

GETTING IT RIGHT –

Drawing Together Key Stakeholders To Shape The Real-World Data Revolution

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During an expert panel convened by Parexel and Pharma Intelligence in Barcelona, industry leaders discussed the challenges and solutions for early payer involvement in real-world data clinical trials.

MODERATOR

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GETTING IT RIGHT – DRAWING TOGETHER KEY STAKEHOLDERS TO SHAPE THE REAL-WORLD DATA REVOLUTION

Real-world data (RWD) provides an opportunity to help address the challenges of rising R&D costs and tougher access hurdles, supporting more sustainable drug development. RWD is also allowing the sector to revisit and evolve the way that product value is established. The sources of real-world, patient-generated data are multiplying and expanding, in part thanks to digital technologies. This growth offers new ways to use RWD and brings in new and different stakeholders. It also requires effective management of huge volumes of data.

A recent study from The Economist Intelligence Unit, commissioned by Parexel, identified RWD trials used in Phase II or Phase III as one innovative approach to help improve drug development efficiency and launch success. It also provided early signs that such data can positively impact market access.¹ During an expert panel convened by Parexel and Pharma Intelligence in Barcelona, 10 industry leaders discussed the challenges and solutions for key stakeholders to become involved earlier in RWD trials to ensure the data is relevant to the needs of different parties.

There are compelling case studies supporting greater, and earlier, use of RWD. GlaxoSmithKline's (GSK) Salford Lung Study broke new ground in providing evidence, pre-approval, of the real-world effectiveness of asthma and chronic obstructive pulmonary disease (COPD) product Relvar Ellipta. The study's unique design overcame the challenge of generating RWD pre-launch – most RWD is collected only after a product is on the market. The study also catalyzed engagement and cooperation among multiple UK health system stakeholders. In the US, Roche is us-

ing high-quality clinical and medical records as a source of ready-made, up-to-date control arm data in cancer, where rapidly-shifting and locally-divergent standards-of-care make trial design challenging.

CHALLENGES FACING THE WIDER USE OF RWD

Still, there are many obstacles to more widespread use of RWD by regulators and payers to support expedited regulatory approval and market access. RWD encompasses a huge range of data types and sources, from health records, to claims and registry data, survey data, observational trials and pragmatic trials like the Salford Lung Study. Social media and wearables are also now capturing even larger, potentially more powerful sources of RWD, around individuals' behavior, preferences and physiology. Yet standards, definitions and transparency are lacking. There is little agreement on the most appropriate study designs, methodologies and analysis tools.

Crucially, neither regulators nor payers currently demand RWD as part of drug manufacturers' regulatory or access packages. Some do not take it into consideration even if it is provided. That lack of consistent RWD standards – and, as a result, huge national and even regional variation in what payers are looking for – means “reluctance among pharma to make significant investment decisions,” pointed out panel participant Eunice Kim, Global Market Access Head, Hematology at Shire.

Fragmented data infrastructure, divergent data privacy and ownership laws across different jurisdictions and the recently-enacted European Union General Data Protection Regulation (GDPR) provide further obstacles to the wider collection

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*– Oriol Solà-Morales,
CEO of HITT,
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and use of RWD. GDPR is also one example of how different regions of the world will have varying standards and guidelines for utilizing and combining data.

SOLUTIONS ARE GROWING

“There are lots of challenges [facing greater use of RWD], but there are probably even more solutions,” commented Oriol Solà-Morales, CEO of HITT, Health Innovation Technology. Examples of engagement among manufacturers, regulators, payers, providers and patients are increasing as stakeholders recognize the growing importance of data in supporting value-based care. Requirements for greater acceptance and use of RWD, to support more sustainable drug development, more successful launches and wider access, will drive a shift away from today’s heavy reliance on randomized controlled trials (RCTs) toward including more innovative approaches. While that idea could be daunting for some, key developments are beginning to materialize.

Among the most important needs are clear policy guidelines and leadership from regulators and/or other institutions across markets, to support greater investment in high-quality RWD. Critically, such guidance must begin to address how RWD can be used pre-launch, during the development process, to support approval and access. Regulators are beginning to consider how and where RWD may support some aspects of drug approval. For example, the FDA has recently announced a real-world evidence framework, looking at how RWD can support label changes and, potentially, product effectiveness.

This kind of change to the traditional evidence-base used for drug approval demands earlier engagement from, and alignment among, multiple stakeholders. Pharma, clinical investigators, patients, regulators and payers must communicate more often and more effectively during evidence-generation to ensure that data meets all needs as fully as possible, with similar clarity and

alignment to that achieved with RCT data. *“Transparency and dialogue,”* summed up Carme Pinyol, Head of Pricing and Market Access Southern Europe at Pierre Fabre.

Traditional stakeholders must also bring in newer players such as those with expertise in digital health and analytics, whose approaches to and experience with data collection, analysis and consumer relationships are becoming more relevant. *“There are newcomers out there that have to be sitting at the table,”* said Véronique Inès Thouvenot, Co-Founder, CCO and Scientific Director at Millennia2025 Women and Innovation Foundation, PUF Director of The Women Observatory for eHealth – WeObservatory. And patients’ voices must continue to be heard, particularly in addressing data privacy issues. The growing professionalism of patient organizations and the rise of the “citizen-patient” should support this, though systematic patient involvement may require legislative changes.

Engagement means a willingness to be open and share early experiences with RWD in order to build greater trust among all parties, and to address concerns as they arise. Embracing RWD will require a mindset shift among many players – a commitment to moving beyond the RCT-based evidence paradigm that has dominated the last half-century, toward one that includes more RWD and data driven by other innovative trial designs.

The value proposition supporting greater use of RWD must be clear to everyone. Payers in particular must buy in to RWD’s potential to efficiently provide more relevant data to support product value, help demonstrate efficacy and safety, and reduce uncertainty around cost-effectiveness and budget-impact. Payers often have quite different demands and needs across geographies that must be taken into account, but the increased availability of high-quality RWD and the alignment of standards may ultimately help meet multiple perspectives.

BUILDING ON POSITIVE EXPERIENCES

Concrete steps to encourage greater RWD acceptance and use among regulators and payers should build on existing, positive examples of RWD studies and of multi-stakeholder collaborations – including across regulators, payers and patient groups.

Pioneering RWD Studies

The Framingham Heart Study was a multi-thousand patient cardiovascular cohort study of the residents of Framingham, MA, begun in 1948. It helped generate much of our current knowledge about the effects on heart disease of diet, exercise and medications such as aspirin. More recently, GSK’s Salford Lung Study of over 2,800 patients with asthma and COPD in Greater Manchester broke new ground in terms of trial design and the degree of collaboration required – and achieved – across National Health Service GPs and hospitals, pharmacies, regulators, academia, patients and pharma. The infrastructure set up for the trial is supporting other initiatives to collate primary and secondary care data. These studies showcase how RWD and early stakeholder involvement can be integrated into trial design and create impactful data.

Existing Multi-Stakeholder Collaborations

Since mid-2017, the European Medicines Agency (EMA) has been offering drug sponsors advice on evidence-generation jointly, alongside the European Network of Health Technology Assessment (EUnetHTA). The process aims to support more efficient, targeted data-generation to satisfy both regulator and payer needs. Although not focused on RWD, the parallel consultation process provides a highly appropriate forum for discussing and introducing RWD. Patients and healthcare professionals are included. EUnetHTA itself was set up to identify and promote common ground across multiple European payers, in itself helping

streamline evidence-generation and access processes for sponsors.

EMA’s PRIME scheme for priority medicines engages pharma early in the drug development process, providing advice to support efficient trial design and data generation, ultimately to accelerate access. The scheme may provide fertile ground for early engagement around greater use of RWD – including with payers.

Similarly, EMA’s Adaptive Pathways Pilot, investigating a more iterative development and approval process to accelerate patient access, accepted RWD as a complement to RCTs.

The multi-stakeholder, IMI-funded ADAPT-SMART project aiming to put the process into practice demonstrated the challenges of changing established systems within a complex, highly-regulated domain such as healthcare. There were few binding outcomes, but the initiative proved that it is possible to engage multiple stakeholders, including around the use of RWD.

Examples are also emerging of more focused projects, driven by highly-motivated patients or family members, which provide an opportunity for introducing new data-types and ways of working. Project Hercules (Health Research Collaboration United in Leading Evidence Synthesis) is a collaboration between charity Duchenne UK and pharmaceutical companies. It aims to engage patients, payers and Health Technology Assessment (HTA) agencies early on, collaboratively and in transparent fashion, in order to expedite patient access to new treatments for Duchenne’s muscular dystrophy, an inherited muscle wasting disease. Several of the program’s goals relate to RWD and its use, including developing shared tools for mapping clinical trial endpoints onto clinical outcomes, an HTA-relevant quality of life metric, and a cross-sectional study looking at true burden of illness.

Growing instances of European payer cooperation could also potentially be expanded to discuss and share experiences of RWD, and feed

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Integrated Market
Access Solutions,
Parexel*

into broader stakeholder efforts to determine RWD standards. These include MEDEV, which assembles health insurers and HTA from Austria, Finland, Germany, Luxembourg, the Netherlands and Switzerland; MoCA, a framework for coordinated access to orphan medicines across Europe, based on voluntary, open-minded and respectful dialogue among key stakeholders; and collaborations among payers within the Benelux region and Iberian Peninsula.

While these examples illustrate the positive impact of greater cooperation, it will take time, continued proven cases and an openness to embrace innovation to ensure more, and earlier, stakeholder involvement around RWD trials.

BUILDING RWD INFRASTRUCTURE

Generating robust, high-quality RWD requires a reliable, expansive data infrastructure, spanning disease registries, integrated out-patient and hospital records, medical databases and, increasingly, cloud-based storage and mobile data-collection hardware. Existing data-troves include the UK's Systemic Anti-Cancer Therapy (SACT) dataset, the Clinical Practice Research Datalink (CPRD) connecting doctors' practices, Imperial College Health Partners' Discover de-identified dataset that links GP data from 370 GP practices with acute, mental health and community health data and social care data for 2.3 million patients in North West London; France's SNIIRAM database of medicines use, Germany's regional payer databases and Italy's cancer registries.

New components of this infrastructure are emerging. The UK government, for instance, has committed to create integrated care records for patients across 5 regions (including London) under the Local Health and Care Record Exemplars (LHCRES) partnerships that will in 2019 be supplemented by a UK-wide initiative, Digital Innovation Hubs Programme that aims to enable the

safe and responsible use of health-related data at scale for research and innovation. Such initiatives offer Europe the opportunity to lead in the greater, more effective use of RWD.

PROPOSED ACTIONS

The roundtable participants suggested concrete actions to encourage early payer and other stakeholder engagement around greater use of RWD. They noted that the ongoing data and digital revolution offers an ideal opportunity to challenge and evolve the traditional RCT-dominated approach to evidence-generation.

Mathieu Boudes, Public/Private Partnership Coordinator at European Patients' Forum (EPF), called for the European Commission to advocate for and support greater use of RWD. Such an authority could convene a multi-stakeholder dialogue and encourage mutual trust. This or a similar, neutral organization would need to engage with manufacturers, regulators and payers to reinforce that RWD can be used to reliably demonstrate many aspects of the value of innovations.

Building data standards would be a key part of such a multi-stakeholder initiative. This would involve agreement on which kinds of RWD are optimal in particular settings, building experience and overseeing the construction of a fit-for-purpose data infrastructure. "No data is perfect," even in the RCT realm, pointed out Richard Tolley, Vice President, Integrated Market Access Solutions, Parexel. "Yet products get developed and approved. We must do the same with RWD as we have done with RCTs - agree the data that is put together, so people can trust them, and be open to building on the experience."

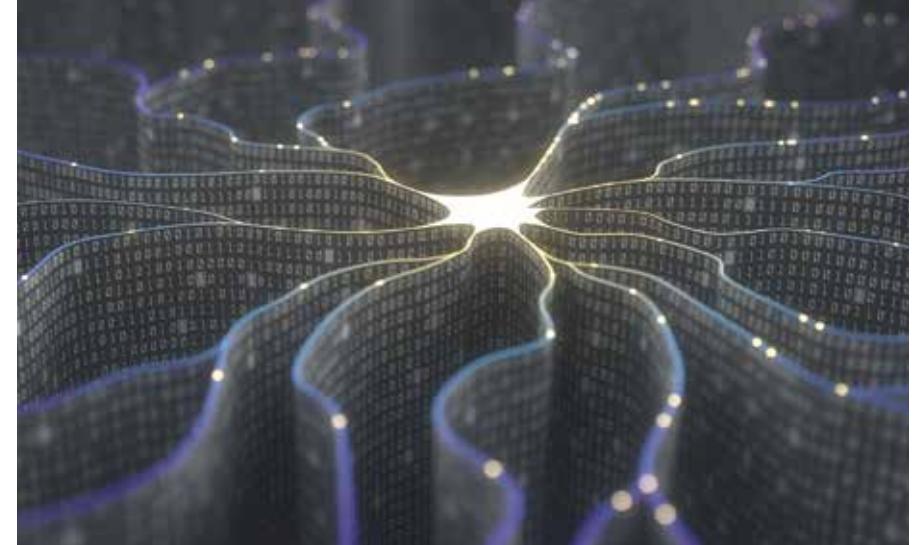
Creating and disseminating a portfolio of positive case studies around the use of RWD to demonstrate the value case across multiple indications and settings was another idea. "We should collaborate to provide our payers and regulators with more evidence of how good research can benefit everyone," said Amanda Lu-

cas, Programme Director at Imperial College Health Partners. The case studies would be agreed with sponsors in collaboration with payers and regulators.

Regulators are more likely than payers to accept RWD, according to Jorge Mestre-Ferrandiz, independent economics consultant. "We have to correctly target what we are trying to do and what we intend to say," he said. Compelling EMA to accept sponsors' RWD plan alongside their RCT plan, in order to establish and understand the connections and relationships between the data-types, was also suggested. "We must move the regulators to accept different types of evidence," said Solà-Morales. This may eventually lead to regulators accepting different kinds of evidence, on the continued understanding that RWD will not replace RCTs but should become a more important complement to them.

Within the payer realm, a European- or national-level think tank was proposed, convened by one or several payer(s) without direct pharma influence. The agenda and leadership of such a think tank would need to be clarified but must address affordability and the budget impact of new medicines, pointed out Gurmit Sandhu, Patient Engagement Specialist at Gurmit Sandhu Consulting GmbH. "Payers need to work out for themselves how they want to look at RWD and digital," he stated.

With or without their own think tanks, payers will need to see hard evidence that appropriate medicines use can help save downstream costs in order to shift their mind-sets, as appropriate, toward "investing" in new drugs, as opposed to "bearing their cost," noted Marco Marchetti, Director of the National Center for Health Technology Assessment, Istituto Superiore di Sanita. Such a change could be accomplished by testing annuity-based payments, value-based insurance design, pooled re-insurance models or other new approaches already being discussed. In short, the data revolu-



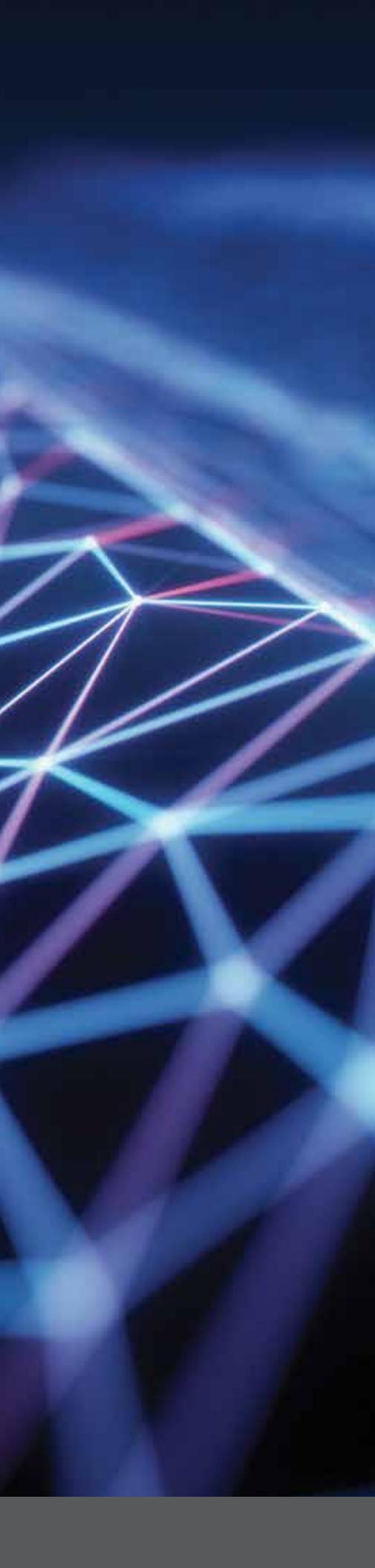
tion could change the way payers assess pricing and reimbursement, and thus proactive input from those payers will be critically important.

Indeed, panelists proposed building upon existing instances of "forced creativity" in reimbursement, when newly-approved, high-priced technologies addressing an unmet need compel payers and pharma to consider novel payment structures. CAR-T therapies are one recent example. These novel cancer medicines generated many discussions (and some deals) around outcomes-based reimbursement and instalment payments. There were calls for a more proactive approach, using new kinds of data and "getting ahead of the curve, rather than being reactive," said Tolley.

Experience with such new payment structures is increasing, both in Europe and the US, as payers grapple with the growing cost of highly specialized therapies in particular. This will continue as science drives more personalized medicines, including cell- and gene-based therapies. Some pharma companies are beginning to engage earlier and more proactively with payers in order to smooth their products' route to patients.

In most cases, payer involvement in such discussions is hindered not by a lack of will, but by a lack of resources or legislative flexibility, pointed out

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Boudes. Even with those things, however, “*early payer involvement will be a long, collective effort to efficiently engage stakeholders to participate in systematic discussions of RWD clinical trials,*” noted Boudes.

A NEW ERA IN CLINICAL DEVELOPMENT

The panel agreed that the growing availability of RWD marks a new era in clinical development. Existing evidence hierarchies and the RCT-dominated paradigm must change, along with regulatory, access and

payment structures. This will not happen overnight. Determining and agreeing upon which kinds of RWD and analysis methods are most useful and trustworthy will take time and collaboration, including among stakeholders that have historically been at odds. “*There is an increasing amount of information out there. The challenge for all stakeholders – now and in the future – is to be innovative in how this is used, realizing the benefits of using this data to support regulatory, market and patient access,*” concluded Parexel’s Tolley.

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