Towards an implementation roadbook for Real World Data collection on ATMPs in Belgium

A pilot in DMD gene therapy

With clinicians, BNMDR and patient association

authored by

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achieving outcomes

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In collaboration with:
DMD clinicians from the Belgian neuromuscular reference centres,
the Belgian Neuromuscular Diseases Registry (BNMDR),
Parent Project Duchenne,
and Pfizer

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Disclaimer	Other multi-stakeholder external experts have contributed via in-depth interviews and a survey. Input from these interviews were analysed and discussed in this Ad Board and resulted in this report. External experts did not co-author these minutes and therefore do not necessarily agree with every element and/or recommendation in this report. However, the report will be shared to inform the external experts concerning the output of the Ad Board.

1 Executive Summary

An increasing amount of paradigm shifting therapies are being developed. These have the potential to offer life-changing solutions for patients with few or no alternative treatments. Among these new therapies, Advanced Technology Medicinal Products (ATMP) including gene and cell therapies, play an important part. Despite the enormous potential these therapies hold, some challenges remain such as funding and clinical uncertainty in long-term efficacy and safety. A policy report following multi-stakeholder round tables held in 2018-2019 on "Innovative funding solutions for paradigm changing advanced therapy medicinal products (ATMP) in Belgium, a multi-stakeholder consensus on gene therapy funding solutions", published in November 2019[1] proposed outcome-based managed entry agreements (MEA) as a possible innovative funding solution for ATMPs. The complexity to prepare outcome-based agreements has however been identified by all stakeholders as a major roadblock hampering the implementation. Therefore, an initiative was set up to prepare a roadbook enabling implementation of RWD solutions and outcome-based MEA for ATMPs in Belgium. This initiative used RWD on gene therapy in Duchenne Muscular Disorder (DMD) as a case study.

Based on literature and recommendations specified in a publication of the RWE4decision project[2], a proposal for a RWD framework for Belgium was designed. This framework formed the basis of an advisory board with clinical experts, project managers from the Belgian Neuromuscular Disease Registry (BNMDR) and a patient representative. During the advisory board the following questions were discussed:

- What data (core dataset) should be collected in a DMD RWD infrastructure for gene therapy follow-up?
- How should this data be collected?
- What would be the appropriate governance model for such a RWD infrastructure?

This report summarises the recommendations from the advisory board regarding a governance model and action plan to facilitate the collection of a real-world data for future gene therapies. In this respect, requirements as well as roles and responsibilities of Belgian stakeholders will need to be clarified. This report will be presented in a broader multistakeholder round table inviting all relevant stakeholders and authorities to implement a RWD framework for Belgium. This project has by commissioned by Pfizer and executed by Inovigate.

Goal of the DMD RWD infrastructure

RWD collection on gene therapies allows for evaluation of long-term efficacy and safety. The advisory board indicated that a DMD RWD infrastructure should ideally fulfil a broad spectrum of objectives and serve all stakeholders involved:

- Long-term follow-up of patients after clinical trials
- Support physicians in medical decision making
- Support well-founded decisions on pricing and reimbursement
- Facilitate post-marketing surveillance and fulfilment of post-marketing obligations

In order to fulfil the above mentioned objectives, a DMD infrastructure should be created based on the BNMDR disease registry and adapted toward future treatments including gene therapy. Through a pre-

[1] Maes, I. Boufraioua, H. Van Dyck, W. Schoonaert, L. (2019). *Innovative solutions for paradigm changing new therapies*. *https://www.inovigate.com/media/filer_public/e8/9c/e89ca2b0-1dcf-48fb-9afc-9e911ddcef84/innovative_funding_solutions_-_short_version_without_appendix_vs09.pdf*

[2] De Cock, J., & Kurz, X. (2021). *Co-Creating Real-World Evidence Excellence for Decision-Making: Meeting Regulatory and HTA/ Payer needs.* RWE4Decisions.

meeting survey, the major hurdle to set up such a DMD infrastructure was identified to be general lack of resources and time, especially relating to data entry and collection.

Question 1: What data (core dataset) should be collected in a DMD RWD infrastructure for gene therapy follow-up?

Alignment on the purpose of the RWD infrastructure should be the first step before a core dataset can be defined taking into account the following recommendations:

- A minimal required dataset should be aligned with international/EU core datasets to maximize harmonization (especially in rare diseases it is important that data can come together on an international level, such as in a federated network or registry)
- Reflect the needs of all stakeholders involved
- Ensure flexibility so that additional datapoints can be added over time
- Include appropriate Quality of Life (QoL) measures, preferring disease-specific QoL measure with a limited burden on patients
- Parameters should:
    - Be easy to capture
    - Provide sufficient data granularity
    - Focus on long-term disease progression in real life
- The frequency of data collection should range between once or twice a year and could differ between parameters
- Duration of follow-up should be decided by the clinician, but lifelong data collection for certain parameters is desirable to evaluate disease progression
- The datasets per patient need to be as complete as possible with room for data enrichment.
- All data should be standardized to facilitate data sharing.

Question 2. How should this data be collected?

The following recommendations were made to transform the current registries, such as BNMDR, to a RWD infrastructure that is future-proof and compatible for gene therapy:

- The burden on patients and physicians should be as low as possible and automated data harvesting from the EPD was considered as a solution. A well-structured EPD at hospital level is needed to facilitate automated harvesting. Web-based QoL questionnaires are preferred, and clinical routine should be optimized to limit patient burden.
- The data collection must be flexible and adjustable.
- Quality checks and validation at data entry are required to ensure high quality data.
- One joined analysis support group should be set up to perform analysis of the data.

Question 3: What would be the appropriate governance model for such a RWD infrastructure?

Once data is collected, an appropriate governance is essential to be agreed on:

- Clinicians were considered as initiators of the data infrastructure with support of companies. The voice of patients should always be considered, and payers should also be involved in an early multi-stakeholder dialogue.
- The government and industry will be essential to assure sustainability of the data infrastructure.
- Collaboration among different companies is strongly preferred.
- Data inclusion could be based on a common consent model as is currently done in the BNMDR, or through an opt-out model.
- Transparency is key to establish trust: web-based tool for patients to consult their data will support this.
- Implementation of a data validation group for data analysis, consisting of clinicians.
- A web-based interface for patients to consult their data was proposed.

- A specific working group is needed per disease/subgroup (paediatric, spinal muscular atrophy (SMA) and DMD) to take subgroup-specific decisions on the RWD infrastructure.
- Appropriate data access and reuse rules are required.
- A reform of current conventions into one overarching convention between RIZIV, the BNMDR and NMRCs is needed to make it workable and sustainable, as well as get recognition for the work done on RWD collection .

Recommendations for a DMD RWD infrastructure for gene therapy follow-up

As discussed above, several conditions will have to be met to create a successful RWD infrastructure that will allow for gene therapy. To fulfil these conditions and to implement a RWD framework for ATMPs in Belgium supported by all stakeholders, several actions are recommended based on a combined top-down and bottom-up approach.

- Multi-stakeholder collaboration will be necessary to set up a RWD framework that is initiated by clinicians, supported by companies, with patient input.
- Start with a minimal required dataset preferably aligned to international datasets and add additional datapoints over time when setting up the RWD framework.
- Set-up of well-structured data, via EPD, in the hospitals, allowing automated data extraction for further analysis and reporting.
- A flexible RWD framework which is easily adapted to other registries (a.o. international registries) or new needs
- A dashboard/web-interface with an overview of the data collection and insights for patients.

a) Top-down

The government will have to take the following top-down actions:

- Impose data standards, including interoperability standards for hospital EPD (e.g. OMOP, preferably EU).
- Reform conventions to assure sustainable financing of data infrastructure, collection and analysis. Sustainable funding requires collaboration with the industry
- Update the HealthData.be architecture to support automated data harvesting and quality checks.
- Provide clear guidance on legal requirements for (re-)use of RWD (e.g. possibility of opt-out system).
- Harmonize data infrastructures across diseases and international initiatives.
- Set up a governance model for RWD infrastructures, i.e. local translation of RWE4Decision.

b) Bottom-up

Bottom-up, hospitals and clinicians will have to take the following actions:

- Hospitals have to work on restructuring the EPD to be compatible with different RWD infrastructures.
- Clinicians need to define core data sets per disease including clinical outcomes, PROMs, QoL, etc.
- Clinicians need to define the necessary frequency and duration of data collection.
- Clinicians need to optimize their clinical routine based on data collection needs and adapt clinical guidelines to reflect these needs.

Next steps

This report provides input to multi-stakeholder discussions for a RWD framework for ATMPs in Belgium. Multi-stakeholder engagement and dialogue will be key to further define the priority actions and build consensus on how to implement them in practice. By working together, we can advance the adoption of ATMPs in healthcare and pave the way forward for patient access in Belgium.

Contents

1 RWD and RWE definitions and need for a RWD re-use framework

RWD and RWE definitions

Since the digital revolution, data is being generated at an extremely high pace. One type of data that is increasingly generated is medical data in real-world settings, also referred to as real world data (RWD). This is the data collected about the patient and their treatment in a real-life setting. The data can come from different RWD sources (Figure 1). Real world data can be used to generate clinical evidence. This evidence generated by RWD is called RWE or real-world evidence.

The need for collecting RWD

Patient health data are classically captured and stored for 2 main reasons: optimization of the health status of patients through adequate medical follow-up, and for medical billing and insurance purposes. This RWD could be re-used and leveraged for big data analysis to gain new insights in specific disease characteristics, patient trajectories, potential biomarkers, etc. Also data from wearables, will probably become more important in the future.

Real world data (RWD) and real-world evidence (RWE) are increasingly used in health care decisions[3]:

- Medical product developers are using RWD and RWE to understand disease mechanisms, support clinical trial designs (e.g., large simple trials, pragmatic clinical trials) and observational studies to generate innovative, new treatment approaches.
- Regulators and payers are using RWD/RWE to monitor post-market safety, to make regulatory decisions, and to support coverage decisions.
- The health care community is using these data to develop guidelines, decision support tools for use in clinical practice, and improve quality of care. In personalised medicine, RWD can be used to identify patients most likely to benefit from a given treatment.

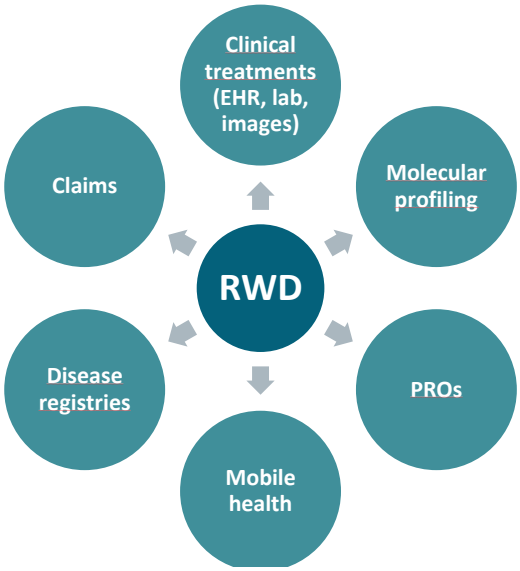

Figure 1: RWD sources

Figure 2: Longitudinal data collection and data enrichment

[3] https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

Challenges in RWD re-use

Secondary use of RWD may play an important role in: (1) quality of care improvement, (2) research, (3) outcome-based healthcare & reimbursement, and (4) economic & ecosystem development (Figure 3).

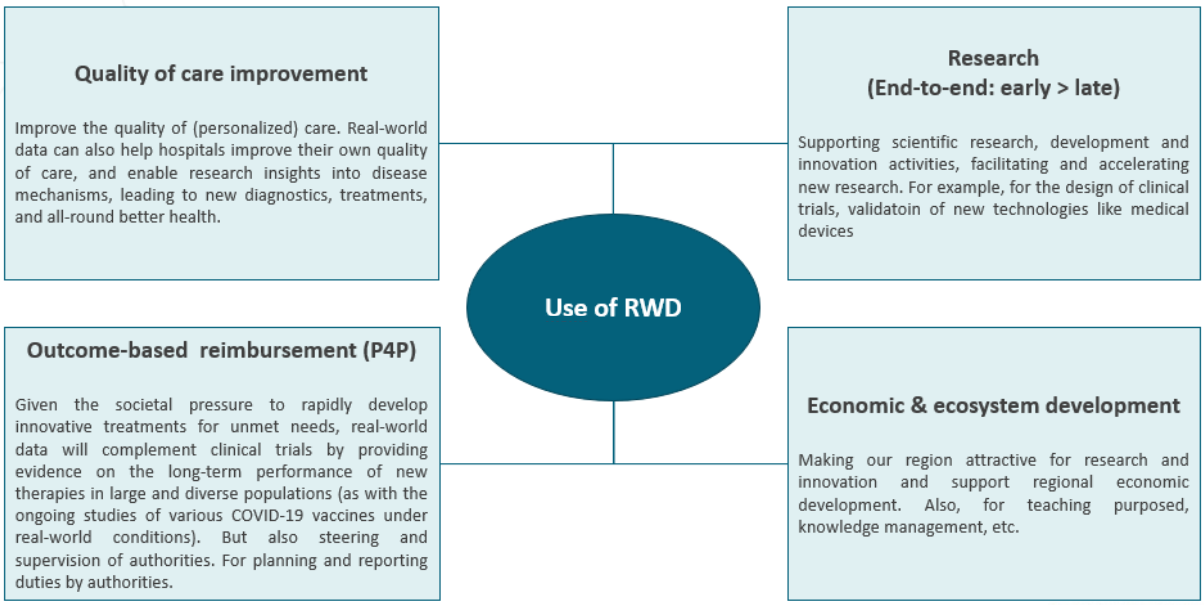

Figure 3: Application areas of secondary use of RWD

To use and re-use data there are a couple of challenges to overcome.

1. Quality and integrity of the data. For example, quality issues can be related to missing data, wrong inputs, and issues with definitions. Data integrity refers to maintaining and assuring the accuracy and consistency of data.
2. Lack of agreement between different involved parties regarding what data are needed, at which point in time, and for which purpose.
3. Difference in structure, set-up and content of different databases, leading to lack of interoperability that hampers pan Belgium and European use of RWD.
4. Differences in medical management between hospitals and within Member States, leading to wide heterogeneity in the data.
5. Scientific rigor of the data management and analysis. Without a good data management and analysis plan, the data may be incorrectly analyzed, which results in poor evidence.
6. Access to, and availability of, data. Excellent data sources may exist in a given jurisdiction, but due to access rules and restrictions regarding re-use of data, the data may be difficult, and sometimes even impossible, to access.
7. Time to collect, analyze and report the data may take too long so that the evidence based on RWD comes in too late to serve their purpose.
8. Cost of collecting the data. In some circumstances, access is possible but at a high cost for the party that needs the data for a given purpose.
9. Need for clarity on legal, privacy and data security aspects.
10. Lack of governance: for example, no or poor standards for collaboration, and lack of incentives.

RWD re-use framework

To solve the faced challenges of RWD re-use and to facilitate the establishment of suitable solutions and a framework for Belgium, first, an extensive literature research was performed in January – February 2021 (Figure 4). To further investigate the Belgian situation and system, interviews with stakeholder were performed between March – June 2021.

Literature research has been performed to map stakeholders in the Belgian RWD, DMD and gene therapy landscape and to gather information about current policies. In addition, literature has been consulted to investigate systems, policies and processes in other countries and to benchmark Belgium. Best practices and key learnings were identified and detailed to inform DMD RWD framework for Gene therapy proposals for Belgium. Two key publications were:

- RWE4Decisions publication "Real-world evidence to support Payer/HTA decisions about highly innovative technologies in the EU—actions for stakeholders"[4] coauthored by Jo De Cock (CEO NIHDI in Belgium): Calls stakeholders to collaborate on RWD pilot projects to inform healthcare decisions. For each stakeholder group, recommended actions (roles and responsibilities) to support the generation, analysis, and interpretation of RWD to inform decision making were developed.
- Zorgnet-Icuro report 2020 on (re-) use of health data for research[5]: Discussed how clinical data can be accessed for societal relevant research in an ethical and judicially sound manner, and managed by a transparent and equitable governance structure representing key stakeholders.

Next to the literature research, key elements and potential solutions were identified through interviews. These interviews covered all stakeholder groups in the Belgian healthcare system.

Based on these insights, a **RWD framework** was designed that can be supported by all stakeholders (Figure 5), and that could support the formulation of solutions. The proposed structure for the RWD framework consists of two layers:

1) Data processing steps: data collection, data quality and data processing.
2) Enabling foundation that is needed to support the data process steps, like: governance, funding and data privacy and security.

For all elements of this framework, responsibilities should be aligned on with stakeholders and an action plan should be created to facilitate access to RWD, (secondary) use of RWD and generation of RWE.

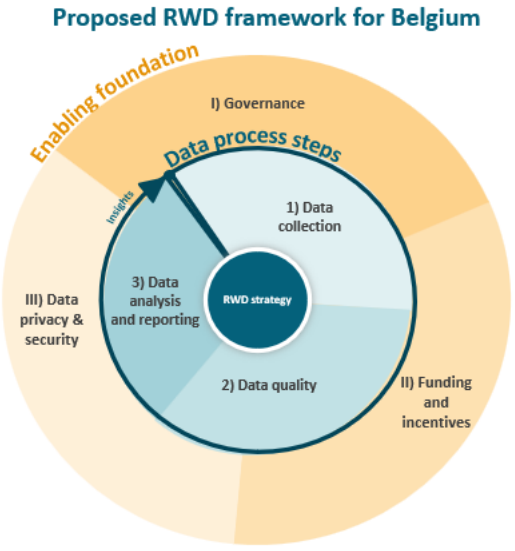

Figure 4: Proposed RWD Framework

[4] Facey KM, Rannanheimo P, Batchelor L, Borchardt M, de Cock J (2020). Real-world evidence to support Payer/HTA decisions about highly innovative technologies in the EU—actions for stakeholders.
International Journal of Technology Assessment in Health Care 1–10. https://doi.org/10.1017/ S026646232000063X

[5] Raeymaekers, Peter; Balthazar, Tom & Denier, Yvonne (2020), Big data in de gezondheidszorg. Technische, juridische, ethische en privacy-gerelateerde randvoorwaarden vor (her)gebruik van gezondheidsgegevens voor onderzoek. Brussel: Zorgnet-Icuro

2 Pilot case: Duchenne muscular dystrophy (DMD) RWD infrastructure for gene therapy follow-up based on multi-stakeholder engagement

The current BNMD registry

The Belgian Neuromuscular Disease Registry, also called BNMDR, is a collaboration between the NIHDI, the reference centres for neuromuscular disorders and Sciensano (formerly the Scientific Institute of Public Health (WIV-ISP)). The BNMDR has been in operation since 2008 and contains medical data of patients who have been diagnosed with a neuromuscular disease. This information is collected annually by the neuromuscular reference centres. This information exchange is on a voluntary basis, in an anonymous way and the data is kept in a secure manner.

The goals of the Belgian Neuromuscular Diseases Registry (BNMDR)[6] are:

- Facilitate clinical, epidemiological and etiologic research in the field of neuromuscular diseases.
- Support and promote the quality of care in the NMRCs.
- Provide information to the public health authorities for the management of the convention and the planning of care.
- Facilitate the recruitment of patients for research on new treatments.

The data in the register contains basic demographic data such as age, gender, geographical origin (district), the diagnosis, the functional status of the person, the reference centre where he/she is receiving care. For two disease groups, DMD and SMA, additional clinical data are included in the registry for sharing at an international level, within the TREAT-NMD network. The registry and its contents are monitored annually by a scientific committee composed of specialists from the NMRCs, a physician from the College of Physicians of NIHDI, two members from Sciensano and representatives from patient associations. A restricted scientific council, made up of NMRC specialists and two members of Sciensano, also meets at least annually to discuss more specific scientific issues.

DMD RWD infrastructure for gene therapy follow-up

Following the multi-stakeholder round tables held in 2018-2019 on innovative funding solutions for ATMP in Belgium[7] and acknowledging the overall importance of RWD collection and re-use for ATMPs, a multi-stakeholder project is started to develop a RWD framework for Gen therapies in Belgium. The objective of this project is to define a governance model and action plan to facilitate the implementation of a RWD infrastructure for future gene therapies. Given its high societal relevance, this project has been endorsed by the NIHDI.

To formulate an implementation framework for the re-use of RWD for ATMPs in Belgium, DMD gene therapy is studied as a pilot case. An advisory board was organized in December 2021 to gather feedback on the proposed RWD framework (described in Section 1.4.2) based on the example of DMD gene therapy in Belgium. In preparation of the advisory board, a survey was sent to the participants of the advisory board. This survey aimed to create preliminary insights concerning the data types to be included in a DMD RWD framework for gene therapy and further details regarding data collections.

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[6] BNMDR, Jagut M., Doggen K., & Cosyns M. (2017, September). *Belgian Neuromuscular Disease Registry (BNMDR) Annual Report*.

[7] Maes, I. Boufraioua, H. Van Dyck, W. Schoonaert, L. (2019). *Innovative solutions for paradigm changing new therapies*. *https://www.inovigate.com/media/filer_public/e8/9c/e89ca2b0-1dcf-48fb-9afc-9e911ddcef84/innovative_funding_solutions_-_short_version_without_appendix_vs09.pdf*

The next sections of this report describe the feedback of the advisory board on the following topics:

1) What data (core dataset) should be collected in a DMD RWD infrastructure for gene therapy follow-up?
2) How should this data be collected?
3) What would be the appropriate governance model for such a RWD infrastructure?

3 What RWD should be collected for ATMPs based on the DMD gene therapy example

The goal of a RWD infrastructure will determine the type of data that will need to be collected. RWD collected for gene therapy should aim to demonstrate whether a gene therapy has long term effect in the real-life setting. To ensure feasibility, it is required to start from the data that are easy to capture and that can only be collected via RWD in contrast to a clinical trial setting. Ideally, RWD collection should fulfil a broad spectrum of objectives, serving several involved stakeholders and covering the full lifecycle of a therapy. Therefore, disease registries encompassing different therapies including gene therapies are preferred over separate gene therapy registries. First, the RWD collection for gene therapy aims to follow-up on patients after clinical trials to gather real-life evidence on the therapy. Further, RWD collection provides support for well-founded decisions on pricing and reimbursement and facilitates post-marketing surveillance as well as post EMA regulatory obligations. Finally, RWD captured for gene therapy should support physicians and hospitals in medical decision making. For DMD, RWD collection for gene therapy should start from the current BNMDR which will be adapted for gene therapies based on the needs of all stakeholders involved.

A RWD framework should contain data that are as complete as possible with room for data enrichment. A RWD framework with limited parameters but complete datasets for each patient are more valuable compared to a RWD framework tracking a broad spectrum of parameters but containing incomplete datasets per patient. Besides this overarching requirement, RWD parameters for gene therapy need to answer several conditions:

- Focussed on progression of patients in real life from a long-term perspective.
- Sufficient granularity should be captured to allow evaluation of disease progression, e.g. a better transition between key parameters such as walking and standing.
- Be easy to capture and able to be collected by the clinician or patient. This in contrast to parameters measured in clinical trials such as biopsies, muscle MRI etc.
- International datasets (if available) should be leveraged and adapted to the Belgian context, which is especially important in a rare disease setting. For DMD the international core dataset, TREAT-NMD should be leveraged. To facilitate data sharing and re-use of data across organizations and countries, international data standards should be used.
- Data sets must be flexible and adjustable to allow for updates and addition of parameters if needed, in order for the RWD infrastructure to offer enough flexibility.

Special attention should be paid to monitoring Quality of Life (QoL), which is especially valued from a patient perspective. Therefore, the right QoL survey should be selected for RWD collection while limiting the burden on patients. Moreover, the survey must be measurable, feasible, easy to capture, disease-specific and with a focus on real life. Given the fact that QoL surveys are not routinely included in patient monitoring for DMD, there is no consensus on which QoL survey would be preferred for DMD gene therapy. However, the ACTIVLIM (activity and participation survey) might be a good base to start from.

Finally, frequency and duration of data collection is said to depend on several conditions. The frequency depends on the parameter and consultation frequency (generally twice a year for DMD). A minimum of once per year and maximum of twice per year was agreed upon. In general, the burden for the patient

should be limited. When further designing the RWD infrastructure, clinicians will have to decide on the duration data collection, ranging from one-time measurements to life-long follow-up. In general, duration of RWD collection should be as long as possible.

4 How RWD for gene therapy should be collected

The second key question that was answered concerned the way these parameters have to be collected. Primarily the burden on patients and clinicians should be limited, and could be reduced by using automated harvesting from the EPD. To achieve this, clinical care and patient visits needs to be optimized. Within the BNMDR and many other RWD infrastructures, data is currently extracted from hospital systems or EPDs through manual input, creating an unsustainable situation. To make automated harvesting possible, the EPD will need to be restructured at hospital-level. A general dataset template that fits the hospital IT system could be provided to the hospitals. Besides automated data harvesting to lower the burden on patients, QoL data could be collected by a web-based survey. Alternatively, a specific dedicated role or function to collect data within hospitals could help to limit the burden on patients and clinicians.

Data analysis should be a joined effort from the medical experts and data scientists. Therefore, one common support for data analysis for all NMRCs is needed. This support group needs to be institutionalized.

5 A governance model for RWD collection for gene therapy

An appropriate governance is essential to support appropriate data collection, analysis and reporting. Multi-stakeholder alignment on this governance model as well as the minimal requirements necessary for the gene therapies RWD framework is key. Multi-stakeholder collaborations to implement RWD solutions should be initiated by clinicians and by industry. Involvement of companies could help to assure sustainability of RWD collection for gene therapy and a collaboration between several companies is preferred. Involvement of other clinicians and endorsement from the medical society is necessary from the beginning. Evidently, the voice of patient must always be considered, and the payer must be involved in early dialogue.

Second, data privacy plays an important part in the governance model. Data inclusion in the RWD infrastructure could be based on a consent model. For example, the BNMDR is using common consent (broad consent on inclusion and use of data in the RWD framework). As sharing of data could be seen as a societal duty of patients, an opt-out model could also be considered. Nevertheless, it remains a personal choice and patients should be able to stop sharing data at any point in time. Further, patients and clinicians would value the possibility to see data through a web-interface.

Third, for RWD collection in NMD, currently three conventions exist between NIHDI, Sciensano and NMRC on the collection, validation, analysis and reporting of the data. To make RWD collection workable and sustainable, as well as get recognition for the work done, current conventions should be reformed into one overarching convention between RIZIV, the BNMDR and NMRCs.

To facilitate an agile way of working & governance of the RWD framework, specific working groups per disease/subgroup (paediatric, SMA and DMD) are needed to take subgroup-specific decisions on the RWD infrastructure. For DMD specifically a separate working group for paediatric NMD was suggested.

6 Recommendations

Based on the insights collected during the Ad Board, recommendations can be split in two types:

- General recommendations which can be applied for registries for all types of ATMPs in all kind of disease areas.
- Specific recommendations for the implementation of the DMD RWD framework for gene therapy.

General recommendations for the implementation of registries for ATMPs in all kind of diseases

To make RWD collection for ATMPs a success, multi-stakeholder collaboration will be necessary to set up an RWD framework that is initiated by clinicians, supported by companies, with patient input. When setting up RWD solutions, collaboration between companies is preferred. Further along the road, industry support could help to assure sustainability of the platform. Upon initiation of the RWD framework, it is advisable to start with a minimal required dataset based on international initiatives that is flexible so that additional datapoints can be added over time if new needs arise. Additionally, to reduce the burden on clinicians and patients, automated data harvesting via well-structured data, in the EPD, in the hospitals needs to be setup. Finally, to raise patient's trust and increase their confidence in the system, a dashboard/web-interface with an overview of the data collection and insights could be provided to patients. To fulfil these conditions and to achieve a good governance model for RWD collection for ATMPs, several actions are recommended and should be supported by all stakeholders. To put this into practice, both a top-down and a bottom-up actions as proposed below are needed.

6.1.1 Top-down

The government will have to take the following top-down actions:

- Impose data standards, including interoperability standards for hospital EPD (e.g. OMOP, preferably EU)
- Reform conventions to assure sustainable financing of data infrastructure, collection and analysis. Sustainable funding requires collaboration with the industry
- Update the HealthData.be architecture to support automated data harvesting and quality checks
- Provide clear guidance on legal requirements for (re-)use of RWD (e.g. possibility of opt-out system)
- Harmonize data infrastructures across diseases and international initiatives
- Set up a governance model for RWD infrastructures, i.e. local translation of RWE4Decision

6.1.2 Bottom-up

Bottom-up, hospitals and clinicians will have to take the following actions:

- Hospitals have to work on restructuring the EPD to be compatible with different RWD infrastructures
- Clinicians need to define core data sets per disease including clinical outcomes, PROMs, QoL, etc.
- Clinicians need to define the necessary frequency and duration of data collection
- Clinicians need to optimize their clinical routine based on data collection needs and adapt clinical guidelines to reflect these needs

Actions and recommendations for the implementation of RWD collection for DMD gene therapy

The specific coreset for DMD should be collectively agreed on international core dataset, i.e. the TREAT-NMD core dataset, translated to the Belgian context. This dataset can act as a starting point and can be adjusted in a later stage. QoL were especially valued by patient representatives. Disease specific QoL measures that are disease-specific are preferred. ACTIVLIM is recommended as a good starting point and use of the new DMD QoL could be explored. Data types should represent real life needs and support long-term follow-up. To ensure feasibility, a start should be made with data that is easy to capture. In summary, the BNMDR should be upgraded to a future proof RWD infrastructure that is more flexible and less burdensome.

7 Conclusions & Call to action

This report provides input to hold multi-stakeholder dialogues to discuss RWD infrastructure for ATMPs. Multi-stakeholder engagement and dialogue will be key to further define priority actions and build consensus to put them in practice.

To support preparedness for future treatments for DMD patients, we should start by setting-up a task force with clinicians, the BNMDR, patient representatives and representation of pharmaceutical companies. This task force should define a concrete plan with all stakeholders to update the current registry, such as the BNMDR registry, towards a less burdensome and more flexible registry that will also include data on gene therapies and future novel therapies.

Data use is integral to the future of healthcare, which is why stakeholders from across the ecosystem must come together to drive data collection regarding gene therapies in Belgium. By joining forces, we'll be able to make a real difference to the patient's experience and infrastructure of care, while also supporting the best interests of different stakeholder groups. By working together, we can advance personalized healthcare and the utilization of gene therapies, and at the same time pave a way forward for the improvement of quality of care and better utilization of resources. The input of this report will be used in a broader multi-stakeholder discussion to define a model and action plan to facilitate the implementation of future cell and gene therapies in Belgium, held in the first half of 2022.

Abbreviations list

BVZD	Belgische vereniging van ziekendirecteurs
BNMDR	Belgisch register van neuromusculaire aandoeningen
DMD	Duchenne Muscular Dystrophy
ERN	European reference networks
EPD	Electronic patient record
FAIR	Findable, accessible, interoperable, re-usable
GP	General Practitioner
HCP	Health Care Professional
HTA	Health technology assessment
KPI	Key Performance Indicators
MA	Marketing authorization
MD	Medical doctor
OB-MEA	Outcomes-based managed entry agreement
PLEG	Post-licensing evidence generation
RCT	Randomized controlled trials
NIHDI	National Institute Health and Disability Insurance
NMRC	Neuromuscular Reference Centre
RWE	Real world evidence
RWD	Real world data
ROI	Return on Investment
SMART	Specific, Measurable, Achievable, Relevant, Timely
SMA	Spinal Muscular Atrophy
WHO	World Health Organization

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