innovative health initiative

IHI workshop on real-world data, digital health & artificial intelligence

Event Report

October 1-2 2024, Brussels, Belgium.

COCIR Advancing Healthcare · efpia · EuropaBio The European Association for Bioindustries · MedTech Europe from diagnosis to cure · Vaccines Europe

Co-funded by the European Union

Table of Contents

1 About this report and the workshop

On 1-2 October 2024, the Innovative Health Initiative organised a workshop examining project outcomes, challenges and opportunities regarding real-world data, digital health and artificial intelligence in Europe. The workshop attendees discussed how challenges and opportunities could be addressed within the scope of future IHI public-private projects and how connections could be made to the emerging EHDS.

Real-world data (RWD) are routinely-collected data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources, and real-world evidence (RWE) is evidence derived from the analysis of RWD[1]. Examples of RWD include data derived from electronic health records, medical claims databases, data from registries, and data gathered from other sources (such as digital health technologies) that can inform on health status[2]. Other important data resources for data-driven health research and artificial intelligence are cohorts and clinical trials.

Artificial intelligence will have a transformative impact on health research and care. Almost every project describes the use of AI technologies, and future developments and implementations will take place with rapidly developing technologies and legislation. The EU Artificial Intelligence Act[3] describes an artificial intelligence (AI) system as 'a machine-based system that is designed to operate with varying levels of autonomy and that may exhibit adaptiveness after deployment and that, for explicit or implicit objectives, infers, from the input it receives, how to generate outcomes such as predictions, content, recommendations or decisions that can influence physical or virtual environments'.

The potential of AI and RWD for healthcare is immense – 30% of the world's data volume is generated by the healthcare industry[4] and according to a report by MedTech Europe, between 380,000 and 403,000 lives could be saved per year by AI[5]. In addition, the Draghi report estimates that gains of EUR 55-95 billion per year are estimated from use cases of AI in the pharma and medical device industries worldwide[6]. Artificial intelligence provides opportunities to transform care, for instance through guidance, better diagnosis and development of patient-centric outcomes. Although AI presents great opportunities for healthcare[7], new AI-based innovations must ensure that the benefits outweigh the risks and that patient safety and their rights are protected[8].

IHI projects are public-private, multi-stakeholder partnerships that address cross-sectoral challenges and aim to have a transformative impact on the health ecosystem. Public-private partnerships are uniquely placed to bring researchers, healthcare professionals, regulators, civil society and industry experts together in an impartial, transparent and trustworthy framework. The Data and Digital Workshop examined the role that IHI projects have played, and continue to play, in strengthening the EU's capabilities in RWD/RWE and digital health towards the opportunities offered by the European Health Data Space. This report summarises the main findings and take-aways from the workshop and identifies future areas where IHI projects could address important problems.

[1] https://www.ema.europa.eu/en/documents/other/guide-real-world-evidence-provided-ema-support-regulatory-decision-making_en.pdf

[2] https://www.ema.europa.eu/en/about-us/how-we-work/big-data/real-world-evidence

[3] https://artificialintelligenceact.eu/

[4] https://www.sciencedirect.com/science/article/pii/S2414644724000034#:~:text=The%20healthcare%20industry%20generates%20approximately,it%20available%20for%20scientific%20discovery

[5] https://www.medtecheurope.org/wp-content/uploads/2020/10/mte-ai_impact-in-healthcare_oct2020_report.pdf

[6] https://commission.europa.eu/document/download/ec1409c1-d4b4-4882-8bdd-3519f86bbb92_en?filename=The%20future%20of%20European%20competitiveness_%20In-depth%20analysis%20and%20recommendations_0.pdf

[7] https://web-assets.bcg.com/5b/4f/303736c54b92bd203db2d5e3e92f/disrupt-ds-roundtable-nrdd-publication-2024-1.pdf

[8] https://www.europarl.europa.eu/RegData/etudes/STUD/2022/729512/EPRS_STU(2022)729512_EN.pdf

2 Key take-aways

- **The importance of the patient perspective:** Engaging patients from the beginning to the end of a project is key to delivering transformative results. Patient perspectives help to design projects more effectively, provide continuous feedback throughout a project's lifecycle and contribute to the scientific outcomes and overall success of a project by bringing in the lived experience of diseases. Several examples of IHI and IMI projects where the benefits of involving patients as partners and participants from the outset were highlighted, including Screen4Care, HARMONY+, OPTIMA, PIONEER and IDERHA.

- **The use of real-world data, digital health or AI applications are game-changers for many areas of health**. Some examples of the potential impacts include faster diagnoses for people with rare diseases, more precise diagnostics for personalised care, improved medicine safety evaluations, the conduct of clinical trials in hard-to-reach populations, or the development of patient-centric markers of diseases. However, to use real-world data and AI safely and efficiently in healthcare systems, structure, scientific rigour and quality, trust, transparency, access and interoperability must be ensured.

- **Legitimacy and Trust:** Legitimacy (i.e. making sure that actors have a legitimate reason to access data) and trust (i.e. making sure that access, analysis and outcomes are for the benefit of individuals and society, on the basis of transparency) are critical for research and the rolling-out of real-world data/real-world evidence, digital health and AI applications. It's essential to ensure that the data that is used is of high quality, that AI tools are delivering trustworthy results, and that patient data will be used responsibly. However, transparency, legitimacy and trust can be elusive concepts and building a shared understanding is critical for the success of European Health Data Space (EHDS). Research projects in public-private partnerships are an opportunity to build transparency and trust between a large number of stakeholders across all sectors of health care for the future implementation of the EHDS.

- **Adopted standards drive utility, scale and value of real-world data**: Real-world data is collected in many forms and in various ways and needs to be harmonised before it can be used effectively. For instance, several systems for standardising real-world data for clinical research are currently in use in different areas - establishing consistent definitions and tools can enhance the efficiency and reliability of RWD applications. Public-private partnerships such as EHDEN have supported the adoption of standards at scale and have trained European companies, healthcare organisations and SMEs in the use of these standards. Building alignment and capacity is key for the success of the developing European Health Data Space (EHDS). It was noted that guidance is emerging on initiatives and standards in use[9].

- **The value of public-private partnerships:** A lot of work still needs to be done – to further improve interoperability of data, to develop trustworthy AI tools, to facilitate the education of healthcare professionals that will generate and use real-world data and AI in their daily practice, and to find solutions to address the tensions between fostering data-driven innovation and ensuring data protection and privacy. We often refer to these public-private partnerships as precompetitive – they drive joint actions between many companies, government agencies, researchers, healthcare and patient organisations that aim to develop and deliver value for the health ecosystem as a whole. Ultimately, the goal and outcome of the joint research should be to provide clear guideline and inform regulation that drives uptake, applicability and value.

[9] Hussein, R., et al (2024). Getting ready for the European Health Data Space (EHDS): IDERHA's plan to align with the latest EHDS requirements for the secondary use of health data. *Open Res Eur*, *4*, 160. https://doi.org/10.12688/openreseurope.18179.1

- **The European context:** Any innovations using real-world data or AI will need to take the AI Act, Medical Devices Regulation and General Data Protection Regulation (GDPR) into consideration. New potential projects should support the operationalisation of research in the European Health Data Space (EHDS) as well. IHI launched a call in 2025 aiming to develop a framework for safeguarding intellectual property within EHDS to support innovation. This is one example of public-private partnerships that offers an opportunity for companies, SMEs and research organisations to build capacity for driving innovation in a landscape of rapidly changing technology and innovation.

- **Start with an end in mind:** Early engagement with the technical companies who are making the devices that are retrieving real-world data, or those that are creating the AI tools, can minimise the risk of encountering difficulties at a later stage and will help drive progress from innovation to implementation.

- **Regulatory science**[10]**:** Regulators need to both uphold and advance standards to inform decision making and to facilitate novel medical products. For the practical use of real-world data and AI in healthcare settings, requirements at national and European level have to be considered. Public-private partnership projects can serve to deliver robust, tested, neutral data and methods to help regulators to make decisions on health innovations that are using real-world data and AI[11]. These partnerships also develop important areas such as the use of real-world evidence and the definition and validation of digital and AI-driven outcome measures.

- **Scaling and implementing innovation:** IMI and IHI projects have delivered clear impact, but one of the key challenges is how to ensure that the infrastructures, frameworks, tools, and other results are sustained and adapted past the project's end and continue to deliver benefits to the health and research community. During the workshop, the participants highlighted the need to determine how to scale and implement project innovation and consider longevity from the earliest phase of the project – when the grant proposal is being written. IHI provides guidance building from project experiences, captured in the "Field manual for scaling innovation"[12]. Options include forming non-profit legal entities or securing support from other funding sources or from private companies to continue the work[13].

- **Reuse invented wheels:** Consortia that are applying to new IHI calls for proposals should try to integrate the work of previous projects into their solutions or build on the foundations laid by previous projects. For example, the OPTIMA project build on some of the outcomes from both the PIONEER and the EHDEN projects, and the urology-specific data resources from all three projects are enabling the UroEvidenceHub, which is federating and leveraging real-world data for better outcomes in urology.

- **Upskilling medical professionals**: Healthcare professionals are overworked and under time pressure and investing in learning how to use AI tools or collect real-world data can be seen as an additional burden on resource-constrained healthcare systems. However, efforts should be made to engage healthcare professionals and healthcare systems to address the usefulness of digital health and AI and recognise the importance of upskilling, and developing roles and responsibilities so that patients can have better outcomes, faster. AI tools can also help to reduce the burden on healthcare systems, making them more resilient. Improving digital health literacy and skills using digital and AI tools is critical across the healthcare ecosystem, including patients, healthcare professionals, regulators and developers. Common training frameworks and cross-disciplinary education can enhance trust and adoption[14].

[10] EMA defines regulatory science as the range of scientific disciplines that are applied to the quality, safety and efficacy assessment of medicinal products and that inform regulatory decision making throughout the life cycle of a medicine.

[11] https://www.ihi.europa.eu/sites/default/files/uploads/Documents/ProjectResources/RegulatoryScienceSummit_Feb2024_Report.pdf

[12] https://www.ihi.europa.eu/sites/default/files/uploads/Documents/ProjectResources/ScalingPPPInnovationFieldManual.pdf

[13] https://www.ihi.europa.eu/news-events/newsroom/crossing-bridge-project-non-profit

[14] https://eupati.eu

3 Setting the scene: the need, the potential and the challenges

The opportunity presented by AI and real-world data is massive. At the beginning of the workshop, Julian Isla of Foundation 29 described how AI tools could have helped his young son, who has a rare disease, to get a diagnosis faster. Julian's son saw seven experts and had to undergo several treatments that were not correct and even aggravated his condition. Once, he experienced more than twenty seizures in one day. Isla, a computer engineer and data and artificial intelligence resource manager working for Microsoft, developed an online decision support tool that uses AI to deliver fast potential diagnoses. Doctors input the patient's symptoms and a list of possible diseases is sent back, as well as the treatment options for these diseases. Doctors will then make the final decisions on the treatment plan. Isla hopes that this tool can help to reduce the time that patients with rare diseases have to wait before they receive the correct diagnosis and get access to treatment. It has already been deployed in Madrid's healthcare system, and dozens of patients have been diagnosed as a result.

Maja Fjaestad, the former Swedish State Secretary for Health during the COVID pandemic, described the challenges encountered when devising and implementing the Swedish plan to become a world leader at using opportunities offered by digitalisation and eHealth. However, the collaborative focus groups set-up throughout Sweden to discuss digitalisation in health and the associated challenges were a great resource for a policymaker and she emphasised that while policymakers need data to make effective and safe policies surrounding the use of digital tools in healthcare, they also need to be aware of the challenges that healthcare practitioners may face, the technical limitations of digital health technologies, as well as the concerns of patients.

> *"Real-world data is a blessing because of its richness. But there's a small curse that comes with it – its lack of structure."*
>
> – **RAJ LONG, GATES VENTURES**

Raj Long of Gates Ventures set out the known challenges in using real-world data. "Real-world data is a blessing because of its richness," she said. "But there's a small curse that comes with it – its lack of structure." She described how concerns about data quality, the lack of interoperability between different data, ethics and privacy challenges as well as barriers to access have translated into uncertainty for regulators, leading to limited adoption despite the potential benefits that real-world data can bring. She also said that links should be made between existing data platforms and new initiatives, so that work is not being replicated.

Jan Beger of GE Healthcare emphasised the impact that real world data and artificial intelligence could have in healthcare. "Innovation, especially in the digital space, is a team sport. It requires cooperation from all stakeholders including healthcare professionals, researchers, industry, payers, and patients alike," he said.

4 Trust

The workshop discussed trust in AI, real-world data, and real-world evidence from several angles. Can regulators and the public have trust in the real-world data that is being collected – is it being collected in a robust and stringent way? Can academic researchers and the pharmaceutical and medical technology industry work together to use real-world data to monitor and improve medicines and medical products? Can manufacturers of devices prove that the real-world data is of a high quality and reproducible for decision-making? How can public-private research projects help to provide the answers to these questions? When it comes to AI, can we trust AI tools when generative AI tools are inventing information and sources, and public mistrust in AI is sky-high? How will the health field manage the drift of models over time and requirements of traceability of AI medical devices? What are the priority areas for public-private research projects to develop Europe's global competitiveness for trustworthy AI tools in healthcare?

4.1 Trust in data quality

If the quality of real-world data can be assured, then it could unlock many new insights into health research. However, not all real-world data is of high quality and not all data is collected in a systematic and rigorous way. Regulators need proof that methods of collecting real-world data are robust enough and are comparable to the current state-of-the-art. If already-existing datasets are being used, then evidence is needed to demonstrate that the data within these datasets has been harmonised, standardised and validated, and that it is reliable. This is one area where public-private projects can play an important role. IMI projects such as EHDEN, Mobilise-D, IDEA-FAST, Conception, IDERHA and several more have already made strides in this field.

4.2 Trust that data will be used responsibly

Most patients may be open to sharing their real-world data to further understanding of a particular disease so that others can benefit from research breakthroughs and new treatments can be found. However, while the primary use of health data usually aligns well with citizens' expectations, the secondary use of real-world data for future innovations can lead to scepticism and mistrust. Some people expect to have agency over their data and to decide where and when their data is used. They are protective of their data due to the extensive use of data in tailored marketing, and increasingly, AI-driven decision-making within the US healthcare insurance industry[15]. The EU's General Data Protection Regulation (GDPR) was the first piece of legislation protecting people's rights over their data worldwide, and health systems and researchers have to ensure that a person's data is not used without their consent[16]. However, for health research to gain ground, a balance needs to be struck between fair data protection and access to information that is needed to make advances in medical research. The European Health Data Space is Europe's response. It aims to ensure that Europe has a consistent, trustworthy and efficient system for both primary and secondary re-use of health data for research, innovation, policy-making and regulatory activities, and future IHI projects should align with the European Health Data Space's objectives. Ensuring consent, transparency and proper data security is key to maintaining public trust in healthcare data practice and innovation.

4.3 Lack of trust blocking uptake of AI tools

One roadblock to AI uptake is that healthcare providers may not trust AI tools. Widely publicised reports of generative AI inventing data erodes trust in AI, even in clinically validated versions of AI. Innovations like the

[15] E.g. https://www.forbes.com/sites/shashankagarwal/2024/03/28/the-ai-revolution-in-medical-claims-processing/

[16] https://gdpr-info.eu/

"Testing and Experimentation Facility for Health AI and Robotics" (TEF Health), which was presented by the coordinator of the TEF Health, Petra Ritter of the Charité Univ Berlin and the Berlin Institute of Health, can help to build trust in new AI tools and will help innovators to meet the requirements of the European AI Act. TEF-Health[17] is a public-private facility where companies can test medical devices that are using AI and robotics in a safe setting. Tests can be conducted for interoperability and trustworthiness as well as examining whether AI can accurately solve existing problems in a risk-free environment. TEF-Health offers both physical and virtual testing environments. TEF-Health is also actively involved in standardising testing protocols and certifications for technology, and in establishing specific codes of conduct for using the technology. The success of TEF-Health illustrates the value of public-private collaboration by providing a safe environment to conduct tests that can be trusted by regulators.

5 The impact of public-private partnerships

5.1 Data harmonisation and standardisation

Healthcare data collection uses different tools, methods, and (based on the setting) different criteria. Across Europe a wide variety of datasets exist and the universal healthcare systems in Europe together with the diverse populations provide a unique opportunity to develop effective and representative digital health and AI-enabled solutions. However, to turn this diverse richness into a competitive advantage, Europe must overcome the challenge of data access and interoperability. Although a hospital in Poland and a hospital in Italy may be collecting data about the same disease, they might use different systems, and their datasets might be incompatible. These heterogeneous features of healthcare data can also impact its quality, and there is a need to put the different data resources into the same model and to describe the content and limitation of diverse data resources. After establishing that data is of high quality (consistent and complete), the harmonisation of data standards is the next step towards the collection of massive datasets which can then be mined for new insights about health based on real-world data. Widespread agreements on data standards are the foundation of the federated European data ecosystem that is now emerging in the European Health Data Space and other EU-wide initiatives.

If a standard system for collecting high-quality data could be established and agreed upon, this could remove a lot of the work involved in data harmonisation and greatly improve data interoperability. Standardisation refers not just to the type of data that is collected, but also how it is collected. Standardisation projects have been ongoing, and participants at the workshops pointed out that there are now several standardisation systems, and choices need to be made about which system to use globally, to improve data interoperability.

The IMI EHDEN project, presented by Peter Rijnbeek of Erasmus University Medical Centre, successfully harmonised and standardised more than 400 million anonymous electronic health records from 187 data partners in 29 countries into the OMOP Common Data Model[18], delivering a vital resource to health researchers in a first step towards the vision of the European Health Data Space. EHDEN generated new insights into COVID-19 vaccines, and characterised diabetes, cancer, and the effects of different types of knee surgery. More recently, EHDEN conducted the largest real world evidence study to date: using 52 databases from 18 European countries and USA, they illustrated the impact of drug shortages on patient care. EHDEN demonstrated that improving the syntactic and semantic interoperability of data enables the use of standardised analytics for generating real world evidence at scale. A new non-profit foundation, the EHDEN Foundation, has been established which will continue the work of the project after its end. The EHDEN project demonstrates how large-scale public-private partnerships can have transformative impact by

[17] https://tefhealth.eu/home

[18] https://www.ihi.europa.eu/news-events/newsroom/new-non-profit-organisation-help-usher-eus-networked-and-harmonised-health

embedding standards, practises and trust in all actors in the health ecosystem: companies, SMEs, regulatory bodies and healthcare providers.

European Medicines Agency (EMA) representatives at the workshop also highlighted the IMI project EHDEN (which transformed real world data into the OMOP Common Data Model) as an example of a public-private partnership that provides results that regulators can use. Leveraging this extensive work done, EMA's DARWIN EU enables the conduction of studies to generate real-world evidence for EMA. The EHDEN-transformed datasets are known to contain harmonised data (with a common structure and terminology) which is what makes them interoperable and helps them to be used for multi-database studies of regulators.

The IMI Mobilise-D project broke new ground by developing digital mobility outcomes based on data from wearable devices that can be used in clinical settings. They developed and validated a system for collecting robust real-world data from wearable devices that can reliably be used to assess health status for certain conditions. When it came to establishing standards for the wearable device data, though, the team had to start from scratch:

"We had a real problem in the area of wearables because there were literally no standards whatsoever," said Brian Caulfield of University College Dublin, who presented the IMI Mobilise-D project at the workshop. He added that if using wearable devices for clinical studies is to become a widespread and inexpensive way of collecting high quality data, then standardisation across wearable devices and the methods for their use must become a reality. Mobilise-D has taken important steps towards this standardisation and the solutions developed in the project have now been licensed to several companies and incorporated into commercial digital health products.

To make the best use of digital health data, an interconnected data infrastructure with fast, reliable, and secure interfaces is needed, international standards for data exchange must be defined, and medical terminologies must be harmonised[19]. Unfortunately, a large amount of health data is hidden in isolated databases or within incompatible systems and proprietary software, rendering the data difficult to exchange, analyse and interpret.

The IMI Combine-CT project, presented by Robert Hofsink of Philips, used real-world data and AI to make the case for using interventional cardiology approaches, which are image-based, minimally invasive alternatives to open surgery. Despite the benefits, coronary computed tomography angiography (CCTA) – a diagnostic test that produces detailed 3D images of the arteries in your heart to detect abnormalities in how blood flows through your heart – is not widely used in cardiovascular healthcare today. That is largely because of issues with interoperability with existing hospital systems, so the COMBINE-CT project developed an automated workflow which will make it easy and efficient for hospitals to roll out interventional cardiology tests that can be used across the care pathway from diagnosis to treatment planning, treatment procedure, and follow-up.

5.2 Access to data / Data sharing

To have the biggest impact, researchers need access to large datasets that may be in the public or the private domain. However, accessing and / or sharing data – particularly health data – raises legal, technical, and ethical challenges. In a federated, cross-national data ecosystem, aspects other than technical compatibility must also be managed for systems to be interoperable and to enable the sharing of information. For instance, data must be registered in suitable data catalogues, necessitating compatible access procedures, data processing and use agreements and often also mechanisms to recover the costs associated with access for the data holder. Furthermore, the reuse of health and patient data will also require

clarity on consent and approval from ethics committees or institutional review boards. IMI and IHI projects have been using a federated system for sharing data repeatedly in our projects with remarkable success over the past decades, which could provide a blueprint for other projects and initiatives to follow.

Niklas Blomberg, IHI's Executive Director, pointed to the Data Sharing Playbook which was recently published by IHI and EFPIA and has many examples of best practices of data sharing. IHI and EFPIA also organised a Data Sharing Masterclass which was held on 4 September and is available online as a recording.

MAKING BETTER USE OF IMAGE-BASED DATA THANKS TO RWD AND AI

More than 90% of health data is images[20] – MRI scans and X-rays for instance, as well as renderings of microscope slides, all of which need to be analysed by healthcare providers to determine a patient's health status.

The IMI BIGPICTURE project, presented by Jeroen van der Laak of Radboud University Medical Centre, is creating a digital repository consisting of images of three million slides covering a range of disease areas. The project will simultaneously develop a series of new AI tools to analyse this data and deliver novel insights about these diseases. This task is not without its challenges – most notably, image files are much heavier than text data files, and training AI to identify diseases via images is more difficult than training AI to find specific words in a database.

The IHI IMAGIO project, presented by Robert Hofsink of Philips, aims to make strides in the field of interventional oncology (IO), where imaging is used to guide miniaturised instruments through the body to target cancer cells more precisely. The project is collecting and validating real-world data to achieve widespread acceptance of IO, and is using AI-based image processing to help accelerate this work.

5.3 Changing how we run clinical trials

Since the pandemic, the value of running decentralised clinical trials has become clear. The IMI Trials@Home project is investigating how robust real-world data can be elicited from clinical trials taking place in participants' own homes through digital technologies and PROs, while Mobilise-D's results indicate that mobility assessment as part of clinical trials for certain diseases can be done at home or even in the outside world.

If clinical trials can be carried out at home or other remote settings, then they can lead to the inclusion of a more diverse group of participants and consequently result in better trials that are more representative of the real patient population. For instance, people who live far from clinical sites can be included, as well as those who have caring responsibilities at home, people who have limited mobility, and people who cannot make the time commitment necessary to participate in an on-site clinical trial. Decentralised clinical trials may be cheaper and have a lower carbon footprint than traditional clinical trials.

The Trials@Home project, presented by Mira Zuidgeest of the University Medical Center Utrecht, is carrying out a clinical trial with three innovative arms – one as a conventional clinical trial with participants attending a clinic on a regular basis, a second as a completely remote trial, and a third which is half remote and half in a

[20] https://pubmed.ncbi.nlm.nih.gov/38157463/

clinic. The project will compare which approaches are better from the viewpoint of the patient, data quality and other parameters.

5.4 Revolutions in diagnostics

If AI can identify patterns in how people develop diseases based on real-world datasets, then it will become easier and faster to predict how a person's disease might progress and identify which treatment might work best for subgroups of patients. Several IHI and IMI projects are investigating how AI and real-world data could yield such insights so that doctors can deliver more personalised prognoses and treatment plans to patients.

Multiple sclerosis (MS) is a disease that presents with a wide range of symptoms and patients may respond differently to various treatments. The IHI CLAIMS project, presented by Annemie Ribbens of Icometrix, is developing a platform based on real-world data and AI models seeking to predict how a person's multiple sclerosis will progress depending on which treatments are administered. This is a step towards more personalised care for people with MS, and it will help clinicians to make better, evidence-based decisions regarding treatment plans. It will also feed into the goals of the European Health Data Space.

The IHI iCARE4CVD project, presented by Nicholas Ciccone of Novo Nordisk, is using real-world data and AI to enhance early diagnosis of patients at risk of cardiovascular disease. It is still unknown how risk factors such as diabetes and high blood pressure influence who will develop heart disease and how their disease will progress. By gathering real-world data from more than one million patients and using artificial intelligence to analyse the data, iCARE4CVD seeks to define subgroups of patients and follow their disease progression. The project will use their findings to predict which patients will develop cardiovascular disease as well as how individual patients will respond to various treatments. In particular, the project will examine people with Type 1 diabetes, who are at a high risk for developing cardiovascular disease.

People with neurodegenerative disorders and immune-mediated inflammatory diseases often report problems with sleep, fatigue and other symptoms that negatively affect their quality of life. The IMI IDEA-FAST project, presented by Nikolay Manyakov of Johnson & Johnson, is identifying and validating digital endpoints as well as establishing real-world data collection methods based on wearable devices. If the digital endpoints are validated, this will mean that fatigue can be better monitored and clinical trial endpoints will be developed. The project is also developing a database containing a wide range of real-world data points that will be coupled with and compared to existing clinical data.

6 The developing European legislation and innovation in digital health and AI

6.1 The setting

The EU is a complex and developing legislative setting. For digital health and AI, a set of legal requirements and overarching EU principles, legislation on AI (including the AI act and AI liability directive), data protection (including GDPR, EHDS and national requirements), cybersecurity (including the Cybersecurity Act), as well as EU regulations and certain national provisions for medicinal products, medical devices and *in vitro* diagnostics exist. Regulatory constraints can be perceived as hurdles to innovation, but Carl Johnson from MSD urged the workshop participants to dig deeper to discover the underlying cause of regulatory concerns, so that new innovations that are compliant with regulatory needs can be developed.

A public-private partnership is one good avenue to build trust through transparency and communication, for instance adding value by providing independent data that the private sector can use and the regulators can refer to. "Are we not innovating because of the regulatory handcuffs? Or are we cautious about going forward because of our lack of understanding of regulatory constraints? Let's try to understand – through IHI projects," said Johnson.

> *"Are we not innovating because of the regulatory handcuffs? Or are we cautious because of our lack of understanding of regulatory constraints?"*
>
> – CARL JOHNSON, MSD

6.2 The European Health Data Space

The goals of the European Health Data Space (EHDS) are to empower individuals to take control of their health data and facilitate the exchange of data for the delivery of healthcare across the EU, foster a genuine single market for electronic health record systems and provide a consistent, trustworthy and efficient system for reusing health data for research, innovation, policy-making and regulatory activities[21].

"We need a set of rules for primary and secondary access to data, and that is the EHDS," said Marco Marsella, Director for Digital, EU4Health and Health Systems Modernisation at DG SANTE of the European Commission.

> *"We need a set of rules for primary and secondary access to data, and that is the European Health Data Space."*
>
> MARCO MARSELLA, EUROPEAN COMMISSION

IMI led the way in harmonising health data across Europe through projects like the EHDEN project, PIONEER, HARMONY+ and more. The EHDEN project was one of the first initiatives in Europe to contribute towards the European Health Data Space's goal, and new IHI projects will align with the EHDS going forwards.

[21] https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en

For instance, the aim of new IHI project IDERHA, presented by Christian Muehlendyck of Johnson & Johnson, is to set up an EU-wide health data space that is aligned with the principles of the EHDS and that will facilitate the access to and analysis of diverse types of health data to improve lung cancer diagnosis and care. Focusing on lung cancer as a case study, the project will link up various datasets from the public and private sector, including imaging data, data from wearables, trial data, electronic health records and individual patient health data. They will develop new tools which clinicians and researchers can use to access this data and receive outputs advising on detection, diagnosis, prognosis and management of various diseases. IDERHA is starting with lung cancer as a case study, which is responsible for 400 000 deaths in Europe each year.

IHI is continuing to search for new projects that can make the ambitions of the European Health Data Space a reality. A new call 10 topic will focus on how to safeguard innovation in secondary use of health data in the EHDS[22]. IHI's tenth call will search for future IHI projects that can help to define new ways to use clinical trial data for secondary purposes while respecting patient privacy and data protection rights, in line with the European Health Data Space. Another goal is to identify paths for innovation while protecting trade secrets and intellectual property.

6.3 The European AI Act

The European AI Act lays down a uniform legal framework for the development, marketing and use of AI systems across the EU member states. Its objective is to promote the uptake of trustworthy AI while ensuring a high level of protection of health, safety and fundamental rights[23].

Under the EU AI Act, medical devices with AI systems are classified as "high risk", meaning that a conformity assessment is needed before they can be used in Europe. Petra Ritter outlined how the "Testing and Experimentation Facility for Health AI and Robotics" is providing technical and scientific support and a neutral space where AI systems can be tested to ensure that they conform with the AI Act. A potential IHI project could similarly support a safe and trustworthy space for testing that new medtech is compliant.

However, the AI Act is not perfect. Ritter explained to the workshop that the current certification process for medical devices was not designed with AI in mind, and that the process needs to be changed. She envisions a future "AI trust label" and a certification revolution.

6.4 The European competitive edge

Although the EU has a strong track record in research – as evidenced by a high number of peer-reviewed publications published each year – that doesn't always translate into commercial success.

Healthcare has been identified as one of the ten strategic sectors in the EU that would benefit most from the rapid introduction of AI[24], and there is an opportunity for the EU to establish itself as a world leader in safe and trustworthy real-world health data systems and AI innovations for health. But steps must be taken quickly to maintain a competitive edge, the workshop heard.

The new AI Act and European Health Data Space could help Europe to become a world leader in designing safe and trustworthy AI solutions that make use of real-world data in an ethical and transparent way. Opening up the secondary use of health data for research purposes also has significant potential to anchor pharma R&I activities within the EU.

[22] https://www.ihi.europa.eu/apply-funding/future-opportunities

[23] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:L_202401689

[24] Draghi report: https://commission.europa.eu/topics/strengthening-european-competitiveness/eu-competitiveness-looking-ahead_en

"We can be very proud of this regulation [the AI Act] – it is the first regulation in the world to enforce trustworthy AI," said Ritter.

On the other hand, if the new regulations do not always complement each other well or are not fit-for-purpose, then they could become barriers to innovation. The workshop heard how the complexity of the European regulatory landscape, in comparison to the US, can discourage industry from investing in innovation in Europe. In 2022, the median approval time for new medicines by regulatory agencies in Europe was 430 days compared with 334 days in the US[25].

7 The patients' perspective

7.1 A patient-centric approach

The workshop started with the focus on patients (or as one participant eloquently phrased it, "persons with conditions") and heard how they should be involved from the earliest stages of health care and research in the design and development of innovative technologies and approaches using AI and real-world data.

> *"Patients should be placed at the centre of data collection, data management and utilisation."*
>
> – **MARIA DUTARTE, EUPATI**

"Patients should be placed at the centre of data collection, data management and utilisation," said Maria Dutarte of EUPATI, emphasising that patient perspectives can help to design projects more effectively, provide continuous feedback throughout a project's lifecycle and contribute to the overall success of a project. Several examples of IHI and IMI projects where patients were involved from the outset were highlighted, including Screen4Care, HARMONY+, OPTIMA, PIONEER and IDERHA.

The Screen4Care project, presented by Gulcin Gumus of EURORDIS, is one example where patient perspectives are continually integrated into the project's activities. Screen4Care focuses on genetic newborn screening as well as the use of real-world data and machine learning tools to accelerate the diagnosis of people with rare diseases. Because people with rare diseases are, by definition, rare and few in number, real-world data can prove extremely valuable. Machine learning tools can also help to rapidly make connections that doctors may miss. The Screen4Care project has a patient advisory board consisting of 11 rare disease patient representatives. The board is co-designing the tools being developed by the project, as well as providing advice for the project's work on genetic screening for newborns.

7.2 Education as a first step

Representatives of patients' organisations present at the workshop stressed the importance of educating patients so that they can have real and meaningful impact on project and trial design. Moreover, patient representatives told the workshop that if the impact of including patients in a project is to be fairly evaluated, then the patients involved should receive proper training before taking part in a project.

Providing patients with effective training tools presents a significant challenge as patients have diverse levels of health literacy and experience a variety of diseases at different stages and from various perspectives.

[25] Draghi report : https://commission.europa.eu/topics/strengthening-european-competitiveness/eu-competitiveness-looking-ahead_en

EUPATI – a non-profit foundation which was originally an IMI project – has developed a suite of patient education programmes and reported that they have more than 330 graduates from their training for patient advocates and that more than 9000 learners have already accessed their module on digital health.

7.3 Data protection, data governance and data sharing

Patients' data is protected by the GDPR, and the workshop heard how increasingly, patients in clinical trials are asking for their data back once the trial has concluded. Many patients agree that their data can be used for a specific clinical trial, but do not consent to the use of their data for secondary research purposes. Discussions revolved around how trial participants should be viewed as "continual contributors of data" and that a framework was needed through which data could be retrieved and requested, and where patients could give and withdraw their consent for data to be used in a transparent and ethically sound system. Peter Arlett of the European Medicines Agency told the workshop that better "data protection literacy" was needed and said that "the projects that are most successful at EU level are those that have understood data protection literacy and the sharing of data across borders."

The IMI FACILITATE project, presented by Johanna Blom, was set up to investigate how a trusted patient-driven and ethical ecosystem could be established for the use and re-use of clinical trial data. The project found that 83% of clinical trial participants want access to their own data or results, 80% want access to the overall results of the study and most participants want their data used for research for new treatment options. The work of FACILITATE can help to inform how the European Health Data Space will function, taking into account the wishes of trial participants. The workshop attendees discussed the fact that many clinical trial participants are never informed about the result of their trial, and how this could be resolved going forwards without compromising the trial.

Christian Muehlendyck from Johnson & Johnson, who presented the IDERHA project, said: "all of us have been in hospitals and we know that we can feel like subjects. We need to change our mindset from subject to partner, because patients as partners can be powerful."

> *"Patients as partners can be powerful."*
>
> – **CHRISTIAN MUEHLENDYCK, JOHNSON & JOHNSON**

Jolanda Koenders of Takeda presented the IMI Health Outcomes Observatory (H2O) project, outlining how their goal is to better integrate patient recorded information into healthcare systems. Up until now, many measures of disease and disease outcomes have been based largely on clinician's inputs. H2O aims to amplify the patient voice by providing patients with digital tools to record their health outcomes, which can be easily accessed by healthcare providers. Using patient reported outcomes will highlight the issues that concern patients the most, such as those that impact quality of life, and this will help clinicians to make better decisions regarding treatment plans. A key pillar of the project is that patients always maintain control of their own data and decide who has access to it.

Susan Evans Axelsson from Bayer of the PIONEER project highlighted that some of the data solutions that sound promising may in fact hamper research goals. For instance, if data is completely anonymised, then it is difficult to determine which patients have co-morbidities and other conditions that may influence their performance in a clinical trial. A person's name may not be essential for a researcher to know, but details including their gender, their age and their health history can be relevant.

Petra Ritter agreed, saying that for TEF's research, such information is crucial. "Anonymisation is not the answer. An anonymous "average brain" would not allow us to do our research."

The workshop heard that these are the discussions that need to be had between patient advisory boards and researchers, so that enough relevant data is available to conduct important research while the patient's privacy is respected.

8 Co-designing with AI experts

Around the table at the workshop, the participants discussed the need for experts in AI to be present when beginning to design new proposals for IHI projects, particularly those that involve healthcare. Technical expertise is necessary from an early stage to understand whether there are hurdles in development or implementation which could impede a project's success. AI experts can understand the complexities of the healthcare ecosystem, while they innovate to identify shortcuts and new or accelerated ways to solve existing problems. It is highly recommended that AI experts be involved in the early phases of the grant application process.

9 Boosting digital health literacy

Collecting high-quality real-world data in a harmonised way requires specific training. The EHDEN project established the EHDEN academy, which delivers training courses for healthcare providers and researchers on how to collect and use real-world data and real-world evidence.

During the workshop, participants discussed the "data explosion in healthcare" and the impact that this has had on healthcare providers. "Every 26 seconds a new medical article is published," said Jan Beger of GE Healthcare. "A dermatologist would need to read about 3900 articles per year to be up-to-date on the latest research."

These figures demonstrate that it is impossible for doctors and clinicians to keep up with the tide of information. AI tools could help them, as well as providing more timely and efficient access to the most relevant information needed to make medical decisions, improving the efficiency of hospital workflows, accelerating diagnoses, and more. The value of AI needs to be emphasised so that hospital and healthcare workers set aside the time needed to train and learn how to use these tools.

The tool developed by Foundation 29 relies on doctors using it. But one of the key issues blocking its uptake was that doctors are learning how to use the resource, according to Isla. "We are so demanding for technology but less so for people. Clinicians aren't required to do additional training after getting their license, and they have no time. We need to rethink this system," he said.

Johanna Blom of the University of Modena who presented the FACILITATE project at the workshop described physicians as the "missing link" between the development of solutions and the benefit that they can bring to patients. "We need higher participation from physicians," she said, "but they often have no time, no interest and no knowledge of the educational tools that are available."

> *"We are so demanding for technology but less so for people."*
>
> – JULIAN ISLA, FUNDACIÓN 29

The Mobilise-D project experienced challenges in engaging clinicians in their trials because there was a lack of understanding about the digital tools that were involved. The project had to dedicate extra time towards explanatory training for the clinicians. “We need the clinical investigators who are looking at these studies to be digitally literate,” said Brian Caulfield.

10 Building on previous projects and longevity

10.1 Sharing data, insights and results with other projects

One key message from the workshop was that innovation cannot happen in silos. The public-private projects that are funded by IHI and IMI should share results and avoid re-inventing the wheel, so that innovation can be accelerated. Data should also be shared and interoperable between projects.

Barbara Bovy of UCB Biopharma described how there was a need to develop a “collective intelligence” so that learnings pass seamlessly between one project and another.

Susan Evans Axelsson from Bayer spoke about how the PIONEER and OPTIMA projects used the OMOP Common Data Model and onboarded a number of datasets (or data partners) harmonised into this model by EHDEN. The results of all three projects will live on as a new independent membership-based entity, the UroEvidenceHub, which is leveraging real-world data to find better outcomes in urology.

The goal of PIONEER was to develop a European network of excellence for big data in prostate cancer, the second most common cancer in men, as it is difficult to predict which patients will respond best to different treatments. Using anonymised data from hospitals, pharmaceutical companies, research institutes, biobanks and biotech companies, the project harmonised the data and set up data tools that can help clinicians to make better diagnostic and treatment decisions. The results could provide answers to important prostate cancer research questions, pave the way towards individualised evidence-based medicine in prostate cancer and optimise care for prostate cancer patients.

OPTIMA aims to harness AI to develop Europe’s first large scale oncology data and evidence generation platform, using data from over 200 million people. Focusing on prostate, breast and lung cancer, the project aims to help clinicians to make more personalised decisions about a patient’s treatment plan. Like PIONEER, OPTIMA is making use of the OMOP Common Data Model and using some of the EHDEN harmonised datasets, and is aligned with the goals of the European Health Data Space. OPTIMA has also learned from data sharing agreements developed in HARMONY+, which helped to speed up the initial phases of the project.

By taking learnings and results from other projects and implementing them, OPTIMA and PIONEER can accelerate their progress and avoid duplicating efforts.

10.2 From innovations to operations: scaling use and impact beyond the projects

All IHI and IMI projects end. But from the start, applicants should consider how to sustain the project’s impact. At the workshop participants discussed how it was important to see the ‘sustainability’ requirement of the grant application as a vitally important question rather than a ‘tick-the-box’ exercise. One recommendation was to apply a start-up approach and focus on developing solutions that can be easily implemented, driving health innovation forwards while envisaging a working business model.

Several projects present at the workshop mentioned their models of sustainability. Some formed non-profit associations, like the EUPATI Foundation, the EHDEN Foundation and the PharmaLedger Association. Other projects secured follow-up funding from other sources – Mobilise-D’s work will continue as the SUSTAIN Mobilise-D project.

10.3 Real World Data and Evidence for understanding disease, planning programmes and pharmacovigilance

DARWIN EU is operated by EMA for use by European regulatory agencies. In Europe there is no large-scale real-world data/evidence infrastructure accessible for research and innovation in academia or industry. This is an important gap that a public-private project, building on the transformative outcomes of IMI/IHI data projects such as EHDEN, H2O, Gravitate Health, IDERHA and others, should aim to fill. DARWIN EU is already part of the European Health Data Space and further development would naturally take the EHDS regulation into consideration. Organised access to these potential networks – facilitated through public-private partnerships or fees from healthcare sector companies – could contribute to the long-term operation and development of innovations using healthcare data and real world evidence.

Other areas where IHI projects could fill current gaps include improving accessibility and linkage of many complementary types of real-world data, so that a more holistic view of the patient and their data is available. For instance, a project could extend the work of projects such as EHDEN towards establishing a common data model for real-world evidence for medical devices. There is also scope for projects focused on how best to integrate real-world data into clinical trials, understanding the limitations of single-arm trials, point-of-care randomisation, and on how RWD could be used in prevention of disease. One area highlighted in the workshop was the opportunities posed by AI in the area of pharmacovigilance.

The EMA is systematically growing and publicly sharing the experience with real-world evidence used for answering questions in medicine development, assessment and use, such as disease epidemiology, clinical management and drug utilisation to support the design and feasibility of studies, evaluate the representativeness and validity of completed studies, and investigate effectiveness and safety studies as well as the impact of regulatory actions about DARWIN EU. Involving regulators in public-private projects is highly recommended, the workshop heard.[26] “If you want the outputs of a project to be relevant to decision-makers, add the decision-makers as partners or advisors in your project,” the European Medicines Agency said.

10.4 Opportunities for project collaborations and future actions

The establishment of the European Health Data Space over the coming years will have a transformative impact on European health research, accelerating data sharing and data access and potentially transforming work on data processing as national centres and European nodes (such as EMA DARWIN) are being established. European research projects and public-private partnerships will be important implementation mechanisms but to fully realise the value IHI must stimulate and increase cross-project collaborations and help projects orient themselves towards the emerging EHDS. These implementation efforts could also support increased dialogue with national health care organisations, regulators and other actors so the ecosystem supports that data is being captured by health care systems and medical devices at a granularity that can actually be used for research purposes.

Another area for reflection and future action is to ensure that the knowledge, experience and infrastructure of current and past IMI/IHI projects are being made available to new IMI projects and in this way contribute to research efficiency and the development of a robust and internationally competitive European health data landscape. A particular area highlighted was the negotiation of contracts, access and processing agreements. Mechanisms should be sought where IHI projects should be allowed to use contracts from earlier projects. For instance, could there be long-term association agreements between institutes that facilitate data access for research purposes – such as mutual recognition of data agreements to benefit research in the same way as the mutual recognition of courses benefit students in Erasmus networks?

[26] https://www.ihi.europa.eu/resources-projects/engaging-regulators

As data-driven health research becomes more complex and relies on ever-larger data collections, the operational implementation of IHI (and other European) projects must be improved. It was noted that the long-term operation and scaling of project outcomes requires a clear value proposition. For most projects there is a clear value statement at the beginning of a 5-year project but it doesn't always develop that way. There should be a way of creating an IHI project to support implementation and scaling for projects that recognise the evolution of the value proposition.

The opportunities provided by AI came up in many areas of data-driven health research discussed at the workshop: medical devices, early-stage drug discovery, RWD, pharmacovigilance and pharmaceutical manufacturing were all highlighted.

It was also noted that cross-sectorial research projects support the development of innovations but importantly also help develop clarity on the acceptance and use of different technologies such as AI in medicines development. For instance, there is great potential for AI in the early stages of drug development. What is in the line-of-sight is to ensure that these solutions are accepted at the regulatory assessment stage. AI in medicine is a rapidly evolving field. Many projects provide excellent use cases that could help inform discussions, but a challenge is to make sure that the project outcomes, challenges and reflections are summarised and so provide relevant feedback to policy.

Contact

Tel +32 (0)2 221 81 81
infodesk@ihi.europa.eu

Postal address:
IHI JU - TO56
1049 Brussels – Belgium

Visiting address:
Ave de la Toison d'Or 56-60
1060 Brussels – Belgium