Big Multiple Sclerosis Data Network

11th Progress Report – June 2025

Introduction

The Big Multiple Sclerosis Data (BMSD) Network constitutes a collaboration of MS registries working together to provide a real-world dataset for researchers, marketing authorization holders and regulatory bodies. Currently, BMSD includes five national registries from the Czech Republic, Denmark, France, Italy and Sweden, as well as the international MSBase. To date the collection of data from all the BMSD registries creates a very rich combined dataset of over 340,000 patient records.

From 2019 to 2023, Karolinska Institutet, representing the Swedish MS Registry, coordinated the activities of BMSD network. In December 2023, the BMSD Steering Committee discussed the idea of having a rotating coordination task among the registries every three years, and the Italian MS Registry (RISM) has been appointed as the new coordinating centre. In 2024, the Network was coordinated jointly by the Italian MS Registry (RISM) group and the Karolinska Institutet to allow the gradual and practical transfer of the coordination tasks to the Italian group, who became responsible for the coordination from January 2025. Activities related to the EMA's request for a qualification opinion on post-authorisation safety studies (PASS) (see the following section for details), currently being finalised, were coordinated by the Karolinska Institutet.

The RISM group includes personal resources belonging to the Italian Multiple Sclerosis Foundation (FISM), a not for profit organization which acts as the legal representative of RISM, and the University of Bari "Aldo Moro".

This report outlines the activities carried out within the Network in the first half of 2025.

Activities and current topics

a) Support from pharmaceutical companies

Over the years, the coordination of the BMSD Network has benefitted from financial contributions by several pharmaceutical companies, including Biogen, BMS, Merck, Novartis, Roche, and Sanofi. At June 2025, Alexion and Merck confirmed their contribution to the network, while Sandoz and Juvisè expressed their interest in providing support within the end of 2025.

b) BMSD Annual Meeting and Statistical Workshop 2025

The Network will hold its Annual Meeting in Matera, Italy, on 18-19 September. Other than BMSD members, pharma representatives have been invited to participate. Topics of interest for the Network will be addressed, including: the new application for the EMA Qualification Opinion, the current and future efforts to collect specific types of data such as Patient Reported Outcomes in MS and data on related disorders (NMOSD and MOGAD), the inclusion of new MS registries, and proposals of new academic projects by representatives from each registry. Together with the BMSD Annual Meeting, a Workshop on Statistics titled "Advanced Statistical Methods for Observational Studies in MS" will also be held on 19-20 September. Internationally recognised statisticians have

been invited to discuss the state-of-the-art of statistical methods for generating real-world evidence in MS.

c) Qualification Opinion by EMA

BMSD submitted a qualification opinion to EMA in 2021 and received Scientific Advice and a Letter of Support describing the methodology under evaluation which also has been published by EMA (January 2022). After having recognised the value of the Network and having encouraged its development and validation, EMA indicated that a **feasibility study** is needed to evaluate the ability of each registry to capture safety data, together with the introduction of a **harmonized approach** to improve quality assurance.

BMSD hopes to receive an **EMA Qualification Opinion** (QO) primarily for PASS. BMSD will submit a renewed application, following the Scientific Advice and the Letter of Support received from EMA, which outlined the key information needed to better demonstrate the potential of the Network for the conduction of real-world safety studies. This EMA QO application is focused on presenting the registries and their data as well as demonstrating data quality and the ability of the registries to collect serious adverse events (SAEs) in a reliable manner as well as the registries' ability to perform PASS. The EMA QO application includes a **briefing document** outlining the rationale for the application, along with four additional documents that further illustrate the BMSD network, the available data, and provide additional evidence of the registries' ability to conduct PASS. In particular, a **Core Safety Protocol** was agreed between BMSD and Marketing authorisation holders and serves as a basis to provide common data requirements for PASS. A **Common Data Model** (CDM) was developed by BMSD to ensure that data collected according to local standards can be transformed into a common format, enabling robust and reproducible cross-border research while maintaining local data collection practices. A **feasibility study** was conducted to describe how SAEs are collected by the respective registries and how the rates of reported SAEs compare between the BMSD registries. The aforementioned documents are integrated by the **REQuEST Tool**, which details the data content and characteristics of the variables collected by the respective registries.

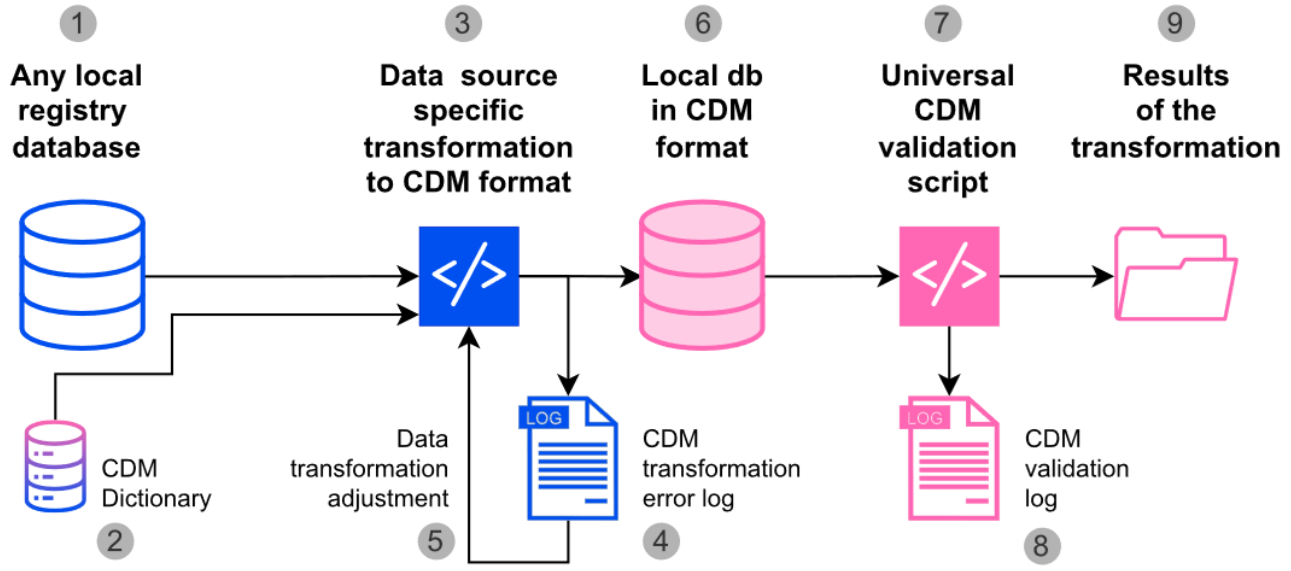

Figure 1 General Common Data Model concept

The package was recently finalised and is ready for submission, which is expected to take place in July 2025.

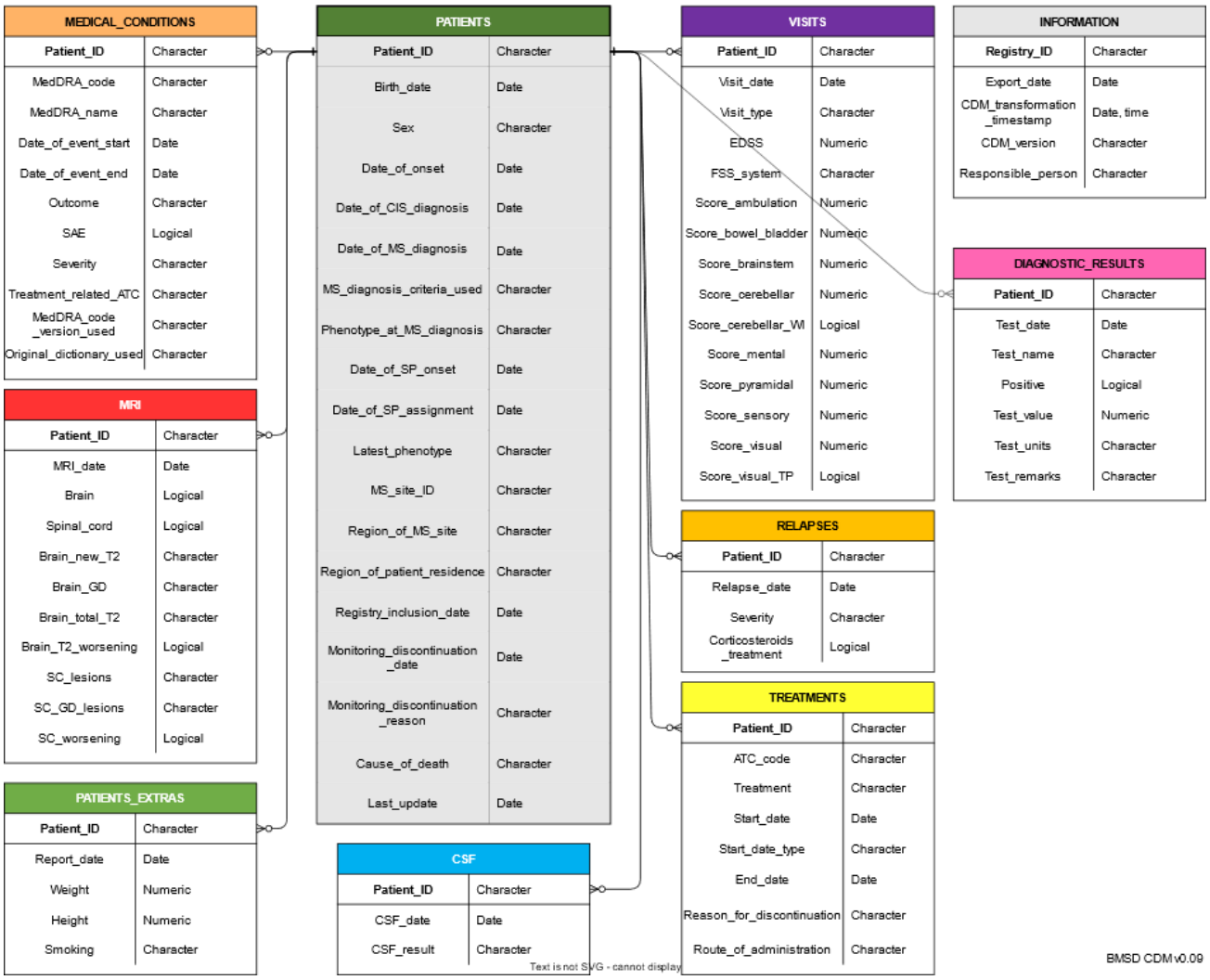

Figure 2 BMSD Common Data Model structure Jiri Drahota

d) Communications

The **BMSD website** (https://bigmsdata.org/) has been updated throughout 2025. In the public area, information regarding the description and the organisational structure of the Network were revised. The reserved area for Network members is constantly updated with the most recent documents.

In 2025, the article "**Disease-modifying treatment and disability progression in subclasses of patients with primary progressive MS: results from the Big MS Data Network. Lorscheider et al, J Neurol Neurosurg Psychiatry, May 2025**" was published. Researchers investigated the potential effect of Disease Modifying Therapies (DMTs) on disability worsening among patients with Primary Progressive MS (PPMS) stratified by different disability trajectories. Overall, data suggest that DMTs do not significantly slow disability progression in PPMS. However, a beneficial effect was observed in patients with more aggressive predicted disability trajectories.

In September 2025, the Network will attend the **ECTRIMS Congress** in Barcelona and will present the initiative to all the participants.

e) Inclusion of new registries

The Network is open to the inclusion of new MS registries. The Network is currently developing a set of criteria for the inclusion of new data sources, based on factors such as registry structure, national coverage, data quality, technical capabilities, and ethical compliance (the document will be presented and discussed during the September Annual Meeting). In September and October 2024, two meetings have been held with the Finnish and German national registries to present the initiative and discuss their potential inclusion in the Network. Both registries have been working throughout 2025 to implement the BMSD Common Data Model into their local datasets and to demonstrate that the level of data quality is adequate for inclusion in the Network. The results of their activity will be presented in September during the Annual Meeting in Matera.

f) TC meetings

Regular monthly Network meetings were held from January to June. The main topics of the meetings included the finalization of the submission package for EMA Qualification Opinion, ongoing and new collaborative research projects, and the inclusion of new MS registries.

Conclusion

We can conclude that the first half of 2025 has seen encouraging progress in BMSD activities. We are pleased that new collaborative research projects are in the pipeline, and we hope that these initiatives, along with the upcoming joint event in Matera, will further strengthen collaboration within the Network. We sincerely thank all Sponsors for their invaluable support.

June, 2025

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