

## Appendix e-1. International Survey of Priorities for Comorbidity Research

We aimed to identify the most relevant comorbidities and health behaviors to evaluate with respect to incidence, prevalence, or their impact on MS outcomes based on expert consensus. Therefore we conducted a cross-sectional pilot study using an anonymous questionnaire. The project was approved by the Research Ethics Board of the University of Manitoba. Consent to participate was considered to be implied by participation in the survey after review of the study information letter.

Initially we developed two versions of the questionnaires which differed with respect to the ranking schema used. We pilot-tested the questionnaire with 10 participants from various clinical and research disciplines (neurology, pharmacoepidemiology, nutrition sciences, occupational therapy, biostatistics, epidemiology) to determine which version of the questionnaire participants preferred, interpretability of the data, and time required to complete the questionnaire. Based on the responses we chose one version of the questionnaire and made some minor changes to the response options. The final questionnaire included questions regarding the most important research gaps with respect to comorbidity in MS and with respect to health behaviors in MS, the most important comorbidities with respect to their impact on outcomes with MS and with respect to clinical trial design in MS, and demographic characteristics of the respondents (see below).

The study population of interest included individuals involved in the care of patients with MS, conducting research related to MS, and patient advocacy organizations. Recruitment was conducted by asking the National MS Society, Consortium of MS Centers, and ECTRIMS to distribute the survey link to their members in January 2014. These organizations did not provide direct access to their distribution lists and some of the distribution lists overlapped. ECTRIMS used the Congress mailing list used to reach potential attendees to their annual meetings and thus was not restricted to their members. We did not obtain written consent from study participants. The questionnaire included an introduction to the study, and a consent statement indicating that completion of the questionnaire would imply consent.

We performed simple descriptive analyses. For questions specifying particular comorbidities, comorbidities were initially analyzed in groups (e.g. Psychiatric disorders), then as individual conditions (e.g. depression, anxiety).

We obtained 351 responses. Nearly half of our participants were women (45.3%), and 59.3% identified themselves as health professionals (Table 1). Of those, most were physicians. Based on the organizational affiliations reported most respondents were from North America and Europe, as expected based on the organizations who distributed the survey for us.

Table 1. Characteristics of survey respondents

Characteristic	Percent
<b>Gender (n = 351)</b>	
Female	45.3
Male	39.0
No response	15.7

<b>Sector of work* (n = 300 responders)</b>	
Health care/health professional	59.3
Research in academic or health care setting	38.2
Government	7.98
Non-profit organization:	4.27
Research in commercial/industry	3.13
Industry/setting, non-research	1.99
Other	2.28
<b>Occupation* (n = 296 responders)</b>	
Clinical care	63.3
Research and evaluation	47.01
Administrative	9.97
Patient advocacy	6.84
Other	3.99
<b>Professional background* (n = 306 responders)</b>	
Physician	53.9
Researcher-clinical	33.3
Researcher-biomedical	10.5
Nurse	9.97
Researcher-population health/epidemiology	7.98
Physiotherapist	6.27
Administrator	5.98
Researcher-health systems and services	4.27
Occupational therapist	1.42
Social worker	0.57
Speech therapists	0.28
Other	2.85
<b>Organization Affiliations* (n = 300 responders)</b>	
National or local Multiple Sclerosis Societies	45.9
ECTRIMS	40.7
Consortium of MS centers	30.8
American Academy of Neurology	26.8
EFNS	12.0
ACTRIMS	11.7
MSIF	9.12
LACTRIMS	3.99
PACTRIMS	2.28
Other	0.57

\* More than 1 field could be applicable

With respect to the comorbidities in greatest need of study with respect to their impact on outcomes, the top five were psychiatric disorders, cancer, autoimmune disease, endocrine and metabolic disorders and neurologic disease. Among individual comorbidities the top five were depression, autoimmune thyroid disease, diabetes, anxiety and inflammatory bowel disease.

Participants ranked the most important gaps with respect to the issue of comorbidity in MS. The most important gap identified was comorbidity as a prognostic factor for MS, followed by estimates of the frequency of comorbidity, comorbidity as an etiologic factor for MS, comorbidity and the impact on diagnosis of MS, the risk of comorbidity secondary to novel therapies, impact of comorbidity on pharmacologic therapy, comorbidity and the impact on health services use, the impact of comorbidity on non-pharmacologic therapy, and other.

With respect to health behaviours, participants ranked the most important research gaps. The highest ranked gap was health behaviours as a prognostic factor for MS, followed by the impact of health behaviours on pharmacologic therapy, health behaviours and impact on diagnosis of MS, health behaviours as an etiologic factor for MS, health behaviours and impact on health services use, impact of health behaviours on non-pharmacologic therapy, estimates of the frequency of comorbid health behaviours and other.

With respect to the health behaviours in greatest need of study with respect to their impact on outcomes, they were ranked as substance use, alcohol use, diet, and cigarette smoking followed by physical activity.

Limitations of the survey should be recognized. This was not a random sample of all potential stakeholders. Further, physicians, a key part of the target audience generally have poor response rates to surveys.<sup>83</sup> The survey was distributed in English due to the costs of translation and time constraints. These limitations may have contributed to selection bias. However, this was a pilot study aimed more at gaining a broad perspective on research priorities. Further, we were unable to determine response rates as we will be asking organizations to forward the survey link to their members by email, as they will not provide us with their distribution lists. A low proportion of respondents were from Asia, Africa, Central or South America thus the priorities for study may not generalize to these regions, although these regions are underrepresented in the comorbidity literature.