

Table of Contents

Appendix 1. Data analysis overview and analytic notes for some of individual studies	4
Appendix 2. Acronyms or abbreviations for studies included in the current report and their key references linked to the Web references	7
Appendix 3. Acknowledgements and funding for collaborating cohorts	8
Table S1. Medication use in different cohorts	10
Table S2. Risk factors of potassium levels <3.5 mmol/L, >5 mmol/L, and >5.5 mmol/L in general and high cardiovascular risk cohorts.	12
Table S3. Risk factors of hypokalemia and hyperkalemia in CKD cohorts	13
Table S4. Odds ratios (95% confidence intervals) of serum potassium level >5.5 mmol/L in patients categorized by baseline levels of estimated GFR and albuminuria in general population and high cardiovascular risk cohorts.	14
Table S5. Odds ratios (95% confidence intervals) of serum potassium level >5.5 mmol/L in subgroups of patients categorized by baseline levels of estimated GFR and proteinuria level in CKD cohorts.	15
Table S6. Outcomes by cohort	16
Figure S1. Distribution of serum potassium concentrations, overall and by baseline estimated glomerular filtration rate in CKD cohorts.	17
Figure S2. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by their age in general population and high cardiovascular risk cohorts.	18
Figure S3. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by their gender in general population and high cardiovascular risk cohorts.	19
Figure S4. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by their race in general population and high cardiovascular risk cohorts.	20
Figure S5. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by the presence or absence of diabetes mellitus in general population and high cardiovascular risk cohorts.	21
Figure S6. Continuous association of estimated GFR (panel A) and albuminuria (Panel B) with the risk of serum potassium level >5.5 mmol/L, and of estimated GFR (panel C) and albuminuria (Panel D) with the risk of serum potassium level <3.5 mmol/L, in CKD cohorts.	22
Figure S7. Adjusted relative hazard of cardiovascular mortality for potassium of 3.0 mmol/L (A) and 5.5 mmol/L (B), compared to a potassium of 4.2 mmol/L in individual general population/high risk cohorts	23
Figure S8. Adjusted relative hazard of end-stage renal disease for potassium of 3.0 mmol/L (A) and 5.5 mmol/L (B), compared to a potassium of 4.2 mmol/L in individual general population/high risk cohorts.	24

Figure S9. Adjusted hazard ratio of cardiovascular mortality (A) and end stage renal disease (B) associated with serum potassium concentration in general population and high cardiovascular risk cohorts, in subgroups divided by baseline eGFR level.	25
Figure S10. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different age subgroups in general population and high cardiovascular risk cohorts.	26
Figure S11. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different gender subgroups in general population and high cardiovascular risk cohorts.	27
Figure S12. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different race subgroups in general population and high cardiovascular risk cohorts.	28
Figure S13. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of diabetes mellitus in general population and high cardiovascular risk cohorts.	29
Figure S14. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups with different albuminuria levels in general population and high cardiovascular risk cohorts.	30
Figure S15. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with ACEI/ARB/potassium sparing diuretics in general population and high cardiovascular risk cohorts.	31
Figure S16. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with thiazide or loop diuretics in general population and high cardiovascular risk cohorts.	32
Figure S17. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in CKD cohorts.	33
Figure S18. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in CKD cohorts, in subgroups divided by baseline eGFR level.	34
Figure S19. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different age subgroups in CKD cohorts.	35
Figure S20. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different gender subgroups in CKD cohorts.	36
Figure S21. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different race subgroups in CKD cohorts.	37

Figure S22. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of diabetes mellitus in CKD cohorts.....	38
Figure S23. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups with different albuminuria levels in CKD cohorts.....	39
Figure S24. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with ACEI/ARB/potassium sparing diuretics in CKD cohorts....	40
Figure S25. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with thiazide or loop diuretics in CKD cohorts.....	41
References.....	42

Appendix 1. Data analysis overview and analytic notes for some of individual studies

Overview:

As previously described,¹ the collaborating cohorts were asked to compile a dataset with approximately 40 variables (key exposures [serum creatinine to estimate GFR, serum potassium and albuminuria], covariates [e.g., age, sex, race/ethnicity, diabetes, hypertension], and outcomes [event variables and corresponding follow-up times]). To be consistent across cohorts, the CKD-PC Data Coordinating Center sent definitions for those variables to participating cohorts. We instructed studies not to impute any variables.

For 21 of the 26 cohorts in this specific study of potassium, the Data Coordination Center at Johns Hopkins University conducted the analysis; the remainder ran the standard code written in STATA by the Data Coordinating Center and shared the output with the Data Coordinating Center. The standard code was designed to automatically save all estimates and variance-covariance matrices needed for the meta-analysis. Then, the Data Coordinating Center meta-analyzed the estimates across cohorts using STATA. Cohorts needed to have at least 50 outcome events overall to be included in this study, and any cohorts with fewer than 10 outcome events in any particular analysis were excluded.

As detailed in our previous reports,^{2,3} each cohort was instructed to standardize their serum creatinine and report its method when available. The reported creatinine standardization allows grouping studies into studies that reported using a standard IDMS traceable method or conducted some serum creatinine standardization to IDMS traceable methods (CanPREDDICT, Geisinger, Gubbio, Maccabi, MASTERPLAN, NHANES, PREVEND, Rancho Bernardo, RCAV, SCREAM, SRR-CKD, Takahata) and studies where the creatinine standardization was not done (AASK, ADVANCE, BC CKD, Beijing, CIRCS, CRIB, KHS, MDRD, MRC, Sunnybrook, Taiwan MJ, ZODIAC). For those cohorts without standardization, the creatinine levels were reduced by 5%, the calibration factor used to adjust non-standardized MDRD Study samples to IDMS.^{2,4} We did not adjust creatinine levels in those studies with unknown standardization status (Mt Sinai and PSP-CKD).

We calculated eGFR using the CKD-EPI equation: $eGFR_{CKD-EPI} = 141 \times (\text{minimum of standardized serum creatinine [mg/dL]/}\kappa \text{ or } 1)^{\alpha} \times (\text{maximum of standardized serum creatinine [mg/dL]/}\kappa \text{ or } 1)^{-1.209} \times 0.993^{\text{age}} \times (1.018 \text{ if female}) \times (1.159 \text{ if black})$, where κ is 0.7 if female and 0.9 if male and α is -0.329 if female and -0.411 if male.⁵ The selection of knots for eGFR and ACR was based on clinical thresholds.⁶

Notes for individual studies:

1. General population cohorts

Beijing: History of heart failure was not available.

CIRCS: History of heart failure was not available. Sudden cardiac death and heart failure were not included in this cohort's definition of cardiovascular mortality.

KHS: History of heart failure was not available.

MRC: Total cholesterol was not available.

PREVEND: Sudden cardiac death was not included in this cohort's definition of cardiovascular mortality.

Rancho Bernardo: Sudden cardiac death was not included in this cohort's definition of cardiovascular mortality.

Taiwan MJ: History of heart failure was not available. Heart failure was not included in this cohort's definition of cardiovascular mortality.

Takahata: History of heart failure was not available. Sudden cardiac death and heart failure were not included in this cohort's definition of cardiovascular mortality.

2. High-risk cohorts

ADVANCE: This study is an intervention study which includes participants with diabetes only. Smoking status was not available.

Geisinger: Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

Maccabi: Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

Mt Sinai BioMe: Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

RCAV: This cohort does not have data on smoking and high-density lipoprotein cholesterol. Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort.

SCREAM: This cohort does not have data on smoking and blood pressure. Due to the requirement of ACR measurement for analyses and the clinical indications that are associated with measurement in this health system dataset, this cohort was categorized as a high-risk cohort. Sudden cardiac death and heart failure were not included in this cohort's definition of cardiovascular mortality.

ZODIAC: History of heart failure was not available.

3. CKD cohorts

AASK: Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

CanPREDDICT: This cohort does not have data on smoking. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women. Sudden cardiac death was not included in this cohort's definition of cardiovascular mortality.

CRIB: History of heart failure was not available. Use of thiazide diuretics, loop diuretics or potassium sparing diuretics was combined. Individual use of each type of diuretics was not available.

MASTERPLAN: This study measured urine albumin-to-creatinine ratio in patients with albuminuria in the low range, urine protein-to-creatinine ratio in patients with overt proteinuria. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

MDRD: History of heart failure was not available. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

PSP-CKD: Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

SRR-CKD: This cohort does not have data on smoking and high-density lipoprotein cholesterol. There may be some overlap with the SCREAM cohort, which would capture participants with advanced CKD in the region of Stockholm. Use of thiazide diuretics, loop diuretics or potassium sparing diuretics was combined. Individual use of each type of diuretics was not available.

Sunnybrook: This cohort includes patients seen in the nephrology clinics at Sunnybrook Hospital in Toronto, Ontario, Canada with CKD stage 3-5 or proteinuric CKD stage 1-2. Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women.

Percent with missing covariates:

Study	DM	History of CHD/ Stroke	History of HF	Current smoker	SBP	BMI	Total Cholesterol
General Population							
Beijing	59 (4%)	0 (0%)	1528 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CIRCS	0 (0%)	0 (0%)	8034 (100%)	0 (0%)	5 (0%)	2 (0%)	0 (0%)
Gubbio	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
KHS	0 (0%)	0 (0%)	111532 (100%)	0 (0%)	6 (0%)	0 (0%)	3 (0%)
MRC	0 (0%)	93 (1%)	11838 (100%)	30 (0%)	96 (1%)	710 (6%)	11840 (100%)
NHANES	60 (0%)	2838 (6%)	2660 (6%)	2562 (6%)	1194 (3%)	503 (1%)	63 (0%)
PREVEND	248 (3%)	0 (0%)	0 (0%)	0 (0%)	3 (0%)	74 (1%)	24 (0%)
Rancho Bernardo	0 (0%)	0 (0%)	0 (0%)	8 (1%)	2 (0%)	7 (0%)	0 (0%)
Taiwan MJ	3 (0%)	32268 (23%)	140488 (100%)	43348 (31%)	9 (0%)	56 (0%)	2 (0%)
Takahata	22 (1%)	0 (0%)	1923 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
High Risk Cohorts							
ADVANCE	0 (0%)	0 (0%)	0 (0%)	11003 (100%)	1 (0%)	4 (0%)	6 (0%)
Geisinger	0 (0%)	0 (0%)	0 (0%)	837 (1%)	9719 (15%)	10998 (16%)	13363 (20%)
Maccabi	0 (0%)	0 (0%)	0 (0%)	0 (0%)	18233 (7%)	54857 (22%)	7584 (3%)
Mt Sinai BioMe	0 (0%)	0 (0%)	0 (0%)	561 (7%)	1274 (15%)	1894 (23%)	1698 (20%)
RCAV	0 (0%)	0 (0%)	0 (0%)	277226 (100%)	9937 (4%)	19166 (7%)	36702 (13%)
SCREAM	0 (0%)	0 (0%)	0 (0%)	224285 (100%)	224285 (100%)	224285 (100%)	83477 (37%)
ZODIAC	0 (0%)	0 (0%)	1153 (100%)	6 (1%)	1 (0%)	2 (0%)	0 (0%)
CKD Cohorts							
AASK	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	16 (1%)
BC CKD	0 (0%)	0 (0%)	0 (0%)	6270 (52%)	2577 (21%)	4150 (35%)	1561 (13%)
CanPREDDICT	0 (0%)	0 (0%)	0 (0%)	2017 (100%)	36 (2%)	1960 (97%)	1002 (50%)
CKD-JAC	0 (0%)	0 (0%)	0 (0%)	397 (15%)	37 (1%)	253 (10%)	419 (16%)
CRIB	0 (0%)	0 (0%)	373 (100%)	0 (0%)	4 (1%)	4 (1%)	13 (3%)
MASTERPLAN	0 (0%)	9 (1%)	25 (4%)	14 (2%)	0 (0%)	0 (0%)	0 (0%)
MDRD	0 (0%)	0 (0%)	832 (100%)	1 (0%)	0 (0%)	2 (0%)	725 (87%)
PSP-CKD	0 (0%)	0 (0%)	0 (0%)	5905 (35%)	2220 (13%)	6234 (37%)	3479 (21%)
SRR-CKD	0 (0%)	0 (0%)	0 (0%)	2618 (100%)	67 (3%)	356 (14%)	1472 (56%)
Sunnybrook	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1214 (39%)	2015 (65%)	1652 (53%)

Appendix 2. Acronyms or abbreviations for studies included in the current report and their key references linked to the Web references

AASK:	African American Study of Kidney Disease and Hypertension ⁷
ADVANCE:	The Action in Diabetes and Vascular Disease: Preterax and Diamicon Modified Release Controlled Evaluation (ADVANCE) trial ⁸
BC CKD:	British Columbia CKD Study ⁹
Beijing:	Beijing Cohort Study ¹⁰
CanPREDDICT:	Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events ¹¹
CIRCS:	Circulatory Risk in Communities Study ¹²
CKD-JAC:	Chronic Kidney Disease Japan Cohort
CRIB:	Chronic Renal Impairment in Birmingham ¹³
Geisinger:	Geisinger Health System ¹⁴
Gubbio:	Gubbio Study ¹⁵
KHS:	Korean Heart Study
Maccabi:	Maccabi Health System ¹⁶
MASTERPLAN:	Multifactorial Approach and Superior Treatment Efficacy in Renal Patients with the Aid of a Nurse Practitioner ¹⁷
MDRD:	Modification of Diet in Renal Disease Study ¹⁸
MRC Older People:	MRC Study of assessment of older people ¹⁹
Mt Sinai BioMe:	Mount Sinai BioMe Biobank Platform ²⁰
NHANES:	US National Health and Nutrition Examination Survey, using both NHANES III and the continuous NHANES from 1999-2010 ²¹
PREVEND:	Prevention of Renal and Vascular End-stage Disease Study ²²
PSP-CKD:	Primary-Secondary Care Partnership to Prevent Adverse Outcomes in Chronic Kidney Disease
Rancho Bernardo:	Rancho Bernardo Study ²³
RCAV:	Racial and Cardiovascular Risk Anomalies in CKD Cohort
SCREAM:	Stockholm CREATinine Measurements Cohort ²⁴
SRR-CKD:	Swedish Renal Registry CKD Cohort ²⁵
Sunnybrook:	Sunnybrook Cohort ²⁶
Taiwan MJ:	Taiwan MJ Cohort Study ²⁷
Takahata:	Takahata Study ²⁸
ZODIAC:	Zwolle Outpatient Diabetes project Integrating Available Care ²⁹

Appendix 3. Acknowledgements and funding for collaborating cohorts

Study	List of sponsors
AASK	AASK was supported by grants to each clinical center and the coordinating center from the National Institute of Diabetes and Digestive and Kidney Diseases. In addition, AASK was supported by the Office of Research in Minority Health (now the National Center on Minority Health and Health Disparities, NCMHD) and the following institutional grants from the National Institutes of Health: M01 RR-00080, M01 RR-00071, M0100032, P20-RR11145, M01 RR00827, M01 RR00052, 2P20 RR11104, RR029887, and DK 2818-02. King Pharmaceuticals provided monetary support and antihypertensive medications to each clinical center. Pfizer Inc, AstraZeneca Pharmaceuticals, Glaxo Smith Kline, Forest Laboratories, Pharmacia and Upjohn also donated antihypertensive medications.
ADVANCE	National Health and Medical Research Council (NHMRC) of Australia program grants 358395 and 571281 and project grant 211086
BC CKD	BC Provincial Renal Agency, an Agency of the Provincial Health Services Authority in collaboration with University of British Columbia.
Beijing	The research for this study was supported by the Program for New Century Excellent Talents in University (BMU2009131) from the Ministry of Education of the People's Republic of China, and the grants for the Early Detection and Prevention of Non-communicable Chronic Diseases from the International Society of Nephrology Research Committee.
CanPREDDICT	
CIRCS	
CKD-JAC	
CRIB	British Renal Society Project Grant Award British Heart Foundation Project Grant Award.
Geisinger	Geisinger Clinic
Gubbio	Municipal and Health Authorities of Gubbio, Italy; Center of Gubbio Epidemiological Studies, Gubbio, Italy; University of Salerno, Salerno, Italy.
KHS	
Maccabi	
MASTERPLAN	The MASTERPLAN study is a clinical trial with trial registration ISRCTN registry: 73187232. Sources of funding: The MASTERPLAN Study was supported by grants from the Dutch Kidney Foundation (Nierstichting Nederland, number PV 01), and the Netherlands Heart Foundation (Nederlandse Hartstichting, number 2003 B261). Unrestricted grants were provided by Amgen, Genzyme, Pfizer and Sanofi-Aventis.
MDRD	NIDDK U01 DK35073 and K23 DK67303, K23 DK02904
MRC Older People	UK Medical Research Council, Department of Health for England, Wales and the Scottish Office and Kidney Research UK
Mt Sinai BioMe	
NHANES	United States Center for Disease Control
PREVEND	The PREVEND study is supported by several grants from the Dutch Kidney Foundation, and grants from the Dutch Heart Foundation, the Dutch Government (NWO), the US National Institutes of Health (NIH) and the University Medical Center Groningen, The Netherlands (UMCG). Dade Behring, Marburg, Germany supplied equipment and reagents for nephelometric measurement of urinary albumin.

PSP-CKD	The PSP-CKD study was funded by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) East Midlands. Ongoing support for the study is funded by NIHR CLAHRC East Midlands and Kidney Research UK (Grant TF2/2015).
Rancho Bernardo	NIA AG07181 and AG028507 NIDDK DK31801
RCAV	This study was supported by grant R01DK096920 from NIH-NIDDK and is the result of work supported with resources and the use of facilities at the Memphis VA Medical Center and the Long Beach VA Medical Center. Support for VA/CMS data is provided by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Health Services Research and Development, VA Information Resource Center (project numbers SDR 02-237 and 98-004).
SCREAM	This study was supported by Stockholm County Council and the Swedish Heart and Lung Foundation.
SRR-CKD	The SRR-CKD is a national health care quality register funded by The Swedish Association of Local Authorities and Regions, which is an organization that represents and advocates for local government in Sweden. All of Sweden's municipalities, county councils and regions are members.
Sunnybrook	
Taiwan MJ	This study was supported by Taiwan Department of Health Clinical Trial and Research Centre of Excellence (DOH 101-TD-B-111-004)
Takahata	A Grant-in-Aid from the 21st Century Center of Excellence (COE) and Global COE program of the Japan Society for the Promotion of Science
ZODIAC	

Table S1. Medication use in different cohorts

Study	Region	N	Any anti-HTN medications	ACE Inhibitor	ARB	Thiazide Diuretics	Loop Diuretics	K-sparing Diuretics	Betablocker	Renin Inhibitor	NSAID	Kayexalate
General Population												
Beijing	China	1528	546 (36%)	-	-	-	-	-	-	-	53 (3%)	-
CIRCS	Japan	8034	1025 (13%)	-	-	-	-	-	-	-	-	-
Gubbio	Italy	1683	332 (20%)	90 (5%)	-	100 (6%)	9 (1%)	59 (4%)	60 (4%)	-	35 (2%)	-
KHS	South Korea	111532	4614 (4%)	-	-	-	-	-	-	-	-	-
MRC	UK	11840	3984 (34%)	-	-	-	-	-	55 (0%)	-	1327 (11%)	-
NHANES	USA	46526	11117 (24%)	3727 (8%)	1419 (5%)	3585 (8%)	1398 (3%)	1265 (3%)	3768 (8%)	10 (0%)	3164 (7%)	-
PREVEND	Netherlands	7319	1028 (17%)	289 (5%)	47 (1%)	150 (2%)	57 (1%)	13 (0%)	499 (8%)	-	583 (9%)	-
Rancho Bernardo	USA	1481	436 (29%)	-	-	203 (14%)	57 (4%)	4 (0%)	142 (10%)	-	340 (23%)	-
Taiwan MJ	Taiwan	140488	7191 (7%)	-	-	-	-	-	-	-	-	-
Takahata	Japan	1923	637 (38%)	-	-	-	-	-	-	-	-	-
Subtotal		332354	30910 (10%)	4106 (8%)	1466 (4%)	4038 (7%)	1521 (3%)	1341 (2%)	4524 (7%)	10 (0%)	5502 (8%)	-
High Risk Cohorts												
ADVANCE	Multi	11003	8203 (75%)	4488 (42%)	569 (5%)	1536 (14%)	-	-	2695 (25%)	-	-	-
Geisinger	USA	67023	39498 (59%)	19905 (30%)	5547 (8%)	12789 (19%)	7620 (11%)	2781 (4%)	18686 (28%)	32 (0%)	8777 (13%)	50 (0%)
Maccabi	Israel	254379	115619 (45%)	47483 (19%)	23746 (9%)	14287 (6%)	5258 (2%)	2588 (1%)	53196 (21%)	6 (0%)	10900 (4%)	79 (0%)
Mt Sinai BioMe	USA	8393	4476 (53%)	2214 (26%)	994 (12%)	1634 (19%)	567 (7%)	242 (3%)	1721 (21%)	9 (0%)	1401 (17%)	188 (2%)
RCAV	USA	277226	210979 (76%)	156601 (56%)	-	54616 (20%)	26920 (10%)	11085 (4%)	96609 (35%)	-	50615 (30%)	17 (0%)
SCREAM	Sweden	224285	105345 (47%)	36991 (16%)	28962 (13%)	9037 (4%)	20719 (9%)	6115 (3%)	55073 (25%)	1 (0%)	41012 (18%)	357 (0%)
ZODIAC	Netherlands	1153	-	-	-	-	-	-	-	-	187 (16%)	-
Subtotal		843462	484120 (57%)	267682 (32%)	59818 (11%)	93899 (11%)	61084 (7%)	22811 (3%)	227980 (27%)	48 (0%)	112892 (16%)	691 (0%)
CKD Cohorts												
AASK	USA	1081	1081 (100%)	651 (60%)	15 (1%)	-	-	-	593 (55%)	-	-	-
BC CKD	Canada	11990	10058 (84%)	5963 (50%)	4089 (34%)	3969 (33%)	5926 (49%)	1339 (11%)	6397 (53%)	39 (0%)	5587 (47%)	2123 (18%)
CanPREDDICT	Canada	2017	1855 (92%)	861 (43%)	754 (37%)	614 (30%)	900 (45%)	118 (6%)	1019 (51%)	8 (0%)	1120 (56%)	112 (6%)
CKD-JAC	Japan	2639	2419 (92%)	726 (28%)	1967 (75%)	211 (8%)	638 (24%)	156 (6%)	272 (10%)	-	144 (5%)	14 (1%)
CRIB*	UK	373	308 (83%)	117 (31%)	16 (6%)	151 (40%)			108 (29%)	-	-	-
MASTERPLAN	Netherlands	670	629 (94%)	343 (51%)	254 (38%)	216 (32%)	119 (18%)	24 (4%)	320 (48%)	-	-	-

MDRD	USA	832	-	-	-	-	-	-	-	-	-	-
PSP-CKD	UK	16828	13546 (80%)	7674 (46%)	3038 (18%)	3508 (21%)	3893 (23%)	781 (5%)	5658 (34%)	-	1768 (11%)	-
SRR-CKD*	Sweden	2618	2405 (92%)	0 (0%)	1012 (39%)	1821 (70%)			-	1 (0%)	-	-
Sunnybrook	Canada	3122	-	-	-	-	-	-	-	-	-	-
Subtotal		42170	32301 (85%)	16335 (46%)	11145 (29%)	8518 (25%)	11476 (34%)	2418 (7%)	14367 (40%)	48 (0%)	8619 (26%)	2249 (14%)
Total		121798	547331 (46%)	288123 (31%)	72429 (11%)	106455 (11%)	74081 (8%)	26570 (3%)	246871 (26%)	106 (0%)	127013 (15%)	2940 (1%)

* Use of thiazide diuretics, loop diuretics or potassium sparing diuretics was combined. Individual use of each type of diuretics was not available.

Table S2. Risk factors of potassium levels <3.5 mmol/L, >5 mmol/L, and >5.5 mmol/L in general and high cardiovascular risk cohorts.

	(K<3.5 mmol/L)	(K>5 mmol/L)	(K>5.5 mmol/L)
Age, per 10 years	0.92 (0.88, 0.96)	1.02 (0.97, 1.08)	0.90 (0.84, 0.97)
Female	1.49 (1.27, 1.75)	0.75 (0.67, 0.85)	0.77 (0.62, 0.96)
Black	1.81 (1.56, 2.09)	0.76 (0.57, 1.02)	0.59 (0.44, 0.79)
SBP, per 20 mmHg	1.32 (1.12, 1.54)	0.96 (0.93, 0.99)	0.99 (0.94, 1.05)
ACE-I/ARB/K Sparing	0.78 (0.69, 0.89)	1.34 (1.23, 1.47)	1.57 (1.30, 1.88)
Other Diuretics	3.69 (2.99, 4.56)	0.68 (0.63, 0.73)	0.68 (0.58, 0.80)
Beta blockers	1.05 (0.92, 1.19)	1.04 (0.98, 1.11)	1.00 (0.94, 1.07)
Cholesterol, per 1 mM	0.95 (0.92, 0.99)	1.03 (1.00, 1.06)	1.04 (0.99, 1.09)
Diabetes	0.76 (0.68, 0.85)	1.53 (1.38, 1.70)	1.60 (1.46, 1.75)
BMI, per 5Kg/m ²	0.92 (0.88, 0.96)	0.88 (0.83, 0.93)	0.86 (0.78, 0.94)
Current smoker	0.88 (0.76, 1.03)	1.28 (1.14, 1.42)	1.37 (1.15, 1.64)
History of CHD or stroke	0.91 (0.86, 0.96)	1.10 (1.06, 1.15)	1.18 (1.10, 1.26)
History of HF	1.06 (0.86, 1.32)	1.06 (1.01, 1.11)	1.10 (0.95, 1.27)
eGFR <30, per -15ml	1.43 (1.04, 1.95)	1.37 (1.22, 1.54)	1.57 (1.32, 1.87)
eGFR 30-59, per -15ml	0.90 (0.81, 0.99)	1.98 (1.77, 2.22)	2.90 (2.39, 3.51)
eGFR 60+, per -15ml	0.97 (0.93, 1.01)	1.35 (1.28, 1.42)	1.55 (1.42, 1.70)
ACR, per 10 fold	1.28 (1.14, 1.43)	1.08 (1.01, 1.16)	1.16 (1.04, 1.29)

Results indicate multivariable adjusted odds ratios (95% confidence intervals). Covariates include all risk factors included in the table.

Table S3. Risk factors of hypokalemia and hyperkalemia in CKD cohorts

	Hypokalemia (K<3.5)	Mild hyperkalemia (K>5)	Moderate hyperkalemia (K>5.5)
Age, per 10 years	0.90 (0.81, 0.99)	0.94 (0.89, 1.01)	0.92 (0.83, 1.01)
Female	1.11 (0.87, 1.42)	0.87 (0.78, 0.97)	0.80 (0.63, 1.01)
Black	1.82 (0.36, 9.24)	0.93 (0.39, 2.22)	1.42 (0.58, 3.48)
SBP, per 20 mmHg	1.16 (1.01, 1.34)	0.98 (0.95, 1.02)	1.00 (0.93, 1.08)
ACE-I/ARB/K Sparing	0.55 (0.41, 0.74)	1.30 (1.11, 1.52)	1.23 (0.98, 1.55)
Other Diuretics	4.27 (2.80, 6.51)	0.65 (0.51, 0.83)	0.72 (0.51, 1.03)
Beta blockers	1.28 (0.73, 2.24)	1.02 (0.93, 1.12)	1.14 (0.94, 1.38)
Cholesterol, per 1 mM	0.97 (0.88, 1.06)	0.99 (0.96, 1.02)	1.00 (0.97, 1.03)
Diabetes	0.86 (0.63, 1.16)	1.31 (1.13, 1.52)	1.51 (1.24, 1.84)
BMI, per 5Kg/m ²	0.97 (0.82, 1.14)	0.96 (0.88, 1.05)	0.96 (0.86, 1.06)
Current smoker	0.98 (0.67, 1.44)	1.26 (1.14, 1.41)	1.34 (0.95, 1.90)
History of CHD or stroke	0.98 (0.75, 1.28)	1.01 (0.93, 1.11)	1.08 (0.90, 1.28)
History of HF	1.48 (0.78, 2.82)	1.09 (0.96, 1.22)	1.03 (0.81, 1.31)
eGFR <30, per -15ml	0.97 (0.51, 1.86)	1.47 (1.21, 1.80)	1.48 (1.18, 1.86)
eGFR 30-59, per -15ml	1.09 (0.85, 1.41)	1.84 (1.57, 2.17)	2.56 (1.71, 3.84)
ACR, per 10 fold	0.87 (0.73, 1.04)	1.11 (0.98, 1.25)	1.28 (1.12, 1.47)

Table S4. Odds ratios (95% confidence intervals) of serum potassium level >5.5 mmol/L in patients categorized by baseline levels of estimated GFR and albuminuria in general population and high cardiovascular risk cohorts. The group with estimated GFR of 60-90 ml/min/1.73m² and albuminuria level <30 mg/g served as referent.

Moderate hyperkalemia (K>5.5 mmol/L)	ACR/PCR/Dipstick* (mg/g)			
	eGFR (ml/min/1.73m ²)	<30	30-299	300+
90 +		0.54 (0.36, 0.81)	1.09 (0.55, 2.16)	1.31 (0.87, 1.99)
60-90		ref	1.60 (1.08, 2.36)	2.11 (1.22, 3.66)
45-59		2.36 (1.88, 2.94)	2.57 (2.08, 3.19)	4.16 (3.04, 5.71)
30-44		5.36 (3.16, 9.09)	5.47 (3.58, 8.36)	8.30 (5.16, 13.36)
15-29		11.97 (5.41, 26.47)	13.89 (10.45, 18.47)	14.56 (10.68, 19.86)
<15		28.80 (14.84, 55.89)	19.68 (10.57, 36.64)	20.40 (13.85, 30.05)

Adjusted for age, gender, black race, systolic blood pressure, renin-angiotensin aldosterone system inhibitor use, loop or thiazide diuretics use, beta blocker use, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure

*Urine protein-to-creatinine ratio was converted to urine albumin-to-creatinine ratio by dividing by 2.655 for men and 1.7566 for women. Dipstick proteinuria was classified as < 30 mg/g for values of negative and trace, 30-299 mg/g for 1+, and 300+ mg/g for 2+ and higher.

Table S5. Odds ratios (95% confidence intervals) of serum potassium level >5.5 mmol/L in subgroups of patients categorized by baseline levels of estimated GFR and proteinuria level in CKD cohorts. The group with estimated GFR of 30-44 ml/min/1.73m² and albuminuria level 30-299 mg/g served as referent.

Moderate hyperkalemia (K>5.5 mmol/L)	ACR/PCR/Dipstick (mg/g)		
	eGFR (ml/min/1.73m ²) <30	30-299	300+
60 +	0.27 (0.19, 0.39)	0.32 (0.15, 0.67)	0.27 (0.14, 0.50)
45-59	0.45 (0.34, 0.59)	0.52 (0.39, 0.70)	0.64 (0.44, 0.93)
30-44	0.92 (0.74, 1.15)	ref	1.21 (0.96, 1.53)
15-29	1.69 (1.08, 2.63)	1.66 (1.26, 2.19)	1.84 (1.49, 2.28)
<15	3.95 (1.96, 7.96)	2.95 (2.13, 4.07)	3.01 (2.34, 3.88)

Table S6. Outcomes by cohort

Study	Region	Total N	Follow-up time, years	All-cause mortality, N (%)	Cardiovascular mortality, N (%)	ESRD, N (%)
General Population						
Beijing	China	1528	6.1 (0.9)	85 (6%)	-	-
CIRCS	Japan	8034	18.9 (4.4)	1330 (17%)	73 (1%)	-
Gubbio	Italy	1683	16.8 (3.2)	234 (14%)	-	-
KHS	South Korea	111532	13.2 (2.6)	4854 (4%)	809 (1%)	375 (0%)
MRC	UK	11840	7.1 (3.6)	7939 (67%)	2962 (25%)	-
NHANES	USA	46526	10.0 (6.7)	7336 (16%)	2157 (5%)	-
PREVEND	Netherlands	7319	11.3 (3.0)	745 (10%)	200 (3%)	-
Rancho Bernardo	USA	1481	13.0 (6.0)	633 (43%)	354 (24%)	-
Taiwan MJ	Taiwan	140488	11.1 (2.6)	8228 (6%)	1683 (1%)	-
Takahata	Japan	1923	7.0 (3.3)	98 (5%)	-	-
Subtotal		332354	11.7 (4.1)	31482 (9%)	8238 (2%)	-
High Risk Cohorts						
ADVANCE	Multi	11003	4.8 (0.9)	982 (9%)	514 (5%)	-
Geisinger	USA	67023	6.0 (4.3)	12097 (18%)	-	1745 (3%)
Maccabi	Israel	254379	5.4 (2.1)	21383 (8%)	-	1904 (1%)
Mt Sinai BioMe	USA	8393	4.3 (3.1)	-	-	638 (8%)
RCAV	USA	277226	5.3 (1.6)	46212 (17%)	-	1240 (0%)
SCREAM	Sweden	224285	4.1 (1.8)	28239 (13%)	-	1973 (1%)
ZODIAC	Netherlands	1153	10.0 (4.3)	524 (45%)	223 (19%)	-
Subtotal		843462	5.1 (2.2)	109437 (13%)	737 (0%)	7500 (1%)
CKD Cohorts						
AASK	USA	1081	1081	209 (19%)	-	298 (28%)
BC CKD	Canada	11990	11990	5191 (43%)	-	3065 (26%)
CanPREDDICT	Canada	2017	2017	468 (23%)	145 (7%)	430 (21%)
CKD-JAC	Japan	2639	2639	73 (3%)	-	528 (20%)
CRIB	UK	373	373	147 (39%)	73 (20%)	185 (50%)
MASTERPLAN	Netherlands	670	670	116 (17%)	-	147 (22%)
MDRD	USA	832	832	440 (53%)	178 (21%)	621 (75%)
PSP-CKD	UK	16828	16828	2267 (13%)	-	108 (1%)
SRR-CKD	Sweden	2618	2618	779 (30%)	301 (11%)	734 (28%)
Sunnybrook	Canada	3122	3122	544 (17%)	-	275 (9%)
Subtotal		42170	4.0 (3.3)	10234 (24%)	697 (2%)	6391 (15%)
Total		1217986	6.9 (4.1)	151153 (12%)	9672 (1%)	14266 (1%)

Figure S1. Distribution of serum potassium concentrations, overall and by baseline estimated glomerular filtration rate in CKD cohorts.

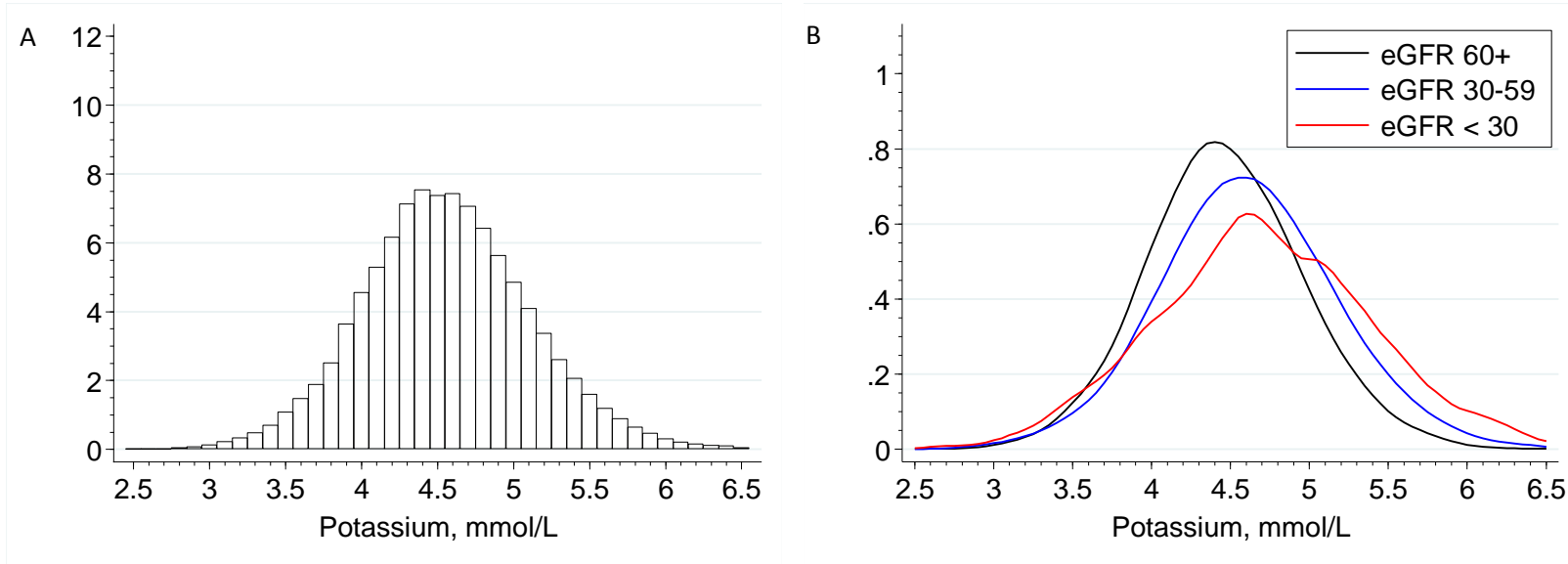


Figure S2. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by their age in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) estimated GFR of 80 ml/min/1.73m² and albuminuria of 10 mg/g. Red triangles indicate significant interactions.

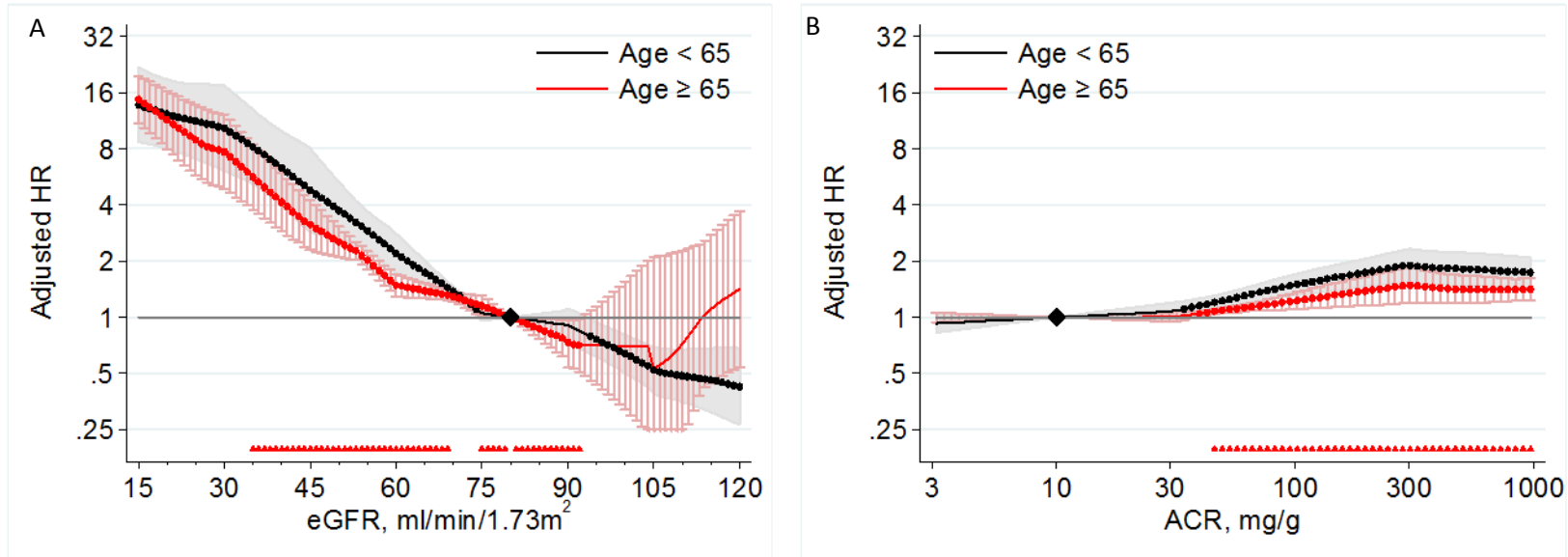


Figure S3. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by their gender in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) estimated GFR of 80 ml/min/1.73m² and albuminuria of 10 mg/g. Red triangles indicate significant interactions.

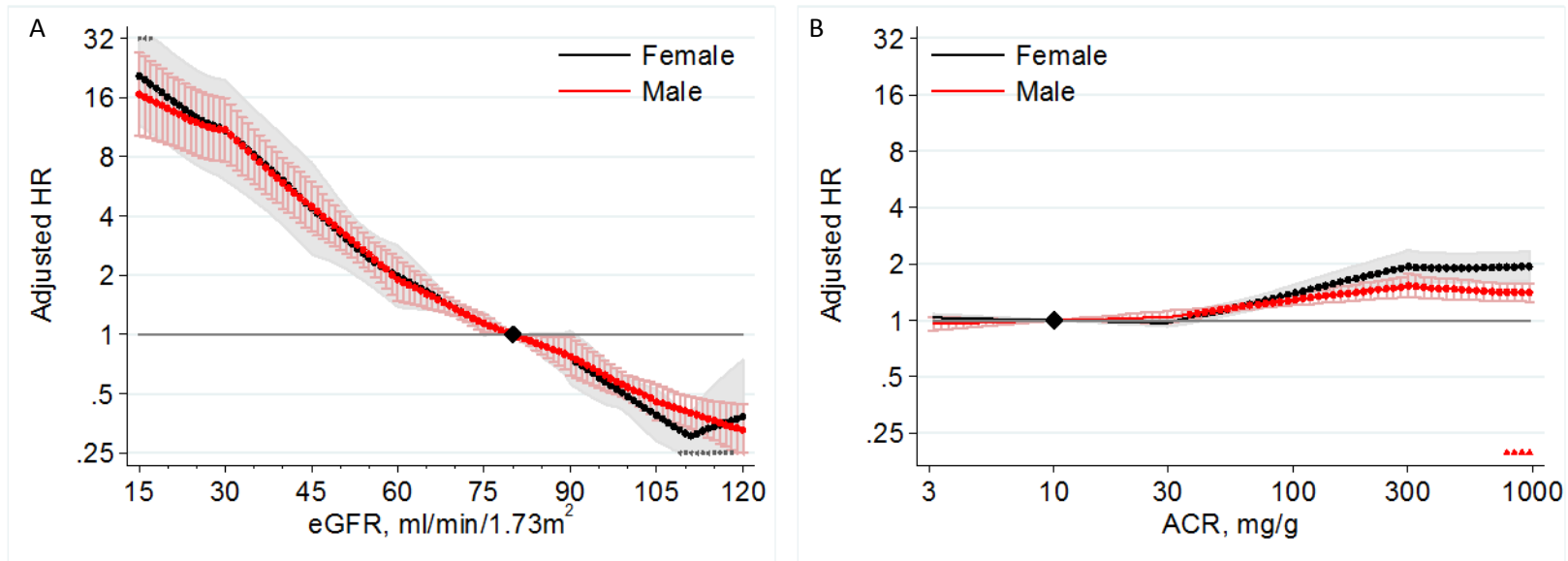


Figure S4. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by their race in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) estimated GFR of 80 ml/min/1.73m² and albuminuria of 10 mg/g.

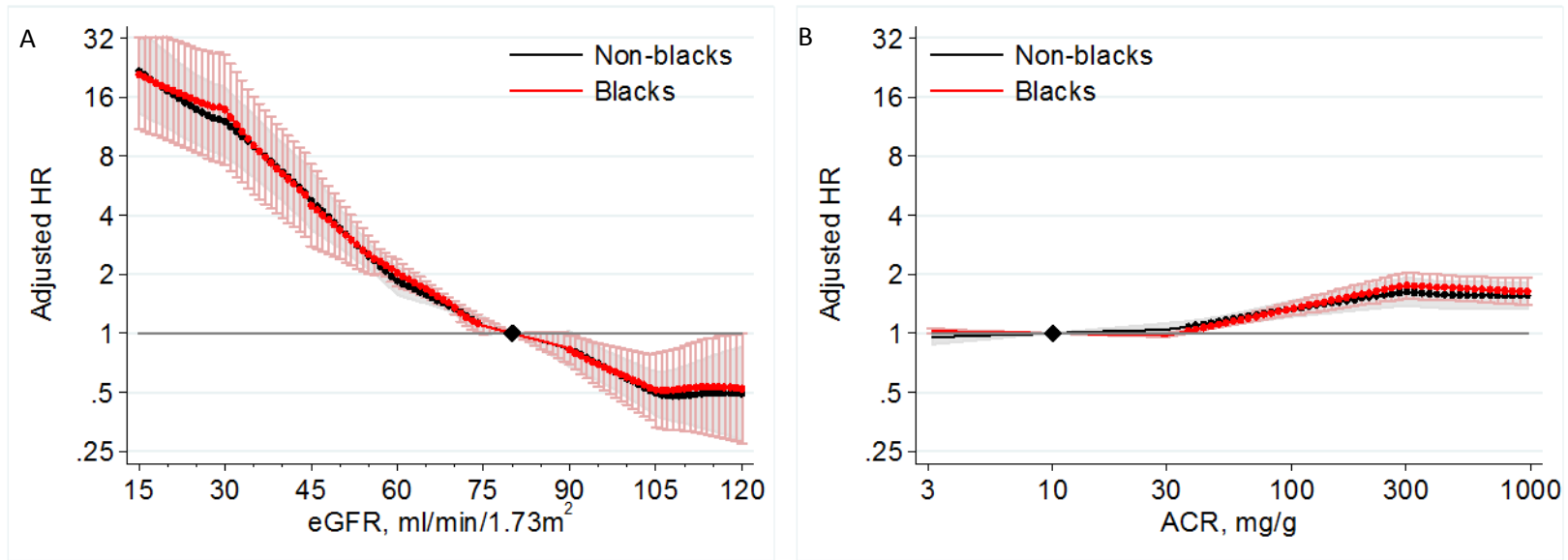


Figure S5. Continuous association of estimated GFR (A) and albuminuria (B) with the risk of serum potassium level >5.5 mmol/L, in subgroups of patients divided by the presence or absence of diabetes mellitus in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) estimated GFR of 80 ml/min/1.73m² and albuminuria of 10 mg/g. Red triangles indicate significant interactions.

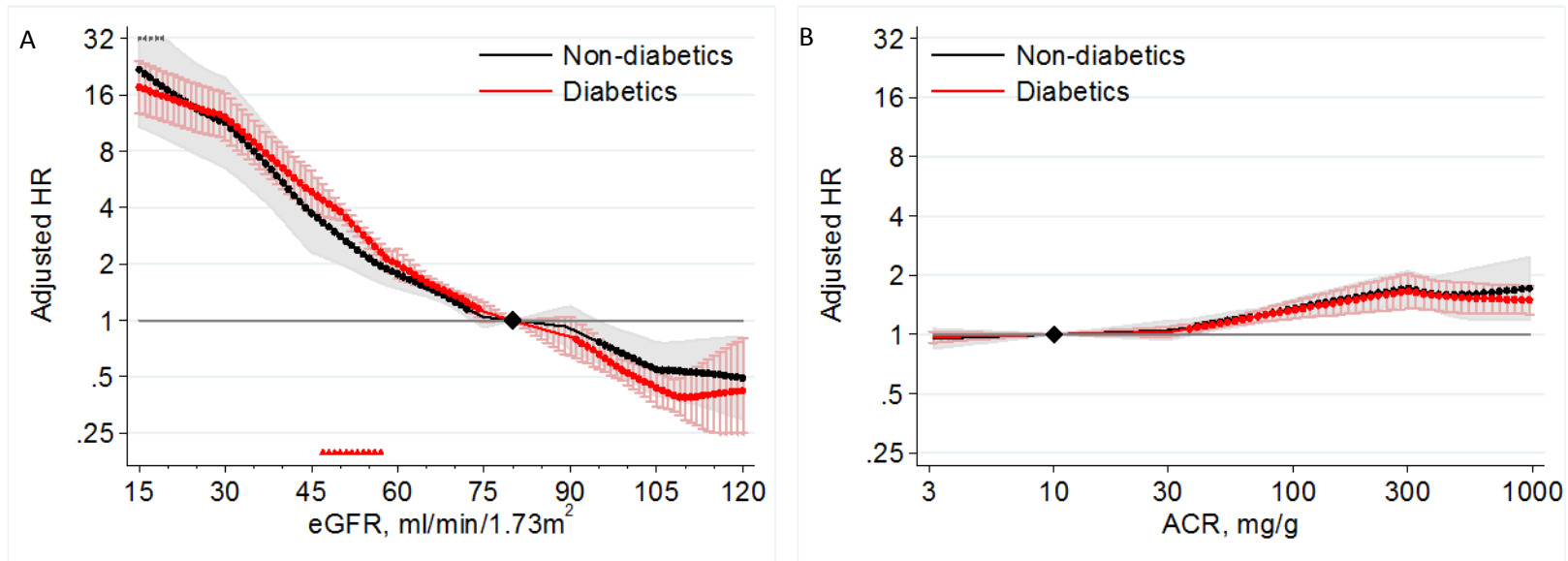


Figure S6. Continuous association of estimated GFR (panel A) and albuminuria (Panel B) with the risk of serum potassium level >5.5 mmol/L, and of estimated GFR (panel C) and albuminuria (Panel D) with the risk of serum potassium level <3.5 mmol/L, in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) estimated GFR of 50 ml/min/1.73m² (panel A) and albuminuria of 50 mg/g (panel B). Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

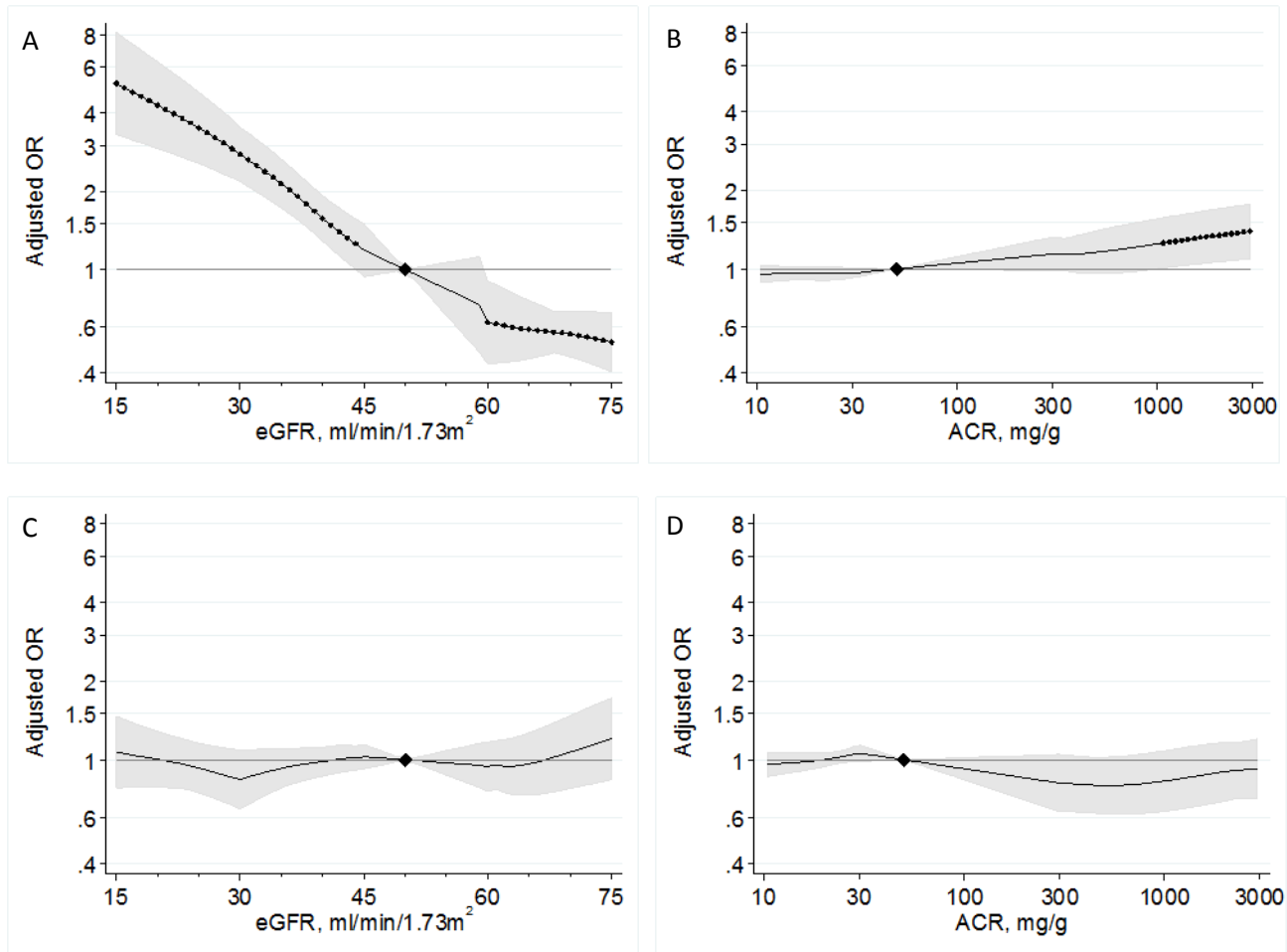


Figure S7. Adjusted relative hazard of cardiovascular mortality for potassium of 3.0 mmol/L (A) and 5.5 mmol/L (B), compared to a potassium of 4.2 mmol/L in individual general population/high risk cohorts.

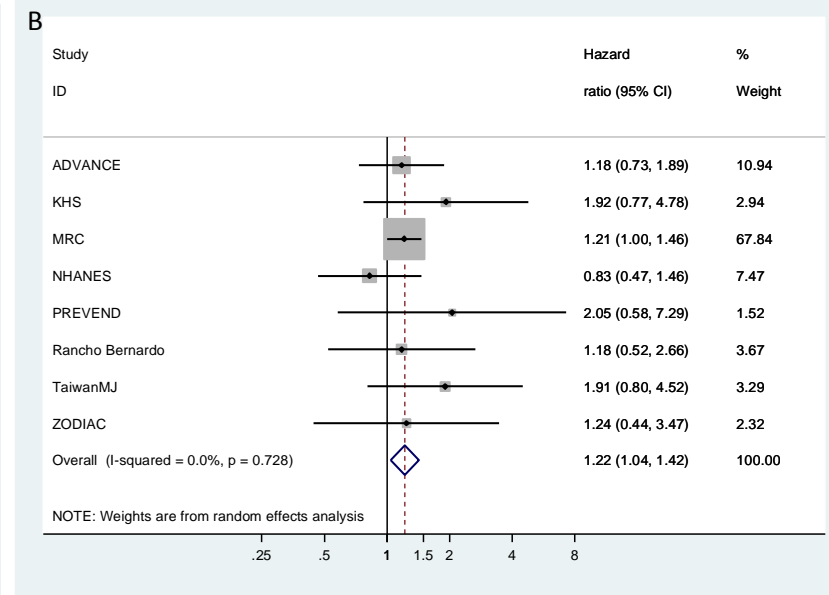
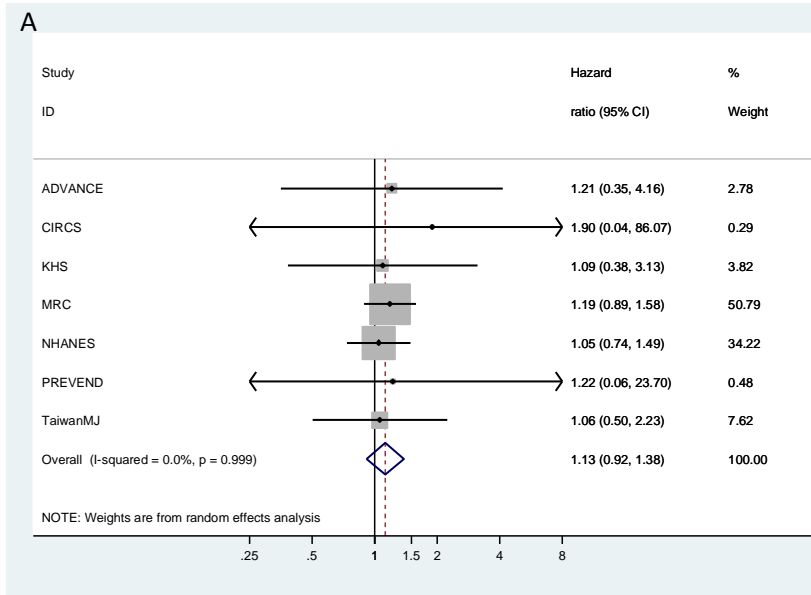


Figure S8. Adjusted relative hazard of end-stage renal disease for potassium of 3.0 mmol/L (A) and 5.5 mmol/L (B), compared to a potassium of 4.2 mmol/L in individual general population/high risk cohorts.

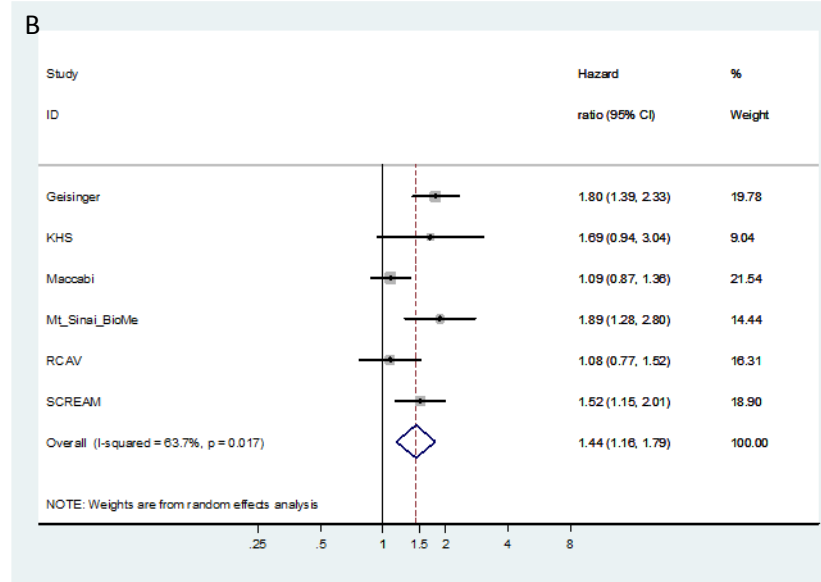
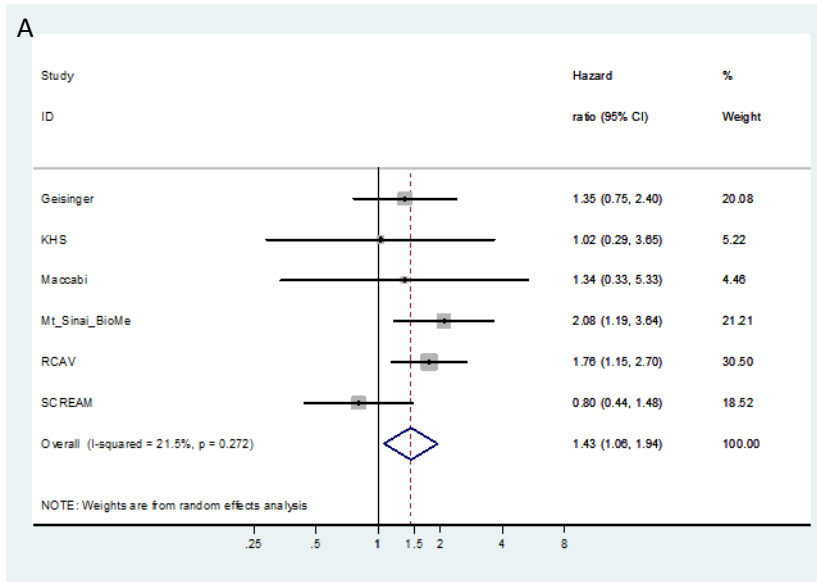
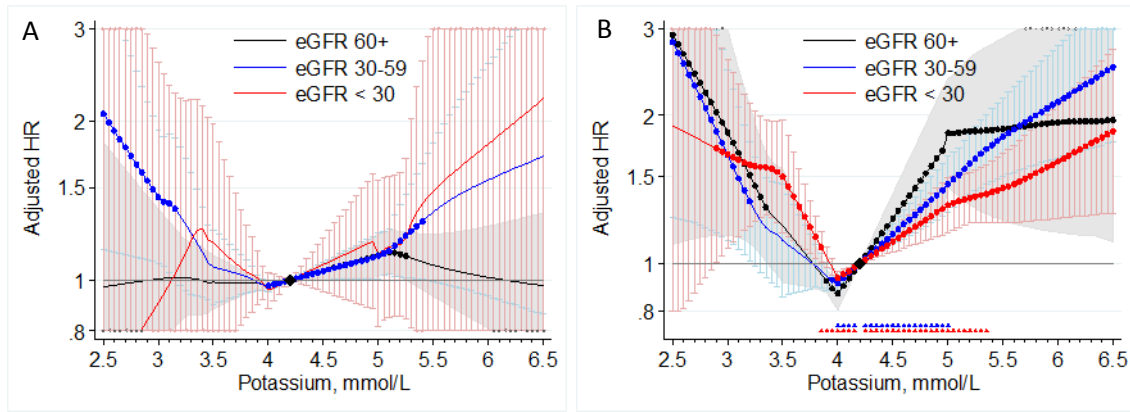


Figure S9. Adjusted hazard ratio of cardiovascular mortality (A) and end stage renal disease (B) associated with serum potassium concentration in general population and high cardiovascular risk cohorts, in subgroups divided by baseline eGFR level. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Red or blue triangles indicate significant interactions. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.



Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure

Figure S10. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different age subgroups in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Models adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

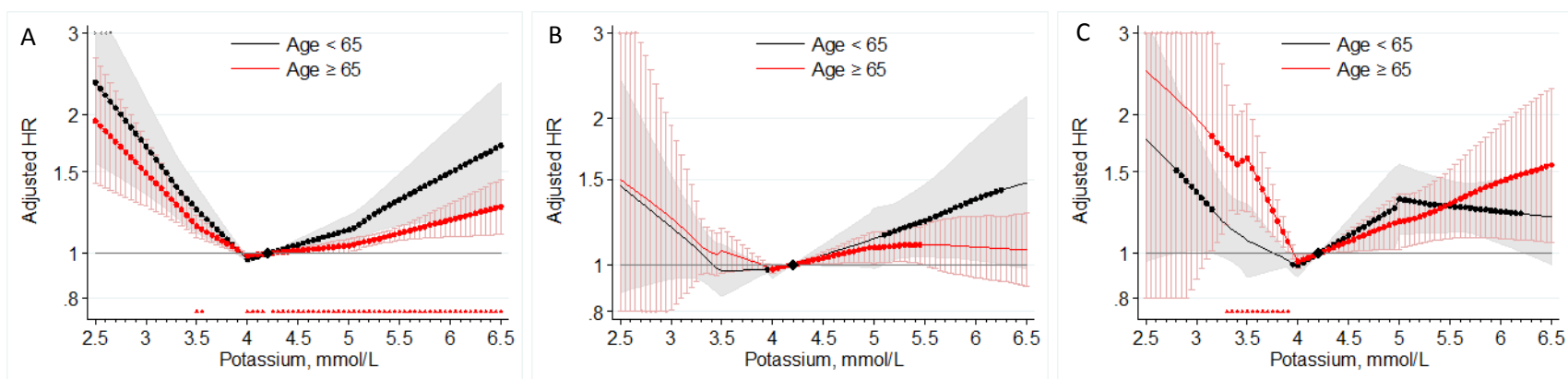


Figure S11. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different gender subgroups in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Models adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

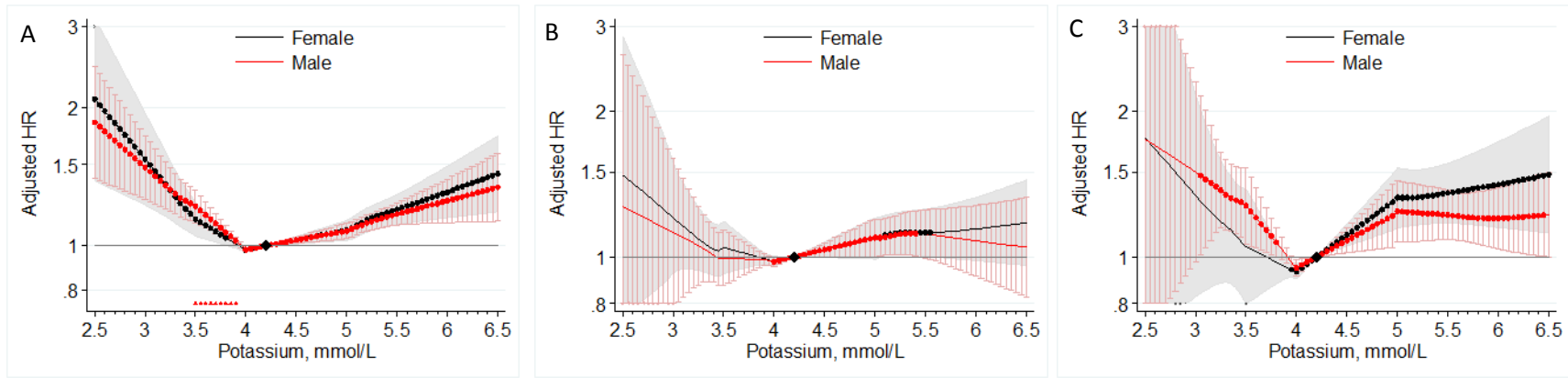


Figure S12. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different race subgroups in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Models adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

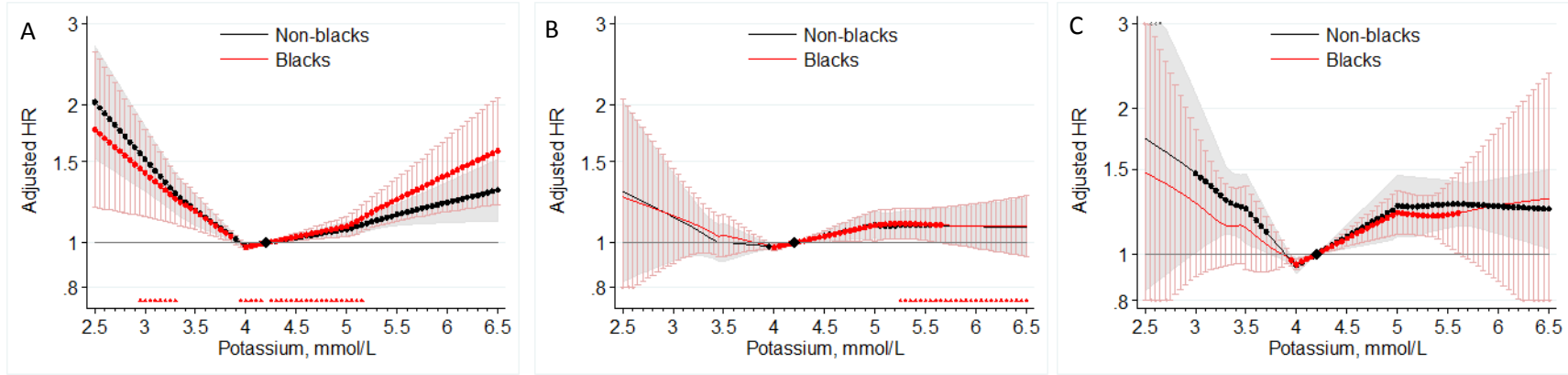


Figure S13. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of diabetes mellitus in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Models adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

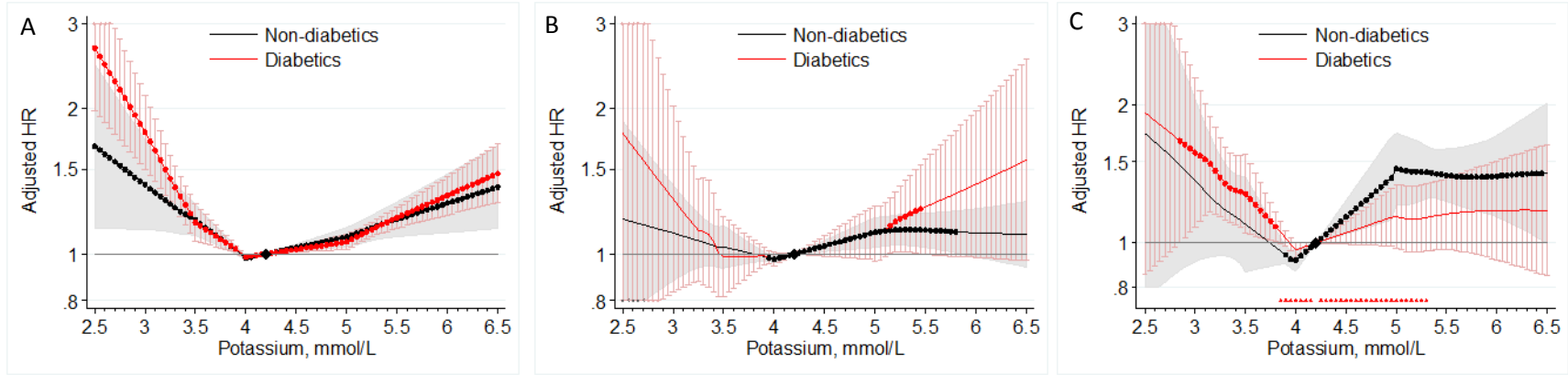


Figure S14. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups with different albuminuria levels in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Models adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

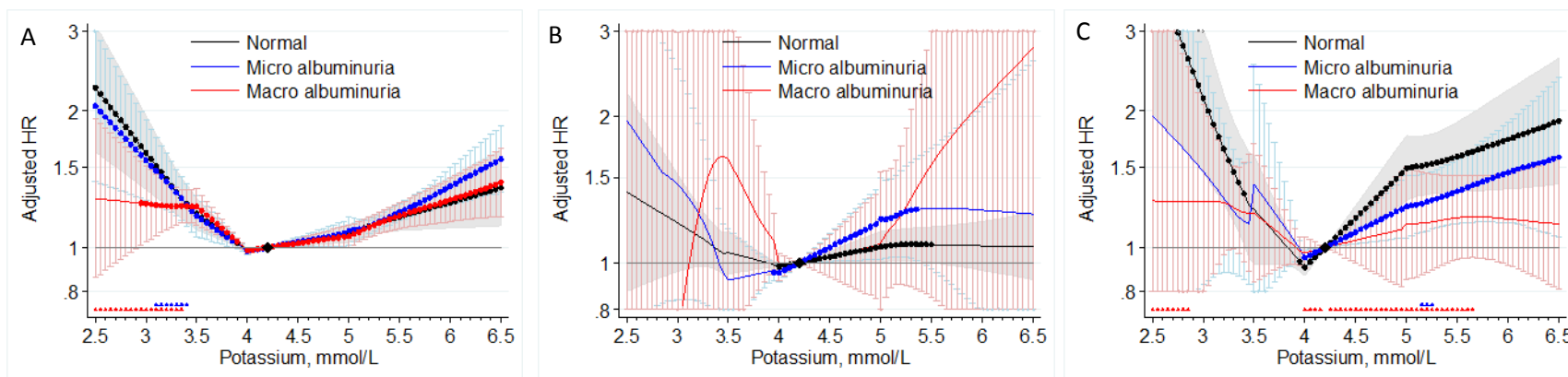


Figure S15. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with ACEi/ARB/potassium sparing diuretics in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Models adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

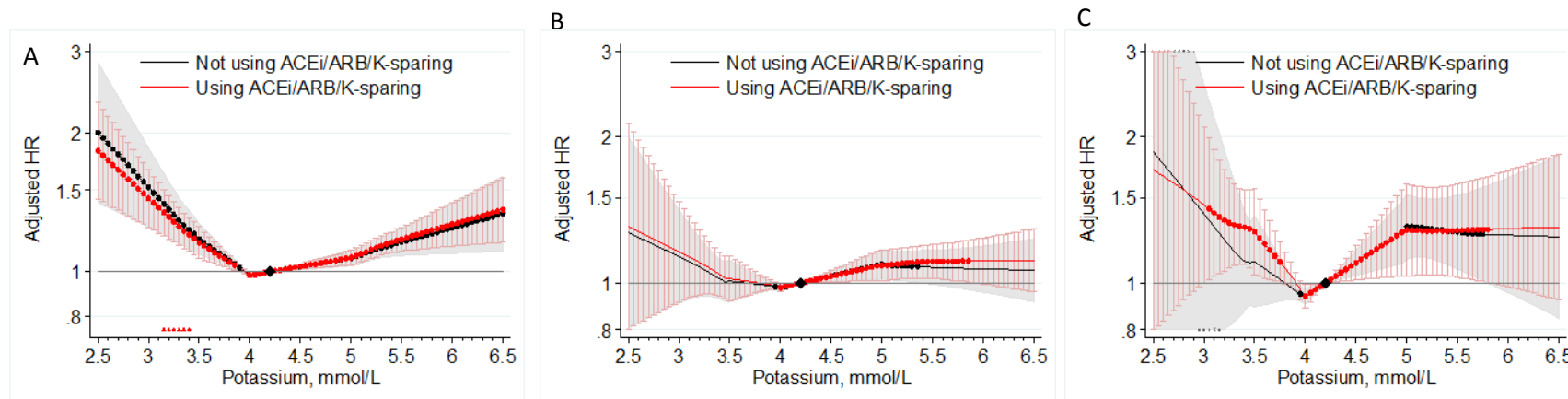


Figure S16. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with thiazide or loop diuretics in general population and high cardiovascular risk cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Models adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

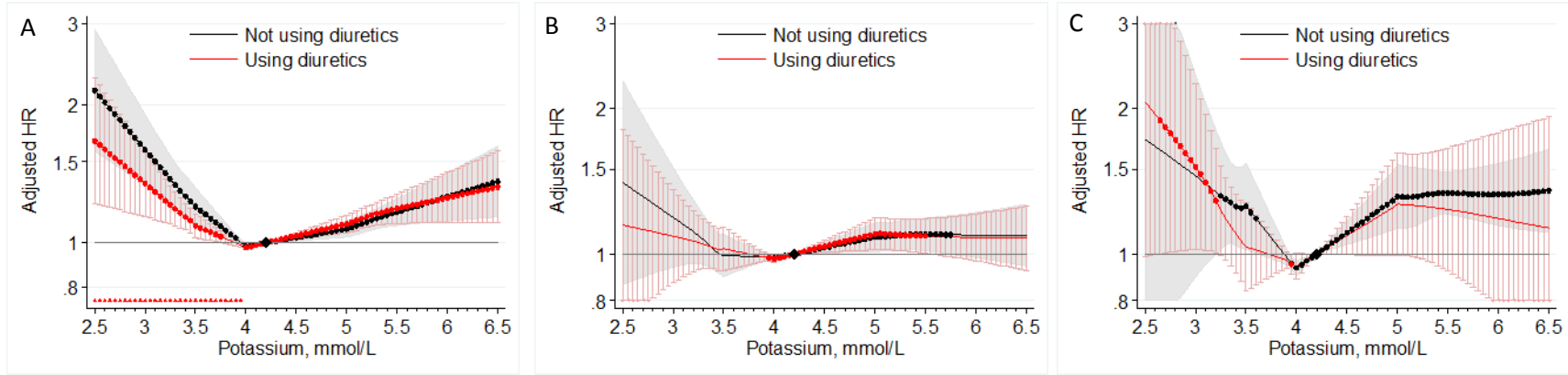


Figure S17. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

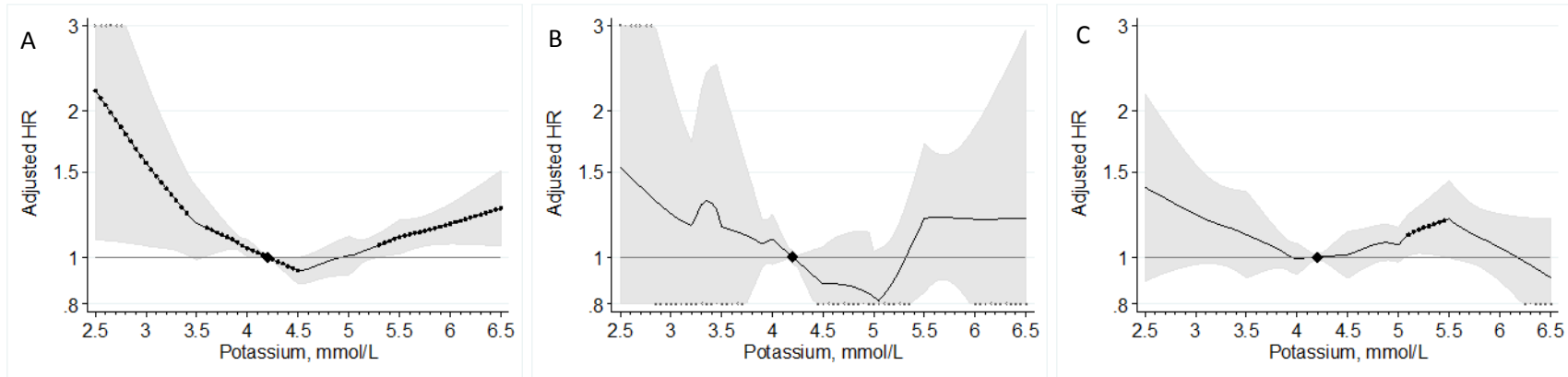


Figure S18. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in CKD cohorts, in subgroups divided by baseline eGFR level. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

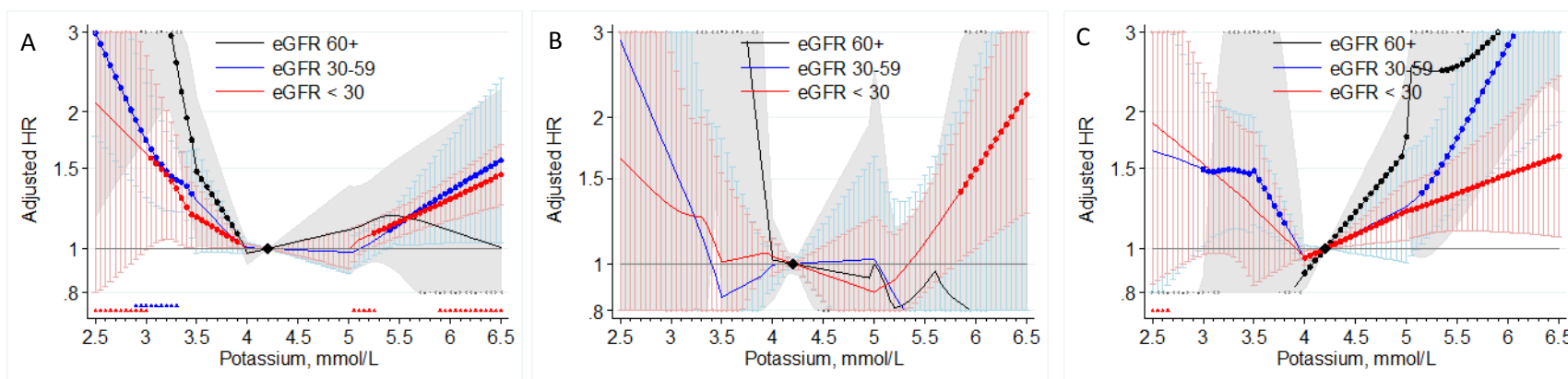


Figure S19. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different age subgroups in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

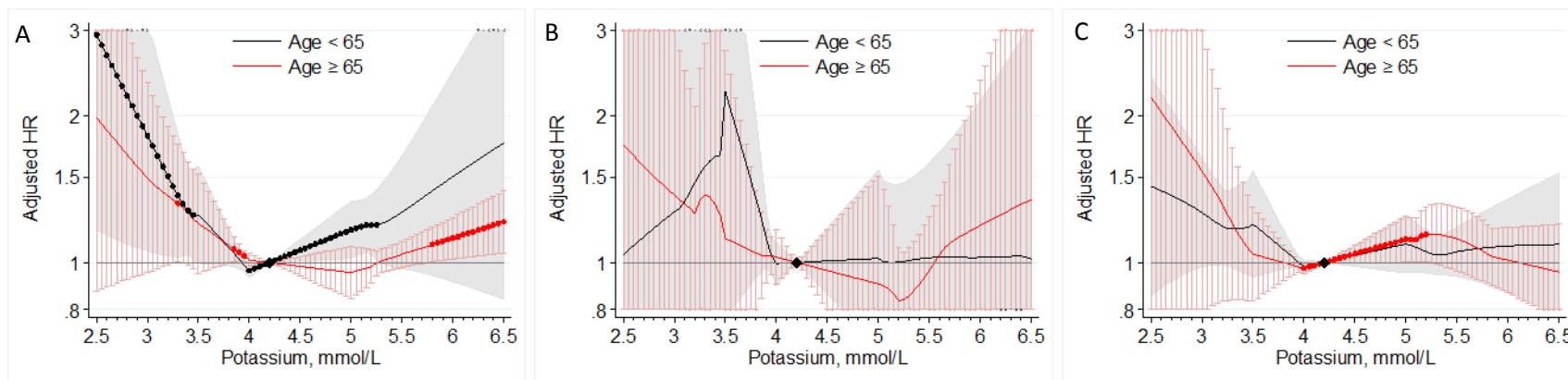


Figure S20. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different gender subgroups in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

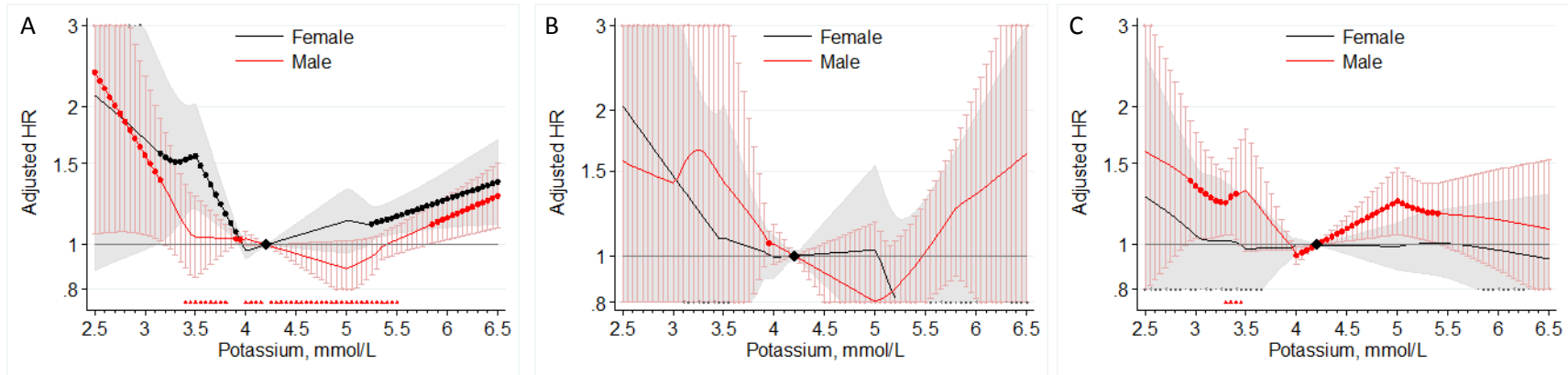


Figure S21. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in different race subgroups in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

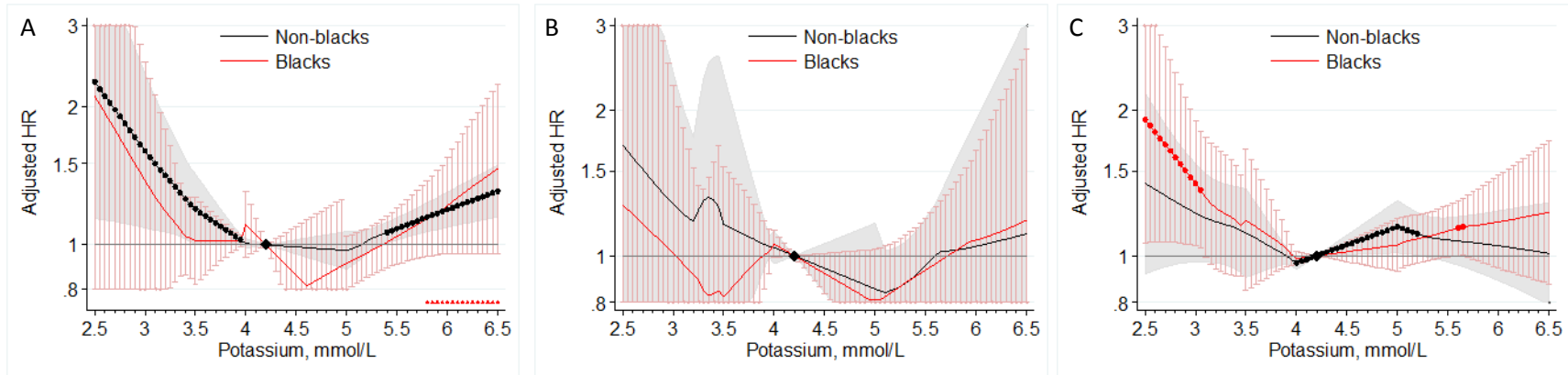


Figure S22. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of diabetes mellitus in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

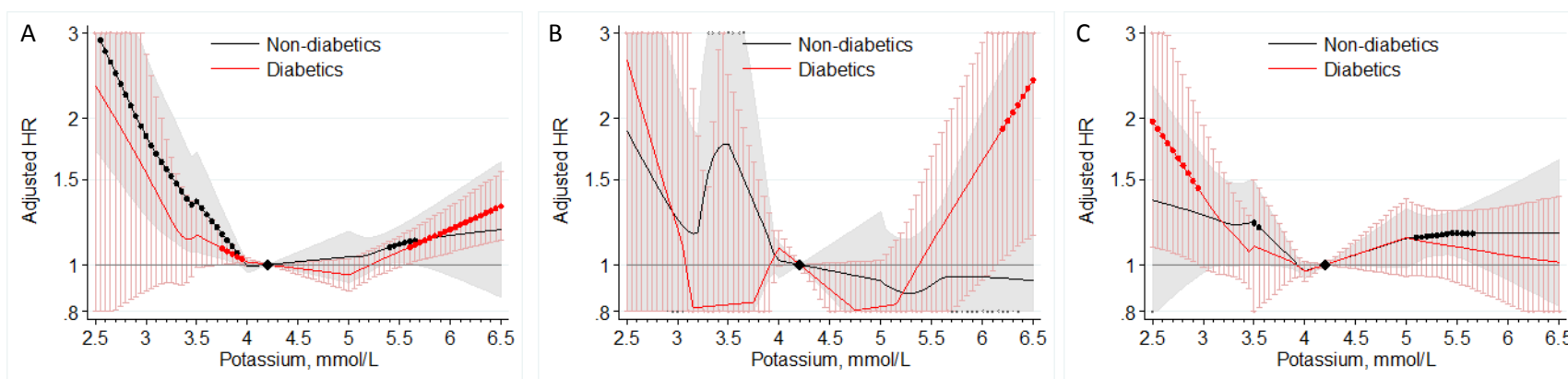


Figure S23. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups with different albuminuria levels in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

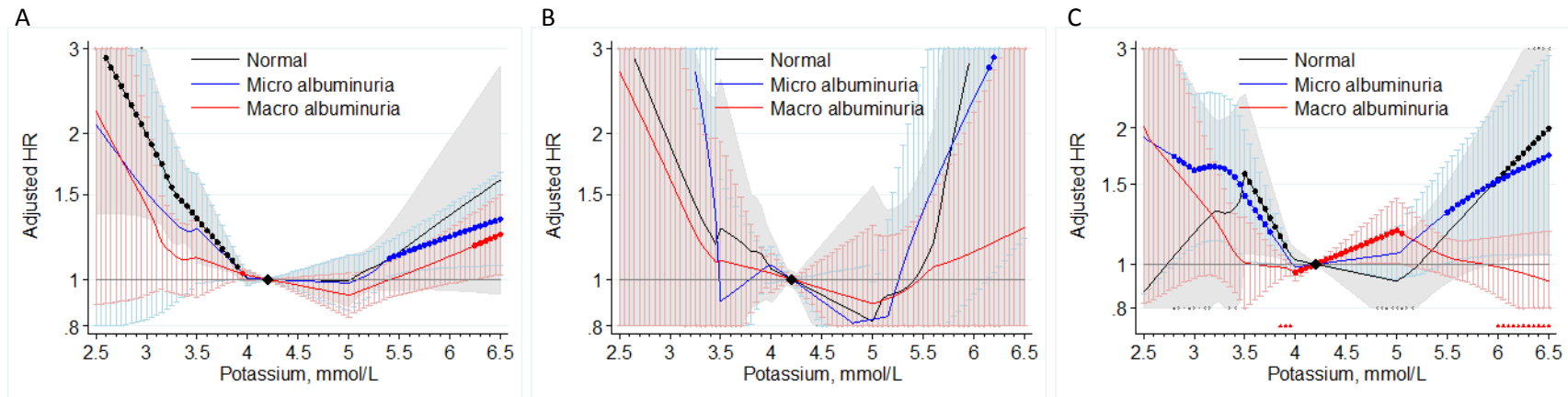


Figure S24. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with ACEi/ARB/potassium sparing diuretics in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.

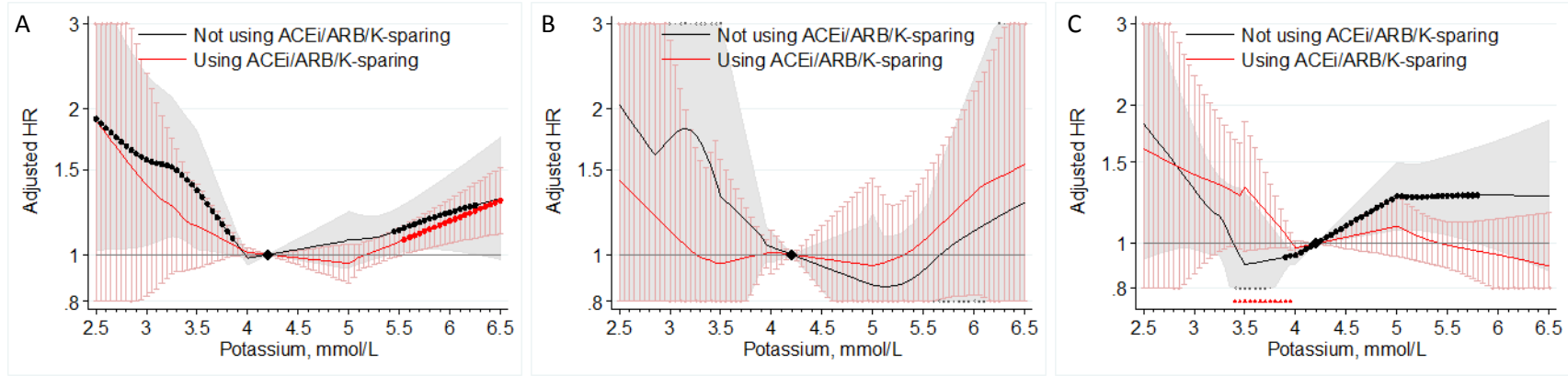
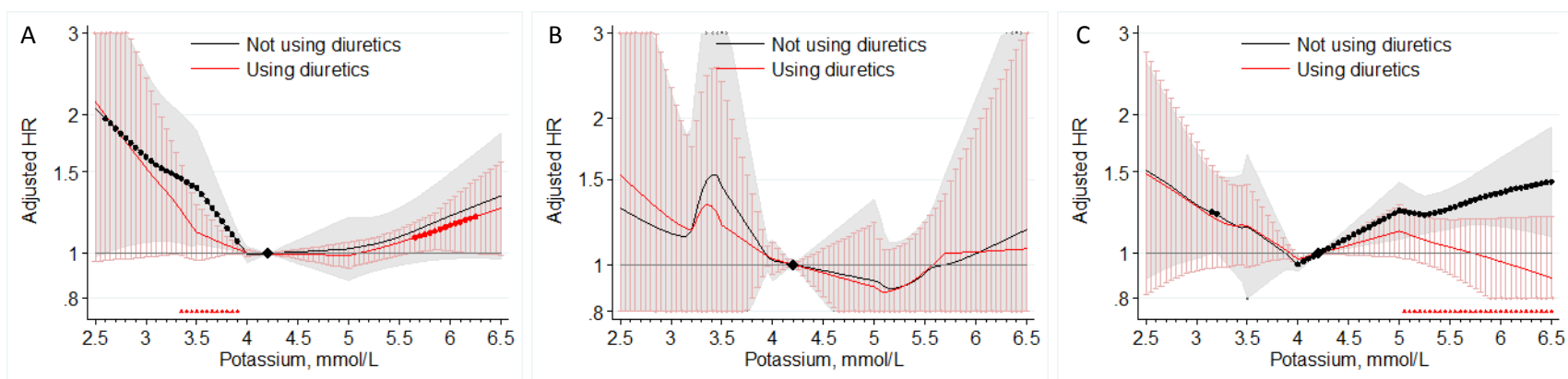


Figure S25. Adjusted hazard ratio of all-cause mortality (A), cardiovascular mortality (B), and end stage renal disease (C) associated with serum potassium concentration in subgroups divided by presence or absence of treatment with thiazide or loop diuretics in CKD cohorts. Black dots indicate statistical significance compared with the reference (diamond) serum potassium of 4.2 mmol/L. Adjusted for age, gender, race, systolic blood pressure, antihypertensive drugs, total cholesterol, diabetes, body mass index, smoking, history of coronary heart disease or stroke, history of heart failure.



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