The big Multiple Sclerosis data network

3rd progress report - June 2021

Big MS Data Network (BMSD)

Karolinska Institutet (KI) will perform the coordination of the Big MS Data Network and the tasks are described in the BMSD coordination synopsis. The Big MS Data Network has reached out to several pharmaceutical companies asking for financial support for the coordination efforts and has had agreements for 1-5 years with Biogen, BMS, Merck, Novartis, Roche and Sanofi.

This is the **3rd progress report**, covering the period until June 2021.

The BMSD network has been able to maintain coordination, active collaborations, an EMA qualification opinion application and further efforts to develop and ensure the progression of the BMSD network. Although the ongoing pandemic of course has been challenging, we have managed to replace face to face meetings with virtual meetings in a satisfactory way.

Support for BMSD co-ordination

At the moment, we have ongoing contractual agreements with five pharma sponsors and awaiting a finalized renewed agreement with a sixth company.

BigMS Data PASS Forum

Currently BMSD registries individually take part in PASS projects run by Biogen, Merck, Roche and Sanofi. Interactions with pharma in the MS area are central to the activities of BMSD.

On March 26, 2021, BMSD held its annual **BigMS Data PASS Forum** virtually, gathering representatives of six pharma with ongoing or planned BMSD formatted Post Authorization Safety Studies, and common activities were discussed. These included the EMA qualification opinion application, pharma and registry PASS updates, the proposal of updating the BMSD PASS core protocol, a BMSD PASS workforce and the possibility of pooled data from the BMSD registries. Pharma interest in patient level data, pregnancy studies and BMSD managed PASS was also explored as were non-PASS projects and other BMSD future projects.

Seeking qualification opinion by EMA

BMSD has the ambition to play a role in developing the standards of PASS in the MS area and in order to be recognized by EMA, a qualification opinion would be important, both for BMSD as a network and for the participating registries as such.

A pre-submission for an EMA qualification opinion was made in October, 2020 followed by a submission in January, 2021. The EMA application was shared with the BMSD sponsors. BMSD received a list of issues from EMA to consider prior to an EMA SAWP meeting with BMSD on 7 April to discuss the application and the EMA comments.

BMSD has subsequently been informed of the EMA decision to issue BMSD a EMA Qualification Advice. BMSD has been made aware of SAWP's considerations and concerns regarding the BMSD application and these will need to be addressed if BMSD would like to proceed with a Qualification Opinion in the future.

Although EMA acknowledges that the use of MS registries participating in BMSD may have several advantages in terms of efficiency and consistency in the preparation and conduct of future MS PASS, there are two major aspects that, in the opinion of EMA, hamper qualification at this stage. The first one concerns perceived uncertainties regarding the extent to which the individual registries and the proposed generic protocol are able to capture the relevant safety endpoints required for successful conduct of a PASS. A feasibility study is recommended. The second concern is in regard to what EMA perceives as a lack of a concrete set of minimum quality requirements that apply equally to all participating registries. Harmonization of minimum quality requirements to improve quality assurance across the individual registries in a coordinated approach is needed.

We have the opportunity of asking for a Letter of Support describing the methodology under evaluation which can be published by EMA. A draft proposal of a LoS is under preparation and will be submitted to EMA.

Data management

Data management development within BMSD is ongoing. The mapping of **MedDRA** codes (i.e. using the same codes) has been planned and will be done in the same way as what is currently up and running in MSBase. The flowchart below describes the possibility of analyzing pooled individual data as well as a federated data approach. The choice of approach will likely depend on the type of project to be performed as well as the extent to which data sharing is permitted by local restrictions.

In connection with one of the BMSD demonstrator projects, a script was developed as part of the checking and data merging. This will be combined with other data management approaches and further developed by the data manager group.
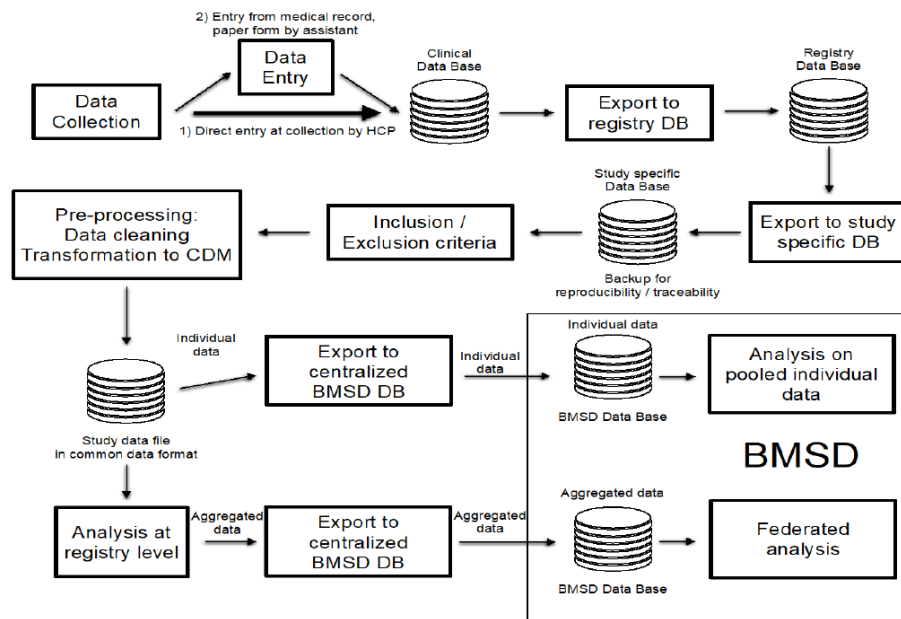
MS-Covid19

As a consequence of the **SARS-CoV2 pandemic**, all BMSD registries have adapted their data collections to allow the gathering of information of MS patients with COVID-19. All registries have used their data for scientific analysis and reported results in different contexts. Based on this data, the Danish, Czech and Swedish registries and MSBase have contributed to the COVID-19 & MS global data-sharing initiative (GDSI). The French and Italian teams have been leaders in their national MS-Covid19 efforts. Altogether, the BMSD registries have been critical in capturing data allowing the identification of treatment related risks for severe Covid19 infection.

Finally, in order to put our data to the best use, we have agreed to enter a BMSD organized MS-COVID-19 project aimed at the analysis of risk factors associated with development and severity of COVID-19 in MS patients which will be led by the Italian team. This analysis will build on previously collected data on the MS-Covid19 patients including disability progression and treatment sequencing that other MS-COVID19 data sets lack. This effort has recently been initiated and the coordination of data is ongoing.

Horizon2020 application: EuCoMS

BMSD decided last year to embark on a joint project application and an application with the acronym EuCoMS (a **Eu**ropean study of **Co**-morbidities in **MS**) was submitted to the European Commission for **Horizon 2020** – Work Program 2018-2020 - Health, demographic change and wellbeing. The project was focused on MS and comorbidities and coordinated by the French OFSEP team under the leadership of Sandra Vukusic. Although the project received excellent

scores and was rated as number eight out of 78 applications, there were only seven applications that received funding. This of course was very disappointing, but BMSD will now prepare for another EU application – "HORIZON-HLTH-2021-TOOL-06-03: Innovative tools for use and re-use of health data (in particular of electronic health records and/or patient registries)". Although this call is more geared towards novel solutions to improve quality and re-use of health data, the comorbidity focus from the previous application will also make a substantial part of the application. Deadline for this call is 21 September 2021.

Communications

The **BMSD homepage** https://bigmsdata.org/ is up and running. There is separate login information to access protocols and reports to be shared with pharma. The sponsor page is also available.

A **review paper** on the BigMS Data effort is in preparation. Two **manuscripts** have been published for the Biogen sponsored demonstrator projects: "Early treatment delays long-term disability accrual in RRMS: Results from the BMSD network" Iaffaldano P et al, Mult Scler. 2021 Apr 26 and "Treatment Switching and Discontinuation Over 20 Years in the Big Multiple Sclerosis Data Network". Hillert J et al, Front Neurol 2021 Mar 17. The DMD effectiveness in progressive MS project has not yet been published.
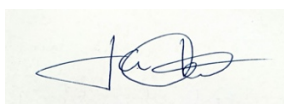
There have been two abstract submissions pertaining to the BigMS Pilot projects to **ECTRIMS 2021** and BMSD will also participate at the ECTRIMS 2021 exhibition as a non-profit organization.

Upcoming meetings

Given the uncertainty due to the pandemic, we will come back with dates for the next meetings.

We conclude that this year so far has been productive for the BigMS Data network and we thank the sponsors for their support.

7 July, 2021

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