REpositioning of Medications IN Dementia (REMIND): Evaluating the fitness for purpose of the French Nationwide Claims Database (SNDS)

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Background

- Alzheimer's disease and related dementia, (ADRD), cause pathological changes in the brain leading to progressive cognitive decline ≥10 years before diagnosis (**Figure 1**).
- ADRD impacts over 55 million worldwide and are major causes of disability.
- ADRD currently has no curative or preventative treatment.

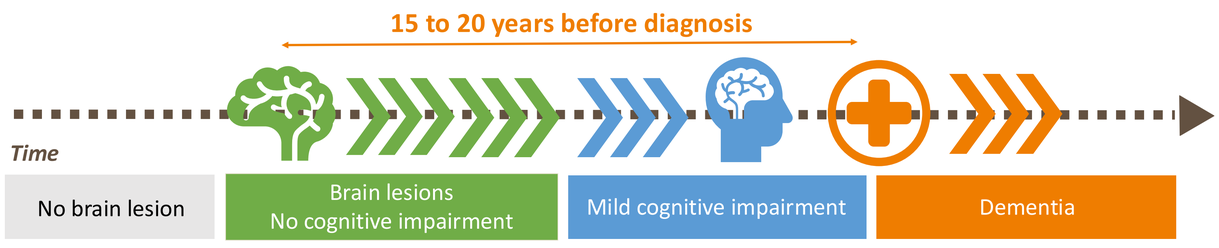

Figure 1: ADRD progression schema

- Drug repurposing offers an opportunity to evaluate the benefit of drugs already approved for other indications for ADRD.
- As part of the **REMIND** project, we will identify ADRD drug candidates using agnostic signal detection and validate these signals using causal inference methods. Additionally, we will validate drug candidates targeting dysfunctional metabolic pathways which were detected in a previous study (DREAM[1]) using a Multi-Omics approach.

Objective

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To assess the feasibility of conducting REMIND in the French Nationwide Claims Database, the SNDS.

Methods

We evaluated key parameters (e.g., ADRD identification, sample size over the follow-up) necessary for conducting an ADRD drug repurposing study in the SNDS.

The SNDS captures the medical claims of **~55 million individuals with over 20 years of follow-up (Figure 2).** Captured claims include medications, hospitalizations, procedures, lab tests and imaging (no results). Some sociodemographic variables are also available (e.g., age, sex, social deprivation index).

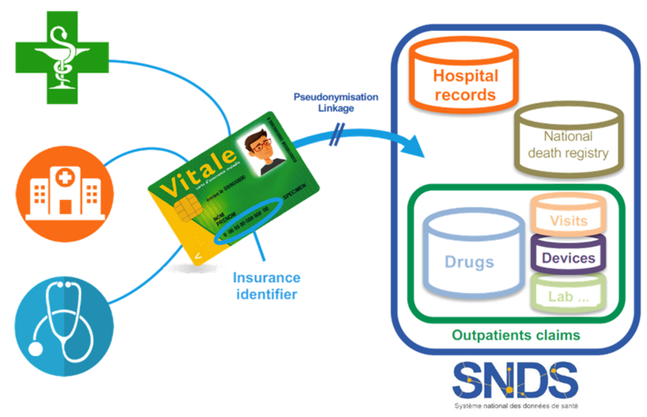

Figure 2: Schema of the SNDS

Results

Identification of Alzheimer's disease and related dementias

Since outpatient diagnosis codes are not available in the SNDS, ADRD can be captured using an algorithm incorporating dementia treatments, hospitalizations and long-term disease registration for ADRD. Results from external validation[2,3] indicate :

- *Lack of sensitivity >70 years:* ~170,000 new cases / year (60% of expected)
- *Good sensitivity <70 years:* ~4,000 new cases / year

Ability to identify drug candidates

A case-control design for signal detection is feasible. **Table 1** indicates that, for example, with an inclusion period of 4 years (n > 680,000), using a 1:1 case-control ratio we can capture an odds ratio (OR) of 0.85 with a power of 80% and an alpha of 5%, for a 0.1% exposure among cases and controls. Multiple time-windows will be tested for drug exposure (e.g., 8 years and 5-years before diagnosis).

Table 1: Estimated sample size as a function of the minimum OR

	OR=0.80		OR=0.85		OR=0.90	
Nb of controls per cases	N cases	N controls	N cases	N controls	N cases	N controls
1	353,478	353,478	**645,897**	**645,897**	1,492,626	1,492,626
2	261,120	522,240	479,132	958,264	1,111,572	2,223,144
3	230,283	690,849	423,494	1,270,482	984,506	2,953,518

Capture of DREAM medications in the SNDS

Exposures are defined in the SNDS by medications claims dispensed from outpatient pharmacies. Except for dipyridamole, all DREAM medications and comparators recommended were captured in the SNDS in 2020 (**Table 2**).

Table 2: DREAM medications and active control users in the SNDS in 2020

DREAM Medications	Population (n)	Active Comparators (n)	Population (n)
Efavirenz	1,670	Dolutegravir, Nevirapine	11,716
Deferiprone, Deferoxamine	189	Deferasirox	3,182
Tofacitinib	5,718	Abatacept	5,254
Tocilizumab	5,737	Abatacept	5,254
Anti TNF*	39,817	Abatacept	5,254
Dipyridamole	0	Acetylsalicylic acid	5,273,293
Anastrozole	89,506	Exemestane, Letrozole	191,000
Valproic acid	138,577	Lamotrigine	120,290
Dihydropyridine calcium channel blocker*	3,863,465	Hydrochlorothiazide	3,059,095
Amiloride	71,183	Triamterene	56,552
Salbutamol	1,105,656	Long-acting muscarinic antagonist*	625,985
Probenecid (2016)	1,234	Allopurinol	993,502
Montelukast	300,000	Fluticasone	1,482,042

*medication class

Ability to conduct a robust validation study

Causal inference analyses will be possible. Minimum sample size is estimated using an inclusion period of 2 years (2011-2013), 5 years of history to guarantee the identification of incident cases, a 13-year follow-up (until end of 2024), and an age and sex adjusted ADRD incidence rate of 11.4/1000 person-years anticipated in the SNDS. Sample size estimation enabled us to determine a minimum number of patients ranging from 114 to 3,812, to detect a Hazard Ratio (HR) of 0.4 to 0.8, respectively **(Table 3)**.

Table 3: Estimated sample size as a function of the minimum HR and type of test

Minimum HR	**0.8**	0.7	0.6	0.5	**0.4**
Log rank test	**3,812**	701	390	215	**114**
Exponential Maximum Likelihood	3,675	681	380	212	114

Conclusions

- The French nationwide claims database, the SNDS, is a valuable resource for identifying and validating drug repurposing candidates in ADRD due to its large population, long follow-up, and high number of drugs captured.
- In the context of the REMIND project, the SNDS captures ADRD diagnoses via an algorithm, drug candidates via dispensing claims, and contains a sufficient sample size to identify drug signals and conduct robust causal inference analyses to validate candidates with precision.
- More to follow : the REMIND project has received funding from the 2025-2027 health sponsorship programme of the AXA Mutuelles.

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Disclosure:
The authors affiliated to Bordeaux PharmacoEpi are researchers from the BPE platform of the University of Bordeaux and its subsidiary the ADERA (LCB, HB, JJ, AB, PB) , which performs financially supported studies for public and private partners in compliance with the ENCePP Code of Conduct.
MT is currently a full-time employee of Novartis. AE is a researcher at INSERM which performs financially supported studies by Michael J Fox Foundation, the French Ministry of Agriculture, ANR (French national funding agency for research), France Parkinson (French patient association). He is part of the Scientific advisory board for the pharmaco-epidemiology group at the French government drug agency (no salary or fees received).
Support by Prada Foundation for attending the Preserving the brain meeting on October 2024 and Honoraria for a lecture at the Preserving the brain meeting on October 2024. There is nothing to disclose in relation to this submission for CH, TG and RJD.

ISPE's 41st Annual Meeting, scheduled for August 22-26 2025 at Washington DC Convention Center, USA

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