# Novel Use of Harmonized Data Quality Indicators in Long-term Safety Studies Using Multiple Sclerosis Registries: Approach in CLARION study

**M. Magyari[1], N. Moore[2], S. Wergeland[3], J. Sõnajalg[4], M. Sabidó[5], A. Aydemir[6], I. Bezemer[7], T. Ziemssen[8], J. Kuhle[9], M. Soilu-Hänninen[10], H. Butzkueven[11], J. Hillert[12]**

[1]Department of Neurology, Danish Multiple Sclerosis Center and The Danish Multiple Sclerosis Registry, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark; [2]Bordeaux PharmacoEpi (BPE), Université de Bordeaux, Bordeaux, France; [3]Department of Neurology, Haukeland University Hospital, Bergen, Norway; [4]Global Database Studies, IQVIA, Tartu, Estonia; [5]the healthcare business of Merck KGaA, Darmstadt, Germany; [6]EMD Serono, Billerica, MA, USA; [7]Global Epidemiology and Outcomes Research, IQVIA, Amsterdam, The Netherlands; [8]Center of Clinical Neuroscience (T.Z.), Neurological University Clinic Carl Gustav Carus, University of Technology, Dresden, Germany; [9]Neurology Clinic and Policlinic, MS Center and Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel, Basel, Switzerland; [10]Turku University Hospital Neurocenter and Department of Neurology, University of Turku, Turku, Finland; [11]Department of Neuroscience, Central Clinical School, Monash University, Melbourne, Victoria, Australia; [12]Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden.

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# Disclosures

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- **MM** has served on scientific advisory boards for AbbVie, Alexion (Janssen/J&J), Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, and Sanofi; has received honoraria for lecturing from Biogen, Genzyme, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, and Sanofi; and has received research support and support for congress participation from Biogen, Genzyme, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, and Roche.
- **NM** has consulted with the healthcare business of Merck KGaA, Darmstadt, Germany.
- **SW** has served on scientific advisory boards for Biogen, Novartis, and Sanofi; has received honoraria for lecturing from Biogen and Novartis; and is currently engaged in sponsor-initiated research by Biogen, EMD Serono, and the healthcare business of Merck KGaA, Darmstadt, Germany.
- **JS** and **IB** are employees of IQVIA, a contract research organization that performs commissioned pharmacoepidemiological studies for several pharmaceutical companies.
- **MS** is an employee of the healthcare business of Merck KGaA, Darmstadt, Germany.
- **AA** is an employee of EMD Serono, Billerica, MA.
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- **MS-H** has served on scientific advisory boards for Biogen, Celgene (BMS), the healthcare business of Merck KGaA, Darmstadt, Germany, Roche, and Sanofi; has received honoraria for lecturing from Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Sanofi, and Teva; and has received research support and support for congress participation from Biogen, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, and Roche.
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CLARION

# INTRODUCTION

- The EMA Initiative for Patient Registries aims to harmonize standard indicators and solutions to ensure consistent data quality across registries in the EEA.[1]
- CLARION is a multi-country, comparative, long-term cohort safety study based on primary and mainly secondary data collection, and involves 9 MS registries. It evaluates the safety profile in terms of AESI for patients newly initiating cladribine tablets versus those newly initiating fingolimod tablets.

**Objectives:** **To evaluate CLARION data quality over time through the use of pre-defined DQIs in participating MS registries.**

1. Patient Registry Initiative. European Medicines Agency: Report on Multiple Sclerosis Registries - Workshop 7 July 2017. 2017 Oct. Report No.: EMA/548474/2017

**AESI**, adverse events of special interest; **DQI**, data quality indicator; **EEA**, European Economic Area; **EMA**, European Medicine Agency; **MS**, multiple sclerosis

# METHODS

- Twenty-eight DQIs were pre-defined to address four aspects of data quality:
  - **Representativeness** (5 DQIs): To assess distribution and representativeness of key patient characteristics.
  - **Consistency** (4 DQIs): To evaluate uniformity of the core data elements entered over time (data recording density and frequency over time).
  - **Accuracy** (7 DQIs): To assess how well the data are entered (identify discrepant values).
  - **Completeness** (12 DQIs): To assess data missingness (proportion of missing values in the key outcomes and variables).
- Data are available from 7 participating registries (DMSR, FMSR, MSBase, MSDS 3D, NMSRB/NTD, SMSC and SMSR).
- At each data cut-off (01May2021 [H1 2021], 01May2020 [H1 2020], 01Nov2019 [H2 2019], and 01May2019 [H1 2019]), DQIs were summarized by the respective registries and overall.

**DMSR**, Danish MS Register; **DQI**, data quality indicator; **FMSR**, Finnish MS Registry; **MSBase**, Multiple Sclerosis Database; **MSDS 3D**, Multiple Sclerosis Management System 3D; **NMSRB**, Norwegian Multiple Sclerosis Register and Biobank; **NTD**, NeuroTransData database; **SMSC**, Swiss Multiple Sclerosis Cohort; **SMSR**, Swedish Multiple Sclerosis Register

# RESULTS

**Demographics by cohort in H1 2021 (01May2021 data cut-off)**

- Data were included for 2393 patients from the 7 participating registries in H1 2021. Patient demographic characteristics in various registries changed over time.
- **Representativeness**: The data appeared representative of the MS population;
  - majority (70.4%) of patients are female,
  - average age at onset of MS is in the early thirties.
- Over 90% of patients included in the study at the latest data cut-off had a confirmed diagnosis of relapsing MS (not shown).

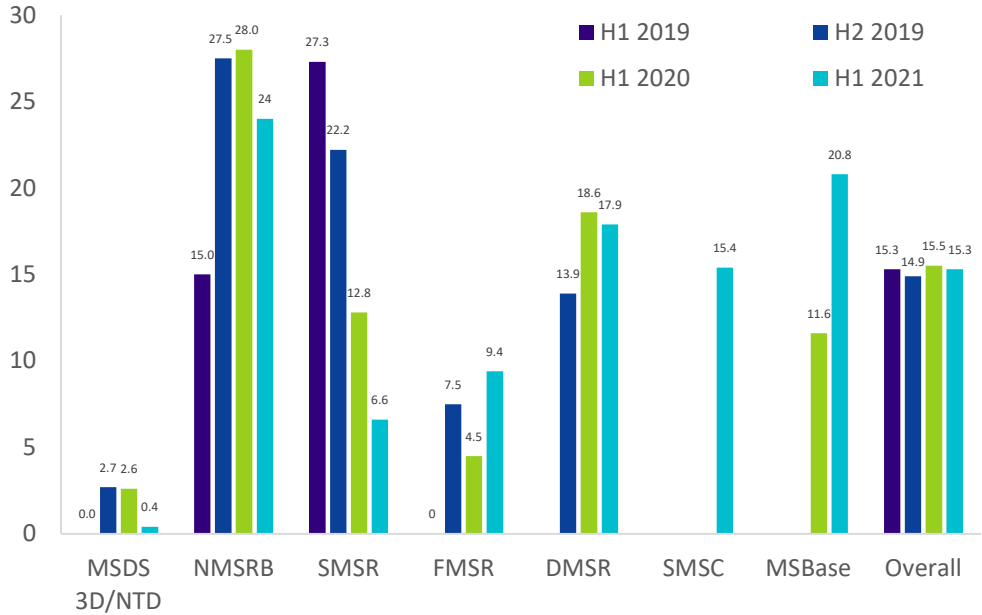
| | Number of patients | | Female sex (%) | | Mean age at MS onset (years) | |
|---|---|---|---|---|---|---|
| **Registry** | Cladribine | Fingolimod | Cladribine | Fingolimod | Cladribine | Fingolimod |
| MSDS 3D/NTD | 294 | 192 | 77.5 | 65.1 | 30.1 | 30.5 |
| NMSRB | 360 | 159 | 70.3 | 64.8 | 33.1 | 33.9 |
| SMSR | 137 | 64 | 70.8 | 68.8 | 29.3 | 30.8 |
| FMSR | 128 | 159 | 85.2 | 76.7 | 27.4 | 28.9 |
| DMSR | 180 | 458 | 62.8 | 67.2 | 31.5 | 30.6 |
| SMSC | 13 | 27 | 46.1 | 48.1 | 34.1 | 34.9 |
| MSBase | 154 | 68 | 72.7 | 75.0 | 35.1 | 29.8 |
| **Overall** | **1266** | **1127** | **72.5** | **68.0** | **31.5** | **30.9** |

**DMSR**, Danish MS Register; **DQI**, data quality indicator; **FMSR**, Finnish MS Registry; **H1 2021**, 01May2021 data cut-off; **MS**, multiple sclerosis; **MSBase**, Multiple Sclerosis Database; **MSDS 3D**, Multiple Sclerosis Management System 3D; **NMSRB**, Norwegian Multiple Sclerosis Register and Biobank; **NTD**, NeuroTransData database; **SMSC**, Swiss Multiple Sclerosis Cohort; **SMSR**, Swedish Multiple Sclerosis Register

# RESULTS

**Percent of patients with no visit during the past year at data cut-off**

- **Consistency**: The proportion of patients with no visits during the one-year period before the data cut-off changed little overall despite the COVID-19 pandemic in 2020–2021;
  - 15.3% in H1 2021,
  - 15.5% in H1 2020,
  - 14.9% in H2 2019, and
  - 15.3% in H1 2019.
- Nevertheless, some changes were observed for individual MS registries.




**DMSR**, Danish MS Register; **DQI**, data quality indicator; **FMSR**, Finnish MS Registry; **H1 2019**, 01May2019 data cut-off; **H2 2019**, 01Nov2019 data cut-off; **H1 2020**, 01May2020 data cut-off; **H1 2021**, 01May2021 data cut-off; **MS**, multiple sclerosis; **MSBase**, Multiple Sclerosis Database; **MSDS 3D**, Multiple Sclerosis Management System 3D; **NMSRB**, Norwegian Multiple Sclerosis Register and Biobank; **NTD**, NeuroTransData database; **SMSC**, Swiss Multiple Sclerosis Cohort; **SMSR**, Swedish Multiple Sclerosis Register

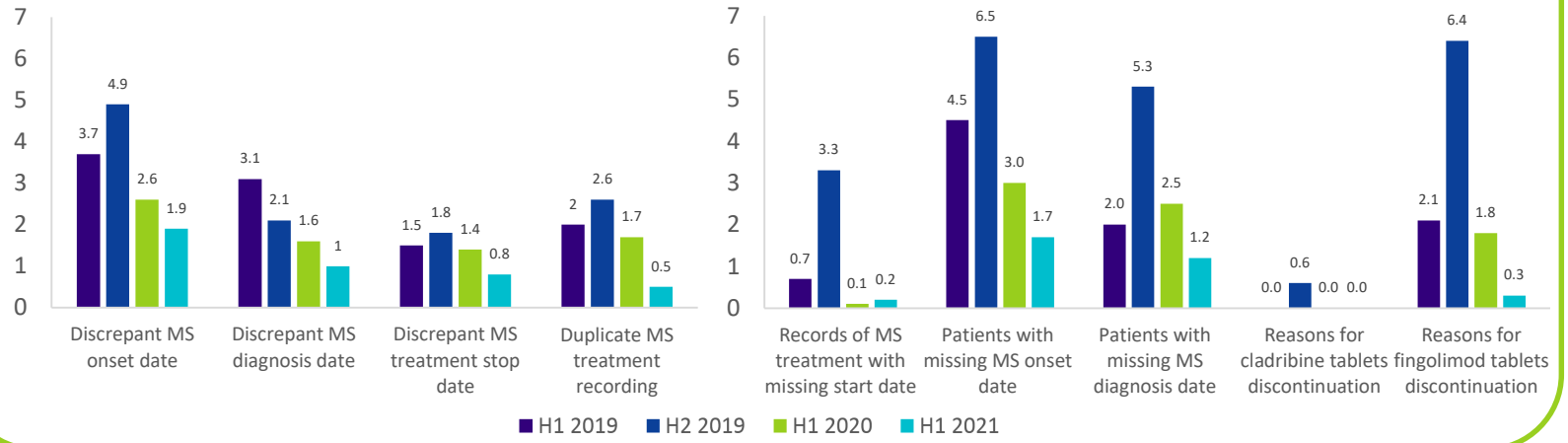
# RESULTS

**Percent of patients with data discrepancies**

- **Accuracy**: Indicators were of acceptable quality with better values in H1 2021 than in H1 2020 and H2 2019, signaling improvements in terms of accuracy.

**Percent of patients with missing values (completely missing)**

- **Completeness**: No missing data for demographics (sex, birth date*) were recorded. The completeness DQIs showed improvement over time regarding reasons for treatment discontinuation and for key dates such as MS diagnosis/onset date.




*Only birth year is available for Germany (MSDS3D [and NTD])
**DQI**, data quality indicator; **H1 2019**, 01May2019 data cut-off; **H2 2019**, 01Nov2019 data cut-off; **H1 2020**, 01May2020 data cut-off; **H1 2021**, 01May2021 data cut-off; **MS**, multiple sclerosis; **MSDS 3D**, Multiple Sclerosis Management System 3D; **NTD**, NeuroTransData database

# CONCLUSIONS

**DQIs have helped to identify potential data inconsistencies and methodological differences in the CLARION study, including outcome definitions such as treatment discontinuation, across participating registries.**

**The DQIs help to identify potential data issues at an early stage, which can be corrected before statistical analyses are performed.**

**Introducing and applying DQIs in the CLARION study improved data quality over time, in terms of completeness and accuracy.**

**DQI**, data quality indicator