

Patient-Reported Outcomes & their Interconnectivity in Multiple Sclerosis

Short title: Patient-Reported Outcomes Measures in MS

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INTRODUCTION

Multiple sclerosis (MS) clinical studies often include patient-reported outcome measures (PROMs) to quantify treatment effects not addressed by clinical measures. Fatigue, cognitive impairment, depression, and pain are burdensome symptoms that often co-occur in people living with MS (PlwMS). Interconnections between these symptoms, including explanatory biological processes, are poorly understood.

OBJECTIVES

To determine the extent of symptom interconnectivity and its impact on quality of life (QoL) in PlwMS; to understand how well PROMs reflect the reality of patients' symptoms; and explore biological processes driving symptom interconnectivity.

METHODS

A quantitative survey (N=2,052 PlwMS from 23 countries) was used to determine the occurrence and impact of symptom interconnectivity, and semi-structured interviews (N=25 patient experts) were used to explore symptom experience and PROMs that are most relevant to PlwMS. A literature search was conducted to identify potential biological processes driving symptom interconnectivity.

RESULTS

Of the 2,052 survey respondents, 63% reported co-occurrence of symptoms (i.e. ≥ 2) impacting their QoL. Fatigue was the most commonly reported symptom (by 13%) among those impacted by a single symptom. For patients impacted by two/three symptoms, fatigue was a key driver. Insights from interviews revealed that fatigue makes it difficult to manage emotions; memory of

previous cognitive abilities and fear of future cognitive decline leads to depressive emotions; fatigue, pain, and cognitive impairment all contribute to depression; and there is a clear relationship between fatigue and pain. Interviewees emphasized the importance of assessing symptom interconnectivity in PROMs and questions of relevance to PlwMS. Literature search returned 76 relevant papers, and identified neuroanatomical brain changes, inflammation, and monoamine disruption as potential biological processes explaining symptom interconnectivity.

CONCLUSIONS

These findings provide evidence of symptom interconnectivity that impacts QoL in PlwMS. The development of more effective PROM strategies and investigation of underlying biological processes will together help to better understand symptom interconnectivity.

This study was previously presented at 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), 13-15 October 2021 and was supported by Novartis Pharma AG, Switzerland.