# IMPROVE

Framework to IMPROVE the Integration of Patient Generated Health Data to Facilitate Value Based Healthcare

# D2.7: Practices report and updates V2

Version 1.0

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## History of Changes

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| 14.10.2025 | 0.1 | ToC of the deliverable |
| 24.10.2025 | 0.2 | Set-up of the methodology to analyse the practices and train the evaluators |
| 20.12.2025 | 1.0 | Final deliverable for peer review |
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## Statement of Originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

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## Abbreviations and Acronyms

| | |
|---|---|
| ConcePTION | Continuum of Evidence from Pregnancy Exposures, Reproductive Toxicology and Breastfeeding to Improve Outcomes Now |
| EHDS | European Health Data Space |
| EHDEN | European Health Data & Evidence Network |
| GDPR | General Data Protection Regulation |
| GREG | Generating Real-world Evidence to support Guidelines |
| HTA | Health Technology Assessment |
| IDEA-FAST | Identifying Digital Endpoints to Assess Fatigue, Sleep and Activities of Daily Living in Neurodegenerative Disorders and Immune-mediated Inflammatory Diseases |
| IHI | Innovative Health Initiative |
| IMPROVE | Integration of Patient Generated Health Data to Facilitate Value-Based Healthcare |
| PaLaDIN | Patient-centric Large-scale Data Integration for Health |
| PGHD | Patient Generated Health Data |
| PPIs | Patient Preference Information |
| PREMs | Patient-Reported Experience Measures |
| PROMs | Patient-Reported Outcome Measures |
| RWD | Real World Data |
| RWE | Real World Evidence |
| VBHC | Value-Based Health Care |

## Table of Content

## Executive Summary

This second version of the Practices Report presents an updated overview of the progress made in identifying, analysing, and structuring real world practices relevant to the collection and use of patient generated health data within the IMPROVE project. The work focuses on expanding the practice tracker, refining its methodology, and strengthening links with ongoing European initiatives that promote the adoption of patient reported outcomes, digital monitoring tools, and data driven decision making. Since the first version of the deliverable, the practice tracker has been further developed through systematic desk research, targeted outreach to organisations, and an expanded review of existing repositories of good practices. The mapping now covers a broader range of national and regional ecosystems that are implementing patient centred data approaches across clinical, research, and public health contexts in other Innovative Health Initiatives (IHI). The updated dataset also includes additional IHI projects that are relevant to PGHD and real world data infrastructures, which are outlined in Appendix A of the deliverable. These projects offer valuable methodological and organisational insights and strengthen the comparative value of the tracker. The work conducted in this update has focused on three areas. First, the identification of practices across Europe has been enhanced by clearer indicators for screening, selection, and assessment. This ensures higher consistency in the information captured and supports more robust comparison across contexts. Second, the project has increased engagement with programme managers and stakeholders from other IHI projects to gather insights into data collection workflows, governance structures, and barriers that affect the integration of PGHD. Third, exploratory work has begun with Utrecht University to investigate opportunities for partial automation of the practice tracker. This includes the potential use of structured extraction techniques and AI supported pattern recognition to reduce manual workload and improve scalability in the next project phase. The practices identified through this process contribute to a growing knowledge base that captures the diversity of approaches used across Europe to implement PGHD and patient reported measures in real settings. These insights support the co-creation of the IMPROVE framework and inform work in WP4 and WP5 by highlighting practical enablers and barriers related to interoperability, patient engagement, data governance, and organisational readiness.

Overall, this updated Practices Report demonstrates clear progress toward building a structured and actionable repository of implementation experiences. It provides a foundation for cross project learning, supports alignment with European evidence generation initiatives, and reinforces IMPROVE's aim to develop a sustainable, patient centred, and practice informed model for PGHD integration.

**Keywords**: Scientific; Policy; Practices; Tracker; Artificial Intelligence; Machine Learning

# 1. Introduction

## 1.1. IMPROVE approach

The IMPROVE project focuses on unlocking the value of Patient Generated Health Data through the use of m-health and e-health technologies. Its aim is to reduce the persistent fragmentation of patient-contributed data and strengthen the understanding of daily experiences, needs, and challenges of people of all ages living with complex chronic conditions and multiple comorbidities. The scientific, policy, and practice trackers play a central role in this effort. By integrating these components into the IMPROVE platform, the project creates a comprehensive mechanism for analysing ongoing initiatives, existing evidence, and practices across Europe. This approach enhances current methodologies for Patient Centered Outcome Measures by enriching them with real world insights that reflect the lived realities and preferences of patients.

IMPROVE is centred on the development of an advanced platform that enables the meaningful use of patient input and generated evidence. The platform supports three major areas of progress. First, it strengthens treatment selection by incorporating patient preferences and experiences to support more personalised decision-making. Second, it contributes to better medical device development by enabling direct integration of patient feedback into design and evaluation processes. Third, it supports faster adoption of innovative care models by helping bring patient focused and cost-efficient integrated care solutions to the market sooner. Through these developments, IMPROVE aims to foster broader uptake of Value-Based Health Care (VBHC) and increase the impact of research and innovation investments across European health systems. The project includes 10 use cases across at least five clinical domains: ophthalmology, oncology, cardiovascular disease, chronic inflammation, and neurology. A range of implementation strategies is applied, all based on design thinking principles that guide the testing, refinement, and validation of the project's data collection methods and their translation into actionable insights and structured change.

The project is expected to benefit significantly from implementation science to ensure that all relevant stakeholders are actively involved and that the solutions developed are realistic, scalable, and sustainable. By aligning in clinic and out of clinic PGHD with existing data streams, IMPROVE advances the use of Patient Reported Outcome Measures (PROMs), Patient Reported Experience Measures (PREMs), Patient Preference Information (PPIs), and other forms of patient derived data. This integrated approach supports the development of personalised and cost-effective care pathways, improves understanding of conditions and treatments, and enables patients, families, and clinicians to make more informed decisions based on transparent and meaningful evidence.

## 1.2. Overview of the deliverable

It is essential that the project connects also to other initiatives and projects to ensure effective synergies and lessons learned, to make sure that the outcomes are useful and integrated into existing knowledge and processes. In this deliverable, we have established the first version of this work, that will be continued over the full trajectory of the project, updating the current version with more information to support the work in the project. Specifically, the deliverable comprises:

- Section 2: Describing the methodology used for analysing the projects. In particular, an analysis of practice template is proposed for collecting information from the relevant projects.
- Section 3: Five key projects will be analysed following the analysis of practice template.
- Section 4: Concludes the deliverable and defines the next steps.

The ultimate goal of this task is that the information, collected about the practices, is visualized within the practice tracker in the IMPROVE platform.

## 2. Methodology

In this chapter, we will explain the main methodology to analyse the practices that are relevant for IMPROVE, as we also did in the first version of this deliverable. In order to standardize the analyses of the practices, we provide here an Analysis of Practice Template.

The template is organised into four main categories. The first category captures high-level descriptive information about each project, including its name, funding source, and a short summary of its objectives. The second category focuses on methodological aspects and collects information on the research problem addressed, the approach taken, and specific elements relevant for IMPROVE. This includes the types of Patient Generated Health Data used, the data collection methods applied, the target population, the disease areas of interest, and the samples used for empirical validation. These elements are essential for enabling consistent categorisation and future searchability of practices within the IMPROVE practice tracker. The third category documents the results produced by the project to date. As many of the initiatives examined are still in progress, this section will be updated continuously as new deliverables become available. The final category assesses the project's relevance to IMPROVE and outlines potential implications. This includes identifying gaps that IMPROVE can address and recognising resources, knowledge, or methods that other projects may contribute. In doing so, the template supports the identification of synergies that can be further explored through collaboration and stakeholder engagement.

### Rationale for the selection of initiatives

The initiatives included in the IMPROVE Practice Tracker were selected through a purpose-driven and relevance-based approach, rather than a comprehensive or exhaustive mapping of all existing projects. The overarching objective was to identify initiatives that generate directly transferable knowledge for the integration of PGHD into VBHC and Health Technology Assessment (HTA) contexts.

First, priority was given to Innovative Health Initiative (IHI) projects, as these operate within the same European funding, governance, and regulatory ecosystem as IMPROVE. This alignment ensures comparability in terms of legal frameworks (e.g. GDPR, EHDS), data governance requirements, interoperability standards, and expectations regarding real-world evidence generation. Selecting IHI initiatives therefore increases the practical relevance and applicability of the identified practices for IMPROVE's own use cases.

Second, the selected initiatives demonstrate substantial experience with real-world data (RWD), patient-reported outcomes (PROMs), patient-reported experience measures (PREMs), and other forms of PGHD. These projects move beyond conceptual discussions and provide concrete implementation examples, including data collection strategies, digital tools, governance models, and integration into clinical or research workflows. This makes them particularly suitable for analysing how PGHD is operationalised in real settings, which is a central objective of the Practice Tracker.

Third, the initiatives were chosen to reflect diversity across disease areas, populations, and methodological approaches, while still maintaining a manageable and analytically coherent sample. The selected projects span multiple clinical domains (e.g. oncology, neurology, cardiovascular disease,

chronic conditions), use heterogeneous PGHD sources (wearables, mobile applications, questionnaires), and apply different analytical and organisational models. This diversity enables cross-project comparison and supports the identification of common patterns, barriers, and success factors.

Fourth, selection was guided by the potential for mutual learning and synergy with IMPROVE. The analysed initiatives either address challenges that are directly relevant to IMPROVE (such as data standardisation, interoperability, patient engagement, or secondary data use), or offer resources, methods, or infrastructures that IMPROVE could reuse or build upon. Conversely, the analysis also helps identify gaps where IMPROVE can contribute novel solutions, thereby positioning the project within the broader European research landscape.

Finally, the selected initiatives have demonstrated a willingness to engage in deeper collaboration. Project leaders from the analysed IHI initiatives have already expressed interest in follow-up interviews and knowledge exchange. This practical consideration ensures that the Practice Tracker is not a static repository but a living instrument, enriched over time through direct dialogue, validation of findings, and co-creation of best practices. As a result, the tracker supports both systematic analysis and sustained stakeholder engagement

Information for completing the template is drawn from project websites, IHI resources, and the CORDIS database, ensuring that the collected data is consistent, structured, and reliable. During next year we will also conduct individual interviews with the project leaders of the IHIs selected in this analyses as they have already confirmed to be interested in this and work together more intensively. At the same time, for the Science Tracker the Utrecht University has worked on several Large Language Models to analyse the scientific papers in more detail. The same is now being tested to analyse the projects collected from the Policy tracker.

**Analysis of Practice Template**

**1. Project Overview**

- **Title**: The formal title of the research project.
- **Principal Investigator(s)**: Name(s) of the lead researcher(s).
- **Consortium partner(s)**: Organization(s) or institution(s) involved.
- **Funding Source(s)**: Identify funding agencies or sponsors.
- **Project Duration**: Start and end dates of the project.

**2. Methodology**

- **Summary of the project**: Short summary of the project
    - **Research Problem**: Clearly state the central problem or issue being addressed.
    - **Objectives**: Specific goals of the project.
- **Population, Disease Area and Sample**: Population, sample size, disease area(s).
- **PGHD used**: What kind of PGHD is mainly analysed in the project.
- **Data Collection Methods**: Tools and techniques for data collection (e.g., surveys, interviews, experiments, archival research, etc.).

**3. Results & Findings**

- **Key Findings**: A summary of the main findings (if available).
- **Data Representation**: Any charts, graphs, or tables that represent the data (if available).
- **Patterns/Trends**: Noteworthy patterns or trends observed from the data.

**4. Discussion & Conclusion**

- **Interpretation of Findings**: Discuss the meaning and implications of the results in relation to the IMPROVE project
- **Gap analyses and Implications for Future Research related to IMPROVE**: Discuss any limitations or constraints exhibited by the project as well as recommendations for future studies or areas for further investigation.

## 3. Analysis of Practices

In this section we analyse five significant IHI projects that are highly relevant to IMPROVE, as all of them have been or still are collecting RWE and RWD and experience the same difficulties and strengths as IMPROVE does: EHDEN, PaLaDIn, IDEA-FAST, ConcePTION, and GREG. The projects are all IHI initiatives that approach and use Patient-Generated Health Data (and related real-world data) in different ways, which makes them an excellent starting point for mapping practices and for subsequent engagement relevant to IMPROVE. These projects (EHDEN, ConcePTION, IDEA-FAST) have been selected because they are explicitly referenced in the call context as foundational or complementary infrastructures and methodologies for cross-project alignment, while synergies with PaLaDIn and GREG are already developing through shared consortium membership and overlapping technical aims. In addition, we have agreed with the project managers of these project that during 2026 we will execute individual interviews with them to further analyze the inputs needed to make IMPROVE a success and how we can learn from these projects.

### 3.1. Practice EHDEN

#### 1. Project Overview

- **Title:** European Health Data & Evidence Network (EHDEN)
- **Principal Investigator(s):** Peter Rijnbeek (Erasmus MC), Patrick Ryan (Janssen) and Carlos Díaz (Synapse)
- **Consortium partner(s):**

a) EFPIA companies
   i. Abbvie Inc, North Chicago Il, United States
   ii. Astrazeneca AB, Sodertaelje, Sweden
   iii. Bayer Aktiengesellschaft, Leverkusen, Germany
   iv. Boehringer Ingelheim Internationalgmbh, Ingelheim, Germany
   v. Celgene Management SARL, Boudry, Switzerland
   vi. Eli Lilly And Company LTD, Basingstoke, United Kingdom
   vii. F. Hoffmann-La Roche AG, Basel, Switzerland
   viii. H. Lundbeck As, Valby, Denmark
   ix. Institut De Recherches Internationales Servier, Gif-Sur-Yvette, France
   x. Janssen Pharmaceutica Nv, Beerse, Belgium
   xi. Novartis Pharma AG, Basel, Switzerland
   xii. Pfizer Limited, Sandwich, United Kingdom
   xiii. Sanofi-Aventis Recherche & Developpement, Gentilly, France
   xiv. UCB Biopharma, Bruxelles / Brussel, Belgium

b) Universities, research organisations, public bodies, non-profit groups
   i. Erasmus Universitair Medisch Centrum Rotterdam, Rotterdam, Netherlands
   ii. Forum Des Patients Europeens, Brussels, Belgium
   iii. National Institute For Health And Care Excellence, Manchester, United Kingdom

iv. Stiftelsen WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden
v. Tartu Ulikool, Tartu, Estonia
vi. Universidade De Aveiro, Aveiro, Portugal
vii. University of Oxford, Oxford, United Kingdom

c) Small and medium-sized enterprises and mid-sized companies (<€500 m turnover)
i. International Consortium For Healthoutcomes Measurement LTD, Erith, United Kingdom
ii. Odysseus Data Services Sro, Praha, Czechia
iii. Synapse Research Management Partners SL, Madrid, Spain
iv. The Hyve BV, Utrecht, Netherlands

- **Funding Source(s):** EU, EFPIA and Other
- **Project Duration:** 01/11/2018 to 31/10/2024

## 2. Methodology

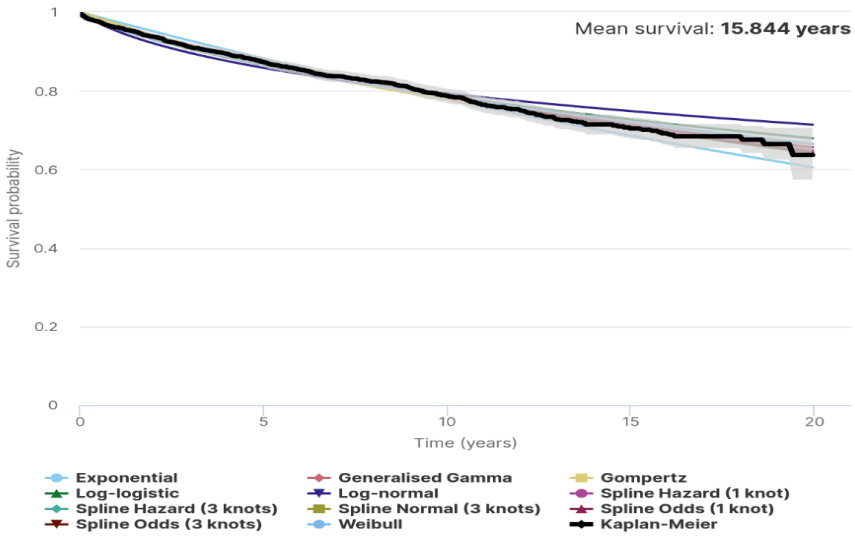
- **Summary of the project:** Healthcare data has the potential to transform our understanding of health, disease and outcomes, yet it is currently scattered across multiple institutions and countries, stored in different formats, and subject to different rules. This makes it very difficult to fully utilise this data to benefit patients. The goal of EHDEN is to make the large-scale analysis of health data in Europe a reality. The project aims to do this by building a federated data network of allowing access to the data of 100 million EU citizens standardised to a common data model. At the heart of the project will be a group of trained, certified small and medium-sized enterprises (SMEs) responsible for transforming the data owned by hospitals to the common data model. The data will remain under complete control of the original data owner, thereby ensuring ethical and local data privacy rules are respected. EHDEN is part of IMI's Big Data for Better Outcomes (BD4BO) programme.
- **Research Problem:** Healthcare data has the potential to transform our understanding of health, disease and outcomes, yet it is currently scattered across multiple institutions and countries, stored in different formats, and subject to different rules. This makes it very difficult to fully utilise this data to benefit patients.
- **Objectives:** The European Health Data & Evidence Network (EHDEN) aimed to transform real-world evidence (RWE) generation in Europe by building a large-scale, federated network of healthcare data sources harmonized to the OMOP Common Data Model. EHDEN supported 187 Data Partners across 29 countries, enabling GDPR compliant, reproducible research on over 350 Million European healthcare records. EHDEN developed IT infrastructure such as the EHDEN Portal, ETL tooling, and the EHDEN Academy for training. These platforms support study feasibility, federated analytics, and data quality assessment, facilitating regulatory and HTA decision-making. The project also trained and certified over 60 SMEs in common data model mapping and ETL, to further a thriving European RWE ecosystem. The EHDEN Foundation was created and is leveraging the project results and expanding them further with a variety of stakeholders.
- **Population:** Established a network of 187 Data Partners across 29 countries, harmonizing over 550 million health records to the OMOP Common Data Model (CDM). The project developed

case studies on multiple therapeutic areas including oncology, COVID-19, dementia, diabetes, and rare diseases like alopecia areata, among others.

- **PGHD used:** Benchmarking dashboards for PROMs and quality improvement, supporting HTA and payer use (D2.5).
- **Data Collection Methods:** EHDEN recruited data partners through structured open calls. Selected data partners received funding and technical support to harmonize their data to the Observational Medical Outcomes Partnership Common Data Model (OMOP CDM), with assistance from certified small-to-medium enterprises trained through the EHDEN Academy. Each data source underwent an extract-transform-load process and data quality assessment using the data quality dashboard. Metadata, including country, care setting, capture method, and population criteria, were compiled in the publicly accessible EHDEN Portal.

## 3. Results & Findings

- **Key Findings:** As of 1 September 2024, the EHDEN Portal contains 210 harmonised data sources across 30 countries, with the largest contributions from Italy (13 per cent), Great Britain (12.5 per cent), and Spain (11.5 per cent). These data sources are substantial in scale, with a mean population size of 2,147,161 individuals and a median of 457,664, demonstrating EHDEN's capacity to support large, high-quality real-world evidence generation. In terms of care settings, almost half of all data sources (46.7 per cent) originate from secondary care, followed by mixed care settings (42.4 per cent) and primary care (11 per cent). Regarding population inclusion criteria, the majority (55.7 per cent) are based on health care encounters, with 32.9 per cent derived from disease-specific data collections and 11.4 per cent from population-based sources. EHDEN has also demonstrated its scientific robustness by replicating within a five-day "study-athon" the findings of a systematic review that originally took twenty years to complete, as well as those of a multi-year clinical trial, highlighting the power, speed and reproducibility of federated analytics at scale.
- **Data Representation:** EHDEN Cancer survival dashboard which uses the IMASIS (Barcelona) dataset for Breast Cancer, unstratified (no subgrouping), over a 0–21 year period:



- **Patterns/Trends:** The survival analysis shows that breast cancer patients in the IMASIS (Barcelona) dataset have a mean survival of 15.844 years, with a gradual decline in survival probability over two decades, indicating strong long-term outcomes.

## 4. Discussion & Conclusion

- **Interpretation of Findings:** EHDEN has demonstrated that large-scale, federated health data infrastructures are not only feasible but can meaningfully transform the speed, reproducibility and breadth of real-world evidence generation in Europe. The success of harmonising more than 550 million health records to the OMOP Common Data Model, and enabling federated analytics across 29 countries, provides a mature blueprint for any downstream project seeking to build patient-centred evidence ecosystems. For IMPROVE, the key implication is that sound technical architecture, transparent governance, harmonised data models and trusted federated methodologies are prerequisites for generating credible PGHD-driven insights across Europe.

  Besides, EHDEN shows that investing in community building, training and certification amplifies ecosystem growth. By establishing the EHDEN Academy, certifying SMEs, and providing open-access tooling, the project created a sustainable pipeline of technical expertise that ensures continuity beyond the project lifespan. For IMPROVE, this underscores the importance of establishing educational resources, documented standards and reusable tools to ensure that PGHD pipelines remain coherent and scalable in the long term

  Finally, the project's demonstration that complex evidence generation exercises, such as systematic reviews and clinical trial replication, can be reproduced within days reflects the broader potential of federated analytics for reducing research timelines and supporting regulatory and HTA assessments. IMPROVE stands to benefit from this precedent by aligning its PGHD approaches with federated, GDPR compliant methods so that its eventual endpoints and analytical outputs are compatible with regulatory expectations and the European Health Data Space.

- **Gap Analyses and Implications for Future Research related to IMPROVE:** A core gap in EHDEN is the limited integration of patient-generated health data (PGHD). While the project advanced clinical RWD harmonisation at unprecedented scale, its primary focus remained on institutional data, electronic health records, insurance claims, disease registries and more sources. PGHD such as PROMs, PREMs, wearable-derived data and home-based monitoring are not yet systematically mapped into OMOP CDM in Europe. This leaves an opportunity for IMPROVE to extend EHDEN's architecture by defining validated PGHD extensions, ensuring that patient-reported information is standardised, interoperable and analytically compatible with clinical RWD. Doing so would enable richer mixed-source evidence and foster patient-centred analytics across disease areas.

  Moreover, a second gap concerns the level at which insights generated through EHDEN primarily operate. The network has excelled in supporting regulatory bodies, health technology assessment agencies and population-level epidemiology, yet less attention has been devoted to closing the loop back to individual patients or frontline clinicians. For IMPROVE, which aims to develop more immediate, patient-facing value, this is a strategic

opening. By building dashboards, feedback loops and near-real-time insights from PGHD, IMPROVE can bridge a space that EHDEN does not fully occupy, translating federated evidence into actionable tools that improve individual-level care, self-management and personalised intervention strategies.

Finally, another gap relates to long-term sustainability and interoperability across future European data infrastructures. EHDEN has made important strides through the EHDEN Foundation, yet the broader data governance landscape is evolving with the European Health Data Space (EHDS) and parallel initiatives. Ensuring that federated networks remain compatible with emerging policy, technical and semantic standards will be essential. For IMPROVE, this signals the need to design PGHD processes, metadata models and interoperability guidelines that anticipate future cross-project alignment. By integrating FAIR principles, transparent provenance tracking and modular data governance frameworks, IMPROVE can establish itself as a future-proof PGHD contributor within the wider European health data ecosystem.

## 3.2. Practice PaLaDIn

### 1. Project Overview

- **Title:** Patient lifestyle and disease data interactium (PaLaDIn)
- **Principal Investigator(s):** Serena Cogoni (Parent Project Italy) and Rebecca Leary (UNEW)
- **Consortium partner(s):**
  a) Contributing partners (SMEs)
    i. Fshd Society, Randolph, United States
    ii. Treat-Nmd Services LTD, Newcastle Upon Tyne, United Kingdom
  b) Universities, research organisations, public bodies, non-profit groups
    i. Academisch Ziekenhuis Leiden, Leiden, Netherlands
    ii. Duchenne Uk, London, United Kingdom
    iii. Ludwig-Maximilians-Universitaet Muenchen, Munchen, Germany
    iv. Parent Project Aps, Roma, Italy
    v. Stichting Amsterdam Umc, Amsterdam, Netherlands
    vi. University Of Newcastle Upon Tyne, Newcastle upon Tyne, United Kingdom
  c) Third parties
    i. Klinikum Der Ludwig-Maximilians-Universitat Munchen, Munchen, Germany
  d) Small and medium-sized enterprises (SMEs) and mid-sized companies (<€500 m turnover)
    i. Aparito Netherlands BV, Leiden, Netherlands
- **Funding Source(s):** EU and Contributing partners
- **Project Duration:** 01/01/2024 to 31/12/2027

### 2. Methodology

- **Summary of the project:** The aim of PaLaDIn is to develop a state-of-the-art platform dubbed the 'Interactium' to drive innovative, real-world data collection from patients with rare diseases. The project focuses on rare neuromuscular diseases (NMDs), specifically Duchenne muscular dystrophy (DMD) and facioscapulohumeral muscular dystrophy (FSHD). The team plans to leverage the TREAT-NMD Global Registry Platform, which brings together over 60 NMD patient registries which collect patient data following a harmonised data model.
- **Research Problem:** Developing new treatments for rare diseases is highly challenging. Because there are, by definition, very few patients with each rare disease, there is a major lack of data on patients' needs, preferences and experiences of living with the disease. Furthermore, what little data exists is often fragmented and hard to access.
- **Objectives:** PaLaDIn aims to improve healthcare outcomes for individuals with neuromuscular diseases (NMD) and other rare diseases (initially working in DMD and FSHD) through the development of 'The Interactium' data platform. By gathering comprehensive patient data on health status and experiences, we will ensure that patients' voices are integral to healthcare decision-making. Our platform will collect data from patient registries, data reported directly from patients including PROMs and PREMs, and patient data from wearable devices. We are currently in the tender process to select a vendor to build the Interactium and will appoint a vendor in October 2025. The data will be used to accelerate the development of effective treatments, improve patient-reported outcome measures (PROMs), and inform healthcare and regulatory decisions. Ultimately, we strive to share our insights and tools to benefit other rare diseases, empowering patients and advancing better healthcare outcomes.
- **Population:** PaLaDIn aims to improve healthcare outcomes for individuals with neuromuscular diseases (NMD) and other rare diseases (initially working in DMD and FSHD) through the development of 'The Interactium' data platform. It is expected that, as a result of the PaLaDIn initiative there will be up to 4000 patients worldwide who submit data to The Interactium
- **PGHD used:** The Interactium will be able to integrate data from diverse sources, including patient-reported outcome/experience measures (PROMs and PREMs), as well as digital outcome measures from wearable devices, all of which will be co-created with patients.
- **Data Collection Methods:** The team plans to leverage the TREAT-NMD Global Registry Platform, which brings together over 60 NMD patient registries which collect patient data following a harmonised data model. A patient interface will facilitate the collection of data and information on preferences and also allow users to visualise their data and control how it is used.

## 3. Results & Findings

- **Key Findings:** Not available
- **Data Representation:** Not available
- **Patterns/Trends:** Not available.

## 4. Discussion & Conclusion

- **Interpretation of Findings:** Although PaLaDIn has not yet produced outcome data, the early development work provides meaningful insights relevant to the IMPROVE project. PaLaDIn demonstrates the importance of building integrated, interoperable platforms capable of combining registry data, PGHD from wearables, and direct patient-reported outcomes in a harmonised manner. This approach shows that meaningful PGHD ecosystems require strong foundational design work before clinical insights can emerge. For IMPROVE, this underscores the value of prioritising early architectural decisions, patient involvement, and transparent data governance so that future digital endpoints can be built on robust and scalable infrastructure.

  Furthermore, PaLaDIn places strong emphasis on co-creation with patient communities, especially given the unique needs of individuals with Duchenne muscular dystrophy and facioscapulohumeral muscular dystrophy. This highlights the importance of embedding patients early in the design of data collection, interface usability and preferences. For IMPROVE, which also relies on PGHD for cardiovascular populations, the implication is clear. Patient experience, device acceptability and data ownership need to guide design choices from the outset to ensure adherence, acceptance and reliability of PGHD-derived endpoints.

- **Gap analyses and Implications for Future Research related to IMPROVE:**

  Firstly, a major gap visible in PaLaDIn is the current lack of mature results due to its early stage. Building a large-scale PGHD platform requires extensive preparation, vendor selection, interface design and registry integration before meaningful analytics can begin. For IMPROVE, this highlights the need to budget sufficient time for early development phases. Expectations around the timing of digital endpoint generation should be realistic, iterative and aligned with progressive platform maturity.

  Furthermore, a second gap concerns the challenge of scaling data integration across diseases. PaLaDIn begins with two neuromuscular diseases and aims to expand to other rare conditions. Designing a flexible system that can incorporate diverse diseases while allowing disease-specific nuances is inherently difficult. The implication for IMPROVE is that data models, ontologies and PGHD frameworks must be built for both specificity and scalability. Cardiovascular diseases differ fundamentally from neuromuscular conditions, yet the structural lessons around interoperability, harmonisation and registry integration remain directly applicable.

  Finally, a relevant gap relates to patient engagement and long-term retention in PGHD ecosystems. PaLaDIn intends to create a patient interface supporting ongoing PROMs, PREMs and wearable-derived data. Sustaining participation in long-term PGHD programmes is a well-known challenge in digital health, particularly in rare disease communities who already face clinical and logistical burdens. IMPROVE should integrate sustained engagement strategies early, including co-design workshops, testing of device burden, transparent consent models, and mechanisms for returning meaningful information back to patients to reinforce engagement.

## 3.3. Practice IDEA-FAST

### 1. Project Overview

- **Title:** Identifying digital endpoints to assess fatigue, sleep and activities in daily living in neurodegenerative disorders and immune-mediated inflammatory diseases (IDEA-FAST)
- **Principal Investigator(s):** Wan-Fai Ng (University Of Newcastle Upon Tyne), Walter Maetzler (University Hospital Schleswig-Holstein), Nikolay Manyakov (Janssen Pharmaceutica NV), Geert Van Gassen (Takeda Pharmaceuticals)
- **Consortium partner(s):**

a) EFPIA companies
   i. Abbvie Inc, North Chicago Il, United States
   ii. Astrazeneca AB, Sodertaelje, Sweden
   iii. Biogen Idec Limited, Maidenhead, United Kingdom
   iv. Bristol-Myers Squibb Company Corp, New York, United States
   v. Eli Lilly And Company LTD, Basingstoke, United Kingdom
   vi. F. Hoffmann-La Roche AG, Basel, Switzerland
   vii. Janssen Pharmaceutica Nv, Beerse, Belgium
   viii. Orion Oyj, Espoo, Finland
   ix. Pfizer Limited, Sandwich, United Kingdom
   x. Sanofi-Aventis Recherche & Developpement, Gentilly, France
   xi. Takeda Pharmaceuticals International AG, Glattpark, Switzerland
   xii. UCB Biopharma, Bruxelles / Brussel, Belgium

b) Universities, research organisations, public bodies, non-profit groups
   i. Academisch Ziekenhuis Leiden, Leiden, Netherlands
   ii. Erasmus Universitair Medisch Centrum Rotterdam, Rotterdam, Netherlands
   iii. European Clinical Research Infrastructure Network (ECRIN), Paris, France
   iv. Fciencias.Id - Associacao Para A Investigacao E Desenvolvimento De Ciencias, Lisbon, Portugal
   v. Fundacao Gimm - Gulbenkian Institute For Molecular Medicine, Lisboa, Portugal
   vi. Helse Stavanger Hf, Stavanger, Norway
   vii. Imperial College Of Science Technology And Medicine, London, United Kingdom
   viii. Institut Mines-Telecom, Palaiseau, France
   ix. Instytut Psychiatrii I Neurologii, Warszawa, Poland
   x. Medizinische Universitat Innsbruck, Innsbruck, Austria
   xi. Queen Mary University Of London, London, United Kingdom
   xii. Teknologian Tutkimuskeskus Vtt Oy, Espoo, Finland
   xiii. Tmf - Technologie Und Methodenplattform Fur Die Vernetzte Medizinische Forschung Ev, Berlin, Germany
   xiv. Universidad Autonoma De Madrid, Madrid, Spain
   xv. Universita Degli Studi Di Brescia, Brescia, Italy
   xvi. Universitatsklinikum Schleswig-Holstein, Lübeck, Germany
   xvii. University College Cork - National University Of Ireland, Cork, Cork, Ireland
   xviii. University Of Glasgow, Glasgow, United Kingdom

xix. University Of Limerick, Limerick, Ireland
xx. University Of Newcastle Upon Tyne, Newcastle upon Tyne, United Kingdom
xxi. University of Cambridge, Cambridge, United Kingdom

c) Small and medium-sized enterprises (SMEs) and mid-sized companies (<€500 m turnover)
i. Asociacion Parkinson Madrid, Madrid, Spain
ii. Byteflies, Antwerpen, Belgium
iii. Cambridge Cognition Limited, Cambridge, United Kingdom
iv. Empirica Gesellschaft Fur Kommunikations Und Technologieforschung Mbh, Bonn, Germany
v. George-Huntington-Institut GMBH, Munster, Germany
vi. Ixscient Limited, Twickenham Middlesex, United Kingdom
vii. Let It Care, Antony, France
viii. Mcroberts BV, 's-Gravenhage (Den Haag), Netherlands
ix. Medibiosense LTD, Doncaster, United Kingdom
x. Pluribus One SRL, Cagliari, Italy
xi. Stichting Lygature, Utrecht, Netherlands

d) Patient organisations
i. European Federation Of Crohn'S And Ulcerative Colitis Associations, Bruxelles / Brussel, Belgium

e) Associated partners
i. Parkinson'S Disease Society Of Theunited Kingdom Lbg, London, United Kingdom

f) Third parties
i. Christian-Albrechts-Universitaet Zu Kiel, Kiel, Germany
ii. Faculdade De Ciencias Da Universidade De Lisboa, Lisboa, Portugal
iii. Fundacion Para La Investigacion Biomedica Del Hospital Universitario Clinico San Carlos, Madrid, Spain
iv. Greater Glasgow Health Board, Glasgow, United Kingdom
v. Kks-Netzwerk Ev -Netzwerk Der Koordinierungszentren Fur Klinische Studien, Berlin, Germany
vi. UNIVERSITAET zu LUEBECK, Lubeck, Germany

g) Other companies
i. CHDI Foundation, Inc., New York, United States

- **Funding Source(s):** EU, EFPIA, Associated partners and Other
- **Project Duration:** 01/11/2019 to 30/04/2026

## 2. Methodology

- **Summary of the project:** The aim of IDEA-FAST is to identify digital endpoints for fatigue and sleep disturbances that will provide a more sensitive, reliable measure of the severity and impact of these symptoms in a real-life setting. They will do this by identifying the characteristics of fatigue and sleep disturbances and the digital endpoints that could quantify them. They will then select the digital devices and technologies that could measure and record

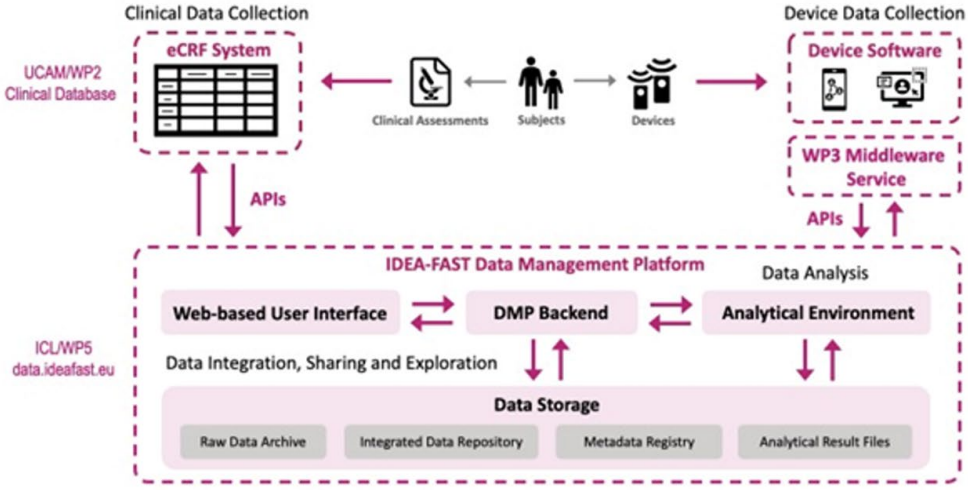
these symptoms. They will also design a secure digital management platform to support the acquisition, storage and analysis of the data.

- **Research Problem**: Fatigue and sleep disturbances are common symptoms of many chronic diseases and are associated with a poor quality of life and greater healthcare costs. Today, efforts to measure these symptoms, e.g. in clinical trials, are based largely on standardised paper questionnaires, which do not give very reliable results.
- **Objectives:** IDEA-FAST aims to identify digital endpoints for fatigue, sleep and activities of daily living in patients with neurodegenerative diseases (Parkinson's disease, Huntington's disease) and immune-mediated inflammatory diseases (Inflammatory bowel disease, rheumatoid arthritis, lupus, Sjogren's disease). The project involves two clinical studies, both of which involve collection of RWD using wearables and other digital health technologies together with relevant electronic patient-reported outcomes. The feasibility study has been completed and included 146 subjects with RWD for four 5-day period over 6-8 weeks. The recruitment phase of the clinical observation study has also been completed. Over 1900 subjects have been recruited, and upon study completion, we will have RWD for four 7-day period over 6 months for the research participants. The data management platform including an analytical environment (based at Imperial College London) is fully operational. The DMP integrates detailed clinical information as well as RWD collected during the clinical studies.
- **Population:** The feasibility study has been completed and included 146 subjects with RWD for four 5-day period over 6-8 weeks. Over 1900 subjects have been recruited, and upon study completion, the project will have RWD for four 7-day period over 6 months for the research participants. Diseases included Parkinson's Disease (PD), Huntigton's Disease (HD), Systemic Lupus Erythematosus (SLE), Inflammatory Bowel Disease (IBD), Primary Sjögren's syndrome (PSS) and Rheumatoid Arthritis (RA).
- **PGHD used: The** project involves two clinical studies, both of which involve collection of RWD using wearables and other digital health technologies together with relevant electronic patient-reported outcomes (PROs).
- **Data Collection Methods**: In order to select the most promising digital devices for the Clinical Observation Study (COS), the patient perspective in combination with device data quality and results were taken into account. Besides some quantitative research using questionnaires, two focus groups and 61 semi-structured interviews were conducted (i.e. views of nearly half of all participants were recorded). The data management platform (based at Imperial College London) integrates detailed clinical information as well as RWD collected during the clinical studies.

**3. Results & Findings**

- **Key Findings:** Despite being highly prevalent in our society, symptoms of fatigue and sleep disturbances remain difficult to treat, measure, and to conceptualise. Digital technology and digital endpoints may provide a novel way to measure fatigue and sleep disturbances more accurately. In general, single small wearable devices and stationary devices were tolerated well, while many participants were bothered by having to use multiple sensors, especially when these included visible electrodes.

- **Data Representation:**




- **Patterns/Trends:** Recruitment for the IDEA-FAST COS reached 265 participants in the first six months, a positive achievement given challenging circumstances and an incomplete network of recruiting centres. Study teams report that assessments are easy to perform across all visits, and participants perceive the study as meaningful and future-oriented, demonstrating strong engagement, good compliance, and promising retention. However, the current recruitment rate remains below what is required, prompting several strategic adjustments: shifting from batch to continuous recruitment, expanding the number of departments involved at existing sites, and increasing support for local study teams through frequent meetings and timely feedback on data quality. The impact of these measures will be closely monitored over the coming months, with additional strategies considered if needed. Despite the recruitment shortfall, overall sentiment from study teams, participants, and broader stakeholders remains strongly positive, reinforcing confidence in the future of the IDEA-FAST COS.

## 4. Discussion & Conclusion

- **Interpretation of Findings:** IDEA-FAST demonstrates that carefully designed, cross-disease digital endpoint development is feasible and, importantly for IMPROVE, that success depends on combining patient-centred methods, robust data infrastructure and early regulatory engagement. The main implications for IMPROVE are threefold.

  Firstly, the project shows that cross disease digital endpoints can be developed and tested at scale by combining multi-sensor passive monitoring, short active tasks and repeated electronic patient reported outcomes. This provides a blueprint for IMPROVE to adopt when aiming to produce generalisable, regulatory relevant PGHD based measures across different disease areas. Evidence that IDEA-FAST engaged regulators and sought EMA advice on qualification emphasises the importance of planning regulatory strategy early, and this is directly relevant to IMPROVE if regulatory impact is an objective.

  Moreover, IDEA-FAST highlights the centrality of a robust data management and analysis environment. The project's centralised data platform at Imperial College London that

integrates clinical metadata with device streams and PROs shows how to operationalise FAIR principles, secure data flows and repeatable analytic pipelines. For IMPROVE this means investing early in platform requirements, data quality metrics and provenance tracking so downstream analyses and eventual regulatory conversations are credible and reproducible.

Finally, the feasibility work and publications demonstrate that patient acceptability and device burden materially affect data completeness and signal quality. IDEA-FAST's finding that single small wearables and stationary sensors were better tolerated than multi-sensor setups underline the trade-off between richer signal acquisition and participant burden. IMPROVE should adopt a patient centric device selection process that balances signal value against adherence risk; this will improve retention and data quality in long observational cohorts.

- **Gap analyses and Implications for Future Research related to IMPROVE:** A central gap illustrated by IDEA-FAST is the challenge of maintaining recruitment momentum and securing a sufficiently representative cohort in large, multi-country digital studies. Although the project ultimately achieved strong engagement and retention, recruitment progressed more slowly than anticipated and required operational adjustments such as a shift to continuous enrolment and enhanced site level support. This underscores that digital health studies, even when perceived positively by participants, face structural barriers relating to site capacity, participant burden and variation in local workflows. For IMPROVE this highlights the necessity of early investment in a recruitment strategy that is adaptable, adequately resourced and monitored in real time, with a particular emphasis on reaching diverse demographic groups to avoid under-representation and downstream bias in PGHD based endpoints.

  Besides, a second substantial gap concerns the balance between device burden and the richness of the data collected. IDEA-FAST's feasibility findings demonstrate that although participants tolerate small, unobtrusive wearables well, adherence drops when device ecosystems become too complex or include visible electrodes or multiple sensors. Across disease areas, this introduces variability in data completeness and threatens the robustness of derived digital endpoints. For IMPROVE this means that a patient centred device strategy is essential. It should prioritise minimal, yet informative sensor sets and incorporate early usability testing to quantify the marginal value of additional devices against the practical burden they impose. Without such optimisation, adherence driven data loss could affect endpoint validity and limit the generalisability of any digital measures developed under IMPROVE.

  Lastly, a major gap relates to the analytical and regulatory maturity of cross disease digital endpoints. IDEA-FAST has made significant progress in defining candidate endpoints for fatigue and sleep, but the project also demonstrates that analytical validation, clinical interpretation and regulatory readiness remain challenging when endpoints must perform consistently across multiple heterogeneous conditions. Ensuring that digital signals capture meaningful, clinically anchored constructs rather than disease specific artefacts requires rigorous validation pipelines, transparent methods and early scientific dialogue with regulators. For IMPROVE, these signals the importance of designing analytical plans that include disease stratified performance assessments, independent replication and clear linkage to patient reported outcomes. Establishing these foundations early will be critical for producing digital endpoints that are both clinically relevant and positioned for future regulatory uptake.

## 3.4. Practice ConcePTION

### 1. Project Overview

- **Title:** ConcePTION
- **Principal Investigator(s):** Marjolein Willemen (Novartis Pharma AG) and Miriam Sturkenboom (Universitair Medisch Centrum Utrecht)
- **Consortium partner(s):** Organization(s) or institution(s) involved.

**a) EFPIA companies**

i. Abbvie Inc, North Chicago Il, United States
ii. Bristol-Myers Squibb Company Corp, New York, United States
iii. Eli Lilly And Company LTD, Basingstoke, United Kingdom
iv. Glaxosmithkline Research & Development Limited, London, United Kingdom
v. Janssen Pharmaceutica Nv, Beerse, Belgium
vi. Labcorp Early Development Laboratories Limited, Harrogate, United Kingdom
vii. Merck Kommanditgesellschaft Auf Aktien, Darmstadt, Germany
viii. Novartis Pharma AG, Basel, Switzerland
ix. Novo Nordisk A/S, Bagsvaerd, Denmark
x. Pfizer Limited, Sandwich, United Kingdom
xi. Sanofi-Aventis Recherche & Developpement, Gentilly, France
xii. Takeda Pharmaceuticals International AG, Glattpark, Switzerland
xiii. Teva Pharmaceutical Industries Limited, Petach Tivka, Israel
xiv. UCB Biopharma, Bruxelles / Brussel, Belgium

**b) Universities, research organisations, public bodies, non-profit groups**

i. Academisch Ziekenhuis Groningen, Groningen, Netherlands
ii. Agenzia Regionale Di Sanita, Firenze, Italy
iii. Alma Mater Studiorum - Universita Di Bologna, Bologna, Italy
iv. Biobanks And Biomolecular Resources Research Infrastructure Consortium (Bbmri-Eric), Graz, Austria
v. Centre Hospitalier Universitaire De Toulouse, Toulouse Cedex 3, France
vi. Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
vii. Consiglio Nazionale Delle Ricerche, Roma, Italy
viii. European Forum For Good Clinical Practice, Bruxelles / Brussel, Belgium
ix. European Institute Of Women'S Health Company Limited By Guarantee, Dublin, Ireland
x. Fundacion Para El Fomento De La Investigacion Sanitaria Y Biomedica De La Comunitat Valenciana, Valencia, Spain
xi. Institut National De La Sante Et De La Recherche Medicale, Paris, France
xii. Karolinska Institutet, Stockholm, Sweden
xiii. Katholieke Universiteit Leuven, Leuven, Belgium
xiv. Medicines And Healthcare Products Regulatory Agency, London, United Kingdom
xv. Region Stockholm, Stockholm, Sweden
xvi. Region Uppsala, Uppsala, Sweden

xvii. Rijksinstituut Voor Volksgezondheid En Milieu, Bilthoven, Netherlands
xviii. St George'S Hospital Medical School, London, United Kingdom
xix. Stichting Entis (European Network Teratology Information Services) Foundation, Hertogenbosch, Netherlands
xx. Stichting Lareb, S Hertogenbosch, Netherlands
xxi. Swansea University, Swansea, United Kingdom
xxii. Terveyden Ja Hyvinvoinnin Laitos, Helsinki, Finland
xxiii. The European Institute For Innovation Through Health Data, Oosterzele, Belgium
xxiv. The European Medicines Agency, Amsterdam, Netherlands
xxv. The Newcastle Upon Tyne Hospitals Nhs Foundation Trust, Newcastle-Upon-Tyne, United Kingdom
xxvi. The University Of Manchester, Manchester, United Kingdom
xxvii. Universita Degli Studi Di Ferrara, Ferrara, Italy
xxviii. Universitair Medisch Centrum Utrecht, Utrecht, Netherlands
xxix. Universitetet I Oslo, Oslo, Norway
xxx. University Of Kwazulu-Natal, Westville, South Africa
xxxi. University Of Ulster, Coleraine, United Kingdom
xxxii. Uppsala Universitet, Uppsala, Sweden

**c) Small and medium-sized enterprises (SMEs) and mid-sized companies (<€500 m turnover)**

i. Bionotus, Temse, Belgium
ii. Elevate BV, Utrecht, Netherlands
iii. Ellegaard Gottingen Minipigs As, Dalmose, Denmark
iv. Orcion BV, Asten, Netherlands
v. The Synergist, Bruxelles / Brussel, Belgium

**d) Third parties**

i. Masarykova univerzita, Brno, Czechia
ii. Medizinische Universitat Graz, Graz, Austria
iii. Ministry Of Health, Jerusalem, Israel
iv. Nearshore Macedonia LTD Skopje, Skopje, North Macedonia
v. Shamir Health Corporation, Zrifin, Israel
vi. Synergist Services, Bruxelles / Brussel, Belgium
vii. Universitaet Leipzig, Leipzig, Germany

- **Funding Source(s):** EU and EFPIA
- **Project Duration:** 01/04/2019 to 31/12/2024

## 2. Methodology

- **Summary of the project:** The ultimate goal of ConcePTION is to create a trusted biomedical ecosystem capable of providing evidence-based information on the safety of medications during pregnancy and breastfeeding in an efficient, systematic and ethically responsible way. The information will be provided in a form that is usable by both healthcare providers and patients alike. The project will achieve this in a number of ways. Firstly, it will improve and

unify existing approaches to data collection in this area by re-using existing, de-identified data generated during routine patient care. The project also aims to deliver procedures and tools for the collection of digital data and samples directly from pregnant women. They will also create the first Europe-wide breast milk biobank for research purposes, and develop tools to predict which drugs are likely to be transferred to breast milk. Finally, the team will establish a web-based drug information knowledge bank.

- **Research Problem:** Women who are pregnant or breastfeeding are traditionally excluded from medical research due to safety concerns. As a result of this, only 5% of medications have adequate safety information on their use in pregnant or breastfeeding women, and this makes it very hard for doctors and women to make informed decisions about their treatment. Nonetheless, some 90% of women are exposed to a prescription medication at some point during their pregnancy.
- **Objectives:** IMI ConcePTION (Grant No. 821520) aimed to reduce uncertainty about the safety of medicines used during pregnancy and breastfeeding by building a sustainable European ecosystem for evidence generation and dissemination. The project developed harmonised methods, data governance models, and IT tools to transform Real-World Data (RWD) into actionable Real-World Evidence (RWE). ConcePTION focused on maternal, perinatal, and child health, using population-based data, pharmacovigilance reports, primary data collection and biological samples to assess medicine safety in real-life use. The project established a federated RWE platform using a generic common data model, FAIR data catalogue, and secure distributed analytics environment, now adopted by RWD research networks such as VAC4EU, EU PE&PV and SIGMA. ConcePTION also created Europe's first non-commercial breast milk biobank and launched MUMS.eu, a public knowledge bank on medicine safety in pregnancy and lactation.
- **Population:** Medicines in pregnancy and breastfeeding. Up to 90% of women take medication at some stage during pregnancy and breastfeeding. Even though many of those medicines are safe to use, only 3,7% of them are explicitly labelled as safe. 1 in 3 choose to discontinue treatment, with potentially serious consequences to their health. With around 5,000,000 pregnancies in Europe ever year, the number of women who are affected is staggering. Of the available medicines, 71% include no information on use when pregnant, and 83% include no information on use when breastfeeding. Of the women, 25% experience anxiety due to a lack of information about medicines. 52% encounter inconsistencies in the available information, 40% report difficulty understanding what is available, and 20% cannot find any relevant information at all.
- **PGHD used:** The ConcePTION project does not use Patient-Generated Health Data (PGHD) as a primary or main data source. Instead, it relies predominantly on population-based, secondary real-world data, such as healthcare databases, registries, prescription records, and linkable administrative datasets. These sources are used to generate robust evidence on medicine safety during pregnancy and breastfeeding through large-scale pharmacoepidemiological studies and data linkage across Europe. However, it is important to note that ConcePTION does incorporate some patient-reported outcomes and experiences, particularly through its MUMS knowledge bank and the Meds4Mums2B app. These tools allow women to share their experiences and outcomes, which are then aggregated and used to enrich the evidence base and inform public guidance. While this element does involve patient-generated information, it is not the core data source for the project's primary research or

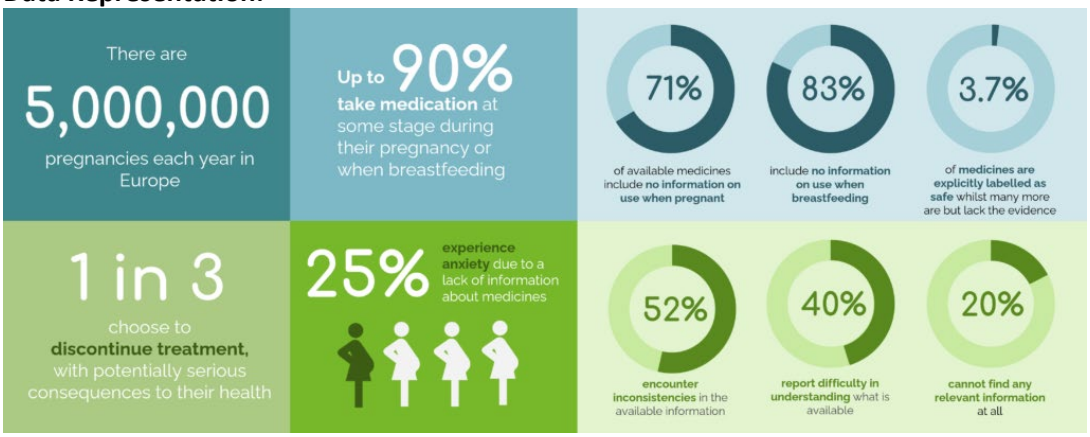
regulatory-grade evidence generation. The main analytical work is based on structured, secondary data from healthcare systems and registries, not on continuous, real-time PGHD from apps, wearables, or patient diaries.

- **Data Collection Methods:** ConcePTION, as shown in its D1.2 deliverable, relies mainly on secondary population-based data such as healthcare databases, administrative records, disease registries and birth cohorts, which are often linked to improve completeness and accuracy. Specifically, D1.2 focuses on observational research using routinely collected data and does not involve experiments or intervention-based studies. Although D1.2 is centred on secondary data, the wider ConcePTION project also develops approaches for primary source data collection in other work packages, particularly through the creation of core data elements for prospective studies. The project also incorporates document-based evidence such as literature reviews, EU PAS Register studies and information from European medicines labels. While these activities support evidence mapping rather than classical data collection, they are an integral part of the project's methodology. Throughout, ConcePTION places strong emphasis on harmonisation of definitions, data structures and linkage processes to ensure high quality, comparable and reliable evidence for pregnancy safety research.

## 3. Results & Findings

- **Key Findings:** The ConcePTION project has demonstrated that it is possible to move from a fragmented, largely anecdotal evidence base on medicine use in pregnancy and breastfeeding to a structured ecosystem that can routinely generate regulatory-grade real-world evidence and translate it into practical guidance for women and health professionals. By harmonising population-based health data, pharmacovigilance reports, primary data collection, and biological samples within a federated platform built on a common data model and FAIR catalogue, the consortium has shown that robust pregnancy pharmacoepidemiology can be conducted across countries, and that these methods are mature enough to be adopted by major European real-world data networks such as VAC4EU, EU PE&PV, and SIGMA. The project has also established Europe's first non-commercial breast-milk biobank, and a validated non-clinical and physiologically based pharmacokinetic framework for lactation studies, demonstrating that quantitative predictions of medicine transfer into breast milk and infant exposure can be generated even when clinical data are sparse, which has led to formal regulatory dialogue, including EMA Qualification Advice. On the knowledge-translation side, ConcePTION has delivered the MUMS online knowledge bank and the Meds4Mums2B mobile application as trusted public resources, which combine up-to-date safety evidence with user-reported experience, thereby both informing individual decisions and continuously enriching the underlying evidence base. Collectively, these outputs show that ConcePTION has not only reduced uncertainty around medicine safety in pregnancy and breastfeeding for a growing set of products, but has also produced enduring ethical data-governance frameworks, data-quality pipelines, and methodological guidance that are now reused in EMA-linked infrastructures and provide a reference model for future IHI and regulatory initiatives in maternal and child health.

- **Data Representation:**




- **Patterns/Trends:** For many years, pregnant and breastfeeding women have been excluded from clinical trials. This was for a good reason – to ensure the baby would not come to any harm. But the knock-on effect of that is that for many medications, there is no strong body of evidence to say whether the drug is safe or not to take during pregnancy and breastfeeding. A staggering 71% of available medicines in the EU do not include information on whether or not it's safe to use them while pregnant.

## 4. Discussion & Conclusion

- **Interpretation of Findings:** ConcePTION has shown that a disease- and population-specific, federated evidence ecosystem for medication safety in pregnancy and lactation can be operationalised at European scale. By delivering harmonised methods, governance frameworks, a federated RWE platform, a FAIR catalogue, a breast-milk biobank and public-facing knowledge translation (MUMS.eu / Meds4Mums2B), the project demonstrates how regulatory-grade pregnancy pharmacoepidemiology can be produced and communicated to clinicians and patients. For IMPROVE, the primary implication is that rigorous governance, transparent metadata, and purpose-built translational resources (knowledge banks, validated PBPK tools) are essential to turn mixed-source data into actionable, trustable outputs for both regulators and patients.

  Firstly, ConcePTION provides a clear technical blueprint for federated, multi-source evidence generation: common data elements, a generic common data model and distributed analytics that preserve privacy while enabling cross-country analyses. IMPROVE can adopt these design principles to ensure that PGHD pipelines are interoperable with clinical RWD and compatible with federated analytics.

  Moreover, ConcePTION's successful regulatory engagement, including PBPK modelling for lactation and formal dialogue with EMA, shows the value of packaging methodological work (models, validation pipelines, data quality metrics) alongside stakeholder-facing outputs. For IMPROVE this emphasises early, documented regulatory strategy and building reproducible validation artifacts that are usable in qualification or advice interactions.

  Finally, ConcePTION's emphasis on public knowledge translation (MUMS.eu) and tools that incorporate patient-reported information highlights that evidence ecosystems should not end at publication: they must return understandable, evidence-based guidance to patients and

clinicians. IMPROVE should therefore plan both analytic pipelines and user-facing translation mechanisms from the start to maximise uptake and trust.

- **Gap analyses and Implications for Future Research related to IMPROVE:** A central gap in ConcePTION is that PGHD was not the primary analytical backbone. ConcePTION relied chiefly on secondary, population-based RWD (healthcare records, registries) and pharmacovigilance, with patient-reported inputs playing a supplementary role. For IMPROVE, which aims to position PGHD (PROMs/PREMs/PPI and device/wearable streams) at the centre of value assessment, this signals a need to define validated PGHD metadata, quality checks and OMOP/CDM extensions so that patient-generated streams are first-class citizens in federated analyses.

  Besides, scaling a pregnancy-focused architecture to other clinical domains (e.g., cardiovascular populations targeted by IMPROVE) will require careful adaptation of clinical concepts, ontologies and exposure/outcome definitions. ConcePTION's models and governance are disease-tailored; IMPROVE will need to invest in disease-specific mapping and validation work to avoid semantic drift when combining continuous PGHD with episodic clinical records.

  Lastly, sustainability and bidirectional value-loops remain challenging. While ConcePTION created durable outputs (biobank, knowledge bank, governance templates), maintaining funding, updating metadata, and keeping patient engagement active beyond project lifetimes is not trivial. IMPROVE should therefore codify sustainability plans (funding models, maintenance responsibilities, local adoption pathways) and design mechanisms that feed informative results back to participants and clinicians to preserve long-term engagement and data quality.

## 3.5. Practice GREG

### 1. Project Overview

- **Title:** Testing, improving, and co-creating guidance and tools for real world evidence generation in Europe and use for decision-making in Europe (GREG)
- **Principal Investigator(s):** Name(s) of the lead researcher(s). Daniel Prieto-Alhambra (Erasmus Universitair Medisch Centrum Rotterdam)
- **Consortium partner(s):**

  a) Universities, research organisations, public bodies, non-profit groups
  i. Erasmus Universitair Medisch Centrum Rotterdam, Rotterdam, Netherlands
  ii. Erasmus Universiteit Rotterdam, Rotterdam, Netherlands
  iii. Getreal Institute, Utrecht, Netherlands
  iv. Instituto Aragones De Ciencias De La Salud, Zaragoza, Spain
  v. National Institute For Health And Care Excellence, Manchester, United Kingdom
  vi. Societe Europeenne De Cardiologie, Biot Sophia Antipolis, France
  vii. Statens Legemiddelverk, Oslo, Norway

viii. Stichting Eupati Foundation, Utrecht, Netherlands
ix. Stichting European Health Data And Evidence Network, Rotterdam, Netherlands
x. Universidade De Aveiro, Aveiro, Portugal
xi. University Of Dundee, Dundee, United Kingdom
xii. University Of Galway, Galway, Ireland
xiii. University of Oxford, Oxford, United Kingdom

b) EFPIA including Vaccines Europe
i. Actelion Pharmaceuticals LTD, Allschwil, Switzerland
ii. Amgen, Diegem, Belgium
iii. Aventis Pharma Limited UK, Reading, United Kingdom
iv. Bayer Aktiengesellschaft, Leverkusen, Germany
v. Boehringer Ingelheim Internationalgmbh, Ingelheim, Germany
vi. Bristol-Myers Squibb Company Corp, New York, United States
vii. Glaxosmithkline Research & Development Limited, London, United Kingdom
viii. Institut De Recherches Internationales Servier, Gif-Sur-Yvette, France
ix. Janssen Cilag SA, Madrid, Spain
x. Janssen Research & Development, LLC, Raritan, United States
xi. Medical Device Business Services Inc, Warsaw, United States
xii. Novo Nordisk A/S, Bagsvaerd, Denmark
xiii. Pfizer AB, Sollentuna, Sweden
xiv. Pfizer Hellas S.A., Athens, Greece
xv. Pfizer Inc, New York City, United States
xvi. Pfizer Limited, Sandwich, United Kingdom
xvii. Pfizer R&D UK Limited, Sandwich, United Kingdom
xviii. Sanofi-Aventis Recherche & Developpement, Gentilly, France
xix. Sanofi-Aventis gulf F.Z.E., Dubai, United Arab Emirates
xx. Sanofi Pasteur Limited Canada, Toronto, Canada
xxi. Sanofi Pasteur SA, Lyon, France
xxii. Sanofi US Services Inc., Cambridge, Massachusetts, United States
xxiii. Sanofi Winthrop Industrie, Gentilly, France

c) MedTech Europe
i. Edwards Lifesciences Belgium BV, Dilbeek, Belgium
ii. Edwards Lifesciences GMBH, Garching B. Munchen, Germany
iii. Edwards Lifesciences Llc, Irvine California, United States
iv. Edwards Lifesciences SARL, Nyon, Switzerland
v. Edwards Lifesciences SAS, Guyancourt, France
vi. Edwards Lifesciences SL, Valencia, Spain
vii. Edwards Lifesciences SRL, Milano, Italy
viii. Medical Devices & Diagnostics Global Services, LLC, Bridgewater, United States
ix. Medtronic, Inc., Minneapolis, United States
x. Medtronic Bakken Research Center B.V., Maastricht, Netherlands
xi. Medtronic France, Boulogne, France
xii. Medtronic Italia S.p.A., Milano, Italy

xiii. Medtronic Ltd, Watford, United Kingdom
xiv. Molnlycke Health Care AB, Goteborg, Sweden
xv. W.L. Gore & Associati S.R.L., Verona, Italy
xvi. W.L. Gore et Associés S.A.R.L., Paris, France
xvii. W L Gore & Associates BV, Tilburg, Netherlands

d) Third parties
   i. Region Uppsala, Uppsala, Sweden

e) Small and medium-sized enterprises (SMEs) and mid-sized companies (<€500 m turnover)
   i. Synapse Research Management Partners SL, Madrid, Spain
   ii. The Hyve BV, Utrecht, Netherlands

- **Funding Source(s):** EU and Industry
- **Project Duration:** 01/05/2025 to 30/04/2030

## 2. Methodology

- **Summary of the project:** The aim of GREG is to generate guidance and tools to advance the use of RWE in the development and evaluation of medicines, medical devices and drug-device combinations, and to support regulatory and health technology assessment (HTA) decision-making. The consortium comprises leaders from key European RWE initiatives including academics, regulators, HTA agencies, and industry leaders from the medicines, medical device and drug-device sectors. The team will start by compiling libraries of use cases where RWE was used, successfully or unsuccessfully, in different settings (e.g. regulatory decision-making, HTA…) at different stages of the development life cycle. They will also gather information on what different stakeholders need when it comes to RWE. All of this will feed into studies that will generate the evidence needed to draft guidance and recommendations, to be co-created with stakeholders and subsequently tested in additional pilot studies. This process will allow the project to deliver much-needed resources on the use of RWE, including evidence-based guidance documents and tools; training on their use; and structured templates for regulatory and HTA submissions. Ultimately, these will help those developing medicines, devices and drug-device combinations to prepare more robust and consistent RWE evidence to regulators and HTA agencies. In turn, the GREG outputs will also allow regulators and HTA bodies to assess these submissions more easily and consistently. Once implemented, the GREG project's results should therefore help to speed up the development and evaluation of medicines, devices and drug-device combinations, and patients' access to them.
- **Research Problem:** Real-world data and evidence (RWD/RWE) have immense potential to contribute to the development and evaluation of medicines, medical devices, and drug-device combinations. Guidance on how this could work exists, but is high level, not evidence-based, and implementing it in practice is far from easy.
- **Objectives:** The GREG project aims to improve decision-making processes across Europe by generating, pilot-testing, and disseminating practical, evidence-based guidance and tools for Real World Evidence (RWE). Its focus includes supporting the development and evaluation of medicines, medical devices, and drug-device combinations by using Real World Data (RWD). GREG will leverage European RWD platforms (e.g., EHDEN, OncoValue, and EuroHeart) and

federated analytics via OMOP-CDM to harmonize data and enable analyses across clinical trial stages, regulatory submissions, HTA assessments, and post-market evaluations.

- **Population:** The GREG project encompasses a broad population across diverse disease areas by leveraging large-scale European real world data platforms, including EHDEN, EuroHeart, and OncoValue, which together cover extensive healthcare populations. It addresses the generation and evaluation of Real-World Evidence (RWE) for medicines, medical devices, and drug-device combinations through federated analyses of millions of patient records harmonised via the OMOP Common Data Model. While the project covers multiple therapeutic areas, its key focus includes oncology, cardiovascular diseases, and diabetes, reflecting the clinical diversity and geographical breadth of European healthcare settings.
- **PGHD used:** The GREG project primarily analyses patient-generated health data (PGHD) related to lifestyle and health behaviour monitoring, which is essential for enriching real-world evidence in chronic disease management. The types of PGHD mainly include data from mobile health applications, wearable devices such as fitness trackers and glucose monitors, and patient-reported outcomes gathered via digital surveys and diaries. This encompasses biometric measurements like blood glucose and blood pressure, activity levels, medication adherence, symptom tracking, and quality of life measures. Such PGHD complements traditional clinical data by providing continuous, real-life context outside healthcare visits, supporting a more comprehensive understanding of treatment effectiveness and patient outcomes.
- **Data Collection Methods:** The GREG project employs a diverse set of data collection methods tailored to generate high-quality Real-World Evidence for medical products across Europe. Key techniques include mining large-scale secondary data from harmonised real world data platforms such as EHDEN and EuroHeart, integrating electronic health records, registries and administrative databases. Complementing this, the project also utilises patient-generated health data collected via mobile health apps, wearable sensors, and digital patient-reported outcome tools to capture lifestyle, symptom, and adherence information outside clinical settings. Additionally, GREG employs surveys and qualitative methods such as interviews and focus groups to co-create evidence generation tools and guidance with stakeholders. These combined archival, observational, and primary data collection approaches enable a comprehensive patient and population level understanding for regulatory and Health Technology Assessment decision-making in Europe. The methodologies follow best practice frameworks for data quality, privacy, and interoperability, leveraging iterative co-creation and testing across Europe's federated data landscape.

## 3. Results & Findings

- **Key Findings:** Not available.
- **Data Representation:** Not available.
- **Patterns/Trends:** Not available.

## 4. Discussion & Conclusion

- **Interpretation of Findings:** Although GREG has not yet produced empirical results due to its early stage, the project design already offers clear implications for IMPROVE. GREG demonstrates that the creation of practical, evidence-based RWE guidance in Europe requires iterative co-creation across regulators, HTA bodies, data platform leaders, industry and patient representatives. This multi-stakeholder approach ensures that methodological recommendations and submission templates are not merely theoretical but grounded in operational feasibility and shared expectations. For IMPROVE, this signals that the development of PGHD-based value elements and endpoints will only achieve long-term legitimacy if similar cross-stakeholder engagement is embedded from the outset.

  Firstly, GREG's plan to build libraries of real-world use cases, including both successful and unsuccessful RWE applications, highlights the importance of learning directly from real regulatory and HTA precedents. IMPROVE can adopt this strategy by cataloguing early PGHD pilots, documenting methodological challenges, and using these lessons to iteratively refine the project's endpoint frameworks, analytical pipelines, and evidence submission strategies.

  Moreover, GREG's emphasis on harmonised, federated analytics leveraging OMOP-CDM and major European data platforms demonstrates that methodological consistency is essential for scalable and regulatory-credible evidence generation. This is directly relevant for IMPROVE, where PGHD will need to coexist with clinical RWD inside distributed analytics environments. Designing PGHD standards, metadata structures and preprocessing pipelines aligned with emerging European RWE frameworks will ensure that IMPROVE's outputs are compatible with wider federated infrastructures and downstream regulatory needs.

  Finally, GREG's intention to deliver structured templates for regulatory and HTA submissions shows that clarity of expectations is a determinant of adoption. IMPROVE should therefore develop parallel PGHD-focused templates that articulate what constitutes high-quality signal processing, adherence metrics, validation steps, and patient-centred interpretability. Such templates will position IMPROVE to engage early with regulators and HTA bodies, facilitating smoother translation of PGHD-derived endpoints into decision-making contexts.

- **Gap analyses and Implications for Future Research related to IMPROVE:** A central gap in GREG, from an IMPROVE perspective, is the project's broad focus on generic RWD/RWE rather than the specific challenges posed by continuous, granular, behavioural PGHD streams. Methodological topics such as sensor calibration, signal quality, algorithmic transparency, missingness patterns, and patient adherence dynamics are not yet integrated into the early GREG work plan.

  Besides, cross-stakeholder alignment on evidentiary expectations, particularly between regulators and HTA bodies, remains an unresolved challenge for GREG. Divergent priorities (e.g., causal inference strength for regulators versus comparative effectiveness and real-world value for HTA) mean there is no unified template yet. For IMPROVE, this highlights the need to design PGHD validation strategies that meet both perspectives simultaneously, including disease-specific performance assessments, bias quantification, and outcome relevance for both clinical and economic evaluation.

  Lastly, the maturity timeline for GREG introduces a practical gap: substantial portions of its guidance, tools and templates will only emerge several years from now. IMPROVE, operating on a faster horizon, cannot afford to delay methodological development until GREG

deliverables become available. This necessitates a dual strategy: progressing independently with PGHD-specific standards, validation frameworks and evidence generation pilots, while ensuring full compatibility with the principles emerging from GREG so that alignment is seamless once tools and guidance are formally released.

## 4. Conclusions

This second version of the Practices Report marks a clear progression in the identification, analysis, and organisation of real world practices relevant to the IMPROVE project. Building on the foundations established in the first version, the work has expanded significantly in scope, depth, and methodological maturity. The enhanced analysis covers five major IHI projects that collectively span real world data infrastructures, patient generated data ecosystems, digital endpoint development, maternal and child health evidence networks, and guidance creation for regulatory and HTA decision making. These projects include EHDEN, PaLaDIn, IDEA-FAST, ConcePTION, and GREG, each offering unique perspectives on the opportunities and challenges associated with the generation, governance, and use of real world and patient generated health data.

Across these analyses, several overarching insights have emerged. First, there is growing recognition across Europe that PGHD and broader RWD infrastructures must be designed for interoperability, federated analytics, and long term sustainability. Projects such as EHDEN and ConcePTION demonstrate that large scale, harmonised data ecosystems are feasible when supported by strong governance, common data models, and transparent quality frameworks. Second, patient centric design and engagement, as illustrated by PaLaDIn and IDEA-FAST, are critical for ensuring the usability, acceptability, and durability of PGHD driven approaches. These projects highlight the importance of co creation, iterative usability testing, and careful management of participant burden to maintain high quality data collection. Third, the analysis reveals that methodological and regulatory alignment remains an ongoing challenge. GREG in particular shows that clear, evidence based guidance for RWE and PGHD integration is urgently needed, and that multi stakeholder co creation is essential for producing practical and credible frameworks.

The refined methodology introduced in this deliverable, including the updated Analysis of Practice Template, has proven effective in structuring diverse information streams and identifying both transferable practices and domain specific requirements. It also provides a consistent foundation for expanding the practice tracker, improving searchability, and linking real world examples to specific needs across WP4 and WP5. Importantly, the work completed in this iteration confirms that the practice ecosystem surrounding PGHD is dynamic, heterogeneous, and rapidly evolving, which underscores the need for continuous updates and systematic engagement with external projects.

Looking ahead, several priority actions emerge. The methodology will be validated and refined in collaboration with stakeholders, including direct interviews with project leaders from the IHI initiatives analysed in this version. The practice tracker will be expanded with additional projects identified in Appendix A, enabling a more comprehensive and representative mapping of practices relevant to IMPROVE. Finally, the insights gathered here will serve as inputs for the development of IMPROVE's conceptual, technical, and implementation frameworks, especially regarding PGHD standardisation, device selection, regulatory readiness, engagement strategies, and long term sustainability planning.

Overall, this second version of the Practices Report provides a strengthened and actionable evidence base that supports cross project learning, promotes alignment with European data initiatives, and informs the co creation of a robust, patient centred, and practice grounded PGHD framework within IMPROVE.

## About IMPROVE

IMPROVE aims to be a dynamic, ready-to-use framework for seamlessly integrating patient-reported information. This adaptable system constantly evolves with the latest evidence, using PGHD and health system data to provide cost-effective solutions for diverse treatment conditions in real settings. The project follows Ontology, Epistemology, and Methodology principles. Ontology defines structures in patient-reported outcomes; Epistemology ensures valid knowledge; Methodology links techniques to outcomes, systematically addressed in its work.

IMPROVE optimizes patient-reported information in real settings, offering a deep understanding of patient behaviors. The project sets up ontology, epistemology, and methodology to minimize the burden on stakeholders cost-effectively. It adopts a scalable, data-driven approach with NLP-driven knowledge extraction. Real World Data is integrated into the Federated Causal Evidence module for comprehensive understanding. Evidence collected enables visualizing attributes affecting patient-reported outcomes through IMPROVE Engagement Factors and Indicators Knowledge Graphs.

IMPROVE's toolkit includes resources for decision-makers, featuring plausible scenarios via the Copenhagen Method. Patient engagement via the MULTI-ACT model ensures sustainable healthcare aligned with patient priorities. This project delivers a modular, open access strategy, providing a trustworthy ecosystem of evidence-based applications. Patient engagement and co-creation scenarios solidify its role in transforming healthcare research and care.

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