

Dose-dependent relationships observed for prescribing cascades: a cohort study

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Background

Prescribing cascades occur when new medications are prescribed to manage adverse drug reactions (ADRs) caused by an initial (index) medication. This phenomenon can lead to polypharmacy and increased healthcare costs [1]. Although dose reduction is frequently suggested as a strategy to prevent prescribing cascades, the impact of the index medication's dosage on the development of these cascades remains unclear [2].

Aim

This study aimed to investigate the dose-dependence of prescribing cascades across a range of index medications.

Methods

This study is a retrospective cohort study using Prescription Sequence Symmetry Analysis (PSSA). Dispensing data from over 600 pharmacies were analyzed to assess the relationship between various doses of index medications and 18 prescribing cascades, including ACE inhibitors, statins, proton pump inhibitors (PPIs), and diuretics.

Doses were classified according to the World Health Organization's defined daily dose (DDD):

- Low: <0.50 DDD
- Medium: ≥0.50 and ≤1.50 DDD
- High: >1.50 DDD

Data-analysis

- Adjusted sequence ratios (aSRs) were calculated (aSR > 1 indicates a prescribing cascade).
- Dose-dependence was confirmed when aSRs increased with higher doses and the 95% confidence intervals (CIs) between dose groups did not overlap.
- A positive control group was included to validate the method.

Results

Overall Findings:

- 18 prescribing cascades analyzed, see figure 1, 2 and 3
- 12 (67%) showed a dose-dependent relationship
- For an overview of mean age, and total patients included, see table 1.

Results Positive control group aSR [95% CI]:

- aSR low dose 1.53 [1.22-1.84]
- aSR medium dose 1.70 [1.65-1.74]
- aSR high dose 2.23 [2.14-2.31]

Table	Mean Age (SD)	Women N (%)	Mean Total Users
ACEI	67.5 (13.5)	7620 (51.0%)	14927
Statins	67.0 (12.7)	14102 (54.8%)	25748
Other Medications	66.2 (16.2)	2210 (35.5%)	6217

Table 1: Overview of the mean age, women, and total included patients per cascade category

References

1. McCarthy LM, Visentin JD, Rochon PA. Assessing the Scope and Appropriateness of Prescribing Cascades. *J Am Geriatr Soc.* 2019;67(5):1023-6.
2. Morris EJ, Hollmann J, Hofer AK, Bhagwandass H, Oueini R, Adkins LE, et al. Evaluating the use of prescription sequence symmetry analysis as a pharmacovigilance tool: A scoping review. *Res Social Adm Pharm.* 2022;18(7):3079-93.

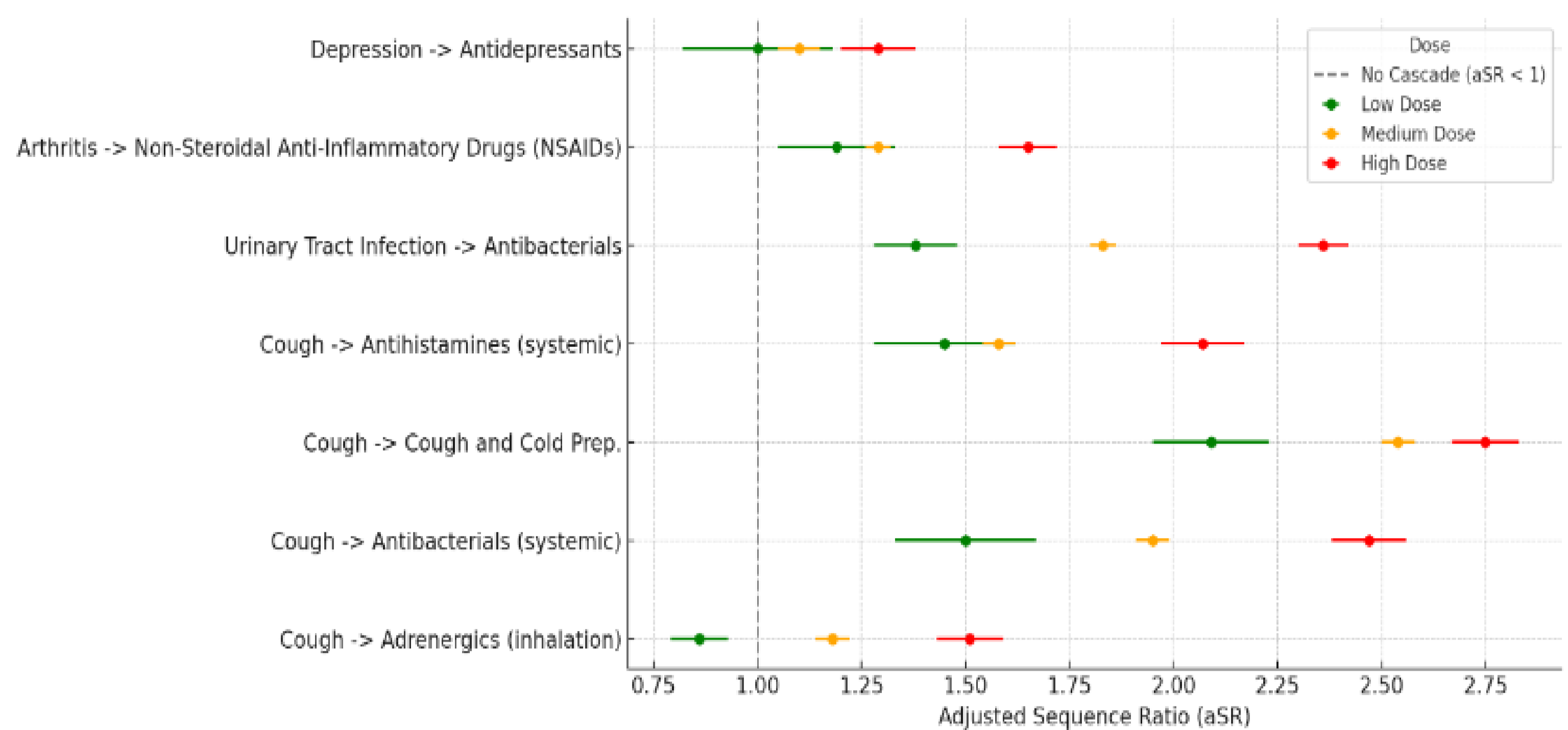


Figure 1: Adjusted sequence ratios (aSRs) and the 95% confidence interval for seven angiotensin-converting enzyme inhibitor related prescribing cascades by dose category.

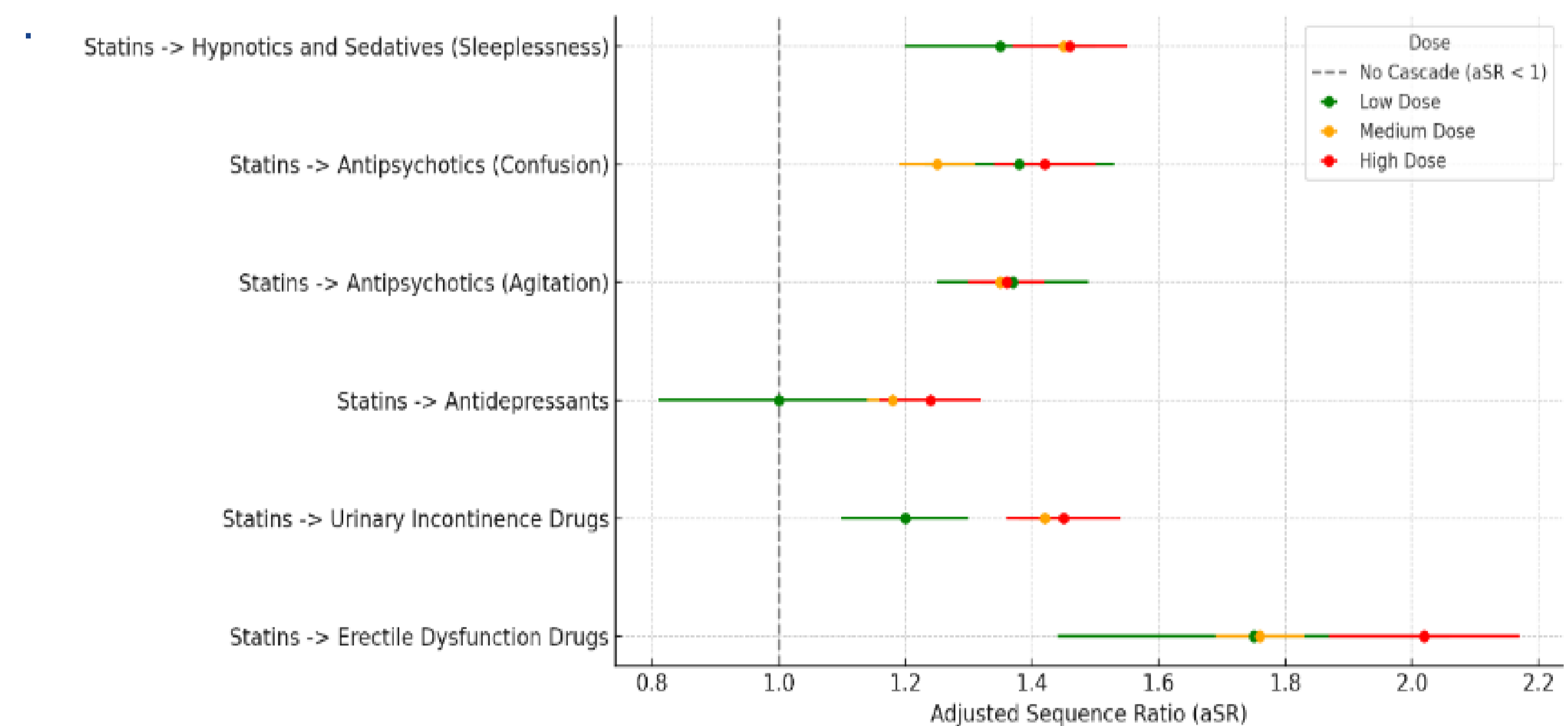


Figure 2: Adjusted sequence ratios (aSRs) and the 95% confidence interval for six statin-related prescribing cascades by dose category.

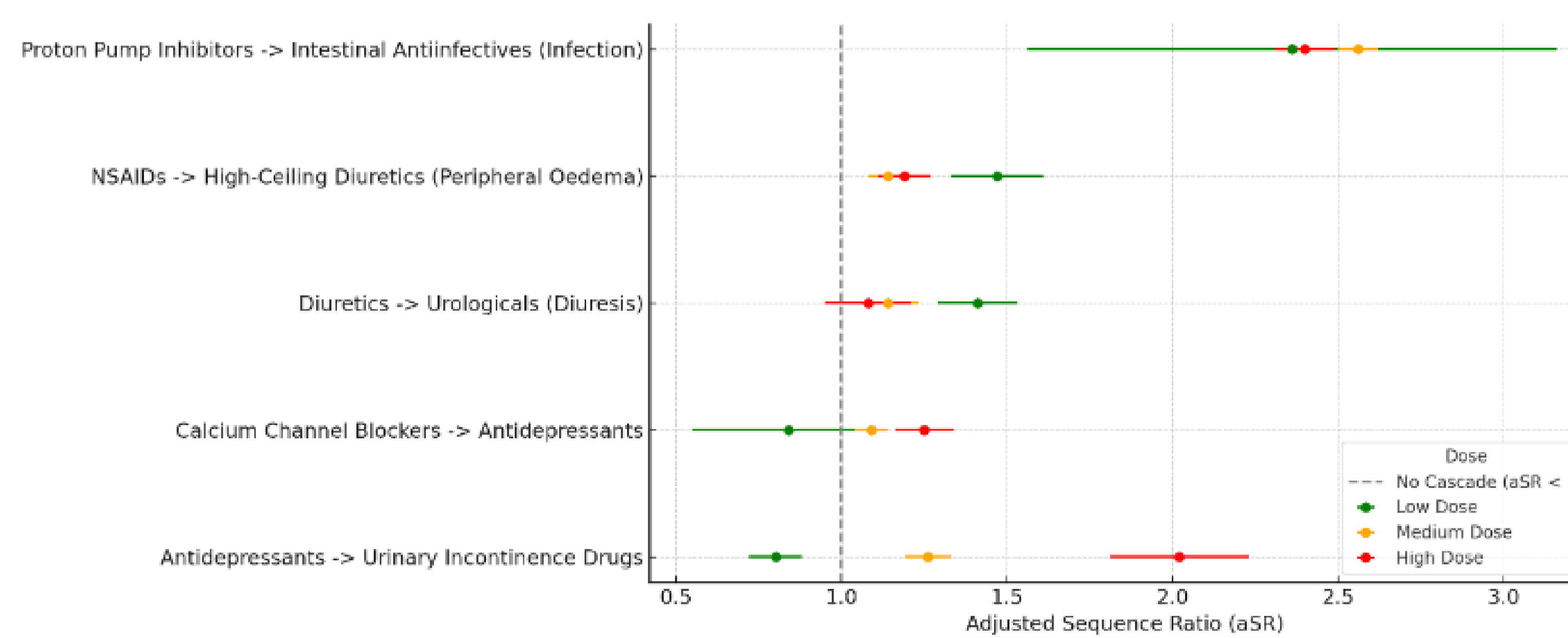


Figure 3: Adjusted sequence ratios (aSRs) and the 95% confidence interval for antidepressants, Dihydropyridine calcium channel blockers, diuretics, non-steroidal anti-inflammatory drugs and proton pump inhibitors prescribing cascades by dose category.

Conclusion

Dosage plays a crucial role in managing prescribing cascades, particularly for ACEi and potentially for statins. Hospital pharmacists should monitor ADRs at higher doses and consider dose reduction as a preventive measure. Further research is necessary to assess the effectiveness of dose adjustments in preventing ADRs and prescribing cascades.



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