EUROPEAN PATIENT OBSERVATORY:

NAVIGATING THE HEALTHCARE LANDSCAPE

The Observatory
a European Patients Observatory study by HealthTech For Care

To promote and defend a European policy that encourages medical innovation while ensuring fair access to care for all European patients.

4 European initiatives for a better equity in Europe:

- *Diga fast-track procedure*
- *National plans for rare diseases*
- *EU Patient-Centric Clinical Trial Platform or EU-PEARL*
- *Early Access and/or Compassionate Care Initiative*

Maryvonne Hiance,
Honory President of HealthTech For Care, initiator of this observatory

Dear fellow citizens,

It is with immense pleasure and undisguised pride that I address you with these few lines on the occasion of the first edition of our European Patients Observatory. As the president of this innovative initiative, I feel profound gratitude towards all those who have contributed to making this project a tangible and promising reality.

The Observatory aims to defend a European policy that promotes cutting-edge medical innovation while ensuring fair access to care. It represents, etc. The European Patients Observatory represents a significant milestone in our shared quest to improve access to healthcare for patients across Europe. We are witnessing an unprecedented convergence of efforts, bringing together healthcare professionals, policymakers, researchers, and most importantly, the true architects of our healthcare system - the patients.

Our vision for this Observatory is clear: to ensure that these initiatives do not remain isolated cases but become models replicated throughout Europe. Borders should not be barriers to health, and our commitment to equal access to healthcare is unwavering. Accessibility to quality healthcare is a fundamental right, and by sharing our successes and learning from our challenges, we can build a stronger and more resilient European healthcare system. Every patient should have the assurance that medical excellence is within reach, regardless of their geographical location.

I invite each of you to explore the presented initiatives, share them widely, and actively participate in building a future where health is truly universal.

Together, we are the architects of change. Thank you for joining us in this vital quest for equitable access to healthcare in Europe.

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Introduction

The challenge of ensuring equitable patient access to healthcare in a project for a Health Europe.

If the life expectancy of populations in Europe and the ease of access to healthcare they enjoy continue to be benchmarks worldwide, the crisis related to the Covid-19 epidemic at the beginning of the decade has highlighted weaknesses and threats to the sustainability of these healthcare systems and the economic ecosystem they rely on.

The following observations are evident:

- **The weakening of healthcare systems** caused by the Covid-19 epidemic, leading to a state of saturation in healthcare infrastructure and human capacities, especially in primary care (general practitioners and nurses).

- **Delays in the management of many pathologies,** with a particularly concerning situation in the fields of mental health, the follow-up of chronic diseases, and the diagnosis of cancers, especially in relation to the goals set by the «Europe's Beating Cancer Plan» proposed by the European Commission. This situation is perceived as worrisome for young populations regarding issues such as overweight or mental health.

- **A situation of dependence on Europe** from other geographical areas in terms of supply, and even control, of certain technologies, whether they are everyday products or critical technologies.

- **A widening gap compared to the United States** in terms of financing capabilities for disruptive innovation and, ultimately, patient access to innovation when it is not sourced in Europe.

Among the priorities defined by the European Commission through its report «Health at a Glance» and the EU4Health initiative, the requirement for equity in patient access to healthcare and innovation emerges as the foundation for numerous challenges, including:

- **Enabling as many patients as possible to benefit** from the contributions of digital innovation in health.

- **Strengthening efforts for early diagnosis and access to therapies in rare and complex diseases** where inequalities in care are most pronounced.

- **Ensuring equity in access to innovations under development and reducing inequities** related to the market entry delays of new therapeutic innovations.

- **Increasing the functional and technological resilience of healthcare systems** in the face of major health crises.

- **Enabling a larger number of people to** access clinical trials and experimental therapies **in areas where medical needs remain massively unmet.**

Presentation of the initiator of this observatory

What is HealthTech For Care?

HealthTech For Care is an endowment fund created in 2020 after the success of the first edition of HealthTech Innovation Days. The objective of HTFC is to support and promote access to care for all patients and, more specifically, access for all to new medical technologies and new drugs.

Our mission statements

Fostering

the growth and development of the entire health ecosystem

Advocating

for the advancement of innovative therapies and treatments to benefit patients

Promoting

enhanced access to care for patients within the European healthcare ecosystem

Our activities

HealthTech For Patients

The creation of HealthTech For Patients (HTFP) serves as a platform for patients to express their needs and discover innovations in healthcare. For the past three years, HealthTech For Care has been hosting HealthTech For Patients events centered around themes dedicated to enhancing patient access to care.

HealthTech Innovation Days

This event provides a valuable platform for actors in the innovation and science sectors to come together and expedite the delivery of solutions to patients, placing them at the heart of innovation. HTID facilitates interactions among companies, investors, industrial and pharmaceutical entities, and various stakeholders in the industry, including patients and patient associations. Additionally, the event features conferences on significant topics of general interest, led by international experts.

Science For Care

«Science For Care» is a podcast that delves into the narratives behind the scientific and medical breakthroughs that have driven innovation for patients.
Its aim is to empower listeners with insights into the narratives behind remarkable scientific and technological advancements, whether they are in the process of development or already in use, all geared towards providing care for everyone.

Observatory

Based on the current situation of health care in Europe, the Observatory aims to highlight and support initiatives taken in favor of health equity, particularly in the area of patient access to innovative care.
By promoting these initiatives, the Observatory aims to defend a European policy that promotes cutting-edge medical innovation while ensuring fair access to care for all European patients.

Missions & concept of this observatory

What are HTFC missions through this observatory?

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Understand European patients' expectations and highlight the differences between European countries.

Bring useful knowledgeable information to the European Commission to support dedicated actions and tools to secure equitable access to solutions for all patient across Europe.

Bring all stakeholders together from patient associations, patients, national clusters, regulatory bodies, innovative healthtech, pharmaceutical companies, … to discuss their input to develop faster patient-oriented projects.

Equal access to healthcare is a cornerstone of the social contract that binds the people of Europe: regardless of income or location, everyone must benefit from the best existing standards of care. This foundation must be consolidated.

The material produced by the Observatory, in the form of a report, must be used to feed the public debate and to support the arguments of the elected representatives who, at the European level, plead for this double requirement of innovation and equity.

TheObservatory
a European Patients Observatory study by HealthTech For Care

1st initiative: A fast-track procedure for digital medical innovation (Germany)

Digital therapies are revolutionising the world of healthcare, altering treatment paths and the options available to patients. But the massive arrival of so many innovations on the market's doorstep is forcing the regulatory authorities to adapt. Germany took the lead four years ago with the DIGA. A system that is inspiring other countries.

Pioneering in patient access to digital therapies, Germany has become a model for many European countries. It was on December 19, 2019, that the Digital Healthcare Act (known as DIGA) was launched in Germany. This act enables digital medical devices to be prescribed by healthcare professionals as part of patient care in Germany. This means that approximately 73 million insured Germans are entitled to these digital health services through health applications. Prescriptions can be initiated by physicians and psychotherapists and reimbursed by health insurers. The Federal Institute for Drugs and Medical Devices in Germany, known as BfArM, is responsible for evaluating DiGA candidates so that they can be listed in the catalog of reimbursed services.

A strict framework for being a DiGA

To be eligible for the DiGA, a digital solution must be a medical device of class I or IIa and have obtained a CE medical marking. It must be intended for the identification, monitoring, treatment, or alleviation of diseases, injuries, or disabilities. «What is important, notes Vincent Vercamer from the Digital Health Delegation (DNS) at the Ministry of Health and Prevention, is that the primary function of a DiGA must rely on digital technologies». Therefore, the main medical purpose must be achieved through digital functions. Thus, a DiGA is for individual use and focused on the patient. Moreover, it must provide evidence of at least one positive health effect, such as a medical benefit to health or quality of life, a contribution to improving structures and relevant processes for patient care, or an organizational benefit such as therapeutic education and better access to care. For instance, a connected watch that reminds the patient to take their medication and tracks their biological values would be considered a DiGA, unlike a platform with multiple connected medical devices where the patient adds their data, as this would then be a passive device.

Early access via Fast Track

To make these digital therapies available to patients as quickly as possible, the German regulatory agency, BfArM, has developed a process to expedite reimbursement. This Fast Track requires the developer of the digital solution to submit an application for either definitive or provisional listing in the DiGA Directory. The candidate submits their application either for a request for definitive listing, which, if approved, allows entry into the DiGA directory, or for a request for provisional listing, which permits provisional entry into the DiGA directory for a duration of 12 months. At the end of this period, the digital medical device will be evaluated based on the results of its clinical studies for potential inclusion in the directory. The reimbursement price is re-evaluated at the end of this year, typically decreasing.

In the application process, two options are possible: a DiGA-Fast-Track without provisional listing. In the first option, after the application is submitted, the manufacturer will consult the BfArM (which incurs costs) for their decision regarding the DiGA candidate. A provisional reimbursement for 12 months will be made at the manufacturer/publisher's rate. During this period, the digital medical device (DMD) will be provisionally listed in the DiGA directory. This timeframe allows for conducting a clinical study to demonstrate its clinical or organizational benefit. Subsequently, the DMD will apply for definitive listing. The BfArM's final decision will occur within a three-month period, involving negotiation of the reimbursement price and the definitive listing.

The French PECAN inspired by the German DiGA

Early access to digital therapies in Germany has inspired a similar approach in France. Since March 30, 2023, digital medical devices (DMDs) can also benefit from early coverage. When the first Early Coverage for Novel Health Technologies (PECAN) is granted, it allows for provisional reimbursement for a non-renewable period of one year, enabling the finalization of their request for standard coverage. Candidate DMDs can either aim for therapeutic purposes, eventually intended for inclusion in the List of Reimbursable Services and Products (LPPR) similar to DiGAs, or be dedicated to medical telemonitoring.

«To benefit from PECAN and ensure rapid patient access to innovations, it's not always necessary to have an ongoing clinical study. It depends on the level of evidence available at the time of submission. In all cases, it's the role of the French Health Authority (HAS) to assess these aspects of the PECAN application, and the standard application should be submitted within 6 to 9 months after the start of PECAN,» explains Vincent Vercamer.

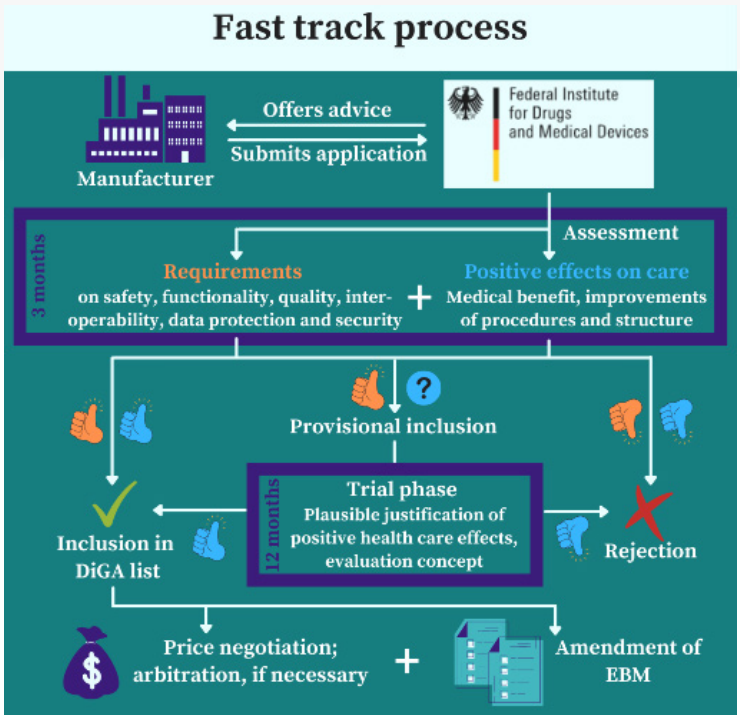
Concurrently with the introduction of PECAN, teams at Yves Lorillard's Digital Health Agency (ANS) are working on creating standards regarding the safety of digital health devices, including interoperability, accessibility, and ethics. «Obtaining the PECAN label and subsequent certification from ANS will be crucial to access reimbursement from the Health Insurance,» emphasizes the Telehealth Projects Manager at ANS. To obtain the PECAN label, digital devices must jointly apply to both the Digital Health Agency and the French Health Authority, which will evaluate the innovative nature of the solution.

A long road to European harmonisation

After Germany followed by France, countries like Italy could follow this movement of Fast Track for Digital Medical Devices (DMDs). «We are very vigilant from an ethical standpoint regarding the hosting of health data in Europe. In all standards, numerous safeguards have been established to ensure that the data is not misused in Europe where it is hosted,» explains Yves Lorillard.

The health ministries of France, Germany, Belgium, and Luxembourg have initiated a series of meetings aimed at laying the foundations for a true European digital health framework.

... to be continued.



Interview with Stefan De Keersmaecker, Spokesperson for the European Union in the field of health

Currently under discussion in the European Parliament and the European Council, the establishment of a new health data ecosystem would promote access to higher quality healthcare for all European patients and open up possibilities for academic and private researchers.

Stefan De Keersmaecker, Spokesperson for the European Community in the field of health

What measures are being taken in Europe to facilitate access to digital health for all European patients?

While the field of public health falls within the jurisdiction of each member state, the European Commission legislates, assists, coordinates, supports, and issues recommendations to create a European Union, particularly a digital health union. That's why, in May 2022, it proposed a draft regulation for the future European Health Data Space (EHDS) common to the member states. This ecosystem would become a cornerstone of a robust European health union. It would, for example, enable the sharing of data, under very strict conditions, for research or industrial performance, improve the management of pandemics such as COVID-19, or study rare diseases through the pooling of data.

What does this project of a European Health Data Space consist of?

Its establishment is considered one of the priorities of European health policy. Currently the vast amount of available data in Europe is not adequately utilized. In primary use - sharing health data with doctors and hospitals - such an ecosystem would promote access to higher quality healthcare for all European patients, with guarantees of data protection and privacy.

Doctors and hospitals would have easier access to patient health data originating from their home country via a shared record. Control over this data would be facilitated at both the national and European Union levels.

In the context of secondary use - the use of health data by public authorities, research centers, and the industry - the Commission's proposal aims to establish a coherent, reliable, and effective framework for the use of health data for research, innovation, policy development, and regulation (anonymized data).

The goal is to provide more room for maneuver and open up possibilities for academic and private researchers, enabling them to develop new drugs. All of this would be done within a strict framework to protect health data.

How can the protection of the data used be ensured?

Trust is a fundamental factor for the success of this project. Hence the establishment of a reliable framework for secure access to a wide range of health data and for the processing of this data.
In addition to the protections already applicable in the healthcare sector, more specific rules are developed in the regulation on the European Health Data Space, considering their sensitivity.

Where is this European Health Data Space project at?

It is currently under discussion in the European Parliament and the Council (which brings together the competent ministers of each member state and votes by qualified majority). In its facilitating role, the Commission is involved in discussions with co-legislators. It seeks to persuade these co-legislators and enable both institutions to reach an agreement in case modifications are made to the project.
Moreover, the draft regulation also proposes a framework for the cross-border use of health data with the establishment of a European infrastructure called MyHealth@EU (for primary use) and

HealthData@EU (for secondary use). It guides actors to facilitate the identification and reuse of data on a European scale. Finally, the text envisions the establishment of European governance through the creation of a European Health Data Space Board.

Are some countries more driving forces in the construction of the European health union?

The Commission never makes comparisons between different members. However, it is true that some member countries have made progress in the field of health data sharing, such as Estonia, Finland, and Croatia. **On a European scale, a shared health data space would indirectly improve equity among all patients, regardless of the European country in which they live.**

What budgets are allocated for the digital health Europe?

The EHDS will be financed through contributions from the European Commission and member states. To make the European Health Data Space a reality, digitization at the local, regional, and national levels is necessary. At the same time, it is also essential to establish interoperable infrastructures at the EU level to enable cross-border use of health data within the EU. The EU and member states must jointly take this bold step.
Member states have allocated €12 billion under the Recovery and Resilience Facility for investments in digital health and the secondary use of health data. The European Regional Development Fund and Invest EU provide additional investments in digital health based on national needs.

In total, at the EU level, the Commission will provide over €810 million to support the EHDS. Out of this amount, over €330 million is allocated to the activities and infrastructure of the European Health Data Space: €280 million under the EU4Health program, of which €110 million is already allocated, and an additional €50 million under the «Digital Europe» program.
The remaining amount, over €480 million from the «Digital Europe» program, the Connecting Europe Facility, and Horizon Europe, can be used by member states and entities involved in the EHDS, as well as other sectors.

The «Digital Europe» program will support the deployment of necessary infrastructures to securely make Health data accessible beyond the EU borders, to develop common data spaces (with over €140 million under the 2021-2022 work programs).
Where physical connectivity is lacking, the Connecting Europe Facility will promote the interconnection of cloud infrastructures in member states, including those needed in the European Health Data Space (€130 million).
Horizon Europe will continue to support the needs of the European Health Data Space through specific research projects and support actions focused on the interoperability of health data and research infrastructures (around €170 million allocated until 2022).

Key points - 1st initiative:

1. The rapid evolution of digital innovation is reshaping various aspects of healthcare, spanning prevention, diagnostics, and treatment follow-up.

2. The Digital Health Innovation Act (DIGA) stands out as a pioneering legal framework that expedites the introduction of digital healthcare innovations for the benefit of all patients, ensuring broad access and coverage. Recognized as a benchmark, DIGA serves as a model adopted by several European countries.

3. This framework lays the foundation for a European plan that establishes regulations for the market entry of innovative medical digital devices. The objective is to prevent innovation from becoming a source of inequity based on resources or geographical location, while also catalyzing the growth of the European startup ecosystem in the field of digital medicine.

2nd initiative: National plans dedicated to rare disease patients (France, Belgium)

National rare disease plans and the organization of European rare disease networks aim to reduce diagnostic delays, stimulate clinical research, and establish cross-border networks between healthcare practitioners and patient associations. France and Belgium have been pionners in France for the past ten years in that field, implementing ambitious programs that could inspire others in Europe.

300 million people worldwide, 30 million in Europe, are affected by rare diseases. Half of the affected patients are children under the age of 5. The unmet need is critical: less than 5% of the 7,000 rare diseases currently have a curative treatment.

Certainly, the management of rare diseases has improved in recent years thanks to the rare disease plans implemented in most European countries. Pioneering in 2005, France has so far conducted three national plans, resulting in the establishment of dedicated networks around reference and expertise centers, as well as a network across the country to ensure optimal care regardless of the patients' place of residence. In parallel, Public-Private research partnerships in rare diseases have been strengthened.

Towards a 4th National Rare Diseases Plan (PNMR) in France

Today, the French organization includes experts and patient associations within a Rare Diseases community in the country. Over 300 national diagnostic and care protocols (PNDS), good practice guidelines for rare diseases, have been developed by reference and expertise centers for rare diseases in France. These PNDS aim to «explain to the professionals involved the optimal diagnostic and therapeutic management and the care path of a patient with a given rare disease,» according to the French Health Authority.»

For Paul Gimenès, director of the Rare Diseases Alliance, 'the 3rd PNMR has led to numerous advancements such as the establishment of national diagnostic and care protocols (PNDS), the implementation of therapeutic education programs, the establishment of diagnostic observatories to assess individuals in diagnostic deadlocks, a better understanding of diagnostic delays based on various groups of rare diseases, and the establishment of a treatment observatory.'

The fourth French plan, currently in the process of being developed, must measure up to the new technological solutions available to patients today to improve diagnosis, treatment, research, and the life journey of those with illnesses. Revolutions are underway everywhere:

The fourth French plan, currently in the process of being developed, must measure up to the new technological solutions available to patients today to improve diagnosis, treatment, research, and the life journey of those with illnesses.

Revolutions are underway everywhere: high-throughput DNA sequencing, gene therapies, cell therapies, artificial intelligence and machine learning, precision medicine, data-sharing platforms, and connected medical devices.

They open up very promising new perspectives in the field of rare diseases. But all these technologies cannot fully unleash their potential without significant dedicated human and financial resources, and beyond that, without strong leadership, an interministerial strategy (Health, education, research, digital, industry...), coordination of all stakeholders in the rare diseases ecosystem, and a comprehensive and adapted communication strategy,' concludes Paul Giménès.

Paul Gimenès,
director of the Rare Diseases Alliance

Eva Schoeters, coordinator of the Belgian association RaDiOrg

8 functions for rare diseases in Belgium

Belgium launched its national rare diseases plan in 2014, in its final version. But as early as 2009, a Rare Diseases and Orphan Drugs Fund (King Baudouin Foundation) had been tasked by the Ministry of Public Health at the time to formulate recommendations for the development of a plan.

This plan is structured around 20 action modalities, divided into four domains: diagnosis and patient information, optimization of care, knowledge and information, and finally, governance in sustainability. According to ***Eva Schoeters, coordinator of the Belgian association RaDiOrg***, the assessment is positive: 'Our rare diseases plan is 10 years old. Among the progress made, we note the establishment of eight rare disease functions in seven university centers and one non-university hospital in collaboration with a genetics center, all of which are funded by the Federal Public Service for Public Health.'
But there is still work to be done, according to her: 'Specialized expertise centers are still lacking, and the establishment of a more comprehensive registry, documenting patients with rare diseases (currently less than 2% of affected Belgian patients are included), is needed. This is to improve knowledge and to be able to adapt policies for people with rare diseases

For example, some Belgian patients with a rare bone disease, progressive ossifying myositis (MOP or FOP), seek treatment in the Netherlands for optimal care of their condition, while others cross the French border to consult with specialists,» she laments.

24 Rare Disease Networks in Europe

The appropriate geographical scale for rare diseases can only be European, given the rarity of reference centers, experts, and patients for each country. That is why the Commission launched its first call for proposals to establish European Reference Networks in 2016. Today, 24 labeled rare disease reference networks are dedicated to various pathologies to assist doctors, researchers, and national expertise centers in sharing their knowledge.

France coordinates eight of them. Beyond borders, the goal is to make expertise travel rather than the patient. The coordinators and other leaders of these European networks convene 'virtual' advisory panels of physicians specialized in various fields, using a platform specifically designed for this purpose and telemedicine tools.

However, diagnostic delays remain high in Europe - the average duration that people with rare diseases wait before obtaining the correct diagnosis is 5 years, according to Eurordis figures. And significant disparities persist across the 27 countries of the Union.

To promote better European coordination, by specialization by country, closer cooperation between public and private research sectors and to improve the diagnosis and access to treatments for European patients, two organizations are playing a critical part :

- Eurordis : represents 57 national patient alliances for rare diseases, such as the French Alliance Maladies Rares, the Belgian RaDiOrg, and the Luxembourgish Alan

- The European Joint Program (EJP), dedicated to rare diseases, which aims to create an effective research ecosystem for rare diseases.

Interview with Philippe Berta, Member of french Parliament

Author of a report containing 51 proposals for a new policy on medical research and innovation, to be submitted to the French President in 2021, Philippe Berta is currently working on a report focusing on rare diseases

What are the main findings of the new analysis you are about to present ?

Last May, at the Institut Curie, President Emmanuel Macron announced the creation of five globally-oriented bioclusters and called for the launch of a comprehensive reformation of the organization of health biology research. This reformation aims to expand into discussions about funding methods and a reconsideration of our valorization-transfer tools.

It's crucial to involve all stakeholders in this discussion, including fundamental research, clinical and translational research, industry-led R&D, scientific societies, and to involve patient associations. This rationalization of our health biology research tool should provide better clarity and efficiency, essential elements to counteract the continual decline of our country on all indicators (publications, patents, creation of new activities) over several decades.

How can we improve access to care for patients suffering from rare diseases?

A new distribution of roles, for instance by pathology, should be organized at the European level. This would enable the pooling of costs, treat more patients, and potentially encourage industry to continue their research and development. With the increasing number of biotherapies - which is good news - and the advancement of increasingly personalized medicine, our model for evaluating these therapies must evolve.

France is the European country where the percentage of medications approved by the European Medicines Agency (EMA) that remain unvalidated by the High Health Authority is the highest.
As a result, one-third of medications are inaccessible to French patients.

Philippe Berta, PhD, geneticist, Member of french Parliament

The Social Security Financing Bill for 2024 must increase resources allocated to medication, particularly benefiting new biotherapies, especially for rare diseases. Other countries are more efficient, and it would not be shameful to replicate their methods. We need to collectively contribute to the establishment, development, and success of the Health Innovation Agency (AIS), led by Dr. Lise Alter. This cross-disciplinary agency should be given more power, flexibility, and resources. It should be able to intervene throughout the entire value chain, from fundamental research to market access for innovations.

What other improvements could be made in France?

The evaluation and reimbursement method for biotherapies need to be reconsidered, moving towards a multi-year model adjusted based on the assessment of medical services provided (SMR). Regarding clinical trials, response times should be shortened and standardized on a European scale to prevent diversion to third countries and harmful competition.
The impetus for change could come from Europe to evolve both our way of thinking and our way of acting.

Interview with Simone Boselli, Director of Public Affairs for Eurordis

Can you tell us more about the origins of Eurordis?

Established in 1997, Eurordis-Rare Diseases Europe is a non-profit alliance that brings together over 1,000 patient organizations representing individuals with rare diseases from 74 countries. It collaborates with European national associations from France, Germany, Italy, Spain, Belgium, Luxembourg, the Netherlands... Its mission is to contribute to changing the lives of European patients affected by rare diseases.

Are patient organisations driving change?

Since 1997, Eurordis has consistently championed the voice of patients. The associations have advocated for European patients with rare diseases to access the same level of care as the general population.
In reality, there's a need to facilitate the development of therapies for rare but common diseases like Sickle Cell Disease at both the European and international scales. At the national level, the cost of medication will differ as it is determined by each country. Significant differences also persist based on diseases and countries, such as a higher prevalence of Sickle Cell Disease in France compared to Ireland. Ultimately, it's important to draw from international strategies but adapt them locally to raise awareness of the disease and provide access to the best possible care.

What is the current state of organisation of care for patients suffering from rare diseases in Europe?

Access to treatments and diagnosis, especially in neonatal cases, significantly varies among countries and even within a single nation across different regions, as well as depending on various pathologies. The healthcare journey for each rare disease is not equitable at the European level. To address this challenge, the 24 European Reference Networks for Rare Diseases were established in 2017.

Wouldn't it be within Europe's remit to provide care for all patients suffering from rare diseases to ensure equal treatment in all countries?

This is the direction that Europe will need to work towards. The most effective strategies are supranational since countries cannot have expertise in all pathologies.
The European Parliament is, in fact, preparing a report on amending the Community Treaty, which would include rare diseases in the scope of European competences. This is a very important goal for us. **However, while many parliamentarians and countries would like health to fall under the action scope of the European Community, the obstacle remains tied to the health system specific to each country.**

Simone Boselli,
Director of public Affairs for Eurodis

Key points - 2nd initiative:

1. Rare diseases pose a significant public health emergency, primarily attributable to inadequate diagnoses and a scarcity of approved treatments.
2. The pioneering initiatives of the French and Belgian National Plans for Rare Diseases represent a pivotal step in Europe, bringing together diagnostic and therapeutic research efforts. These plans played a crucial role in the establishment of the European Reference Network (ERN), to which France and Belgium made substantial contributions.
3. While the ERN stands as an initial stride, there is a pressing need for a comprehensive European policy. Such a policy would ensure that no European Union patient is left without access to the most advanced diagnostics and treatments available to date. The aim is to create a framework that guarantees equitable and optimal healthcare outcomes for all individuals affected by rare diseases across the European Union.

3rd Initiative:
A patient-centric clinical trial platform (Spain, Europe)

Ensuring swift access to clinical trial is a moral requierement toward european patients as well as a condition to create a favorable environment for research and development of new medication. Launched in Spain with the support of IHI and spread in all Europe, EU-Pearl is an inspiring initiative responding to thoses challenges.

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Created in 2019, EU-PEARL (EU-Patient Centric Clinical Trial Platforms) is a public-private partnership funded by the Innovative Health Initiative (IHI, which replaced IMI) and notably supported by the European Patient Forum. This consortium has developed a generic framework and a set of tools for conducting collaborative trials in Europe: Patient-Centric Integrated Research Platforms (IRPs). Their goal is to facilitate the design and implementation of collaborative trials to improve drug development and enable patients' faster access to innovation.

For nearly four years, 36 organizations representing patients, clinicians, researchers, authorities, and the industry have been working together. Under the leadership of the Vall d'Hebron Research Institute (VHIR) and Johnson & Johnson Innovative Medicine, the EU-PEARL consortium brings together diverse expertise from the international clinical research ecosystem.

Optimizing Clinical Trials

In a conventional clinical trial, half of the participants receive the tested drug, and the other half receives a placebo. When multiple trials are conducted simultaneously in the same therapeutic area, it can be challenging to find a sufficient number of patients to conduct them successfully.

Conversely, when recruitment is conducted separately by each sponsor, patients may not necessarily be offered the trial most suited to their needs.

Dr. Hugh Laverty, Interim Executive Director of the Innovative Health Initiative (IHI)

«EU-PEARL allows testing multiple treatments simultaneously for a given pathology and comparing the results of all these trials to a single control arm,» explains Dr. Hugh Laverty, Interim Executive Director of the Innovative Health Initiative (IHI).

This decentralized approach has two immediate advantages: improving the chances for patients, who are more likely to receive an experimental treatment rather than a placebo, and reducing the total number of patients required for the development process.
It also promises a more collaborative approach among different drug candidate sponsors.

Sharing a single control arm among multiple sponsors involves collecting a greater number of parameters, enhancing knowledge of pathologies, understanding patient experiences better, and ultimately developing a truly patient-centered approach.

«In addition to being more effective, this approach is more patient-friendly; in the EU-PEARL framework, patients play a key role in trial design and, once enrolled, are more likely to receive a new treatment rather than a placebo,» notes Hugh Laverty.

Four «ready-to-use» collaborative trials have been established within this program, each focusing on specific pathological areas: **major depressive disorder, tuberculosis, non-alcoholic steatohepatitis (NASH), and neurofibromatosis.**

The project's results, which have been closed since April 2023, will be widely disseminated and utilized. The ambition of the European Commission is to transform the clinical trial system based on the evaluation of an asset through the development of integrated research platforms at the EU level.

From a Partnership to Multisectoral Collaboration

EU-PEARL relies on the Innovative Medicines Initiative (IMI), which has now evolved into the Innovative Health Initiative (IHI). The IMI was established in 2008 as a public-private partnership between the European Union (EU) and the European pharmaceutical industry with the aim of improving and accelerating the drug development process.
Building on the successes of the IMI while expanding the scope and composition of the partnership, the Innovative Health Initiative (IHI) replaced it in 2021. While the IMI was a collaboration between the EU and the pharmaceutical industry, the IHI involves a broader spectrum, including medical device manufacturers, biotechnology, digital health, and vaccines. «The multisectoral approach reflects the fact that health R&D covers different sectors, and future advances are likely to arise at the intersection of various disciplines, such as combinations of medical devices and drugs or AI-based diagnostics,» explains Dr. Hugh Laverty.

The IHI, and before it, the IMI, contribute to shaping European policies supporting innovation in health, such as the Cancer Mission and the European Health Data Space.

Financial Allocations to Selected Projects

In total, nearly 200 projects have been funded under the IMI1 and 2 programs. Some are dedicated to health issues such as antimicrobial resistance, dementia, diabetes, cancer, and autoimmune diseases. Others have aimed to address broader challenges in treatment development, such as drug and vaccine safety, the use of big data in research, and digital health. «The budgets of our projects vary considerably and are tailored to the objectives and scope of each project,» notes Hugh Laverty. The project funding model reflects the public-private nature of the partnership. Half of the funding comes from EU research programs and primarily finances the participation of universities, small and medium-sized enterprises, patient groups, etc.

The other half is contributed by industrial members of the partnership, mainly in the form of in-kind contributions, meaning that companies share the time of their researchers, access to resources, etc. The combination of these public and private resources enables us to address the significant challenges of research and innovation in health on a large scale.

In total, the overall budget of the IHI for the period 2021-2027 amounts to €2.4 billion, with:

- €1.2 billion coming from Horizon Europe, the EU framework program for research and innovation.
- €1 billion to be contributed by industrial partners of the IHI.
- €200 million coming from other industries or life sciences associations that choose to contribute to the IHI as contributing partners.

Three European projects dedicated to improving the accessibility of clinical trials for patients:

- The European FACILITATE program aims to establish a transparent and ethical framework for access to and reuse of patient data from clinical trials for the individuals themselves (with their consent). The project, led by IMI and supported by the European Commission and EFPIA, was launched at the beginning of 2022.
- Trials@Home aims to develop and pilot standards, recommendations, and tools to enable the decentralization of trials, particularly by leveraging digital technologies and wearable medical devices to remotely collect data from participants' homes in clinical trials.
- The COMBACTE projects have established networks of hospital sites and laboratories to facilitate the implementation of clinical trials for antimicrobials.

Interview with Michel Goldman, Emeritus Professor of Immunology at the Université Libre de Bruxelles

Michel Goldman, professor emeritus of immunology at the University of Brussels

What are the missions and vision that IHI (Innovative Health Medicine) in 2022, has carried since its creation?

The fundamental objective of IHI could undoubtedly be expressed as follows: to contribute to translating the progress of science and research in the field of health into tangible benefits for patients and society as a whole. It is also about ensuring that Europe remains competitive in the field of medical innovation and interdisciplinary research.

We also had the intuition that the ecosystem would benefit from better cooperation among the various actors involved in innovation. By bringing together not only academic and pharmaceutical actors but also SMEs and biotech and medtech start-ups, patient associations, regulatory agencies, and all related industries (imaging, diagnostics, etc.).

So, the goal was to facilitate, through tools and programs, partnerships and alliances that bring together enough expertise and different skills to overcome the numerous obstacles - intellectual property, manufacturing, competition, etc. - that hinder developments in the medical field.

What need does this address?

I would start by saying that a second intuition has also been confirmed: populations are increasingly unwilling to accept that treatments that could save their lives exist and are available somewhere in the world, but not accessible to them in Europe.

This missed opportunity, as we know, can result from a lack of financial means, too restricted access to clinical trials, or too slow and complex regulatory approval. In any case, it is perceived today as a serious injustice.

There is, on one hand, a very strong societal expectation, and on the other, the experience gained since the creation of IHI, that partnerships help overcome barriers and obstacles. Advances in science must be translated as quickly as possible into new products with "multi-stakeholder" partnerships.

How do collaborative programs create concrete synergies?

The goal is to target therapeutic areas that are relatively unattractive to the pharmaceutical industry in terms of profitability and promising products that are not developed due to a lack of outlets. By providing innovative tools or new financing modalities, we open up new development perspectives. Very interesting results have been obtained with projects focusing, for example, on autism, Alzheimer's disease, the Ebola virus, etc.

These projects operate through calls for proposals to which consortia formed by different actors respond, and their proposals are selected by a scientific jury. In these consortia, industry players work together, and competition is set aside while research progresses and reveals the potential of a technology to define the indication of a drug or the application of a program.
When it is possible to suspend, for a time, the mechanisms of competition and prioritize cooperation and sharing, strong synergies are generated, and discoveries are accelerated.

I mentioned earlier that one of the pillars of the IHI approach is to involve patients. I have personally committed to the EUPATI program, which helps patients gather information, contribute to the training of other patients, and communicate what is important to developers.
By systematically involving patients in the development of therapeutic innovations, a virtuous circle is formed. Patient experts become interlocutors and stakeholders in projects, participating in consortium decisions, and proposing ideas for clinical trials.

Finally, in Europe, where we often lament the lack of bridges between the academic and university world and the business world, we have an advantage: the spirit of competition between universities is less prevalent than in North America. There is a real culture of collaboration between teams, which is also a factor in synergy.

What challenges do you identify behind the EU Pearl project?

Collaborative trials, which the EU Pearl program promotes, meet an obvious need. As research advances, we better understand diseases and, in doing so, segment them more and more. Diseases that could be considered common - such as breast cancer, for example - tend to be, so to speak, fractionated into a multitude of "rare" indications.

In this context, the traditional model of "randomized" trials has its limitations. Adaptive trials, umbrella or basket trials, are gaining popularity. With the approach proposed by EU Pearl, a new collaborative space is opened in clinical development, generating synergies and shared benefits

Key points - 3th initiative:

1. Patient-Centric Collaborative Clinical Trials represent a groundbreaking approach, enabling the simultaneous testing of multiple drug candidates within a single trial using an adaptive design that emphasizes extensive collaboration and information sharing.

2. These trials, managed collaboratively with active participation from various industrial sponsors, academic partners, and patient associations, provide a formidable mechanism to expedite development in neglected diseases facing stagnation in research and where economic viability is uncertain. Furthermore, they facilitate patients' access to potential new therapies.

3. Originating in Spain and subsequently extended to several countries, this innovative approach has garnered significant support from the Institute for Healthcare Improvement (IHI), a prominent European body. The EU Pearl initiative, underpinned by this collaborative model, has already produced noteworthy outcomes, serving as compelling evidence for potential partners to embrace this clinical revolution.

4th Initiative: A framework for Early Access to innovative Medecines (Italy, France)

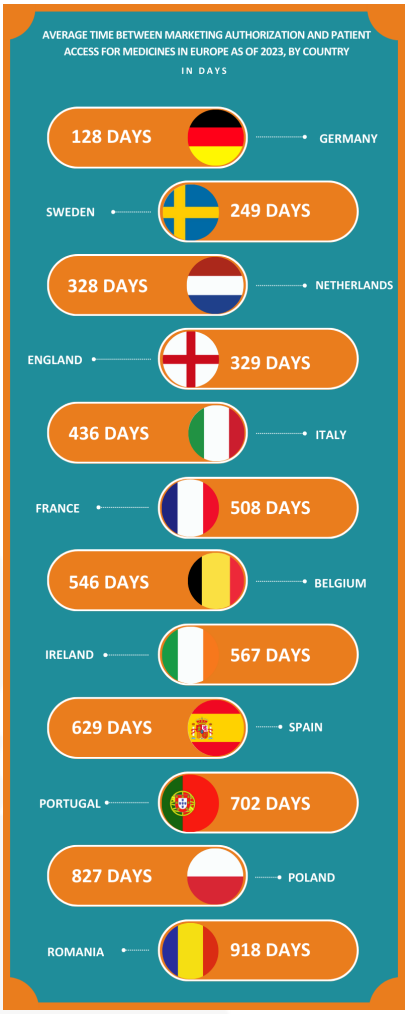
In Europe, there is a wide variety of mechanisms allowing patients in therapeutic impasse to benefit from unapproved treatments, often still in development. However, the conditions and timelines for access, as well as the allocated budgetary resources, vary significantly from one country to another, creating situations of inequity. Harmonization of these systems in Europe is necessary. The French and Italian systems, among the oldest, can serve as a model.

TheObservatory
a European Patients Observatory study by HealthTech For Care

Monica Mazzucato, MD, PhD Rare Diseases Coordinating Centre, Veneto Region, Padua University Hospital

Early access targets medications that address an unmet therapeutic need, likely to be innovative, and for which the pharmaceutical company commits, ultimately, to submit an application for marketing authorization (MA) or reimbursement.

Compassionate access pertains to medications that may not necessarily be intended to obtain marketing authorization but can address an unmet therapeutic need. This is, for example, the case with treatments for certain rare diseases.



Average time between marketing authorization and patient access for medicines in Europe as of 2023, by country in Days

Multiple programs in Italy

In Italy, there is no general program, but multiple possibilities to access treatments through early access programs,» emphasizes Monica Mazzucato, MD PhD, from the Rare Diseases Coordination Center of the Veneto Region. This national system was structured as early as 2014, through laws 648/1996 and 326/69 (the 5% Fund).

Law 648 covers both early access for patient cohorts and off-label use, while the 5% Fund covers drugs in development for orphan diseases. Although the Italian Medicines Agency (AIFA) plays a central role in the approval process, various stakeholders can apply for these different programs. «It is worth noting, among them, the role of patient associations, through law 648/96,» emphasizes Monica Mazzucato.

No specific budget is dedicated to list 648, and in practice, payers differ depending on the program (industrial, regional funds, NHS-AIFA). This is not the case for the «5% Fund,» composed of 50% of the pharmaceutical companies' annual contribution, which corresponds to 5% of the annual expenses of the laboratories' promotional activities. However, this budget can vary from year to year. Furthermore, no specific timeframe for the validity of the programs is set a priori (unlike in France, for example).

The compassionate use program, on the other hand, was first authorized in 2003 in the country and revised in 2017. Compassionate use involves the direct and free delivery of the drug by the laboratory that developed the treatment and is subject to approval by an ethics committee before AIFA evaluation.
Also, an article in law 94/98 - the former Di Bella law - provides for the possibility of off-label access, even in the presence of therapeutic alternatives on the market. Again, the treatment is at the patient's expense or the hospital structure in the case of hospitalization.

«Italy has made a general effort in information and transparency regarding access modalities and data on these programs. However, the various possibilities still require a good understanding of the conditions and processes to apply,» notes Monica Mazzucato.

France, a structured model, funded by Health Insurance

Early and compassionate access have undergone successive reforms in recent years in France. The Social Security Financing Bill (PLFSS 2024) indeed envisages strengthening these exceptional access mechanisms to innovative products for patients.

Between 2021 and mid-2023, early access (formerly Temporary Authorization for Use) benefited more than 100,000 patients, according to the Ministry of Health, more than any other country in Europe. This authorization can be granted for a treatment, after dossier examination, for a period of one year, renewable. Medications benefiting from this are fully covered by Health Insurance.

Compassionate access can be requested for an unapproved and unavailable drug in France. The request is made by a hospital prescriber for a specific patient. It can also, at the initiative of the National Agency for the Safety of Medicines and Health Products (ANSM), frame a medical practice to secure off-label prescribing of a drug available in France but indicated for another pathology. Finally, a derogatory system allows nominative access to drugs in development for a specific indication.

In other countries, such as Germany, between marketing authorization and reimbursement decision, the laboratory can provide the drug for immediate patient access, and this is for six months before official commercialization. Price negotiation takes place during this period. Once the negotiation is completed, the drugs enter the standard reimbursement system. This applies to all drugs and not just innovative or orphan treatments, as in France. Therefore, one cannot speak of an early access system in this country where, it is true, the process of bringing approved drugs to market is the fastest in Europe.

Other mechanisms exist in Europe, but are less structured. In Spain, the United Kingdom, and Belgium, the possibility is only open at the initiative of physicians.

European harmonization for greater equity

Early and compassionate access vary significantly from one European Union member state to another, creating an evident source of inequity in patient access to care, as emphasized by Alice Tarantola, the lead author of the first comparative study of early access systems in Europe, featured in an article published in May in the Journal of Pharmaceutical.*

The authors of this publication underscore that the systems implemented by France and Italy are both the oldest and most generous and can be considered as models to follow for several reasons: the establishment of clear selection criteria based on innovation and unmet medical needs, the continuity of access to medications in clinical trials, before marketing authorization (MA) and between MA and price approval to cover price negotiation delays, and finally, by opening the possibility for industry players to request early access.

These mechanisms are not without criticism. In France, there is a stark contrast between the quality of the early access system and the post-marketing authorization (MA) price negotiation timelines, among the longest in Europe. In Italy, the inclusion of «off-label» products on list 648, which are sometimes cheaper than the prescribed ones, is sometimes driven more by economic than medical logic.

A necessary harmonization of early access systems in Europe should rely on several pillars:
1 - **A clear distinction** between compassionate access and early access in both procedures and funding modalities.
2 - **Standardization** of application procedures to enable various stakeholders to request early access, including pharmaceutical companies, physicians, and patient associations.
3 - **A systematic and effective procedure** for collecting clinical data from early access to create a lever for accelerating clinical trials.
4 - **Coordination** of early access funding at the European level.

** Early access programs for medicines: comparative analysis among France, Italy, Spain, and UK and focus on the Italian case", Journal of Pharmaceutical, 2023*

Interview with, Antoni Montserrat Moliner, Vice President of the Luxembourg National Committee for Rare Diseases

Faster access to innovations for European patients

In April 2023, the European Medicines Agency (EMA) launched a proposal to revise the PRIME (PRIority Medicines) mechanism, accelerating the approval of drugs for unmet medical needs. If adopted, what advances will result from it?

This initiative, as part of the pharmaceutical legislation revision, is currently being discussed in the European Parliament. It will create a regulatory environment conducive to innovation for the development of new treatments and the repurposing of existing molecules. On one hand, it aims to shorten timelines to provide urgent access to certain drugs; on the other hand, it offers pharmaceutical companies the opportunity to launch their products on the market earlier.

The European Medicines Agency (EMA) will provide enhanced early regulatory and scientific support to these promising treatments, facilitating their rapid approval and assisting SMEs and non-profit developers.
Scientific evaluation and drug authorization will be expedited. As a result, market authorization procedures in Europe are expected to take 180 days, contributing to a reduction from the current average of about 400 days. Regulatory burden will also be eased through simplified procedures and digitization (electronic submission of applications, electronic product information, etc.). This includes eliminating the need for most market authorization renewals and introducing simpler procedures for generic drugs. The most rigorous standards for the quality, safety, and efficacy of drug authorization will be maintained.

How do the various member states of the European Union respond to this revision?

The program, established since 2016 on a voluntary basis (see inset), is expected to become a real lever for promoting patient access to treatments in European legislation. In this post-Covid period, the EMA has reacted with a certain imagination and speed to address the pandemic and facilitate the acceleration of clinical trials, which has profoundly influenced this European reform.

In the face of this reform, extreme positions coexist, with some countries being unfavorable to the current framework for rare diseases and orphan drugs, while others consider PRIME to be a fantastic instrument for promoting research.

Antoni Montserrat Moliner, Vice President of the Luxembourg National Committee for Rare Diseases

Will this reform improve equality in patient care within Europe?

The only way to ensure equity for all European patients would have been to create a common fund that would have allowed patients in European countries without access to certain expensive medications to finance them. This proposal was not adopted.
The consequence: medical tourism has developed.

How do the various member states of the European Union respond to this revision?

France has implemented the best early access system in Europe. It could be a model to follow. More decentralized systems like those in Spain and Italy are more complex. In Luxembourg, we are highly dependent on the Belgian system. In Germany, due to the lack of a national authority, early access depends on the federal states (Länder) in which patients live.

As for compassionate access, it is often used for drugs that have received approval in the United States but not in Europe, with prices that impose an additional cost on national healthcare systems. This has led to some resistance to granting this access.

Some argue that the compassionate drug system is very expensive and does not ensure long-term patient treatment. It does not have unanimous support, especially among health economists. This is particularly true as gene therapies, expensive but life-saving, are increasingly entering the market. Regarding access to innovative treatments, I would recommend adapting the mountaineer theory. **When a person is injured or lost in the mountains, no one contests the exorbitant cost of helicopters and rescuers who go to find and treat them. Why should it be any different when it comes to access to a medication that prolongs life or saves a patient?**

PRIME for faster access to medications in Europe

Since 2016, the European PRIority MEdicines (PRIME) mechanism aims to support the development of drugs intended to address unmet medical needs. It is a voluntary program that involves early and proactive collaboration between regulators and laboratories.

Today, laboratories that have developed a drug benefiting from PRIME can benefit from an accelerated assessment when applying for marketing authorization (MA) from the EMA. This PRIME mechanism is expected to be enhanced if the pharmaceutical reform proposed by the European Commission in April 2023 is adopted.

Based on a 12-month pilot project, which will conclude in March 2024, a new framework for scientific advice should allow for quicker responses to PRIME applicants. Additionally, pre-submission MA preparation meetings are planned, occurring about a year before the submission of the application dossier to assist PRIME drug developers. This should provide robust support for MA applications and, consequently, expedite the process.

Key points - 4th initiative:

1. The time lapse between the final stages of drug development and its availability to patients can be a matter of life or death for many individuals.

2. In France and Italy, comprehensive legal frameworks have been established to delineate a transparent pathway for the expedited distribution of the most promising medications before formal approval. This framework is open for applications from all stakeholders, ranging from patient associations and physicians to industrial entities.

3. However, both responses are still in need of refinement, and these ongoing efforts should not exempt each country from further reducing the time it takes to gain market access. While these initiatives serve as examples of processes that safeguard the fundamental rights of patients and promote equitable access to innovation, they also prompt a critical examination of Europe's role in this context. This includes contemplating the creation of a funding body to enhance the collective ability to address this crucial aspect of healthcare.

SKEZI: actively involve patients in research

Since 2022, Mapi Research Trust has partnered with SKEZI to promote the consideration of patients' quality of life in both practice and clinical trials.

Spin-off from AP-HP and the University Paris-Cité, SKEZI entered into a partnership in 2022 with Mapi Research Trust, a non-profit organization that develops questionnaires assessing the quality of life of patients in clinical trials or in their healthcare journey, and facilitates access to them. Specializing in cohorts, SKEZI, in turn, develops the data collection software initially designed to follow the ComPaRe cohort (the Patients' Community for Research) in 2017, now available to everyone under the name SKEZIA.

Jean-Philippe Bertocchio, Physician and CEO of Skezi

«Our partnership aims to place patients at the heart of research, to involve them in sharing their daily lives with scientifically validated tools,» says Jean-Philippe Bertocchio, physician and CEO of SKEZI. The questionnaires filled out online by patients, or Patient Reported Outcomes, are used by researchers worldwide. Cataloged and described by Mapi Research Trust, these measurement tools allow, among other things, the comparison of the health status of the French with that of other Europeans. The data collected with patients are hosted in France.

A better understanding of diseases for improved diagnosis

«Already, over 80,000 patients in France and Europe have chosen to collaborate online to share their health data. This has led to the publication of about thirty scientific articles and the identification of patients, including those who had contracted long COVID, to monitor the progression of their symptoms and the duration of their illness,» explains the CEO of SKEZI. Other questionnaires are under consideration, still based on patient experiences but incorporating pre-validated tools and open-ended questions.

In the future, researchers will be able to use the SKEZIA platform and identify the most appropriate questionnaire for monitoring their patients.

SKEZI has already begun collaborating with several cohorts, including Le French Gut, which collects stool samples from healthy individuals. The goal is to study the occurrence of diseases over the years based on microbiota imbalances. Launched in 2022, French Gut aims to include nearly 100,000 people and become one of the largest French cohorts.

Reducing territorial inequalities

Participating in decentralized trials reduces access inequalities to research for patients. Some limitations for patients include access to a computer or smartphone. This is why SKEZI has established a second partnership with the USPO, the Union Syndicale des Pharmacies d'Officine (Union of Community Pharmacies). This could involve pharmacists in clinical trials and include more patients, especially the elderly.

The initiatives undertaken by both partners are also transferable on a European scale. «Our solutions/questionnaires can be translated into all languages very quickly, in less than 48 hours. We already include individuals from French-speaking countries: Benelux, Canada, the Maghreb, and have developed English-language versions,» the physician explains.
Other expertise areas, such as organizing Multidisciplinary Consultation Meetings (RCP) online and tele-expertise, have also been developed. Particularly utilized in rare diseases, they enable patients, regardless of their place of residence, to access the expertise of a few specialists located in major cities.

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