Why France is the Go-To Country to Conduct Real-World Studies

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Foreword

The growing use of real-world data is dramatically changing many businesses. Look at how safety is improving in the airline industry or how the customer experience is changing in retail business.

The healthcare industry is undergoing the same revolution. With real-world patient data, we can continuously monitor epidemiology, assess the impact and safety of treatments, or study the patient care pathway.

Data can also be used to improve healthcare professionals' activity and to develop new tools and treatments. Its use is limitless. This was proven by the management of Covid-19.

In France, the French National Health Data System (SNDS) is an important patient-level database that provides an impressive overview of the care provided to 66 million people. Access to the SNDS was opened in 2017. The SNDS has proven to be one of the essential sources of health data to meet many needs, especially those of the life science industry and health authorities.

Whilst committed to protecting individual privacy, IQVIA is investing heavily in using this data source and linking it to several others to help healthcare stakeholders improve care.

This document presents the fruits of our five year-experience in conducting studies on these health data records. It covers:

- The establishment of data governance and access arrangements
- The immense potential for the development of innovative health care practices
- The limitations that need to be overcome

It also concludes with our key recommendations for conducting successful real-world studies in France.

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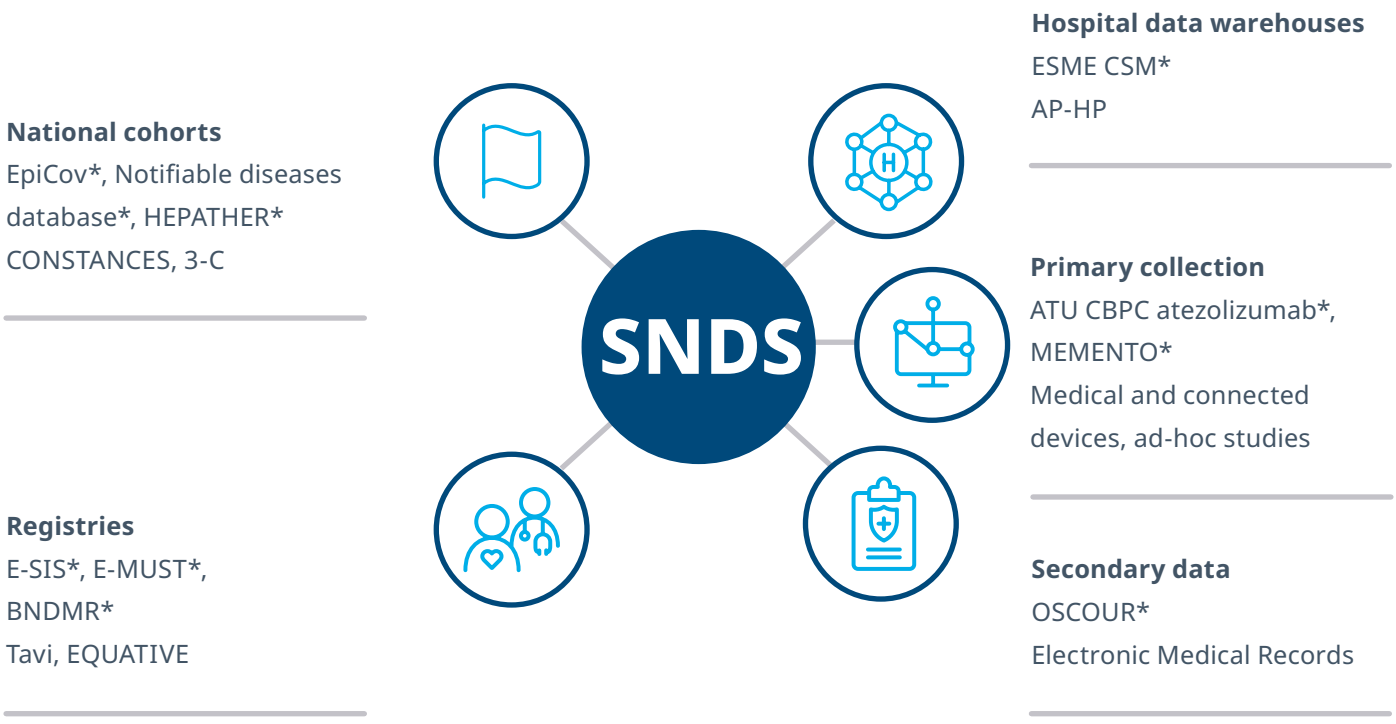
The unique French health data ecosystem

The French National Health Data System (SNDS) is the largest claims database in Europe. This medico-administrative database covers both primary and secondary care claims for 99% of French citizens, representing 66 million people. The SNDS is the pinnacle of almost two decades of regulatory amendments aiming to structure, organize and compile multiple datasets owned by different public health bodies.

- 2002: The French National Health Insurance Fund (CNAM, Caisse Nationale d'Assurance Maladie) combines all primary care claims into a single database (i.e., Système National InterRégimes de l'Assurance Maladie: SNIIRAM)
- 2009: SNIIRAM is linked to secondary care data (i.e., Hospital Discharge Database: PMSI)
- 2017: Health Data Commission provides access to the combined dataset, renamed SNDS, to the private sector, upon a robust evaluation process ensuring patient privacy and ethical use of the data
- 2019: The Health Data Hub (HDH) is created to facilitate data access and promote the use of Artificial Intelligence (AI)
- 2022: The National Health Insurance Fund releases a user-friendly interface for the public to access high level analysis of its data
- 2023: Health data warehouses are funded and deployed

Today, the SNDS has established itself as the backbone of the French data ecosystem and efforts are underway to expand its capabilities even further. Secure data warehouses will allow SNDS to be permanently linked to rich external data (Figure 1).

Figure 1: Linking datasets to gain insights on the full patients' picture



*These datasets are already included in the Health Data Hub catalog. Constances, 3-C, Tavi, Equative, AP-HP are linked to the SNDS (non exhaustive) but their inclusion in the Health Data Hub catalog is not planned or is still ongoing.

Setting up the data warehouses is a current focus of public authorities, and the French government launched a call for project proposals in March 2022 for the establishment of a France-wide hospital data warehouse network, with a fund of 50 million euros.[1] The HAS (Haute Autorité de Santé) published a report in October 2022 and the permanent connection of the SNDS to hospital data warehouses is one of its key recommendation:[2] "Combining outpatient data and hospital data would finally provide a complete picture of patient care. The HAS recommends that consideration be given to systematizing the reconciliation of hospital data warehouses and billing data".

Claims data will be enriched with clinical data coming from private and public hospitals, increasing the depth of accessible healthcare data that can further improve treatment pathways and patient outcomes. For healthcare stakeholders, the data landscape in France is growing in complexity, but also in opportunity. The use of clinical datasets linked to the SNDS will save time and money in setting up replicative studies to obtain similar data for regulatory and exploratory studies. Rare diseases will benefit the most from linking registries to the SNDS, which will significantly reduce study costs for this market, facilitate patient enrolment, and speed up and simplify the data access process. This is the near future: the National Data Bank for Rare Diseases (BNDMR) has already submitted its future registration to the HDH, ensuring its permanent linkage to the SNDS.[3]
The French health data ecosystem is evolving and mutating rapidly, catapulting new uses in real-world evidence generation.

Leveraging innovative study designs

Since 2017, the number of studies using SNDS data conducted by national and international companies has considerably risen. The use of SNDS data was mainly limited to epidemiological, safety and economic studies. As the experience of both providers and pharmaceutical companies increased, the discussion on study design evolved accordingly. Aware of the access timelines, pharmaceutical companies want to optimize trials and new designs have emerged. These new designs are based on the newly available data sources, methods and technologies and are increasingly recognized by regulatory authorities such as the FDA,[4] EMA[5] and HAS.[6]

- **Randomized Controlled Trial (RCT) enrichment:** Phase III trials or roll-over (extension) studies can be enriched with real-world data (RWD) bringing new information about patients and allowing new types of insights.
- **Artificial intelligence (AI) & Machine Learning (ML):** Predictive algorithms applied to real-world data can help identify patients or groups of patients at risk.
- **External comparators:** Access to pseudonymized individual-level data enables the use of propensity score-based methods or outcome modeling, paving the way for external comparator studies using the SNDS. External comparators may complement or even replace controls (Single Arm Trials: SAT) in randomized clinical trials.
- **Pragmatic clinical trials aim** at improving both the efficiency of generating clinical evidence and the relevance of that evidence to real-world practice. Pragmatic trials may differ from traditional or explanatory clinical trials in several ways, including the recruitment of more heterogeneous participants from typical practice settings, greater flexibility, and variability in the delivery of interventions, and the ascertainment of outcomes from real-world datasets.
- **Organizational Impact:** Real-world data can be used to assess or monitor the impact of a device or a drug on the healthcare system (e.g., patient pathways, approach to care, efficiency).

These methods are just the beginning of the new possibilities offered by the breadth and depth of SNDS data.

The future new capabilities of the SNDS will place it at the forefront of Real-World Evidence (RWE) generation for pharmaceutical companies and researchers to improve patient outcomes.

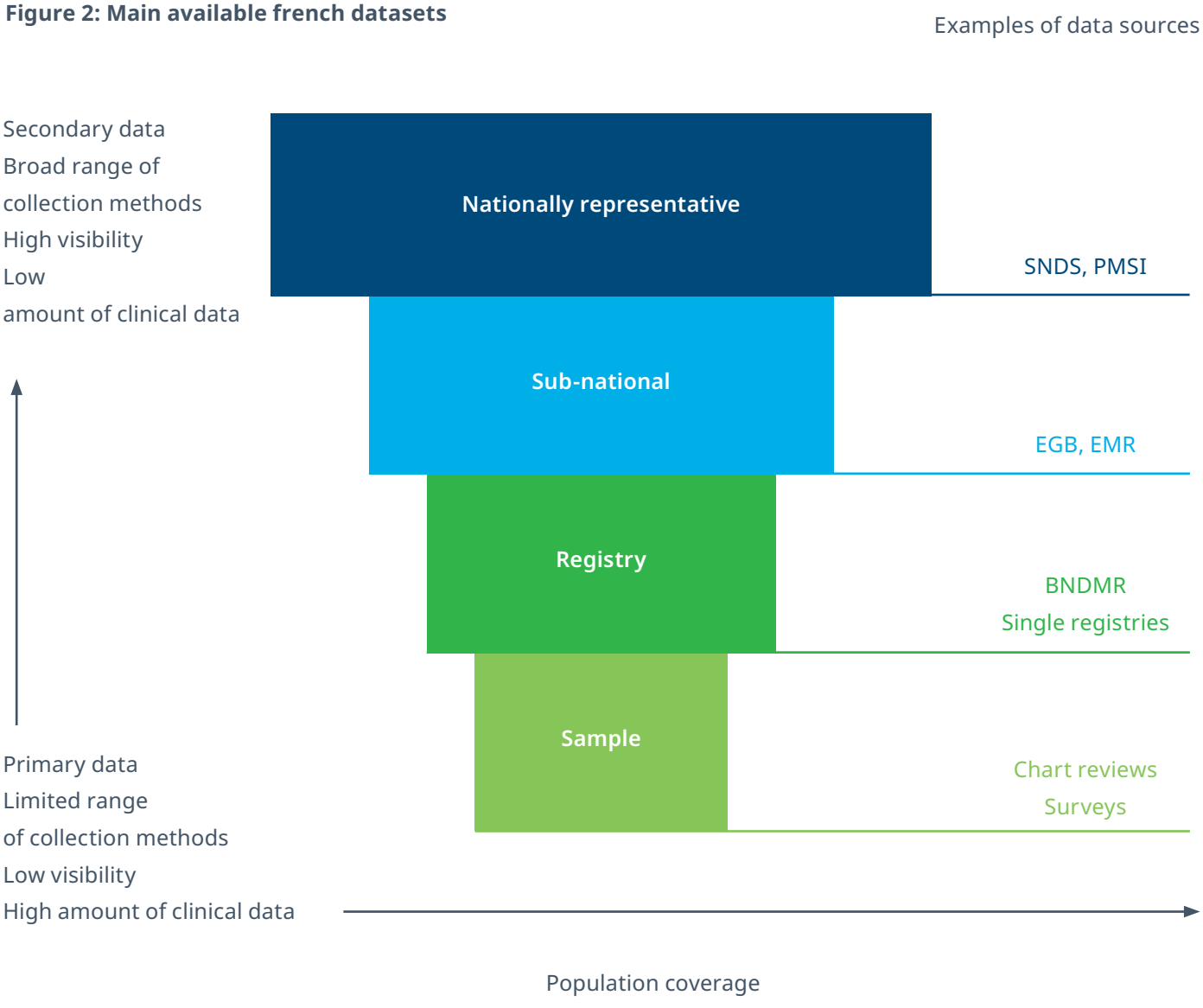
However, the SNDS must overcome challenges such as regulatory delays and data quality to truly fulfill its promises. These considerations are a priority, and constitute the first axis of the HDH multi-year plan for 2023-2025.[7] The choice of dataset still needs to be carefully considered when generating RWE, as the SNDS may not be the optimal choice.

Generating insights from a wide range of French datasets

The SNDS is not a one-size-fits-all database for all study needs.

Discussions with data experts are critical during the early feasibility and design phases of the projects to tailor the best solution in the real-world data landscape. Existing datasets have different characteristics, including data collected or time to access, which must be carefully considered (Figure 2).

Figure 2: Main available french datasets



The IQVIA Real-World Solutions team has recently made available and summarized the IQVIA and French databases available for research (Figure 3).[8]

Depending on the research question(s), we can easily assess the relevance and quality of these databases and identify the right ones.

Figure 3: Example of datasets regulatory needs for access

	LRx	EMR	PMSI	New ESND	SNDS	SNDS enriched with database	SNDS enriched with PDC
Requires protocol	✓ (but not mandatory)	✓ (but not mandatory)	✓	✓	✓	✓	✓
Requires publication	✗	✗	✓	✓	✓	✓	✓
Regulatory process (excluding physicians' implication)	Simple and fast track (MR004)	Simple and fast track (MR004)	Fast track (MR006)	Fast track vs. SNDS (CESREES + CNIL+CNAM)	CESREES+ CNIL+ CNAM	CESREES+ CNIL+ CNAM	CPP+ CNIL+ CNAM
Data access timelines	Immediate	Immediate	Immediate once protocol submitted	4-6 months	8-10 months	10-16 months	18-24 months
Data access fees (situation in 2023)	✓	✓	✓	✗	✗	✓	✗
Study timelines	5-8 months	5-8 months	3-8 months	8-10 months	18-20 months	20-30 months	30-36 months

Conducting successful studies from design through to insights: our recommendations

Using a wide variety of privacy-enhancing technologies and safeguards to protect individual privacy, our Real-World Solutions experts can generate and analyze information on a scale that helps healthcare stakeholders identify disease patterns and correlate with the precise treatment path and therapy needed for better outcomes. With more than 50 projects completed, the IQVIA Real-World Solutions team has more than 80 person-years of combined experience with the SNDS. In Figure 4, we present several key success factors we identified in conducting RWE studies at each stage.

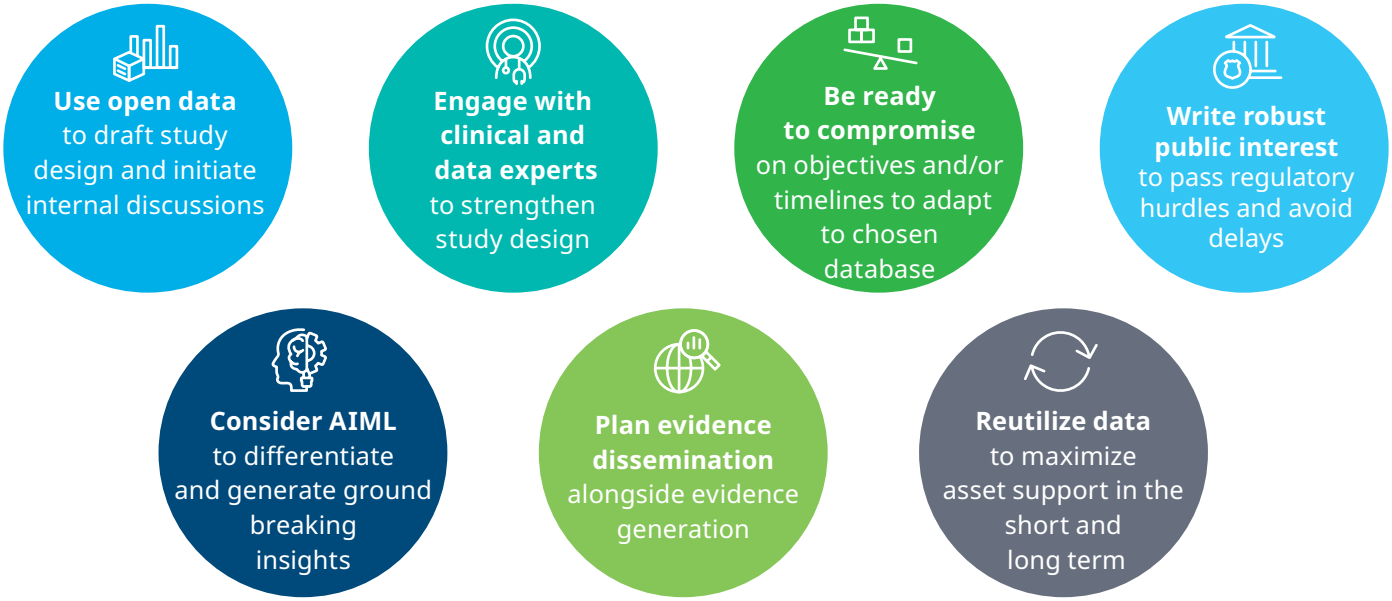
In the early phase of the study, open data, such as CNAM open Damir or open Medic datasets,[9] can provide initial metrics for the study design and enrich internal discussions about the study requirements. Bringing clinical experts and data scientists into the process as early as possible is critical to refine the study design and objectives. Experts are also critical to carefully select a dataset, considering feasibility and adjusting the objectives or timelines accordingly.

After the design phase, data access depends on the regulatory process. The public interest of the study must be carefully written to overcome regulatory hurdles, with optimized study objectives, study periods, sample size estimation, and a mindful evaluation of the need for external data and clinical practice. Nearly half (25 out of 55) of the projects submitted in 2022 did not receive regulatory approvals.[10] In addition, the datasets extracted by the CNAM must be quality controlled for consistency in population targeting and linkage. Delays may occur if data do not meet quality requirements and need to be re-extracted.

Once the data are available, the analysis may be extended in ways that were not planned at the early design stage, such as analysis of sub cohorts that were later identified. This may delay the end of the study but also provide interesting results. In addition, innovative methods such as AI-ML may be considered to provide differentiation and breakthrough insights.

After or in parallel with the end of the study, the evidence generated must be communicated to the public in the form of publications or scientific communications on platforms such as congresses. Data can be reused in future projects.

Figure 4: Key success factors to consider when conducting RWE studies



Abbreviations

AI	Artificial Intelligence
BNDMR	Banque Nationale de Données Maladie Rares; National Data Bank for Rare Diseases
CESREES	Comité Ethique et Scientifique pour les Recherches, les Etudes et les Evaluations dans le domaine de la Santé; Ethical and scientific Committe for health research
CNAM	Caisse Nationale d'Assurance Maladie; National Health Insurance Fund
CNIL	Commission Nationale de l'Informatique et des libertés; French Data Privacy Agency
EMA	European Medicines Agency
EMR	Electronic Medical Records
ESND	Nouvel Echantillon du Système National de Données; Novel Generic Sample of Benificiaries
EU	European Union
FDA	United states of America Food & Drug Administration
Insee	Institut National de la Statistique et des Etudes Economiques; National Statistics Institute
HAS	Haute Autorité de Santé
HDH	Health Data Hub
ML	Machine Learning
PMSI	Programme de Médicalisation des Systèmes d'Information; Hospital Discharge Database
RCT	Randomized Clinical Trials
RWD	Real-World Data
RWE	Real-world Evidence
SAT	Single Arm Trials
SNDS	Système National des Données de Santé, National Health Data System
SNIIRAM	Système National InterRégimes de l'Assurance Maladie

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Prior to joining IQVIA in 2018, Cédric has held different roles, lately in the French Health Product Agency (ANSM) both in the Health Product Epidemiology department and in the Psychotropic and Narcotic Drugs Department (misuse, off-label use of psychotropic drugs from SNDS data).

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