

# Hyperkalaemia in patients receiving co-trimoxazole for complex infections

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## Background

- Co-trimoxazole (SXT) is classed as an ‘access antibiotic’ by WHO<sup>(1)</sup>
- Its use is promoted by the Scottish Antimicrobial Prescribing Group (SAPG) as part of a strategy to reduce use of co-amoxiclav and quinolones, mitigate antimicrobial resistance, and reduce the risk of C. difficile infection<sup>(2)</sup>.
- Routine use of SXT for a range of conditions was introduced in NHSD&G in 2020
- SXT is also known to cause raised serum creatinine and hyperkalaemia<sup>(3)</sup>.
- We investigated the incidence of hyperkalaemia in patients receiving outpatient SXT for complex infections in this period, aiming to identify risk factors

## Methodology

- Retrospective cohort study with study population of patients treated with SXT for complicated infections between 2020 and 2024
- Data was collected on age, sex, diagnosis, medications, co-morbidities, incidence of hyperkalaemia, and what, if any, treatment required
- Significant hyperkalaemia was defined as K > 5.5mmol/L ; renal impairment was defined as eGFR<60 prior to commencing SXT
- Logistic regression was used to identify risk factors associated with hyperkalaemia

## Results

- 55 patients were identified during the study period
- 13 (23.6%) patients developed significant hyperkalaemia while taking SXT
- 15 (27.2%) required intervention; 12 (21.8%) had to stop SXT
- 6 (10.9%) were admitted to DGRI for emergency treatment of hyperkalaemia
- There was moderate evidence of association between renal impairment and increased likelihood of developing hyperkalaemia.
- Co-prescribed medicines had high collinearity with renal impairment so was removed.

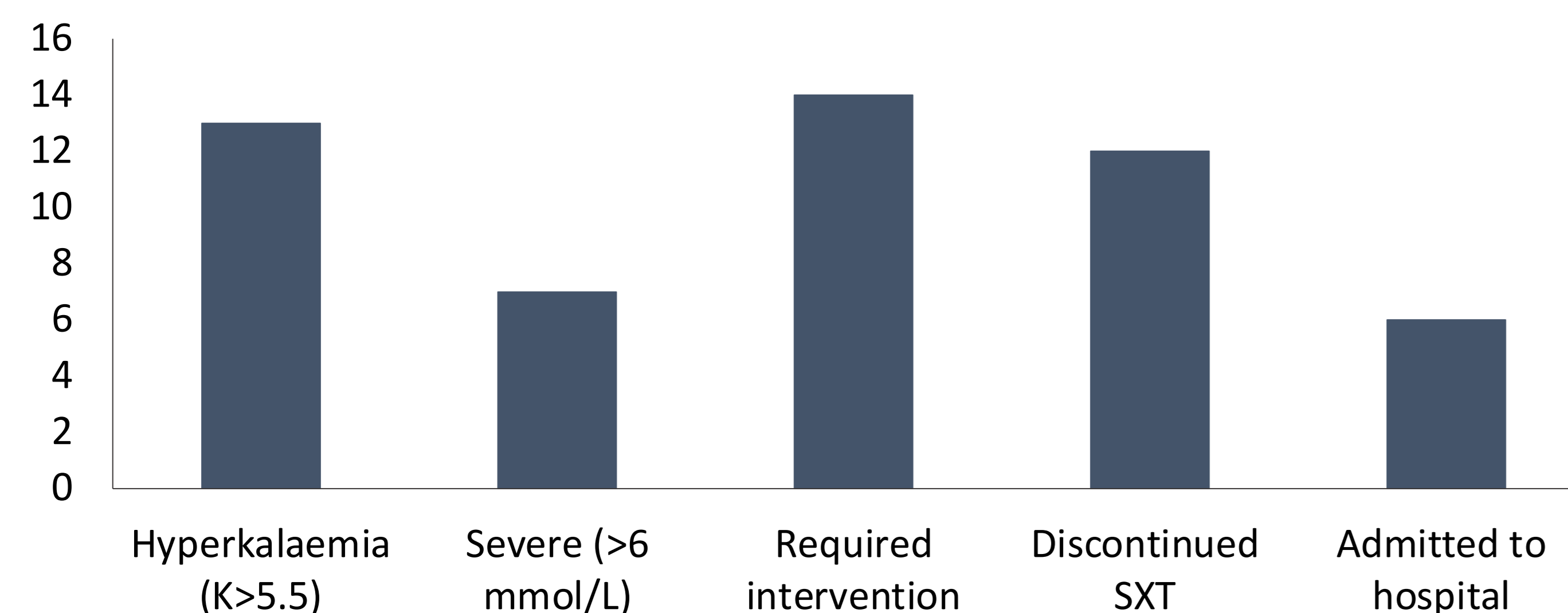


Fig 3: Complications of co-trimoxazole during study period (N=55)

## Key points

- Co-trimoxazole use is promoted by WHO and SAPG as part of AMR strategy
- We identified a high risk of hyperkalaemia in patients treated with SXT for complex infections
- There was moderate evidence that renal impairment was associated with an increased risk of hyperkalaemia
- Prescribers should exercise caution and consider an alternative antibiotic in patients with renal impairment

Patients	N=55
<b>eGFR prior to treatment</b>	
>60	45
<60	10
<b>Co-prescribed medicines</b>	
Yes	24
No	31
<b>Diabetes mellitus</b>	
Yes	27
No	28
<b>Sex</b>	
Male	38
Female	17
<b>Age (mean + SD)</b>	
	63.8 (49.3 – 78.3)

Fig 1: Patient demographics

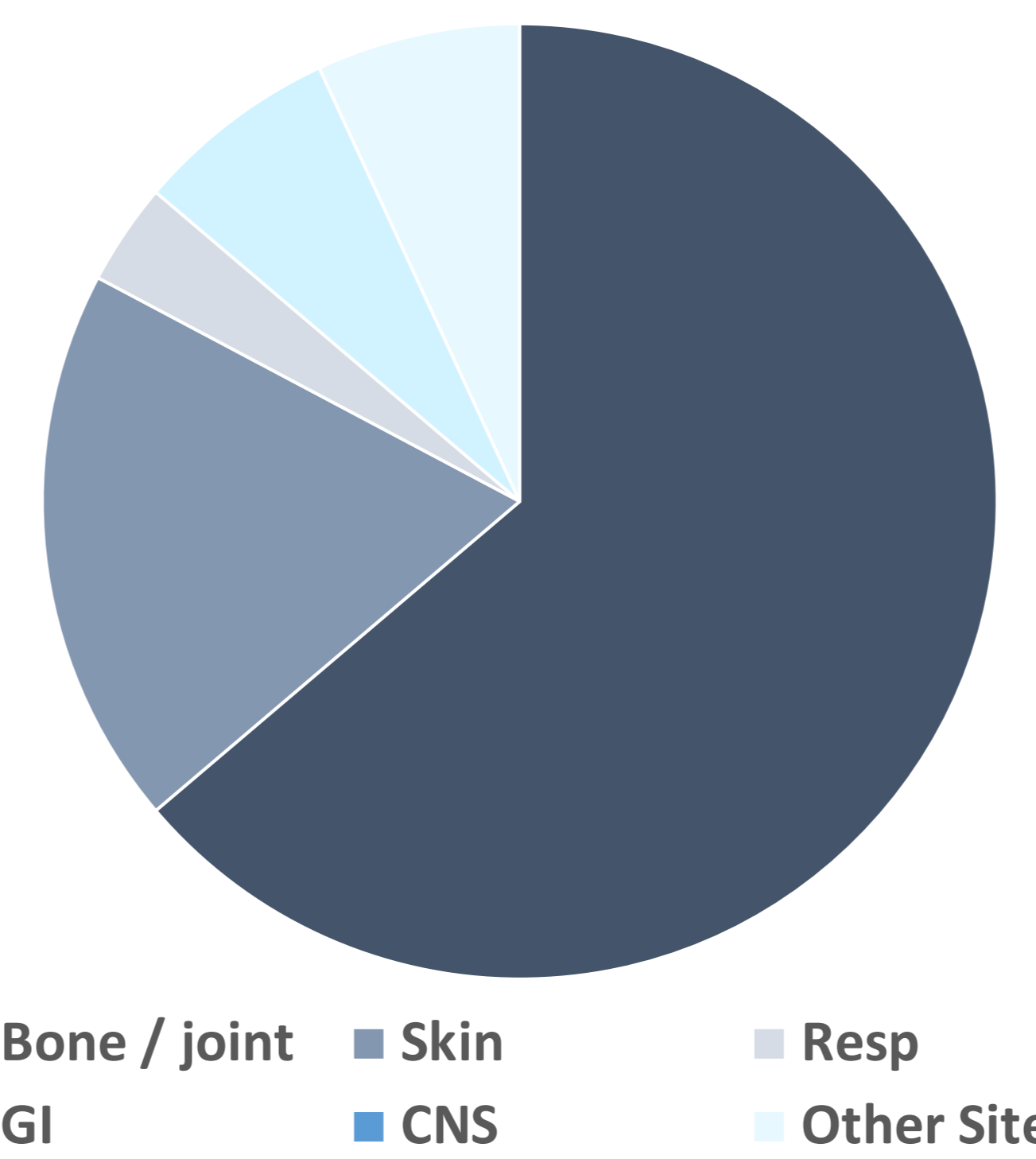


Fig 2: Site of underlying infection

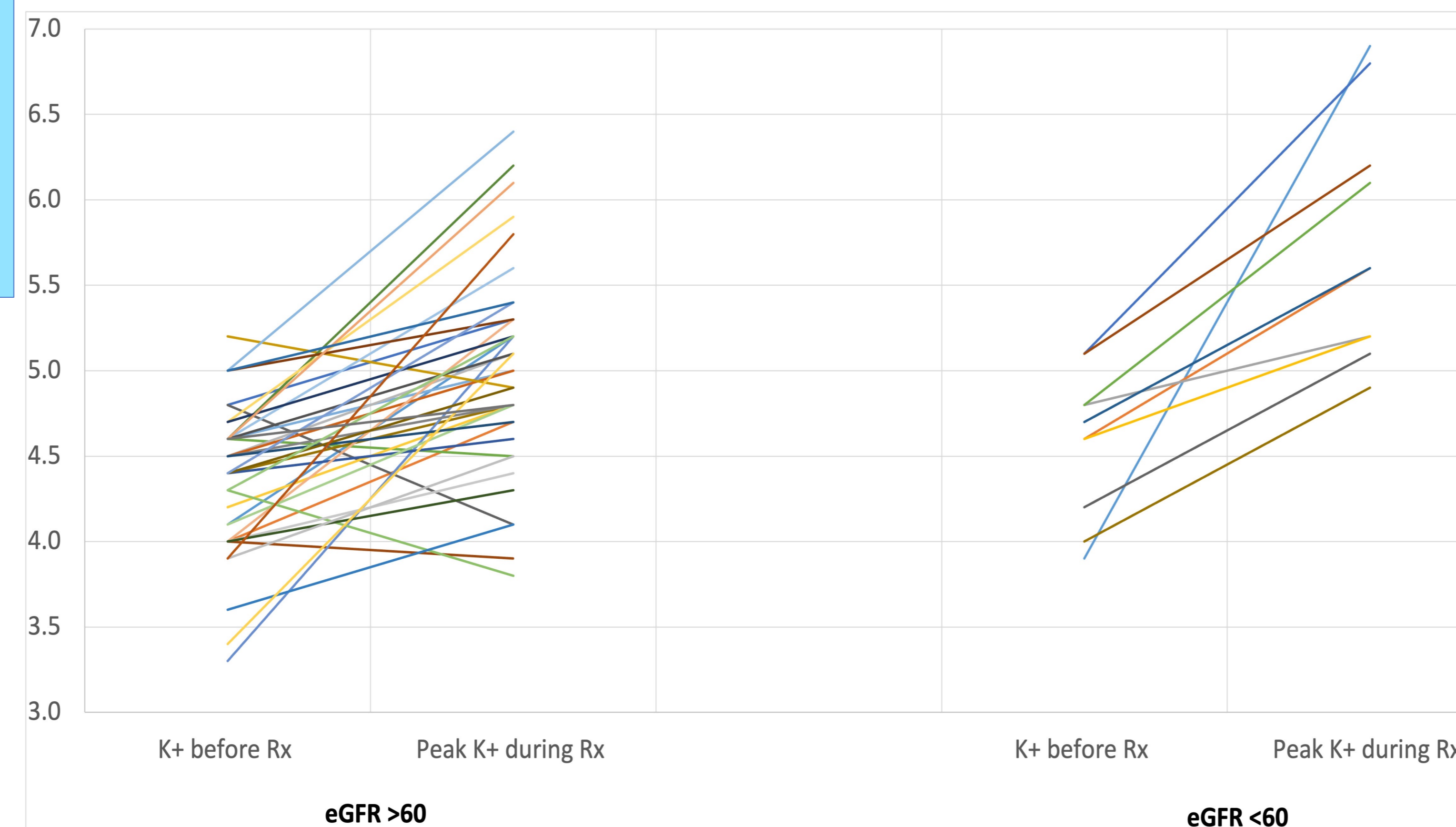


Fig 4: Serum potassium before and during SXT therapy, stratified by renal function

## Discussion

- Recent efforts to encourage use of SXT as part of AMR agenda are reflected in its increasing use for complex infections in NHSD&G
- A high proportion of patients developed hyperkalaemia, and a high proportion in turn required SXT discontinuation and/or hospitalisation for emergency treatment of hyperkalaemia
- There was moderate evidence that renal impairment was associated with a higher risk of developing hyperkalaemia in patients prescribed SXT.

## So what?

- Patients and clinicians prescribing SXT should be aware of the high risk of SXT-associated hyperkalaemia
- We suggest that clinicians should exercise caution prescribing co-trimoxazole in those with renal impairment and consider an alternative antibiotic.
- Future research could investigate the safety and efficacy of reduced dose regimens of co-trimoxazole in this population, or co-prescription of potassium binders
- A larger sample size would allow further characterization of risk factors associated with hyperkalaemia

Variable	Risk of hyperkalaemia		
	Odds ratio	95% CI	P value
Sex (female)	1.13	0.21 – 5.44	0.878
Age	4.02	0.87 – 24.01	0.089
Renal impairment	5.52	0.97 – 36.17	0.057
Diabetes	3.39	0.71 – 18.93	0.134

Fig 5: Risk factors for hyperkalaemia with odds ratios: results of logistic regression

## References

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2. Scottish Antimicrobial Prescribing Group. Guidance on the use of co-trimoxazole in secondary care in NHS Scotland [Internet]. 2023 [cited 2024 Mar 18]. Available from: <https://www.sapg.scot/media/7364/20230116-sapg-statement-in-support-of-co-trimoxazole.pdf>
3. Chan WY, Clark AB, Wilson AM, Loke YK, Investigators on behalf of the T. The effect of co-trimoxazole on serum potassium concentration: safety evaluation of a randomized controlled trial. Br J Clin Pharmacol. 2017;83(8):1808–14.