

Sequence symmetry analysis finds different alerts based on prescriptions in Danish and Dutch data

Title: Identifying Adverse Drug Reaction: Using Sequence Symmetry Analysis Design on OMOP data from the IPCI database compared to Danish register data

Background: Sequence symmetry analysis is a tool for hypothesis-free screening for potential (un)known adverse drug reactions. We apply this method to incident use of ACE inhibitors and investigate all prescribed medications as outcomes in Danish national data (the National Patient Registry) and in Dutch data from general practitioners (the Integrated Primary Care Information (IPCI) Database)

Method:
This study uses the CohortSymmetry package to perform sequence symmetry analysis (SSA). Sequence ratios (SR) were calculated for all ATC 5th-level medications as outcomes. The top 100 outcomes from both dataset were compared, and those that were present in both and had a SR with a lower bound >1 in at least one database were evaluated.

Results:
42 outcomes codes were present in both analyses
40 outcomes had SRs with a lower bound of the 95% confidence interval above 1 in both analysis (see figure 2)
2 outcomes had a SR with a lower bound > 1 in the IPCI data but below 1 in the Danish analysis (see figure 3)
0 outcomes had SR with a lower bound > 1 in the Danish data but below 1 in the IPCI analysis
3 outcomes were present in top 10 in both analyses:
- C09BA02 (enalapril/hydrochlorothiazide)
- C08CA01 (amlodipine)
- C03DA01 (spironolacton)

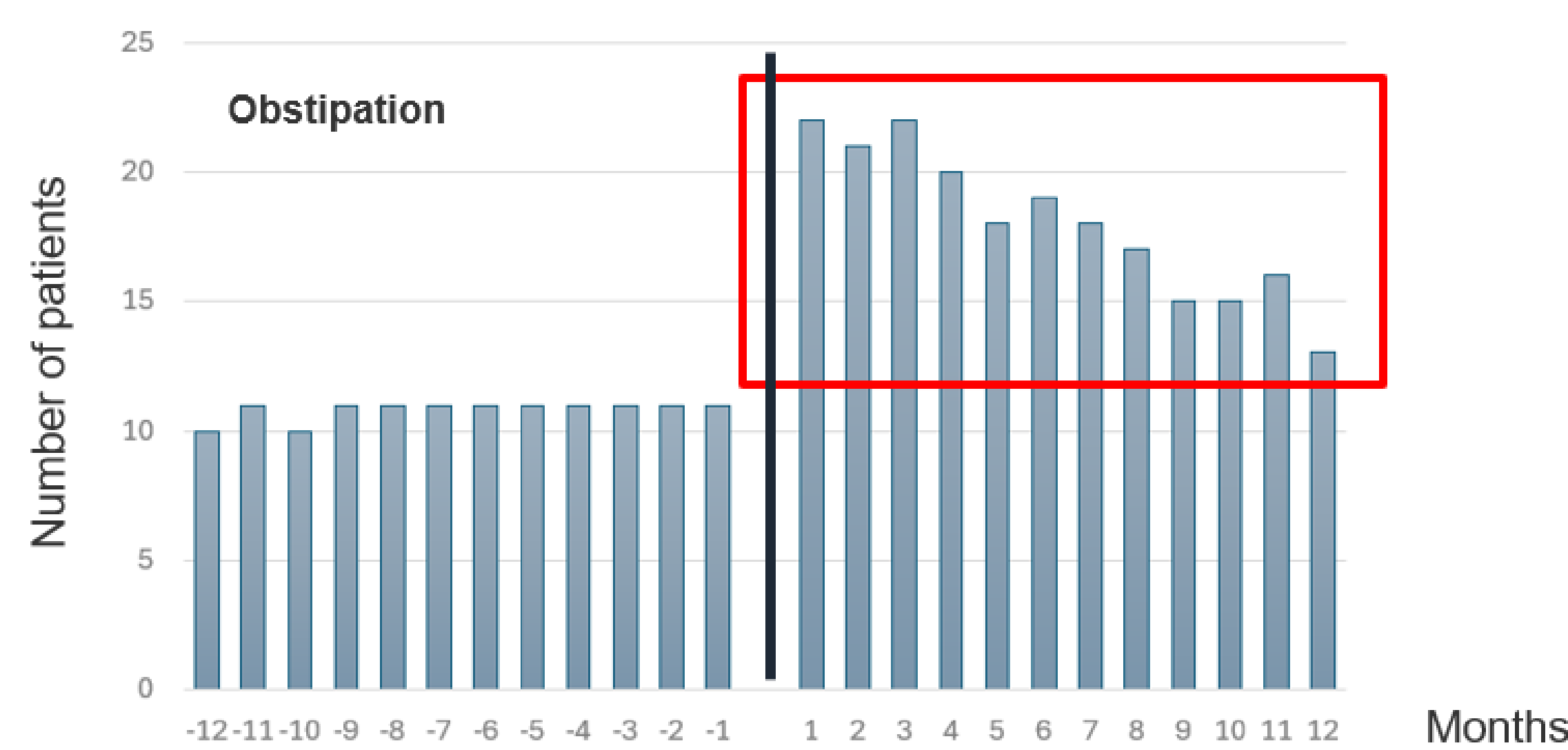


Figure 1: The SSA looks at event-timing for patients with an incident exposure (ACE inhibitors) and then investigates distribution of an outcome 1 year before and after exposure across the study population.

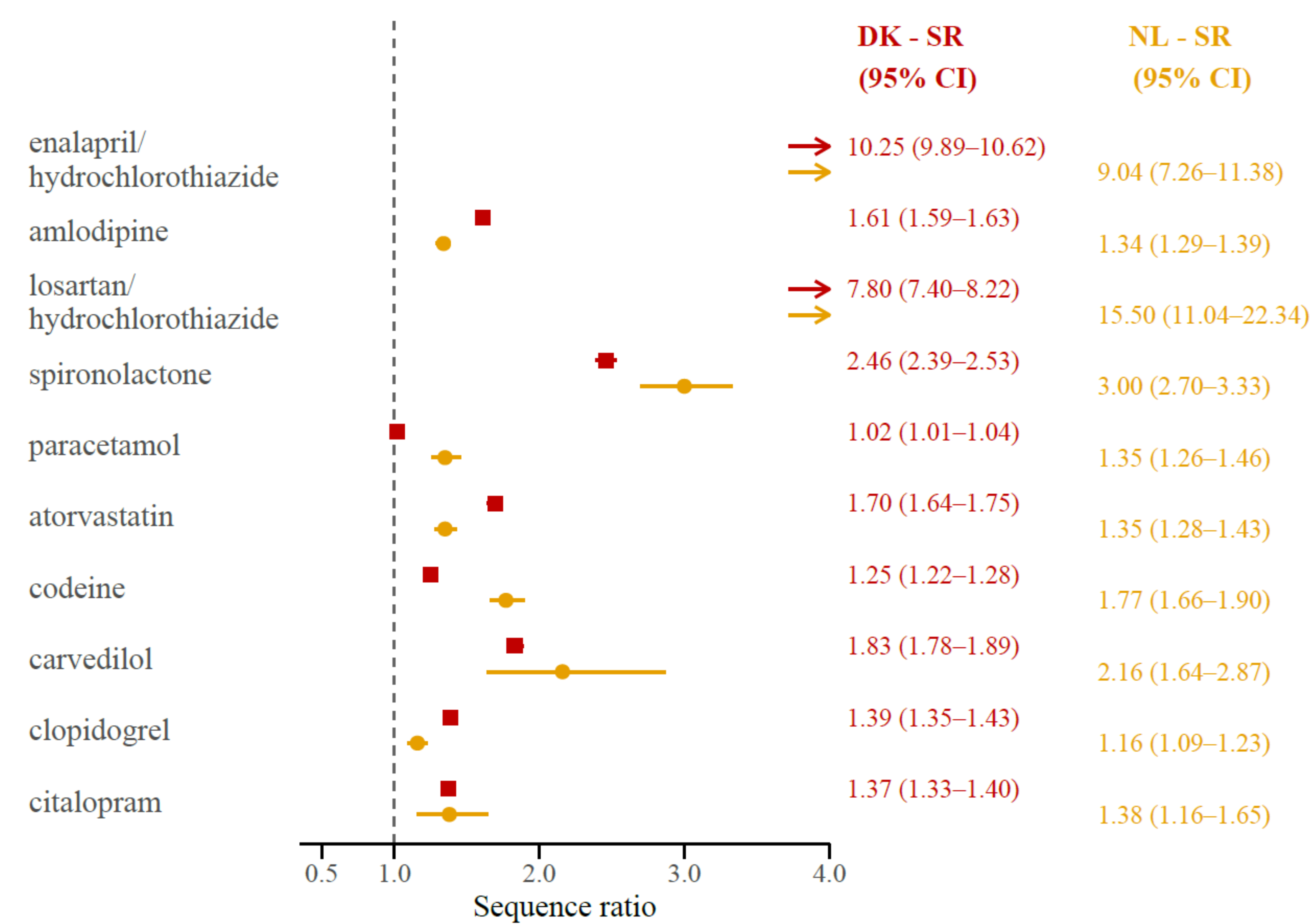


Figure 2: Top 10 of outcomes that were identified in both datasets with a lower bound above 1 in both datasets. DK: Denmark, NL: IPCI, SR: Sequence Ratio

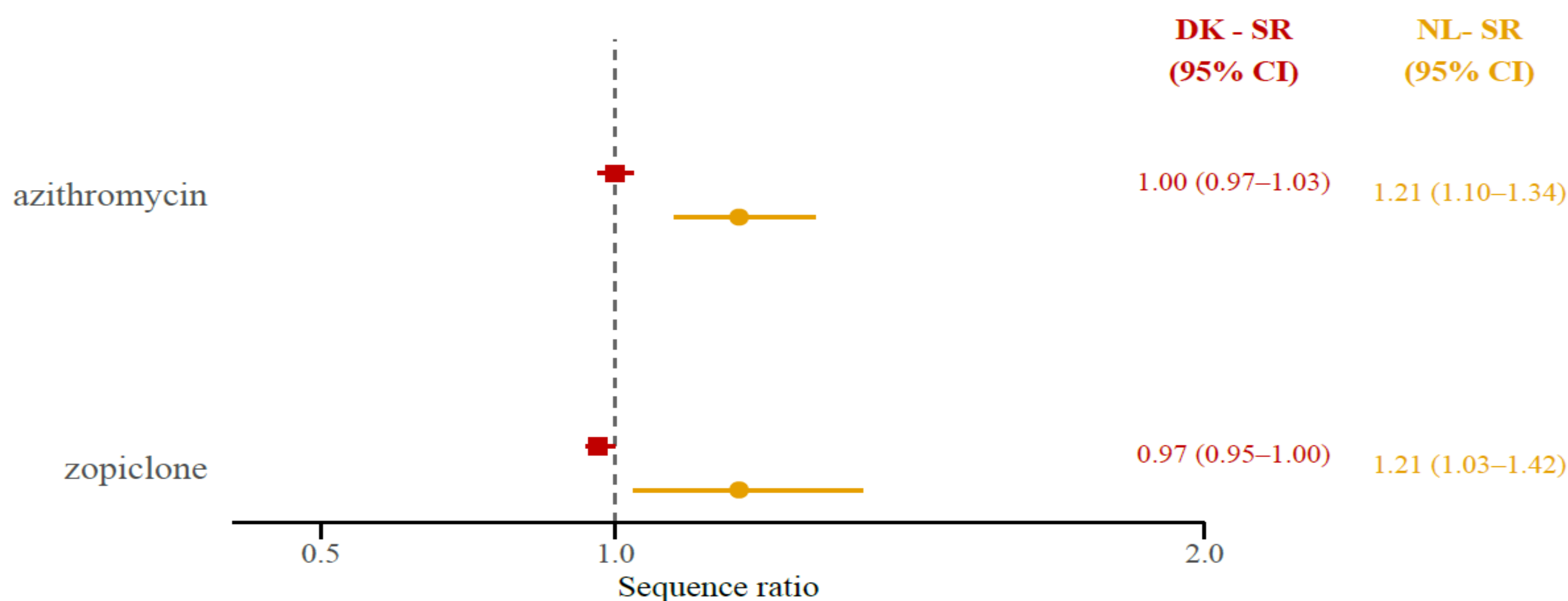


Figure 3: Sequence ratios for 2 outcomes that were significant for the SSA performed on IPCI data but not on Danish data

	Denmark	IPCI
Number of exposed	958 400	86 200
Mean age (years)	62.3	62.3
SD Age (years)	13.4	13.2
Female (%)	48	48

Table 1: Cohort sizes and basic demographics

Future work: The analysis applied will be extended to run on any outcome defined as any RxNorm ingredient level drug, or any SNOMED coded condition outcome in the OMOP CDM dataset. An active comparator SSA will be performed, and results will be compared with results from a similar SSA run on Danish register data,

