



# Validation of an algorithm identifying relapses in multiple sclerosis using the French nationwide claims database

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## Background

### Multiple sclerosis (MS)

- Incapacitating, progressive, chronic neurological disorder that involves a selective, chronic inflammation and demyelination of the central nervous system
- Relapsing-remitting MS form (RRMS) is the most common, and are characterized by the presence of relapses without disability progression between relapses
- In France, prevalence in 2015: 135 per 100 000 inhabitants and 87 000 cases in 2017

### Relapses

- Clinically defined as the occurrence of new neurologic symptoms or the recurrence of old neurological symptoms that last at least 24 hours
- SNDS (national healthcare system database): No direct indicator available, complex algorithm based on:
  - hospitalization(s) related to relapse or related to MS,
  - or outpatient dispensation(s) of IV or oral high dose corticosteroid therapy,
  - or combination of hospitalization(s) related to relapse or related to MS and outpatient dispensation(s) of IV or oral high dose corticosteroid therapy.

### Validation of the algorithm

- Conducted by clinician using all information of the database (as a patient's medical file, see below) for a random sample of patients

## Objectives

- To assess the validity of an algorithm identifying relapses in MS patients in SNDS database

## Methods

- **Data source:** extraction of SNDS data from 2011 to 2016 (EVIDEMS cohort)

### General approach

- 1 Execution of the algorithm for relapses identification
- 2 Assessment of randomly selected cases by a committee of experts
- 3 Calculation of positive (PPV) and negative (NPV) predictive values of the algorithm
- 4 Adjustment of algorithm
- 5 Calculation of positive (PPV) and negative (NPV) predictive values of the algorithm

### SNDS data formatting for cases review (Figure 1)

- For each case, pseudonymized medical chart was reconstructed using data of SNDS extraction:
- age class, sex, drugs dispensing, hospitalization, medical procedures (during history period and follow-up period)
  - healthcare data possibly related to MS: the dispensing of corticosteroids, hospitalizations for potential MS relapse or for administration of high dose of steroids...

### Validation committee (Figure 2)

- Random selection of 200 patients among 37 986 MS patients of the cohort:
  - 100 MS patients with at least one relapse during follow-up period detected by the algorithm
  - 100 MS patients without relapse (not detected by the algorithm)
- Double blind review of 100 patients (50 with at least one relapse and 50 without relapse) per expert pair
- By 2 expert pairs (each pair with 1 neurologist member of the Scientific Committee of EVIDEMS study + 1 independent neurologist)

### Algorithm validation (Figure 2)

- Assessment by each expert of the presence or absence of relapses and the number of relapses
- In case of discrepancy within a pair of experts: the case was discussed by the 4 experts to reach consensus
- Algorithm performance was estimated using the positive and negative predictive values (PPV, NPV).

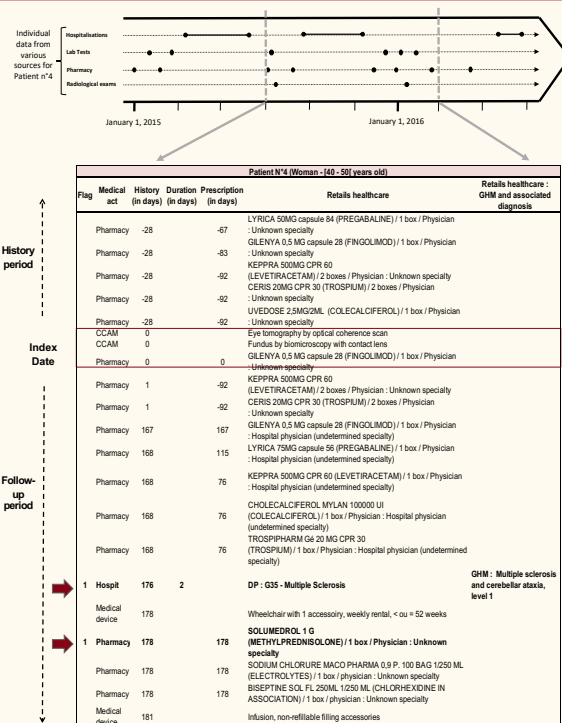


Figure 1. Reconstructed medical chart of patient

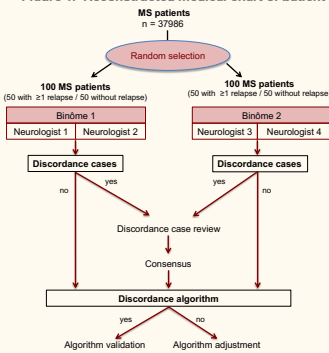


Figure 2. Validation Committee

## Results

### Inter-expert and algorithm discrepancy

- Inter-expert discrepancy: among the 200 MS patients selected, the summary sheets of 35 patients were reviewed in a collegiate manner, in order to reach a consensus.
- Algorithm discrepancy: finally 11 discordant cases (9 patients because a patient may have many relapses) have been identified by the experts: 7 related to the criteria "relapse presence" and 4 to the criteria "relapse absence".

### PPV and NPV calculation (Table 1)

- Confirmation of 95 out of 100 MS patients with at least one relapse and 96 out of 100 patients without relapse
- PPV = 95.0% and NPV = 96.0%

Table 1. PPV and NPV calculation

Algorithm		Experts		Total
		Relapse	Without relapse	
	Relapse	95	4	100
	Without relapse	5	96	100
	Total	100	100	200

### PPV and NPV calculation after algorithm adjustment (Table 2)

- Discordant cases have been discussed by the experts in order to adjust the algorithm
- Finally, the algorithm was revised to include all changes proposed by the experts.
- The proposed changes increased algorithm performance: the PPV and NPV of the revised version of the algorithm became 95.2% and 100% respectively.

Table 2. PPV and NPV calculation after algorithm adjustment

Algorithm		Experts		Total
		Relapse	Without relapse	
	Relapse	99	5	104
	Without relapse	0	96	96
	Total	99	101	200

## Conclusion

### The wealth of data available in the SNDS enables

- The implementation of algorithms to detect complex events
- The validation of these algorithms via the reconstitution of pseudonymized medical charts based on SNDS data

### This claim-based algorithm

- Appeared to successfully detect MS relapses
- Could thus be applied to future observational MS studies in SNDS database such as those aiming to assess effectiveness of MS treatments on relapses

**Declaration of Interest Statement:** The validity assessment of this algorithm is linked to a study using it (EVIDEMS) and carried out by the Bordeaux PharmacEpi platform in collaboration with Biogen and supervised by an independent scientific committee. The study was supported by an unconditional grant from Biogen.