Big Multiple Sclerosis Data Network

10th Progress Report – December 2024

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 tasks of BMSD. In December 2023, the BMSD Steering Committee discussed the idea of having a rotating coordination task among the registries every three years. 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 will be responsible for the coordination from January 2025. The activities related to the EMA Qualification Opinion application for Post Authorisation Safety Studies - PASS (see Section 2 for details) will be coordinated by Karolinska Institutet until completion.

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 2024, with a particular focus on the second half of the year.

Activities and current topics

a) Support from pharmaceutical companies

Over the years, the coordination of the Big MS Data Network has benefitted from financial contributions by several pharmaceutical companies, including Biogen, BMS, Merck, Novartis, Roche, and Sanofi. Recently, Alexion and Sandoz have expressed their interest in providing support.

b) BMSD Annual Meeting and Statistical Workshop 2025

The Network will hold its Annual Meeting in Italy. Other than BMSD members, pharma representatives will be invited to participate. The joint activities the Network is conducting will be presented, together with future efforts that can be pursued. Together with the BMSD Annual Meeting, a Workshop on Statistics will also be held on 19-20 September. Internationally recognised statisticians will be 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.

In the context of the BMSD application for a Qualification Opinion from EMA, a **feasibility study** has been proposed where data from ongoing PASS studies are used to demonstrate the level of adverse event (AE) capture in each registry. This study is made up of three parts. In the 1st part, each registry describes the routines applied in their countries regarding the collection of AEs. This includes aspects such as what is expected from neurologists, what is the procedure, and what fields/variables are used in their respective platforms. This gives a wider image and better understanding of how each registry works. In the 2nd part, for those registries that have the possibility to link their patient data to national healthcare databases that contain all possible diagnoses, a comparison of AE incidence rates calculated separately from the two sources is performed using data from ongoing PASS studies. The outcomes of interest are malignancies and serious infections, and the incidence rates will be calculated as described in the respective studies' statistical analysis plans (SAP). Finally, in the 3rd part, for registries where access to national healthcare databases is not available and a direct comparison as described in part 2 is not possible, an indirect evaluation of the AE capture is performed. Data from ongoing PASS studies are used, as before, to calculate incidence rates of malignancies and serious infections for all BMSD registries according to the study's SAP. The incidence rates are adjusted for sex and age to account for possible differences in population structure between countries (direct standardization).

Following EMA's recommendations, BMSD mapped the member registry datasets to a minimum dataset and **Common Data Model** (CDM) of variables, definitions and data structure. The CDM developed by BMSD ensures 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. By focusing on data harmonization rather than modifying local data collection methods, the CDM allows diverse data sources to contribute to comprehensive, large-scale studies. The basis of the CDM is the **BMSD data dictionary** which contains close to a hundred items with agreed upon common definitions and descriptions. In addition, a BMSD CDM software will translate a local database into the BMSD data format and generate a report on the success of the transformation of data and a second report on data quality. The CDM has been piloted in three registries—Czech, Swedish, and the international MSBase registry. This phase focused on transforming existing data into the CDM format, ensuring that each registry's locally collected data could be accurately harmonized. Key aspects of validation included aligning medical conditions, treatment records, and diagnostic results. This process highlighted areas for refinement and has successfully demonstrated the model's ability to integrate data from diverse sources without altering local data collection practices.

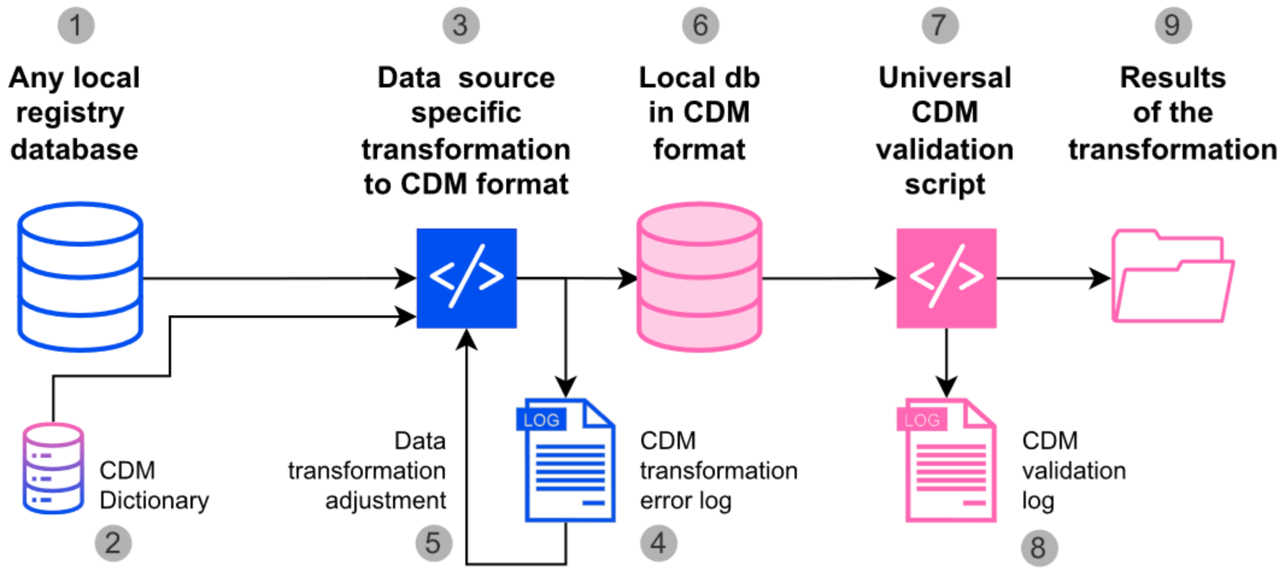

Figure 1 General Common Data Model concept

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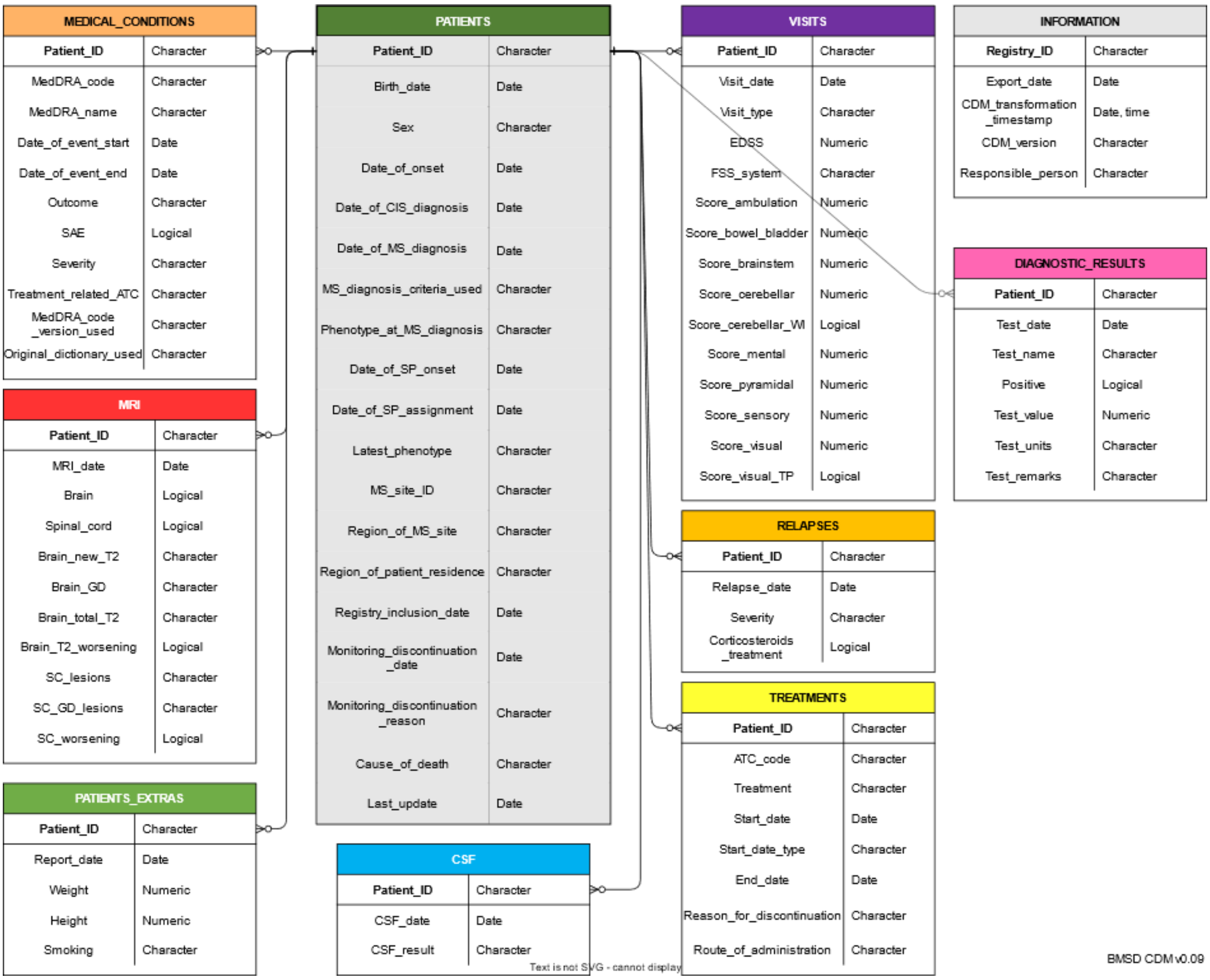

MEDICAL_CONDITIONS	
Patient_ID	Character
MedDRA_code	Character
MedDRA_name	Character
Date_of_event_start	Date
Date_of_event_end	Date
Outcome	Character
SAE	Logical
Severity	Character
Treatment_related_ATC	Character
MedDRA_code_version_used	Character
Original_dictionary_used	Character

MRI	
Patient_ID	Character
MRI_date	Date
Brain	Logical
Spinal_cord	Logical
Brain_new_T2	Character
Brain_GD	Character
Brain_total_T2	Character
Brain_T2_worsening	Logical
SC_lesions	Character
SC_GD_lesions	Character
SC_worsening	Logical

PATIENTS_EXTRAS	
Patient_ID	Character
Report_date	Date
Weight	Numeric
Height	Numeric
Smoking	Character

PATIENTS	
Patient_ID	Character
Birth_date	Date
Sex	Character
Date_of_onset	Date
Date_of_CIS_diagnosis	Date
Date_of_MS_diagnosis	Date
MS_diagnosis_criteria_used	Character
Phenotype_at_MS_diagnosis	Character
Date_of_SP_onset	Date
Date_of_SP_assignment	Date
Latest_phenotype	Character
MS_site_ID	Character
Region_of_MS_site	Character
Region_of_patient_residence	Character
Registry_inclusion_date	Date
Monitoring_discontinuation_date	Date
Monitoring_discontinuation_reason	Character
Cause_of_death	Character
Last_update	Date

CSF	
Patient_ID	Character
CSF_date	Date
CSF_result	Character

Text is not SVG - cannot display

VISITS	
Patient_ID	Character
Visit_date	Date
Visit_type	Character
EDSS	Numeric
FSS_system	Character
Score_ambulation	Numeric
Score_bowel_bladder	Numeric
Score_brainstem	Numeric
Score_cerebellar	Numeric
Score_cerebellar_WI	Logical
Score_mental	Numeric
Score_pyramidal	Numeric
Score_sensory	Numeric
Score_visual	Numeric
Score_visual_TP	Logical

RELAPSES	
Patient_ID	Character
Relapse_date	Date
Severity	Character
Corticosteroids_treatment	Logical

TREATMENTS	
Patient_ID	Character
ATC_code	Character
Treatment	Character
Start_date	Date
Start_date_type	Character
End_date	Date
Reason_for_discontinuation	Character
Route_of_administration	Character

INFORMATION	
Registry_ID	Character
Export_date	Date
CDM_transformation_timestamp	Date, time
CDM_version	Character
Responsible_person	Character

DIAGNOSTIC_RESULTS	
Patient_ID	Character
Test_date	Date
Test_name	Character
Positive	Logical
Test_value	Numeric
Test_units	Character
Test_remarks	Character

Figure 2 BMSD Common Data Model structure

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A **BMSD core protocol** has been drafted and is close to being finalised. This document will be used as a reference standard and will provide a common background for all registries to develop protocols for drug-specific safety studies.

The aforementioned documents and activities performed will be integrated by the **REQuEST Tool**, which has already been finalised and provides details on the technical, methodological and governance aspects of BMSD registries to respond to EMA requests. The documents complement each other and once defined will form the submission package to apply for the EMA Qualification Opinion.

d) Communications

It is planned to update the **BMSD website** (https://bigmsdata.org/). In the public area, information regarding the description and the organisational structure of the Network will be revised. The reserved area for Network members will also be updated with a new login access and the most recent documents will be uploaded as well.

In 2024, the article "**Big Multiple Sclerosis Data network: an international registry research network**. Glaser A. et al, J Neurol, June 2024" presenting the initiative, methodological aspects and future perspectives, was published.

In 2024, the Network participated at the **ECTRIMS Congress** in Copenhagen with a stand open to the public. USB flash drives containing a presentation of each registry within the Network were distributed to visitors at the stand.

e) Inclusion of new registries

The Network is open to the inclusion of new MS registries. In September and October 2024, two meetings were held with the Finnish and German national registries to present the initiative and discuss their potential inclusion in the Network.

f) TC meetings

Regular monthly Network meetings were held from September to December. Members shared their updates on the current activities, such as the finalisation of the submission package for EMA Qualification Opinion and collaborative research projects conducted within the Network

Conclusion

In conclusion, the second half of 2024 has witnessed significant progress in the activities carried out by the Network. We anticipate that 2025 will be a challenging year, but one that also offers valuable opportunities for the Network's development. We sincerely thank the Sponsors for their continued support.

December, 2024

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BMSD Coordination Leaders