POSITION PAPER

10 RECOMMENDATIONS TO TURN BELGIUM INTO A LEADER ON REAL-WORLD DATA EVIDENCE GENERATION

Executive summary

With a constructive, solution-oriented mindset, the American Chamber of Commerce in Belgium (AmCham Belgium) aims to contribute to the discourse on transforming Belgium into a leader in real-world data (RWD) evidence generation, presenting ten concrete recommendations to achieve this goal.

- Unique selling value propositions should be created in the Belgian healthcare data to become relevant. These value propositions should first be elaborated through a series of consultations with key stakeholders, in a view to be proposed, prioritized, and tested through business cases.
- Explicit governmental support to highlight the importance of RWD for the Belgian healthcare system is needed. It is essential that the next government funds, supports and facilitates the secondary use of health data not only for clinical research and practice, but also for regulatory decision making.
- Awareness campaigns should be launched for healthcare practitioners, decision makers and the broader public. Today, the added value of the secondary use of data is underestimated and underrated.
- A clear legal framework and regulation for the processing of RWD should be implemented. The lack of consensus on the approval and access to RWD for the purpose of studies is limiting the further development and use of these processes.
- By implementing such a framework, study timelines could be accelerated. Transparent and fast procedures should be defined to allow access to RWD. This recommendation should include the development of a standard contract and a transparent remuneration model.
- The lack of standards in data structures and content implies that data is not accessible to answer research questions. We recommend that data are standardized and harmonized by structuring the data using a well-defined coding system and data modeling principles.
- AmCham recommends to fund and stimulate the deployment of innovative technologies to help make the health data findable, accessible, interoperable and reusable (FAIR-ify), ensuring the technical maturity of healthcare organizations to be better balanced across regions.
- Federated data networks and data lakes should be created to support the uniformity and interoperability of health data. This would provide the opportunity to combine data.
- The international private and public initiatives should be encouraged to participate. The more Belgian data holders are involved in these highly visible and international initiatives, the more they will be able to demonstrate Belgium's capabilities and expertise. The Belgian Health Data Authority (BE HDA) could play a central role as the contact point, connecting all stakeholders.
- The application of RWD in regulatory decision-making should be increased.

The rapid changes in scientific, technological, and regulatory landscapes and the need for patient centricity in healthcare decision-making make RWD increasingly important. The 10 recommendations are proposals on how Belgium can be at the forefront for the use of RWD. The implementation of these recommendations requires a close collaboration between government, care providers, industry and finally citizens and patients. Ultimately, a legal basis or consensus among stakeholders is needed to implement, to facilitate adoption and enforce many of these recommendations.

Context

The Innovative Healthcare Committee (IHC) of the American Chamber of Commerce in Belgium (AmCham Belgium) is a cross-industry platform which aims to create a sustainable ecosystem empowering patients and improving the quality of care. Comprising senior experts from innovative pharmaceutical and medtech companies, technology firms, data specialists, insurance providers, and various other sectors, it possesses the unique capability to offer unparalleled insights into real-world data.

Belgium is uniquely positioned as second in Europe for clinical trials. However, Belgium is on par with the EU average for the secondary use of health data and is behind the Scandinavian countries. The Belgian Health Data Agency was recently set up to address this competitive gap, striving for a high-quality, data-driven healthcare system in which health data are available for secondary use in a uniform, transparent and secure manner. This paper outlines ten recommendations for Belgium to strengthen its position for the re-use of health data, elaborating on challenges and solutions.

In April 2018, the Innovative Healthcare Committee of AmCham Belgium published a cross-industry white paper: "Real World Data, the key to securing an innovative Belgian Healthcare landscape." This reflection paper explains the huge potential of Real-World Data (RWD), expresses the challenges, and formulates some recommendations.

Since the publication of the RWD white paper, major evolutions have happened in the Belgian healthcare system related to Real-World Evidence (RWE) such as the COVID-19 crisis, the development of new technological solutions, the creation of the Belgian Health Data Agency (BE HDA), and the upcoming European Health Data Space (EHDS) regulation. The objective of today's paper is to outline the means for Belgium to be a leader with a high standard of quality and with an ecosystem that allows for dialogue and implementation of policies articulated around infrastructure, capability, innovation, ethics, equity and engagement for the secondary use of health data. This is particularly relevant considering the significant progress other European countries are making regarding the use of RWD and setting up their national health data networks for secondary use.

Therefore, through the implementation of these ten concrete recommendations, Belgium can level up and become a hub for the secondary use of health data. More detailed information on the different recommendations can be found in the annexes.

Recommendations

1. Create unique selling value propositions in Belgian healthcare data to become relevant

The Belgian Health Data Agency (BE HDA) is currently well-positioned to outline and develop unique selling value propositions on the secondary use of health data and how it brings value to the research community, impacts healthcare delivery, quality of care and health outcomes, informs health policy or supports assessment of new health technologies. Next to that, it ultimately provides health, economic and social benefits to the Belgian population. Elaborating these value propositions through a series of consultations with key stakeholders (e.g., healthcare providers, governments and insurers, researchers, patient associations, and the industry), to then propose, prioritize, and execute business cases could be a step forward. These business cases could be further articulated around the

combination of data from different sources (e.g., longitudinal follow-up of patients through the primary, ambulatory and inpatient pathways), linking OMIC data to existing clinical data sources and making them searchable, structured design of PROMS/PREMS in certain therapeutic domains, etc.

2. Explicit governmental support highlighting importance of RWD for the future of Belgian Healthcare

Unlocking the potential of RWD is high on the Belgian political agenda, driven by the COVID-19 pandemic. Stakeholders such as public and private data holders, policy makers, industry and clinical research organizations have recognized the importance of RWD in making healthcare decisions. The Belgian government's "#dataforbetterhealth" initiative and the BE HDA initiative to get access to healthcare data for secondary use in a General Data Protection Regulation (GDPR)-compliant and uniform manner are a step in the right direction. For AmCham Belgium, it is crucial that the government funds, supports, and facilitates the federated secondary use of health data for clinical research and practice, and regulatory decision-making, underlining thereof its importance for our healthcare ecosystem.

3. Launch awareness campaigns on RWD for healthcare practitioners, decision makers and the public

Research conducted by the King Baudouin Foundation shows that Belgians know relatively little about data related to their health[1]. Nevertheless, more than three in four Belgians are willing to share their personal medical data, should it remain within the medical sector. The limited knowledge of the positive impact of using RWD is also observed among healthcare providers and decision-makers in healthcare organizations. Therefore, specific awareness campaigns should be designed for this audience, in addition to campaigns for the broader public.

The message could focus, for example, on faster identification of rare disease patients, evaluation of quality of care, funding of treatment based on their effectiveness, etc. The message could also help built trust in data processing for secondary use. In addition to raising awareness, pilot projects can be carried out that actively involve patients at the local, regional, or national level and whose results are made public by researchers in scientific communication. Hence, patient-focus studies where the impact on health outcomes of patient behavioral (e.g., eating habits, physical activities, etc.), phenotype (e.g., clinical and family history), social (e.g., education level, economic and social network) and genotype attributes could be significant for healthcare decision-making and personalized medicine.

In this way, information and the value of the data is brought back into the hands of patients, providing further trust in and added value for the secondary use of health data. Patients will have to be informed about their right of access and data portability, as well as their rights to rectify, erase, restrict processing, and object. Patients must also be informed of their right not to be subject to a decision based solely on automated processingwhen applicable, as principles of data protection do not apply to anonymous and aggregated health data.

The latest version of the European Health Data Space (EHDS) legislation, which is an outcome of the trialogue, offers an opt out possibility for citizens/patients at Member State level. The EHDS

[1] https://kbs-frb.be/fr/zoom-prenez-soin-de-vos-donnees-de-sante

legislation needs to be made implementable through implementing acts; should Belgium consider the possibility of an opt-out, then educational and awareness campaigns are recommended to inform citizens and patients about the associated pros and cons.

4. Creation of a clear legal framework and basis for processing RWD to generate real world insights

There is a lack of consensus on approving and providing access to RWD for the purpose of executing RWE studies, with often conflicting interpretations of the requirements of the GDPR. For example, some hospitals add rules for processing on top of the GDPR (e.g., requirement of an informed consent for retrospective studies with scientific or historical purpose), adding more complexities to studies, thus delaying or denying their conduct. Therefore, clear rules would allow sponsors (typically acting as data controllers) and/or Clinical Research Organizations (CROs) (typically acting as data processors) to allocate appropriate resources for the different phases of studies (e.g., regulatory submission and contracting) and speed up study timelines. In some circumstances (e.g., when determining the means for the interoperability and re-use of health data), there may be a collision between sponsors, data holders, and data controllership. Therefore, the possibilities for joint-controllership could be evaluated on a case-by-case basis should there be convergence in determining the purpose and the means of processing health data. A clear legal framework (such as EHDS) could govern the relations between stakeholders and clarify study requirements with unambiguous GDPR interpretation. Guidance on the interpretation of data sharing modalities (e.g., pseudonymization and anonymization standards and methodologies) would streamline the processes, facilitate local collaborations between the public and private sectors and make Belgium more attractive for international RWE studies. The position paper published by the seven university hospitals for a framework for secondary use of RWD (routinely) collected in hospitals could be a starting point.[2]

5. Define transparent, fast procedures to allow access to RWD including a standard contract and transparent remuneration model

Facilitating access to RWD is best supported by legal and regulatory frameworks as well as standard operating procedures. Access to health data for secondary use is usually determined by, among other things, the purpose of RWD use, the nature or type of data, conditions and requirements for data dissemination, and the need for committee approval. The acceptance and use of standard contract templates or data sharing agreements between the industry, CROs and data holder institutions could significantly accelerate the establishment of RWE studies in Belgium. An example of this is the ongoing project between Pharma.be / BeMedTech and hospitals. Moreover, considerations could be made for a fair market value framework based on how labor intensive it is to exploit some data (e.g., unstructured versus structured data and associated data curation steps to make the data fit for purpose), the method of accessing the data (e.g., data query or manual abstraction), the associated time-effort and overhead, and the technical maturity and required contribution of the data holder to make the data readily available, reusable and executable in a timely manner.

[2] https://www.univ-hospitals.be/ [accessed on May 17th, 2024]

6. Continued efforts to Findable, Accessible, Interoperable and Reusable Belgium health data

Identifying, accessing, assessing, and processing RWD can sometimes be difficult due to the lack of standards in data structure and content, making data barely accessible to answer research questions. Standardization and harmonization of data is essential for RWE studies; data must be structured using a well-defined coding system and data modelling principles to be maintained while minimizing information loss. For example, if most data holders would use the same data model with format standards and semantics (terminology, ontology), it would be easier, faster, and more effortless to combine, compare and analyze data from different systems. In Belgium, the lack of interoperability standards across data holders to facilitate a multitude of data use represents a major challenge to achieving this goal. In Finland FINOMOP collects and links data from diverse sources including registries, primary and secondary cares, coordinates data access. Hence, different data standardization such as OMOP, FHIR, ODM, SNOMED, etc., are available to harmonize clinical data into a research infrastructure whilst maintaining a minimal data loss in the information and implementing the FAIR principles. Multiple factors must be considered for selecting the right data standardization, including the nature of the source of the data, the frequency of update, the intended usage, current and expected data modalities, etc. Adopting government-funded interoperability standards for specific therapeutic areas (e.g., rare disease) and data complexity (as operationalizing a one-size-fit-all approach will be challenging) may facilitate data mapping and enable smooth cooperation with both local initiatives and projects outside Belgium.

7. Fund and stimulate the deployment of innovative technologies to help FAIR-ify health data

Advanced technology solutions are critical to accessing RWD and require the technical commitment of data holders. There must be investment in technologies to easily search structured and unstructured data at the hospital level, for example, and in artificial intelligence and machine learning to process and make sense of RWD. Healthcare organizations may struggle in financing the investment needed to deploy these technologies, limiting thereof their contribution to national and international RWE initiatives. Furthermore, the technical maturity of healthcare organizations is disparate across regions. To tackle that, one can cite the Data Capability Program and the Innovative Data Program with the initiative for integrated electronic health records (EHRs) and the vision to have information shared without it being duplicated but retrieved from the original source. The implementation of the integrated EHR is fostered by the Belgian Meaningful Use Criteria (BMUC) with supportive financial incentives. This model can be replicated for FAIR-ify health data, with public funding at the local, regional and/or national level that is critical to the technical adaptation of data holders, especially hospitals.

8. Support the uniformity and interoperability of health data with the creation of federated data networks and Data Lakes

As highlighted earlier, applying data interoperability provides the opportunity to combine data. However, it can be challenging to bring data from multiple sources together in one place to perform analysis at scale. One solution to this is to build a federated data network where multiple datasets remain with their owners, but at the same time are accessible and analyzable from their source locations. To do so, one must consider system architecture and interoperability, data population governing the input of health data to be integrated into a common data warehouse through data

mapping, transformation and harmonization, common data quality frameworks, standards and semantic supporting querying, and advanced metadata for data exploration, as well as clear data governance, security, and privacy. The Data Analysis and Real-World Interrogation Network (DARWIN) project, a project of the European Medicines Agency (EMA) or the European Health Data and Evidence Network (EHDEN) project under the Innovative Medicine Initiative are examples of such a large-scale federated data network. Data are converted into the OMOP common data model (CDM) for these initiatives. In addition to a federated data network model, there are Data Lakes where both structured and unstructured data can be stored at any scale centrally. Data Lakes are central repositories of data with no predefined structure or schema. The Institute of Analytics for Health (INAH) is an example of a Data Lake initiative with a platform that uses distributed data warehouses at the data owners' facilities. Initiatives around federated data networks or Data Lakes are booming in Europe and beyond, highlighting the need for uniformity to provide legitimacy and confidence in operationalizing simultaneous access to multiple datasets. The BE HDA presents the characteristics of a data access body that can play a role in uniformity and interoperability of health data, stimulating public-private collaborations among others.

9. Stimulate the participation to international private and public initiatives

Under the auspices of both private and public stakeholders such as DigiOne and Elixir, there are an increasing number of European and international initiatives enabling access to RWD in multiple countries. The more Belgian data holders are involved in these highly visible and international initiatives, the more they will be in demand and able to demonstrate capabilities and expertise for Belgium to maintain its data leadership position. The BE HDA could play a key role as a central contact point for these initiatives by connecting the relevant data holders with regionally funded innovativeinitiatives, keeping the overview and ensuring that Belgium is represented as a country. Hence, the continued participation of Belgian data holders and the increased use of Belgian data to the Data Analysis and Real-World Interrogation Network (DARWIN) project of the European Medicines Agency (EMA) is a nice example. The role of the DARWIN coordination center is to develop and manage a network of real-world healthcare data sources across Europe and to conduct scientific studies at the request of drug authorities and, at a later stage,[3].

10. Increase the application of RWD in regulatory decision-making

Belgium is in the second place in Europe in terms of number of clinical trials per inhabitant. Randomized clinical trials (RCTs) shall remain the gold standard for the benefit-risk evaluation of medical interventions. However, RWD can complement traditional RCTs. Currently, the United States is the only country where RWE is explicitly mentioned in the legislation with an FDA RWE framework operationalized by the Food and Drug Administration. With the BE HDA now in place, Belgium could strengthen its position in the use of RWD for regulatory decision-making tackling operational, technical, and methodological challenges (OPTIMAL framework[4]). Hence, next to the searchable

[3] https://www.ema.europa.eu/en/news/initiation-darwin-eur-coordination-centre-advances-integration-real-world-evidence-assessment

[4] Cave, A., Kurz, X., & Arlett, P. (2019). Real-world data for regulatory decision making: challenges and possible solutions for Europe. *Clinical pharmacology and therapeutics*, *106*(1), 36.

inventory of Belgian data assets, the BE HDA could publish recommendations on how to use the data catalogue, including use cases and best practices. Belgian health authorities and the BE HDA could also publish guidelines on the use of RWD in clinical studies to support regulatory decisions or promote the use of Belgian RWD in studies in different situations. Such situations where RWD would be determinant include when clinical trials are not feasible (e.g., rare outcomes requiring excessively large sample sizes), when ethical considerations interdict RCTs (e.g., life-threatening disease without an effective standard of care), when RCTs are poorly designed and data could not be generalized, or to better understand the natural disease history and epidemiology or treatment effectiveness and safety in (post-)marketing authorization, and indication extension. This would require a strong data quality framework, such as the one used by EMA, that could be readily deployed in Belgium.

About AmCham Belgium

Founded in 1948, the American Chamber of Commerce in Belgium (AmCham Belgium) is a dynamic non-profit organization dedicated to improving business and investment opportunities for the US-Belgian business community. Supported by more than 400 member companies, AmCham Belgium plays a pivotal role in an evolving business environment by focusing on three key areas: advocacy, networking, and knowledge-sharing. To learn more about AmCham Belgium, visit www.amcham.be.

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