# Empirical assessment of case-based methods for the identification of drug-related health outcome of interest in the French nationwide healthcare database (SNDS)

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# Disclosure statement

- Based on Alcapone
- Funded by the French Ministry of Health (PREPS, 14-0635)
- Designed, conducted and analyzed independently by the Bordeaux PharmacoEpi platform of Bordeaux University
- Supervised by an independent scientific committee
- Registered in EMA EUPAS n°13031

# Background

- Risk identification performances
  - Depends on the method
  - Depends on the method settings
  - Depends on the environment = the **database**

- Tools need to be tested and assessed *in real life* to ensure the generation of meaningful point estimates

# SNDS

- French Nationwide Healthcare System Database
  - 66.6 million persons (99% of the French population)
  - Individual pseudonymised information on
    - Drug dispensings
    - Hospital discharge diagnoses
    - Procedures
    - Death
    - Costs
    - *etc.*
- Database extraction accessible for public health purposes after approval by
  - Data protection agency (CNIL)
  - National Health data institute (INDS)

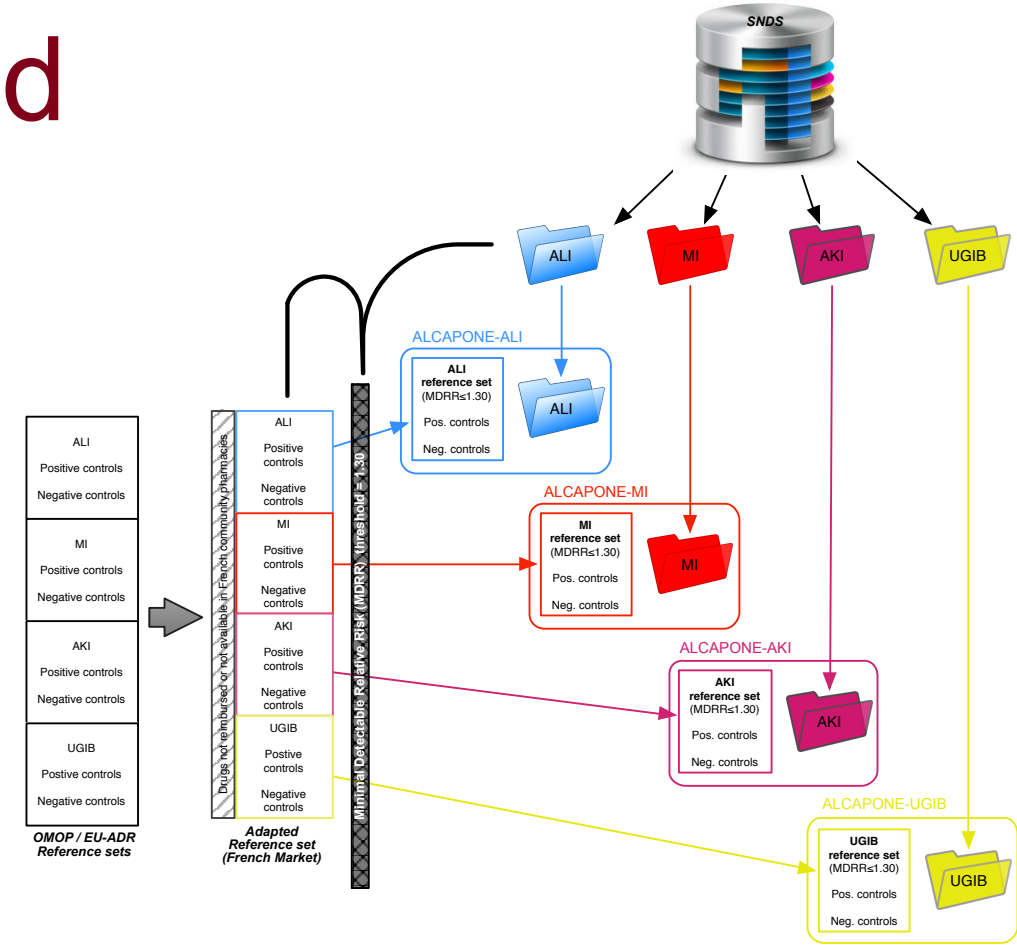
# Objectives

- To evaluate and compare the performances in the SNDS of
  - SCCS (Self-controlled case series)
  - CC (Case-control)
  - CP (Case-population)

- For the identification of
  - ALI (Acute liver injury)
  - AKI (Acute kidney injury)
  - MI (Myocardial infarction)
  - UGIB (Upper gastrointestinal bleeding)

# Method

- 273 drug-outcome pairs
  - Adapted from OMOP and EU-ADR reference sets
    - 4 health outcomes of interest
    - 139 positive and negative controls
  - Restricted to the pairs with MDRR<1.30
- SNDS data extractions based on cases
  - ALI
  - AKI
  - MI
  - UGIB

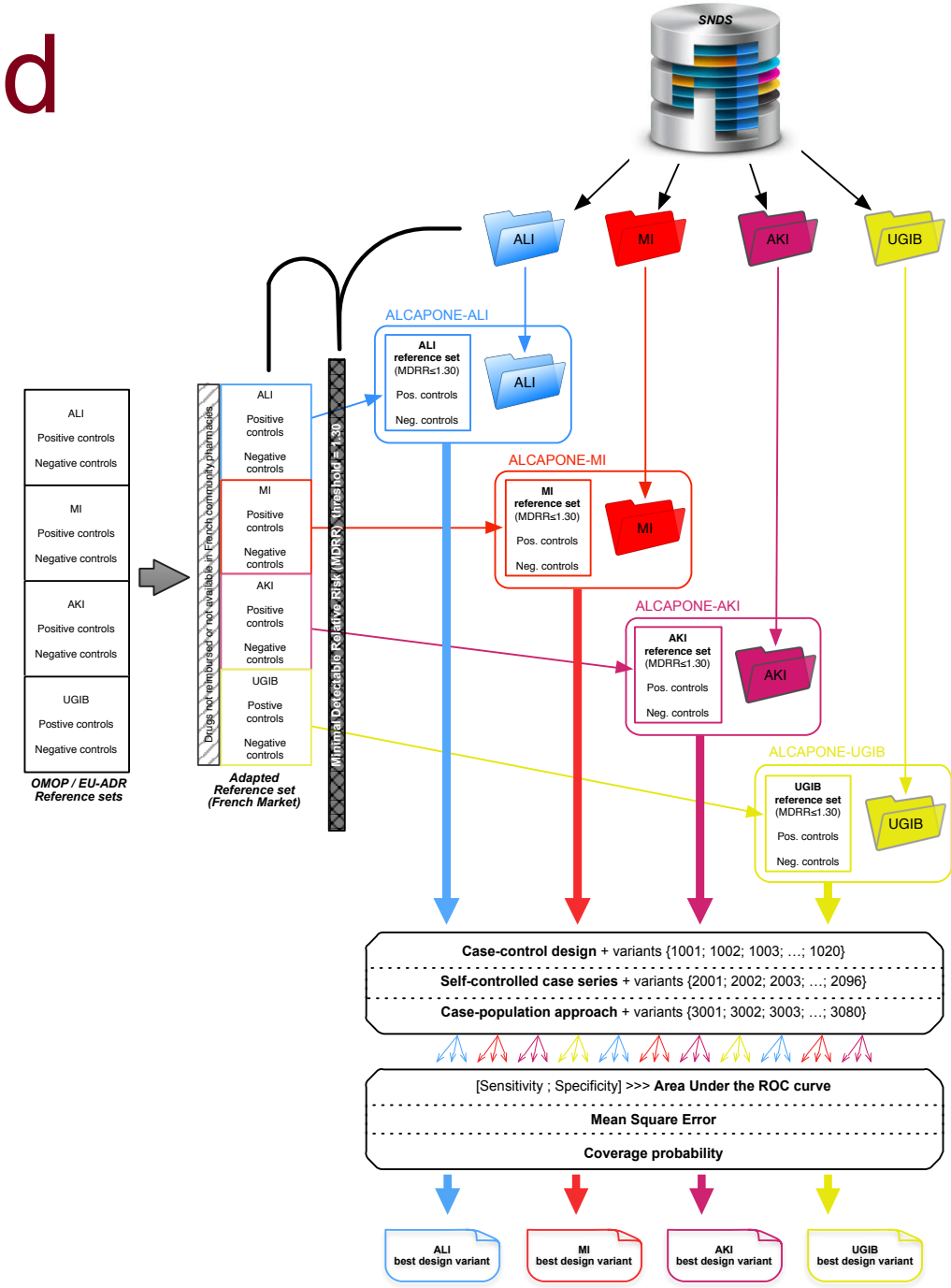


# Method

- Detection of drug-outcome pairs *via*
  - 96 SCCS variants
  - 20 CC variants
  - 80 CP variants

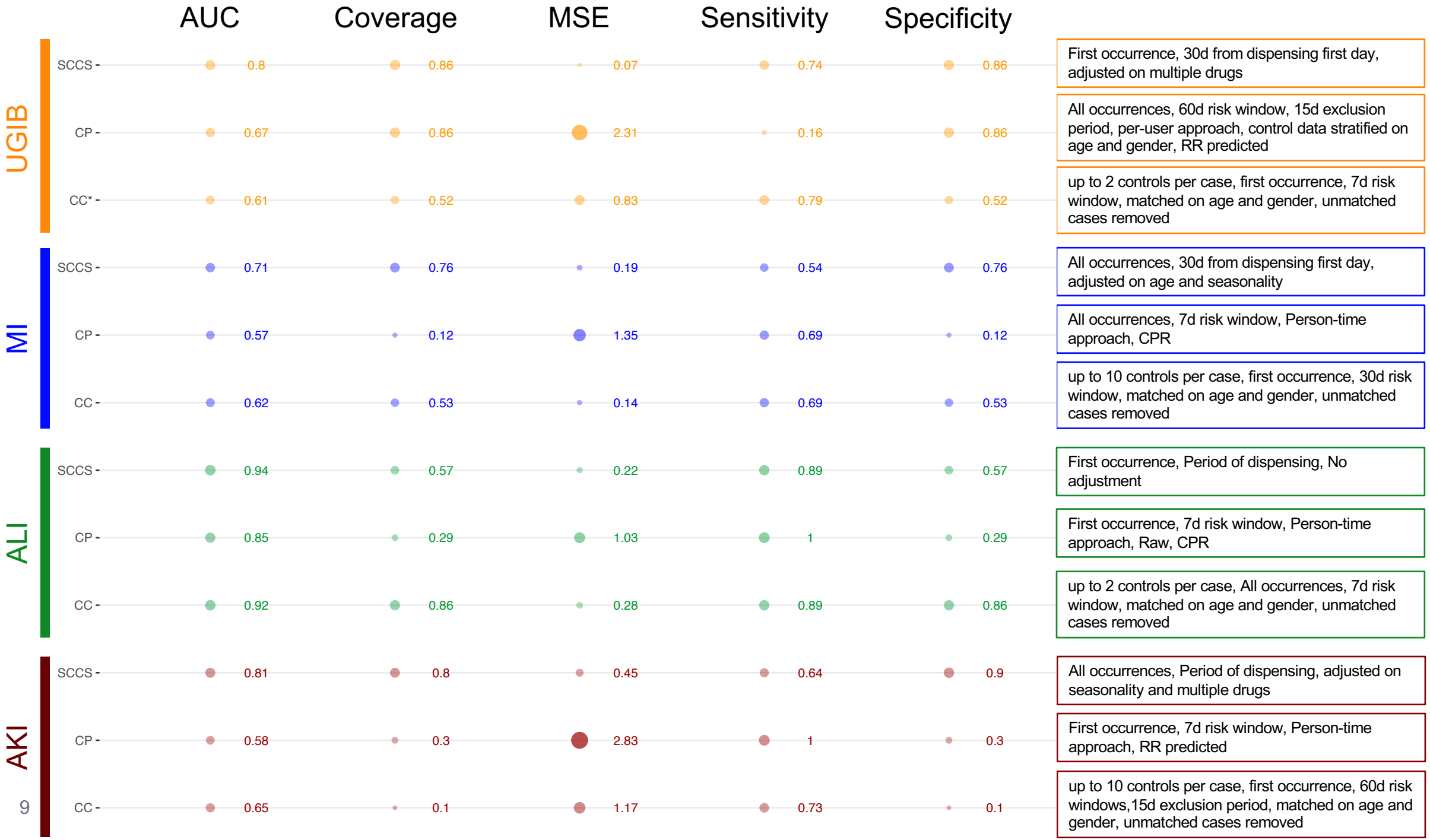
  ➔ Generation of one point estimate per pair for each variant (26 068)

- Performance assessment of the variants
  - Discriminant ability: AUC
  - Accuracy (negative controls):
    MSE, coverage probability



# Results

| Raw data extractions (SNDS) | | HOI | Reference set | | | | | |
|---|---|---|---|---|---|---|---|---|
| Patients | Outcomes | | Drug controls (+/-) | French market Reference set | Number of detectable controls (MDRR<1.30) in the data extraction | | | |
| | | | | | raw sample | 1/3rd sample | 1/10th sample | 1/20th sample |
| 5 152 | 5 225 | ALI | + | 58 | 18 | | | |
| | | | - | 23 | 7 | | | |
| 304 369 | 354 109 | MI | + | 28 | 25 | | | 26 |
| | | | - | 42 | 36 | | | 20 |
| 12 317 | 12 633 | AKI | + | 22 | 17 | 11 | | |
| | | | - | 36 | 13 | 10 | | |
| 139 172 | 156 057 | UGIB | + | 22 | 22 | | 19 | |
| | | | - | 42 | 36 | | 22 | |


AUC
Coverage
MSE
Sensitivity
Specificity
UGIB
SCCS
0.8
0.86
0.07
0.74
0.86
First occurrence, 30d from dispensing first day, adjusted on multiple drugs
CP
0.67
0.86
2.31
0.16
0.86
All occurrences, 60d risk window, 15d exclusion period, per-user approach, control data stratified on age and gender, RR predicted
CC*
0.61
0.52
0.83
0.79
0.52
up to 2 controls per case, first occurrence, 7d risk window, matched on age and gender, unmatched cases removed
MI
SCCS
0.71
0.76
0.19
0.54
0.76
All occurrences, 30d from dispensing first day, adjusted on age and seasonality
CP
0.57
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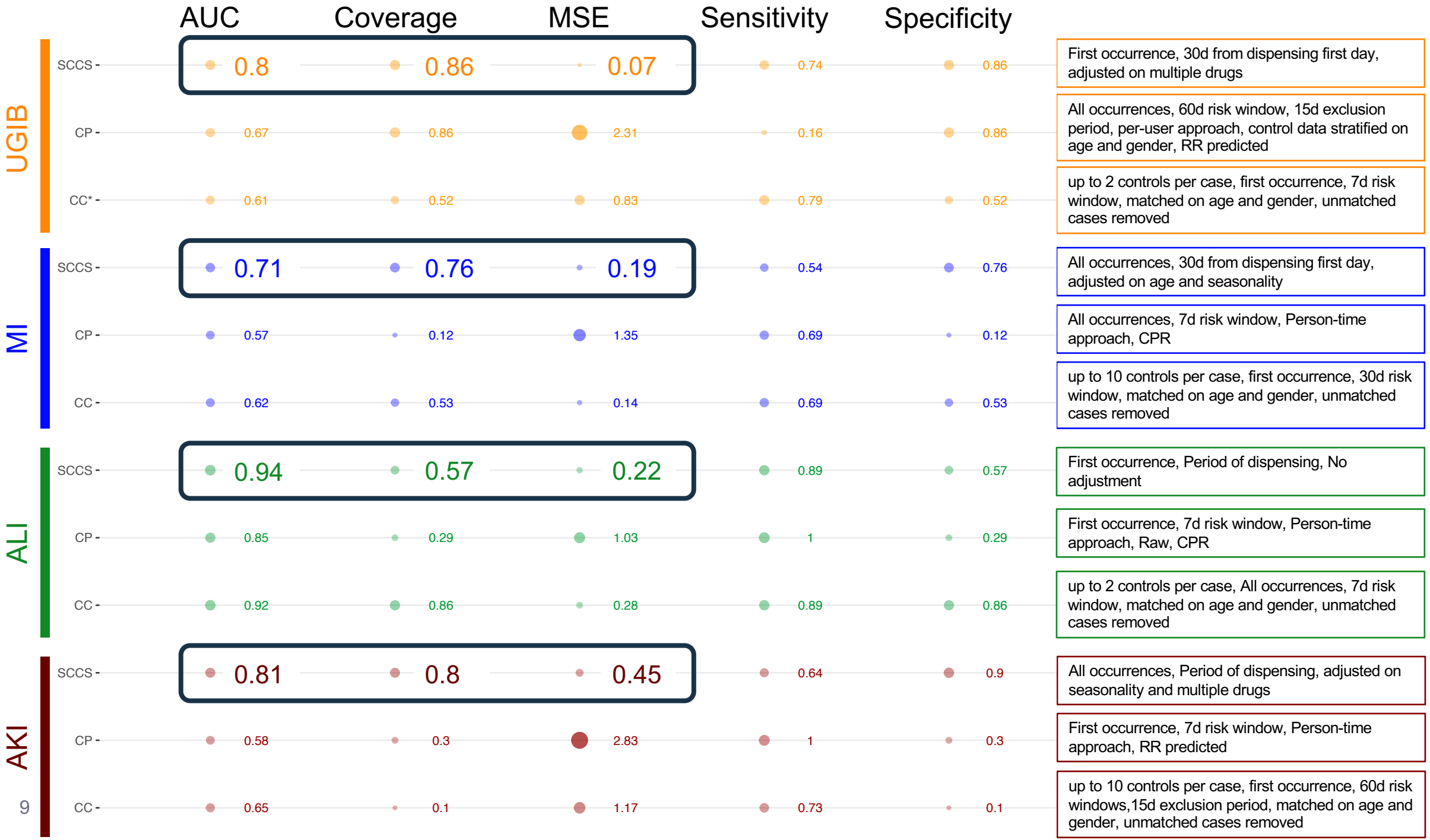
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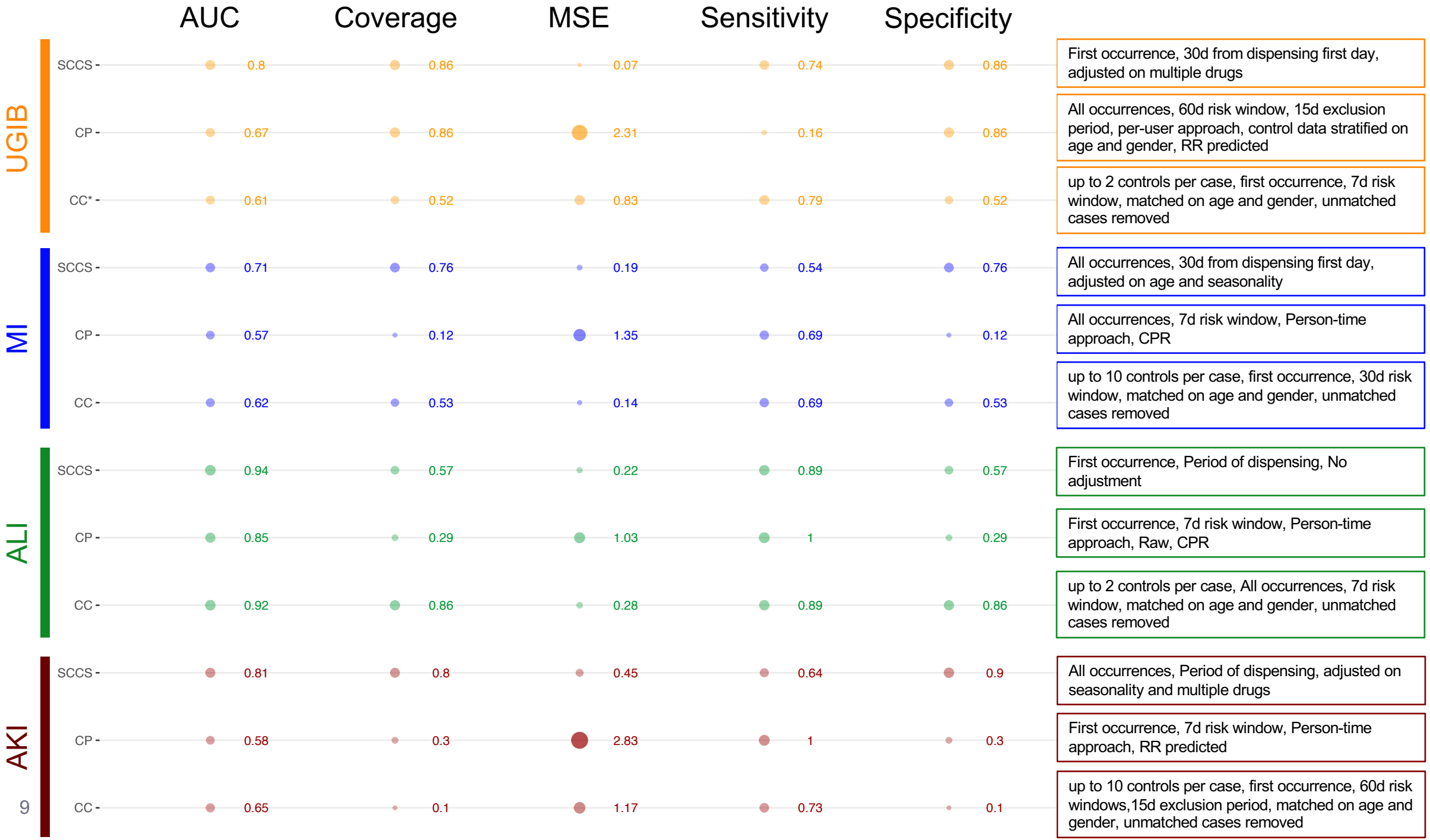
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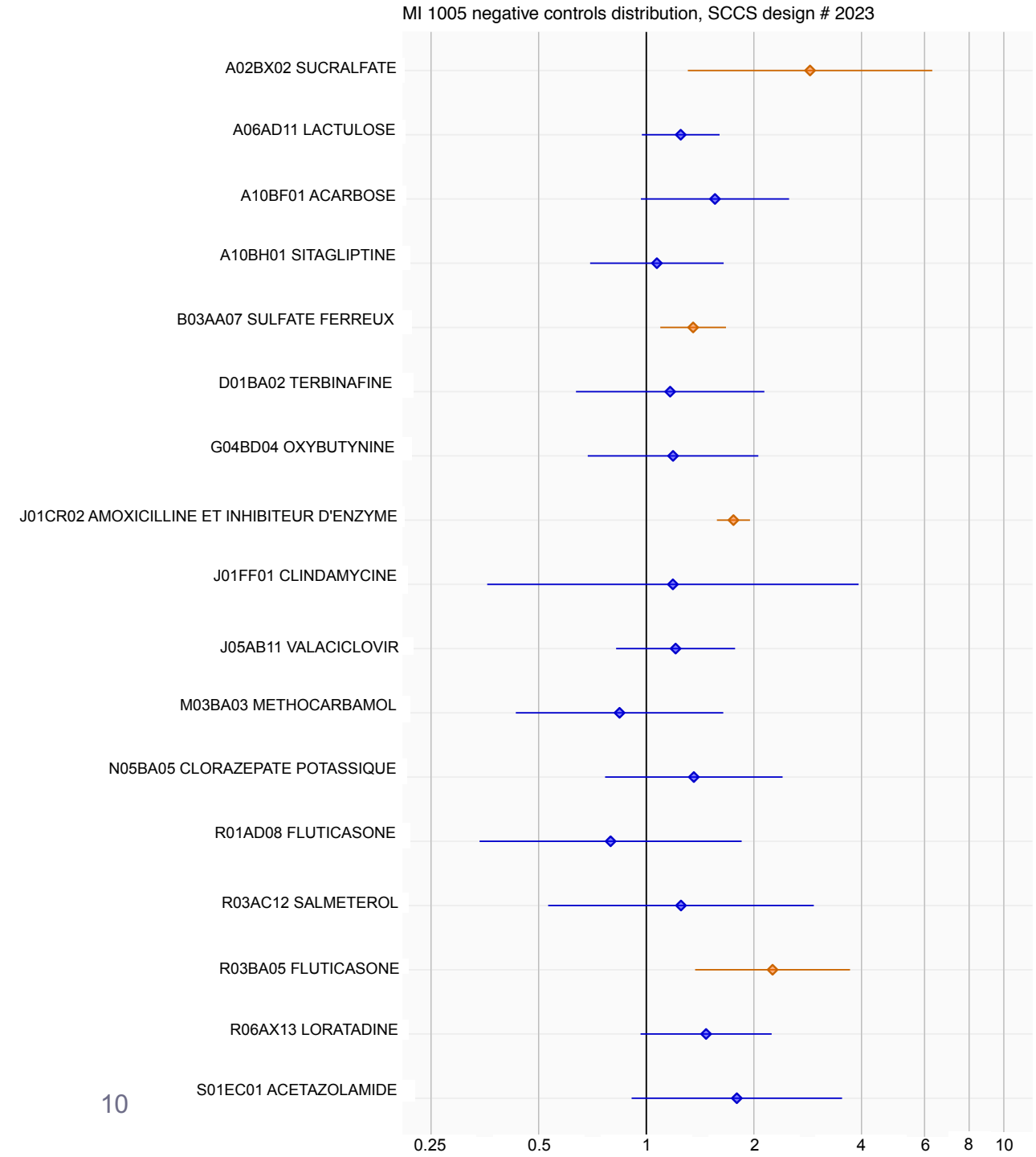
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A02BX02 SUCRALFATE
A06AD11 LACTULOSE
A10BF01 ACARBOSE
A10BH01 SITAGLIPTINE
B03AA07 SULFATE FERREUX
D01BA02 TERBINAFINE
G04BD04 OXYBUTYNINE
J01CR02 AMOXICILLINE ET INHIBITEUR D'ENZYME
J01FF01 CLINDAMYCINE
J05AB11 VALACICLOVIR
M03BA03 METHOCARBAMOL
N05BA05 CLORAZEPATE POTASSIQUE
R01AD08 FLUTICASONE
R03AC12 SALMETEROL
R03BA05 FLUTICASONE
R06AX13 LORATADINE
S01EC01 ACETAZOLAMIDE
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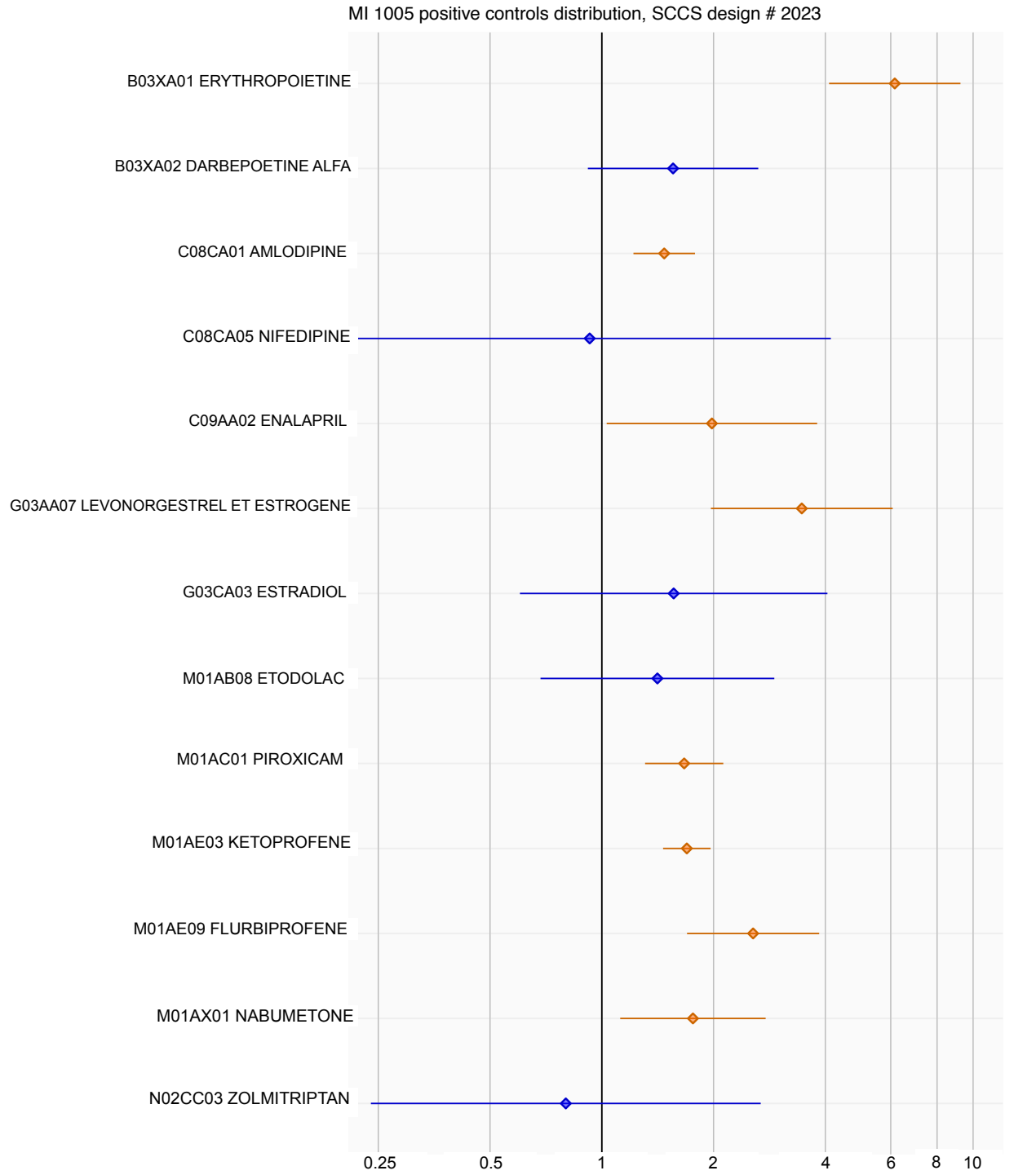
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B03XA02 DARBEPOETINE ALFA
C08CA01 AMLODIPINE
C08CA05 NIFEDIPINE
C09AA02 ENALAPRIL
G03AA07 LEVONORGESTREL ET ESTROGENE
G03CA03 ESTRADIOL
M01AB08 ETODOLAC
M01AC01 PIROXICAM
M01AE03 KETOPROFENE
M01AE09 FLURBIPROFENE
M01AX01 NABUMETONE
N02CC03 ZOLMITRIPTAN
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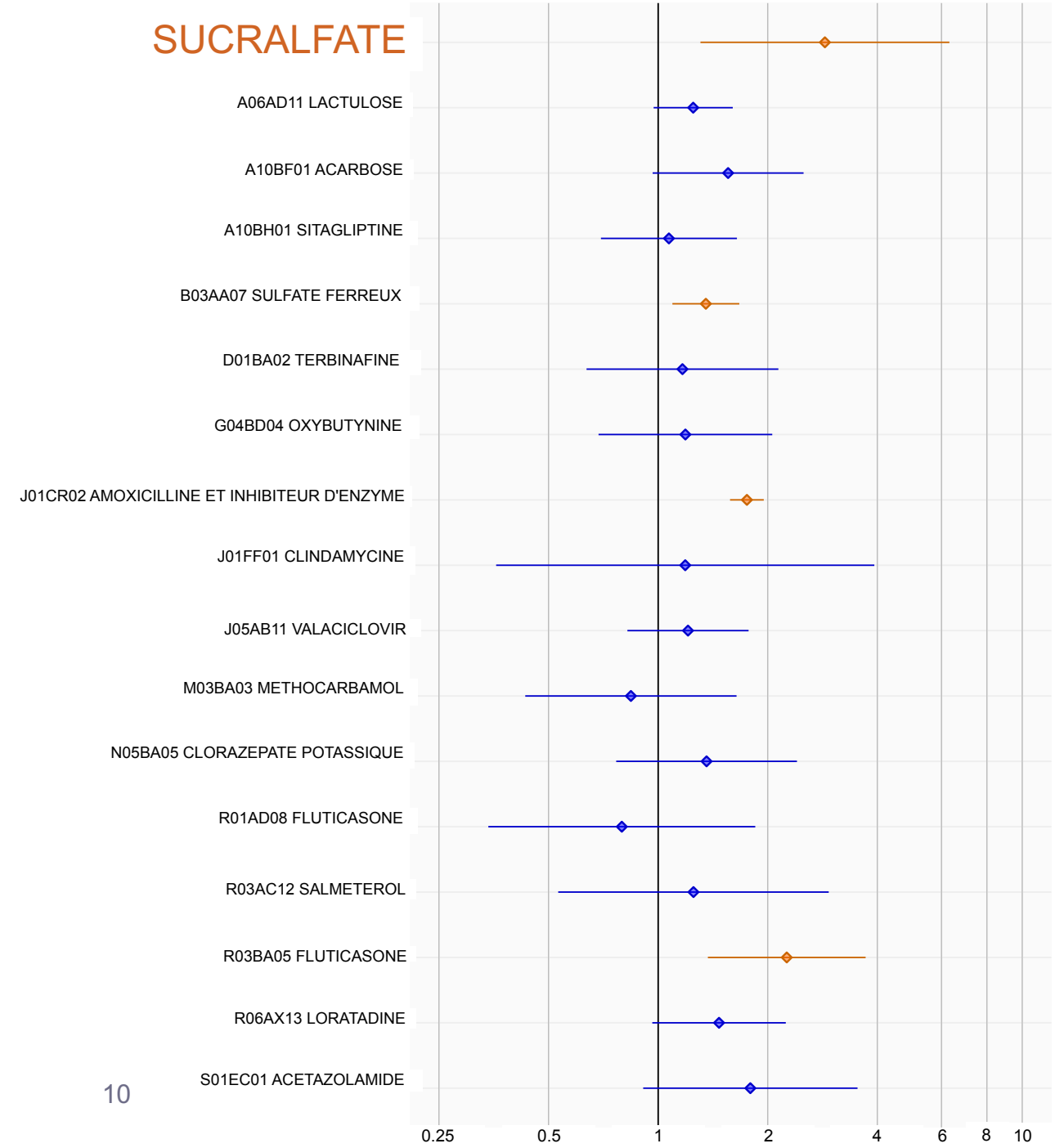


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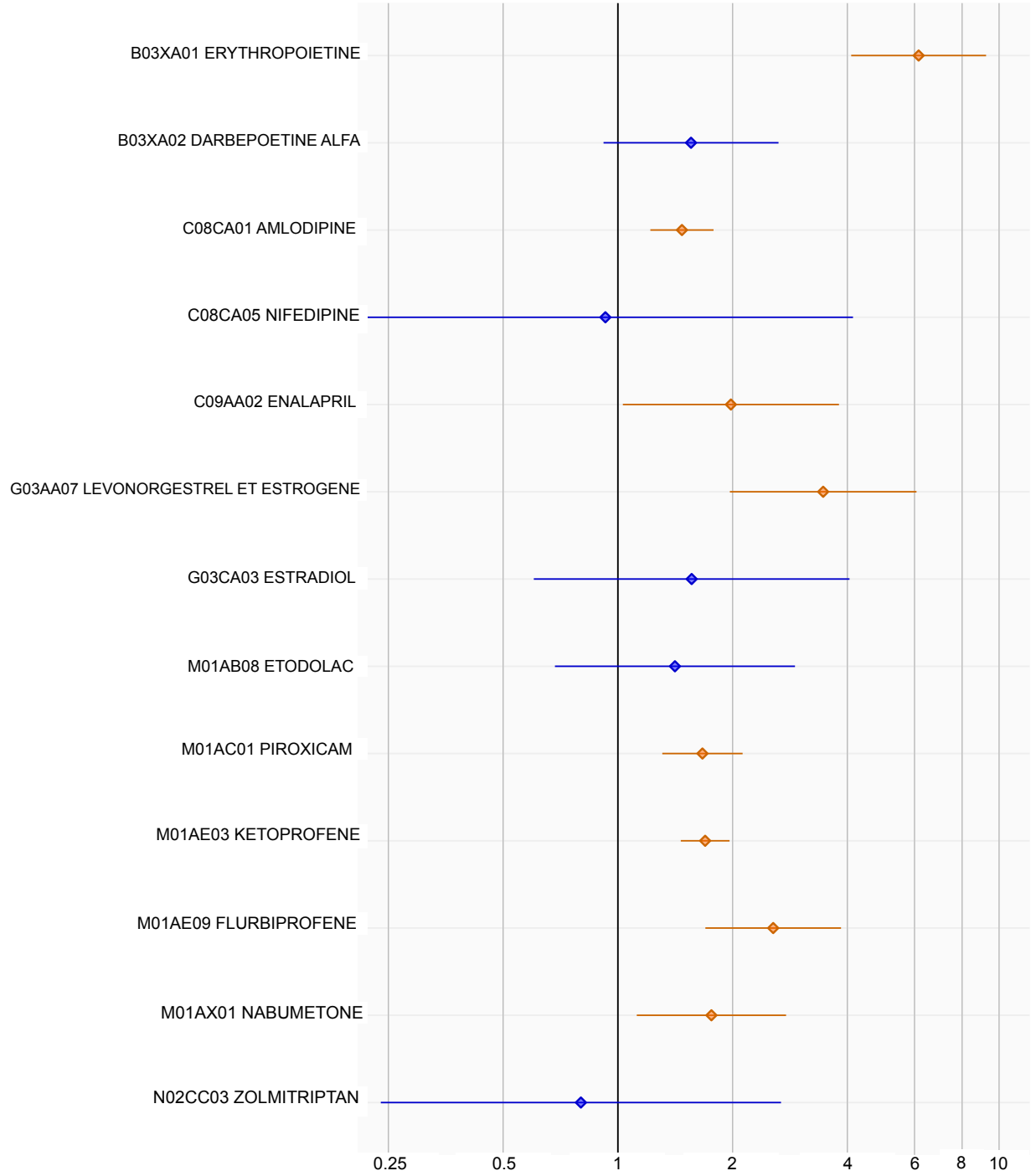

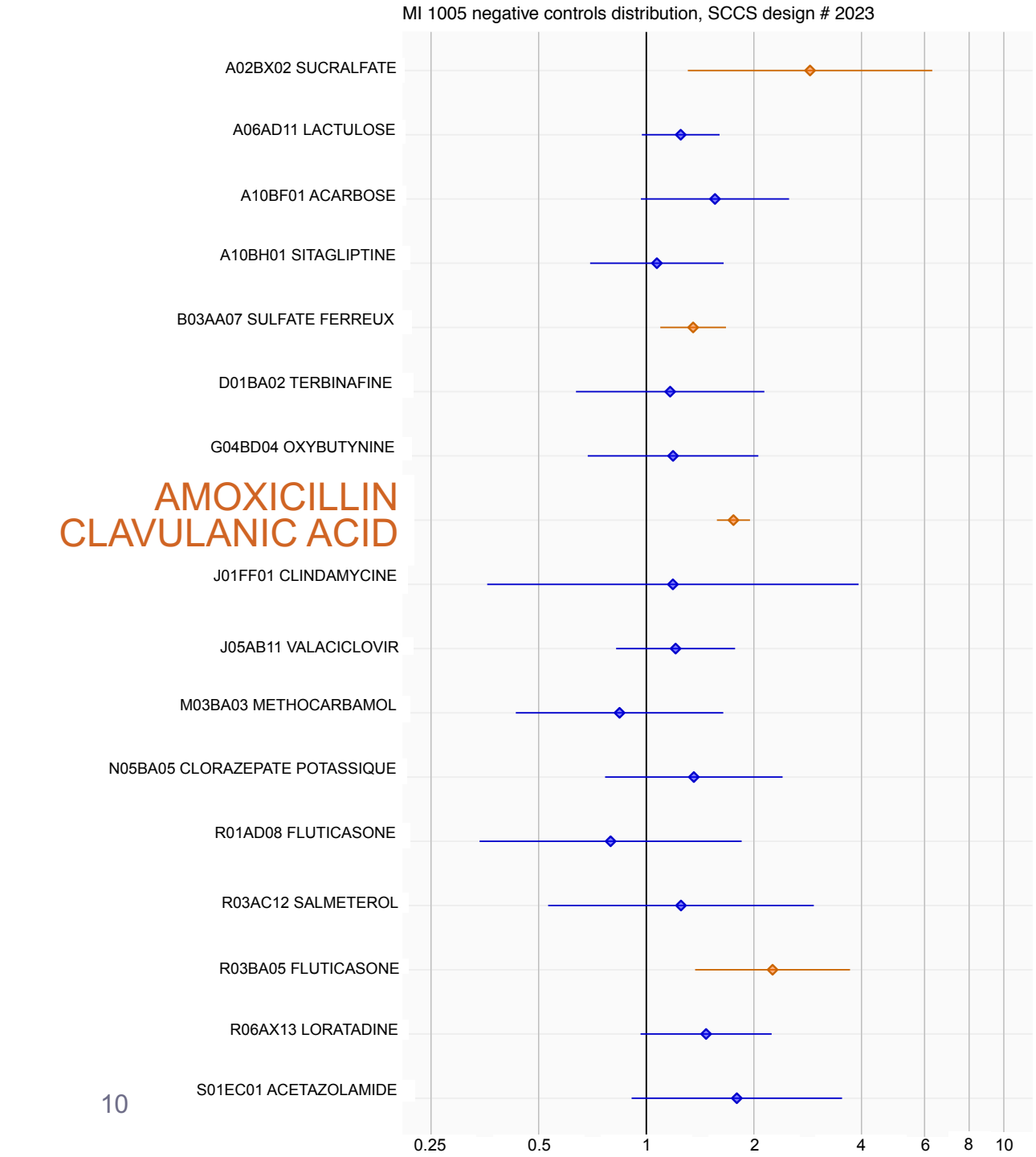
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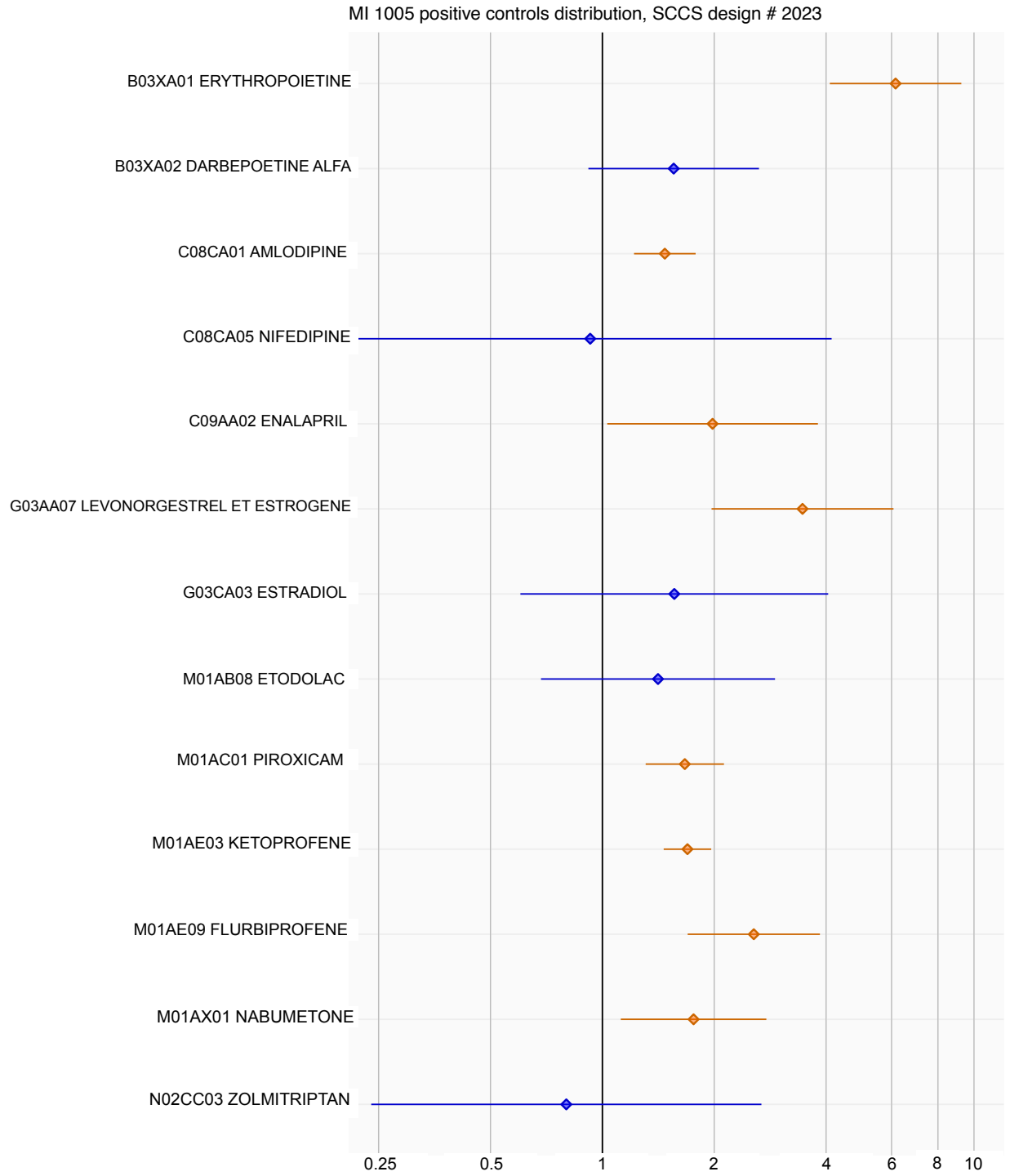
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# Conclusion

- First overview of SCCS, CC and CP performances
- SCCS achieves better performances across all outcomes with
  - High discriminative ability
  - High predictive accuracy
- Controls help to highlight design limits
- For each outcome of interest, a specific variant should be considered for drug-related outcome detection
- Valuable tools for routine alert generation in the SNDS


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