ECTRIMS
EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS

# Abstract Submission ECTRIMS 2022

## Preview

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**Proposed Project Title:** **Multiple Sclerosis disease states as identified by unsupervised machine learning on multimodal longitudinal patient trajectories**

**Type:** Oral or ePoster

**Authors:** H. Ganjgahi* [1], D. A. Häring* [2], G. Graham [3], Y. Sun [4], S. Gardiner [4], W. Su [5], B. C. Kieseier [3], T. E. Nichols [4], D. L. Arnold [6], R. A. Bermel [7], H. Wiendl^ [8], C. C. Holmes^ [9]



author) Novartis Pharma AG, Basel, Switzerland, [2]Novartis Pharma AG, Basel, Switzerland, [3]Oxford Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom, [5]Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, United States, [6]Brain Imaging Centre, Montreal Neurological Institute and Hospital, McGill University, Montréal, Canada, [7]Department of Neurology, Mellen MS Center, Cleveland Clinic, Cleveland, United States, [8](co-last author) Department of Neurology, University Hospital Münster, Münster, Germany, [9](co-last author) Department of Statistics, University of Oxford, Oxford, United Kingdom

### General data

**Topic:** * 7: Natural course

### Abstract text

**Abstract text:** *

**Introduction:** Multiple sclerosis (MS) phenotypes/states have been defined to describe the clinical disease course. However, individual patient journeys remain unpredictable.
**Aims and Objective:** To use advanced data analytical methods to agnostically characterize MS progression by discovering homogenous disease states and transition pathways in longitudinal multidimensional patient trajectories.
**Methods:** A scalable machine learning method (factor analysis followed by hidden Markov model; FAHMM) was developed to analyze longitudinal patient trajectories (up to 15 years of follow-up; >120,000 visits; 5 clinical, 3 MRI features) from the Novartis–Oxford MS clinical trial database [N=8052 MS patients (discovery: 6444; validation: 1608)] to identify 1) key-dimensions of MS (based on feature covariation); 2) homogeneous states of MS (based on composite score changes); 3) transition probabilities between MS states; and 4) the effect of treatment.
**Results:** We discovered three reproducible key-dimensions of MS: 1) physical disability; 2) subclinical disease burden/associated cognitive deficits; and 3) ongoing focal inflammation symptomatic (relapse)/asymptomatic (lesion). Nine distinct MS states, grouped into 4 meta-states: 4 *early MS*, 1 *acute relapse*, 1 *transition* and 3 *late MS* states. *Early MS* patients transition between 4 early MS states depending on subclinical inflammation and cognitive performance. They can move into the *acute relapse* state from where they either recover or move into the *transition state*. The single *transition state* between *early* and *late MS* is characterized by substantial subclinical disease burden, moderate physical and cognitive impairment and high levels of ongoing inflammation. From the *transition state*, patients may recover or move on to *late MS*. *Late MS* is characterized by high levels of subclinical damage, physical and cognitive impairment, very low level of new inflammation, with low/no probability of recovery. Patients in *late MS* states typically have a diagnosis of progressive MS (without distinction between primary- or secondary progressive disease made by FAHMM). Disease modifying therapies significantly lowered the *transition* probability from *early MS* to*late MS*.
**Conclusions:** The FAHMM discovered that MS patients do not transition from *early* to *late MS* unless through accumulation of subclinical damage and confirms that treatment provided to *early MS* patients significantly improves a patient's chance of staying in *early MS*states.

**Disclosure:** *

**Habib Ganjgahi**: Nothing to disclose
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**Gordon Graham:**Full-time employee of Novartis Pharma AG, Basel, Switzerland.
**Yang Sun:** Nothing to disclose
**Stephen Gardiner:**Nothing to disclose
**Wendy Su:** Full-time employee of Novartis Pharma AG, Basel, Switzerland
**Bernd C. Kieseier:** Full-time employee of Novartis Pharma AG, Basel, Switzerland
**Thomas E. Nichols:** Nothing to disclose.
**Douglas L. Arnold:**consulting fees from Biogen, Celgene, Frequency Therapeutics, Genentech, Merck, Novartis, Race to Erase MS, Roche, and Sanofi-Aventis, Shionogi, Xfacto Communications, grants from Immunotec and Novartis, and an equity interest in NeuroRx.
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**Heinz Wiendl:**receivedhonoraria for acting as a member of Scientific Advisory Boards for Biogen, Genzyme, Merck Serono, Novartis, Roche Pharma AG, and Sanofi-Aventis and UCB; as well as speaker honoraria and travel support from Alexion, Biogen, Biologix, Cognomed, F. Hoffmann-La Roche Ltd., Gemeinnützige Hertie Stiftung, Merck, Novartis, Roche Pharma AG, Genzyme, TEVA and WebMD Global. Prof. Wiendl is acting as a paid consultant for Actelion, Argenx, Biogen, Bristol Myers Squibb, EMD Serono, Idorsia, IGES, Immunic, Immunovant, Janssen, Johnson & Johnson, Novartis, Roche, Sanofi, the Swiss Multiple Sclerosis Society and UCB. His research is funded by the German Ministry for Education and Research (BMBF), Deutsche Forschungsgemeinschaft (DFG), Else Kröner Fresenius Foundation, Fresenius Foundation, the European Union, Hertie Foundation, NRW Ministry of Education and Research, Interdisciplinary Center for Clinical Studies (IZKF) Muenster and Biogen, GlaxoSmithKline, Roche Pharma AG and Sanofi-Genzyme.
**Chris C. Holmes:**Nothing to disclose

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