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Real-time monitoring of MS-immunotherapy discontinuation, switching, and restarting with a Visualisation and Analysis Platform (VAP) implemented in the Swedish MS-Registry

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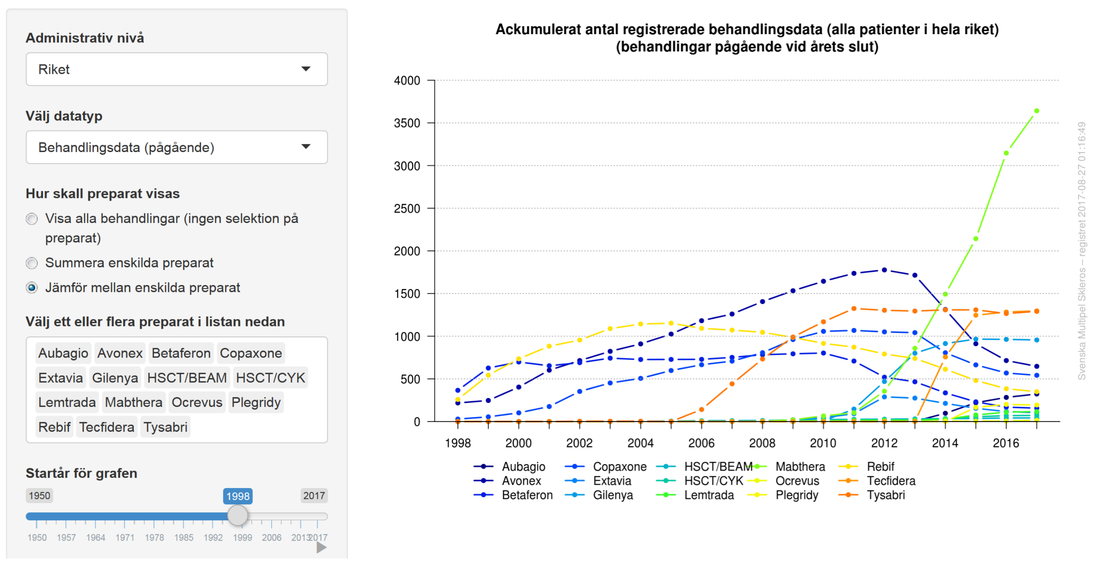
Background

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.

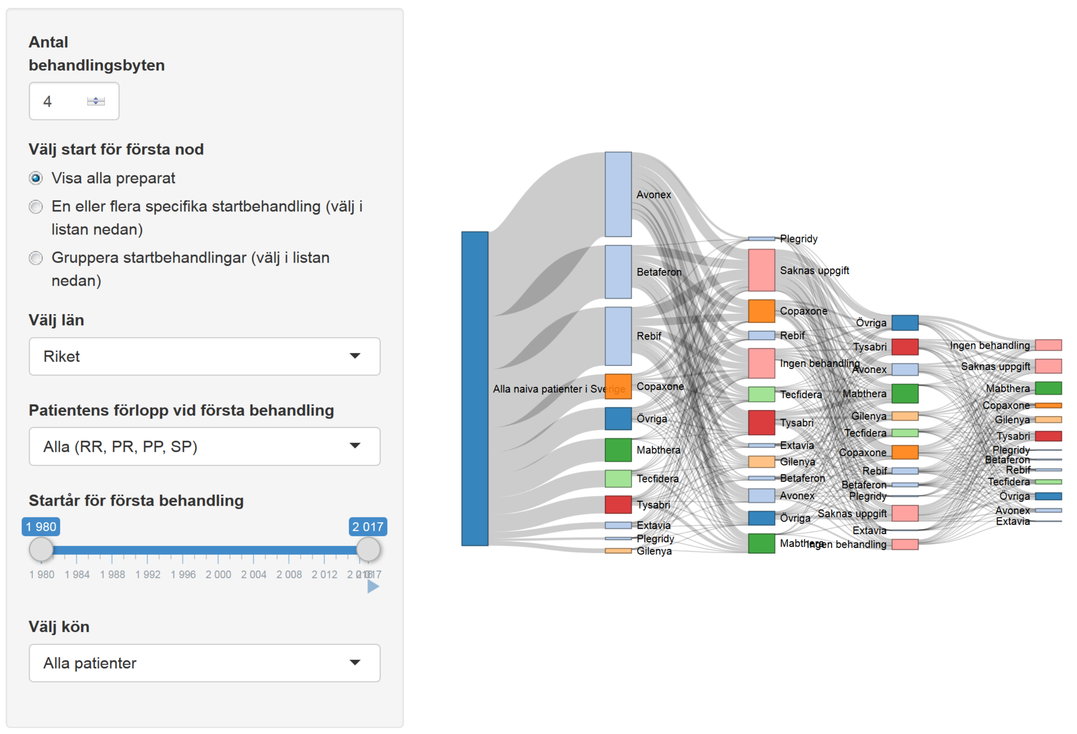
Fig.1 Longitudinal changes in ongoing MS treatment patterns in Sweden.
The figure shows the number of ongoing treatments on a national level over time. It illustrates changes in DMD treatment strategies when novel and more effective drugs have been introduced on the market. Availability of a drug, therapy effect, number of adverse events, national recommendations, personalized medicine approach, an individual neurologist choice, or drug pricing influenced which treatment strategies has been preferred at a specific time point.



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.

Fig.2 Real-time monitoring of treatment switches with the help of Sankey diagram.
The Sankey diagram illustrates transfer between one set of treatment to another. The flows are directional in time and proportional to the amount of patients in the switch. All patients start as naïve patients. The Shiny VAP platform enables a selection of a specific cohort of patients, with user-friendly and flexible graphical control panel. The figure bellow illustrates treatment flow of all naïve patients in Sweden beginning their first treatment between 1980 and 2017.



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.

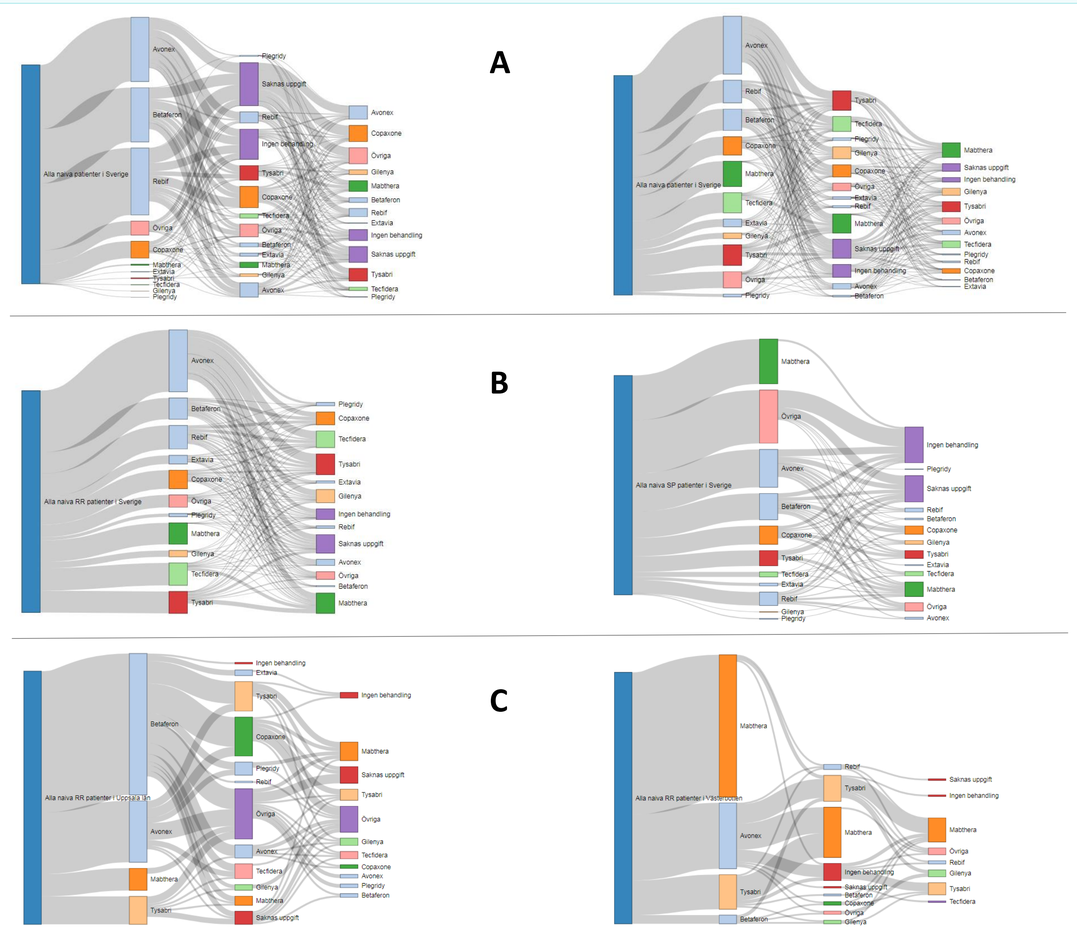
The Sankey diagram is one of the Visualization and Analysis Platform (VAP) tools, providing graphs and tables on SMSreg data in real-time (Ref.2). VAP is built in SQL and R language, with a collection of R libraries. It avails Shiny - a powerful tool for web-visualization, which allows interactive selection 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”.

Conclusions

The system offers flexible, real-time, graphical monitoring of treatment switches. With the help of Sankey diagrams, a unique visualization of this complex issue is possible. It provides complimentary information on treatment patterns, which are already monitored with the help of Visualization and Analysis Platform (VAP) in SMSreg.

Fig.3 Comparing treatment strategies over time, between patient groups and geographical regions.
Figures below compare treatment strategies and switches when selecting different time and geographical cohorts: A) two different time cohorts of first DMD treatment (1997-2006, 2007-2017) for all MS patients; B) two patient groups with different MS clinical courses (RR vs SP) for time cohort of 2007-2017; C) two different counties with selection of four most used naïve/first registered drugs for time cohort of 2007-2017.



Results

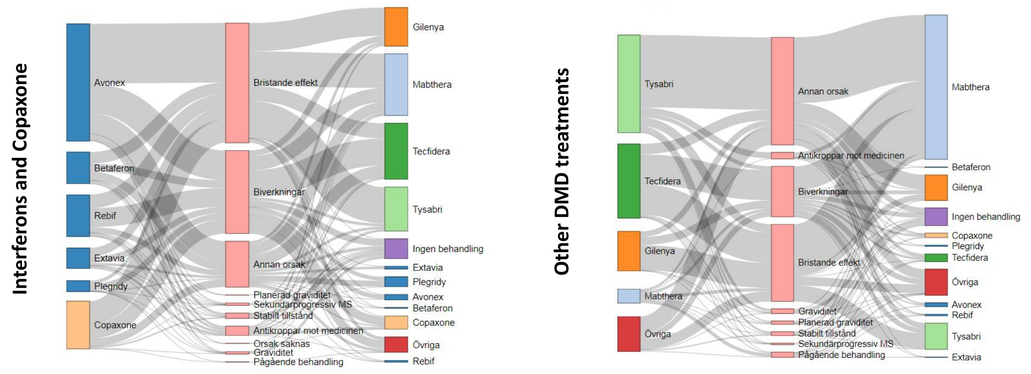
Monitoring of treatment switches in VAP avails customizable Shiny diagrams. The system allows the user to select a specific time cohort of first treatments, to choose gender, region (national and county levels) and disease course as well as the number of treatment switches. A reason for discontinuation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

Fig.4 An example of the Sankey diagram showing switches and reason for discontinuation of DMD treatments.
This Sankey diagram illustrates reason for discontinuation in a reversed order. A node to the right is the current ongoing treatment and nodes on the left hand side illustrate the reason for discontinuation and a previous treatment.
The graphs bellow illustrate all naïve RRMS patients in Sweden beginning their first treatment between 2007 and 2017.



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Conflict of interests / Disclosure

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