Insights Brief

Why You Should Consider France for Your Real-World Evidence Strategy

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Foreword

The growing use of Real-World Data (RWD), data generated in everyday practice, is dramatically changing the field of healthcare. Leveraging RWD enables to continuously monitor epidemiology, assess the impact and safety of treatments, or study the patient care pathway.

Turning RWD into evidence can also be used to improve healthcare practice and to develop new tools and treatments. Its use and potential for improving patient outcomes is limitless. This was proven during the management of COVID-19, where regulatory bodies relied on RWD to complement the benefit-risk profile for marketing authorization of the rapidly-approved vaccines.[1]

The success lies in the quality of the data, its robustness and relevance to address the research question but also its process and analysis. In France, IQVIA have access to the unique French National Health Data System (SNDS), a patient-level database that provides an impressive overview of the care provided to 66 million people. Access to SNDS was made available in 2017; since then the SNDS has proven itself an essential source of health data, meeting needs across both public health and industry to improve patient outcomes. IQVIA was one of the first clinical research organizations (CROs) to be granted access to SNDS, putting them at the center of the health data ecosystem, working closely with health bodies, the SNDS and industry).

IQVIA is investing in optimizing this data source, together with several others, to help healthcare stakeholders improve care. As such, IQVIA recently won the bid to support the Health Data Hub in maximizing SNDS data for the healthcare ecosystem, supporting stakeholders to further leverage RWD.

This document presents the fruits of our seven-year experience in conducting studies in the unique French health data ecosystem. It covers:

- The potential France offers for RWE strategy
- The importance of optimal dataset selection
- Recommendations for conducting successful RWE studies in France and overcoming potential limitations

In conclusion, it is a distinct honor and pleasure to observe the transformative journey of the French healthcare system and witness IQVIA's adept harnessing of Real-World Evidence to enhance decision-making. Our vision is to empower healthcare stakeholders to efficiently generate and disseminate evidence, thereby informing decisions and ultimately enhancing patient outcomes. By sharing insights accumulated over the years, we aim to illustrate that IQVIA Real World Solutions is excellently positioned to offer valuable guidance on optimizing use of RWE stemming from the French healthcare system and ultimately a successful implementation of your RWE strategy.

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Head of Real World Solutions 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. The SNDS is the pinnacle of two decades of regulatory efforts to structure, organize and collate multiple datasets owned by different public health bodies.

This medico-administrative database now covers both primary and secondary care claims for 99% of French citizens, representing 66 million people. The private sector has access to the SNDS, subject to a rigorous approval process ensuring patient privacy and ethical use of the data.

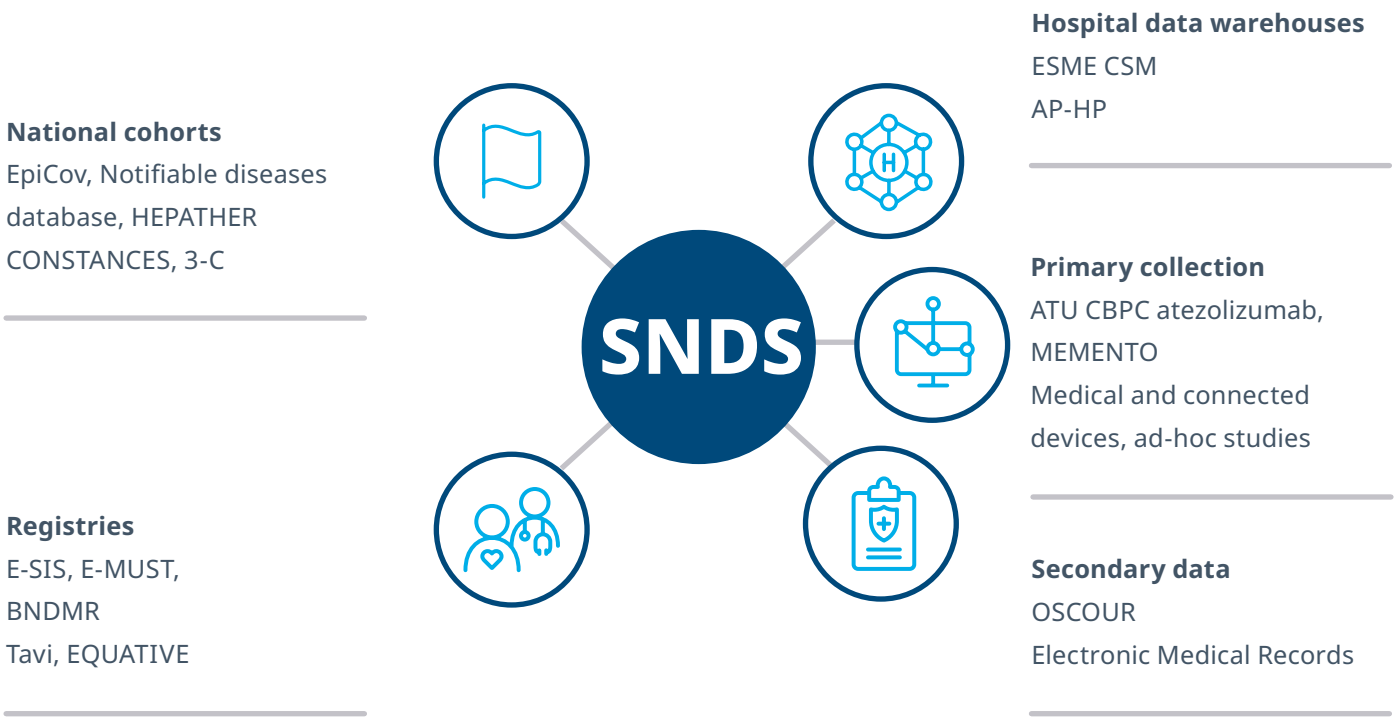
Today's SNDS

Today, the SNDS has established itself as the backbone of the French data ecosystem and efforts are underway to expand its capabilities even further by connecting the SNDS with secure data warehouses, which will allow the SNDS to be enriched with external data (Figure 1).

The French National Authority for Health (HAS) recently recommended the permanent connection of the SNDS to hospital data warehouses: "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".[2]

This is now a current focus, with the French government calling for proposals in March 2022 for the establishment of a France-wide hospital data warehouse network, with a fund of 50 million euros.[3]

Figure 1: Linking datasets to map patient journey and outcomes

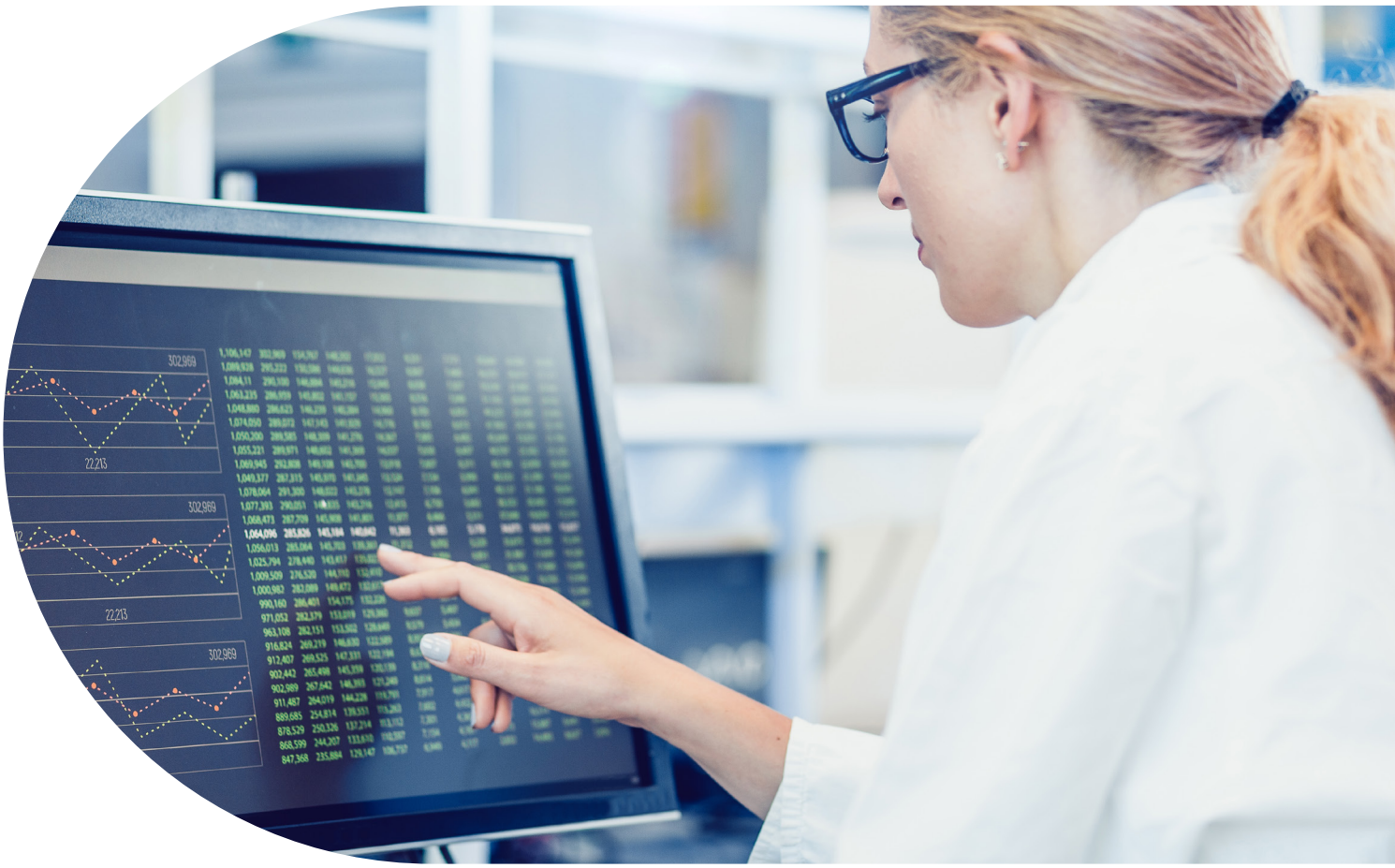


Datasets are already included in the Health Data Hub catalog.
Constances, 3-C, Tavi, Equative, AP-HP are examples of datasets whose inclusion in the HDH catalog are a work in progress or not planned but are linked to the SNDS (non exhaustive).

What's next for the SNDS?

- The enrichment of claims data with clinical data will increase the depth of the SNDS data, enabling further improvement of treatment pathways and patient outcomes
- Optimal 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. Being able to access rare disease data with the SNDS as opposed to via registries will significantly reduce study costs, facilitate patient enrolment, and speed up and simplify the data access process. This is already underway: the National Data Bank for Rare Diseases (BNDMR) has already submitted its future registration to the HDH, ensuring its permanent linkage to the SNDS.[4]

"The French health data ecosystem is maturing and evolving rapidly, pioneering new uses in RWE generation, making it an exciting proposition for RWE strategies."



The French SNDS enables the use of innovative study designs

Since 2017, the number of studies using SNDS data has risen considerably. Previously, the use of SNDS data was mainly limited to epidemiological, safety and economic studies. As healthcare providers, public health and industry have gained experience, the discussion around study designs has evolved accordingly.

Extending the use of the SNDS with innovative study designs

Aware of challenges with SNDS access timelines, pharmaceutical companies aim to optimize their trials, with innovative new designs emerging. These designs take into account newly available data sources, methods and technologies, and are increasingly recognized by HTA authorities such as the FDA,[5] EMA,[6] and HAS:[7]

- **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
- **Organizational impact**: RWD 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)
- **Randomized controlled trial (RCT) enrichment**: Phase III trials or roll-over (extension) studies can be enriched with RWD, providing additional patient information and resulting in new, more meaningful insights
- **Pragmatic clinical trials**: These aim to improve both the efficiency of clinical evidence generation 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 inclusion of more representative participants from typical practice settings, greater flexibility and variability in the delivery of interventions, and the generation of outcomes from RWD
- **Artificial intelligence (AI) & Machine learning (ML)**: Predictive algorithms applied to RWD can help identify patients or groups of patients at risk, leading to the development of tailored and targeted prevention campaigns to improve public health

These innovative study designs are just the beginning of the new possibilities offered by the breadth and depth of SNDS data. The future capabilities of the SNDS will place it at the forefront of RWE generation for public health, industry and research to improve patient outcomes.

Potential yet to be reached

In order to fulfill the promise it offers, the SNDS must overcome challenges such as regulatory delays and data quality issues. These considerations have been prioritized and constitute the first axis of the Health Data Hub multi-year plan for 2023-2025.[8] The choice of dataset still needs to be carefully considered when generating RWE, as the SNDS may not be the optimal choice for every study.

The ESND is an alternative to the SNDS that should be considered, as the study timelines are reduced and the study population is not too rare. In fact, its fast-track access makes it possible to carry out epidemiological studies with shorter milestones.

All studies need to demonstrate they are in the public interest, or they risk being denied regulatory approval. With their experience and in-depth knowledge of the SNDS and other available data sources, the IQVIA Real World Solutions team is well-placed to advise on which dataset would be most suitable for a particular data-generation requirement.

Partnering with IQVIA to devise your RWE strategy

It is critical to work with data experts during the early feasibility and design phases of a study to consider all the available real-world datasets to tailor a solution which answers a particular evidence challenge.

IQVIA Real World Solutions leverages unparalleled data assets, with a deep understanding of the existing datasets, and their different characteristics (including type of data and time to access), factors which should be carefully considered when developing a solution. Figure 2 provides a topline summary of some IQVIA proprietary and public French databases available for research.[9]

IQVIA Real World Solutions works closely with their public health or industry partners to evaluate their complex research questions and decide the right approach to take. With expertise in multiple therapeutic areas, and across functions (medical, regulatory, HTA and RWE), they will assess and identify which data sources will generate the right RWE to meet stakeholders' needs with confidence and get real results.

Figure 2: Example of datasets regulatory needs for access[9]

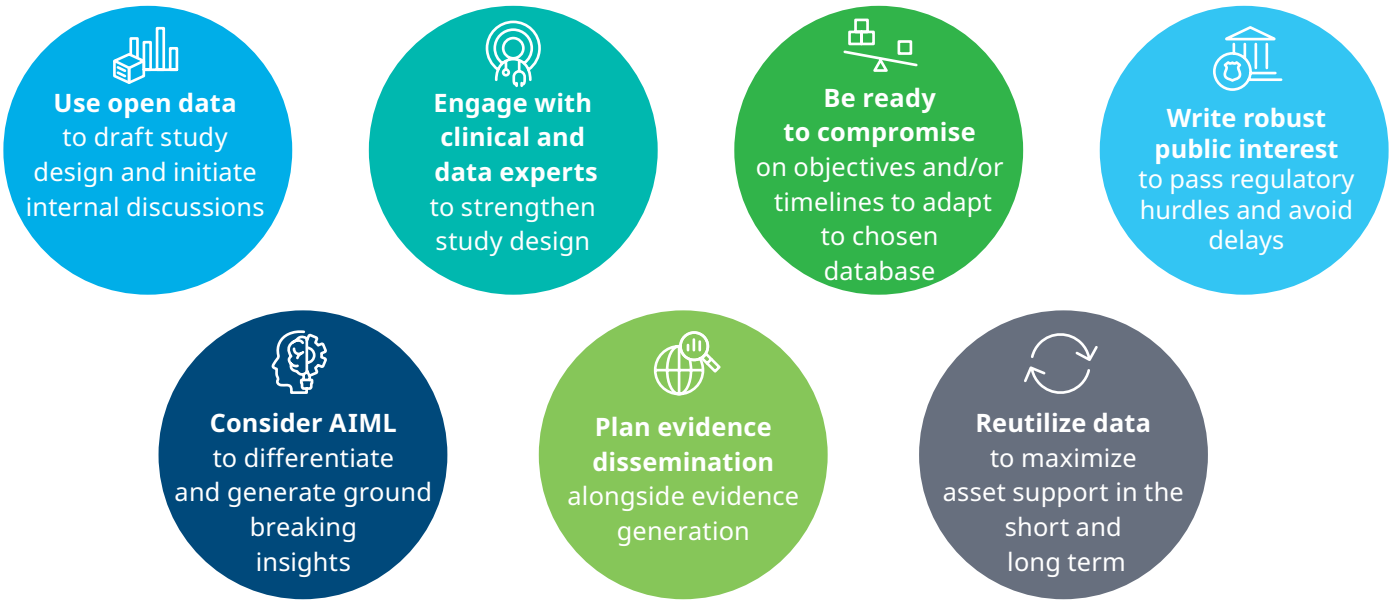
	LRx	EMR	PMSI	ESND	SNDS	SNDS enriched with database	SNDS enriched with PDC
Requires protocol	✓ (but not mandatory)	✓ (but not mandatory)	✓	✓	✓	✓	✓
Requires publication	✗	✗	✓	✓	✓	✓	✓
Regulatory process (excluding physicians' involvement)	Simple and fast track (MR004)	Simple and fast track (MR004)	Fast 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

Generating the right information for a RWE study is critical but finding the right datasets and designing the optimal study design can be daunting. There are several key stages that IQVIA Real World Solutions have identified for conducting successful RWE studies. This includes:

- Bringing clinical and data experts into the process as early as possible is critical to refining the study design and objectives. Experts are also key to carefully selecting a dataset, considering feasibility and adjusting the objectives or timelines accordingly. Privacy protection is also an essential factor throughout the process
- Demonstrating the study's public interest is essential to overcoming regulatory hurdles in accessing the required data. Expert knowledge here is key, with nearly half (25 out of 55) of the projects submitted [to the SNDS] in 2022 not receiving regulatory approval[10]
- Implementing quality control of the datasets for consistency in population targeting and linkage is important to avoid delays
- Once the data is available, as needs evolve, and with the right expertise, the analysis may be extended, e.g. 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 suggested to provide differentiation and breakthrough insights
- Effectively disseminating the evidence generated to the relevant audience is fundamental to a successful RWE study. Experience in how to reutilize data for future projects can maximize assets in the short and long term

Figure 3: Key success factors to consider when conducting RWE studies



Abbreviations

CESREES	Comité Ethique et Scientifique pour les Recherches, les Etudes et les Evaluations dans le domaine de la Santé, Ethical and Scientific Committee 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' covers physicians' activity with access to all the coded medical and clinical information from patients' files
ESND	'Echantillon Système National des Données de Santé' is the 2/100th random permanent representative sample of health insurance database
FDA	United States of America Food & Drug Administration
LRx	'Longitudinal Prescription' data is a longitudinal patient prescription dataset based on retail pharmacy data. It enables the longitudinal tracking of patient prescription activity
PDC	Primary Data Collection — refers to observational studies using, at least partly, data collected directly from healthcare professionals
PMSI	'Programme de Médicalisation des Systèmes d'Information' (national hospital-discharge summaries database system) covers hospital activity on medicine, surgery, obstetrics (MSO), post-acute care and rehabilitation (SSR), hospitalization at home (HAD) and psychiatry (PSY)
SNDS	Système National des Données de Santé (French nationwide claims database) is the nationwide healthcare insurance system database which provides, for defined purposes, pseudonymized individual health data from the main medico-administrative databases

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With over 20 years' experience in Health Economics and Outcomes Research (HEOR) and Real-World Evidence (RWE), Frédérique is the scientific head of the IQVIA Real World Solutions' secondary data team.

Prior to joining IQVIA, Frédérique held various positions in life sciences organizations, including at AstraZeneca France, where she was the Director of the Center of Excellence for Real-World Data (RWD) and Evidence Synthesis Research (ESR) in the Oncology Business Unit.

She holds Postgraduate degrees in Health Economics and Industrial Strategies.

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Cédric has 12+ year experience in epidemiology and SNDS expertise; he is an epidemiology director of the secondary data team.

Prior to joining IQVIA in 2018, Cédric held different roles, most recently 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).

He holds a PhD in Pharmacoepidemiology.

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Building on 20+ years of experience at IQVIA, François is a principal in the secondary data team.

He has extensive experience in project management, particularly focusing on the utilization of existing databases such as Electronic Medical Records (EMR), Longitudinal Patient Databases (LRx), and the National Health Data System (SNDS), as well as observational studies.

François holds a Master's degree in Biochemistry.

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