FITFILE

Driving higher-powered observational studies

with larger populations and more valuable data

fitfile.com

In brief

Observational studies are often sub-scale in size and number, and not properly representative of real world populations.

FITFILE's solution can dramatically increase the size and completeness of studies whilst ensuring subject privacy is preserved at all times.

How? By enabling the previously unachievable unification of fully anonymised data from any source in global regulatory compliance.

I. **Background:** major regulators support the increased use of observational studies and generation of real world evidence (RWE)

Observational studies are increasingly accepted by regulators like the FDA and the EMA as a key route for providing critical RWE on long-term effectiveness and safety in a way that clinical trials cannot, and at a lower cost.[1]

The FDA published a framework for RWE in 2018[2] and has drafted further industry partner advice in December 2021[3] for the use of RWE to support regulatory decision-making for drugs and biological products.

The EMA recently undertook a retrospective analysis which revealed that 40% of initial marketing authorisation applications and 18% of applications for extension of indication for products currently on the market contained some form of RWE[4]. An EMA ambition is that RWE will be used more fully still across a spectrum of use cases by 2025[5].

RWE can support drug development, market authorisation, post-market authorisation requirements (including adverse event reporting) and deepening the understanding of disease epidemiology.

Observational studies typically require:

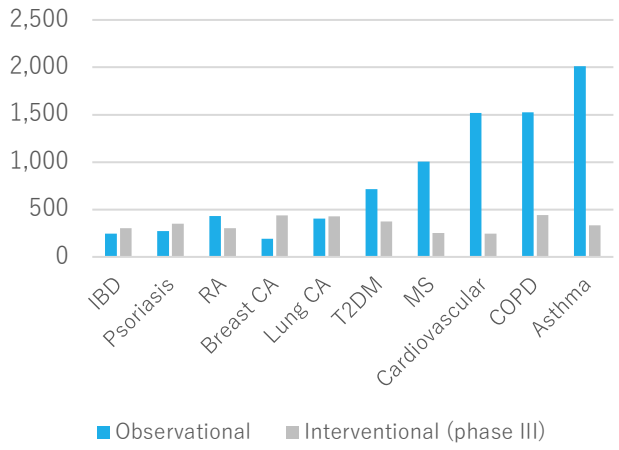
1. Long-term (often multi-year) **consistent** longitudinal monitoring of outcomes
2. An **accurate** granular view of the patient journey and treatment experiences in the real world
3. The largest economically feasible number of study subjects to provide a diverse and realistic population representation in order to generate **complete** insights into real world patient populations and sub-populations through appropriate stratification.

[1] Observational studies and their utility for practice, Gilmartin-Thomas and Liew, 2018
[2] Framework for FDA's Real world evidence program, FDA, 2018
[3] Guidance for Industry: Considerations for the use of real world data and real world evidence to support regulatory decision-making for drug and biological products, FDA, 2021
[4] A vision for use of RWE in EU medicines regulation, EMA, 2021
[5] Real - World Evidence in EU Medicines Regulation: Enabling Use and Establishing Value, Arlett et al, 2021

II. **The problem:** observational studies are still sub-scale

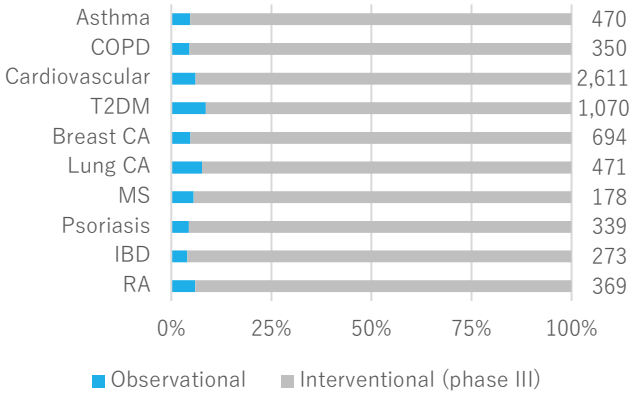
A proprietary FITFILE analysis of key therapeutic areas shows how both median participant enrolment and the total number of studies is frequently *smaller* for observational studies than phase III interventional studies, even though observational studies are supposed to proxy the real world with much larger study populations than earlier phase studies[6].

Median enrolment for key therapeutic areas



This could suggest individual studies as well as the total RWE population pool (i.e. the number of subjects per study multiplied by the number of studies) is arguably sub-scale and severely limiting the current power of observational study activity.

Number of active/ completed studies for key therapeutic areas



As an example, cardiovascular disease has 523 million sufferers around the world and is a leading cause of mortality with 18.6 million deaths a year[7]. This has made it a prime area of research interest, with 2,452 interventional trials taking place globally as at end-2021.

Against that number, the 159 observational studies conducted to date, whilst being the largest for any of the key therapeutic areas, still only represents a miniscule coverage of the global affected population and leaves plenty of room for greater observational study activity to develop a deeper understanding of phenotype, morbidity, mental health and functional impact.

By way of further example, whilst the median enrolment for Multiple Sclerosis (MS) observational studies versus phase III interventional studies is 4x higher, there are

[6] Extensive analysis based on clinicaltrials.gov (1965 – 2022)

[7] Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update from the GBD 2019 Study, Roth et al, 2020

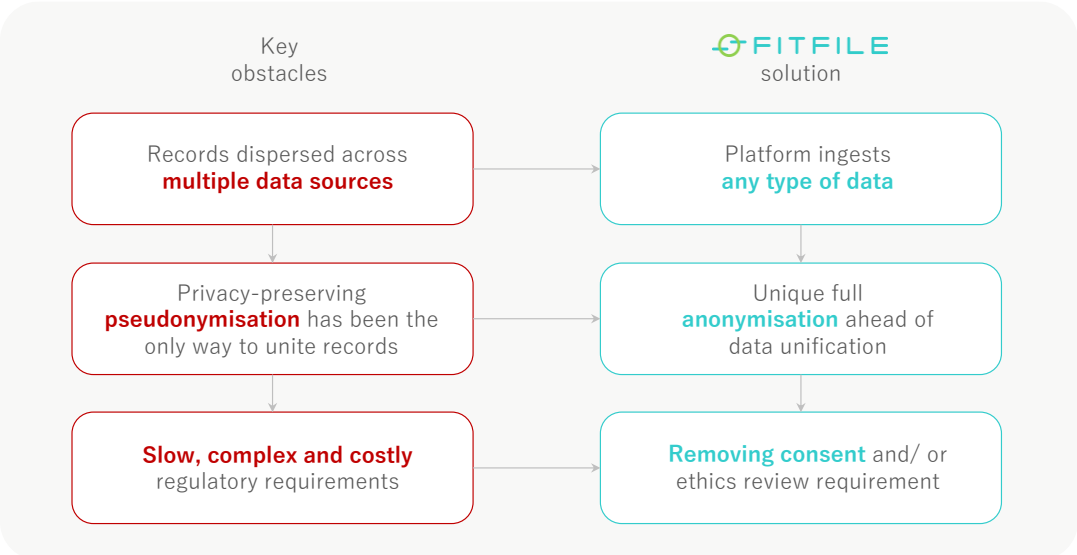
only 10 active/ completed observational studies compared to 168 phase III interventional studies. The total global observational study patient body for MS across the entire measurement period is 46,000, which is a mere 1.6% of global sufferers[8] and again highlights the sub-scale nature of observational studies.

III. **Underlying causes:** uniting data across multiple sources has been difficult

We believe sub-scale observational study activity is primarily due to the following factors:

1. **Multiple data sources** are typically required to generate a complete profile of outcomes
2. Until now, privacy-preserving unification of data across those sources has only been possible with **pseudonymisation**[9], a de-identification procedure whereby a key can reverse the process and restore the original identifiable state
3. This represents a threat to privacy and hence, studies have typically needed institutional review board ethics approval and/or to seek consent. These processes are **slow, complex and costly** – as evidenced by a separate proprietary FITFILE analysis which uses up-to-date calculations based on Noble, Donovan et al. (2009) to derive an estimated consent cost of $0.4 – 6.0 million per study, assuming 3 – 5 records per subject and 500 – 5,000 subjects.

IV. **Our solution:** directly addressing underlying causes



[8] Number of people with MS (2.8 million), Atlas of MS, Feb 2022

[9] Personally identifiable information is replaced by one or more artificial identifiers, typically using token-based approaches

The next-generation FITFILE solution has been purpose-built to address these factors with **consistent**, **accurate** and **complete** record-level evidence.

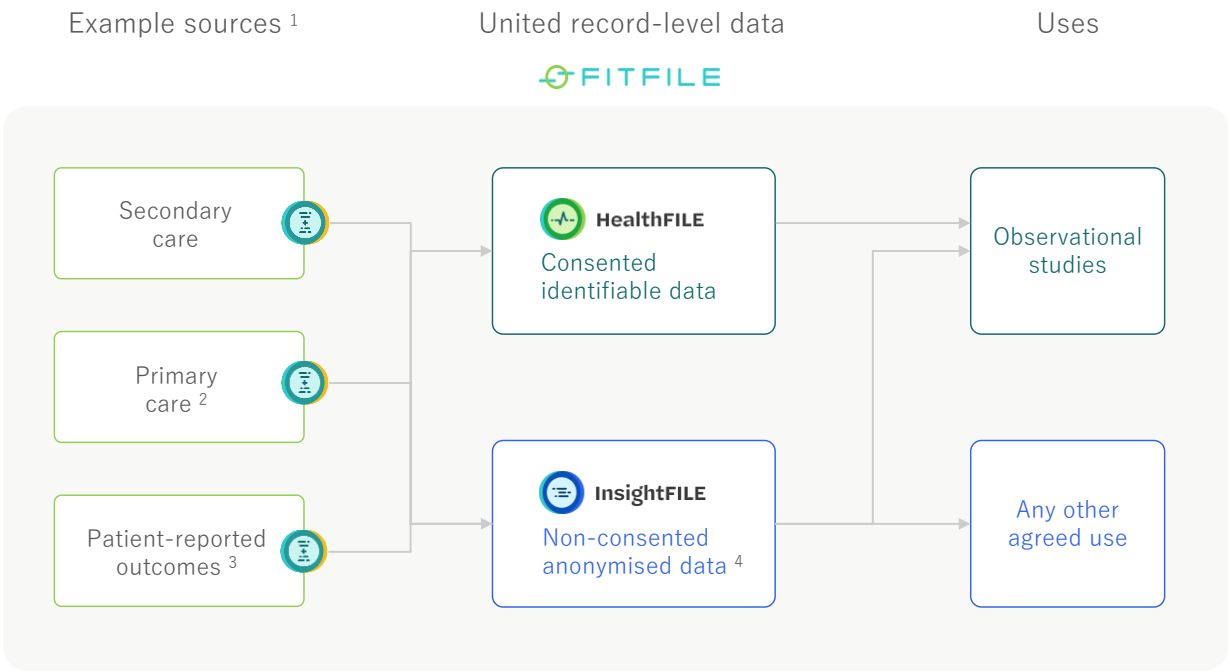
As shown below, a FITConnect software application ( ) is used within each data source regulatory perimeter. FITConnect is an easily deployed, modern data management platform that smoothly connects to any type of data source in any hosting environment. FITFILE has strong expertise of how to navigate governance, data protection and technology stakeholders in data settings.

The FITConnect applications are securely controlled by two separate FITFILE products.

1. **InsightFILE** delivers united record-level evidence from data that has first been *fully anonymised* by FITConnect within each regulatory perimeter, and
2. **HealthFILE** delivers *identifiable* united record-level evidence with consent (e.g. long-term follow-up) or legitimate patient care interest (e.g. for actioning adverse event reporting).

This solution powers **better, safer and faster observational studies at any scale**.

Please email us at contact@fitfile.com for further information and to join our fast-growing list of partners.



[1] Usage of FITFILE's software within regulatory perimeter of each data source is denoted by FITConnect
[2] Example primary care tracking of any signals of interest for expanded population/ triangulation
[3] Example tracking of patient-reported outcomes for enhanced longitudinal data and a more holistic view
[4] Unification of irreversibly anonymised data registered with U.S. Patent and Trademark Office (17/558,636) and with the EPO under priority declaration EP21216054

Better, safer, faster health data