Real-world evidence to support HTA/payer decisions about highly innovative technologies

Actions for Stakeholders v1.0

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1. BACKGROUND TO THIS INITIATIVE

1.1 Context of highly innovative technologies

Highly innovative technologies use ground-breaking, scientifically advanced mechanisms to target the underlying cause of a disease to deliver highly effective, potentially curative, or at least transformative, patient benefit. Examples include direct-acting antiviral therapies for hepatitis C and the cell and gene therapies being developed for a range of conditions. Where large potential benefit is expected in areas of high unmet need, regulators have developed accelerated development and review pathways. These regulatory pathways can result in a small evidence base for HTA/payers who must balance the claim of substantial effectiveness (lasting cure) with a high price arising from the complexity of scientific development and proposed transformative benefit. This leads to major challenges in determining the value of these highly innovative technologies in terms of clinical effectiveness (particularly determining size and durability of effect in the standard healthcare setting), cost effectiveness and budget impact.

1.2 Potential of real-world data

Alongside this, strategic and operational advancements in digital health are enabling access to real-world data (RWD) leading to discussions about their potential to resolve uncertainties in HTA/payer decisions, particularly in the case of highly innovative technologies.

There are differing views and definitions of real-world data, but the HTA community has recently agreed the following definition

> *RWD are collected during the routine delivery of health care from administrative datasets, case notes, surveys, product and disease registries, social media, electronic health records, claims and billing datasets, or mobile health applications.*[1]

As Annemans (2018)[2] indicated, there is a continuum between data collected in strictly controlled conditions and data reflecting what happens in daily practice.

[1] RWD HTA Glossary. Accessed 1 July 2019
[2] Check reference

HTA relies on good scientific evidence that arises from systematic, robust processes and in this context the HTA community has defined that:

> *Real-world evidence (RWE) is derived from the analysis of RWD. RWE is characterized by the actual use of the technology in practice and by findings that are generalizable to the target population for the technology. Real world data are primarily analysed through observational study designs.*[3]

Annemans (2018)[4] stated that RWE can only arise from RWD that are of high quality, accessible and analysed correctly to answer well-formulated questions.

This initiative was commissioned by the Belgian Payer INAMI/RIZIV building on previous multi-stakeholder initiatives exploring the potential of RWE to close evidentiary gaps for HTA/payer decisions:

- 'The use of real-world data throughout an innovative medicine's lifecycle' - outlined nine principles for good RWD practice in Europe
- 'Outcomes based pricing and reimbursement of innovative medicines with budgetary limitations' - defined 10 principles to assess the value for money of a medicine, with a main focus on outcomes-based agreements
- Tool to reduce the uncertainties in the evidence generation for specialised treatments for rare diseases (TRUST4RD)[5] - developed a taxonomy with four types of evidence gaps/uncertainties and emphasized the important role of an early, iterative dialogue between all stakeholders (EMA, HTA bodies/payers, industry, patients, clinicians).

TRUST4RD outlined that RWE may be able to resolve uncertainties about natural history, the interaction between the technology and the disease (including long-term treatment effects), and uncertainties related to the healthcare ecosystem for rare disease treatments. It was recognised that this framework could be applied to highly innovative treatments for rare diseases. For highly innovative technologies in more prevalent diseases, accelerated regulatory pathways may lead exceptionally to approval based on single-arm trials whereby RWE could resolve uncertainties about comparator effectiveness. For both rare and prevalent conditions, RWE could provide important information about long-term safety and effectiveness of a highly innovative technology. The RWE could point to outcomes that are indicative of response, which would be relevant as input to performance-based risk sharing agreements post HTA/reimbursement.

The reference section of this Guidance shows a wide range of other recent initiatives related to digital health and the generation and use of RWD and RWE for health system decision-making that have been reviewed for this initiative. The view of the stakeholders is that past initiatives remain fragmented and lack clarity about mechanisms for implementation.

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[3] RWE HTA Glossary. Accessed 1 July 2019

[4] Check reference

[5] Tool to reduce the uncertainties in the evidence generation for specialised treatments for rare diseases (TRUST4RD), March 2019 (submitted to Orphanet)

1.3 Purpose of this initiative

Regulators have identified that the randomised-controlled trial (RCT) is the best available standard, but due to rapid scientific and technological advancements a framework for regulatory use of RWE has been developed[6]. Now HTA/Payers need to develop their own approaches. This initiative was established to consider how RWD and RWE could be used to support HTA/payer decisions about the specific case of highly innovative technologies. It aims to explore if RWE could be used to resolve important decision uncertainties in a manner that is directive and collaborative, overcoming issues of fragmentation and providing practical actions for implementation by each stakeholder.

This work was commissioned to consider a particular area of decision-making that is challenging HTA/payers so that concrete issues about the use of RWD could be discussed and clear actions agreed. It does not focus on the underpinning issues of data sources, methodologies, governance, analytics and infrastructure[7] that are addressed by many other documents (see reference section). Instead it suggests concrete actions that can be taken by stakeholders now to improve the development of RWE that could inform HTA/payer decision-making for highly innovative technologies. It is hoped that the lessons learned from this particular case can be drawn upon for other situations.

Section 2 explains how this Guidance was developed. **Section 3** provides a framework for consideration of the issues, explaining stakeholder roles, the vision and key principles underpinning the work. **Section 4** presents recommendations for each stakeholder group and **section 5** makes overarching policy recommendations including the call for a multi-stakeholder collaborative network to be resourced and developed.

2. METHODS

This work considered the following questions in relation to highly innovative technologies:

1. How can the potential of RWD/RWE strengthen HTA/payer decision-making and lead to better tailor-made decisions on reimbursement?
2. What is the place of RWE in the lifecycle of these technologies?
3. Can valuable RWE be obtained from RWD? If so, which HTA questions can be answered with RWE, from what data, and under which conditions?

The potential for use of RWD relies on many issues and so this initiative included relevant stakeholders (see acknowledgements) to discuss these questions using a mixed-methods approach:

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[6] Cave, A., Kurz, X., Arlett, P., Real-World Data for Regulatory Decision-Making: Challenges and Possible Solutions for Europe, *Clinical Pharmacology and Therapeutics*, 10 April 2019, https://ascpt.onlinelibrary.wiley.com/doi/full/10.1002/cpt.1426

[7] Plueschke, K., McGettigan, P., Pacurariu, A., Kurz, X., Cave, A., EU-funded initiatives for real world evidence: descriptive analysis of their characteristics and relevance for regulatory decision-making, BMJ Open, Vol 8(6), 2018, https://bmjopen.bmj.com/content/8/6/e021864.full

- stakeholder presentations about the potential for use of RWD when making decisions about medicines
- review of recent international recommendations about the use of RWD in health decision-making[8] and identifying how those recommendations relate to challenges faced by HTA/payers for decisions about highly innovative technologies
- discussion of case studies from HTA authorities, payers and industry about use of RWD in relation to reimbursement decisions about highly innovative technologies to identify what's needed moving forward
- development of actions for each stakeholder group and a framework for a collaborative network.

All work was undertaken in accordance with the 'Bad Gastein' principle of equal representation of all stakeholders.[9] Representatives from HTA bodies, payers, academia, patient groups, healthcare professional organizations, government bodies and industry participated in two face-to-face meetings. The meetings were chaired by INAMI and the policy organisation, FIPRA. Detailed notes of each meeting were agreed by all participants and a sub-group involving all stakeholders brainstormed ideas arising from each meeting. An iterative process involving all participants was then used to refine the stakeholder actions and draft this Guidance.

Karen Facey PhD from the University of Edinburgh led the development of meeting content and drafting of this Guidance. The work was financially supported by EUCOPE, Amgen, AstraZeneca, Gilead Sciences and Roche. Some participants received travel expenses and Dr Facey received a fee for her work up to the provision of the final draft, subsequent work has been undertaken under the auspices of the University of Edinburgh with funding from the EC H2020 grant for the project IMPACT HTA.

3. FRAMEWORK

3.1 Stakeholder roles

Effective use of RWD to inform decisions about use of highly innovative technologies requires a collaborative effort across stakeholders, with each playing their part:

- **Policy-makers and national/European authorities**: enacting legislation to ensure a robust governance framework and enabling effective cross-country collaboration for use of RWD
- **HTA bodies/payers (nationally/regionally or in collaboration)**: identifying the questions that can/should be answered with RWD/RWE, providing guidance on critical assessment of RWE, collaborating with other stakeholders to collect and analyse RWD, implementing conditional payment models such as outcomes-based agreements using RWD

[8] See list of references on page 11-12
[9] https://www.ehfg.org/about-us/ehfg/ Accessed 27 August 2019

- **Regulators – European Medicines Agency (EMA) and National Competent Authorities (NCAs)**: ensuring RWD collection strategies (such as registries) are multi-stakeholder and fit for regulatory purposes and where possible take account of the needs of HTA and payers
- **Pharmaceutical Industry**: actively engaging with other stakeholders to develop and implement plans for RWD collection, analysis and reporting over the lifecycle of a highly innovative technology to generate robust RWE that helps resolve HTA/payer decision uncertainties
- **Registry holders**:[10] involving all stakeholders in the establishment of registries and ensuring good governance that addresses data quality, accessibility and sustainability to ensure the long-term value of registries and avoidance of waste in research
- **Clinicians and patients**: contributing their real-world experience to support collection of RWD that is useful and informs treatment decisions, at the individual and population-level
- **Patient groups:** as authorised representatives of patients, engaging in co-creation of RWE, communicating the possible uses of RWD and good governance processes to encourage patient involvement.

3.2 Vision

Stakeholders agree what RWD can be collected for highly innovative technologies - when, by whom and how - in order to generate RWE that meets the needs of patients and healthcare systems.

3.3 Key principles

To ensure efficient use of RWD and generation of RWE to inform HTA/payer decisions about highly innovative technologies, collaboration and transparency are key.

Collaboration: RWE generation is a shared responsibility and should be pre-specified and planned with all stakeholders. There are challenges in developing and coordinating the necessary collaborative platforms in terms of funding, knowledge[11] and governance mechanisms. So, collaborative strategies are needed to ensure RWD/RWE requirements are aligned amongst stakeholders and across jurisdictions, avoiding fragmentation and duplication. Iterative dialogues should be developed that 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. Furthermore, 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 HTA/payer decisions and improve patient care.

[10] EMA uses the term 'registry coordinator' - a person or entity having a role in the overall coordination of a registry or of a platform of several registries. Registry holders can be patient groups, healthcare professionals, clinical institutes, manufacturers.

[11] TLV. Follow-up of drug utilisation and treatment effects in clinical practice. Stockholm: Dental and Pharmaceutical Benefits Agency, 2019. https://www.tlv.se/download/18.24b9c52f16cc59e80009df2f/1567172243382/rapport_follow_up_of_drug_utilisation_and_treatment_effects%20in_clinical_practice.pdf

Transparency: Plans for RWD collection and generation of RWE should be shared publicly to ensure that data sources can be focused, coordinated and combined by:

- clarifying what questions RWD may be able to address in regulatory and HTA/payer decisions
- publishing methods for critical assessment of RWE
- sharing information about RWD studies underway across different jurisdictions to enable data amalgamation
- use of clear processes for managing conflicts of interest among stakeholders.

4. RECOMMENDATIONS TO EACH STAKEHOLDER GROUP

Working within the principles of collaboration and transparency, each stakeholder can take responsibility for actions that will better enable the use of real-world evidence in HTA/payer decisions about highly innovative technologies. This section proposes actions for each stakeholder group and the final section considers overarching policy recommendations that are needed to drive this work forward.

Recommendations to HTA bodies/payers

1. European or Multi-Country HTA bodies/payers

1.1 When Horizon Scanning identifies that highly innovative technologies might have a small evidence base, encourage industry to engage in multi-stakeholder dialogues to discuss evidence generation including RWD collection.
1.2 Identify the HTA/payer questions that can be answered with RWE and what the "evidence bar" is for each type of question.
1.3 Agree the core outcome set that is required for HTA reassessment.
1.4 Develop methods guides to show how RWE will be critically assessed.

2. National HTA bodies/payers

2.1 Use RWD to monitor the uptake and impact of HTA recommendations about highly innovative technologies.
2.2 Inform national stakeholders about RWE needs for HTA and engage in developments to enable secondary use of health and social care data in the national context.
2.3 Actively explore the opportunity to use RWD from other countries, preferably in collaboration with other HTA bodies, in consultation with industry, taking account of national/context specific limitations of the source of the data.
2.4 Request RWE generation plans from companies with links to protocols or plans for data collection and analysis.
2.5 During assessment, consider the feasibility of RWD collection or an outcomes-based managed entry agreement (nationally or in collaboration with other countries) to resolve important uncertainties and enable reassessment in the future.
2.6 Engage with stakeholders to agree responsibility for the conduct and financing of RWD collection and analysis.
2.7 When an outcomes-based managed entry agreement is used, engage with patients and clinicians to plan for potential routine adoption or disinvestment at the end of the agreement.
2.8 Build capacity in data analytics.

Recommendations to Regulators

3.1 Promote use of Scientific Advice/Early Dialogue processes at various points in the development of a highly innovative technology including all relevant stakeholders.

3.2 Continue to support methodological discussions with industry about non-RCT methodologies through methods qualification and scientific advice.

3.3 Enhance collaboration with HTA on initiatives such as registry qualification, Post-Authorization Safety Studies and Post-Authorization Efficacy Studies to agree a common core outcome set of data for HTA and regulation.

Recommendations to Industry

4.1 Create a RWE generation plan very early in development that addresses what outcomes will be used to determine patient benefit, how natural history and effectiveness of the comparator will be explored and plans for evaluation of long-term effectiveness.

4.2 Discuss the RWE generation plan at various stages throughout the technology life cycle with regulators, payers, HTA bodies, clinicians and patients.

4.3 Ensure analytical plans for RWE studies that are answering major HTA questions are available to HTA bodies.

4.4 Support the development of a public portal that summarizes the design and results of major RWE studies (ala RCT registries).

4.5 Support disease-based registries, instead of product-based registries (particularly for long-term clinical effectiveness).

Recommendations to Registry-holders

5.1 Continue to develop European Reference Networks (ERNs) within healthcare systems and ensure good representation of all stakeholders (including regulatory, payer, HTA) to contribute to discussions about registries and other sources of RWD.

5.2 At an early stage in the development of a highly innovative technology, be prepared to collaborate with regulatory authorities (EMA and NCAs), HTA bodies and industry to identify if existing registries could be used to resolve uncertainties during the development phase or for post-launch data collection, or discuss potential for new registries.

5.3 Review quality standards for registries issued by EMA and EUnetHTA and apply them.

5.4 Collaborate with HTA bodies/EMA and NCAs/manufacturers to determine if relevant outcomes can be collected and shared for analysis.

5.5 Collaborate with European policy makers to develop governance structures that facilitate data quality and accessibility.

5.6 Create disease-based, rather than product-specific, registries.

Recommendations to Clinicians

6.1 European Reference Networks (ERNs) and other clinical networks should systematically collaborate with regulators and HTA/Payers when establishing their registry[12] or other form of RWD collection to ensure it is fit for all purposes including HTA.

6.2 Enhance the H2020 EU Joint-Programme for rare diseases to include regulators and HTA bodies in order to better understand their needs.

6.3 Promote the use of data driven shared decision-making processes for optimization of treatment of the individual and care pathways.

6.4 Understand the importance and relevance of the role of RWD in outcomes-based managed entry agreements in order to align on right usage and adherence to collect the data needed.

Recommendations to Patient Groups

7.1 Develop patient group experts to be co-creators of RWE.

7.2 Develop EU or international patient group collaborations to engage in RWD initiatives and ensure that outcomes that matter to patients are collected.

7.3 Provide recommendations on novel and efficient collection methods for RWD (e.g. devices, wearables, mHealth).

7.4 Help promote the scientific and policy value of data collection and provide access within strict governance frameworks.

7.5 Work with stakeholders to encourage alignment of views on identification, collection, analysis and evaluation of RWD for decision-making.

5. POLICY RECOMMENDATIONS

This Guidance has focused on the specific case of RWE for HTA/Payer decisions about highly innovative technologies to enable work to be undertaken in a specific, high priority area of decision making and to develop learnings for other settings. It recognizes that there are some underpinning cross-country initiatives relating to the use of RWD that are needed to continue the digital transformation of healthcare and support this specific initiative.

Recommendations for Underpinning Cross-Country Initiatives

8.1 Continue the work of the eHealth Digital Service Infrastructure to develop services for cross-border health data exchange including recommendations for the principles and technical specification of electronic health records.

8.2 Share good practices on e-Health strategies which have been successfully implemented - in particular around integrated data systems, encouraging uptake of standardised data collection, quality standards and overcoming legal barriers.

8.3 Enable more efficient RWD collection across Europe by standardisation of electronic health records, core outcome sets and registries.

8.4 Support collaboration across Member States to agree methodologies and specifications for RWD collection and analysis to avoid duplication.

[12] Support for the setting-up of registries of patients affected by rare diseases available for all ERNs, European Reference Networks, 5 June 2019, available here.

8.5 Insist on transparency in reporting of RWE studies (in terms of plans and results) as is required for clinical trials.

8.6 Enact the WHO Global Strategy on Digital Health 2020-2024,[13] which encourages national and regional Digital Health initiatives to be guided by a robust strategy that integrates financial, organizational, human and technological resources.

8.7 Develop a legal framework, platform and governance processes for providing access to health data across Europe that can be accessed via appropriate governance mechanisms for bona fide research and decision-making purposes for technology development by any stakeholder (including health care systems), taking into consideration the implications of commercialisation of patient and health system data.

Recommendations for Overarching Collaborative Network

This Guidance has sought to identify clear actions for each stakeholder group in order to develop the use of RWE and resolve some of the uncertainties that exist in HTA/payer decisions about highly innovative technologies. The Policy Guidance has also stressed that collaboration across stakeholders is needed. **This requires appropriate resourcing, knowledge sharing and governance**.

9.0 To enable appropriate patient access to highly innovative technologies, we call for a multi-stakeholder collaborative learning network to be created involving policy makers, HTA bodies, payers, regulatory agencies, clinicians, patient groups, industry and academic experts that:

9.1 builds on past and existing initiatives about use of RWD in HTA/payer decisions

9.2 encourages implementation of these recommendations in each stakeholder group

9.3 monitors progress of implementation of these recommendations and discusses emerging issues with all stakeholders

9.4 shares case studies of challenges about use of RWE in HTA/payer decisions about highly innovative technologies

9.5 develops learnings to continuously improve approaches

9.6 develops guidance on use of RWE to promote access to highly innovative technologies.

[13] Global Strategy on Digital Health 2020-2024, WHO, Draft 26 March 2019, https://www.who.int/research-observatory/analyses/digitalhealth/en/index2.html

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REFERENCES CONSIDERED IN DEVELOPMENTAL WORKSHOP - BY STAKEHOLDER GROUP

International health policy

- Support for the setting-up of registries of patients affected by rare diseases available for all the ERNs, 5 June 2019, https://ec.europa.eu/health/sites/health/files/ern/docs/2019041052_news_en.pdf
- Global Strategy on Digital Health 2020-2024, WHO, Draft 26 March 2019, https://extranet.who.int/dataform/upload/surveys/183439/files/Draft%20Global%20Strategy%20on%20Digital%20Health.pdf?ua=1
- Using routinely collected data to inform pharmaceutical policies, Analytical Report for OECD and EU countries, February 2019, https://www.oecd.org/els/health-systems/routinely-collected-data-to-inform-pharmaceutical-policies.htm

HTA/Payers

- Widening the evidence base: use of broader data and applied analytics in NICE's work, Consultation on the data and analytics statement of intent, released on 13 June 2019 (open until 13 September 2019), https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-guidelines/how-we-develop-nice-guidelines/consultation-data-and-analytics-statement-of-intent
- EUnetHTA's Work package 5b (WP5B), in particular the Post Launch Evidence Generation and Registries (PLEG), https://www.eunethta.eu/ja3-archive/work-package-5-life-cycle-approach-to-improve-evidence-generation/
- Vision paper on the sustainable availability of the proposed Registry Evaluation and Quality Standards Tool (REQueST), https://www.eunethta.eu/request-tool-and-its-vision-paper-are-now-available-for-public-consultation/ (currently open for consultation)
- Tool to reduce the uncertainties in the evidence generation for specialised treatments for rare diseases (TRUST4RD), March 2019 (submitted to Orphanet)
- Pearson, S., Dreitlein, W., Towse, A., Hampson, G., Henshall, C., Understanding the Context, Selecting the Standards: A Framework to Guide the Optimal Development and Use of Real World Evidence for Coverage and Formulary Decisions, *Journal of Comparative Effectiveness Research*, Vol 7 (12), 14 November 2018, https://icer-review.org/wp-content/uploads/2018/03/ICER-RWE-Framework-Companion-White-Paper-03282018.pdf
- MIT NEWDIGS FoCUS Project. Designing financial solutions to ensure affordable access to cures. An overview of the MIT FoCUS project, August 2018, https://newdigs.mit.edu/sites/default/files/NEWDIGS%20FoCUS%20Frameworks%2020180823.pdf
- The use of real world data throughout an innovative medicine's lifecycle, 7 June 2018, https://www.inami.fgov.be/SiteCollectionDocuments/real_world_data.docx
- Hampson, G., Towse, A., Dreitlein, B., Henshall, C., Pearson, S., Real World Evidence for Coverage Decisions: Opportunities and Challenges. A Report from the 2017 ICER Membership Policy Summit, March 2018, https://www.ohe.org/publications/real-world-evidence-coverage-decisions-opportunities-and-challenges
- Outcomes-based pricing and reimbursement of innovative medicines with budgetary limitations, Discussion document for the multi-stakeholder meeting on pharmaceuticals, 12 September 2017, https://www.inami.fgov.be/SiteCollectionDocuments/innovative_medicines_with_budgetary_limitations.docx
- The use of RWD for the estimation of treatment effects in NICE decision-making, NICE Decision Support Unit, June 2016, updated December 2016, http://nicedsu.org.uk/methods-development/real-world-data/

Regulators

- Cave, A., Kurz, X., Arlett, P., Real-World Data for Regulatory Decision-Making: Challenges and Possible Solutions for Europe, *Clinical Pharmacology and Therapeutics*, 10 April 2019, https://ascpt.onlinelibrary.wiley.com/doi/full/10.1002/cpt.1426
- Olmo, C.A., McGettigan, P., Kurz, X., Barriers and Opportunities for Use of Patient Registries in Medicines Regulation, *Clinical Pharmacology & Therapeutics*, April 2019, https://doi.org/10.1002/cpt.1414
- EMA-Heads of Medicines Agencies Joint Big Data Taskforce Summary Report, 13 February 2019, https://www.ema.europa.eu/documents/minutes/hma/ema-joint-task-force-big-data-summary-report_en.pdf
- Report on CAR-T cell therapy Registries Workshop 9 February 2018, Patient Registries Initiative, 15 May 2018, https://www.ema.europa.eu/en/events/chimeric-antigen-receptor-car-t-cell-therapy-registries-workshop
- Discussion paper: Use of patient disease registries for regulatory purposes – methodological and operational considerations, The Cross-Committee Task Force on Patient Registries, 5 November 2018, https://www.ema.europa.eu/documents/other/discussion-paper-use-patient-disease-registries-regulatory-purposes-methodological-operational_en.docx
  Superseded by
  McGettigan P, Alonso Olmo C, Plueschke K, Castillon M, Nogueras Zondag D, Bahri P, Kurz X, Mol PGM. Patient Registries: An Underused Resource for Medicines Evaluation: : Operational proposals for increasing the use of patient registries in regulatory assessments. Drug Saf. 2019 Jul 13. doi: 10.1007/s40264-019-00848-9.
- Patient registry initiative coordinated by the EMA, https://www.ema.europa.eu/en/human-regulatory/post-authorisation/patient-registries
- ENCePP Guide on Methodological Standards for Pharmacoepidemiology. Chapter 4.3. Patient registrieshttp://www.encepp.eu/standards_and_guidances/methodologicalGuide4_3.shtml
- Framework for FDA's Real-World Evidence Program, December 2018, https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence
- Lim, R., Lee, D., Sabourin, P., *et al*, Recognizing that Evidence is Made, not Born, *Clinical Pharmacology & Therapeutics*, Vol 105(4), April 2018, https://www.ncbi.nlm.nih.gov/pubmed/30472743
- Plueschke, K., McGettigan, P., Pacurariu, A., Kurz, X., Cave, A., EU-funded initiatives for real world evidence: descriptive analysis of their characteristics and relevance for regulatory decision-making, BMJ Open, Vol 8(6), 2018, https://bmjopen.bmj.com/content/8/6/e021864

Industry

- AmCham Belgium, Real World Data, the key to securing an innovative Belgian healthcare landscape, Innovative Healthcare Committee, Cross-industry reflection paper, April 2018, https://amcham.app.box.com/s/eav0s0zch6ezb7ljpk213hoxk6on7n54
- EFPIA, Oncology health data mapping, Barriers to the collection and use of health data, March 2018

Academia

- Swift, B., Lokesh, J., White, C., Chandrasekaran, V., Bhandari, A., Hughes, D., Jadhav, P., Innovation at the Intersection of Clinical Trials and Real-World Data Science to Advance Patient Care, *Clinical and Translational Science*, Vol. 11(5), pp. 450-460, May 2018, https://www.ncbi.nlm.nih.gov/pubmed/29768712

Glossary

BD4BO	Big Data for Better Outcomes (IMI project)
EMA	European Medicines Agency
ERN	European Reference Network
EU	European Union
EUCOPE	European Confederation of Pharmaceutical Entrepreneurs
EUnetHTA	European Network for HTA
FIPRA	Foresight International Political & Regulatory Advisers
H2020	Horizon 2020 (research programme)
HTA	Health technology assessment
IMI	Innovative Medicines Initiative
INAMI	National Institute for Health and Disability Insurance
NCA	National competent authorities
RWD	Real-world data
RWE	Real-world evidence
TRUST4RD	Tool to reduce uncertainties in the evidence generation for specialised treatments for rare diseases (TRUST4RD)
WHO	World Health Organisation
WP	Work Package