REAL WORLD EVIDENCE
RWE4Decisions

First Public Stakeholder Meeting

Realising the Potential of Real-World Evidence for Learning Healthcare Systems

22 September 2020

Memorandum

RWE4Decisions REAL WORLD EVIDENCE

Keynote:

The EU Health Data Space and cross-country collaboration on real-world evidence

Andrzej Rys
Director for Health Systems, Medical Products and Innovation, DG SANTE, European Commission

Health reforms should continue to be based on the principles of resilience, accessibility and effectiveness as these can provide better quality care for all European citizens. Digital solutions, including datafication, can also increase the well-being of citizens. The COVID-19 crisis clearly shows the need for this kind of thinking where access to clinical evidence and the data to track the virus, along with exchange of knowledge and efficient communication with patients and between health professionals, are essential.

One of the main priorities of the European Commission – announced at the end of 2019 – is the creation of the European Health Data Space as part of the European Strategy for Data which was adopted end February 2020. The European Health Data Space should be able to use or reuse health data for better health provision, research and innovation, and policymaking. It will strengthen the access and portability of citizens' data and remove barriers for the cross-border provision of digital health.

To implement this programme we are working on several pillars: governance and rules; quality of data; infrastructure and technical interoperability; and capacity building and digital upskilling. The Commission is currently working with Member States and stakeholders to define the best governance structure and set up appropriate infrastructure for the European Health Data Space. Part of this effort has been addressed through workshops with Presidents of Member States and experts in fields such as data policy, national interpretation of GDPR in the health sector, and the various models of dealing with data. We are currently launching the expert study on regulatory gaps and barriers to cross-border provision of digital health. The main findings of the studies will be taken into account in the preparation of the European Health Data Space which is planned for adoption in 2021. The work of the Commission is being closely coordinated with Member States.

Other important developments include the system for the exchange of electronic data, and an e-prescription patient summary through myhealth.eu which is already helping seven Member States to send data across their borders. We continue to work on the implementation of the recommendation for an electronic health records exchange format to facilitate the exchange of electronic health records across borders. Seven Member States have started this and about 25 are committed to implement it in 2021. Another example of a cross-border and EU-wide solution is a single platform of 24 European reference networks for the exchange of data – the Clinical Patient Management System (CPMS). We also have a project to make a registry of diseases.

A recent and lesser known example is the support of the European Commission on the EU programme of COVID-19 convalescent plasma collection and transfusion. The Commission is working together with the European Blood Alliance to build a database for the collection of data on donation and patient outcome. This is an area that truly incorporates real-world data.

We are conducting additional work with 20 Member States on the 1+ Million Genomes initiative. We also continue to work with both the European Medicines Agency and the European Centre for Disease Prevention on how those two agencies can be incorporated in the European Health Data Space. We believe that Real-World Evidence has a key role to play in the current and future development of the Health Technology Assessment (HTA).

Finally, we have the eHealth Stakeholder Group which includes stakeholders in the field of digital health, the health industry, standardization bodies and other parties. This is where we continue to interact, gain knowledge, learn more and produce better results.

Session 1

Experience to date in the use of RWE - What do we know?

What does it take to use real-world evidence to enable decisions? The role of real-world evidence in scientific advice and in novel outcomes-based reimbursemen approaches.

Jo De Cock
Belgian National Institute for Health and Disability Insurance (INAMI/RIZIV)

Huge challenges still exist in the field of real-world data and evidence, but also great opportunities. The Belgian social health insurance system is trying to address these challenges to see how evidence-based decisions can help in the field of reimbursing new innovative medicines.

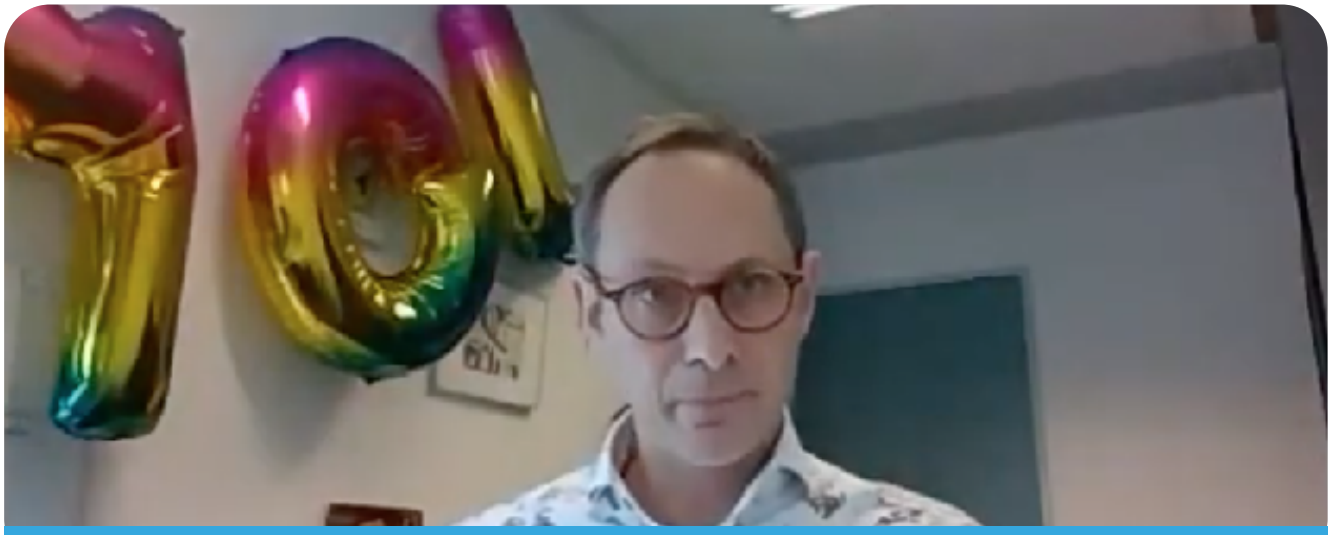
Although payers still have concerns and remain cautious, there is increasing interest regarding the potential of RWD/RWE to support their decisions about highly innovative technologies for different reasons. These include:

- reducing uncertainties at the moment of market launch, especially when clinical results are insufficient to respond to payers needs;
- narrowing the gaps between projected outcomes and clinical benefits in practice;
- pressure as a consequence of the use of fast track access procedures;
- requirements for outcome oriented managed entry agreements
  taking into account patient experience;
- realising the opportunities offered by digitalization;
- policy initiatives.

A basic question is whether agreement can be found for real-world data that could support pricing and reimbursement decisions. It's clear that some elements are not always present at market launch. These include questions about the populations to be treated, the natural history of the disease, the size and durability of the clinical efforts compared to treatment alternatives, and the budget impact. There is a need to see what end points are measurable while taking into account the experiences of patients and quality of life. To make progress, co-creation with different stakeholders is essential such as regulators, HTA, clinicians, patients, and manufacturers.

Also key are the principles on which such initiatives are founded. Two main ones are collaboration, which stresses that real-world evidence is a shared responsibility that should be pre-specified and planned with all the stakeholders, and transparency, to use clear processes for managing conflicts of interest among the different stakeholders and agree on what real-world data can be collected.

A practical proposal is a learning network or action-oriented network to share case studies, enable multi-stakeholder dialogue, provide guidance on how patient experts can be supported to co-design RWE studies, and enable the attainment of common goals. Such a network should be objective, owned by a public institution to enable this interaction, and be sustainable through long-term funding.



Peter Mol

Professor of Drug Regulatory Science (University Medical Center Groningen), Clinical Assessor Dutch Medicines Evaluation Board, Vice-chair EMA Scientific Advice Working Party

Real-world evidence is becoming increasingly important to the regulator, although the experience and the actual use of it in our decision-making is mainly from the area of post-marketing.

A key question is whether real-world data can be used to contextualize single arm trial results and explain why the effects observed in the trial are meaningful. In the post-licensing phases the data might be intended to add new information which could be to maintain efficacy.

Contexts where real-world data can be helpful include in rare diseases to extend the indication; in oncology where a change of drug formulation might be proposed; and in gene therapies to look at long-term effects and safety concerns.
Real-world evidence is useful but will primarily be driven by asking what the data can add to our understanding. It's necessary to look very carefully at data quality as well as the feasibility of data.

It should be a protocol worked out and preferably registered at one of the existing sites (e.g. NCEP at EMA). Transparency is key. If registries are used, an existing one is to be preferred rather than setting one up for a specific company as this will be difficult to

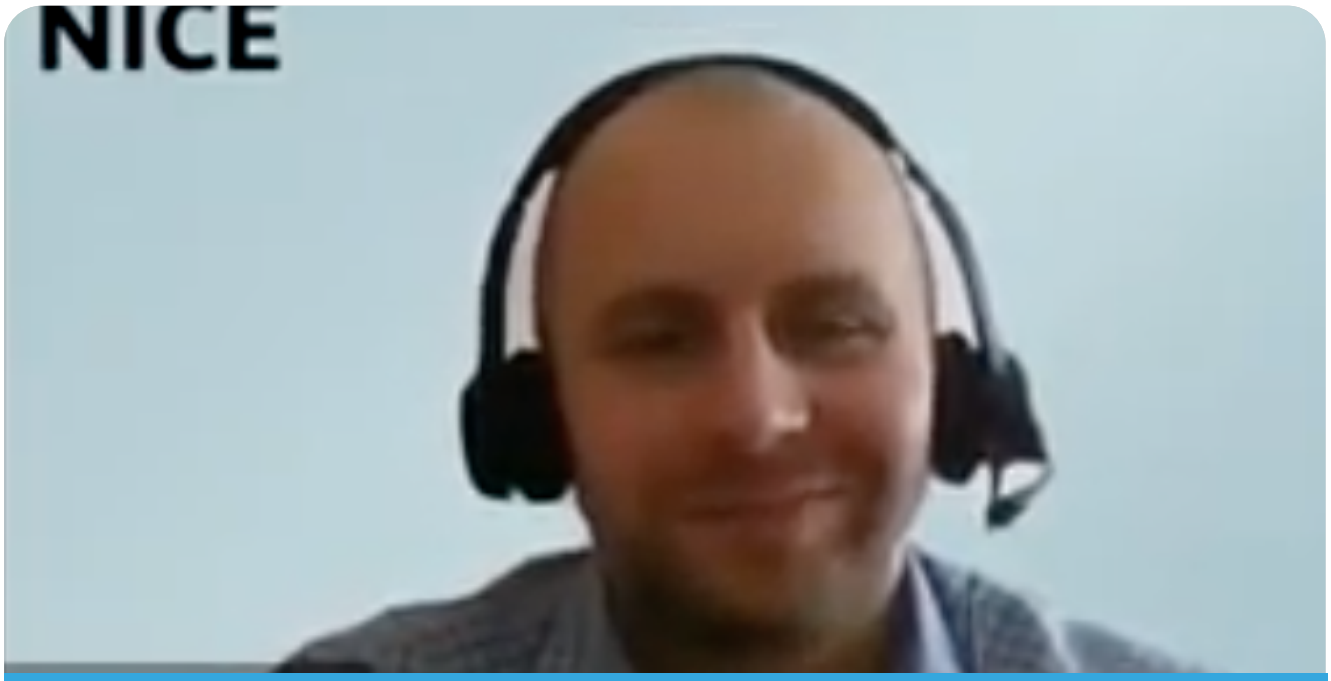
Etienne Jousseaume
Head of Market Access Cell & Gene Europe, Novartis

We see a sub-optimal landscape of real-world evidence. How to make real-world data collection more efficient needs upfront coordination and collaboration between the scientific community, patient groups, the regulator and payers to align on what is a normalized real-world evidence perspective for a specific therapeutic area. Also needed is flexibility of all stakeholders involved.

Second is the data collection. It's difficult enough to get one hospital team to fill in one registry. If they then have to fill in two or three registries then it's mission impossible. This is not just a matter of financial incentive but about prioritization of everyday care; it's about having people that are able and that have the time to fill in this registry.

Third, when it comes to data access models that facilitate the availability of real-world data and interfacing with electronic health records we need the right data protection standards.

Overall, it would be extremely helpful to skip the burdensome manual data collection. We see great initiatives in Europe to move forward and catch up with other parts of the world.



Adrian Jonas
Associate Director for Data and Analytics, UK National Institute for Health and Care Excellence (NICE)

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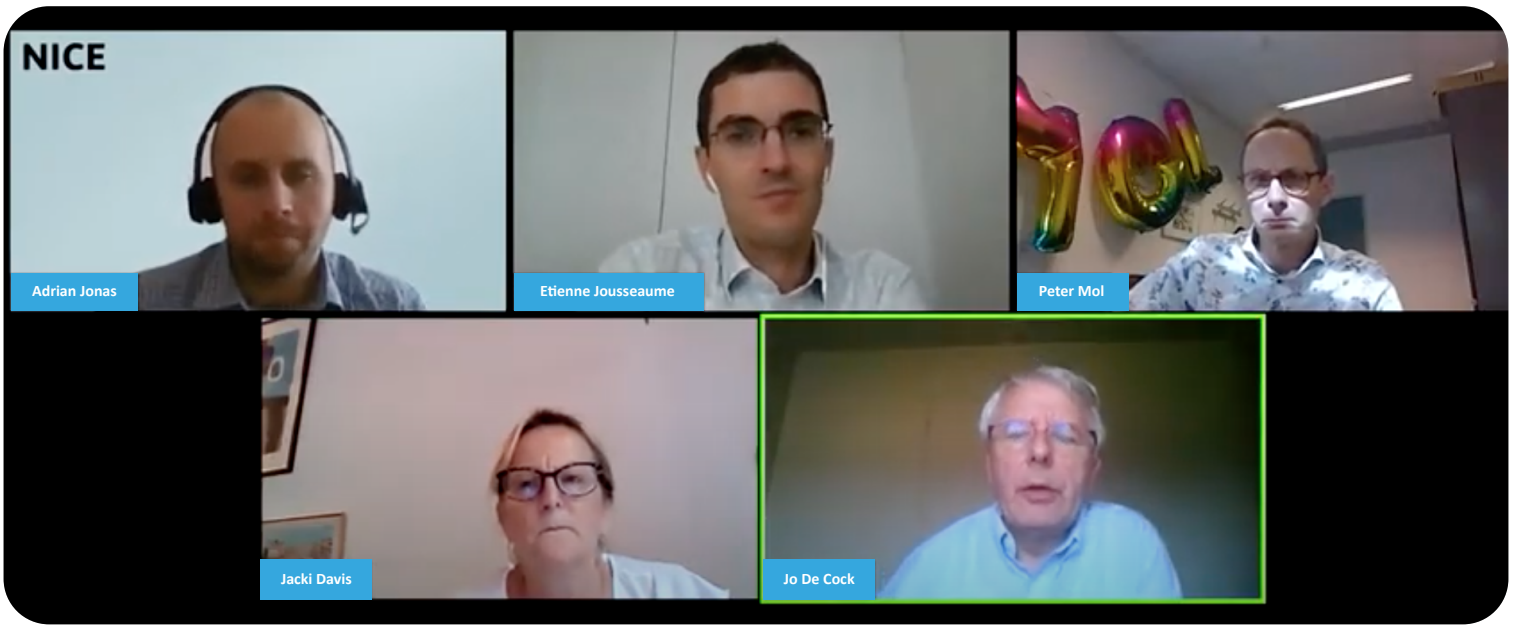
Q&A and interactive debate moderated by Jacki Davis



Moderator: What is the key differentiator of this initiative on real-world evidence? Is it the element of learning by doing?

Jo De Cock

We have set up two workshops together with panels from payers and the industry on practical and concrete products, initiatives and pilots, to consider their questions and what can be improved. Learning by doing is certainly a key element of a health system, especially in these contexts. It's clear that we should try and bring together people in order to reach practical answers and because it's important to have as information as possible to enable evidence-based decision-making.

Special interventions

Denis Lacombe
Director General, European Organisation for Research and Treatment of Cancer (EORTC) and Co-Chair of the European Cancer Organisation's Health Systems and Treatment Optimisation Network

Yann Le Cam
Chief Executive Officer, EURORDIS

Wim Goettsch
Special Advisor HTA, Zorginstituut Nederland (ZIN)

We have done some work with the European Parliament on treatment optimization. It was generated by the observation of many so-called innovative drugs coming to the market which are not holding up to their promises. We also see diminishing opportunities in Europe to question how to optimize drugs in the healthcare system. These questions relate to duration, and combination with other drugs and with other modalities.

One issue with real-world data is access. Today it's extremely difficult to access real-world data, although what is being proposed at the European level may solve that. What is more crucial is research methodology: how to structure real-world data in the continuum from early clinical research through late research and into access.

We cannot speak about real-world data without speaking about artificial intelligence. For diagnostics we can build a model because it's human-made. When it comes to cell biology and cancer biology it's not human-made and we would be presumptuous to say that we understand this biology and that we are going to predict it with artificial intelligence.

From the perspective of rare diseases, currently a number of breakthroughs are coming, particularly in gene and cell therapies, that have potential to be life-transforming or even life-saving. Uncertainties exist, however, such as patient access and the long-term effect of these therapies. It's only possible to know about the clinical benefits of an approved treatment from the moment that this real-world evidence can be collected, post-launch. It can't be known from the artifact of an artificial homogeneous population for the clinical trial.

To address these issues, the project called Rare Impact was launched. It brings together manufacturers and engages with HTA, payers, EMA and stakeholders to identify the barriers. One key challenge identified at the European level which is true across the Member States is that the data required for post-approval regulatory differs from the one that payers and HTA are requesting.

On top of the post-marketing efficacy study and safety studies, each agency has its own data generation requirements, which is highly inefficient. There is no consensus on the collaboration on data collection and on data registries. From a patient advocate perspective this is disappointing as these conversations have been ongoing for ten years. It's a waste of financial resources and data. Also we cannot optimize the treatment options because this data cannot be consolidated and looked at in a consistent way.

The key issue is about ensuring better healthcare for the individual patient while ensuring long-term sustainability of the healthcare system. We are moving away from a one-time HA assessment for a pharmaceutical directly after market authorization to a more lifecycle approach. This means we are going to do more assessments later on and more reassessments.

Many initiatives are looking at issues such as the quality of a patient registry, the type of study designs needed if we have a patient registry, how to collect the data, and what to do with all the information from wearables and questionnaires on quality of life.

It's not only real-world evidence but should be a combination from clinical trial data with real-world evidence to get the best prediction. To bring those data together we need better methods. A first step is towards transparency. If we are going to do studies on reviewable data, what are we going to make public, and how?

My concern is that there are many initiatives at national and international level, and it's important for the European Union to facilitate bringing these initiatives together and find a way to use that money which is already invested to produce methods and outcomes which will be used by HCA, regulators, payers, patients and clinicians.

Moderator: Why is it difficult to bring these initiatives together? How do you see the way forward?

Jo De Cock: I think we have the possibility now to do so with two European strategies coming together: the data one and the pharmaceutical policy one. An issue is the decision making in the European context, which is not an easy one to solve, but nevertheless I think it's possible that these voluntary mechanisms can work together and reach their goals.

One recent initiative is the Horizon Scanning Project which involves 16 Member States along with Canada. It's creating awareness to prepare a decision-making process based on the right research questions. The question is how to make an initiative sustainable and not just a pilot. We have to bring together this fragmented landscape and try to join forces and not to launch different initiatives.

Moderator: What is the key barrier and challenge?

Adrian Jonas: There is no single issue but a whole ecosystem that needs to continually evolve. It concerns data quality and data access on the one hand, and only when those mature and standards are in place will we get greater cultural acceptance. Underpinning all of this is collaboration and public trust. Trying to coalesce various initiatives could lead to a risk of paralysis. Some HTAs accept real-world evidence and some don't even open the file when we're bringing real-world evidence. Definitely there are differences in the way a drug is assessed in different countries but coordinated work at this level would be very helpful.

Etienne Jousseaume: GBA recently issued guidelines on how to analyse real-world evidence and under what conditions would real-world evidence be accepted and how might the benefit assessment be affected. It's a positive move forward but such work needs to be coordinated at the united HTA level and not just at GBA or other technology assessment level. Coordination is the key to improve the predictability of the outcome of the analysis.

Peter Mol: The quality of the data is vital. Do you really have a sufficient understanding of the robustness of the data? This refers to not only the outcomes as they are presented or are available from the data, but also the way we analyse it. We are really looking at causality of a drug effect and we want to understand whether this drug causes this outcome. For that, randomization is key. If we get these better data available we might even capture the outcomes that may not be the clinical, more specific ones but the longer-term ones such as the mortality. It's important to capture the patient report outcomes and contributions of patients. Initiatives like IMI and Get-Real have proposed randomized registry based trials that could be very promising for the regulator.

Delegate: Isn't the right question WHAT real-world data will support pricing and reimbursement decisions instead of HOW it will support decisions?

Jo De Cock: The two are interlinked. One relates to the scientific robustness of the data and how can we have sufficient information which allows us to make evidence-based decisions. The other takes into account that these questions are always coming forward in smaller patients group in which randomized clinical trials are not always available; how can we make these decisions nevertheless when no alternative is available? For small patient groups for rare diseases it's important to clarify as soon as possible which data are needed but also how can we bring this to reality.

Delegate: Why is the (proposed) network not owned by the patients? They provide the information and benefit the most from the results.

Jo De Cock: Patients undoubtedly have an important role to play but a learning network or a platform should be organized with sufficient administrative support to have the links between all the stakeholders involved. It's not a political instrument.

Etienne Jousseaume: The openness of the platform is critical. It could belong to the patient groups or owned by an academic institution or a hospital on behalf of a scientific group or a scientific cooperative group. I'm not aware of registers that are owned by an administration. The key is that whether it's owned by the patient, an academic institution, a company or a consortium, it has to remain open, so that all stakeholders are able to discuss with the owner, build analyses, and publish.

Chris Sotirelis: As a patient advocate with a long experience in rare diseases, one of which I have myself, I am interested to see how this initiative could bridge the gap between clinical efficacy and safety, and clinical effectiveness and relative effectiveness and safety. This gap has been increasing rapidly in the last few years, particularly in the field of rare diseases. The elephant in the room is what is the legal status of registries? What is the position of the governance under which this real-world evidence will be collected? This has many issues and knock-on effects in other areas. It is important to have registries that are disease-based registries. Another issue with the legal status is that in several Member States, observational studies are not valid. Finally, within a legal framework, what is the position of the patient? Patients give their data but their involvement finishes when they sign the consent agreement. We want more of a co-creation framework with patients at the centre.

Moderator: What's the top priority or key next step to build on the work that's been done?

Adrian Jonas: Developing a clear, transparent standards and methods programme that will be delivered as a suite of products over the next couple of years. Disease doesn't have geographic boundaries, therefore collaboration across various initiatives is key.

Etienne Jousseaume: The opportunity that we have to analyse large databases without manual data collection is critical but you need to have a framework with adequate data privacy, access, and transparency of usage to help inform decision making.

Peter Mol: Examples of good data sources and a case-by-case understanding of what you can do with real-world data and how it can support our decision making.

Jo De Cock: To bundle forces and get a structure which is sufficiently stable with a good and transparent governance.

Session 2
How to realise a learning healthcare system?
How a Learning Network should involve all stakeholders and the role of a 'Data Analysis and Real-World Interrogation Network'

Karen Facey
Senior Research Fellow, University of Edinburgh and lead author of RWE4Decisions Actions for Stakeholders

The learning healthcare system concept has been around for a decade or more. It aims to use developments in digitalisation of healthcare to improve our health systems. This is a continuous process and links strongly with quality improvement methodology that involves PDSA cycle, starting with the best evidence, then studying small scale changes and scaling up.

So for real-world evidence, Payers decided to take a case study of a particularly challenging case – that of highly innovative treatments – particularly for rare diseases – which often come at a high cost, but with major uncertainties about effectiveness. For these technologies it is difficult to determine their value and real-world data may have a role to play as outlined in the RWE4Decisions paper

A multi-stakeholder workshop was held to provide advice to companies on real-world evidence generation plans for three highly innovative technologies at various stages in their life cycle. The aim was to test some of the recommended actions recommendations for stakeholders in the RWE4Decisions paper by engaging in multi-stakeholder dialogues.

The workshop not only enacted some of the recommendations about open structured dialogue about research questions that could be answered by real-world data, it also tested the two underpinning principles of transparency and collaboration. The workshop showed that there is a need to manage conflicts of interest and be upfront about them. Even "light touch processes" or "demonstration projects" need to be carefully managed when confidential information from drug development is involved. Questions as to what real-world data may be able to address in regulatory and Payer/HTA decisions need to be clarified, and methods for critical assessment of RWE should be published. It's also key to share information about RWD studies that are taking place across different jurisdictions to enable data amalgamation.

Iterative dialogues should involve all stakeholders throughout the lifecycle of a technology to discuss plans for evidence generation and the potential for RWE to resolve important decision uncertainties. RWE generation is a shared responsibility and should be pre-specified and planned with all stakeholders. We need to think about an "onion of core data", with different layers. There is a central part of the onion we should all be able to agree on: one or two key outcomes that should be collected to answer every decision-maker's questions. HTA bodies might then have a different layer to regulators. Countries may have their own specifications.

Each stakeholder needs to take responsibility for aspects they can influence and work collaboratively with other stakeholders to achieve the common goal of developing RWE that can inform (Payer/HTA) healthcare decisions and improve patient care.

A learning network needs to have open governance, reciprocity, and involvement of all stakeholders. It needs to be owned by a public institution, enable full multi-stakeholder interaction, and be sustainable through long-term funding.

Peter Arlett

Head of the Data Analytics and Methods Task Force & Co-Chair of the EMA-HMA Big Data Taskforce, European Medicines Agency

Real-world evidence isn't about the future but about the here and now. As a medicines regulator we recognize that the clinical trial is key, but real-world evidence is crucial to fill in the gaps and answer certain questions that clinical trials can't answer. It's critical to plan early. Ideally a plan for drug development will meet the needs of the different stakeholders. The learnings initiative could either be regarded from a product-specific or a systems basis.

In medicine's regulation disease epidemiology context for clinical trials, safety, risk management, and special populations are all areas where real-world evidence has a well established use case and methodology. Efficacy/effectiveness is more tricky; here the most work is needed to establish where real-world evidence can be used.

Given the COVID-19 crisis, real-world evidence has an important role to play in crisis planning and crisis response, including work on shortages, repurposing medicines, and monitoring therapeutics and vaccines.

We are doing a lot as regulators and with multiple stakeholders to improve the framework and the evidentiary value of real-world evidence. We believe that real-world evidence can support product development for patients as well as the safe and effective use of products on the market for patients. Indeed, all this work should be for patients.

Piia Rannanheimo
Pharmacoeconomist, Finnish Medicines Agency (FIMEA)

From an HTA author perspective it's clear that different organizations are integrating the use of real-world data in their work at a very different pace. Also, mandates related to managed entry agreements, post-launch evidence generation, re-assessment, scientific advice etc. differ in different countries. The mandates different HTA-organisation have may vary particularly in the hospital setting where many of these medicines and new treatments are targeted. So the role that a HTA organisation can take in the use of real-world data can differ in different countries.

Maybe a network of networks is needed, or an implementation network instead of a learning network, because many great initiatives have been done already and are ongoing. Also, a talented team for network coordination and facilitation is necessary because it's such a complex sort of ecosystem and it's a real risk that organisations don't commit to yet another initiative or network. Benefits are possible at multiple levels, such as policy learnings and methodological learnings.

Jakub Boratyński
Acting Director in charge of Digital Society, Trust and Cybersecurity, DG CONNECT, European Commission

We need to make sure that our actions in this area in Europe are interoperable. The exchange of information via European Electronic Health Records is critical. This demands the right technical specification covering lab tests, hospital discharge reports, medical images etc.

It's also essential to ensure a high level of cybersecurity, and in this respect there is a major need for investment in the health sector. We will be supporting these initiatives with the Digital Europe programme to deploy the infrastructures that would underpin these common data spaces. In the area of health this refers to the European Health Data Space, which is essential for making informed, real-world evidence-based decisions in order to improve accessibility, effectiveness and sustainability of the healthcare system. It is essential that we make a great effort to make the data accessible to research at innovators and also that we do not lose the trust of citizens in the process.

Q&A and interactive debate moderated by Jacki Davis

Special interventions

Matthias Rose
Medical doctor at the Charité – Universitätsmedizin Berlin

We are working on what we call the Health Outcome Observatory which builds on the EHDEN project from NICE. It involves conducting a federated data analysis on existing EHR records. So this is a source of real-world evidence. It involves storing the data in a common data format. The next level is access to registries. Then these two sources are combined with the patient perspective. It is starting with four countries (The Netherlands, Austria, Spain and Germany). The aim is to build one central hub in which patients can enter their health data.

Nicola Bedlington
Special Advisor, European Patients' Forum

The proper use of data can increase quality, safety and patient centredness of healthcare systems, and transform care into a more participatory process. It can improve healthcare system sustainability and reduce low-value care and costs. With regard to the recommendations targeted towards patients, they resonate with the thinking and direction of EPF and the specific work already undertaken.

In regard to the emerging European Health Data Space, it's fundamental for patients to be involved meaningfully right from the onset. This involvement should be structured, and facilitated at all levels from shaping real-world evidence ecosystems, governance, and decision-making to implementation of data co-creation and information exchange. Only through this broad and systematic involvement can patient organisations bridge the gap and bring patients closer to health data and real-world evidence, whilst ensuring appropriate ethical frameworks protection, transparency and fit-for-purpose consent mechanisms.

Collecting the right data is only one piece of the puzzle. The patient should also have a say on how data is safely stored, used and analysed to improve their health. Patient organisations can play a fundamental role in providing access to unbiased reliable information about real-world data and how this can lead to real-world evidence and their importance in the context of innovation and value-based healthcare.

Ansgar Hebborn
Head – European Access Policy Affairs, Roche

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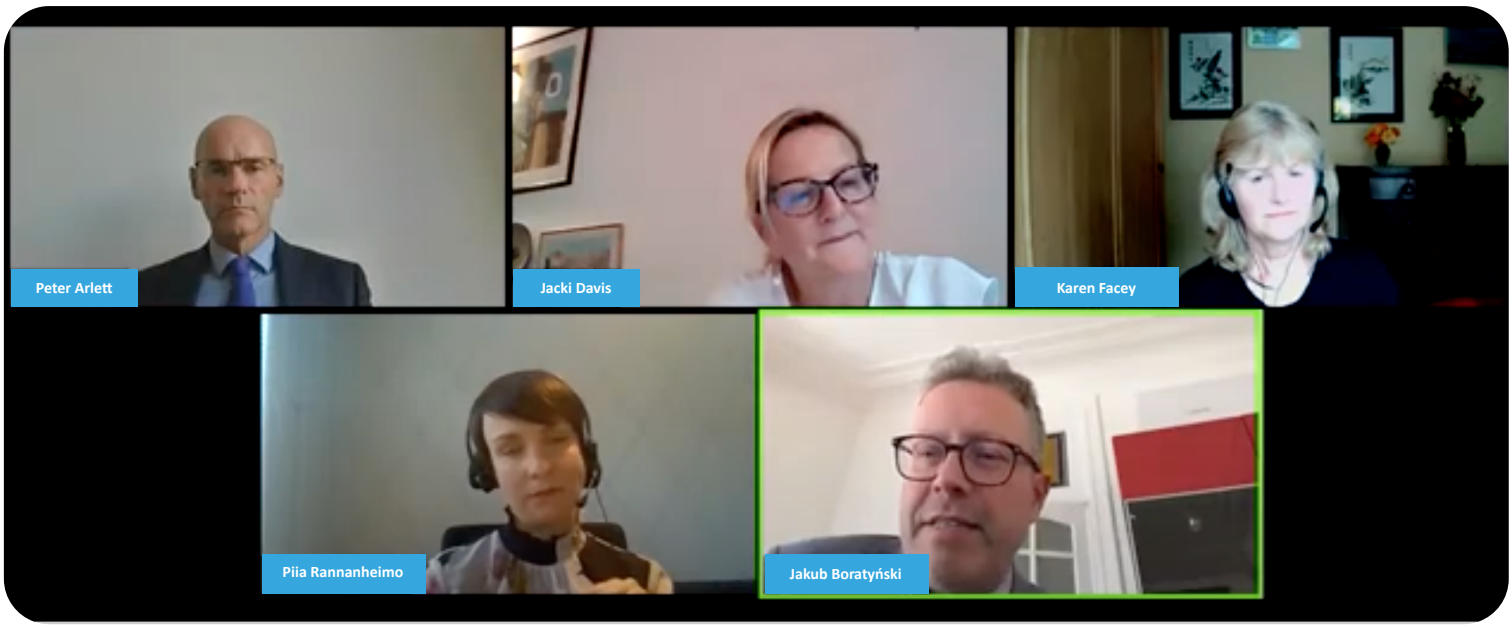

Moderator: What should be the scope and approach of this network?

Peter Arlett: If there is to be such an initiative it needs to have clearer objectives, a structure, and a basis for the participation of different parties. Currently, in regard to specific products, discussions take place that are confidential on individual products that are not on the market. These go on through scientific advice at the EMA. We reach out to healthcare, to HTA bodies and to payers to join that scientific advice. It's radical to think that we need a whole new forum, because EMA has got a legal basis for scientific advice and a whole mechanism and machinery that works very well. We should think twice before interfering with that. One of the recommendations of the heads of EMA's big data taskforce is for a multi-stakeholder forum on the framework for real-world evidence. This could involve guidelines for studies for protocols, a data quality framework, or even on the evidentiary value and use cases where real-world evidence might help.

Moderator: What might an implementation network involve, and what could be its scope?

Piia Rannanheimo: A lot has already been done and a lot is ongoing. We definitely don't need to reinvent the wheel. The EU has also funded many real-world data related projects. However, the implementation has been sub-optimal so this is an important area to work on. A broad perspective makes sense because so many things are inter-linked. I would not like to see specific topics forgotten such as cost-effectiveness, economic value, and managed entry agreements.

Moderator: What is the role for policymakers in terms of owning this process and its funding, because without long-term funding it's not going to be sustainable?

Jakub Boratyński: The idea of the learning network sounds very promising as it is involving a wide range of relevant stakeholders. At this stage I can't say what type of funding support we can provide but clearly this is a priority area. The key question is how can we really make big progress with the use of data?

Karen Facey: The workshop we've just undertaken was simply a case study workshop; it wasn't what the RWE4Decisions initiative intends to do in the future. But it did show the benefits possible in terms of very early dialogue involving the payers and all stakeholders, the potential for iterative dialogue, and a recognition that it could add value alongside existing Early Dialogue processes.

Patient organisations are investing huge amounts of money in registries, working in collaboration with clinicians, but patients can't always get access to the right data from the registry which they've been involved with. Regulators and payers are also saying that some of the data collected isn't sufficient or good enough to make decisions. It would be good to discuss openly what some of the challenges are and how we can resolve them with openness and transparency.

Moderator: What are the key ingredients that support this multi-stakeholder engagement?

Peter Arlett: You definitely need an honest, trusted broker, it needs to be funded in a sustainable way, and the different stakeholder groups need to have an equal footing or certainly a defined place in that forum. I would add clarity on the roles and responsibilities, which links into conflicts of interest.

Piia Rannanheimo: The key is really to understand what are the member benefits that the network is aiming to achieve. The goals should be clear and attractive to all members that join the network. The benefits could be achieved in multiple levels not only related to individual assessments, products or decisions. It's also important to separate whether we are talking about policies at a national or European level. There's a lot to learn from different countries in regard to market access processes and how we use data in managed entry of new products.

Delegate: It is not clear whether summary records for cross-border use are sufficient to support the need for real-world data. The EHR exchange format is a good start but do we need to go further in terms of interoperability and harmonization?

Jakub Boratyński: To build a real system in which medical data can flow with respect to the rules, we need data governance enshrined in European legislation. It cannot be just based on good will or a memorandum of understanding. Cooperation needs a very solid legal framework.

Peter Arlett: The EMA and the heads of the national agencies recently published the work plan of the big data steering group. It comes with a big caveat that some of the deadlines may need to be changed due to COVID-19. It involves launching work before the end of the year on a data standardization strategy with a view to adopting as medicines regulators a data standardization roadmap in 2022.

Delegate: What is the plan and timeframe for key stakeholders to issue clear and concise recommendations on how data quality and data fitness for purpose will be evaluated?

Peter Arlett: In the first quarter of 2021 we will be launching an external study to get an academic or a service provider to review what is already the state-of-the-art in terms of data quality, and what a regulator, HTA or a payer means by data quality, The aim would be to reach a common understanding. We hope then in 2022 to have a data quality framework for regulators which would at least be informed by the needs of other stakeholders.

Karen Facey: We need the same rigour around real-world data analysis that that we have in clinical trials. We need to understand that how we select the data from a retrospective chart review or draw it down from administrative databases is really important. So perhaps we not only need publication of protocol and a statistical analysis plan but also the data extraction plan.

Peter Arlett: EMA is shortly publishing a guideline on studies in patient registries for public consultation which draws on a number of the points being made here about the important role of registries and the need to get it right.

Moderator: What does good, watertight, open governance of a network like this mean?

Karen Facey: There's governance issues around all the kinds of data access. In the UK we find it difficult to link across data sets. Then there's the aspect of roles and responsibilities. I'm an advocate for patient involvement but also for transparency. Decision makers are having to make decisions for the whole of their population, and a patient group may have a specific interest. We need to work with them in an appropriate way to recognise who has responsibility for what and who can take what action.

Peter Arlett: I would come up with three: overall transparency, with transparency of funding in particular; detailed conflict of interest rules; and agreed and crystal-clear roles and responsibilities with the right to be heard of all relevant stakeholders.

Delegate: What about involving HTA bodies to ensure a common understanding across regulators and HTA bodies?

Delegate: One data standardization at EU level, how can the payer interact?

Peter Arlett: On both workstreams there will be outreach to HTA and payers. We will listen very carefully to their needs and perspectives. If we can come up with common data elements or common principles then that's a win-win situation because then we can have one registry that meets the needs of medicines regulators, HGA and payers, or one way of patient reported outcomes.

Moderator: What are the most important key next steps to move the real-world evidence world from pilots to routine structural processes?
Piia Rannanheimo: To clarify the roles of different stakeholders at the national level with regard to the use of real-world data in decision-making. This is the way to improve implementation of learnings from European collaborations. At the European level it would be good to better understand what benefits different stakeholders are expecting from this learning network.

Jakub Boratyński: To have secure accessibility of health data across the EU. Currently a range of financial instruments are on the table such as the Recovery and Resilience Facility, the Digital Europe programme, the Connecting Europe Facility (which could be relevant in terms of connecting infrastructure of Member States), Horizon Europe, and EU for Health. My priority would be for Member States and other stakeholders to come up with ideas on what is the best investment.

Peter Arlett: Darwin EU as a pathfinder project for the European Health Data Space, delivering secure accessibility of health data across Europe.

Karen Facey: Upskilling. An essential element of a learning healthcare system is that every member of staff within a health system has training in quality improvement appropriate to their own level, so that every member of staff understands what quality improvement means. Some will simply know about the methods, others should be experts and lead change. We need that around real- world data, particularly within the HTA/payer community.

Concluding remarks
The way forward
Moderated by Jacki Davis

Jo De Cock
CEO, Belgian National Institute for Health and Disability Insurance (INAMI/ RIZIV)

Andrzej Rys
Director for Health Systems, Medical Products and Innovation, DG SANTE, European Commission

To resolve the research questions, it's not a question of gathering data but of evidence building. This should be done for and with patients, taking into account the different roles of regulators and payers. Value for money also has to be demonstrated; especially in the coming years in the economic context we are facing. Any initiatives taken should of course have public trust.

To clarify the way forward, certain key questions need to be addressed:

- Do participants agree on the usefulness of a multi-stakeholder approach with regard to RWE, which is based on the principle "learning by doing" and underpinned by robust methodologies?
- Can a Learning Network on RWE be part of (or supported by) the EU Strategy for Data & the EU Pharmaceutical Strategy based on a voluntary cooperation mechanism between Member States?
- What steps should be taken to ensure the necessary sustainability of the initiative and for obtaining sufficient political endorsement?
- How could an alignment be realised with other RWE initiatives in order to join forces and avoid duplication?

We can come to a concrete proposal based on what has been heard today. This is what we want to realise in the upcoming period. The German presidency has also hosted a meeting which is linked to this issue and this project.

Learning is doing. If we do not try anything we will not get anywhere. This is the concept of the learning network; we might have to make mistakes to make progress. It should probably be a network of networks because there are many networks out there with their own culture and knowledge. We now have to ensure that these networks are connected. Important here is to collect and share examples and best practices. Another aspect is to work out who is in the system and then ensure trust and transparency throughout.

At the EU political level we have the European Health Data Space which is a joint venture that depends on having as many participants as possible involved. In the coming months, work will be done to achieve interconnectivity between European initiatives, European pharma strategies, the Member States and other stakeholders. Data will be the big winner. However, no-one should be under the illusion that this will be easy. But working together in a close and transparent way will enable the challenges to be overcome.

REAL WORLD EVIDENCE
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