**Designing wellbeing intervention trials for people with progressive multiple sclerosis: The importance of understanding "usual care" comparators**

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**Running head:** "usual care" in wellbeing intervention trials

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For people with progressive forms of multiple sclerosis (MS), there are few disease modifying treatments available[1,2], leaving much of MS care focused on the management of symptoms and resulting disability. Research indicates that pharmaceutical approaches to symptom management can reduce the frequency and severity of symptoms and delay progression[3,4], while rehabilitation and self-management approaches can help people with progressive MS reduce the impact of symptoms [5,6], restore some lost abilities[6,7], and manage everyday life despite disability[8,9]. Approaches tested through research are often applied in clinical practice under the assumption that they will improve the overall wellbeing of people with progressive MS, even if available evidence has not included this sub-group of the MS population or explicitly reported this broader outcome.

Wellbeing (or "wellness") is an individual's capacity to lead a life that is purpose-filled, engaged, and embraces their full potential, including physical, emotional, spiritual, intellectual, social, environmental, and vocational functioning[10]. Therefore, wellbeing is not just the absence of symptoms or the ability to perform daily activities, but about *thriving* in a balanced, meaningful, and fulfilling life. This implies that interventions focused on wellbeing require a wholistic, multidimensional approach and 'intervention targets' that go beyond specific symptoms, physiological parameters, or behaviours.

The importance of broader targets for MS care is apparent in the results of a recent international survey[11] that found >40% of people with MS reported worsening of their ability to perform activities of daily living (ADLs) during the previous 24 months and >60% reported negative changes in physical functioning. Furthermore, respondents indicated that these negative changes were associated with factors beyond symptoms (e.g., emotional and social factors, future outlook, emotional wellbeing, coping, self-esteem, and relationships with friends and family).

This brief background supports the need for a novel approach to address the wellbeing of people with MS, particularly those with progressive MS, whose symptoms and their impact may be particularly burdensome and/or intractable[12]. It is this need that drives our work.

We are an international multidisciplinary consortium of MS researchers and clinicians from eight countries who are developing and evaluating a wellbeing intervention for people with progressive MS[13]. In designing our study, one of the challenges we faced was understanding the similarities and differences in "usual care" across our settings and what that means for evaluating our intervention. The intent of this editorial is to share our insights regarding the "usual care" challenge.

*The "usual care" challenge*

To evaluate our intervention, we are planning a comparative trial with the exact design still under consideration. Comparative studies, including randomised controlled trials, rely on comparisons between the "experimental condition" (intervention to be tested) and a control or "comparator condition". In MS rehabilitation trials focused on symptom management, the comparator is often described as "usual", "routine" or "standard" care, suggesting that participants randomised to this

trial arm receive what is typically/routinely provided to patients in that clinic or region. While published treatment guidelines can encourage the harmonisation of comparator trial arms in *medical* trials, the commitment in *rehabilitation* to patient-centred, goal-directed, and tailored interventions can make such harmonisation challenging. Standardised comparators may be more challenging for wellbeing interventions since the ways in which individuals achieve a meaningful, purpose-filled and engaged life vary socio-culturally and individually[14,15]. Further, usual care can vary widely regionally and nationally, making the generalisation of trial findings difficult without details about usual care comparators.

Notably, the practice characteristics of rehabilitation and the breadth of interventions addressing wellbeing are both consistent with "complex interventions". Complex interventions include several interacting components, require engagement in multiple behaviours by both the provider and the recipient, have multiple targets and outcomes, and offer a degree of delivery flexibility. Thus, a single intervention can vary considerably depending on the recipient, their goals, the provider's implementation of the tailoring process, and the resources made available by the healthcare system, health insurance, or the individual[16–18]. Complexity is further affected by service-level factors and by an individual's clinical characteristics[19].

Given these multiple factors, what constitutes "usual care" to support and promote wellbeing for people with progressive MS is largely unknown. This gap has also been identified in stroke rehabilitation[20]. However, in situations where a trial uses a usual care comparator, or when the experimental intervention is added to usual care, a good understanding of what constitutes usual care is needed to accurately interpret results and their relevance to a particular setting. Although the importance of describing a usual care comparator is recognised in the context of trial reporting[21,22], we argue that understanding and documenting usual care needs to be part of *trial planning* and implementation. Gathering information about usual care in potential study sites will facilitate decision-making about which sites to use, enhance understanding about the overlap between the intervention to be tested and usual care at each site, guide thinking about how to maximise generalisability, and support future implementation if the trial is successful. Indeed, a methodological review summarising the current approaches to determining the components of usual care comparators highlighted the importance of researchers understanding the context in which a trial is going to be implemented[23].

*Moving forward*

As part of our consortium's work[13], we aimed to describe usual care to support improved wellbeing among people with progressive MS in potential study sites in Norway, UK, USA, Canada, Australia, Belgium, Italy, and Denmark. We developed a brief survey for this purpose, with the goal of using the results to inform trial design and planning. We did not intend to conduct formal comparisons across countries, but wanted to understand what services and resources were available to support wellbeing (e.g., disciplines and programmes available, service funding models, referral requirements, care coordination) and what this might mean for our trial comparators. We also wanted to know about the modes of service delivery available, the extent of use of digital technologies, and the outcomes that were being monitored. We received ethical approval from Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (Canada; No. 6041507) for our survey. An invitation to participate, with a link to an online survey,

was sent to all members of our study team, who then purposefully distributed it to colleagues who may be invited to operate a study site for our trial in the future.

In total, 50 individuals responded, with half from the UK. We also had responses from Italy, Australia, Denmark, Belgium, Canada and Norway. Respondents were primarily neurologists (41%) and nurses (23%), with others being physiotherapists (14%), occupational therapists (12%), psychologists (2%), continence specialists (2%), or "other" (5%).Most (50%) worked in an academic hospital , with tertiary care settings and community-based hospitals or practices being the next most common. The vast majority (85%) reported that theirs was a MS specialty centre. Although 98% considered themselves to be MS specialists within their discipline, a third of respondents reported serving <100 people with progressive MS annually, while 16% reported serving >1000 annually.

Despite responses from different countries, 90% of respondents indicated that traditional healthcare services were publicly funded, likely due to the preponderance of European respondents. In comparison, less than one-third of respondents reported that wellbeing services were publicly funded. Instead, a mixed model that included both public and private funding sources was most common, followed by private pay (e.g., through private insurance or out of pocket payments). Of concern is that 56%reported that <25% of their patients with progressive MS have private health insurance to access services that support wellbeing.

Respondents were asked about the sources of the referrals to their service, and they could choose more than one option. Primary care physicians were the most common referral source (56%), followed by general (non-MS) neurologists (50%), and then other healthcare providers (40%). Just over 25% of respondents also reported receiving self-referrals from people with MS. Given our respondents' settings, it is not surprising that the majority (47%) reported that nurses were the team member most likely to coordinate the connections between people with progressive MS and services or resources to support wellbeing. Only 3% had a "case manager or coordinator" who offered such coordination service for people with progressive MS.

The proportion of time respondents spent delivering services to support the wellbeing of people with progressive MS was limited – the majority (58%) reported that they spent ≤25% of their time addressing wellbeing. The availability of other disciplines, services or resources to address wellbeing was also limited; for example, <25% of respondents indicated that their centre offered exercise programmes for people with physical disabilities, and a smaller proportion had a social worker (18%) or offered mental health programmes (14%), spiritual support (12%), or assistive technology services (8%). Service providers such as physiotherapists, occupational therapists, dieticians, speech therapists, continence advisors and psychologists were sometimes available through a centre or through external agencies, where referrals were often required. Availability of digital healthcare technologies (DHCTs) to support wellbeing was not common, except for telehealth technologies, which were available to 56% of respondents. All other DHCTs were available to fewer than a third of respondents. Even when available, DHCTs were integrated into care ≤40% of the time.

*Main considerations*

Our survey uncovered several issues that we must consider as we move forward to develop our intervention to improve wellbeing for people with progressive MS. We believe that attending to these issues may also be useful to others interested in supporting wellbeing of people with progressive MS and improve future research.

1. *Content of Services Still Unknown*: We asked about what services were available, primarily focusing on the person/discipline or service (e.g., nurse, social worker, support group). We cannot assume that the people providing services are focused on wellbeing, consistent with the broad definition provided earlier. However, based on what we found, service provision focused on wellbeing appears to be relatively sparse for people with progressive MS. This may be due to funding structures, time available during appointments, or other service factors. We are left wondering the extent to which wellbeing services reach people with progressive MS and whether any sub-groups (e.g., minoritised individuals) are particularly disadvantaged, given extant literature[24–26].

2. *Gaps in Coordination of Wellbeing Care*: Care to support wellbeing is often coordinated by nurses in the centres where our respondents worked. Nevertheless, we cannot assume that the availability of nurses is ubiquitous[27]. Even when nurses are available, they may not have time to address wellbeing needs of people with progressive MS given the ever-increasing pressures they are under to provide support for disease modifying treatments and other medical issues. Overall, our findings suggest that focusing on wellbeing issues represents a small fraction of most neurologists' and nurses' clinical time. While case-coordinators or "link-workers" have become a useful resource in other areas of healthcare and social prescribing[28], and "patient navigators"[29] are also used to complement traditional healthcare professionals' roles, very few MS centres have such personnel or offer these models of care provision.

3. *Wellbeing Supports Beyond Healthcare:* We need to consider whether the types of supports and services needed to address wellbeing - "thriving in a balanced, meaningful and fulfilling life" - are aligned with traditional healthcare settings, which primarily operate in a medical model of care. If we think broadly about "usual care" for wellbeing, we need to recognise that care can be obtained from services that are not commonly linked to healthcare (e.g., recreation, leisure and social programmes), and from informal systems of support. These aspects of care can be invisible if they are not consistently recorded in patient records or during clinical trials. Our survey only captured aspects of usual care that were provided in the context of the clinical setting. We need to capture other aspects of wellbeing support when describing usual care comparator arms.

4. *Availability and Use of Digital Healthcare Technologies (DHCTs)*: Despite the growth in the use of DHCTs in neurological trials )[30] our findings indicated limited use of such technologies in clinical care. We need a better understanding of the factors contributing to this implementation gap so that evidence-based DHCTs can be considered as an adjuvant or alternative to traditional in-person services[31–34]. Given technological improvements and increased technological literacy, providing patients *choices* in accessing and receiving services that include evidence-based DHCTs is worth considering. The use of DHCTs is particularly relevant if we want to provide accessible wellbeing services in the community.

5. *Importance of Describing Usual Care*: Finally, in a trial, we can often control aspects such as access to the intervention, the method and timing of its delivery, and the training of personnel

providing it. As our survey revealed, usual care to support the wellbeing of people with progressive MS varies widely. This highlights the need for a consistent way to collect data and report on the components of usual care (see definition of complex interventions) so that we fully understand the comparator arm of our wellbeing trials.

*Conclusion and Implications*

Our consortium is committed to developing and evaluating a programme to support people with progressive MS to live well and thrive in daily life. Our small survey of clinicians in potential study sites has helped inform our thinking and planning. Although our approach and sample size have limitations, our findings highlighted variability in available services, care team composition, and access to wellbeing supports. Understanding these variations is a critical step in designing interventions that are feasible, able to be implemented at scale, and truly centred on the diverse needs of people with progressive MS. For a clinical audience, our team's efforts highlight that "usual care" looks different across clinics, regions and countries, which highlights the importance of interpreting the results of trials with usual care comparators carefully. Our work also highlights the potential value of monitoring and addressing gaps in the provision and coordination of wellbeing-focused services in routine care.

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