

Appendix

Supplementary Table 1: STROBE Statement for *cohort studies*

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	5-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(b) For matched studies, give matching criteria and number of exposed and unexposed	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	

		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9 Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	10

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

Supplementary Table 2. Code definitions for baseline comorbidities

Category	ICD-9	ICD-10	ATC codes	Laboratory Data
Chronic Kidney Disease (excluding End Stage Renal Disease)	250.4, 403, 404, 580, 581, 582, 583, 585, 586, 587, 588, 591, 593, 753	E10.2, E11.2, I12, I13, N18, N19, N00-N16, N25, N26, N28.82, N39.1, Q60-Q64	A11CC04, A11CC03, H05BX03, H05BX02, V03AE02, V03AE03, V03AE04, B03XA01, B03XA02, B03XA04, V03AE03, V03AE01, A02AC01, A12AA04, H05BX01	Two abnormal eGFR tests at least 90 days apart. Abnormal eGFR was defined as an eGFR below 60 mL/min/1.73m ²
Diabetes Mellitus	250.x	E10-E14	A10	n/a
Heart Failure	428.0, 428.1-5, 428.9	I50, I50.9, I50.1, I50.20-23, I50.30-33, I5040-43	n/a	n/a
Hypertension	401.xx, 402.00, 402.1, 402.10, 402.90, 403.xx-405.xx	I10-I13, I15	C02AB01, C02AB02, C02AC01, C02CA04, C02CA05, C02DB02, C02DC01, C02KX01, C02LA01, C02LB01, G04CA03, C03AA03, C03BA04, C03BA11, C03CA01, C03CA02, C03CC01, C03DA01, C03DB01, C03DB02, C03EA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA12, C07AB02, C07AB03, C07AB04, C07AB07, C07AG01, C07BA05, C07BA06, C07CA03, C07CB03, C08CA01, C08CA02, C08CA04, C08CA05, C08CA06, C08DA01, C08DB01, C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA07, C09AA08, C09AA09, C09AA10, C09BA02, C09BA03, C09BA04, C09BA06, C09BA08, C09CA01, C09CA02, C09CA03, C09CA04, C09CA06, C09CA07,	N/a

			C09DA01, C09DA02, C09DA03, C09DA04, C09DA06, C09DA07	
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Supplementary Table 3: Baseline Characteristics stratified by Serum Potassium levels

<u>Characteristic</u>	<u>Overall</u> <u>n=93,667</u>	<u>≥5.0 K+ <5.5</u> <u>(n =75,364)</u>	<u>≥5.5 K+ <6.0</u> <u>(n =12,139)</u>	<u>≥6.0 K+ <6.5</u> <u>(n =3,349)</u>	<u>≥6.5 K+ <7.0</u> <u>(n=1,378)</u>	<u>K+ ≥ 7.0</u> <u>(n= 1,437)</u>
Demographics						
<u>Age (years)</u>	<u>64.15±18.09</u>	<u>64.45±17.81</u>	<u>65.06±18.30</u>	<u>63.25±19.33</u>	<u>61.95±19.20</u>	<u>60.24±19.77</u>
<u>Sex (% female)</u>	<u>43,541</u> <u>(45.64%)</u>	<u>34,432</u> <u>(45.69%)</u>	<u>5,537</u> <u>(45.61%)</u>	<u>1,579</u> <u>(47.15%)</u>	<u>637</u> <u>(46.23%)</u>	<u>693</u> <u>(48.23%)</u>
Comorbidities						
<u>CKD</u>	<u>26,566</u> <u>(28.4%)</u>	<u>20,683</u> <u>(27.44%)</u>	<u>3,917</u> <u>(32.27%)</u>	<u>1,095</u> <u>(32.70%)</u>	<u>437</u> <u>(31.71%)</u>	<u>434</u> <u>(30.20%)</u>
<u>Hypertension</u>	<u>65,161</u> <u>(69.6%)</u>	<u>52,316</u> <u>(69.42%)</u>	<u>8,683</u> <u>(71.53%)</u>	<u>2,320</u> <u>(68.74%)</u>	<u>943</u> <u>(68.43%)</u>	<u>917</u> <u>(63.81%)</u>
<u>Diabetes Mellitus</u>	<u>33,548</u> <u>(35.8%)</u>	<u>26,520</u> <u>(35.19%)</u>	<u>4,683</u> <u>(38.58%)</u>	<u>1,283</u> <u>(38.31%)</u>	<u>522</u> <u>(37.88%)</u>	<u>540</u> <u>(37.58%)</u>
<u>Heart Failure</u>	<u>19,374</u> <u>(20.7%)</u>	<u>14,861</u> <u>(19.72%)</u>	<u>2,974</u> <u>(24.50%)</u>	<u>870</u> <u>(25.98%)</u>	<u>345</u> <u>(25.04%)</u>	<u>324</u> <u>(22.55%)</u>
Medications						
<u>RAAS inhibitors</u>	<u>33,381</u> <u>(35.6%)</u>	<u>26,599</u> <u>(35.29%)</u>	<u>4,620</u> <u>(38.06%)</u>	<u>1,234</u> <u>(36.85%)</u>	<u>485</u> <u>(35.20%)</u>	<u>443</u> <u>(30.83%)</u>
<u>Beta Blockers</u>	<u>22,019</u> <u>(23.5%)</u>	<u>17,438</u> <u>(23.14%)</u>	<u>3,094</u> <u>(25.49%)</u>	<u>836</u> <u>(24.96%)</u>	<u>341</u> <u>(24.75%)</u>	<u>310</u> <u>(21.57%)</u>
<u>Azole Antifungals</u>	<u>211</u> <u>(0.2%)</u>	<u>168</u> <u>(0.22%)</u>	<u>33</u> <u>(0.27%)</u>	<u>7</u> (0.21%)	<u>*</u>	<u>*</u>
<u>Cyclosporine</u>	<u>114</u> (0.1%)	<u>97</u> (0.13%)	<u>11</u> (0.09%)	<u>*</u>	<u>*</u>	<u>*</u>
<u>Digoxin</u>	<u>3,136</u> <u>(3.4%)</u>	<u>2,412</u> <u>(3.20%)</u>	<u>464</u> <u>(3.82%)</u>	<u>140</u> <u>(4.18%)</u>	<u>69</u> <u>(5.01%)</u>	<u>51</u> <u>(3.55%)</u>
<u>Heparin</u>	<u>545</u> (0.6%)	<u>417</u> (0.55%)	<u>84</u> (0.69%)	<u>21</u> (0.63%)	<u>13</u> <u>(0.94%)</u>	<u>10</u> <u>(0.70%)</u>
<u>NSAIDs</u>	<u>5,090</u> <u>(5.4%)</u>	<u>4,036</u> <u>(5.36%)</u>	<u>689</u> <u>(5.68%)</u>	<u>196</u> <u>(5.85%)</u>	<u>87</u> <u>(6.31%)</u>	<u>82</u> <u>(5.71%)</u>
<u>K Supplements</u>	<u>2,872</u> <u>(3.1%)</u>	<u>2,090</u> <u>(2.77%)</u>	<u>503</u> <u>(4.14%)</u>	<u>129</u> (3.85%)	<u>80</u> <u>(5.81%)</u>	<u>70</u> <u>(4.87%)</u>
<u>Tacrolimus</u>	<u>108</u> (0.1%)	<u>99</u> (0.13%)	<u>9</u> (0.07%)	<u>0</u>	<u>0</u>	<u>0</u>
<u>Trimethoprim</u>	<u>1,929</u> <u>(2.1%)</u>	<u>1,484</u> <u>(1.97%)</u>	<u>300</u> <u>(2.47%)</u>	<u>89</u> <u>(2.66%)</u>	<u>28</u> <u>(2.03%)</u>	<u>28</u> <u>(1.95%)</u>

Abbreviations: CKD: Chronic Kidney Disease; DM: Diabetes mellitus; HF: Heart Failure; HTN: Hypertension; K+: Potassium; NSAIDs: Nonsteroidal anti-inflammatory drugs.

*Not reported due to small numbers

Supplementary Table 34. Outcomes, time at risk and crude rates by high-risk subgroup

All-cause mortality			
Cohort	Events	Time at risk (person-years)	Crude rate (per 100 person-years)
CKD	12,729	83,970	15.16
Diabetes Mellitus	12,044	111,106	10.84
Heart Failure	11,395	52,427	21.73
Hypertension	24,478	203,831	12.01
Short Term mortality¹			
Cohort	Events	Time at risk (person-years)	Crude rate (per person-year)
CKD	2,230	2,057	1.08
Diabetes Mellitus	2,285	2,625	0.87
Heart Failure	2,614	1,441	1.81
Hypertension	5,368	5,045	1.06
Long term Mortality²			
Cohort	Events	Time at risk (person-years)	Crude rate (per 100 person-years)
CKD	10,499	81,913	12.82
Diabetes Mellitus	9,759	108,481	9.00
Heart Failure	8,781	50,985	17.22
Hypertension	19,380	198,785	9.75
Cardiovascular Events			
Cohort	Events	Time at risk (person-years)	Crude rate (per 100 person-years)
CKD	11,112	83,586	13.29
Diabetes Mellitus	13,063	110,731	11.80
Heart Failure	9,237	52,128	17.72
Hypertension	20,544	203,205	10.11
Acute Dialysis			
Cohort	Events	Time at risk (person-years)	Crude rate (per 1,000 person-years)
CKD	584	83,956	6.96
Diabetes Mellitus	580	111,091	5.22
Heart Failure	335	52,417	6.39
Hypertension	718	203,814	3.52

ICU Admission			
Cohort	Events	Time at risk (person-years)	Crude rate (per 100 person-years)
CKD	560	8,674	6.46
Diabetes Mellitus	570	4,911	11.61
Heart Failure	369	3,389	10.89
Hypertension	2317	70,152	3.30
All-cause Hospitalizations			
Cohort	Events	Time at risk (person-years)	Crude rate (per person-year)
CKD	7,777	8,480	0.92
Diabetes Mellitus	7,862	13,606	0.58
Heart Failure	2,814	3,301	0.85
Hypertension	39,763	69,242	0.57

Supplementary Table 45. Baseline characteristics: propensity-score match of patients with and without Hyperkalemia*.

Characteristic	With Hyperkalemia† (n = 18,247)	Without Hyperkalemia (n = 18,247)	SMD
Demographics			
Age (years)	64.1 ± 18.7	65.1 ± 18.8	0.058
Sex (% female)	8,429 (46.2%)	8,401 (46.0%)	0.003
Baseline Comorbidities			
Chronic Kidney Disease	5,827 (31.9%)	5,792 (31.7%)	0.041
Diabetes Mellitus	6,984 (38.3%)	7,097 (38.9%)	0.012
Heart Failure	4,463 (24.46%)	4,468 (24.49%)	0.0006
Hypertension	12,835 (70.3%)	13,180 (72.2%)	0.042
Medications			
RAAS inhibitors			

<i>Current users</i> ¹	6,738 (36.9%)	6,866 (37.6%)	0.012
<i>Non-users</i> ²	2,402 (13.2%)	2,564 (14.0%)	0.026
<i>Never users</i> ³	9,107 (49.9%)	8,817 (48.3%)	0.032
Azole antifungals			
<i>Current users</i>	43 (0.2%)	33 (0.2%)	0.012
<i>Non-users</i>	990 (5.4%)	990 (5.4%)	0
<i>Never users</i>	17,214 (94.3%)	17,224 (94.4%)	0.002
Beta-blockers			
<i>Current users</i>	4,544 (24.9%)	4,771 (26.1%)	0.002
<i>Non-users</i>	1,558 (8.5%)	1,551 (8.5%)	0.028
<i>Never users</i>	12,145 (66.5%)	11,925 (65.3%)	0.025
Cyclosporine			
<i>Current users</i>	17 (0.1%)	13 (0.1%)	0.008
<i>Non-users</i>	14 (0.1%)	16 (0.1%)	0.004
<i>Never users</i>	18,216 (99.8%)	18,218 (99.8%)	0.003
Digoxin			
<i>Current users</i>	711 (3.9%)	668 (3.6%)	0.012
<i>Non-users</i>	315 (1.7%)	282 (1.5%)	0.014
<i>Never users</i>	17,221 (94.4%)	17,297 (94.8%)	0.018
Heparin			
<i>Current users</i>	126 (0.7%)	109 (0.6%)	0.012
<i>Non-users</i>	625 (3.4%)	627 (3.4%)	<.001
<i>Never users</i>	17,496 (95.8%)	17,511 (95.9%)	0.004
Prescription NSAIDs			
<i>Current users</i>	1,045 (5.7%)	1,010 (5.5%)	0.008
<i>Non-users</i>	5,607 (30.7%)	5,714 (31.3%)	0.013

<i>Never users</i>	11,595 (63.5%)	11,523 (63.1%)	0.008
Potassium Supplements			
<i>Current users</i>	765 (4.2%)	717 (3.9%)	0.013
<i>Non-users</i>	1,202 (6.6%)	1,134 (6.2%)	0.015
<i>Never users</i>	16,280 (89.2%)	16,396 (89.9%)	0.020
Tacrolimus			
<i>Current users</i>	9 (0.1%)	9 (0.1%)	0
<i>Non-users</i>	‡	‡	-
<i>Never users</i>	18,236 (99.9%)	18,236 (99.9%)	0
Trimethoprim			
<i>Current users</i>	431 (2.4%)	349 (1.9%)	0.031
<i>Non-users</i>	3,333 (18.3%)	3,454 (18.9%)	0.017
<i>Never users</i>	14,483 (79.4%)	14,444 (79.2%)	0.005

*Subgroup of patients with Serum Potassium ≥ 5.5 mmol/L

†Defined as a Serum Potassium ≥ 5.5 mmol/L

‡Not reported due to small numbers

Abbreviations: NSAIDs: nonsteroidal anti-inflammatory drugs; RAAS: renin-angiotensin aldosterone system;

¹A patient will be defined as a current user if 150% of the days' supply of the last prescription of a given exposure covers the date of incident hyperkalemia. ²Non-users (or former users) were defined as patients with a prescription for a given exposure for which 150% of the days' supply of the last prescription days' supply did not overlap with the index date. ³Patients with no record of any prescription for an exposure prior to index date were classified as never-users.

Supplementary Table 56: Hazard ratios with 95% confidence interval and p-values of Cox proportional hazards regression models*

Model Type	All-cause mortality		Cardiovascular events	
	HR (95% CI)	p	HR (95% CI)	p
Propensity matched ¹	1.66 (1.58-1.74)	<0.001	1.31 (1.17-1.45)	<0.001

*Subgroup of patients with Serum Potassium ≥ 5.5 mmol/L

Abbreviations: CI - confidence interval; HR - hazard ratio; p - p-value.

¹Multivariate analysis in the propensity scored-matched sample was adjusted for the following covariates at baseline: age, sex, serum potassium value, comorbidities and medications.