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Multiple Sclerosis Data Alliance – A global multi-stakeholder collaboration to scale-up real world data research

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ABSTRACT

The Multiple Sclerosis Data Alliance (MSDA), a global multi-stakeholder collaboration, is working to accelerate research insights for innovative care and treatment for people with multiple sclerosis (MS) through better use of real-world data (RWD). Despite the increasing reliance on RWD, challenges and limitations complicate the generation, collection, and use of these data. MSDA aims to tackle sociological and technical challenges arising with scaling up RWD, specifically focused on MS data. MSDA envisions a patient-centred data ecosystem in which all stakeholders contribute and use big data to co-create the innovations needed to advance timely treatment and care of people with MS.

1. The Multiple Sclerosis Data Alliance (MSDA) is a global multi-stakeholder collaboration working to accelerate research insights for innovative care and treatment for people with multiple sclerosis (MS) through better use of real-world data (RWD).

RWD are defined as health data that are routinely collected through the course of health and care services, including prevention and self-care. RWD exists in a number of sources that provide care, such as hospitals, general practices, charities but also patients themselves. Disease registries either collect new RWD from patients, concentrate data of interest extracted from healthcare provider EHR systems, or a combination of both. High quality RWD are required for many different purposes beyond direct patient care provision, such as quality improvement, safety monitoring and research. Despite the increasing reliance on RWD, challenges and limitations exist that complicate the collection, combination and analysis of these data. MSDA aims to tackle sociological as well as technical challenges that arise in scaling-up RWD, with a specific focus on MS data.

The MSDA initiative originated from the advocacy work for better use of RWD performed by the European Multiple Sclerosis Platform (EMSP). EMSP is a Pan-European umbrella of 43 European MS patient representative groups. It consists of a network of member societies in 37 European countries. The European Register for Multiple Sclerosis (EUReMS, 2011-2014) was one of the first cross-border data collections in the field of MS to highlight the feasibility of using RWD for specific research questions [1]. In 2015, the European Medicine Agency (EMA) [2] launched its Patient Registries Initiative, aiming to optimize and facilitate the use of existing patient registries for benefit-risk monitoring of medicinal products throughout their life cycles. In 2017, this EMA Patient Registry initiative selected MS as one of their pilot projects and an MS-specific workshop was organized in 2017. This workshop aimed to agree on the factors that would be expected to help assure the quality and interoperability of MS registry data for supporting regulatory evaluations while ensuring that appropriate governance arrangements are adopted.

The workshop report of this meeting [3] was one of the major inspirations for the discussions of the first MSDA working group brought together by EMSP in 2017. The MSDA working group consisted of representatives of data custodians, patient organisations, academia and industry. Several brainstorm sessions of the working group during 2018 resulted in an official kick-off year in 2019. At that time, the MSDA initiative was a joint initiative of Hasselt University (UHasselt, Belgium) and EMSP.

Today, the MSDA is an independent multi-stakeholder initiative under the umbrella of the European Charcot Foundation (ECF) with ECF acting as the legal entity. ECF is an independent non-profit organization for advancing MS research. Six core partners drive the MSDA initiative forward: EMSP, ECF, the European Institute For Innovation Through Health Data (i~HD), and the academic partners UHasselt, KU Leuven and the University Medical Center Göttingen.

The MSDA focuses on the following strategic objectives (Fig. 1):

1 **Raise awareness about the importance of research using real-world MS data.** The support of people with MS is key to establishing a trustworthy ecosystem for reusing health data for research and for learning health care systems. Like many other patients, people with MS (PwMS) are supportive of the use of their data to accelerate research and learning. However, there is an urgent need to explain how and why data can be used for care and research, how their data and identity must be protected and how the data must be used ethically. MSDA aims to launch a multi-faceted motivation campaign to engage PwMS in decisions about the use of their personal data. A close collaboration has therefore been set up with the European Patients' Forum (EPF) and their "Data Saves Lives" initiative (www.datasaveslives.eu). Data Saves Lives is a new multi-stakeholder initiative with the aim of raising wider patient and public awareness about the importance of health data, improving the understanding of how it is used and establishing a trusted environment for multi-stakeholder dialogue about responsible use and good practices across Europe. The MSDA believes that an informed and engaged patient community will lead to increased compliance to data

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collection procedures (more specifically when it comes to patient-reported and patient relevant outcome measures) and increased patient-driven advocacy by use of RWD in (regulatory and therapeutic) decision-making.

2 **Build a multi-stakeholder MS data ecosystem:** The MSDA envisions a multi-stakeholder synergetic approach to tackle the socio-technical challenges related to scaling-up RWD. The EMA workshop on MS [3] clearly stated that there is an urgent need for community engagement and communication between stakeholders. MSDA actions are intended to *improve collaborations between stakeholders involved* (registry custodians, Marketing Authorisation Holders, regulators, academia, patient societies) so that a mutual understanding concerning the nature and quality of data needed for several purposes is accomplished. MSDA aims to regularly bring together all relevant stakeholders to discuss different MS data science topics. The first MSDA stakeholder meeting [4] was held on the 20th of November 2019 in Baveno (Italy). Representatives of patient organizations, industry partners, regulatory decision-makers, health technology assessors, clinicians and researchers were informed about the initiative and challenges and opportunities were extensively discussed.

3 **Promote trustworthy and transparent practices in the use of real-world MS data.** MSDA respects and promotes the FAIR guiding principles for scientific data management and stewardship [5] for all MS data sources, so that the data are findable, accessible, interoperable, and reusable. A code of practice and data sharing principles are developed to encourage the use of data transparently and in a manner that builds trust. Through educational sessions, MSDA aims to support greater understanding within the community about the use of RWD. Data custodians will be informed on the importance and mechanism for safely and respectfully sharing data. For example, we aim to touch upon concepts like interoperability standards and information security measures.

4 **Catalogue existing and emerging MS data sources.** The MS data landscape consists of many local and regional data initiatives featured by considerable heterogeneity. A growing number of data collection efforts are underway [6] (Table 1). These efforts differ, among others, in their genesis, population criteria, types of collected data (clinical, patient-reported outcomes, biospecimens, imaging) and duration of follow-up [7]. Every dataset has its own strengths, and limitations. Improved awareness of existing and planned cohorts and registries is needed to better coordinate these efforts and maximize the impact of the limited resources available to support them [6]. The MSDA has created a meta-data catalogue of existing cohorts and registries to help improve the discovery and appropriate use of these RWD sources [7].

5 **Support local harmonization efforts by developing and promoting the adoption of an MS specific common data model.** The diversity of the variables used across different MS data sources and their representative values within those data cohorts are heterogeneous. We will not be able to scale up learning on sub-populations unless we can pool the data, or pool the analysis of distributed data, that is homogenous in its representation. Collaborative research therefore requires extensive and labour-intensive harmonisation efforts. The MSDA strives towards the development of an MS specific "common data model" (CDM). A CDM can be defined as a

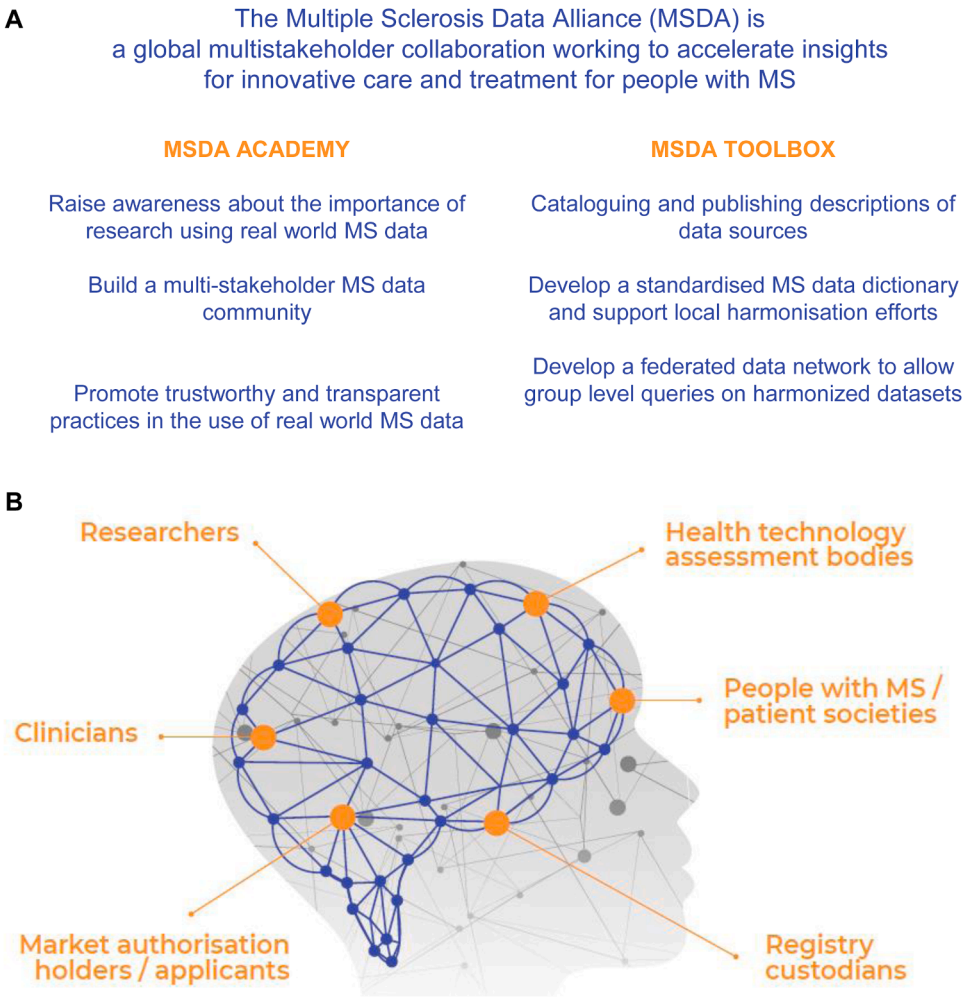


Fig. 1. Aims, strategic objectives and parties concerned of the MSDA. A: Through the MSDA Toolbox and the MSDA Academy, the MS Data Alliance aims to realize their strategic objectives, thereby accelerating research insights for innovative care and treatments for people with MS. **B:** The fulfilment of MSDA strategic objectives is beneficial for researchers, clinicians, market authorisation holders/applicants, health technology assessment bodies, people with MS/ patient societies and registry custodians.

Table 1
Examples of real-world data sharing initiatives pragmatically categorized in 6 categories.

Category	RWD sharing initiatives
Regional- or National Longitudinal follow-up	British Columbia MS Database, Danish MS Registry, Italian MS Registry, New York State MS Consortium, OFSEP, Swedish MS Registry@@@@Many other existing and emerging (Canadian Progression Cohort in MS, Corona MS Registry, Czech MS registry, German MS registries (>3), MS Clinical Database and Registry Health Sciences Centre Winnipeg, SJ MS Center Face to Face Registry, Sonya Slifka Longitudinal MS Study, United Kingdom MS Registry, …)
Deep phenotyping/ Biobanking	Accelerated Cure Project Registry,@@@@CEMCAT CIS Cohort, CLIMB Study, John Hopkins Precision Medicine Center of Excellence for MS, MS EPIC Study, MS Partners Advancing Technology and Health Solutions (MSPaths), MS Sunshine Study, NARCRMS, Norwegian MS Registry & biobank, Swiss MS Cohort, …
Research Collaborations	BMSD, IMSG, MSBase Neuro-Immunology Registry, MultipleMS, RADAR-CNS, SUMMIT, …
Patient-centered	Australian MS Longitudinal Study, iConquerMSTM People-Powered Research Network, NARCOMS, PatientsLikeMe, PROMOPRO-MS, …
Special target population	MS in the Hispanic Population (USC Registry), PeMSDD, Sylvia Lawry Centre for MS Research, Veterans Health Administration MS Surveillance Registry (MSSR), …
Improve care path concept	Cleveland Clinic Knowledge program, MS Documentation System, OptimiseMS, …

Abbreviations: BMSD: Big MS Data Network; CEMCAT: Centre D'esclerosi Multiple De Catalunya; CIS: clinically isolated syndrome; CLIMB: Comprehensive Longitudinal Investigation of MS; EPIC: MS genetics-, expression, proteomics, imaging clinical; IMSG: International MS Genetic Consortium; MS: multiple sclerosis; MSPaths: Multiple Sclerosis Partners Advancing Technology and Health Solutions; NARCOMS: North American Research Committee on Multiple Sclerosis; NARCRMS: North American Registry for Care and Research in Multiple Sclerosis; OFSEP: Observatoire Français de la Sclérose en Plaques; PeMSDD: Pediatric MS and Other Demyelinating Diseases; PROMOPRO-MS: new functional PROfile to MOnitor the PROgression of disability in MS; RADAR-CNS: Remote Assessment of Disease and Relapse; SUMMIT: Serially Unified Multicenter Multiple Sclerosis Investigation.

mechanism by which the raw data are standardised to a common structure, format and terminology independent from any particular study in order to allow a combined analysis across several databases/ datasets. The adoption of a CDM can be realized as a re-modelling of the operational database of an existing registry and its prospective use for new data, or as a mapping target for datasets intended for sharing or distributed analysis. The latter is a frequently-used approach before migrating to operational adoption.

6 **Build a federated ecosystem to allow local queries of different cohorts and registries, while respecting autonomy and ownership of data sources.** Patient-level cross-border data sharing is challenging because national terminology systems have to be cross-mapped, and because of the need to comply with the GDPR or other jurisdictional data protection laws beyond Europe. It is also important that technical solutions, as well as governance solutions, are developed that create an ecosystem in which all stakeholders are comfortable to work together for the benefit of patients. We believe the implementation of a global federated data sharing governance model can enable this ecosystem. In a federated ecosystem, individual MS data cohorts and registries retain custody over their data and implement their preferred governance and standard operating procedures, while they can cross-check and validate their results with the other parties' databases.

The importance of the MSDA has been clearly showcased by its role within the recent COVID-19 pandemic. Only a few months after the formal launch of the MSDA in November 2019, the MS International Federation invited the MSDA to jointly set-up a global data sharing initiative to scale up COVID-19 data collection efforts and provide the MS community with data-driven insights on the effect of COVID-19 in people with MS as soon as possible [8]. Within a month, this joint effort managed to define an MS COVID-19 core dataset, build a central platform to allow data sharing and to have first successful pilot uploads within the platform. On the 10th of August, the initiative consisted of 20 data partners across the globe, sharing patient-level or aggregated data of 7161 people with MS (clinician reported data: patient-level data sharing n=603, aggregated data sharing n=835; patient reported data: patient-level data sharing n=3794, aggregated data sharing n=1929). Besides this data shared by the data partners, clinicians and people with MS from all over the world entered data directly into the platform leading to another 1366 data records (n=119 and n=1247 for clinician and patient reported data, respectively). Thanks to the prompt efforts of intercontinental clinicians, people with MS and registries to share their data, we were able to generate some first results (presented at the special COVID-19 session on MSVirtual 2020 [9] and recently submitted for peer review) and acquire initial insights on COVID-19 in MS. Furthermore, the MS International Federation incorporated these results in their global and national advice to inform people with MS and their clinicians on how to act during this pandemic [10]. This project clearly showcases that although individual cohorts can achieve important results, scaling-up at global scale is required, specifically when rare events are being investigated. Next to this, the COVID19 in MS global data sharing initiatives illustrates how the principles of the MSDA, including early alignment of a common data model and the use of federated data sharing principles, can greatly speed-up collaborative research projects.

In conclusion, RWD can transform the care of people with MS. MSDA envisions a patient-centred data ecosystem in which all stakeholders contribute and use big data to co-create the innovations needed to advance the timely treatment and care of people with MS.

Declaration of Competing Interest

Liesbet M. Peeters has no personal pecuniary interests to disclose, other than being the chair of The MS Data Alliance (MSDA), which receives income from a range of corporate sponsors, recently including: Biogen, BristolMyersSquibb (formerly Celgene), Canopy Growth Corporation, Genzyme, Icometrix, Merck, Mylan, Novartis, QMENTA, Quanterix, Roche.

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