

Epidemiology of HK in HF

**Supplement for *Epidemiology and risk factors for hyperkalaemia in heart failure***

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**Supplementary Table** Prevalence and incidence of hyperkalaemia and hypokalaemia, and risk factors for hyperkalaemia in studies that include patients with HF

Study	Population studied	Years	Overall <i>n</i> number and population breakdown	Prevalence		Risk factors for hyperkalaemia
				Hyperkalaemia	Hypokalaemia	
Retrospective study of population-based healthcare database in Spain <sup>1</sup>	55 years or older with ≥1 sK <sup>+</sup> measurement	2015–2017	Overall 375,233  Prevalence of conditions: <ul style="list-style-type: none"> <li>• CHF 2–3% + CKD and DM 50–54%</li> <li>• HT 48–49%</li> <li>• DM 15%</li> </ul> Prevalence of drug use: <ul style="list-style-type: none"> <li>• ACEis 53–58%</li> <li>• ARBs 31–32%</li> <li>• RAASis 75–77%</li> </ul>	<b>Prevalence:</b> <ul style="list-style-type: none"> <li>• 10.6–12.8% per year               <ul style="list-style-type: none"> <li>○ 1.8–2.6% recurrent</li> </ul> </li> <li>• 12% per year with chronic condition on RAASi               <ul style="list-style-type: none"> <li>○ 20–22% on MRAs</li> </ul> </li> <li>• <b>23.3–24.6% per year in the subgroup with both CHF and CKD</b> <ul style="list-style-type: none"> <li>○ 6.7–8.0% recurrent</li> </ul> </li> </ul>	<b>Prevalence:</b> <ul style="list-style-type: none"> <li>• 1.0–1.2% per year</li> <li>• 1.1% per year with chronic condition on RAASi</li> </ul>	RRs in 2015–2017 for strongest predictors ( <i>P</i> < 0.001) were: <ul style="list-style-type: none"> <li>• CKD 1.8–1.9</li> <li>• DM 1.85–1.9</li> <li>• ACEis 1.39–1.5</li> <li>• MRAs 1.34–1.4</li> </ul>
Retrospective study of Medicare claims database in the USA <sup>2</sup>	65 years or older, <65 years with disabilities and all ages with	2010–2014	Overall 1,964,905 With hyperkalaemia 90,814 <ul style="list-style-type: none"> <li>• HF 25,603 (28%)</li> <li>• HT 85%</li> <li>• Diabetes 49%</li> <li>• CKD 30%</li> </ul>	<b>Prevalence:</b> <ul style="list-style-type: none"> <li>• 2.6–2.7% per year overall</li> <li>• <b>8.6–9.4% per year in HF</b></li> <li>• 8.9–9.3% per year in CKD and/or HF</li> </ul>	NA	Patients with hyperkalaemia vs. without hyperkalaemia were (all <i>P</i> < 0.001): <ul style="list-style-type: none"> <li>• Older (72.8 vs. 71.8 years)</li> <li>• Female (55.4% vs. 54.0%)</li> <li>• More likely to require inpatient (37.8% vs. 2.2%) and ED (9.5% vs. 4.0%) services</li> <li>• More likely to have hypertension (84.7% vs. 71.5%) and diabetes (48.8% vs. 35.1%)</li> <li>• Higher CCI (3.2 vs. 2.6)</li> </ul>
Retrospective cohort study of administrative databases in Canada <sup>3</sup>	<i>De novo</i> hyperkalaemia	2007–2015	Overall 93,667 <b>HF 19,374 (21%)</b>  HT 69% DM 36% CKD 28%	Of hyperkalaemia events: <ul style="list-style-type: none"> <li>• 80.5% were mild</li> <li>• 13.0% were moderate</li> <li>• 3.6% sK<sup>+</sup> 6.0–6.5 mEq/L</li> <li>• 1.5% sK<sup>+</sup> 6.5–7.0 mEq/L</li> <li>• 1.5% sK<sup>+</sup> of ≥7.0 mEq/L</li> </ul>	NA	NA

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Retrospective cohort study of electronic medical record data from REACH-net in the USA <sup>4</sup>	Adults with $\geq 1$ mild hyperkalaemia event	2012–2018	Overall 35,369 with mild hyperkalaemia <b>HF 5132 (15%)</b>  HT 32% DM 32% Stage 3 CKD 22% Stage 4 CKD 5% Stage 5 CKD 5%  On RAASis 39%	<ul style="list-style-type: none"> <li>• 16.9% progressed from mild to moderate/severe               <ul style="list-style-type: none"> <li>○ <b>28.0% HF</b></li> <li>○ 20.3% HT</li> <li>○ 23.3% DM</li> <li>○ 12.0% no CKD</li> <li>○ 21.7% stage 3 CKD</li> <li>○ 32.2% stage 4 CKD</li> <li>○ 43.6% stage 5 CKD no dialysis</li> <li>○ 50.2% stage 5 CKD on dialysis</li> </ul> </li> <li>• 6.3% progressed from mild to severe               <ul style="list-style-type: none"> <li>○ <b>12.0% HF</b></li> <li>○ 7.7% HT</li> <li>○ 8.9% DM</li> <li>○ 3.9% no CKD</li> <li>○ 7.5% stage 3 CKD</li> <li>○ 12.4% stage 4 CKD</li> <li>○ 22.8% stage 5 CKD no dialysis</li> <li>○ 31.3% stage 5 CKD on dialysis</li> </ul> </li> </ul>	NA	HR (95% CI) for mild to moderate/severe hyperkalaemia progression ( $P < 0.0001$ ): <ul style="list-style-type: none"> <li>• Female 0.90 (0.85–0.95)</li> <li>• White 0.83 (0.78–0.88)</li> <li>• Stage 3 CKD 1.57 (1.46–1.68)</li> <li>• Stage 4 CKD 2.19 (1.97–2.43)</li> <li>• Stage 5 CKD 3.32 (3.03–3.64)</li> <li>• DM 1.2 (1.13–1.28)</li> <li>• sK<sup>+</sup> at index 1.12 (1.10–1.15)</li> </ul>
Retrospective cohort study of SCREAM project in Sweden <sup>5</sup>	Adults with eGFR $< 60$ mL/min/1.73 m <sup>2</sup> and $\geq 1$ plasma or sK <sup>+</sup> measurement in outpatient care	2006–2011	Overall 36,511 with K <sup>+</sup> measured and stage 3–5 CKD <b>HF 11,735 (32%)</b>  HT 65% DM 25% CVD 21% MI 20% PVD 11%  ACEis 32% ARBs 23% MRAs 13% BB 51%	<ul style="list-style-type: none"> <li>• Transient               <ul style="list-style-type: none"> <li>○ 15% stage 3a CKD</li> <li>○ 50% stage 5 CKD</li> </ul> </li> <li>• Chronic               <ul style="list-style-type: none"> <li>○ 4% stage 3a CKD</li> <li>○ 17% stage 5 CKD</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Transient               <ul style="list-style-type: none"> <li>○ 14% stage 3a CKD</li> <li>○ 18% stage 5 CKD</li> </ul> </li> <li>• Chronic               <ul style="list-style-type: none"> <li>○ 5% stage 3a CKD</li> <li>○ 3% stage 5 CKD</li> </ul> </li> </ul>	OR (95% CI) of chronic or transient hyperkalaemia vs. stage 3a CKD reference were similar: <ul style="list-style-type: none"> <li>• Age per 10 years older 0.84 (0.82–0.86) and 0.86 (0.83–0.90)</li> <li>• Female 0.72 (0.68–0.75) and 0.67 (0.61–0.74)</li> <li>• Stage 5 CKD 8.05 (7.20–9.00) and 8.74 (7.16–10.66)</li> <li>• Diabetes 1.44 (1.36–1.52) and 1.60 (1.44–1.77)</li> <li>• HF 1.33 (1.25–1.41) and 1.14 (1.01–1.28)</li> </ul>

			Thiazide-loop diuretics 49% SPS 1%			<ul style="list-style-type: none"> <li>• PVD 1.16 (1.09–1.25) and 1.21 (1.07–1.38)</li> <li>• ACEi/ARBs 1.55 (1.48–1.63) and 1.66 (1.50–1.84)</li> <li>• MRAs 1.76 (1.66–1.87) and 1.26 (1.10–1.45)</li> <li>• SPS 8.41 (7.12–9.93) and 12.66 (10.28–15.6)</li> </ul>
<b>Patients requiring an ED visit</b>						
Retrospective study of Intermountain Healthcare database in the USA <sup>6</sup>	Adults with ≥2 separate, non-urgent care or ED visits	2003–2018	Overall 1,208,815 With hyperkalaemia 161,849 <ul style="list-style-type: none"> <li>• <b>HF 32,370 (20%)</b></li> <li>• HT 63%</li> <li>• Hyperlipidaemia 55%</li> <li>• Diabetes 33%</li> <li>• Smoking 26%</li> <li>• ASCVD 21%</li> <li>• Renal insufficiency 16%</li> <li>• AF 14%</li> <li>• ACEis 39%</li> <li>• ARBs 16</li> <li>• Aldosterone inhibitors 6%</li> <li>• BBs 32%</li> <li>• Diuretics 42%</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Prevalence*</b> 13%</li> <li>• Average annual incidence 0.81%</li> </ul>	NA	<p>Patients with vs. without hyperkalaemia were:</p> <ul style="list-style-type: none"> <li>• Older (60 vs. 43 years)</li> <li>• Male (51% vs. 41%)</li> <li>• Higher CCI (3.5 vs. 1.7)</li> </ul> <p>Patients with vs. without hyperkalaemia had:</p> <ul style="list-style-type: none"> <li>• HT (63 vs. 20%)</li> <li>• Hyperlipidaemia (55% vs. 17%)</li> <li>• Diabetes (33% vs. 7%)</li> <li>• Smoking (26% vs. 13%)</li> <li>• ASCVD (21% vs. 4%)</li> <li>• HF (20% vs. 2%)</li> <li>• Renal insufficiency (16.3% vs. 0.7%)</li> <li>• AF (14% vs. 2%)</li> </ul> <p>Patients with vs. without hyperkalaemia received:</p> <ul style="list-style-type: none"> <li>• ACEis (39% vs. 8%)</li> <li>• ARBs (16% vs. 3%)</li> <li>• Aldosterone inhibitors (6% vs. 0.6%)</li> <li>• BBs (32% vs. 6%)</li> <li>• Diuretics (42% vs. 9%)</li> </ul>
Retrospective study in Spain <sup>7</sup>	Cases of severe hyperkalaemia in an ED	2016–2017	Overall 277,280 In patients with severe hyperkalaemia (n=160): <ul style="list-style-type: none"> <li>• <b>Congestive HF 35%</b></li> </ul>	<ul style="list-style-type: none"> <li>• 1444 moderate/severe episodes</li> <li>• <b>Prevalence* severe:</b> 0.06% of patients (172 severe)</li> </ul>	NA	NA

- CKD 29%
  - DM 57%
  - HT 57%
  - CHD 36%
  - CVD 13%
  - PVD 18%
- episodes in 160 patients with mean sK<sup>+</sup> 6.6 mEq/L
- 47.1% had sK<sup>+</sup> >5.5 mEq/L at discharge
- 786 sK<sup>+</sup> measurements over mean follow-up 14.5 months
    - 39.5% recurrence moderate/severe
    - 22.8% within first month of discharge
    - 16% one recurrence
    - 13.6% two recurrences
    - 9.9% three recurrences
- Loop diuretics 50%
  - RAASis 43%
  - BBs 37%
  - MRAs 28%

Study	Population studied	Years	Overall n number and population breakdown	Incidence		
				Hyperkalaemia	Hypokalaemia	Risk factors for hyperkalaemia
Retrospective cohort study of SCREAM project in Sweden <sup>8</sup>	Adults with ≥1 ambulatory serum creatinine measurement in inpatient or outpatient care within the preceding year	2006–2011	Overall 364,955 with K <sup>+</sup> measured <b>HF 29,684 (8%)</b>  HT 54% CVD 19% DM 16%  On RAASis 23%	<ul style="list-style-type: none"> <li>• <b>Incidence</b> 7% overall over 3 years                             <ul style="list-style-type: none"> <li>○ 64.3% transient (once)</li> <li>○ 35.7% recurrent (&gt;once)</li> <li>○ <b>Crude IR</b> 49.9 (95% CI 49.5–50.3) per 1000 person-years</li> </ul> </li> <li>• <b>Incidence</b> 2.5% moderate/severe over 3 years                             <ul style="list-style-type: none"> <li>○ 72.0% transient (once)</li> <li>○ 28% recurrent (&gt;once)</li> <li>○ <b>Crude IR</b> 14.6 (95% CI 14.4–14.9) per 1000 person-years</li> </ul> </li> <li>• <b>Incidence 24.0% (range 4.33–43.3%) with HF and ≥1 sK<sup>+</sup> &gt;5.0 mEq/L within 3 years</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Incidence</b> 13.6% over 3 years</li> <li>• <b>Crude IR</b> 61.3 (60.9–61.7) per 1000 person-years</li> </ul>	OR (95% CI), <i>P</i> < 0.05 <ul style="list-style-type: none"> <li>• 18–44 years ref</li> <li>• 45–64 years 1.52 (1.42–1.63)</li> <li>• 65–74 years 1.82 (1.69–1.95)</li> <li>• ≥75 years 1.87 (1.74–2.01)</li> <li>• HF 1.14 (1.09–1.19)</li> <li>• DM 1.73 (1.67–1.79)</li> <li>• HT 1.05 (1.00–1.10)</li> <li>• PVD 1.22 (1.15–1.28)</li> <li>• Stage 1–2 CKD ref</li> <li>• Stage 3 CKD 2.14 (2.07–2.22)</li> <li>• Stage 4+ CKD 5.60 (5.24–5.98)</li> <li>• ACEi 1.51 (1.46–1.57)</li> <li>• ARBs 1.21 (1.17–1.26)</li> <li>• MRAs 1.66 (1.41–1.95)</li> <li>• BBs 1.06 (1.03–1.10)</li> <li>• Loop/thiazide diuretics 0.94 (0.90–0.97)</li> <li>• Other BP medication 0.88 (0.85–0.91)</li> <li>• 1–2 sK<sup>+</sup>/year ref</li> <li>• 3–4 sK<sup>+</sup>/year 4.17 (3.99–4.36)</li> </ul>

Retrospective cohort study of Clinical Practice Research Datalink and linked Hospital Episode Statistics databases in the UK <sup>9</sup>	≥1 of the following conditions: <b>HF</b> , resistant HT, diabetes, stage 3+ CKD, dialysis and/or RAASis	2003–2018	Overall 931,460 <b>HF 84,210 (9%)</b>  Resistant HT 34% Diabetes 31% Stage 3+ CKD 31% Dialysis 0.5%  RAASis use 81% RAASis and in no other group 28%	<ul style="list-style-type: none"> <li>• Crude rate (95% CI) per 1000 patient-years in patients overall               <ul style="list-style-type: none"> <li>○ Any 223.5 (223.1–224.0)</li> <li>○ Moderate/severe 48.1 (47.9–48.3)</li> <li>○ Severe 7.7 (7.6–7.8)</li> </ul> </li> <li>• <b>Crude rate (95% CI) per 1000 patient-years in HF</b> <ul style="list-style-type: none"> <li>○ Any 490.6 (487.8–493.3): highest rate of cohorts studied</li> <li>○ Moderate/severe 125.6 (124.2–127.0)</li> <li>○ Severe 23.4 (22.8–24.0)</li> </ul> </li> <li>• Crude rate (95% CI) per 1000 patient-years in RAASi users               <ul style="list-style-type: none"> <li>○ Overall 211.04 (210.54–211.55): lowest rate of cohorts studied</li> </ul> </li> </ul>	NA	<ul style="list-style-type: none"> <li>• &gt;4 sK<sup>+</sup>/year 17.26 (16.58–17.97)</li> </ul> <p>Reduced kidney function (lower eGFR, higher serum creatinine) and history of severe renal disease were associated with high sK<sup>+</sup> variability regardless of mean sK<sup>+</sup></p>
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\*Prevalence not stated in the paper, but reference was made to all patients with hyperkalaemia out of those tested and new cases were not specified.

Mild, moderate, and severe hyperkalaemia defined as sK<sup>+</sup> >5.0 to ≤5.5 mEq/L, >5.5 to ≤6.0 mEq/L, and >6.0 mEq/L, respectively. Hypokalaemia defined as sK<sup>+</sup> <3.5 mEq/L.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, aldosterone receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BB, beta-blocker; BP, blood pressure; CCI, Charlson Comorbidity Index; CHD, coronary heart disease; CHF, chronic heart failure; CI, confidence interval; CKD, chronic kidney disease; CVD, cerebrovascular disease; DM, diabetes mellitus; ED, emergency department; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; HT, hypertension; IR, incidence rate; K<sup>+</sup>, potassium; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; NA, not available; OR, odds ratio; PVD, peripheral vascular disease; RAASi, renin–angiotensin–aldosterone system inhibitor; RR, rate ratio; SCREAM, Stockholm CREAinine Measurements; sK<sup>+</sup>, serum potassium; SPS, sodium polystyrene sulphonate.

## References

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