Big Multiple Sclerosis Data Network

12th Progress Report – December 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 380,000 patient records (Table 1).

Country	MS registry	Number of people with MS included	Estimated coverage of prevalent MS population
Czech Republic	ReMuS	24,030 (June 2025)	90%
Denmark	DMSR	34,720 (August 2025)	95%
France	OFSEP	86,180 (August 2025)	55%
Italy	RISM	95,294 (July 2025)	70%
Sweden	SMSreg	24,780 (August 2025)	90%
International	MSBase	122,604 (August 2025)	variable

Table 1 Number of MS patients included in the BMSD Network, by registry

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), 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 second 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. In 2025, the Network received support from Alexion, Merck and Juvisè, while Sandoz confirmed a financial contribution for 2026 and 2027.

b) BMSD Annual Meeting and Statistical Workshop 2025

A joint event was held in Matera, Italy, from 18 to 20 September 2025. On 18 and 19 September, the BMSD Annual Meeting brought together members of the registry network to discuss the latest updates. Other than BMSD members, pharma representatives have been invited to participate. The agenda included the presentation of documents submitted by BMSD to the EMA as part of the Qualification Opinion application, as well as discussions on opportunities to expand the Network. Key topics included criteria for the inclusion of new registries and the collection of specific data, such as those related to NMOSD, MOGAD, and Patient-Reported Outcomes (PROs). A dedicated session focused on proposals for new academic projects to be conducted within the Network. Some of the projects have been accepted and are currently ongoing or under evaluation by the Scientific Committees of each registry.

On 19 and 20 September, the BMSD Statistical Workshop took place, entitled "Advanced Statistical Methods for Observational Studies in MS." The workshop covered key statistical approaches for handling multi-source real-world data, strategies for integrating different MS data sources for research purposes, and the development of predictive models for real-world applications. Participants at the meeting are working on a position paper that will highlight the key topics of the workshop.

c) Status of activities related to the European Medicines Agency

I. 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 submitted a renewed application in October 2025, 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 authorization holders and serves as a basis to provide common data requirements for PASS. A **Common Data Model** (CDM, see the following section II for details) 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** (see section III) 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.

The package was successfully submitted in October 2025. The EMA, through the Scientific Advice Working Party (SAWP), is currently reviewing the application and is expected to contact the Network in February should any issues require clarification or resolution.

II. Common Data Model (CDM)

During the reporting period, the activities of the BMSD Network related to the **Common Data Model** progressed substantially, consolidating the CDM as a core infrastructure for data harmonization and for enabling reproducible multi-registry analyses.

The CDM was designed to capture the main domains of multiple sclerosis research, including demographics, disease history, relapses, treatment exposure, comorbidities, disability outcomes, magnetic resonance imaging, paraclinical results, and laboratory data, for a total of approximately 120 standardized variables (Figure 1).

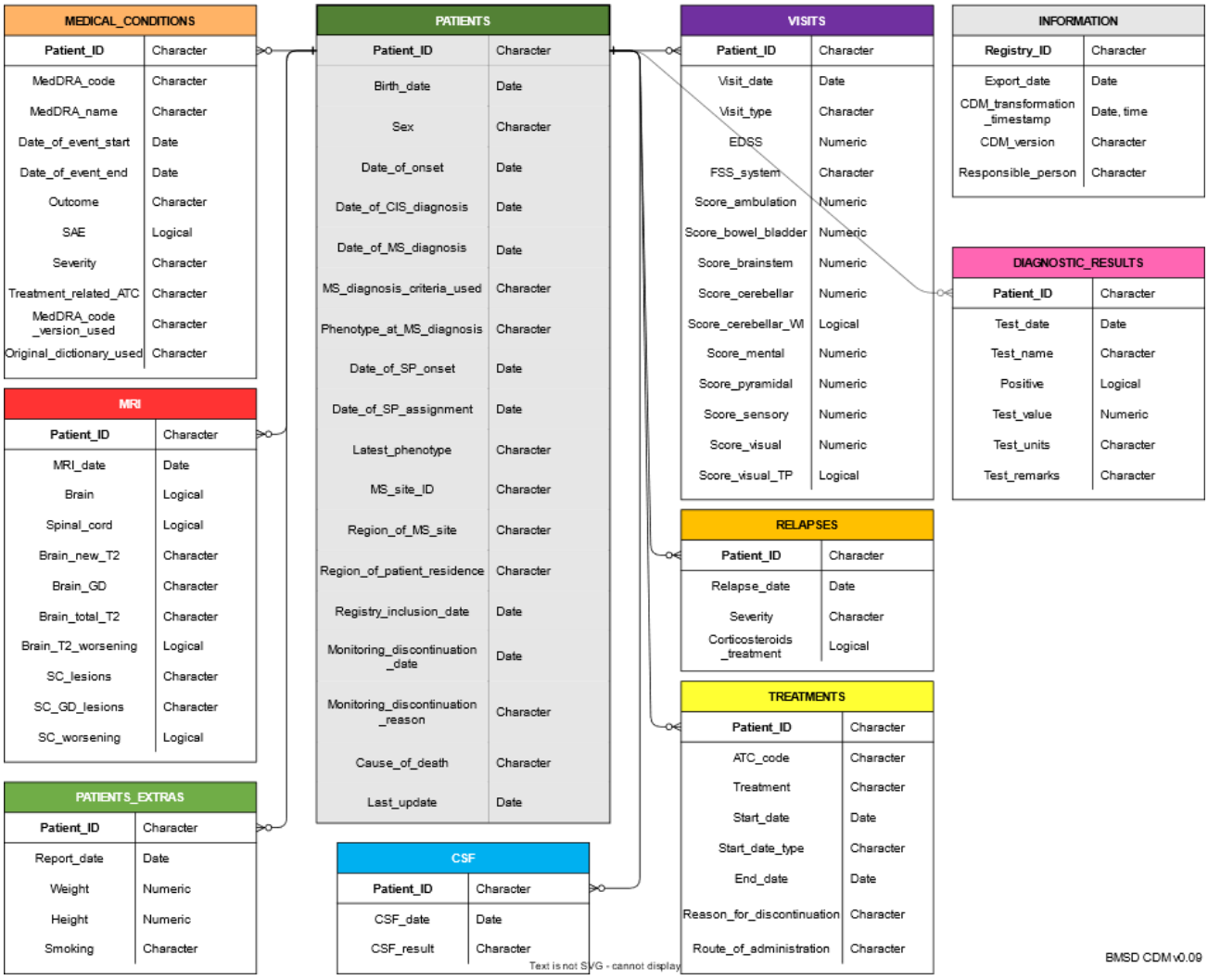

Figure 1 BMSD Common Data Model structure Jiri Drahota

Participating registries mapped their local datasets to the common variable definitions and transformed the data into the CDM format using reproducible R-based pipelines (Figure 2). The transformation process generated automated validation and data quality reports, allowing systematic monitoring of mapping success and information integrity. All participating registries

successfully completed the transformation of their datasets into the CDM, achieving high levels of information retention, ranging from 98% to 100% (Table 2).

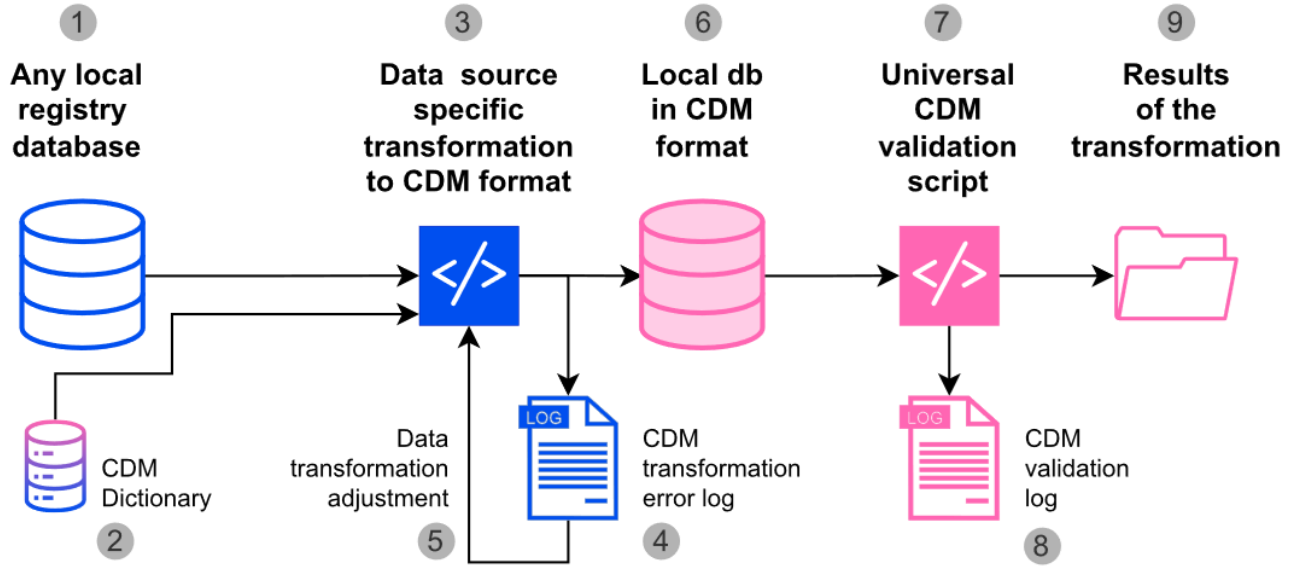

Figure 2 General Common Data Model concept Jiri Drahota

Variable groups						MSBase
PATIENTS	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
PATIENTS EXTRAS	98.74%	NA	100.0%	51.55%	100.0%	97.04%
VISITS	100.0%	100.0%	100.0%	100.0%	100.0%	99.68%
RELAPSES	100.0%	100.0%	100.0%	99.98%	100.0%	96.75%
MEDICAL CONDITIONS	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
CSF	99.9%	99.89%	99.89%	99.96%	100.0%	93.82%
TREATMENTS	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
MRI	99.53%	100.0%	100.0%	100.0%	100.0%	71.23%
DIAGNOSTIC RESULTS	99.82%	NA	NA	100.0%	100.0%	98.66%
PREGNANCY	100.0%	NA	NA	100.0%	100.0%	100.0%

Table 2 CDM transformation success rate among participating registries [1]

[1] Drahota J, Forsberg L, Pontieri L, et al. **MS Research Without Borders – Accelerating Collaboration with a BMSD Common Data Model**. In: Proceedings of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) Congress; 2025 Sep; Barcelona, Spain. Poster presentation. Mult Scler J. 2025;31(3 Suppl):136–762. doi:10.1177/13524585251358344

Overall, the first implementation of the CDM enabled the harmonization of data from 348,371 patients with multiple sclerosis *(CZE 23,401; DNK 19,097; FRA 77,463; ITA 92,851; SWE 23,832; MSB 111,727)*. Standardized validation produced demographic and clinical distributions consistent with current epidemiological knowledge, confirming the robustness and reliability of the model *(e.g.,*

mean age at MS onset: CZE 33.1, DNK 35.4, FRA 33.6, ITA 32.2, SWE 34.2, MSB 31.8 years; ~70% female). In addition, the CDM was used as the basis for a pilot application within a federated learning framework, demonstrating the feasibility of performing distributed statistical analyses without sharing patient-level data. These results confirm the CDM as a mature and operational framework to support international observational research, regulatory initiatives, and future real-world evidence activities within the BMSD Network.

III. Feasibility Study

The **feasibility study** evaluated adverse event (AE) collection procedures across the BMSD registries and examined the comparability of serious AE incidence rates among participating countries. The study was made up of three sections listed below:

1. Adverse event collection routines
2. Comparison between MS registry collected adverse events and events captured in public healthcare databases
3. Comparisons between BMSD registries

In the absence of absolute reference SAE rates, the study exploited the ability of the Swedish and Danish multiple sclerosis registries to link patient-level data with national healthcare databases, including cancer registries, hospitalization records, and outpatient specialist care. Using data derived from ongoing PASS and external cohort comparison studies, the incidence of malignancies and serious infections was assessed through both direct comparisons between registry-based and healthcare database–based estimates and indirect comparisons across BMSD registries. Crude and standardized incidence rates were calculated, with standardization applied to account for differences in age and sex distributions across registry populations. Overall, the results indicated that SAE information is effectively captured across all participating registries, either through structured registry-based data collection systems or via linkage to national healthcare databases. Despite heterogeneity in organizational processes and data capture workflows, SAE incidence rates are largely comparable across countries, supporting the fitness-for-purpose of the BMSD registries for PASS and reinforcing confidence in the robustness of registry-based pharmacovigilance data.

IV. Registration of the BMSD Network in the HMA-EMA Catalogues of real-world data sources and studies

In response to EMA's invitation, the Network is in the process of finalising its registration in the **HMA-EMA Catalogues of real-world data sources and studies** (https://catalogues.ema.europa.eu/), a publicly available online resource that collects metadata on real-world data (RWD) sources and studies. The catalogue will enhance the Network's visibility and transparency, in line with EMA's recommendations encouraging the registration of all real-world data sources and studies. Submission of all required information for publication in the catalogue is expected in January 2026.

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, two articles were published by the Network:

- Lorscheider J, Signori A, Subramaniam S, et al. **Disease-modifying treatment and disability progression in subclasses of patients with primary progressive MS: results from the Big MS Data Network.** J Neurol Neurosurg Psychiatry. 2025 May 14;96(6):606-615. doi: 10.1136/jnnp-2024-334700. 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.
- Trojano M, Iaffaldano P, Copetti M, et al. **Big multiple sclerosis data network: novel modelling approaches for real-world data analysis.** J Neurol. 2025 Nov 8;272(12):754. doi: 10.1007/s00415-025-13439-9. The objective of this study is to present a report from the BMSD statistics workshop (Bari - Italy, June 2023) which focused on advanced statistical approaches for real-world data analyses in multiple sclerosis. The report emphasises the application of these approaches in predicting individual treatment response, assessing comparative effectiveness and safety of therapies and their sequences, and harmonizing data for large-scale federated analyses.

In September 2025, the Network attended the **ECTRIMS Congress** in Barcelona with an exhibition booth to present the initiative together with national MS registries (Figure 3). Four posters presented the organizational structure of the Network, the scientific publications, and the process of the EMA QO submission.

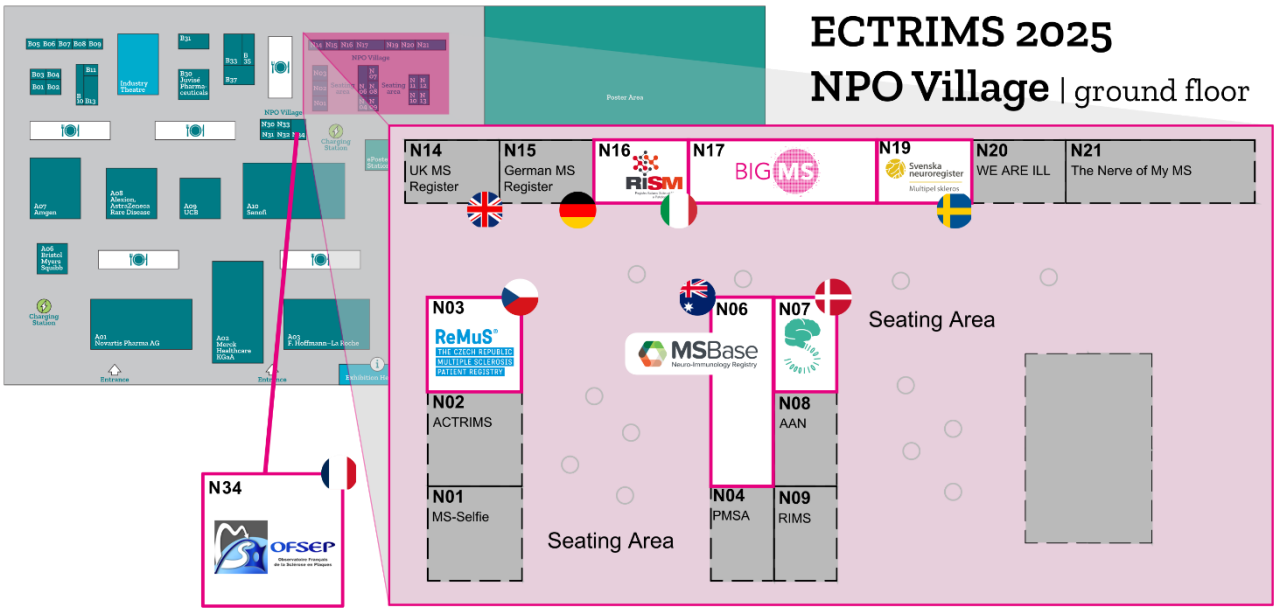

Figure 3 Floor plan of the ECTRIMS 2025 NPO (Not-for-Profit Organization) Village, showing the exhibitor booths dedicated to the BMSD Network and the national registries.

e) Inclusion of new registries

The Network is open to the inclusion of new MS registries. In the second part of 2025, the Network has finalized 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. New

applicants will need to answer and fulfil all the criteria and provide relevant documentation, which will be assessed for the inclusion.

The Finnish and German registries are interested in joining 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. In December 2025, they provided answers to the set of criteria and are currently under evaluation for the final approval.

f) TC meetings

Regular monthly Network meetings were held throughout the year. Key topics discussed included EMA-related activities, such as the renewal of the EMA Qualification Opinion and the registration of BMSD and national registries in the RWD Catalogues, as well as the organization of the 2025 Annual Meeting and the Statistical Workshop. Additional topics covered ongoing and new collaborative research projects, and the definition of procedures for the inclusion of new MS registries.

Conclusion

We are pleased to report that the Network has successfully achieved its objectives for 2025, reflecting the continued commitment and collaborative efforts of all members. Key milestones included the renewal of the EMA QO submission, the publication of new collaborative research articles, and the development of additional research projects currently in the pipeline. Furthermore, the Network is in the process of expanding through the inclusion of new registries, which will further enhance opportunities for future scientific initiatives. We are grateful to our Sponsors for their ongoing support, which contributes to the sustainability of the Network's activities.

December, 2025

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BMSD Coordination Leaders