230
Hypertriglyceridemia Yes	615 (70.1)	989 (65.9)	0.0334	897 (68.0)	707 (66.8)	0.5588
Hyperuricemia Yes	688 (70.4)	1405 (84.1)	<0.0001	1178 (79.3)	915 (78.7)	0.7144
Hypoalphalipoproteinemia Yes	502 (62.1)	833 (60.9)	0.6055	731 (60.6)	604 (62.3)	0.4308
Diabetes mellitus* Yes	310 (31.2)	708 (42.0)	<0.0001	509 (33.8)	509 (43.4)	<0.0001

Appendix Table 2B. Baseline patient characteristics of subcohorts stratified by CKD stage and DM

Variable	CKD stage 3	CKD stage 4–5	a control	Non-DM	DM	
Variable	(N = 1207)	(N = 1471)	p value	(N = 1660)	(N = 1018)	p value
Demographic and Clinical Characteristics						
Age* (yrs)	58.9 ± 12.4	61.7 ± 10.6	<0.0001	58.8 ± 12.5	63.1 ± 9.1	<0.0001
Sex* Male	785 (65.0)	900 (61.2)	0.0399	977 (58.9)	708 (69.5)	<0.0001
BMI (kg/m²)	23.83 ± 3.83	23.25 ± 3.77	<0.0001	22.89 ± 3.63	24.53 ± 3.88	<0.0001
SBP (mmHg)	130.1 ± 17.7	133.3 ± 19.2	<0.0001	129.9 ± 17.8	135.0 ± 19.5	<0.0001
DBP (mmHg)	76.3 ± 11.4	76.1 ± 12.3	0.6674	77.5 ± 11.5	74.0 ± 12.2	<0.0001
MBP* (mmHg)	94.2 ± 12.2	95.2 ± 13.3	0.0590	95.0 ± 12.6	94.4 ± 13.2	0.2384
PP (mmHg)	53.8 ± 13.6	57.2 ± 14.6	<0.0001	52.4 ± 12.6	60.9 ± 15.2	<0.0001
HR (beats/min)	75.3 ± 12.6	76.2 ± 13.0	0.1114	75.5 ± 12.6	76.4 ± 13.2	0.0871
PP × HR* (mmHg-beats/min)	4050.0 ± 1259.1	4352.2 ± 1295.5	<0.0001	3960.5 ± 1149.6	4627.1 ± 1388.4	<0.0001
Pulse wave velocity (cm/s)	1599.4 ± 391.6	1745.1 ± 537.1	0.0021	1594.4 ± 505.5	1789.9 ± 384.7	<0.0001
Ankle brachial index	1.110 ± 0.114	1.111 ± 0.147	0.9549	1.129 ± 0.097	1.081 ± 0.170	<0.0001
Primary cause of CKD						
Diabetic nephropathy	218 (18.1)	342 (23.2)	<0.0001	0 (0.0%)	560 (55.0)	<0.0001
Chronic glomerulonephritis	561 (46.5)	598 (40.7)		948 (57.1)	211 (20.7)	
Nephrosclerosis	201 (16.7)	300 (20.4)		348 (21.0)	153 (15.0)	
Others	227 (18.8)	231 (15.7)		364 (21.9)	94 (9.2)	
CKD stage						
3A	281 (23.3)	0 (0.0%)	<0.0001	193 (11.6)	88 (8.6)	0.0446
3B	926 (76.7)	0 (0.0%)		581 (35.0)	345 (33.9)	
4	0 (0.0%)	1047 (71.2)		637 (38.4)	410 (40.3)	
5	0 (0.0%)	424 (28.8)		249 (15.0)	175 (17.2)	
<u>Laboratory Findings (Whole blood, Serum, Urine)</u>						
Hemoglobin* (g/dL)	12.92 ± 1.79	11.37 ± 1.59	<0.0001	12.21 ± 1.83	11.82 ± 1.86	<0.0001
Albumin* (g/dL)	4.02 ± 0.43	$3.92 \pm 0.43$	<0.0001	4.02 ± 0.38	3.87 ± 0.48	<0.0001

ALT* (IU/L)	17.0 (13.0–24.0)	14.0 (10.0–19.0)	<0.0001 <sup>a</sup>	15.0 (11.0–21.0)	16.0 (12.0–23.0)	<0.0002a
Uric acid* (mg/dL)	6.94 ± 1.43	7.43 ± 1.62	<0.0001	7.11 ± 1.50	7.38 ± 1.62	<0.0001
Creatinine (mg/dL)	1.37 ± 0.27	2.80 ± 1.03	<0.0001	2.11 ± 1.05	2.23 ± 1.08	0.0052
eGFR* (ml/min/1.73m²)	40.23 ± 7.20	19.45 ± 6.14	<0.0001	29.36 ± 12.42	27.93 ± 12.02	0.0033
Potassium* (mEq/L)	4.46 ± 0.48	4.78 ± 0.62	<0.0001	4.63 ± 0.57	4.66 ± 0.59	0.2477
Phosphorus* (mg/dL)	3.30 ± 0.60	3.72 ± 0.72	<0.0001	3.47 ± 0.68	3.64 ± 0.72	<0.0001
iPTH* (pg/mL)	58.0 (43.0–78.0)	111.0 (74.0–169.0)	<0.0001 <sup>a</sup>	78.0 (53.0–122.0)	81.0 (55.0–130.5)	0.1275ª
LDL cholesterol* (mg/dL)	111.3 ± 33.5	105.7 ± 32.8	<0.0001	109.6 ± 33.7	106.4 ± 32.4	0.0268
HDL cholesterol* (mg/dL)	56.1 ± 18.7	52.8 ± 18.3	<0.0001	57.5 ± 19.3	49.8 ± 16.4	<0.0001
Triglycerides* (mg/dL)	136.0 (95.0–202.0)	139.0 (98.0–203.0)	0.5967ª	132.0 (94.0–193.0)	147.0 (100.0–214.0)	0.0001a
Glucose* (mg/dL)	120.2 ± 46.6	120.2 ± 42.5	0.9847	104.7 ± 22.3	142.1 ± 56.8	<0.0001
Hemoglobin A1c (NGSP) (%)	5.98 ± 0.98	5.89 ± 0.87	0.0176	5.47 ± 0.36	6.67 ± 1.05	<0.0001
UACR* (mg/g Cre)	259.35 (56.95–846.85)	764.60 (244.30–1566.90)	<0.0001 <sup>a</sup>	401.60 (101.85–991.95)	776.30 (151.40–2096.90)	<0.0001a
e24hUK* (mEq/day)	41.27 ± 7.92	36.52 ± 7.50	<0.0001	38.11 ± 7.95	39.49 ± 8.14	<0.0001
e24hUNa* (mEq/day)	155.31 ± 46.10	147.98 ± 42.34	<0.0001	147.52 ± 41.25	157.31 ± 48.01	<0.0001
UCACR* (mg/g Cre)	47.0 ± 58.6	27.8 ± 43.1	<0.0001	34.7 ± 48.0	39.1 ± 56.7	0.0391
UPCR* (mg/g Cre)	406.7 ± 184.3	432.8 ± 164.0	<0.0001	407.2 ± 169.8	443.6 ± 177.8	<0.0001
<u>Medications</u>						
Antihypertensive medicine Yes	1034 (85.7)	1360 (92.5)	<0.0001	1445 (87.0)	949 (93.2)	<0.0001
RASI Yes	967 (80.1)	1236 (84.0)	0.0084	1319 (79.5)	884 (86.8)	<0.0001
Ca blockade Yes	542 (44.9)	958 (65.1)	<0.0001	842 (50.7)	658 (64.6)	<0.0001
Statin Yes	498 (41.3)	586 (39.8)	0.4556	583 (35.1)	501 (49.2)	<0.0001
Allopurinol Yes	447 (37.0)	770 (52.3)	<0.0001	800 (48.2)	417 (41.0)	<0.0001
Insulin Yes	120 (9.9)	211 (14.3)	0.0006	0 (0.0)	331 (32.5)	<0.0001
ESAs Yes	31 (2.6)	325 (22.1)	<0.0001	179 (10.8)	177 (17.4)	<0.0001
Active vitamin D Yes	89 (7.4)	136 (9.2)	0.0823	147 (8.9)	78 (7.7)	0.2799
Antiplatelet Yes	234 (19.4)	344 (23.4)	0.0123	236 (14.2)	342 (33.6)	<0.0001
Diuretics* Yes	306 (25.4)	524 (35.6)	<0.0001	340 (20.5)	490 (48.1)	<0.0001

#### **Comorbidities**

Hypertension* Yes	1073 (89.0) 1387 (94.3)	<0.0001	1491 (89.9)	969 (95.2)	<0.0001
Hypercholesterolemia Yes	682 (66.7) 774 (64.1)	0.2092	832 (62.6)	624 (69.3)	0.0012
Hypertriglyceridemia Yes	731 (67.3) 873 (67.6)	0.8934	904 (63.7)	700 (73.1)	<0.0001
Hyperuricemia Yes	839 (70.7) 1254 (85.9)	<0.0001	1301 (79.3)	792 (78.6)	0.6764
Hypoalphalipoproteinemia Yes	593 (59.8) 742 (62.7)	0.1678	699 (54.9)	636 (70.4)	<0.0001
Diabetes mellitus* Yes	433 (35.9) 585 (39.8)	0.0388	0 (0.0)	1018 (100.0)	<0.0001

Values are expressed as n (%), mean ± SD or median (inter quartile range). Imputed variables are marked with an asterisk (\*). Proportions are based on non-missing data. a: p values are calculated by using the Kruskal–Wallis test. Abbreviations: BMI, body mass index; N, number; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; PP, pulse pressure; HR, heart rate; PP × HR, pulse pressure x heart rate; CVD, cardiovascular disease; CKD, chronic kidney disease; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; iPTH intact parathyroid hormone; LDL, low-density lipoprotein; HDL, high-density lipoprotein; UACR, urine albumin-to-creatinine ratio; e24hUK, estimated 24-hour urinary potassium excretion; e24hUNa, estimated 24-hour urinary sodium excretion; UCACR, urine calcium-to-creatinine ratio; UPCR, urine phosphorus-to-creatinine ratio; RASI, renin-angiotensin system inhibitor; ESA, erythropoiesis-stimulating agent; DM, diabetes mellitus.

Appendix Table 3A. Baseline patient characteristics of subcohorts cross-classified by sex and BMI

Variable	BMI < 25, Male	BMI < 25, Female	BMI ≥ 25, Male	BMI ≥ 25, Female
	(N = 1113)	(N = 1113)	(N = 572)	(N = 265)
Demographic and Clinical Characteristics				
Age* (yrs)	62.1 ± 10.9	58.5 ± 12.3	59.9 ± 11.2	59.9 ± 11.5
Sex* Male	1113 (100.0)	0 (0.0)	572 (100.0)	0 (0.0)
BMI (kg/m²)	21.92 ± 2.00	20.87 ± 2.57	27.75 ± 2.45	28.31 ± 2.72
SBP (mmHg)	131.3 ± 17.8	128.3 ± 18.9	135.4 ± 18.6	136.0 ± 19.2
DBP (mmHg)	75.7 ± 11.5	74.6 ± 12.0	78.6 ± 12.1	77.2 ± 11.9
MBP* (mmHg)	94.3 ± 12.3	92.5 ± 13.0	97.5 ± 12.9	96.8 ± 13.1
PP (mmHg)	55.6 ± 13.8	53.6 ± 14.4	56.8 ± 14.5	58.8 ± 14.7
HR (beats/min)	74.8 ± 12.9	77.1 ± 12.5	75.6 ± 13.1	77.1 ± 12.2
PP × HR* (mmHg-beats/min)	4136.1 ± 1219.6	4152.3 ± 1344.9	4288.8 ± 1282.8	4574.3 ± 1358.2
Pulse wave velocity (cm/s)	1732.8 ± 580.1	1584.5 ± 337.1	1676.4 ± 403.5	1605.4 ± 421.8
Ankle brachial index	1.109 ± 0.152	1.100 ± 0.104	1.123 ± 0.127	1.114 ± 0.112
Primary cause of CKD				
Diabetic nephropathy	225 (20.2)	83 (11.4)	173 (30.2)	79 (29.8)
Chronic glomerulonephritis	446 (40.1)	417 (57.3)	179 (31.3)	117 (44.2)
Nephrosclerosis	240 (21.6)	78 (10.7)	146 (25.5)	37 (14.0)
Others	202 (18.1)	150 (20.6)	74 (12.9)	32 (12.1)
CKD stage				
3A	106 (9.5)	63 (8.7)	70 (12.2)	42 (15.8)
3B	390 (35.0)	235 (32.3)	219 (38.3)	82 (30.9)
4	446 (40.1)	302 (41.5)	207 (36.2)	92 (34.7)
5	171 (15.4)	128 (17.6)	76 (13.3)	49 (18.5)
Laboratory Findings (Whole blood, Serum, Urine)				
Hemoglobin* (g/dL)	12.19 ± 1.84	11.28 ± 1.49	12.98 ± 1.94	11.68 ± 1.60

Albumin* (g/dL)	3.95 ± 0.45	3.99 ± 0.40	3.97 ± 0.42	$3.92 \pm 0.40$
ALT* (IU/L)	16.0 (11.0–23.0)	13.0 (10.0–17.0)	18.0 (14.0–26.0)	15.0 (11.0–20.0)
Uric acid* (mg/dL)	7.35 ± 1.53	6.82 ± 1.52	7.49 ± 1.60	7.11 ± 1.43
Creatinine (mg/dL)	2.34 ± 1.10	1.88 ± 0.90	2.29 ± 1.12	1.82 ± 0.91
eGFR* (ml/min/1.73m²)	28.67 ± 11.83	27.88 ± 12.28	30.05 ± 12.59	29.35 ± 13.35
Potassium* (mEq/L)	4.69 ± 0.57	4.59 ± 0.59	4.62 ± 0.59	4.62 ± 0.56
Phosphorus* (mg/dL)	3.38 ± 0.65	$3.81 \pm 0.66$	$3.38 \pm 0.73$	3.81 ± 0.62
iPTH* (pg/mL)	77.0 (52.0–123.0)	83.0 (55.0–133.0)	76.0 (51.5–120.0)	82.0 (58.0–142.0)
LDL cholesterol* (mg/dL)	104.2 ± 32.6	113.5 ± 34.1	106.9 ± 31.9	114.8 ± 33.8
HDL cholesterol* (mg/dL)	53.2 ± 18.0	65.3 ± 19.9	44.9 ± 12.8	52.6 ± 14.0
Triglycerides* (mg/dL)	127.0 (92.0–189.0)	121.5 (88.0–169.0)	169.0 (116.0–252.0)	160.0 (115.0–230.0)
Glucose* (mg/dL)	121.8 ± 44.2	108.0 ± 35.3	129.5 ± 50.1	124.9 ± 46.4
Hamaglahin A1a (NGSD) (9/)	5.85 ± 0.81	5.74 ± 0.86	6.15 ± 0.99	6.32 ± 1.13
Hemoglobin A1c (NGSP) (%)	5.05 ± 0.01	5.7 . = 5.65		0.02 = 1.10
UACR* (mg/g Cre)	497.30 (105.40–1310.00)	414.85 (107.45–1088.70)	615.95 (157.05–1684.40)	600.70 (143.50–1641.40)
UACR* (mg/g Cre)	497.30 (105.40–1310.00)	414.85 (107.45–1088.70)	615.95 (157.05–1684.40)	600.70 (143.50–1641.40)
UACR* (mg/g Cre) e24hUK* (mEq/day)	497.30 (105.40–1310.00) 38.00 ± 7.46	414.85 (107.45–1088.70) 36.82 ± 8.72	615.95 (157.05–1684.40) 41.49 ± 7.47	600.70 (143.50–1641.40) 40.32 ± 7.73
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day)	497.30 (105.40–1310.00) $38.00 \pm 7.46$ $148.33 \pm 40.59$	414.85 (107.45–1088.70) 36.82 ± 8.72 141.71 ± 40.76	615.95 (157.05–1684.40) 41.49 ± 7.47 165.40 ± 49.12	600.70 (143.50–1641.40) $40.32 \pm 7.73$ $160.05 \pm 48.16$
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day) UCACR* (mg/g Cre)	$497.30 (105.40-1310.00)$ $38.00 \pm 7.46$ $148.33 \pm 40.59$ $30.8 \pm 43.5$	414.85 (107.45–1088.70) $36.82 \pm 8.72$ $141.71 \pm 40.76$ $46.3 \pm 63.9$	615.95 (157.05–1684.40) $41.49 \pm 7.47$ $165.40 \pm 49.12$ $32.0 \pm 42.3$	600.70 (143.50–1641.40) $40.32 \pm 7.73$ $160.05 \pm 48.16$ $41.7 \pm 57.8$
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day) UCACR* (mg/g Cre) UPCR* (mg/g Cre)	$497.30 (105.40-1310.00)$ $38.00 \pm 7.46$ $148.33 \pm 40.59$ $30.8 \pm 43.5$	414.85 (107.45–1088.70) $36.82 \pm 8.72$ $141.71 \pm 40.76$ $46.3 \pm 63.9$	615.95 (157.05–1684.40) $41.49 \pm 7.47$ $165.40 \pm 49.12$ $32.0 \pm 42.3$	600.70 (143.50–1641.40) $40.32 \pm 7.73$ $160.05 \pm 48.16$ $41.7 \pm 57.8$
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day) UCACR* (mg/g Cre) UPCR* (mg/g Cre)  Medications	$497.30 (105.40-1310.00)$ $38.00 \pm 7.46$ $148.33 \pm 40.59$ $30.8 \pm 43.5$ $388.9 \pm 152.6$	414.85 (107.45–1088.70) $36.82 \pm 8.72$ $141.71 \pm 40.76$ $46.3 \pm 63.9$ $462.0 \pm 202.1$	615.95 (157.05–1684.40) $41.49 \pm 7.47$ $165.40 \pm 49.12$ $32.0 \pm 42.3$ $404.4 \pm 147.2$	600.70 (143.50–1641.40) $40.32 \pm 7.73$ $160.05 \pm 48.16$ $41.7 \pm 57.8$ $480.5 \pm 188.3$
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day)  UCACR* (mg/g Cre)  UPCR* (mg/g Cre)  Medications  Antihypertensive medicine Yes	$497.30 (105.40-1310.00)$ $38.00 \pm 7.46$ $148.33 \pm 40.59$ $30.8 \pm 43.5$ $388.9 \pm 152.6$ $998 (89.7)$	414.85 (107.45 $-$ 1088.70) 36.82 $\pm$ 8.72 141.71 $\pm$ 40.76 46.3 $\pm$ 63.9 462.0 $\pm$ 202.1	615.95 (157.05–1684.40) $41.49 \pm 7.47$ $165.40 \pm 49.12$ $32.0 \pm 42.3$ $404.4 \pm 147.2$ 539 (94.2)	$600.70 (143.50-1641.40)$ $40.32 \pm 7.73$ $160.05 \pm 48.16$ $41.7 \pm 57.8$ $480.5 \pm 188.3$
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day)  UCACR* (mg/g Cre)  UPCR* (mg/g Cre)  Medications  Antihypertensive medicine Yes  RASI Yes	$497.30 (105.40-1310.00)$ $38.00 \pm 7.46$ $148.33 \pm 40.59$ $30.8 \pm 43.5$ $388.9 \pm 152.6$ $998 (89.7)$ $913 (82.0)$	$414.85 (107.45-1088.70)$ $36.82 \pm 8.72$ $141.71 \pm 40.76$ $46.3 \pm 63.9$ $462.0 \pm 202.1$ $603 (82.8)$ $549 (75.4)$	615.95 (157.05–1684.40) $41.49 \pm 7.47$ $165.40 \pm 49.12$ $32.0 \pm 42.3$ $404.4 \pm 147.2$ 539 (94.2) 505 (88.3)	$600.70 (143.50-1641.40)$ $40.32 \pm 7.73$ $160.05 \pm 48.16$ $41.7 \pm 57.8$ $480.5 \pm 188.3$ $254 (95.8)$ $236 (89.1)$
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day)  UCACR* (mg/g Cre)  UPCR* (mg/g Cre)  Medications  Antihypertensive medicine Yes  RASI Yes  Ca blocade Yes	497.30 (105.40–1310.00)  38.00 ± 7.46  148.33 ± 40.59  30.8 ± 43.5  388.9 ± 152.6  998 (89.7)  913 (82.0)  613 (55.1)	414.85 (107.45–1088.70) 36.82 ± 8.72 141.71 ± 40.76 46.3 ± 63.9 462.0 ± 202.1  603 (82.8) 549 (75.4) 326 (44.8)	615.95 (157.05–1684.40) 41.49 ± 7.47 165.40 ± 49.12 32.0 ± 42.3 404.4 ± 147.2 539 (94.2) 505 (88.3) 390 (68.2)	$600.70 (143.50-1641.40)$ $40.32 \pm 7.73$ $160.05 \pm 48.16$ $41.7 \pm 57.8$ $480.5 \pm 188.3$ $254 (95.8)$ $236 (89.1)$ $171 (64.5)$
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day)  UCACR* (mg/g Cre)  UPCR* (mg/g Cre)  Medications  Antihypertensive medicine Yes  RASI Yes  Ca blocade Yes  Statin Yes	497.30 (105.40–1310.00)  38.00 ± 7.46  148.33 ± 40.59  30.8 ± 43.5  388.9 ± 152.6  998 (89.7)  913 (82.0)  613 (55.1)  367 (33.0)	414.85 (107.45–1088.70) 36.82 ± 8.72 141.71 ± 40.76 46.3 ± 63.9 462.0 ± 202.1  603 (82.8) 549 (75.4) 326 (44.8) 310 (42.6)	615.95 (157.05–1684.40) 41.49 ± 7.47 165.40 ± 49.12 32.0 ± 42.3 404.4 ± 147.2 539 (94.2) 505 (88.3) 390 (68.2) 244 (42.7)	600.70 (143.50–1641.40) 40.32 ± 7.73 160.05 ± 48.16 41.7 ± 57.8 480.5 ± 188.3 254 (95.8) 236 (89.1) 171 (64.5) 163 (61.5)
UACR* (mg/g Cre) e24hUK* (mEq/day) e24hUNa* (mEq/day) UCACR* (mg/g Cre) UPCR* (mg/g Cre)  Medications  Antihypertensive medicine Yes  RASI Yes Ca blocade Yes  Statin Yes  Allopurinol Yes	497.30 (105.40–1310.00)  38.00 ± 7.46  148.33 ± 40.59  30.8 ± 43.5  388.9 ± 152.6  998 (89.7)  913 (82.0)  613 (55.1)  367 (33.0)  579 (52.0)	414.85 (107.45–1088.70)  36.82 ± 8.72  141.71 ± 40.76  46.3 ± 63.9  462.0 ± 202.1  603 (82.8)  549 (75.4)  326 (44.8)  310 (42.6)  222 (30.5)	615.95 (157.05–1684.40) 41.49 ± 7.47 165.40 ± 49.12 32.0 ± 42.3 404.4 ± 147.2 539 (94.2) 505 (88.3) 390 (68.2) 244 (42.7) 309 (54.0)	600.70 (143.50–1641.40) 40.32 ± 7.73 160.05 ± 48.16 41.7 ± 57.8 480.5 ± 188.3 254 (95.8) 236 (89.1) 171 (64.5) 163 (61.5) 107 (40.4)

Antiplatelet Yes	267 (24.0)	101 (13.9)	169 (29.5)	41 (15.5)
Diuretics* Yes	309 (27.8)	173 (23.8)	237 (41.4)	111 (41.9)
<u>Comorbidities</u>				
Hypertension* Yes	1024 (92.1)	634 (87.2)	544 (95.1)	258 (97.4)
Hypercholesterolemia Yes	493 (55.8)	437 (72.6)	330 (66.7)	196 (78.7)
Hypertriglyceridemia Yes	575 (59.3)	395 (63.3)	414 (77.8)	220 (87.0)
Hyperuricemia Yes	919 (83.1)	488 (68.3)	486 (86.2)	200 (76.0)
Hypoalphalipoproteinemia Yes	485 (55.2)	326 (56.9)	348 (71.2)	176 (74.6)
Diabetes mellitus* Yes	419 (37.6)	177 (24.3)	289 (50.5)	133 (50.2)

Appendix Table 3B.Baseline patient characteristics of subcohorts cross-classified by age and BMI

Variable	BMI < 25, Age < 65	BMI < 25, Age ≥ 65	BMI ≥ 25, Age < 65	BMI ≥ 25, Age ≥ 65	
	(N = 1011) (N = 830)		(N = 493)	(N = 344)	
Demographic and Clinical Characteristics					
Age* (yrs)	52.7 ± 9.9	70.3 ± 3.2	52.8 ± 9.3	70.1 ± 3.3	
Sex* Male	570 (56.4)	543 (65.4)	335 (68.0)	237 (68.9)	
BMI (kg/m²)	21.41 ± 2.37	21.63 ± 2.21	28.23 ± 2.69	27.49 ± 2.26	
SBP (mmHg)	128.4 ± 18.6	132.3 ± 17.7	134.1 ± 17.7	137.7 ± 20.1	
DBP (mmHg)	76.8 ± 11.8	73.4 ± 11.3	80.1 ± 11.9	75.4 ± 11.8	
MBP* (mmHg)	94.0 ± 13.1	93.0 ± 12.0	98.1 ± 12.7	96.2 ± 13.2	
PP (mmHg)	51.5 ± 13.1	58.8 ± 14.2	54.0 ± 13.1	62.2 ± 15.3	
HR (beats/min)	76.4 ± 13.0	74.8 ± 12.6	76.8 ± 12.7	75.2 ± 13.0	
PP × HR* (mmHg-beats/min)	3942.0 ± 1216.5	4381.5 ± 1291.7	4130.6 ± 1191.4	4711.7 ± 1394.2	
Pulse wave velocity (cm/s)	1484.3 ± 278.3	1899.2 ± 610.1	1519.0 ± 305.5	1879.1 ± 454.3	
Ankle brachial index	1.124 ± 0.116	1.087 ± 0.153	1.137 ± 0.105	1.096 ± 0.143	
Primary cause of CKD					
Diabetic nephropathy	153 (15.1)	155 (18.7)	148 (30.0)	104 (30.2)	
Chronic glomerulonephritis	560 (55.4)	303 (36.5)	194 (39.4)	102 (29.7)	
Nephrosclerosis	124 (12.3)	194 (23.4)	95 (19.3)	88 (25.6)	
Others	174 (17.2)	178 (21.4)	56 (11.4)	50 (14.5)	
CKD stage					
3A	120 (11.9)	49 (5.9)	81 (16.4)	31 (9.0)	
3B	344 (34.0)	281 (33.9)	180 (36.5)	121 (35.2)	
4	403 (39.9)	345 (41.6)	161 (32.7)	138 (40.1)	
5	144 (14.2)	155 (18.7)	71 (14.4)	54 (15.7)	
Laboratory Findings (Whole blood, Serum, Urine)					
Hemoglobin* (g/dL)	12.06 ± 1.75	11.55 ± 1.74	12.82 ± 1.98	12.20 ± 1.81	

Albumin* (g/dL)	$4.00 \pm 0.44$	3.92 ± 0.43	$3.96 \pm 0.44$	$3.96 \pm 0.38$
ALT* (IU/L)	15.0 (11.0–21.0)	14.0 (11.0–20.0)	18.0 (14.0–27.0)	16.0 (12.0–22.0)
Uric acid* (mg/dL)	7.17 ± 1.54	7.10 ± 1.55	7.44 ± 1.50	7.27 ± 1.64
Creatinine (mg/dL)	2.14 ± 1.08	2.19 ± 1.02	2.15 ± 1.12	2.13 ± 1.04
eGFR* (ml/min/1.73m²)	29.56 ± 12.43	26.90 ± 11.32	31.02 ± 13.36	28.13 ± 11.84
Potassium* (mEq/L)	4.63 ± 0.58	4.67 ± 0.58	4.58 ± 0.56	4.67 ± 0.60
Phosphorus* (mg/dL)	3.53 ± 0.71	$3.56 \pm 0.66$	3.54 ± 0.79	$3.48 \pm 0.62$
iPTH* (pg/mL)	80.5 (53.0–131.5)	78.0 (54.0–123.5)	76.0 (53.0–123.0)	80.0 (54.0–128.0)
LDL cholesterol* (mg/dL)	110.4 ± 33.2	104.5 ± 33.5	111.6 ± 33.2	106.3 ± 31.8
HDL cholesterol* (mg/dL)	60.3 ± 20.6	54.7 ± 17.9	47.7 ± 13.0	46.6 ± 14.5
Triglycerides* (mg/dL)	124.5 (88.0–186.0)	124.0 (94.0–175.0)	170.0 (117.0–260.0)	160.5 (114.0–221.0)
Glucose* (mg/dL)	111.6 ± 38.9	122.2 ± 43.8	128.0 ± 50.7	127.9 ± 46.5
Hemoglobin A1c (NGSP) (%)	5.71 ± 0.82	5.92 ± 0.83	6.20 ± 1.10	6.21 ± 0.95
UACR* (mg/g Cre)	503.10 (148.80–1246.10)	390.80 (72.50–1156.40)	730.70 (199.20–1897.30)	516.80 (98.80–1415.50)
e24hUK* (mEq/day)	38.34 ± 7.92	36.58 ± 8.00	41.95 ± 7.39	39.92 ± 7.68
e24hUNa* (mEq/day)	148.92 ± 39.34	141.89 ± 42.13	167.02 ± 49.44	158.95 ± 47.66
UCACR* (mg/g Cre)	36.2 ± 53.6	37.8 ± 52.4	34.5 ± 46.3	35.9 ± 50.1
UPCR* (mg/g Cre)	417.8 ± 179.8	418.0 ± 174.9	424.7 ± 169.4	433.7 ± 158.4
<u>Medications</u>				
Antihypertensive medicine Yes	869 (86.0)	732 (88.2)	470 (95.3)	323 (93.9)
RASI Yes	816 (80.7)	646 (77.8)	440 (89.2)	301 (87.5)
Ca blocade Yes	433 (42.8)	506 (61.0)	323 (65.5)	238 (69.2)
Statin Yes	367 (36.3)	310 (37.3)	241 (48.9)	166 (48.3)
Allopurinol Yes	426 (42.1)	375 (45.2)	236 (47.9)	180 (52.3)
Insulin Yes	94 (9.3)	101 (12.2)	75 (15.2)	61 (17.7)
ESAs Yes	121 (12.0)	155 (18.7)	31 (6.3)	49 (14.2)
Active vitamin D Yes	102 (10.1)	66 (8.0)	35 (7.1)	22 (6.4)

Antiplatelet Yes	145 (14.3)	223 (26.9)	97 (19.7)	113 (32.8)
Diuretics* Yes	226 (22.4)	256 (30.8)	196 (39.8)	152 (44.2)
<u>Comorbidities</u>				
Hypertension* Yes	896 (88.8)	762 (91.8)	476 (96.6)	326 (94.8)
Hypercholesterolemia Yes	516 (63.9)	414 (61.0)	319 (73.7)	207 (66.6)
Hypertriglyceridemia Yes	524 (60.7)	446 (61.1)	373 (81.6)	261 (79.6)
Hyperuricemia Yes	776 (77.7)	631 (76.9)	402 (82.7)	284 (83.3)
Hypoalphalipoproteinemia Yes	436 (55.6)	375 (56.2)	295 (69.9)	229 (75.6)
Diabetes mellitus* Yes	275 (27.2)	321 (38.7)	234 (47.5)	188 (54.7)

Appendix Table 3C. Baseline patient characteristics of subcohorts cross-classified by CKD stage and BMI

Variable	BMI < 25, stage 3	BMI < 25, CKD stage 4–5	BMI ≥ 25, stage 3	BMI ≥ 25, CKD stage 4–5	
vanable	(N = 794)	(N = 1047)	(N = 413)	(N = 424)	
Demographic and Clinical Characteristics					
Age* (yrs)	59.2 ± 12.5	61.7 ± 10.8	58.3 ± 12.1	61.4 ± 10.3	
Sex* Male	496 (62.5)	617 (58.9)	289 (70.0)	283 (66.7)	
BMI (kg/m²)	21.66 ± 2.19	21.39 ± 2.38	28.00 ± 2.69	27.85 ± 2.40	
SBP (mmHg)	128.4 ± 17.6	131.4 ± 18.8	133.1 ± 17.7	137.9 ± 19.5	
DBP (mmHg)	75.2 ± 11.3	75.3 ± 12.0	78.3 ± 11.3	78.0 ± 12.8	
MBP* (mmHg)	93.0 ± 12.1	94.0 ± 12.9	96.6 ± 12.1	98.0 ± 13.7	
PP (mmHg)	53.2 ± 13.4	56.1 ± 14.4	54.8 ± 13.8	60.0 ± 14.8	
HR (beats/min)	75.0 ± 12.4	76.2 ± 13.1	76.1 ± 13.1	76.1 ± 12.6	
PP × HR* (mmHg-beats/min)	3980.4 ± 1235.5	4264.9 ± 1282.6	4183.1 ± 1294.4	4566.5 ± 1304.0	
Pulse wave velocity (cm/s)	1589.6 ± 376.3	1764.6 ± 599.1	1615.5 ± 417.4	1707.9 ± 394.1	
Ankle brachial index	1.114 ± 0.122	1.099 ± 0.147	1.105 ± 0.097	1.138 ± 0.146	
Primary cause of CKD					
Diabetic nephropathy	112 (14.1)	196 (18.7)	106 (25.7)	146 (34.4)	
Chronic glomerulonephritis	404 (50.9)	459 (43.8)	157 (38.0)	139 (32.8)	
Nephrosclerosis	107 (13.5)	211 (20.2)	94 (22.8)	89 (21.0)	
Others	171 (21.5)	181 (17.3)	56 (13.6)	50 (11.8)	
CKD stage					
3A	169 (21.3)	0 (0.0%)	112 (27.1)	0 (0.0%)	
3B	625 (78.7)	0 (0.0%)	301 (72.9)	0 (0.0%)	
4	0 (0.0%)	748 (71.4)	0 (0.0%)	299 (70.5)	
5	0 (0.0%)	299 (28.6)	0 (0.0%)	125 (29.5)	
Laboratory Findings (Whole blood, Serum, Urine)					
Hemoglobin* (g/dL)	12.64 ± 1.72	11.23 ± 1.54	13.45 ± 1.82	11.72 ± 1.64	

Albumin* (g/dL)	4.03 ± 0.45	$3.92 \pm 0.42$	4.00 ± 0.39	3.91 ± 0.43
ALT* (IU/L)	16.0 (12.0–22.0)	13.0 (10.0–19.0)	20.0 (15.0–29.0)	16.0 (11.0–21.0)
Uric acid* (mg/dL)	6.85 ± 1.38	7.36 ± 1.63	7.13 ± 1.50	7.60 ± 1.58
Creatinine (mg/dL)	1.36 ± 0.27	2.77 ± 1.02	1.37 ± 0.28	2.89 ± 1.05
eGFR* (ml/min/1.73m²)	39.94 ± 7.01	19.57 ± 6.13	40.80 ± 7.52	19.14 ± 6.17
Potassium* (mEq/L)	4.48 ± 0.47	4.78 ± 0.62	$4.43 \pm 0.48$	4.79 ± 0.61
Phosphorus* (mg/dL)	3.32 ± 0.57	$3.71 \pm 0.72$	3.25 ± 0.64	3.75 ± 0.71
iPTH* (pg/mL)	58.0 (41.0–77.0)	109.0 (73.0–164.0)	60.0 (46.0–80.0)	115.5 (74.0–182.0)
LDL cholesterol* (mg/dL)	111.2 ± 34.2	104.9 ± 32.6	111.5 ± 32.2	107.4 ± 33.0
HDL cholesterol* (mg/dL)	60.3 ± 19.8	55.7 ± 19.2	48.1 ± 13.2	46.5 ± 14.1
Triglycerides* (mg/dL)	125.0 (88.0–178.0)	123.5 (92.0–179.0)	166.0 (113.0–234.5)	167.0 (119.0–251.0)
Glucose* (mg/dL)	116.4 ± 43.7	116.5 ± 39.8	127.1 ± 50.7	128.9 ± 47.3
Hemoglobin A1c (NGSP) (%)	5.82 ± 0.84	5.79 ± 0.82	6.27 ± 1.14	$6.13 \pm 0.93$
UACR* (mg/g Cre)	234.95 (51.20–764.90)	689.25 (226.70–1453.20)	341.45 (61.65–1116.40)	923.70 (317.30–2096.90)
e24hUK* (mEq/day)	40.38 ± 7.98	35.44 ± 7.35	42.96 ± 7.54	39.30 ± 7.15
e24hUNa* (mEq/day)	150.12 ± 42.57	142.46 ± 39.11	165.25 ± 50.80	162.21 ± 46.86
UCACR* (mg/g Cre)	48.4 ± 58.0	28.5 ± 47.3	44.3 ± 59.7	25.9 ± 29.5
UPCR* (mg/g Cre)	404.2 ± 187.3	427.9 ± 169.4	411.4 ± 178.5	445.2 ± 148.7
<u>Medications</u>				
Antihypertensive medicine Yes	652 (82.1)	949 (90.6)	382 (92.5)	411 (96.9)
RASI Yes	604 (76.1)	858 (81.9)	363 (87.9)	378 (89.2)
Ca blocade Yes	315 (39.7)	624 (59.6)	227 (55.0)	334 (78.8)
Statin Yes	303 (38.2)	374 (35.7)	195 (47.2)	212 (50.0)
Allopurinol Yes	267 (33.6)	534 (51.0)	180 (43.6)	236 (55.7)
Insulin Yes	67 (8.4)	128 (12.2)	53 (12.8)	83 (19.6)
ESAs Yes	26 (3.3)	250 (23.9)	5 (1.2)	75 (17.7)
Active vitamin D Yes	66 (8.3)	102 (9.7)	23 (5.6)	34 (8.0)

Antiplatelet Yes	137 (17.3)	231 (22.1)	97 (23.5)	113 (26.7)
Diuretics* Yes	161 (20.3)	321 (30.7)	145 (35.1)	203 (47.9)
<u>Comorbidities</u>				
Hypertension* Yes	685 (86.5)	973 (92.9)	388 (93.9)	414 (97.6)
Hypercholesterolemia Yes	424 (64.1)	506 (61.3)	258 (71.3)	268 (70.2)
Hypertriglyceridemia Yes	428 (60.8)	542 (61.0)	303 (79.3)	331 (82.1)
Hyperuricemia Yes	523 (66.9)	884 (85.2)	316 (78.0)	370 (87.7)
Hypoalphalipoproteinemia Yes	352 (54.9)	459 (56.7)	241 (68.7)	283 (75.7)
Diabetes mellitus* Yes	233 (29.3)	363 (34.7)	200 (48.4)	222 (52.4)

Appendix Table 3D. Baseline patient characteristics of subcohorts cross-classified by DM status and BMI

Variable	BMI < 25, Non-DM	BMI < 25, DM	BMI ≥ 25, Non-DM	BMI ≥ 25, DM
	(N = 1245) (N = 59		(N = 415)	(N = 422)
Demographic and Clinical Characteristics				
Age* (yrs)	59.0 ± 12.5	64.1 ± 8.7	58.1 ± 12.6	61.7 ± 9.6
Sex* Male	694 (55.7)	419 (70.3)	283 (68.2)	289 (68.5)
BMI (kg/m²)	21.28 ± 2.33	21.97 ± 2.16	27.70 ± 2.35	28.15 ± 2.72
SBP (mmHg)	128.6 ± 17.9	133.3 ± 18.7	133.7 ± 16.8	137.4 ± 20.4
DBP (mmHg)	76.7 ± 11.4	72.4 ± 11.8	80.0 ± 11.4	76.4 ± 12.5
MBP* (mmHg)	94.0 ± 12.6	92.7 ± 12.6	97.9 ± 12.0	96.7 ± 13.8
PP (mmHg)	51.9 ± 12.5	60.9 ± 15.1	53.7 ± 12.7	61.0 ± 15.3
HR (beats/min)	75.4 ± 12.7	76.3 ± 13.1	75.7 ± 12.3	76.5 ± 13.4
PP × HR* (mmHg-beats/min)	3916.6 ± 1158.9	4604.6 ± 1360.1	4090.9 ± 1112.8	4659.1 ± 1429.1
Pulse wave velocity (cm/s)	1617.2 ± 552.2	1799.6 ± 363.3	1541.3 ± 372.9	1778.8 ± 410.5
Ankle brachial index	1.131 ± 0.088	1.053 ± 0.193	1.126 ± 0.119	1.116 ± 0.127
Primary cause of CKD				
Diabetic nephropathy	0 (0.0%)	308 (51.7)	0 (0.0%)	252 (59.7)
Chronic glomerulonephritis	733 (58.9)	130 (21.8)	215 (51.8)	81 (19.2)
Nephrosclerosis	229 (18.4)	89 (14.9)	119 (28.7)	64 (15.2)
Others	283 (22.7)	69 (11.6)	81 (19.5)	25 (5.9)
CKD stage				
3A	122 (9.8)	47 (7.9)	71 (17.1)	41 (9.7)
3B	439 (35.3)	186 (31.2)	142 (34.2)	159 (37.7)
4	479 (38.5)	269 (45.1)	158 (38.1)	141 (33.4)
5	205 (16.5)	94 (15.8)	44 (10.6)	81 (19.2)
Laboratory Findings (Whole blood, Serum, Urine)				
Hemoglobin* (g/dL)	11.98 ± 1.72	11.53 ± 1.81	12.91 ± 1.95	12.23 ± 1.86

Albumin* (g/dL)	4.02 ± 0.39	3.86 ± 0.51	4.05 ± 0.35	3.87 ± 0.45
ALT* (IU/L)	14.0 (10.0–20.0)	16.0 (11.0–22.0)	18.0 (14.0–26.0)	16.5 (12.0–24.0)
Uric acid* (mg/dL)	7.06 ± 1.49	7.30 ± 1.64	7.25 ± 1.52	7.49 ± 1.59
Creatinine (mg/dL)	2.13 ± 1.05	2.23 ± 1.05	2.05 ± 1.04	2.23 ± 1.12
eGFR* (ml/min/1.73m²)	28.78 ± 12.24	27.47 ± 11.49	31.11 ± 12.81	28.57 ± 12.73
Potassium* (mEq/L)	4.64 ± 0.58	4.67 ± 0.57	4.60 ± 0.55	4.63 ± 0.61
Phosphorus* (mg/dL)	3.51 ± 0.69	$3.63 \pm 0.68$	$3.37 \pm 0.63$	3.66 ± 0.78
iPTH* (pg/mL)	80.0 (54.0–126.0)	78.0 (53.0–130.0)	74.0 (52.0–111.5)	87.0 (56.0–131.0)
LDL cholesterol* (mg/dL)	109.4 ± 34.2	104.6 ± 31.9	110.1 ± 32.4	108.8 ± 33.0
HDL cholesterol* (mg/dL)	60.6 ± 19.9	52.9 ± 18.1	49.1 ± 14.6	45.6 ± 12.5
Triglycerides* (mg/dL)	122.0 (90.0–173.0)	130.5 (90.5–196.0)	167.0 (114.0–241.0)	166.0 (118.0–246.0)
Glucose* (mg/dL)	103.8 ± 22.5	139.2 ± 55.9	107.1 ± 21.8	146.1 ± 58.0
Hemoglobin A1c (NGSP) (%)	5.44 ± 0.36	6.56 ± 1.00	5.56 ± 0.35	6.84 ± 1.10
UACR* (mg/g Cre)	382.50 (94.95–976.65)	697.85 (139.30–1775.30)	449.25 (128.70–1135.10)	889.40 (206.00–2673.30)
e24hUK* (mEq/day)	37.21 ± 7.94	38.19 ± 8.10	40.84 ± 7.31	41.40 ± 7.82
e24hUNa* (mEq/day)	143.09 ± 38.98	151.09 ± 43.78	160.98 ± 44.94	166.43 ± 52.35
UCACR* (mg/g Cre)	35.0 ± 48.0	40.8 ± 62.0	33.5 ± 47.9	36.6 ± 47.9
UPCR* (mg/g Cre)	406.8 ± 175.8	440.6 ± 178.9	408.5 ± 150.3	448.1 ± 176.3
<u>Medications</u>				
Antihypertensive medicine Yes	1058 (85.0)	543 (91.1)	387 (93.3)	406 (96.2)
RASI Yes	952 (76.5)	510 (85.6)	367 (88.4)	374 (88.6)
Ca blocade Yes	576 (46.3)	363 (60.9)	266 (64.1)	295 (69.9)
Statin Yes	407 (32.7)	270 (45.3)	176 (42.4)	231 (54.7)
Allopurinol Yes	571 (45.9)	230 (38.6)	229 (55.2)	187 (44.3)
Insulin Yes	0 (0.0)	195 (32.7)	0 (0.0)	136 (32.2)
ESAs Yes	157 (12.6)	119 (20.0)	22 (5.3)	58 (13.7)
Active vitamin D Yes	117 (9.4)	51 (8.6)	30 (7.2)	27 (6.4)

Antiplatelet Yes	167 (13.4)	201 (33.7)	69 (16.6)	141 (33.4)
Diuretics* Yes	221 (17.8)	261 (43.8)	119 (28.7)	229 (54.3)
<u>Comorbidities</u>				
Hypertension* Yes	1097 (88.3)	561 (94.1)	394 (94.9)	408 (96.7)
Hypercholesterolemia Yes	596 (61.4)	334 (64.9)	236 (65.9)	290 (75.1)
Hypertriglyceridemia Yes	601 (57.7)	369 (67.0)	303 (80.2)	331 (81.3)
Hyperuricemia Yes	953 (77.6)	454 (76.7)	348 (84.5)	338 (81.4)
Hypoalphalipoproteinemia Yes	472 (50.9)	339 (64.7)	227 (65.6)	297 (78.4)
Diabetes mellitus* Yes	0 (0.0)	596 (100.0)	0 (0.0)	422 (100.0)

Values are expressed as n (%), mean ± SD or median (inter quartile range). Imputed variables are marked with an asterisk (\*). Proportions are based on non-missing data. a: p values are calculated by using the Kruskal–Wallis test. Abbreviations: BMI, body mass index; N, number; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; PP, pulse pressure; HR, heart rate; PP × HR, pulse pressure x heart rate; CVD, cardiovascular disease; CKD, chronic kidney disease; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; iPTH, intact parathyroid hormone; LDL, low-density lipoprotein; HDL, high-density lipoprotein; UACR, urine albumin-to-creatinine ratio; e24hUK, estimated 24-hour urinary potassium excretion; e24hUNa, estimated 24-hour urinary sodium excretion; UCACR, urine calcium-to-creatinine ratio; UPCR, urine phosphorus-to-creatinine ratio; RASI, renin-angiotensin system inhibitor; ESA, erythropoiesis-stimulating agent; DM, diabetes mellitus.

Appendix Table 4. Baseline patient characteristics for the assessment of elderly non-obese patients with DM (Left: Subcohorts stratified by age in the cohort of "BMI < 25, DM", Right: Subcohorts stratified by BMI in the cohort of "Age ≥ 65, DM")

Variable	BMI < 25, Age ≥ 65, DM	BMI < 25, Age ≥ 65, Non-DM	p value	BMI < 25, Age < 65, DM	p value	BMI ≥ 25, Age ≥ 65, DM	p value
variable	(N = 321)	(N = 509)	p value	(N = 275)		(N = 188)	p value
Demographic and Clinical Characteristic	<u>:s</u>						
Age* (yrs)	70.4 ± 3.2	70.3 ± 3.3	0.5361	56.8 ± 7.2	<0.0001	70.0 ± 3.3	0.2134
Sex* Male	226 (70.4)	317 (62.3)	0.0165	193 (70.2)	0.9526	130 (69.1)	0.7655
BMI (kg/m²)	21.91 ± 2.11	21.45 ± 2.26	0.0031	22.04 ± 2.22	0.4889	27.56 ± 2.31	<0.0001
SBP (mmHg)	133.6 ± 17.9	131.4 ± 17.5	0.0739	132.9 ± 19.6	0.6081	138.3 ± 20.7	0.0076
DBP (mmHg)	70.6 ± 11.3	75.2 ± 11.0	<0.0001	74.5 ± 12.0	<0.0001	73.5 ± 11.9	0.0065
MBP* (mmHg)	91.6 ± 11.9	93.9 ± 12.0	0.0067	94.0 ± 13.2	0.0223	95.1 ± 13.5	0.0026
PP (mmHg)	63.0 ± 15.0	56.2 ± 12.9	<0.0001	58.3 ± 14.8	0.0001	64.8 ± 15.6	0.2039
HR (beats/min)	74.6 ± 12.5	75.0 ± 12.6	0.6959	78.3 ± 13.5	0.0012	74.3 ± 13.1	0.7984
PP × HR* (mmHg-beats/min)	4692.6 ± 1402.8	4188.2 ± 1178.5	<0.0001	4504.4 ± 1305.4	0.1140	4889.6 ± 1517.5	0.1612
Pulse wave velocity (cm/s)	1931.0 ± 381.8	1879.8 ± 716.6	0.6630	1643.4 ± 270.2	0.0002	1962.5 ± 471.2	0.7448
Ankle brachial index	1.016 ± 0.199	1.129 ± 0.095	<0.0001	1.100 ± 0.177	0.0292	1.094 ± 0.128	0.0359
Primary cause of CKD							
Diabetic nephropathy	155 (48.3)	0 (0.0%)	<0.0001	153 (55.6)	<0.0001	104 (55.3)	0.0863
Chronic glomerulonephritis	58 (18.1)	245 (48.1)		72 (26.2)		35 (18.6)	
Nephrosclerosis	65 (20.2)	129 (25.3)		24 (8.7)		37 (19.7)	
Others	43 (13.4)	135 (26.5)		26 (9.5)		12 (6.4)	
CKD stage							
3A	21 (6.5)	28 (5.5)	0.0318	26 (9.5)	0.3523	15 (8.0)	0.1011
3B	105 (32.7)	176 (34.6)		81 (29.5)		75 (39.9)	
4	149 (46.4)	196 (38.5)		120 (43.6)		66 (35.1)	
5	46 (14.3)	109 (21.4)		48 (17.5)		32 (17.0)	
Laboratory Findings (Whole blood, Seru	m, Urine)						
Hemoglobin* (g/dL)	11.45 ± 1.78	11.62 ± 1.71	0.1657	11.63 ± 1.84	0.2224	12.12 ± 1.78	<0.0001

Albumin* (g/dL)	3.89 ± 0.47	3.94 ± 0.40	0.1175	3.83 ± 0.54	0.1311	$3.90 \pm 0.41$	0.8847
ALT* (IU/L)	16.0 (11.0–22.0)	14.0 (10.0–19.0)	<0.0001 <sup>a</sup>	15.0 (12.0–22.0)	0.8408ª	16.0 (12.0–24.0)	0.5112ª
Uric acid* (mg/dL)	7.25 ± 1.64	7.00 ± 1.49	0.0268	7.37 ± 1.65	0.3722	7.48 ± 1.60	0.1236
Creatinine (mg/dL)	2.13 ± 0.94	2.22 ± 1.06	0.1768	2.34 ± 1.15	0.0115	2.16 ± 1.08	0.6743
eGFR* (ml/min/1.73m²)	27.59 ± 11.18	26.46 ± 11.40	0.1622	27.34 ± 11.85	0.7897	28.05 ± 11.93	0.6594
Potassium* (mEq/L)	4.69 ± 0.59	4.67 ± 0.57	0.5879	4.66 ± 0.55	0.5135	4.69 ± 0.60	0.9267
Phosphorus* (mg/dL)	3.59 ± 0.63	3.54 ± 0.67	0.2935	3.67 ± 0.73	0.2005	3.59 ± 0.65	0.9715
iPTH* (pg/mL)	76.0 (52.0–122.0)	81.0 (55.0–126.0)	0.1438ª	85.0 (56.0–144.0)	0.0280ª	84.0 (57.0–129.0)	0.1106ª
LDL cholesterol* (mg/dL)	102.2 ± 29.7	106.2 ± 35.9	0.1428	107.3 ± 34.0	0.0730	105.4 ± 31.7	0.2896
HDL cholesterol* (mg/dL)	51.5 ± 17.5	57.1 ± 17.8	0.0002	54.4 ± 18.8	0.0802	45.6 ± 13.3	0.0005
Triglycerides* (mg/dL)	128.5 (90.5–187.5)	122.0 (94.0–168.0)	0.5995ª	134.0 (90.5–199.5)	0.2686ª	156.5 (116.0–213.0)	<0.0001 <sup>a</sup>
Glucose* (mg/dL)	143.4 ± 54.4	106.9 ± 24.6	<0.0001	134.3 ± 57.2	0.0549	141.1 ± 54.1	0.6532
Hemoglobin A1c (NGSP) (%)	6.54 ± 0.96	5.53 ± 0.36	<0.0001	6.59 ± 1.05	0.6159	6.70 ± 1.01	0.0928
UACR* (mg/g Cre)	513.25 (105.15–1434.90)	323.60 (60.70–969.60)	0.0006ª	921.75 (216.00–2248.90)	0.0002ª	689.45 (109.35–1802.35)	0.1713ª
e24hUK* (mEq/day)	37.52 ± 8.04	35.98 ± 7.93	0.0097	38.99 ± 8.10	0.0333	40.12 ± 7.43	0.0007
e24hUNa* (mEq/day)	146.32 ± 45.42	139.07 ± 39.68	0.0201	156.75 ± 41.13	0.0053	157.92 ± 48.05	0.0104
UCACR* (mg/g Cre)	40.2 ± 53.8	36.2 ± 51.5	0.3110	41.6 ± 70.5	0.7845	34.4 ± 42.3	0.2368
UPCR* (mg/g Cre)	433.5 ± 179.2	408.1 ± 171.6	0.0499	448.9 ± 178.7	0.3144	442.4 ± 166.3	0.6013
<u>Medications</u>							
Antihypertensive medicine Yes	293 (91.3)	439 (86.2)	0.0288	250 (90.9)	0.8749	182 (96.8)	0.0159
RASI Yes	274 (85.4)	372 (73.1)	<0.0001	236 (85.8)	0.8734	166 (88.3)	0.3498
Ca blocade Yes	214 (66.7)	292 (57.4)	0.0075	149 (54.2)	0.0018	137 (72.9)	0.1442
Statin Yes	139 (43.3)	171 (33.6)	0.0049	131 (47.6)	0.2893	100 (53.2)	0.0310
Allopurinol Yes	136 (42.4)	239 (47.0)	0.1959	94 (34.2)	0.0407	84 (44.7)	0.6111
Insulin Yes	101 (31.5)	0 (0.0)	<0.0001	94 (34.2)	0.4809	61 (32.4)	0.8183
ESAs Yes	70 (21.8)	85 (16.7)	0.0659	49 (17.8)	0.2246	35 (18.6)	0.3907
Active vitamin D Yes	21 (6.5)	45 (8.8)	0.2332	30 (10.9)	0.0574	11 (5.9)	0.7566
Antiplatelet Yes	123 (38.3)	100 (19.6)	<0.0001	78 (28.4)	0.0104	75 (39.9)	0.7249

Diuretics* Yes	140 (43.6)	116 (22.8)	<0.0001	121 (44.0)	0.9245	102 (54.3)	0.0203
<u>Comorbidities</u>							
Hypertension* Yes	303 (94.4)	459 (90.2)	0.0310	258 (93.8)	0.7662	182 (96.8)	0.2146
Hypercholesterolemia Yes	170 (61.4)	244 (60.7)	0.8593	164 (68.9)	0.0741	124 (71.3)	0.0318
Hypertriglyceridemia Yes	194 (65.8)	252 (57.9)	0.0332	175 (68.4)	0.5180	143 (79.9)	0.0010
Hyperuricemia Yes	246 (77.1)	385 (76.7)	0.8887	208 (76.2)	0.7906	153 (82.3)	0.1711
Hypoalphalipoproteinemia Yes	176 (63.5)	199 (51.0)	0.0013	163 (66.0)	0.5574	133 (79.2)	0.0005
Diabetes mellitus* Yes	321 (100.0)	0 (0.0)	<0.0001	275 (100.0)		188 (100.0)	

Values are expressed as n (%), mean ± SD or median (inter quartile range). Imputed variables are marked with an asterisk (\*). Proportions are based on non-missing data. a: p values are calculated by using the Kruskal–Wallis test comparing with "BMI < 25, Age ≥ 65, DM". Abbreviations: BMI, body mass index; DM, diabetes mellitus; N, number; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; PP, pulse pressure; HR, heart rate; PP × HR, pulse pressure x heart rate; CVD, cardiovascular disease; CKD, chronic kidney disease; ALT, alanine aminotransferase; eGFR, estimated glomerular filtration rate; iPTH, intact parathyroid hormone; LDL, low-density lipoprotein; HDL, high-density lipoprotein; UACR, urine albumin-to-creatinine ratio; e24hUK, estimated 24-hour urinary potassium excretion; e24hUNa, estimated 24-hour urinary sodium excretion; UCACR, urine calcium-to-creatinine ratio; UPCR, urine phosphorus-to-creatinine ratio; RASI, renin-angiotensin system inhibitor; ESA, erythropoiesis-stimulating agent

Appendix Table 5. Predictive characteristics of subcohorts for ≥ 50% eGFR decline or ESRD

Cohort	Positive	Sensi	itivity	:	Specificity	Positive l	ikelihood ratio	Negativ	e likelihood ratio	Diagn	ostic odds ratio
		(%)	95%CI	(%)	95%CI	Value	95%CI	Value	95%CI	Value	95%CI
Overall	Age ≥ 65	44.90	(40.96–48.41)	56.58	(54.32–58.87)	1.03	(0.93–1.14)	0.97	(0.90–1.06)	1.06	(0.88–1.27)
	BMI ≥ 25	36.25	(32.70–39.73)	70.91	(68.66–73.08)	1.25	(1.09–1.42)	0.90	(0.84–0.96)	1.39	(1.14–1.69)
	DM	49.49	(45.76–53.01)	67.04	(64.94–69.30)	1.5	(1.36–1.67)	0.75	(0.70–0.82)	1.99	(1.66–2.40)
	Male	71.18	(67.71–74.79)	40.56	(38.29–42.82)	1.2	(1.13–1.28)	0.71	(0.62–0.82)	1.69	(1.37–2.06)
	CKD stage 4–5	84.40	(81.52-87.33)	57.53	(55.10–59.78)	1.99	(1.86–2.12)	0.27	(0.23–0.33)	7.33	(5.69–9.25)
BMI < 25	Age ≥ 65	46.82	(41.84–51.54)	55.56	(52.78–58.13)	1.05	(0.93–1.19)	0.96	(0.87–1.07)	1.10	(0.87–1.37)
	DM	41.70	(37.19–46.12)	71.32	(68.74–73.81)	1.45	(1.26–1.69)	0.82	(0.75–0.90)	1.78	(1.41–2.25)
	Male	69.66	(65.43–73.92)	43.06	(40.12–45.73)	1.22	(1.12–1.33)	0.70	(0.60–0.84)	1.74	(1.35–2.19)
	CKD stage 4–5	87.38	(84.17–90.77)	54.65	(51.77–57.49)	1.93	(1.79–2.07)	0.23	(0.18–0.31)	8.34	(5.90–11.19)
BMI < 25, female	Age ≥ 65	48.03	(39.73–56.38)	62.90	(58.84–67.00)	1.29	(1.05–1.63)	0.83	(0.70-1.00)	1.57	(1.06–2.34)
	DM	31.87	(23.89–39.50)	77.76	(74.32–81.38)	1.43	(1.07–1.99)	0.88	(0.78–1.00)	1.64	(1.07–2.56)
	CKD stage 4–5	91.13	(86.27–96.59)	49.51	(45.43–53.63)	1.8	(1.63–1.99)	0.18	(0.11–0.40)	10.07	(4.21–17.84)
BMI < 25, male	Age ≥ 65	46.22	(40.90–51.75)	50.03	(46.36–53.56)	0.92	(0.80-1.07)	1.07	(0.95–1.23)	0.86	(0.65–1.13)
	DM	45.88	(40.28–51.06)	66.43	(62.90–69.85)	1.37	(1.17–1.60)	0.81	(0.73–0.92)	1.68	(1.28–2.18)
	CKD stage 4–5	85.81	(81.44–90.08)	58.56	(54.78–62.32)	2.07	(1.86–2.28)	0.24	(0.19–0.35)	8.54	(5.52–12.04)
BMI < 25, Age < 65	DM	43.97	(37.61–50.23)	79.16	(75.94–82.25)	2.11	(1.71–2.60)	0.71	(0.63-0.80)	2.98	(2.16–4.10)
	Male	70.25	(64.36–76.30)	48.74	(45.05–52.43)	1.37	(1.22–1.55)	0.61	(0.49–0.78)	2.25	(1.57–3.13)
	CKD stage 4–5	86.39	(82.09–91.18)	57.98	(54.24-61.64)	2.06	(1.85–2.28)	0.23	(0.17–0.35)	8.76	(5.48–13.03)
BMI < 25, Age ≥ 65	DM	38.89	(32.50–45.35)	61.41	(57.40–65.78)	1.01	(0.83–1.26)	1.00	(0.87–1.14)	1.01	(0.72–1.45)
	Male	68.78	(62.22–75.48)	35.92	(31.91–39.98)	1.07	(0.96–1.21)	0.87	(0.69–1.13)	1.23	(0.85–1.77)
	CKD stage 4–5	88.39	(83.42–93.45)	50.53	(46.34–54.78)	1.79	(1.61–1.99)	0.23	(0.16–0.40)	7.77	(4.08–12.43)
BMI < 25, CKD stage 3	Age ≥ 65	46.80	(34.18–59.28)	58.95	(55.30–62.51)	1.14	(0.88–1.55)	0.90	(0.73–1.19)	1.26	(0.73–2.13)
	DM	53.95	(41.92–67.46)	73.11	(69.75–76.28)	2.01	(1.57–2.74)	0.63	(0.49–0.85)	3.18	(1.86–5.59)

	Male	78.31 (68.12–88.85)	39.01 (35.28–42.58)	1.28 (1.12–1.50)	0.56 (0.37–1.04)	2.31 (1.09–4.07)
BMI < 25, CKD stage 45	Age ≥ 65	47.36 (42.32–52.40)	51.93 (47.86–56.24)	0.99 (0.86–1.15)	1.01 (0.88–1.16)	0.97 (0.74–1.30)
	DM	39.70 (34.98–44.39)	69.17 (65.15–73.24)	1.29 (1.06–1.56)	0.87 (0.79–0.97)	1.48 (1.10–1.99)
	Male	68.41 (63.91–73.20)	48.05 (43.96–52.16)	1.32 (1.18–1.47)	0.66 (0.55–0.79)	2.00 (1.51–2.66)
BMI < 25, Non-DM	Age ≥ 65	49.22 (42.89–55.37)	61.67 (58.50–64.95)	1.28 (1.10–1.52)	0.82 (0.72–0.95)	1.56 (1.16–2.12)
	Male	64.47 (58.76–70.25)	46.94 (43.67–50.05)	1.22 (1.08–1.37)	0.76 (0.64–0.92)	1.61 (1.18–2.15)
	CKD stage 4–5	90.54 (86.87–94.65)	56.02 (52.87–59.34)	2.06 (1.89–2.25)	0.17 (0.12–0.28)	12.20 (6.92–18.99)
BMI < 25, DM	Age ≥ 65	43.66 (36.45–50.88)	40.49 (35.49–45.35)	0.73 (0.61–0.90)	1.39 (1.16–1.69)	0.53 (0.36–0.76)
	Male	76.65 (70.75–83.07)	33.30 (28.42–38.02)	1.15 (1.03–1.29)	0.70 (0.52–0.98)	1.64 (1.05–2.47)
	CKD stage 4–5	83.18 (78.03–88.66)	51.29 (46.12–56.30)	1.71 (1.50–1.93)	0.33 (0.24–0.48)	5.21 (3.17–7.79)
BMI ≥ 25	Age ≥ 65	41.42 (35.52–47.57)	59.04 (54.75–63.38)	1.01 (0.84–1.23)	0.99 (0.87–1.14)	1.02 (0.74–1.41)
	DM	63.12 (57.21–68.92)	56.59 (52.30–60.86)	1.45 (1.27–1.67)	0.65 (0.55–0.78)	2.23 (1.64–3.03)
	Male	73.90 (68.66–79.69)	34.54 (30.39–38.59)	1.13 (1.03–1.25)	0.76 (0.59–0.97)	1.49 (1.06–2.10)
	CKD stage 4–5	79.17 (74.03–84.14)	64.52 (60.39–68.57)	2.23 (1.94–2.52)	0.32 (0.26–0.43)	6.91 (4.64–9.63)
BMI ≥ 25, female	Age ≥ 65	42.11 (30.83–53.59)	60.36 (53.42–67.18)	1.06 (0.79–1.52)	0.96 (0.76–1.22)	1.11 (0.65–1.98)
	DM	63.56 (52.79–75.51)	55.40 (48.28–62.67)	1.43 (1.12–1.86)	0.66 (0.48–0.96)	2.17 (1.19–3.92)
	CKD stage 4–5	79.85 (70.42–89.89)	57.59 (50.44–64.54)	1.88 (1.52–2.31)	0.35 (0.23–0.66)	5.38 (2.48–10.04)
BMI ≥ 25, male	Age ≥ 65	41.13 (34.33–48.12)	58.35 (53.12–63.82)	0.99 (0.80–1.24)	1.01 (0.86–1.18)	0.98 (0.68–1.43)
	DM	63.05 (56.12–69.98)	57.28 (51.91–62.62)	1.48 (1.25–1.74)	0.65 (0.53–0.81)	2.29 (1.56–3.30)
	CKD stage 4–5	79.03 (72.90–85.14)	68.26 (63.13–73.04)	2.49 (2.05–2.93)	0.31 (0.23–0.44)	8.11 (4.95–12.26)
BMI ≥ 25, Age < 65	DM	61.49 (54.24–69.29)	60.24 (54.60–66.19)	1.55 (1.27–1.89)	0.64 (0.51–0.81)	2.42 (1.61–3.67)
	Male	74.27 (67.27–81.49)	35.31 (29.95–40.14)	1.15 (1.01–1.31)	0.73 (0.54–1.05)	1.58 (0.97–2.43)
	CKD stage 4–5	78.69 (72.06–85.75)	69.66 (64.39–74.78)	2.59 (2.09–3.11)	0.31 (0.23–0.45)	8.48 (4.86–13.13)
BMI ≥ 25, Age ≥ 65	DM	65.28 (56.41–74.29)	51.37 (44.16–58.13)	1.34 (1.09–1.65)	0.68 (0.51–0.95)	1.99 (1.14–3.23)
	Male	73.39 (64.96–81.74)	33.48 (27.31–39.74)	1.1 (0.95–1.28)	0.79 (0.56–1.24)	1.39 (0.77–2.29)
	CKD stage 4–5	79.86 (72.13–87.93)	57.13 (50.49–64.27)	1.86 (1.53–2.25)	0.35 (0.24–0.58)	5.28 (2.85–9.01)
BMI ≥ 25, CKD stage 3	Age ≥ 65	39.97 (26.05–53.19)	63.75 (58.55–68.84)	1.1 (0.77–1.67)	0.94 (0.76–1.25)	1.17 (0.62–2.20)
	DM	74.64 (63.22–87.19)	56.26 (50.97–61.31)	1.71 (1.39–2.12)	0.45 (0.30–0.83)	3.79 (1.76–7.07)

	Male	74.73	(63.87–88.73)	30.84	(26.02–35.74)	1.08	(0.91–1.33)	0.82	(0.52–1.51)	1.32	(0.61–2.55)
BMI ≥ 25, CKD stage 4–5	Age ≥ 65	41.78	(35.32–48.48)	50.40	(42.95–57.97)	0.84	(0.67–1.06)	1.16	(0.94–1.40)	0.73	(0.48–1.12)
	DM	59.51	(52.74–65.91)	56.66	(48.87–64.15)	1.37	(1.09–1.69)	0.71	(0.58-0.90)	1.92	(1.24–2.93)
	Male	73.78	(67.99–79.93)	41.38	(34.03-48.50)	1.26	(1.08–1.46)	0.63	(0.47-0.85)	1.99	(1.29–3.10)
BMI ≥ 25, Non-DM	Age ≥ 65	38.85	(28.13-48.66)	62.85	(57.29–68.31)	1.05	(0.78–1.44)	0.97	(0.81–1.21)	1.07	(0.64–1.77)
	Male	74.10	(65.54–83.75)	33.81	(28.55–39.42)	1.12	(0.97–1.32)	0.77	(0.53-1.19)	1.46	(0.81–2.51)
	CKD stage 4–5	86.96	(79.49–94.81)	64.14	(58.67–69.72)	2.42	(2.01–2.90)	0.20	(0.12–0.47)	11.92	(4.62–22.37)
BMI ≥ 25, DM	Age ≥ 65	42.84	(35.32–50.56)	54.14	(47.85–60.43)	0.93	(0.74–1.19)	1.06	(0.88–1.27)	0.88	(0.58–1.34)
	Male	73.83	(66.98–80.65)	35.43	(28.96–41.81)	1.14	(1.00-1.31)	0.74	(0.55–1.04)	1.55	(0.97–2.40)
	CKD stage 4–5	74.64	(67.86–81.12)	64.82	(58.63-71.47)	2.12	(1.72–2.60)	0.39	(0.30-0.53)	5.42	(3.38–8.54)

Diagnostic odds ratio of male, Age  $\geq$ 65 years, CKD stage 4–5 and DM according to subcohorts for a decline in eGFR by  $\geq$  50% from baseline or ESRD that requires renal replacement therapy during the follow-up examination period. Abbreviations: CI, confidence interval; DM, diabetes mellitus; BMI, body mass index.

Appendix Table 6. Multivariate analysis for prognostic factors associated with ≥ 50% eGFR decline or ESRD in subcohorts stratified by BMI

	(Full mod 								(Final mo	del)		
Variable		BMI < 25			BMI ≥ 25			BMI < 25			BMI ≥ 25	
	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value
Age (/1 yr)	0.991	(0.981–1.000)	0.0505	0.987	(0.973–1.001)	0.0681	0.990	(0.981–0.999)	0.0377	0.986	(0.973–0.999)	0.0328
Male	2.365	(1.801-3.106)	<0.0001	2.374	(1.634–3.449)	<0.0001	2.629	(2.098–3.295)	<0.0001	2.614	(1.920-3.559)	<0.0001
BMI (/1 kg/m²)	0.970	(0.925–1.017)	0.2011	1.042	(0.978–1.111)	0.2048	0.978	(0.936–1.022)	0.3194	1.042	(0.983-1.105)	0.1682
eGFR (/1 ml/min/1.73m²)	0.937	(0.924–0.951)	<0.0001	0.956	(0.938–0.974)	<0.0001	0.934	(0.921–0.947)	<0.0001	0.953	(0.937–0.970)	<0.0001
MBp (/10 mmHg)	1.063	(0.968–1.167)	0.2037	0.975	(0.863-1.103)	0.6910						
PP × HR (/1000 mmHg-beats/min)	1.134	(1.032–1.245)	0.0090	1.170	(1.029–1.330)	0.0170	1.155	(1.066–1.252)	0.0005	1.137	(1.017–1.271)	0.0241
Hemoglobin (/1 g/dl)	0.831	(0.769–0.897)	<0.0001	0.846	(0.762-0.940)	0.0018	0.829	(0.772–0.890)	<0.0001	0.848	(0.769–0.936)	0.0011
Uric acid (/1 mg/dL)	0.933	(0.876–0.994)	0.0332	1.037	(0.949–1.133)	0.4259						
iPTH (/10 pg/mL)	1.010	(1.000-1.019)	0.0437	1.014	(0.999–1.028)	0.0596	1.009	(1.001–1.018)	0.0338	1.012	(0.998–1.027)	0.0865
Log UACR [/1 log(mg/g Cre)]	1.855	(1.650-2.086)	<0.0001	2.106	(1.756–2.526)	<0.0001	1.829	(1.635–2.045)	<0.0001	1.946	(1.661–2.281)	<0.0001
ALT (/1 IU/L)	0.999	(0.989–1.009)	0.8152	0.991	(0.978–1.004)	0.1635						
Phosphorus (/1 mg/dL)	1.465	(1.226–1.751)	<0.0001	1.524	(1.246–1.865)	<0.0001	1.410	(1.216–1.636)	<0.0001	1.377	(1.146–1.654)	0.0006
Albumin (/1 g/dL)	0.772	(0.599–0.996)	0.0467	0.649	(0.462-0.911)	0.0125	0.778	(0.618–0.980)	0.0331	0.692	(0.512-0.934)	0.0162
HDL cholesterol (/10 mg/dL)	0.970	(0.908-1.036)	0.3631	0.939	(0.828–1.064)	0.3219						
UCACR (/100 mg/g Cre)	0.990	(0.759–1.291)	0.9417	1.602	(0.972–2.640)	0.0644						
UPCR (/100 mg/g Cre)	0.975	(0.900-1.056)	0.5319	0.890	(0.798–0.992)	0.0355						
e24hUK (/10 mEq/day)	0.702	(0.578-0.853)	0.0004	0.841	(0.642-1.101)	0.2067	0.701	(0.598–0.821)	<0.0001	0.850	(0.693-1.042)	0.1173
Potassium (/1 mEq/L)	1.116	(0.942–1.322)	0.2034	1.052	(0.832–1.328)	0.6735						
Diabetes mellitus	1.035	(0.817–1.312)	0.7757	0.899	(0.648–1.247)	0.5241						
Diuretics use	0.910	(0.713-1.161)	0.4466	0.931	(0.684–1.267)	0.6475						
Hypertension	1.075	(0.650-1.780)	0.7774	0.635	(0.227–1.782)	0.3885						

Variables with p-values of <0.1 in the univariate model in total cohort were included in the multivariate model. Multivariate Cox regression analyses using backward selection were performed in the final model. Abbreviations: eGFR, estimated glomerular filtration rate; BMI, body mass index; HR<sup>a</sup>, hazard ratio; CI, confidence interval; MBP, mean blood pressure; PP × HR, pulse pressure x heart rate; iPTH, intact parathyroid hormone; UACR, urine albumin-to-creatinine ratio; ALT, alanine aminotransferase; HDL, high-density lipoprotein; UCACR, urine calcium-to-creatinine ratio; UPCR, estimated 24-hour urinary sodium excretion; e24hUK, estimated 24-hour urinary potassium excretion

Appendix Table 7A. Multivariate analysis for prognostic factors associated with ≥ 50% eGFR decline or ESRD in subcohorts cross-classified by sex and BMI

	(Final model)											
Variable		BMI < 25, Male			BMI ≥ 25, Male			BMI < 25, Female			BMI ≥ 25, Female	)
	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value
Age (/1 yr)	0.989	(0.978-1.000)	0.0489	0.984	(0.969–0.999)	0.0408	0.992	(0.976-1.009)	0.3510	0.994	(0.969–1.021)	0.6744
BMI (/1 kg/m²)	0.992	(0.935–1.052)	0.7853	1.068	(0.997–1.144)	0.0619	0.967	(0.905-1.034)	0.3317	0.985	(0.876–1.107)	0.8021
eGFR (/1 ml/min/1.73m²)	0.940	(0.925–0.956)	<0.0001	0.947	(0.927–0.968)	<0.0001	0.915	(0.888-0.943)	<0.0001	0.971	(0.938–1.006)	0.1032
PP × HR (/1000 mmHg-beats/min)	1.118	(1.006-1.244)	0.0389	1.143	(1.003-1.302)	0.0446	1.194	(1.054–1.353)	0.0053	1.145	(0.890–1.472)	0.2918
Hemoglobin (/1 g/dl)	0.839	(0.772-0.911)	<0.0001	0.853	(0.763–0.955)	0.0055	0.796	(0.694-0.913)	0.0011	0.805	(0.647–1.000)	0.0499
iPTH (/10 pg/mL)	1.018	(1.005-1.032)	0.0089	1.016	(0.999–1.033)	0.0684	1.001	(0.988-1.014)	0.8653	1.011	(0.978–1.045)	0.5101
Log UACR [/1 log(mg/g Cre)]	1.881	(1.629–2.173)	<0.0001	1.794	(1.484–2.169)	<0.0001	1.685	(1.412-2.012)	<0.0001	2.374	(1.693–3.327)	<0.0001
Phosphorus (/1 mg/dL)	1.439	(1.203-1.721)	<0.0001	1.295	(1.055–1.590)	0.0135	1.342	(1.020-1.767)	0.0357	1.887	(1.055–3.376)	0.0325
Albumin (/1 g/dL)	0.846	(0.647-1.106)	0.2212	0.617	(0.438-0.871)	0.0060	0.525	(0.332-0.831)	0.0060	0.886	(0.382–2.057)	0.7775
e24hUK (/10 mEq/day)	0.663	(0.547–0.803)	<0.0001	0.796	(0.629-1.008)	0.0582	0.816	(0.618-1.077)	0.1509	1.000	(0.639–1.566)	0.9988

# Appendix Table 7B. Multivariate analysis for prognostic factors associated with ≥ 50% eGFR decline or ESRD in subcohorts cross-classified by age and BMI

	(Final model)											
Variable		BMI < 25, Age < 65	i		BMI ≥ 25, Age < 6	55		BMI < 25, Age ≥ 65			BMI ≥ 25, Age ≥ 6	5
	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value
Age (/1 yr)	0.990	(0.976–1.005)	0.1930	0.973	(0.954–0.992)	0.0055	1.036	(0.993–1.080)	0.1015	0.993	(0.937–1.053)	0.8207
Male	3.130	(2.305-4.251)	<0.0001	2.591	(1.723–3.895)	<0.0001	2.148	(1.527–3.022)	<0.0001	2.973	(1.778–4.971)	<0.0001
BMI (/1 kg/m²)	0.971	(0.914–1.030)	0.3251	1.010	(0.939–1.085)	0.7953	0.983	(0.921–1.049)	0.5958	1.150	(1.032–1.280)	0.0111
eGFR (/1 ml/min/1.73m²)	0.923	(0.905-0.941)	<0.0001	0.951	(0.930-0.972)	<0.0001	0.942	(0.922–0.962)	<0.0001	0.956	(0.928-0.984)	0.0024
PP × HR (/1000 mmHg-beats/min)	1.146	(1.019–1.290)	0.0230	1.060	(0.914–1.229)	0.4410	1.150	(1.026–1.288)	0.0160	1.226	(1.027–1.464)	0.0240
Hemoglobin (/1 g/dl)	0.826	(0.751–0.908)	<0.0001	0.923	(0.821–1.038)	0.1822	0.808	(0.721–0.905)	0.0002	0.682	(0.569–0.817)	<0.0001
iPTH (/10 pg/mL)	1.009	(0.998-1.019)	0.0960	1.012	(0.993-1.031)	0.2264	1.009	(0.992–1.027)	0.3103	1.015	(0.992-1.039)	0.2021
Log UACR [/1 log(mg/g Cre)]	1.844	(1.570–2.165)	<0.0001	2.101	(1.659–2.662)	<0.0001	1.847	(1.582–2.155)	<0.0001	1.923	(1.539–2.401)	<0.0001
Phosphorus (/1 mg/dL)	1.367	(1.124–1.661)	0.0017	1.492	(1.212–1.836)	0.0002	1.384	(1.081–1.772)	0.0100	1.176	(0.763-1.811)	0.4623

Albumin (/1 g/dL)	0.738 (0.547–0.995)	0.0464	0.670 (0.452–0.992)	0.0457	0.808 (0.565–1.158)	0.2459	0.625 (0.364–1.072)	0.0875
e24hUK (/10 mEq/day)	0.790 (0.631–0.988)	0.0391	0.884 (0.685–1.142)	0.3444	0.633 (0.503–0.795)	<0.0001	0.817 (0.572–1.166)	0.2643

# Appendix Table 7C. Multivariate analysis for prognostic factors associated with ≥ 50% eGFR decline or ESRD in subcohorts cross-classified by CKD stage and BMI

	(Final model)											
Variable		BMI < 25, CKD stag	ge 3	ı	BMI ≥ 25, CKD stag	e 3	В	MI < 25, CKD stage	<b>1–</b> 5	ВГ	VII ≥ 25, CKD stage	4–5
	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value
Age (/1 yr)	1.002	(0.977–1.028)	0.8535	0.984	(0.960-1.009)	0.2007	0.986	(0.977–0.996)	0.0066	0.984	(0.969–0.999)	0.0387
Male	2.121	(1.106-4.070)	0.0237	2.184	(1.087-4.389)	0.0283	2.741	(2.151–3.494)	<0.0001	2.921	(2.055–4.152)	<0.0001
BMI (/1 kg/m²)	0.934	(0.823-1.061)	0.2940	0.985	(0.875–1.109)	0.8000	0.984	(0.939–1.032)	0.5057	1.071	(1.001–1.146)	0.0478
eGFR (/1 ml/min/1.73m²)	0.978	(0.937–1.021)	0.3107	0.991	(0.948–1.036)	0.6933	0.915	(0.895–0.936)	<0.0001	0.928	(0.895-0.961)	<0.0001
PP × HR (/1000 mmHg-beats/min)	1.305	(1.062-1.604)	0.0113	1.269	(0.991–1.625)	0.0587	1.132	(1.036–1.237)	0.0061	1.141	(1.009–1.291)	0.0361
Hemoglobin (/1 g/dl)	0.942	(0.788–1.125)	0.5084	0.873	(0.715–1.065)	0.1794	0.806	(0.743-0.874)	<0.0001	0.842	(0.752-0.943)	0.0029
iPTH (/10 pg/mL)	1.035	(0.961–1.116)	0.3641	1.035	(0.952–1.125)	0.4190	1.005	(0.996–1.015)	0.2475	1.004	(0.988–1.020)	0.6464
Log UACR [/1 log(mg/g Cre)]	1.775	(1.337–2.358)	<0.0001	2.45	(1.735–3.458)	<0.0001	1.825	(1.613–2.066)	<0.0001	1.749	(1.462-2.093)	<0.0001
Phosphorus (/1 mg/dL)	1.232	(0.696–2.180)	0.4744	1.208	(0.789–1.848)	0.3843	1.403	(1.199–1.642)	<0.0001	1.402	(1.099–1.789)	0.0066
Albumin (/1 g/dL)	0.381	(0.204–0.711)	0.0024	0.605	(0.293–1.252)	0.1759	0.881	(0.683–1.136)	0.3291	0.680	(0.484–0.956)	0.0263
e24hUK (/10 mEq/day)	0.800	(0.535–1.197)	0.2779	1.125	(0.736–1.720)	0.5871	0.705	(0.592-0.840)	<0.0001	0.834	(0.662–1.051)	0.1249

## Appendix Table 7D. Multivariate analysis for prognostic factors associated with ≥ 50% eGFR decline or ESRD in subcohorts cross-classified by DM status and BMI

	(Final model)											
Variable		BMI < 25, Non-DI	М		BMI ≥ 25, Non-DN	1		BMI < 25, DM			BMI ≥ 25, DM	
	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value	HRª	95% CI	p value
Age (/1 yr)	0.991	(0.980–1.002)	0.1066	0.982	(0.962–1.002)	0.0751	0.984	(0.967–1.001)	0.0625	0.990	(0.973–1.007)	0.2582
Male	2.927	(2.174–3.940)	<0.0001	3.417	(1.920-6.079)	<0.0001	2.274	(1.579–3.275)	<0.0001	2.383	(1.618–3.512)	<0.0001
BMI (/1 kg/m²)	1.019	(0.961–1.079)	0.5346	1.055	(0.948–1.173)	0.3278	0.924	(0.860-0.992)	0.0291	1.037	(0.964–1.116)	0.3286
eGFR (/1 ml/min/1.73m²)	0.922	(0.904–0.941)	<0.0001	0.943	(0.913-0.975)	0.0005	0.952	(0.933-0.972)	<0.0001	0.961	(0.941–0.982)	0.0003
PP × HR (/1000 mmHg-beats/min)	1.153	(1.030–1.290)	0.0134	1.071	(0.859–1.335)	0.5407	1.156	(1.022–1.308)	0.0213	1.177	(1.026–1.351)	0.0201

Hemoglobin (/1 g/dl)	0.790 (0.713–0.874)	<0.0001	0.815 (0.695–0.956)	0.0118	0.872 (0.786–0.967)	0.0098	0.871 (0.766–0.991)	0.0358
iPTH (/10 pg/mL)	1.003 (0.991–1.014)	0.6429	1.013 (0.986–1.041)	0.3415	1.025 (1.007–1.043)	0.0068	1.014 (0.996–1.032)	0.1178
Log UACR [/1 log(mg/g Cre)]	1.787 (1.545–2.067)	<0.0001	1.893 (1.429–2.508)	<0.0001	1.829 (1.533–2.181)	<0.0001	1.972 (1.599–2.434)	<0.0001
Phosphorus (/1 mg/dL)	1.435 (1.166–1.766)	0.0007	1.705 (1.014–2.866)	0.0441	1.385 (1.098–1.748)	0.0060	1.331 (1.074–1.649)	0.0091
Albumin (/1 g/dL)	0.775 (0.546–1.100)	0.1529	0.514 (0.289–0.914)	0.0234	0.728 (0.526–1.006)	0.0540	0.761 (0.526–1.100)	0.1460
e24hUK (/10 mEq/day)	0.718 (0.588–0.878)	0.0012	0.857 (0.552–1.330)	0.4898	0.676 (0.522–0.874)	0.0028	0.845 (0.658–1.083)	0.1833

Variables with p-values of <0.1 in the univariate model in the total cohort were included in the multivariate model. Multivariate Cox regression analyses using backward selection were performed in final model. Abbreviations: eGFR, estimated glomerular filtration rate; BMI, body mass index; HR<sup>a</sup>, hazard ratio; CI, confidence interval; PP × HR, pulse pressure x heart rate; iPTH, intact para thyroid hormone; UACR, urine albumin-to-creatinine ratio; e24hUK, estimated 24-hour urinary potassium excretion; DM, diabetes mellitus.

Appendix Table 8. Predictive characteristics of prognostic factors based on the cut-off values in respective cohorts for ≥ 50% eGFR decline or ESRD

Cohort	Positive	Sens	sitivity	Specificity	Positive	likelihood ratio	Negative	likelihood ratio	Diagnosti	c odds ratio
conort	rositive	(%) 95	95%CI (%)	95%CI	Value	95%CI	Value	95%CI	Value	95%CI
Overall	Alb ≤ 3.9	62.43 (5	58.80–66.02) 64.85	(62.70–67.12)	1.78	(1.62–1.94)	0.58	(0.52–0.65)	3.07	(2.52–3.70)
	Hb ≤ 11.3	59.05 (5	55.54–62.89) 72.57	(70.53–74.62)	2.15	(1.95–2.38)	0.56	(0.51–0.62)	3.81	(3.18–4.61)
	95 ≤ iPTH	66.17 (6	62.53–69.84) 72.03	(69.83–74.14)	2.37	(2.14–2.61)	0.47	(0.42-0.53)	5.04	(4.12–6.15)
	e24hUK ≤ 36.8	52.25 (4	48.45–56.15) 62.02	(59.75–64.39)	1.38	(1.25–1.53)	0.77	(0.70-0.84)	1.79	(1.49–2.17)
	865.2 ≤ UACR	68.73 (6	65.08–72.43) 78.16	(76.19–80.27)	3.15	(2.82–3.52)	0.40	(0.36–0.45)	7.86	(6.40–9.63)
	3.6 ≤ P	65.08 (6	61.45–68.90) 60.29	(57.89–62.81)	1.64	(1.50–1.79)	0.58	(0.52–0.65)	2.83	(2.33–3.45)
	4216.0 ≤ PP × HR	58.31 (5	54.09–62.22) 62.98	(60.52–65.33)	1.58	(1.42–1.73)	0.66	(0.60-0.74)	2.38	(1.93–2.90)
BMI < 25	Alb ≤ 3.9	63.74 (5	59.16–68.60) 64.82	(62.17–67.39)	1.81	(1.62–2.02)	0.56	(0.49–0.65)	3.24	(2.52–4.10)
	Hb ≤ 11.3	66.25 (6	61.73–70.77) 68.57	(66.04–71.25)	2.11	(1.88–2.35)	0.49	(0.43–0.57)	4.28	(3.32–5.43)
	96 ≤ iPTH	65.72 (6	61.07–70.30) 71.66	(69.10–74.24)	2.32	(2.05–2.60)	0.48	(0.42–0.56)	4.85	(3.68–6.17)
	e24hUK ≤ 36.7	60.91 (5	56.01–65.63) 57.93	(55.16–60.86)	1.45	(1.30–1.62)	0.67	(0.59–0.78)	2.15	(1.67–2.73)
	661.4 ≤ UACR	72.98 (6	69.00–77.27) 71.03	(68.36–73.82)	2.52	(2.25–2.80)	0.38	(0.33–0.45)	6.62	(5.17–8.47)
	3.6 ≤ P	67.93 (6	63.39–72.56) 59.56	(56.75–62.62)	1.68	(1.52–1.86)	0.54	(0.46–0.63)	3.12	(2.41–4.01)
	4240.2 ≤ PP × HR	57.10 (5	52.01–61.97) 65.61	(62.73–68.38)	1.66	(1.46–1.87)	0.65	(0.58–0.75)	2.54	(1.96–3.19)
BMI < 25, female	Alb ≤ 3.9	57.07 (4	48.81–65.34) 64.34	(60.30–68.43)	1.60	(1.32–1.95)	0.67	(0.55–0.84)	2.40	(1.60–3.52)
	Hb ≤ 10.6	65.97 (5	57.12–74.92) 75.97	(72.55–79.56)	2.75	(2.24–3.35)	0.45	(0.35–0.61)	6.13	(3.81–9.37)
	98 ≤ iPTH	66.37 (5	57.89–74.73) 66.27	(62.13–70.36)	1.97	(1.64–2.34)	0.51	(0.40-0.69)	3.88	(2.44–5.78)
	e24hUK ≤ 35.5	64.48 (5	56.54–73.35) 58.24	(53.96–62.51)	1.54	(1.32–1.85)	0.61	(0.48–0.79)	2.53	(1.69–3.84)
	658.5 ≤ UACR	67.51 (5	59.12–75.42) 69.42	(65.52–73.45)	2.21	(1.83–2.66)	0.47	(0.37–0.63)	4.72	(2.98–7.05)
	4.0 ≤ P	55.68 (4	46.61–64.28) 66.66	(62.26–70.99)	1.67	(1.35–2.08)	0.66	(0.54–0.85)	2.51	(1.62–3.80)
	4141.5 ≤ PP × HR	61.97 (5	53.06–70.97) 60.05	(55.81–64.51)	1.55	(1.29–1.87)	0.63	(0.51–0.84)	2.45	(1.54–3.68)
BMI < 25, male	Alb ≤ 3.9	66.85 (6	61.41–72.40) 65.27	(61.79–68.71)	1.92	(1.69–2.20)	0.51	(0.43–0.61)	3.79	(2.80–5.04)
	Hb ≤ 11.7	70.54 (6	65.18–75.76) 68.81	(65.47–72.20)	2.26	(1.96–2.57)	0.43	(0.36–0.53)	5.28	(3.76–7.02)
	96 ≤ iPTH	65.48 (5	59.62–71.16) 76.65	(73.45–79.91)	2.80	(2.36–3.31)	0.45	(0.38–0.54)	6.23	(4.49–8.54)

	e24hUK ≤ 36.8	58.74	(52.83–64.46)	61.96	(57.95–65.55)	1.54	(1.32–1.78)	0.67	(0.57–0.79)	2.32	(1.68–3.12)
			,				,				
	588.4 ≤ UACR	78.00	(73.45–82.81)	70.26	(66.71–73.93)	2.62	(2.29–3.00)	0.31	(0.25–0.39)	8.37	(6.03–11.48)
	3.5 ≤ P	69.18	(63.38–74.65)	69.39	(65.73–73.19)	2.26	(1.93–2.61)	0.44	(0.37–0.55)	5.09	(3.58–6.92)
4	1300.0 ≤ PP × HR	56.15	(50.21–62.02)	69.21	(65.48–72.93)	1.82	(1.53–2.16)	0.63	(0.55–0.75)	2.88	(2.06–3.89)
BMI < 25, Age < 65	Alb ≤ 3.9	61.51	(55.44–68.09)	68.96	(65.48–72.40)	1.98	(1.69–2.33)	0.56	(0.47–0.67)	3.55	(2.57–4.93)
	Hb ≤ 11.3	61.61	(55.52–67.95)	73.24	(69.98–76.65)	2.30	(1.95–2.71)	0.52	(0.44–0.63)	4.39	(3.14–5.99)
	95 ≤ iPTH	68.85	(62.79–75.04)	71.31	(67.60–74.70)	2.40	(2.02–2.81)	0.44	(0.36–0.55)	5.49	(3.79–7.64)
	e24hUK ≤ 37.3	57.95	(51.58–64.45)	57.56	(53.73–61.45)	1.37	(1.19–1.59)	0.73	(0.62–0.88)	1.87	(1.35–2.57)
	901.7 ≤ UACR	68.09	(62.05–74.20)	79.22	(76.01–82.57)	3.28	(2.71–3.94)	0.40	(0.34–0.50)	8.14	(5.57–11.47)
	3.6 ≤ P	65.35	(58.84–71.67)	60.99	(57.16–64.95)	1.68	(1.44–1.94)	0.57	(0.47–0.71)	2.95	(2.03-4.10)
3	3828.0 ≤ PP × HR	65.35	(58.90–71.99)	59.95	(56.28–63.99)	1.63	(1.41–1.89)	0.58	(0.48–0.72)	2.82	(1.99–3.95)
BMI < 25, Age ≥ 65	Alb ≤ 3.9	65.94	(58.66–72.83)	59.75	(55.73–63.80)	1.64	(1.41–1.92)	0.57	(0.46–0.73)	2.87	(1.95–4.11)
	Hb ≤ 11.1	66.06	(59.18–72.62)	67.54	(63.69–71.38)	2.03	(1.72–2.41)	0.50	(0.41–0.63)	4.05	(2.76–5.77)
	87 ≤ iPTH	69.08	(62.07–75.67)	65.68	(61.71–69.80)	2.01	(1.71–2.36)	0.47	(0.38–0.61)	4.27	(2.85–6.16)
	e24hUK ≤ 36.7	69.23	(62.23–76.10)	54.33	(49.87–58.65)	1.52	(1.31–1.75)	0.57	(0.45–0.74)	2.68	(1.80-3.84)
	531.6 ≤ UACR	76.60	(70.92–82.52)	69.33	(65.25–73.44)	2.50	(2.12–2.90)	0.34	(0.27–0.45)	7.40	(4.90–10.53)
	3.6 ≤ P	70.56	(64.00–76.76)	57.89	(53.70–62.24)	1.68	(1.45–1.96)	0.51	(0.41–0.66)	3.29	(2.23–4.78)
4	1416.0 ≤ PP × HR	56.18	(49.34–63.99)	62.18	(57.57–66.69)	1.49	(1.25–1.80)	0.70	(0.59–0.85)	2.11	(1.48–3.05)
BMI < 25, CKD stage 3	Alb ≤ 3.8	74.95	(62.51-87.45)	76.47	(73.36–79.67)	3.19	(2.55–3.97)	0.33	(0.22–0.66)	9.72	(4.09–17.83)
	Hb ≤ 11.8	53.27	(39.88–65.77)	68.79	(65.53–72.24)	1.71	(1.33–2.28)	0.68	(0.53–0.95)	2.51	(1.42-4.26)
	63 ≤ iPTH	62.18	(49.71–76.06)	59.16	(55.31–62.80)	1.52	(1.24–2.00)	0.64	(0.46–0.97)	2.38	(1.28–4.32)
	e24hUK ≤ 39.1	58.41	(45.08–71.80)	56.67	(53.03–60.69)	1.35	(1.08–1.80)	0.73	(0.54–1.09)	1.84	(1.00-3.30)
	519.6 ≤ UACR	77.91	(67.91–89.61)	71.71	(68.23–75.26)	2.75	(2.29–3.35)	0.31	(0.20–0.56)	8.94	(4.20–16.19)
	3.4 ≤ P	58.33	(44.62–71.97)	54.82	(51.02–58.88)	1.29	(1.02–1.72)	0.76	(0.56–1.15)	1.70	(0.88–3.06)
4	1252.5 ≤ PP × HR	61.99	(47.51–76.46)	68.67	(65.16–72.51)	1.98	(1.53–2.65)	0.55	(0.40–0.91)	3.58	(1.72–6.64)
BMI < 25, CKD stage 4–5	Alb ≤ 3.8	51.31	(46.27–56.46)	71.54	(67.61–75.37)	1.80	(1.51–2.15)	0.68	(0.60–0.77)	2.65	(1.96–3.54)
	Hb ≤ 11.0	61.64	(56.58–66.59)	63.66	(59.56–67.60)	1.70	(1.47–1.96)	0.60	(0.52–0.71)	2.81	(2.10-3.71)
	113 ≤ iPTH	63.25	(57.98–68.58)	62.54	(58.30–66.90)	1.69	(1.45–1.94)	0.59	(0.50–0.70)	2.87	(2.10–3.85)

	e24hUK ≤ 36.7	63.48 (58.57–68.30)	48.04 (43.64–52.20)	1.22 (1.08–1.38)	0.76 (0.64–0.91)	1.61 (1.20–2.14)
	861.6 ≤ UACR	65.93 (61.13–70.85)	74.17 (70.06–78.17)	2.55 (2.11–3.01)	0.46 (0.40–0.54)	5.56 (4.01–7.47)
	3.6 ≤ P	71.39 (66.43–76.17)	50.71 (46.46–55.23)	1.45 (1.29–1.63)	0.56 (0.47–0.69)	2.57 (1.87–3.46)
	4524.0 ≤ PP × HR	50.43 (44.98–55.55)	72.11 (68.20–76.54)	1.81 (1.49–2.17)	0.69 (0.61–0.79)	2.63 (1.92–3.54)
BMI < 25, Non-DM	Alb ≤ 3.9	55.01 (48.51–61.66)	64.79 (61.71–68.04)	1.56 (1.35–1.83)	0.69 (0.60–0.82)	2.25 (1.65–3.05)
	Hb ≤ 11.3	63.76 (57.53–69.96)	72.04 (68.97–74.94)	2.28 (1.96–2.64)	0.50 (0.43–0.61)	4.53 (3.24–6.08)
	95 ≤ iPTH	69.29 (63.37–75.42)	71.06 (67.89–74.17)	2.39 (2.07–2.75)	0.43 (0.36–0.53)	5.54 (3.99–7.58)
	e24hUK ≤ 36.5	65.48 (59.41–72.16)	57.10 (53.72–60.43)	1.53 (1.34–1.74)	0.60 (0.50–0.74)	2.53 (1.81–3.45)
	584.6 ≤ UACR	70.95 (65.45–76.88)	70.10 (67.04–73.44)	2.37 (2.07–2.72)	0.41 (0.34–0.52)	5.73 (4.11–7.84)
	3.6 ≤ P	64.74 (58.49–71.26)	60.87 (57.45–64.41)	1.65 (1.44–1.90)	0.58 (0.48–0.71)	2.86 (2.05–3.90)
	3828.0 ≤ PP × HR	61.19 (54.21–68.13)	57.11 (53.85–60.38)	1.43 (1.24–1.66)	0.68 (0.57–0.84)	2.10 (1.50–2.92)
BMI < 25, DM	Alb ≤ 3.8	66.94 (59.87–73.88)	72.95 (68.12–77.42)	2.47 (1.96–3.01)	0.45 (0.37–0.58)	5.46 (3.50–7.98)
	Hb ≤ 11.0	64.09 (56.86–71.05)	68.00 (63.34–72.85)	2.00 (1.64–2.40)	0.53 (0.44–0.67)	3.79 (2.52–5.45)
	81 ≤ iPTH	73.29 (66.84–80.22)	63.45 (58.21–68.61)	2.01 (1.68–2.37)	0.42 (0.33–0.56)	4.76 (3.09–7.02)
	e24hUK ≤ 38.1	63.65 (56.49–71.14)	53.95 (48.63–59.08)	1.38 (1.17–1.65)	0.67 (0.54–0.86)	2.05 (1.39–3.07)
	996.3 ≤ UACR	71.74 (65.23–78.27)	75.96 (71.30–80.82)	2.98 (2.35–3.70)	0.37 (0.30–0.48)	8.02 (5.13–12.15)
	3.8 ≤ P	59.13 (51.90–66.56)	69.62 (64.52–74.57)	1.95 (1.56–2.41)	0.59 (0.49–0.72)	3.31 (2.17–4.91)
	4797.0 ≤ PP × HR	57.34 (49.74–64.77)	67.14 (61.63–72.38)	1.74 (1.38–2.15)	0.64 (0.53–0.79)	2.75 (1.78–4.05)
BMI ≥ 25	Alb ≤ 3.9	59.89 (53.95–65.95)	64.77 (60.63–68.81)	1.70 (1.46–2.00)	0.62 (0.53–0.74)	2.75 (2.03–3.78)
	Hb ≤ 12.2	65.74 (60.01–71.86)	65.92 (61.78–69.91)	1.93 (1.65–2.24)	0.52 (0.43–0.63)	3.71 (2.68–5.18)
	92 ≤ iPTH	68.10 (62.06–74.57)	73.02 (68.91–77.20)	2.52 (2.11–3.02)	0.44 (0.36–0.54)	5.78 (3.98–8.25)
	e24hUK ≤ 39.8	48.56 (42.22–55.33)	59.26 (54.58–63.86)	1.19 (1.01–1.44)	0.87 (0.75–1.01)	1.37 (1.00–1.93)
	896.6 ≤ UACR	73.26 (67.75–78.70)	78.34 (74.48–82.32)	3.38 (2.73–4.06)	0.34 (0.28–0.43)	9.91 (6.66–13.98)
	3.7 ≤ P	56.16 (49.93–62.23)	69.87 (65.48–74.27)	1.86 (1.53–2.24)	0.63 (0.54–0.74)	2.97 (2.09–4.12)
	4209.0 ≤ PP × HR	59.65 (53.28–66.07)	59.39 (54.68–63.58)	1.47 (1.24–1.73)	0.68 (0.57–0.83)	2.16 (1.51–3.04)
BMI ≥ 25, female	Alb ≤ 3.9	67.62 (56.52–79.36)	59.54 (52.34–67.24)	1.67 (1.30–2.17)	0.54 (0.39–0.84)	3.07 (1.60–5.65)
	Hb ≤ 11.2	64.12 (52.26–76.34)	71.33 (64.49–77.96)	2.24 (1.64–2.99)	0.50 (0.37–0.76)	4.45 (2.28–8.02)
	104 ≤ iPTH	69.78 (59.25–80.40)	72.86 (65.53–80.21)	2.57 (1.81–3.47)	0.41 (0.30–0.64)	6.20 (3.13–11.31)

	e24hUK ≤ 42.3	71.93	(61.05–83.81)	44.39	(36.79–51.68)	1.29	(1.05–1.62)	0.63	(0.42–1.06)	2.05	(1.02-3.83)
	910.9 ≤ UACR	79.11	(70.13-88.04)	81.80	(75.26–88.37)	4.35	(2.79–6.02)	0.26	(0.18-0.44)	17.02	(7.56–31.89)
	4.0 ≤ P	67.53	(55.38–80.05)	76.06	(69.50-83.07)	2.82	(1.97–3.89)	0.43	(0.30-0.67)	6.61	(3.08–12.29)
	4628.0 ≤ PP × HR	54.54	(41.47–67.32)	58.95	(51.23–66.84)	1.33	(0.98–1.84)	0.77	(0.57–1.12)	1.72	(0.88–3.20)
BMI ≥ 25, male	Alb ≤ 3.9	57.17	(50.17–64.27)	67.39	(62.29–72.57)	1.75	(1.42–2.16)	0.64	(0.53-0.77)	2.76	(1.89–4.04)
	Hb ≤ 12.8	74.84	(68.60–80.86)	64.84	(59.34–69.89)	2.13	(1.76–2.50)	0.39	(0.31–0.52)	5.49	(3.51–7.99)
	88 ≤ iPTH	70.96	(63.98–78.15)	74.32	(69.31–79.41)	2.76	(2.17–3.43)	0.39	(0.31–0.52)	7.07	(4.32–11.00)
	e24hUK ≤ 39.6	47.81	(39.94–55.17)	62.82	(57.32–68.21)	1.29	(1.02-1.60)	0.83	(0.70-1.00)	1.55	(1.02-2.28)
	896.6 ≤ UACR	71.11	(64.23-77.79)	76.93	(71.92–81.94)	3.08	(2.38–3.88)	0.38	(0.30-0.50)	8.21	(5.12–12.63)
	3.5 ≤ P	56.14	(48.57–63.31)	69.70	(64.14–75.39)	1.85	(1.44–2.32)	0.63	(0.53-0.78)	2.94	(1.89–4.34)
	4267.9 ≤ PP × HR	57.12	(49.72–64.99)	67.06	(61.98–72.67)	1.73	(1.38–2.17)	0.64	(0.53-0.79)	2.71	(1.79–4.08)
BMI ≥ 25, Age < 65	Alb ≤ 3.9	63.72	(56.20-71.76)	64.88	(59.40-70.69)	1.81	(1.47–2.24)	0.56	(0.45-0.72)	3.24	(2.09–4.90)
	Hb ≤ 12.5	65.23	(58.01–73.20)	64.54	(58.93–70.01)	1.84	(1.50-2.26)	0.54	(0.43-0.69)	3.42	(2.23–5.23)
	88 ≤ iPTH	69.54	(61.70–77.49)	71.39	(66.10–76.96)	2.43	(1.91–3.03)	0.43	(0.33–0.58)	5.70	(3.45–8.90)
	e24hUK ≤ 43.4	66.00	(58.38–74.59)	43.36	(37.54–49.17)	1.17	(0.98–1.40)	0.78	(0.59–1.07)	1.49	(0.93–2.38)
	896.6 ≤ UACR	77.73	(70.75–85.09)	75.02	(69.71–80.51)	3.11	(2.40-3.88)	0.30	(0.22–0.43)	10.48	(6.15–16.92)
	3.8 ≤ P	52.58	(44.37–60.79)	74.67	(69.41–80.17)	2.08	(1.59–2.69)	0.64	(0.53-0.79)	3.27	(2.09–5.02)
	4209.0 ≤ PP × HR	52.05	(43.46–60.72)	66.69	(60.99–72.54)	1.56	(1.21–2.01)	0.72	(0.59–0.89)	2.17	(1.37–3.37)
BMI ≥ 25, Age ≥ 65	Alb ≤ 3.9	54.38	(45.01–63.65)	64.61	(57.42–71.73)	1.54	(1.15–2.03)	0.71	(0.56–0.92)	2.18	(1.26–3.61)
	Hb ≤ 11.4	62.02	(52.88–71.65)	76.73	(70.57–82.79)	2.67	(1.90-3.55)	0.49	(0.39–0.66)	5.39	(3.05-8.93)
	92 ≤ iPTH	69.80	(60.55–78.83)	72.15	(65.58–78.82)	2.51	(1.87–3.27)	0.42	(0.31–0.61)	5.99	(3.36–10.28)
	e24hUK ≤ 39.6	55.33	(45.90–65.48)	53.13	(45.99–60.26)	1.18	(0.92–1.55)	0.84	(0.64–1.11)	1.40	(0.83-2.45)
	795.4 ≤ UACR	71.88	(63.28–80.98)	81.20	(74.84–87.41)	3.82	(2.56–5.26)	0.35	(0.26–0.50)	11.04	(5.64–19.37)
	3.7 ≤ P	57.88	(48.49–67.09)	69.94	(63.12–76.86)	1.93	(1.41–2.52)	0.60	(0.48-0.80)	3.20	(1.85–5.15)
BMI ≥ 25, CKD stage 3	4731.4 ≤ PP × HR	60.58	(50.15-71.27)	66.88	(60.35–73.85)	1.83	(1.39–2.41)	0.59	(0.45–0.82)	3.10	(1.76–5.27)
	Alb ≤ 3.9	67.44	(55.29–80.78)	65.51	(60.53–70.82)	1.96	(1.53–2.54)	0.50	(0.35–0.79)	3.93	(1.96–7.28)
	Hb ≤ 12.9	55.82	(42.60–68.76)	63.48	(58.16–68.99)	1.53	(1.17–2.07)	0.70	(0.53-1.01)	2.20	(1.18–3.92)
	61 ≤ iPTH	59.14	(45.44–73.27)	53.34	(47.80–58.53)	1.27	(0.99–1.71)	0.77	(0.56–1.16)	1.65	(0.86–3.07)

	e24hUK ≤ 43.4	58.32 (44.23–72.85)	47.20 (41.68–52.88)	1.10 (0.86–1.51)	0.88 (0.63–1.39)	1.25 (0.62–2.40)
	1159.0 ≤ UACR	76.01 (63.34–88.25)	85.18 (81.07–89.34)	5.13 (3.59–6.85)	0.28 (0.19–0.60)	18.22 (6.96–34.37)
	3.7 ≤ P	38.98 (24.51–53.50)	77.17 (71.95–82.33)	1.71 (1.14–2.87)	0.79 (0.63–1.04)	2.16 (1.11–4.57)
	4209.0 ≤ PP × HR	58.91 (44.17–74.40)	62.80 (57.13–68.36)	1.58 (1.18–2.22)	0.65 (0.47–1.05)	2.42 (1.16–4.75)
BMI ≥ 25, CKD stage 4–5	Alb ≤ 3.9	58.11 (51.51–64.67)	63.73 (56.32–71.18)	1.60 (1.25–2.01)	0.66 (0.54–0.80)	2.44 (1.59–3.71)
	Hb ≤ 11.4	53.91 (46.94–60.65)	68.62 (61.32–75.17)	1.72 (1.26–2.20)	0.67 (0.56–0.82)	2.56 (1.57–3.90)
	109 ≤ iPTH	69.79 (63.52–76.21)	64.57 (56.87–72.40)	1.97 (1.52–2.48)	0.47 (0.37–0.61)	4.21 (2.58–6.58)
	e24hUK ≤ 37.3	41.06 (34.02–48.12)	62.93 (55.36–70.46)	1.11 (0.83–1.46)	0.94 (0.78–1.11)	1.18 (0.76–1.88)
	894.8 ≤ UACR	71.99 (65.67–78.72)	74.65 (67.57–81.87)	2.84 (2.04–3.74)	0.38 (0.29–0.50)	7.57 (4.32–12.28)
	3.9 ≤ P	53.07 (45.95–59.50)	72.45 (65.39–79.68)	1.93 (1.36–2.53)	0.65 (0.55–0.79)	2.97 (1.76–4.62)
	4395.3 ≤ PP × HR	54.54 (47.39–62.10)	60.06 (52.36–68.30)	1.37 (1.06–1.77)	0.76 (0.60–0.95)	1.80 (1.12–2.96)
BMI ≥ 25, Non-DM	Alb ≤ 3.9	52.20 (41.63–62.29)	69.10 (63.68–74.54)	1.69 (1.29–2.24)	0.69 (0.56–0.89)	2.44 (1.49–4.00)
	Hb ≤ 12.7	74.95 (66.06–84.24)	62.50 (56.74–67.94)	2.00 (1.63–2.43)	0.40 (0.29–0.64)	4.99 (2.66–8.50)
	85 ≤ iPTH	73.76 (64.08–83.91)	71.46 (66.27–77.08)	2.58 (2.04–3.31)	0.37 (0.26–0.59)	7.04 (3.65–12.62)
	e24hUK ≤ 39.8	57.58 (47.01–68.78)	58.59 (52.60–64.91)	1.39 (1.11–1.81)	0.72 (0.56–0.98)	1.92 (1.14–3.26)
	696.7 ≤ UACR	68.83 (58.91–78.62)	74.64 (69.27–80.52)	2.71 (2.04–3.47)	0.42 (0.31–0.62)	6.50 (3.51–10.67)
	3.5 ≤ P	58.09 (47.01–68.78)	60.90 (55.02–66.90)	1.49 (1.17–1.93)	0.69 (0.53–0.94)	2.16 (1.26–3.63)
	3763.4 ≤ PP × HR	58.85 (48.10–70.63)	49.38 (43.25–55.39)	1.16 (0.94–1.50)	0.83 (0.62–1.16)	1.40 (0.82–2.42)
BMI ≥ 25, DM	Alb ≤ 3.9	64.40 (57.19–71.34)	59.09 (52.64–65.74)	1.57 (1.28–1.93)	0.60 (0.48–0.78)	2.61 (1.68–4.00)
	Hb ≤ 12.2	67.52 (60.38–74.78)	58.81 (51.91–65.77)	1.64 (1.33–2.00)	0.55 (0.43–0.73)	2.97 (1.86–4.63)
	109 ≤ iPTH	60.02 (52.56–67.77)	79.91 (74.24–85.81)	2.99 (2.12–4.07)	0.50 (0.41–0.62)	5.97 (3.58–9.68)
	e24hUK ≤ 39.2	42.57 (34.28–50.57)	62.89 (56.33–69.84)	1.15 (0.88–1.52)	0.91 (0.76–1.11)	1.26 (0.79–1.99)
	888.8 ≤ UACR	81.99 (75.86–88.26)	74.51 (68.34–80.88)	3.22 (2.42–4.10)	0.24 (0.18–0.37)	13.31 (7.43–21.97)
	3.9 ≤ P	54.04 (45.89–61.71)	76.98 (71.02–83.35)	2.35 (1.69–3.14)	0.60 (0.50–0.74)	3.93 (2.40–6.21)
	4387.7 ≤ PP × HR	63.08 (55.94–70.91)	56.00 (48.98–63.14)	1.43 (1.17–1.75)	0.66 (0.52–0.84)	2.17 (1.43–3.35)

Cut-off values in all cohorts for predicting an eGFR decline by ≥ 50% from baseline or ESRD that requires renal replacement therapy during the follow-up examination period were examined by ROC analyses. Abbreviations: CI, confidence interval; BMI, body mass index; CKD, chronic kidney disease; DM, diabetes mellitus; Alb, Albumin; Hb, Hemoglobin; iPTH, intact parathyroid hormone; e24hUK, estimated 24-hour urinary potassium excretion; UACR, urine albumin-to-creatinine ratio; P, serum phosphorus; PP × HR, pulse pressure x heart rate