Bordeaux PharmacoEpi platform experience using the national healthcare system claims databases in France (SNDS): a powerful tool for pharmacoepidemiology

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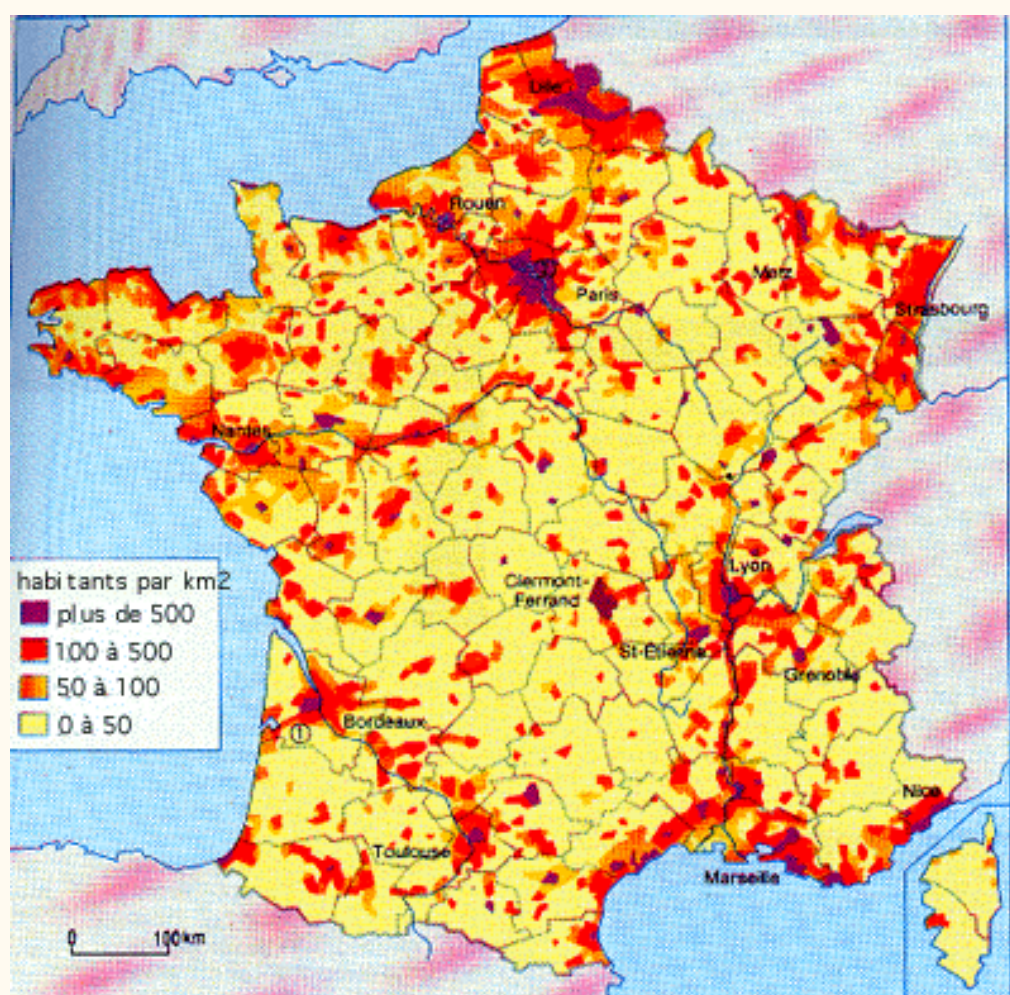
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Introduction

The pharmacoepidemiology or real-world evidence (RWE) studies aim to evaluate the post-authorisation efficacy of drugs in real life settings. This field covers the description of drug utilisation and population risks or benefits of these drugs after they have been marketed and provided to their target populations. Though field studies have existed for a long time, modern pharmacoepidemiology has been made possible essentially by the emergence of large population databases compiled notably from claims data. In France, the use of the medico-administrative database, in particular the French Nationwide Claims database or SNDS (*Système National des Données de Santé*) is a powerful tool for pharmacoepidemiology study.

SNDS Presentation[1]

[1] *Bezin J, Duong M, Lassalle R, Droz C, Pariente A, Blin P, Moore N.*
The national healthcare system claims databases in France, SNIIRAM and EGB: Powerful tools for pharmacoepidemiology.
Pharmacoepidemiol Drug Saf. 2017 May 24.

France key demographics

➢ **66.6 Million inhabitants**
➢ **219 834 Physicians**
  • 102 140 General Practitioners
  • 117 694 Specialists
    – 67 039 Medical
    – 25 802 Surgical
    – 14 831 Psychiatrists
    – 6 796 Cardiologists
    – 4 076 Dermatologists
    – 3 570 GE/Hep
    – 2 598 Rheumatologists
    – 2 289 Neurologists
    – …

➢ **French healthcare system**
  • Universal mandatory coverage (called Social Security, paid on salaries and other gains) complemented by mutual funds or private insurance companies
  • The healthcare system covers, to various degrees, most medical expenses, with patient copay except for diseases with 100% coverage (see below)
  • 3 main programs, 19 smaller ones
  • General practitioners and most specialists are in private practice. Secondary care is by private clinics or local hospitals, and tertiary care by public university hospitals and regional cancer centres
  • Freedom of choice of a referent physician, access to specialist through referent physician, freedom of prescription, and free access to hospital

➢ **French nationwide healthcare data system (SNDS)**
  • Contains continuous data on about 99% of the 66.6 million persons of the French population from birth (or immigration) to death (or emigration), even if a subject changes occupation or retires
  • Making it one of the world's largest homogeneous claims database
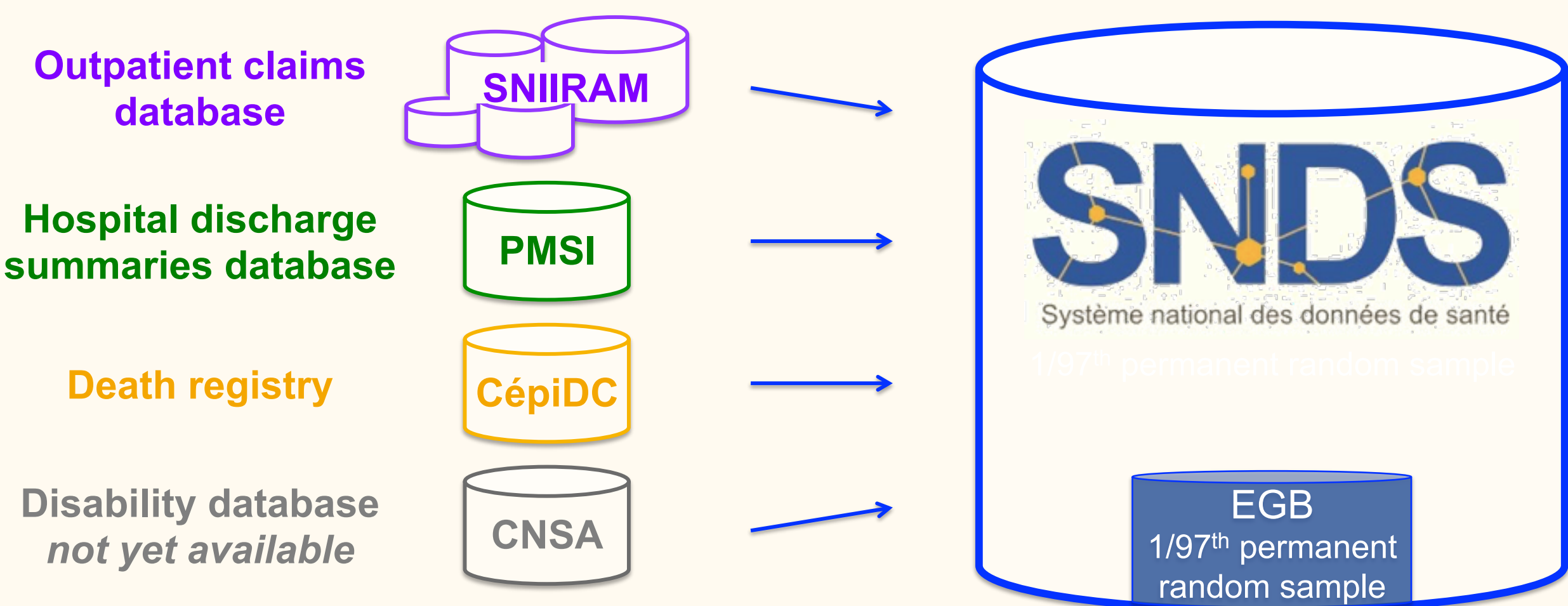 • Merges several databases using unique pseudonymised patient numbers (Figure 1)

Figure 1: Constitution of the French nationwide healthcare data system (SNDS)

➢ **The outpatient claims database (SNIIRAM)**
  • Includes gender, date of birth, localization of residence, indicator of low income
  • Includes Long Term Disease (LTD) registration with start and end dates (costly chronic diseases, with ICD-10 codes). It is requested by the patient's practitioner and medically validated by the health insurance system. Once registered, patients receive full reimbursement for expenditures related to the LTD
  • Contains outpatient reimbursed healthcare expenditures: physician or paramedical visits (e.g. nursing, physiotherapy), drugs prescribed and reimbursed, medical devices, lab tests, imaging (but not medical indication or results) with prescriber and professional caregiver information (specialty, private/public practice), code, dates of prescription and completion, total and reimbursed costs
  • Data are regularly uploaded with a lag time of 6 months to have 98% of information uploaded

➢ **Hospital discharge summaries database (PMSI)**
  • Includes ICD-10 codes for primary diagnosis, associated diagnosis, and linked diagnosis for ICD-10 Z-codes (e.g. chemotherapy), for all private and public medical, obstetric and surgery hospitalizations, with the date and duration of hospitalization, medical procedures, and cost coding system (Diagnostic Related Group), as well as most very expensive drugs. The hospital discharge summary includes the medical unit summaries
  • Data from psychiatry, and rehabilitation centres are also available but not yet in EGB
  • PMSI data are available yearly in the SNDS, during the third trimester of current year for the data of previous year (during the first trimester of following year in the EGB)

➢ **National death registry (CépiDC) :** It provides date of death and causes of death, starting to be included (at this time: years 2013 – 2015)

➢ **SNDS access - https://www.snds.gouv.fr/SNDS/Accueil**
  • A new process was adopted by Parliament in 2016, with the creation of a single gatekeeper, INDS (National Institute of Healthcare Data)
  • Access to SNDS data is authorized only for research with public health interest
  • Access to SNDS itself is subject to approval from national data protection agency (CNIL) after advice from a committee on healthcare data research (CEREES)
  • The linkage of individual patients to their claims data is now possible after authorization by a committee for protection of persons involved in biomedical research (CPP) and CNIL, and of course patient consent
  • Data access can be requested by any legitimate entity, public or private, as long as the study objectives are in the interest of public health, and means are provided to ensure confidentiality, integrity, and traceability of data and its usage, and the information is not used for drug promotion
  • Pharmaceutical companies can access SNDS via accredited public or private research organizations or directly if they can ensure they cannot use the data to promote their drugs
  • Considering the complexity of the data and the step learning curve, it is expected that most accesses will be through specialized entities

BPE's Expertise in SNDS

➢ **Bordeaux PharmacoEpi (BPE)** is a labeled platform of Bordeaux University dedicated to research in pharmacoepidemiology:
  • Created in 2003 and accredited by INSERM since 2008 as the Pharmacoepidemiology Unit of the Bordeaux Clinical Investigation Centre (CIC1401)
  • BPE Quality Management System is certified ISO 9001:v2015
  • Respect of the ENCePP code of conduct (European Network of Centres for Pharmacoepidemiology and Pharmacovigilance)
  • > 30 field studies (from 50 to 46 000 patients) and > 50 studies using population databases (SNDS notably)
  • Over 100 publications in pharmacoepidemiology for the past 5 years

➢ With 15 years of experience in analysis using SNDS data, BPE developed:
  • A dedicated secured IT environment, the "Bulle BPE", compliant with the French safety referential for SNDS data hosting, with the safety requirements set out by the French government and with the EU General Data Protection Regulation GDPR. BPE is able to physically host subsets of SNDS on site, for the application of sophisticated statistical methods or analytic tools other than SAS® that are not accessible on the public access portals (Figure 2).
  • A simplified and optimized SNDS relational Data Model, the "BPE Data Model":
    – Patient-centered: 1 unique joint key (*versus up to 9 in the original SNDS*)
    – With a limited number of tables : 14 tables (*versus 123 for one year and up to 1 000 for long-term follow-up*)
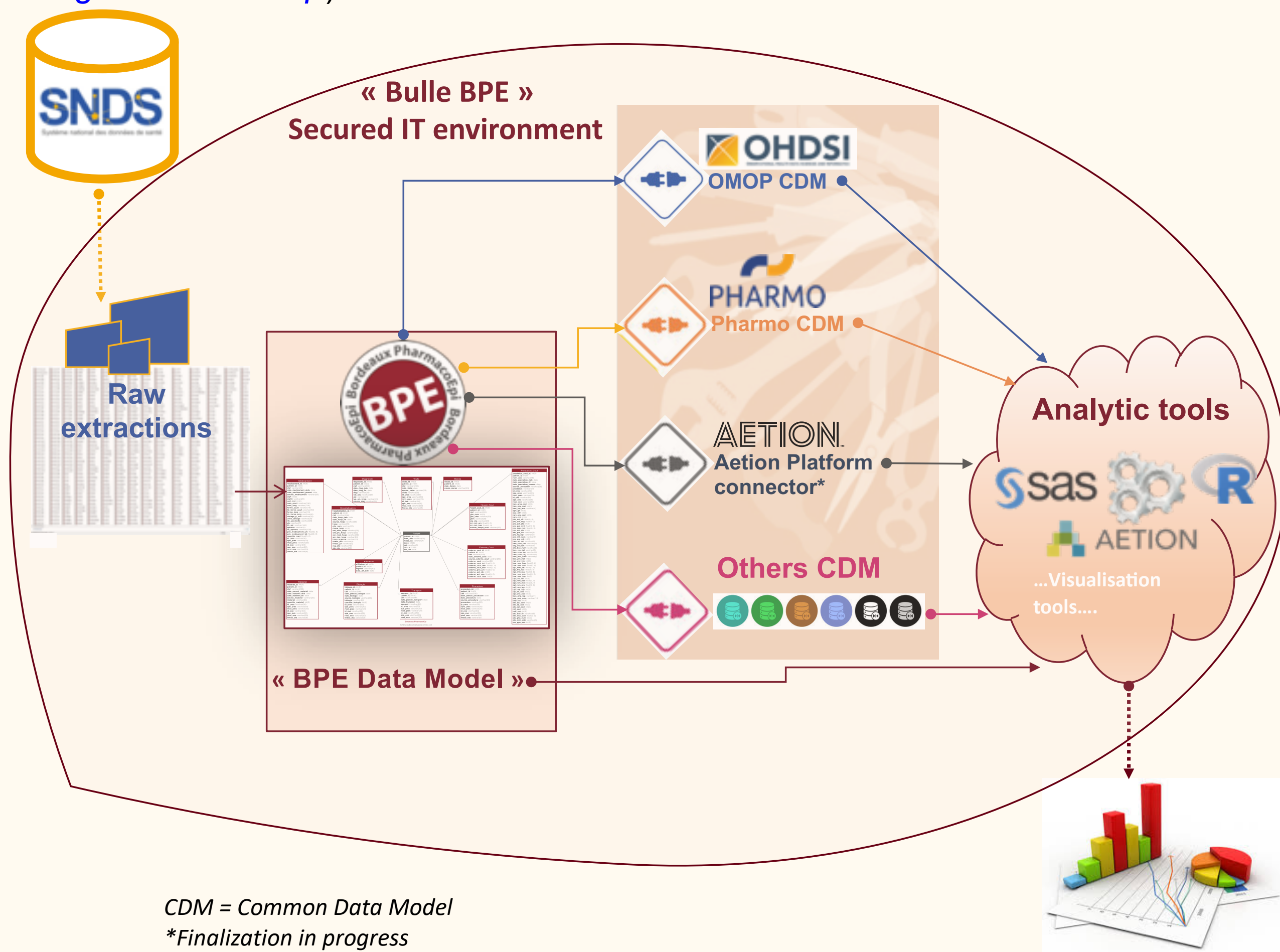

CDM = Common Data Model
*Finalization in progress

Figure 2. Tools for exploiting SNDS data "Bulle BPE" & "BPE Data Model"

➢ Over the last 15 years, BPE has carried out more than 50 studies using national health insurance database, mostly SNDS, such as :
  • Disease-based studies
    – Disease epidemiology and the use of diagnostic algorithms
    – Disease treatment patterns and unmet needs
    – Disease management
    – Drug-related risk identification and alert generation
  • Drug-based studies
    – Drug utilisation studies
    – Risk identification and quantitation,
    – Comparative drug effectiveness and risks
  • Methodological research
  • Mixed studies: cohort or registry with a secondary link to SNDS databases

➢ Some examples of BPE studies are presented on Table 1, see more details and publications on our website **www.bordeauxpharmacoepi.eu/notre-expertise/etudes-snds/**

Table 1: Examples of BPE study using SNDS Database

Cardiology	
ENGEL-1A	REal-life aNticoaGulants bEnefit-risk in atrial fibrilLation in France
ENGEL-2	REal-life aNticoaGulants comparative bEnefit-risk in nonvalvular atrial fibrillation (NVAF) in France
BROTHER	Benefit-Risk Of arterial THrombotic prEvention with Rivaroxaban for atrial fibrillation in daily clinical practice
HORUS	Health Outcomes, Resource Use, costs in patients with Stable coronary artery disease a cohort study in the EGB database
SPACE-AA	Secondary Prevention of Acute Coronary Events with Antiplatelet Agents: A cohort study in the SNIIRAM database
ATTOS	Benefit and risk of AntiThrombotic Treatments after Orthopaedic Surgery in real-life settings: a cohort study in the SNIIRAM claims and hospitalisation database
ATHENA-F	Assessment of The High risk and unmEt Need in patients with coronary artery disease and type 2 diabetes in France
Oncology	
GROC	Glargine and risk of cancer
CAMERRA	Therapeutic strategy in metastatic castration-resistant prostate cancer: target population and changes between 2012 and 2014
Hepatotoxicity	
EPIHAM	Epidemiology of acute hepatotoxicity from medicines
Effectiveness, safety & DUS studies	
EVIDEMS	Effectiveness of Tecfidera® in multiple sclerosis: a French cohort within the nationwide claims and hospital database
DUS	Drug usage patterns of Pylera® in France using the national claims reimbursement database
DIORAMA	Resistant Depression in France, description from the nationwide claims and hospitalization database
Multi-country DB studies	
IV-IRON	Intravenous Iron Postauthorisation Safety Study (PASS): Evaluation of the Risk of Severe Hypersensitivity Reactions
EU-DOAC	Characterising the risk of major bleeding in patients with Non-Valvular Atrial Fibrillation: non-interventional study of patients taking Direct Oral Anticoagulants in the EU
MALBEC	Malignancies in Multiple Sclerosis: multi-country cohort database studies
Methodological research (in addition to methods research embedded in all the other studies)	
ALCAPONE	Alert generation using the case-population approach in the French claims databases
ECOSTIM	Budget impact analysis of discontinuing Tyrosin Kinase Inhibitors in patients with chronic myeloid leukemia achieving a complete molecular response by using probabilistic Markov approach

Conclusion

The SNDS brings a major actor to pharmacoepidemiology, providing a nationwide resource with tremendous power, allowing BPE platform to participate in numerous international multi-country multi-base projects and to access to other databases in Europe and the USA through international collaborations.