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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Background

- **SNDS** is the French Nationwide Healthcare System Database
  - covering 66.6 million persons (99% of the French population),
  - including individual pseudonymised information on
    - Sociodemographics
    - Drug dispensings
    - Hospital discharge diagnoses
    - Procedures
    - Deaths
    - Costs, *etc.*
- SNDS extractions available after approval for public health purposes, including drug-related risk identification
- Risk identification performances depends on
  - the method,
  - the method settings
  - the environment = **the database**

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

Objectives

- To evaluate and compare the performances in the SNDS of
  - Self-controlled case series (SCCS)
  - Case control (CC)
  - Case-population (CP)
- For the identification of
  - ALI (Acute liver injury)
  - AKI (Acute kidney injury)
  - MI (Myocardial infarction)
  - UGIB (Upper gasrtointestinal bleeding)

Methods

- **Construction of a reference set adapted to the French Market**
  - 273 drug-outcome pairs from OMOP and EU-ADR reference sets
    - 4 health outcomes of interest (ALI, AKI, MI and UGIB)
    - 139 drug controls supposed associated (*positive*) or not (*negative*) with the outcome
    - Restricted to the pairs with the minimum detectable relative risk (MDRR) <1.30
- **SNDS data extractions** based on cases (2009-2014 period)
  - ALI, non sampled
  - AKI, sampled at 1/3
  - MI, sampled at 1/20
  - UGIB, sampled at 1/10
- **Detection of the drug-outcome pairs** *via* the 3 designs and different settings
  - **96** SCCS variants
  - **20** CC variants
  - **80** CP variants

  ➔ Generation of one point estimate by pair and variant, in total, 26 068.
- **Performance assessment** of the design variants based on
  - Discriminating power: area under the receiving operator curve (AUC)
  - Accuracy: mean square error (MSE), coverage probability

Results

- Over 6 years, the number of cases extracted from the SNDS ranges from 5 152 (ALI) to 304 369 (MI) [Table 1]

***Table 1**. Outcomes and number of patients extracted from SNDS by health outcome of interest*

	ALI	MI	AKI	UGIB
Outcomes	5 225	354 109	12 633	156 057
Patients	5 152	304 369	12 317	139 172

- Considering the raw data extraction of the SNDS, the number of drug-outcome pairs with a MDRR<1.30 ranged from 25 for ALI to 61 to MI [Table2]
- Sampling data extraction was necessary to reduce execution time. The result is a decrease of the number of detectable drug-outcome pairs, especially the number of negative controls

***Table 2**. Number of positive and negative controls by health outcome of interest available in the French market and detectable in the SNDS*

	Drug controls	French market Reference set	Number of detectable controls[1]				
			SNDS extraction	raw	1/3rd sample	1/10th sample	1/20th sample
ALI	+	58		18			
	-	23		7			
MI	+	28		25			26
	-	42		36			20
AKI	+	22		17	11		
	-	36		13	10		
UGIB	+	22		22		19	
	-	42		36		22	

[1] Drug controls with MDRR<1.30

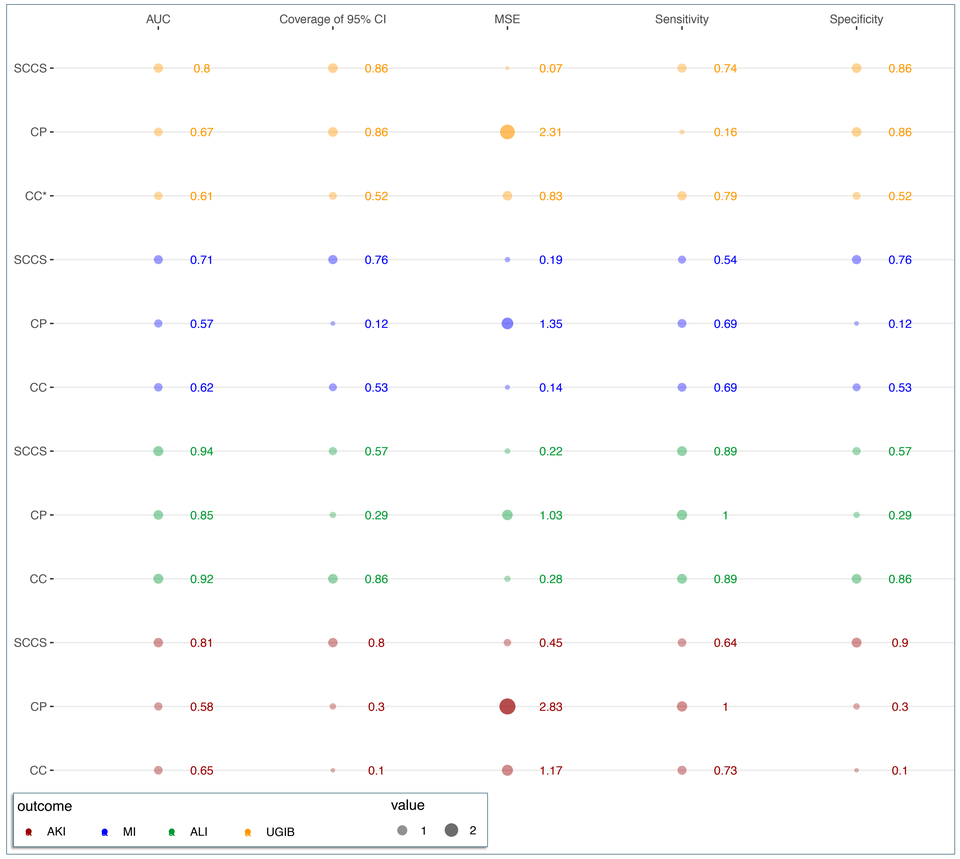

***Figure 1**. AUC, coverage probability, MSE, sensitivity and specificity of the SCCS, CC and CP best design variants across the four health outcome of interest.*

- SCCS variants achieved the best performance across all outcome definitions with AUC ≥0.9 for ALI, ≥0.8 for KI and UGIB and ≥0.7 for MI [Figure 1]
- CC achieved higher AUC than CP for ALI (≥0.89 *vs.* ≥0.85), KI (≥0.62 *vs.* ≥0.58) and MI (≥0.62 *vs.* ≥0.57); and lower for UGIB (≥0.60 *vs.* ≥0.67)
- The best predictive accuracy was observed with SCCS for UGIB (MSE=0.07) and MI (MSE=0.19)
- MSE was lower for the most discriminating CC variants (0.23≤MSE≤1.34) as compared to the most discriminating CP variants (1.07≤MSE≤3)

Conclusions

- **OHDSI Methods Library can be implemented in the SNDS framework**
- **First overview of CP performances: CP seems to be less accurate and discriminant for alert generation than SCCS and CC**
- **SCCS achieves better performances across all outcomes with**
  - **high discriminative ability**
  - **high predictive accuracy**
- **Designs and settings tested can be used as reference methods for the identification of drug-related outcome in the SNDS**

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2019 European OHDSI Symposium, March 29th, Rotterdam, Netherlands

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