Background

Multiple Sclerosis patients and their doctors are nowadays offered a broad choice of immunomodulating therapies (DMTs) which can be individually tailored. However, the treatment is associated with different degrees of effectiveness and risks of adverse events. Reasons for discontinuation can be different and lead to frequent changes of therapy. The complex switching patterns of MS therapy are difficult to monitor with traditional tools.

Objectives

To develop a flexible tool for monitoring of discontinuation, switching and restarting of DMTs. The tool has been designed to allow assessment of the eventual fate of naïve treatments by following subsequent switches in a forward direction, as well as ongoing therapies in a reverse direction, to monitor the path by which patients ended up in the current treatment regime.

Methods

All neurological clinics in Sweden contribute DMT data to the Swedish MS Registry (SMSreg) on a regular, although voluntary basis (Ref.1). SMSreg has over 80% coverage of all prevalent MS patients in Sweden (16,600 of 20,000). The total number of registered DMT episodes is 32,300 on 14,100 unique MS patients with over 10,000 ongoing treatments (status of August 2017) (Fig.1).

A specific type of flow diagrams - the Sankey diagrams were used to visualize DMT switches. The Sankey diagram is one of the Visualization and Analysis Platform (VAP) tools, providing graphs and tables on SMSreg data in real-time (Ref.2). VAP is built in SQL and R language, with a collection of R libraries. It avails Shiny - a powerful tool for web-visualization, which allows interactive selection of a patient cohort and data presentation. The library networkD3 (Ref.3) was used to produce Sankey diagrams.

The input data for the Sankey diagram consist of an interactively selected cohort of patients and their treatment data which are automatically retrieved from SMSreg. The individual treatments are ordered in time and then summarized to calculate the proportional flows within the selected cohort. In order to incorporate all treatments and patients, the node “naïve patient” was introduced when a patient enters the flow for the first time. Patients that are without treatment for more than three months are categorized as “no rx info”.

Results

Monitoring of treatment switches in VAP avails customizable Shiny diagrams. The system allows the user to select a specific time cohort of first treatments, to choose gender, region (national and county levels) and disease course as well as the number of treatment switches. A reason for discontinuation is also implemented as a separate layer, seen between changes of drugs.

The diagram’s first node can be grouped for several first treatment drugs or for monitoring of individual drugs. Treatment flow can then be followed from the first/ naïve DMT episode to the last/current DMT, or from the reverse direction, i.e. starting with the currently ongoing DMT backwards to the first registered treatment.

Hovering the mouse over a specific node or link shows the exact number of observations in that flow. Sankey diagrams are utilized to understand how MS-patients switch between treatment strategies and to determine the reason for discontinuation of treatment. They could reveal new insights into a problem of discontinuation and restarting.

Reference


Conflict of Interests / Disclosure

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