



Empirical assessment of OHDSI case-based methods and case-population for the identification of drug-related outcome in the French nationwide healthcare database (SNDS)

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Disclosure statement

- Based on  Lcapone
- Funded by the French Ministry of Health (PREPS, 14-0635)
- Designed, conducted and analysed 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
 - Deaths
 - Costs
 - *etc.*
- Database extraction accessible for public health purposes after approval by
 - Data protection agency (CNIL)
 - National Health data institute (INDS)



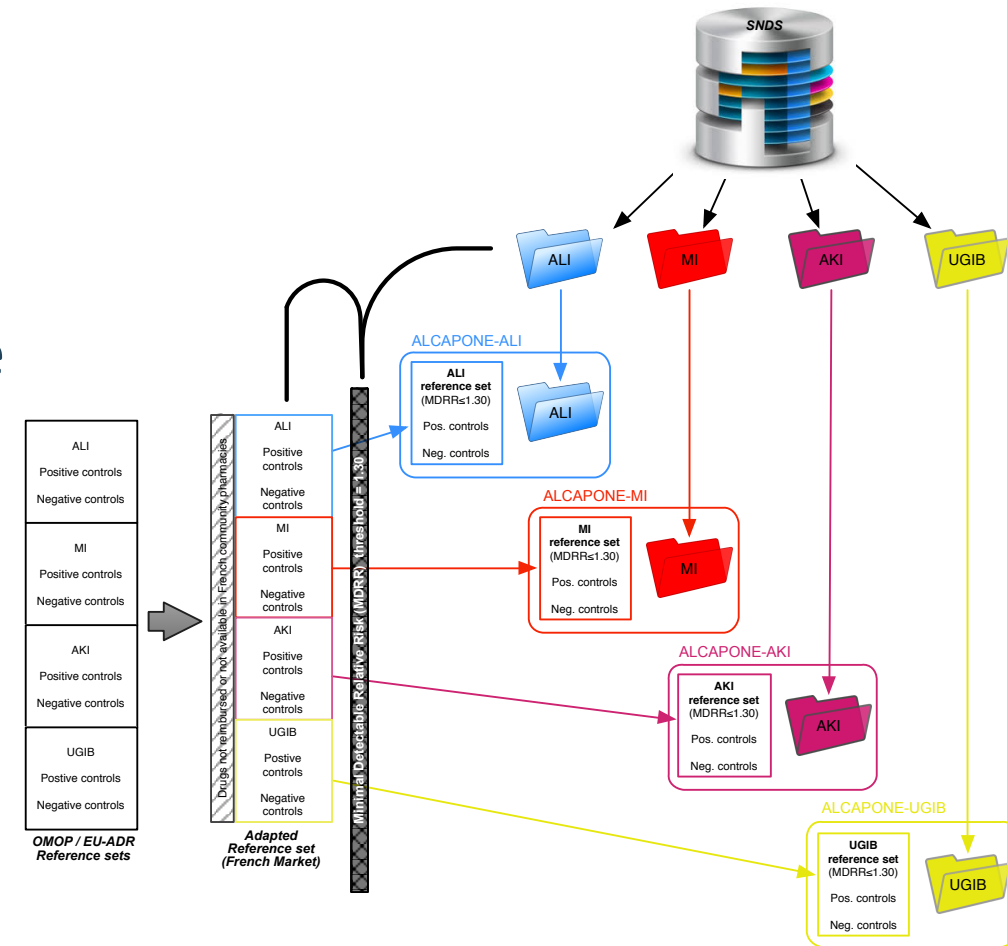
Objectives

- 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)



Methods

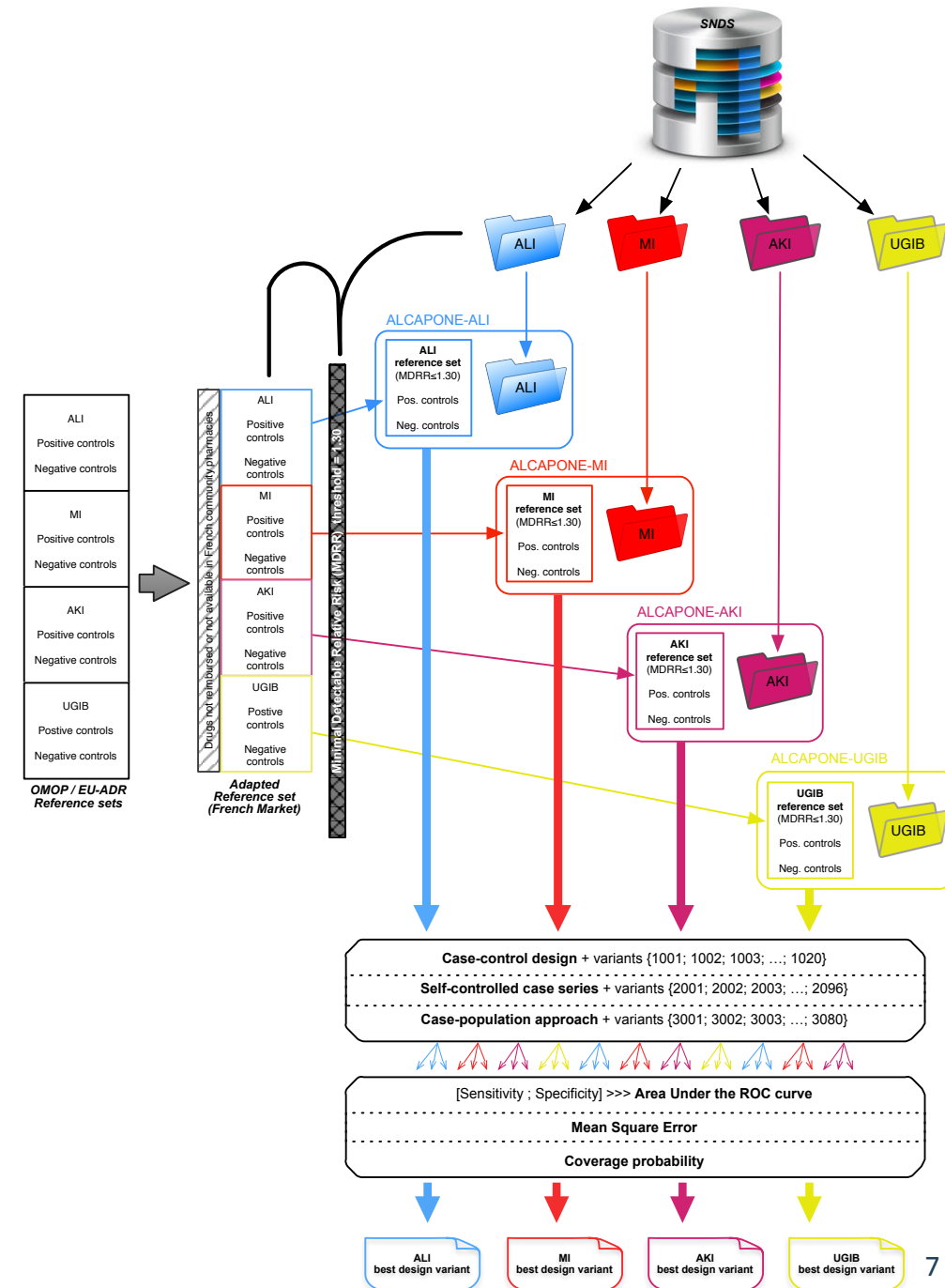
- 273 drug-outcome pairs
 - Adapted from OMOP and EU-ADR reference sets
 - 4 health outcomes of interest
 - 139 positive and negative controls
 - Restricted to the pairs with $MDRR < 1.30$
- SNDS data extractions based on cases
 - ALI
 - AKI
 - MI
 - UGIB





Methods

- 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





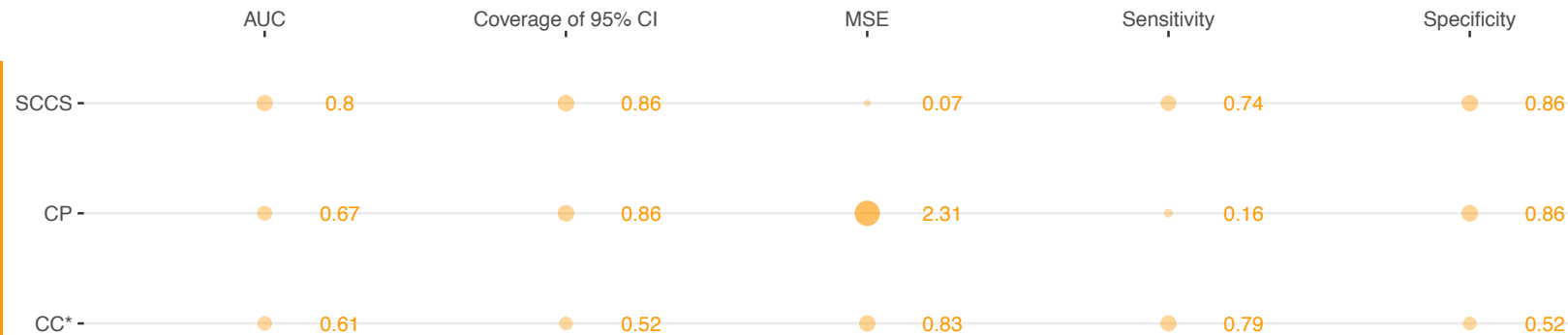
Results

Raw data extractions (SNDS)

Reference set

Patients	Outcomes	HOI	Drug controls (+/-)	French market Reference set	Number of detectable controls (MDRR<1.30) in the data extraction			
					raw sample	1/3 rd sample	1/10 th sample	1/20 th 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	

UGIB



First occurrence, 30d from dispensation first day, adjusted on multiple drugs

All occurrences, 60d risk window, 15d exclusion period, per-user approach, control data stratified on age and gender, RR predicted

up to 2 controls per case, first occurrence, 7d risk window, matched on age and gender, unmatched cases removed

MI

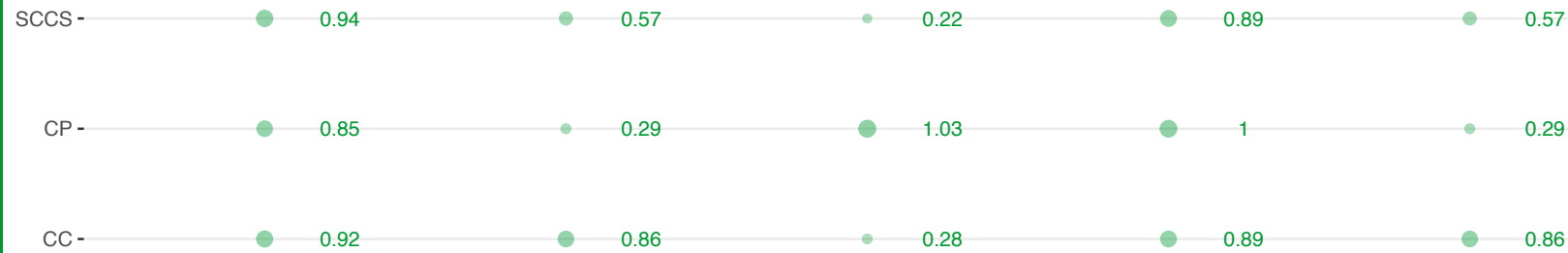


All occurrences, 30d from dispensation first day, adjusted on age and seasonality

All occurrences, 7d risk window, Person-time approach, CPR

up to 10 controls per case, first occurrence, 30d risk window, matched on age and gender, unmatched cases removed

ALI

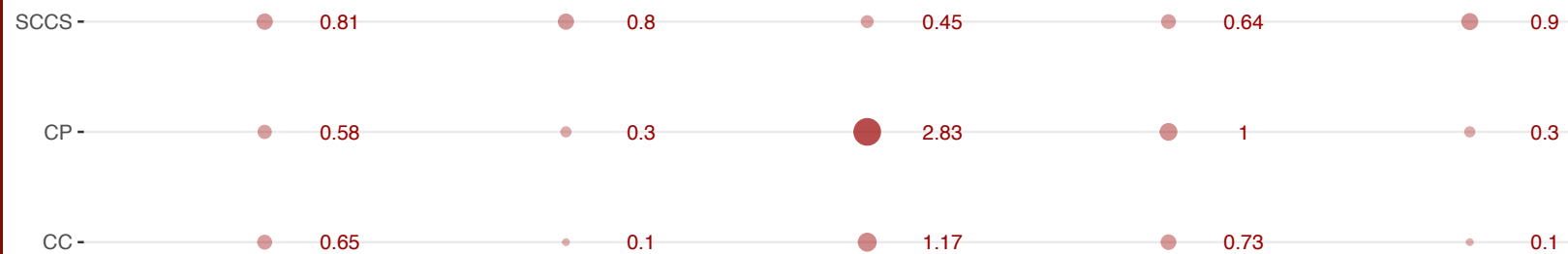


First occurrence, Period of dispensation, No adjustment

First occurrence, 7d risk window, Person-time approach, Raw, CPR

up to 2 controls per case, All occurrences, 7d risk window, matched on age and gender, unmatched cases removed

AKI

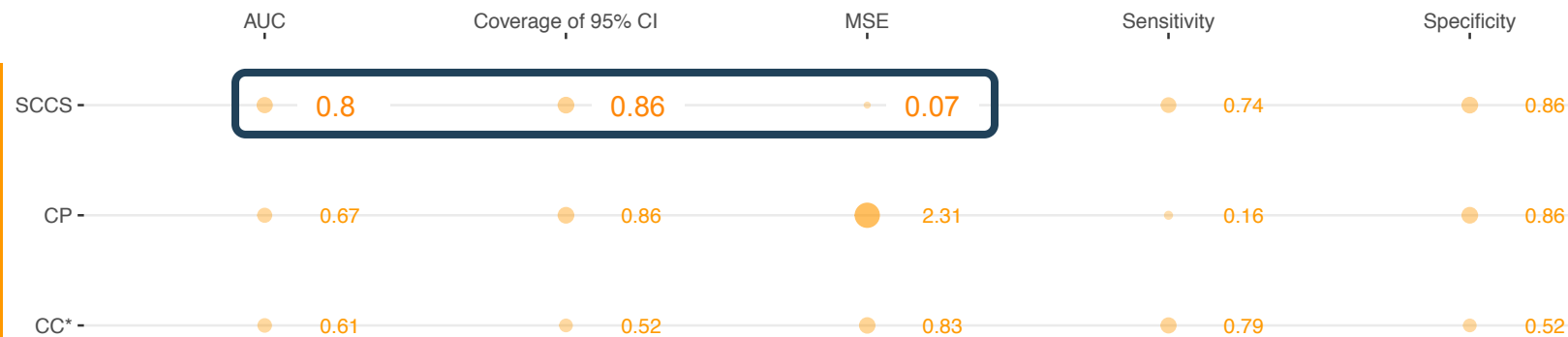


All occurrences, Period of dispensation, adjusted on seasonality and multiple drugs

First occurrence, 7d risk window, Person-time approach, RR predicted

up to 10 controls per case, first occurrence, 60d risk windows, 15d exclusion period, matched on age and gender, unmatched cases removed

UGIB

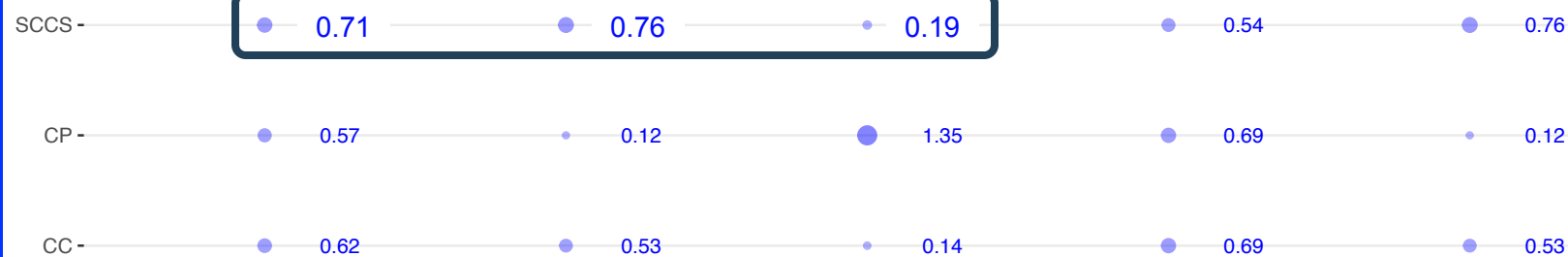


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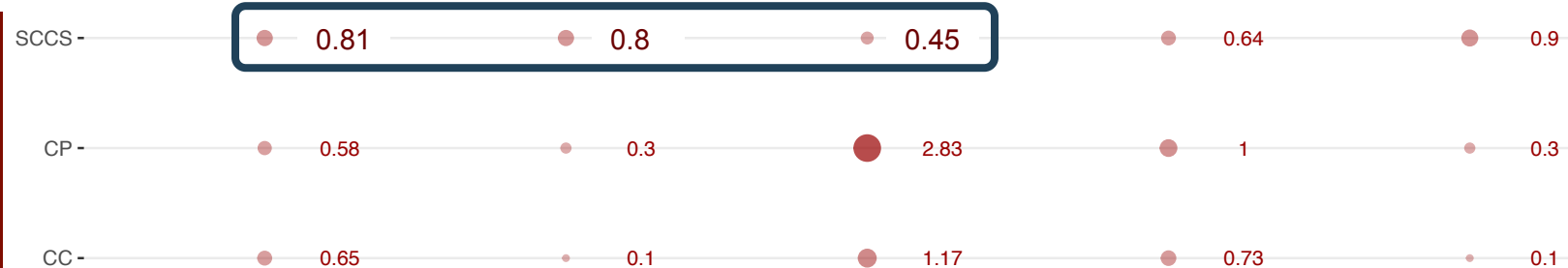


First occurrence, Period of dispensation, No adjustment

First occurrence, 7d risk window, Person-time approach, Raw, CPR

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AKI

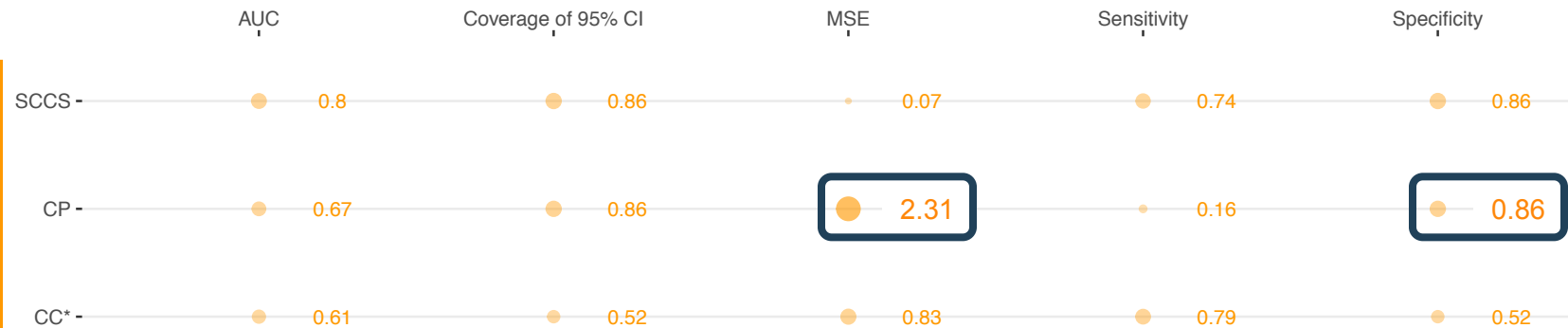


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UGIB

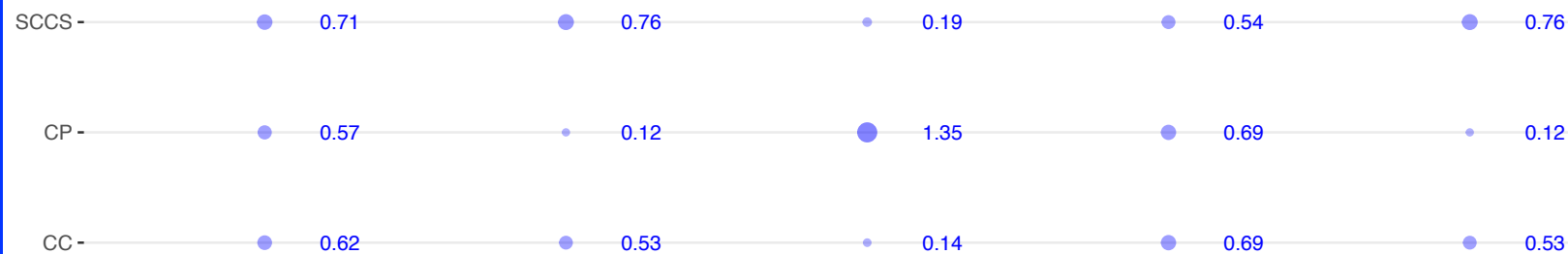


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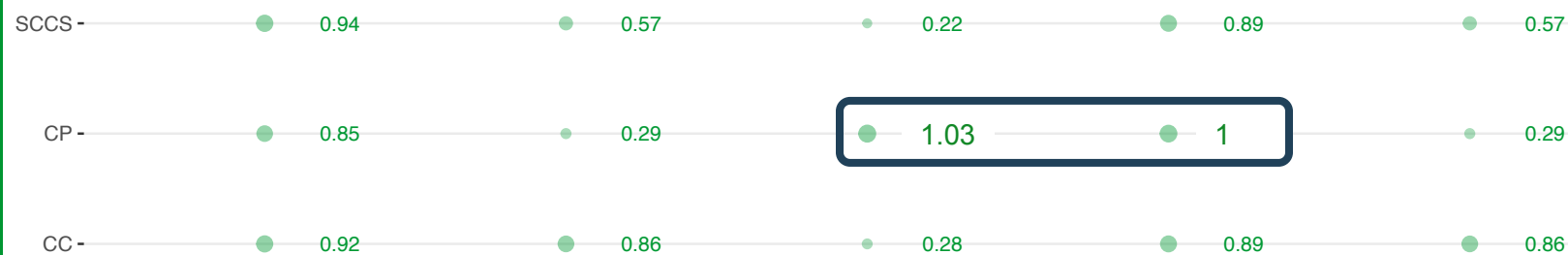


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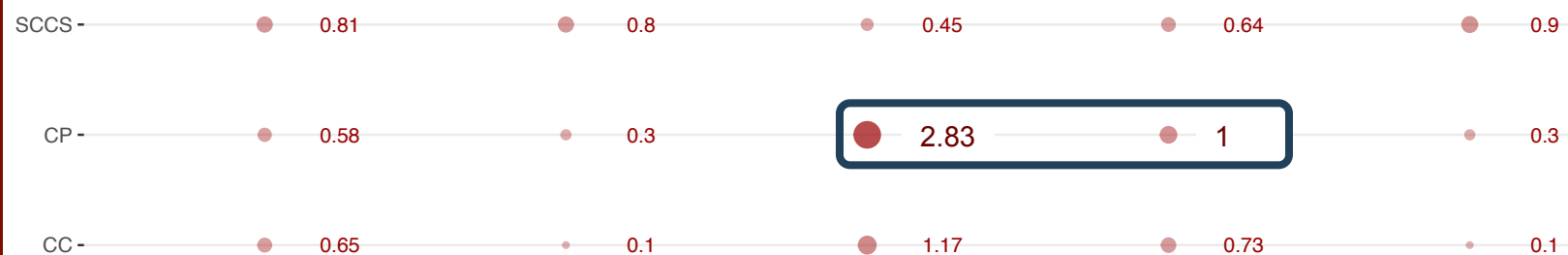


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AKI

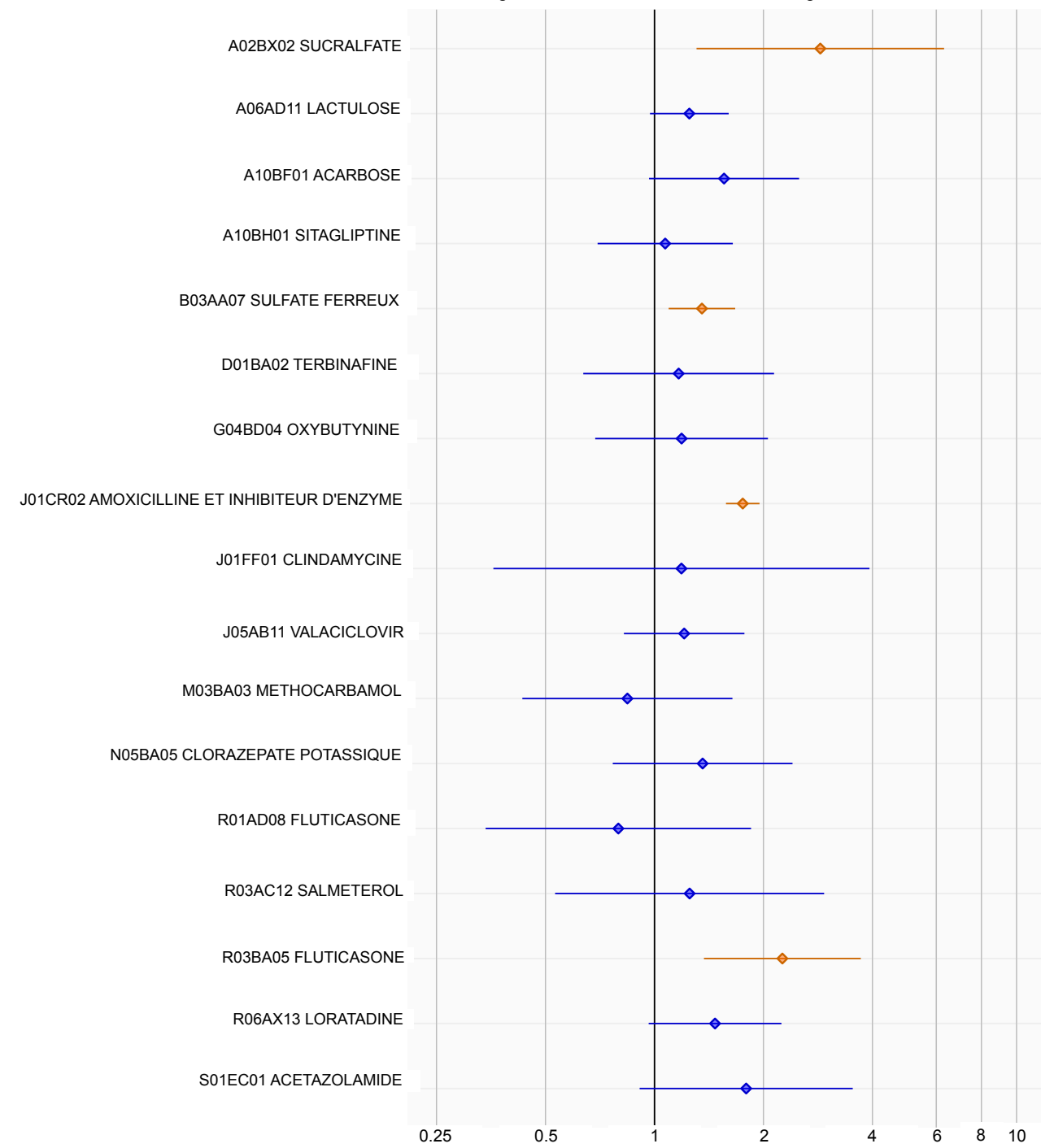


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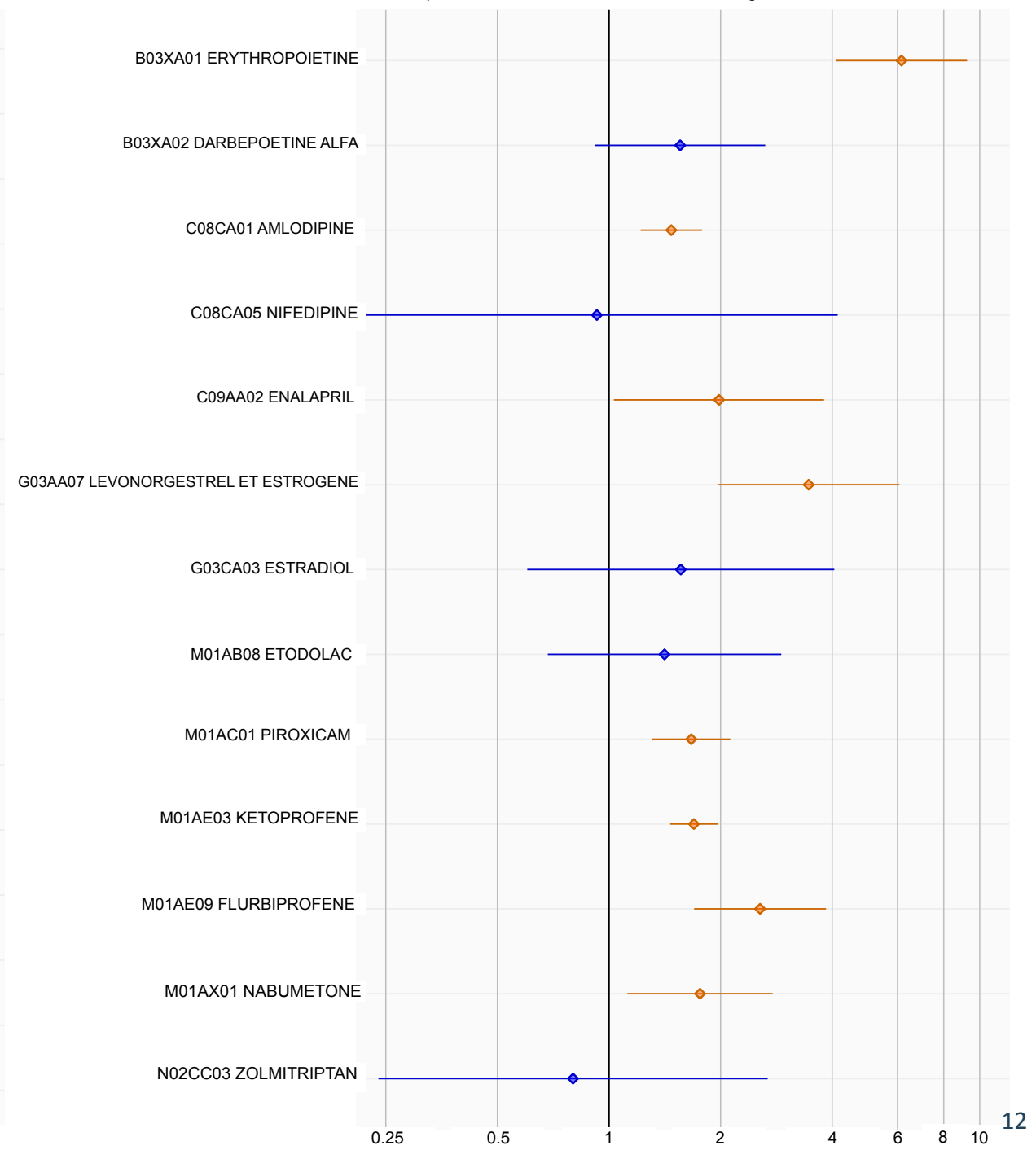
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MI 1005 negative controls distribution, SCCS design # 2023



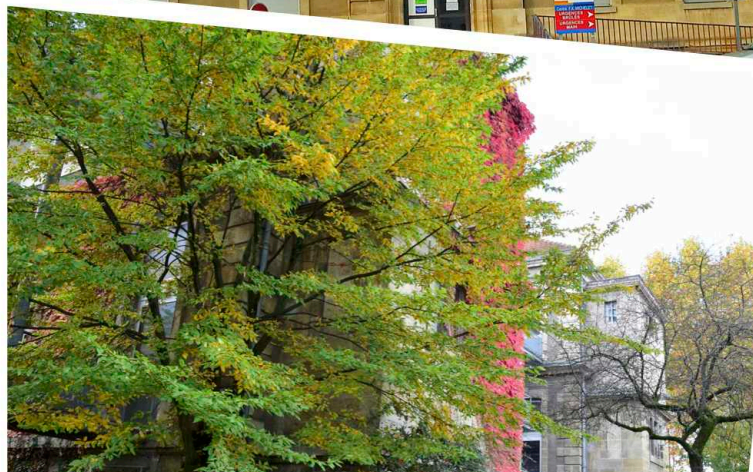
MI 1005 positive controls distribution, SCCS design # 2023





Conclusion

- Ability to implement OHDSI Methods Library in the SNDS
- First overview of CP performances
- SCCS achieves better performances across all outcomes with
 - High discriminative ability
 - High predictive accuracy
- Reference methods and settings for the identification of drug related outcome in the SNDS
- Application for routine alert generation



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