Digital patient experience tools in multiple sclerosis: a landscape analysis of the global Patient-Reported Outcomes in Multiple Sclerosis (PROMS) initiative

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Summary

Background Electronic health (eHealth) applications can increase the uptake of patient-reported outcomes (PROs) in people with multiple sclerosis. We aim to present the findings of the eHealth tools landscaping exercise conducted by the global Patient-Reported Outcomes for Multiple Sclerosis (PROMS) initiative.

Methods A structured survey was disseminated among identified eHealth tool developers. Metadata (up to 10 October 2024) were hosted on the Multiple Sclerosis Data Alliance catalogue, an open-access platform focussing on digital health tools in multiple sclerosis. eHealth tools' clinical domains were compared using a Kruskal–Wallis non-parametric one-way analysis of variance, based on domain-specific scores (each domain received one point for every test in which it was evaluated), followed by Dunn's post-hoc tests with Holm adjustment for multiplicity.

Findings 16 eHealth tools launched between 2014 and 2022 in Europe and North America were included, targeting people with multiple sclerosis, caregivers, and healthcare professionals, and collecting data remotely and in clinic through smartphones (n = 12), smartwatches (n = 1), and tablets or computers (n = 11). Data are used for clinical research, self-management, and real-time or visit-based clinical monitoring. Scoring showed that movement and cognition/behaviour/mood were the most represented domains. The Kruskal–Wallis test indicated significant differences across domains (p = 0.0016), with cognition/behaviour/mood evaluated more frequently than brainstem, sensory, and sleep functions. Twelve tools are implemented in 108 hospitals across Europe and North America, with approximately 33,373 downloads, 7413 people with multiple sclerosis involved in 44 research studies, and 12,503 people with multiple sclerosis using them in real life.

Interpretation We provide the first dynamic and strategic overview of available eHealth tools evaluating PROs in multiple sclerosis. Although movement and cognitive domains dominate current assessments, several clinically

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important domains remain underrepresented. The global PROMS initiative is committed to ongoing updates and stakeholder engagement for identifying gaps and needed action plans.

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Keywords: Multiple sclerosis; Patient-reported outcomes; eHealth; Digital health; Metadata

Research in context

Evidence before this study

We searched PubMed and Web of Science for articles published in English from inception through December 31st, 2024, using the search string "multiple sclerosis" AND ("patient-reported" OR "patient reported" OR PRO OR PROs OR PROM OR PROMs) AND ("digital health" OR "eHealth" OR electronic OR "electronic health"). Despite emphasisising the necessity of patient-reported outcomes (PROs) in personalised care for people with multiple sclerosis (MS), recent systematic reviews have identified and discussed challenges regarding PROs implementation and integration to electronic health (eHealth) tools. Moreover, there is an unmet need for systematic mapping and landscaping of various technical characteristics and properties in existing eHealth tools using PROs, including digital platform, purpose, governance, and domains of interest. Aiming to enhance patient-centred care through eHealth, the global Patient-Reported Outcomes for Multiple Sclerosis (PROMS) initiative has recognised the significance of cataloguing existing eHealth tools to assess functionality, implementation, and usage across real-world settings.

Added value of this study

This study presents the first structured, multinational landscaping exercise of eHealth tools that collect and use PROs in multiple sclerosis. A survey developed by a dedicated PROMS working group was completed by eHealth tool developers and metadata from 16 tools were systematically collected and hosted in a living, open-access online catalogue. We provide a comprehensive overview of the tools' technology and platform, domains of interest, governance, data privacy, and current clinical usage. Moreover, this study quantitatively investigates the domains that are prioritised or underrepresented in existing tools. Through its evolving infrastructure for the collection and presentation of metadata, this work promotes transparency, multidisciplinarity, interoperability, and stakeholder engagement across people with multiple sclerosis (pwMS), clinicians, researchers, and the industry.

Implications of all the available evidence

Although eHealth tools for PROs collection and use are expanding and working towards holistic evaluation of pwMS, our results indicate the prioritisation of a narrow set of domains, especially motor and cognitive function. While this finding may reflect a growing recognition of the need to target the most debilitating symptoms, it may also indicate a tendency to neglect other patient-relevant areas such as vision, sleep, sensory or autonomic symptoms, limiting the usage of eHealth tools in routine practice. Our study underscores the need for balanced domain coverage and through the PROMS eHealth tools living catalogue we support further harmonisation and validation of PROs that can reflect the diverse and fluctuating symptomatology of MS. Moreover, by serving as a shared metadata inventory, the catalogue offers a valuable opportunity for collaboration between eHealth tool developers, researchers, and healthcare systems to promote inclusive, patient-centred innovation in MS care.

Introduction

In recent years, there has been a shift in healthcare delivery models emphasising more patient-centred approaches.[1] Patient engagement in decision-making and disease management is invaluable in chronic neurological conditions like multiple sclerosis, where symptom variability and disease progression pose unique challenges for healthcare providers.[2] Traditional clinical measures, such as clinical or imaging outcomes, often fail to capture the full spectrum of the disease's effects on patients' well-being.[1,2] In this context, patient-reported outcomes (PROs) have emerged as insightful tools, allowing people with multiple sclerosis to report their experiences (actively and passively), symptoms, and quality of life (QOL) factors to clinicians and researchers and providing a comprehensive understanding of multiple sclerosis and its management.[3] With the increasing complexity of multiple sclerosis care, PROs offer valuable complementary information that may support more personalised management and shared decision-making, although their formal incorporation into treatment decision-making is still at an early stage.[2,4,5]

Moreover, developing practical and usable tools (e.g. apps, wearables, other devices) is needed to enable the routine capture of multiple changing outcomes over

time, which requires acceptability and therefore a user-friendly and useful solution from the perspectives of people with multiple sclerosis.[6] Electronic health applications can facilitate continuous PROs collection,[7] while developers and researchers can enhance their analysis and interpretation through emerging data science methods. Innovative and personalised monitoring for people with multiple sclerosis[8] can overcome recall bias often associated with conventional follow-up schedules such as 6-month interval visits, paving the way for tailored and data-driven telemedicine. In light of these advancements, the global Patient Reported Outcomes for Multiple Sclerosis (PROMS) initiative, a multi-stakeholder collaboration enabling science with patient input in multiple sclerosis research and care,[3] has developed a dedicated working group for electronically collected PROs, through the investigation of electronic health (eHealth) using PRO measures.[9] Aligning with the EU-funded MULTI-ACT model for inclusive healthcare and equitable access to treatment or support systems regardless of geographic or socioeconomic barriers,[10] the PROMS initiative aims to set a standard for inclusive, patient-engagement research and care that leverages digital health innovations to better understand and meet the diverse needs of people with multiple sclerosis. This paper introduces the PROMS eHealth tools catalogue, summarising the PROMS landscaping exercise and offering a living reference on eHealth tools using active and passive PRO measures for people with multiple sclerosis.

Methods

Overview

Starting from April 2021, a dedicated PROMS working group, consisting of people with multiple sclerosis, multiple sclerosis neurologists, researchers and industry affiliates, had regular virtual meetings to determine the landscaping exercise's scope and approach. We designed a survey (finalised in April 2022) to collect descriptive information on the organisational information, background/purpose, how and which data are collected, using which technology and platform, governance, data privacy/management, analytics and visualisation, publications, certification and validation, and current state of the available eHealth tools that collect relevant PROs for people with multiple sclerosis.

A list of candidate eHealth tool developers was compiled via internet searches, conference attendance and the PROMS network, including the working group members and collaborators. Consistent with the scope of this landscaping exercise, this approach aimed to capture tools explicitly designed for multiple sclerosis. Forty official invitation letters were sent to these candidate eHealth tool developers (October 2022–March 2023). Additional advertising and an open call was launched via the PROMS website and flyers that were distributed at ECTRIMS 2022 (Amsterdam, 26–28 October). Developers who accepted the invitation were provided with additional information and were asked to update the shared metadata at regular intervals. The collected metadata (as of the 10th of October 2024) were hosted on the Multiple Sclerosis Data Alliance catalogue (https://msda.emif-catalogue.eu/), which can be browsed by interested parties after creating a free account.[11,12] All data custodians who shared metadata can edit and update the metadata of their eHealth tool whenever needed.

Statistics

Differences in domain-specific scores across 12 clinical domains (movement, balance, sensory functions, vision, brainstem functions, bladder/bowel/sexual functions, cognition/behaviour/mood, fatigue, sleep, functional capacity, activities of daily living, and QOL) were evaluated using a Kruskal–Wallis non-parametric one-way ANOVA. Each domain received one point for every test in which it was evaluated across all eHealth tools, yielding a domain-specific score for comparison. This non-parametric approach was selected after violations of normality and variance assumptions were identified (Shapiro–Wilk and Levene's tests). Significant omnibus results were followed by Dunn's post-hoc pairwise comparisons with Holm adjustment for multiplicity. Analyses were performed in R version 4.1.2 (R Foundation for Statistical Computing) using the stats package (version 4.3.1), car package (version 3.1–2), and FSA package (version 0.9.5). A two-sided p value of less than 0.05 was considered statistically significant.

Ethics

This study did not involve human participants, patient-level data, or intervention, and therefore did not require approval from an institutional review board or ethics committee. The landscaping exercise was based on metadata voluntarily provided by eHealth tool developers and on publicly available information hosted in the Multiple Sclerosis Data Alliance catalogue. No identifiable personal data were collected or analysed. Consequently, informed consent from individuals was not required.

Role of funding source

There was no funding source for this study.

Results

Of the 40 invitations sent, 18 responses were received. Two developers did not participate (one did not collect patient-reported or personal data; one considered inclusion premature). The following 16 eHealth tools were identified: Amiria, CogEval, dreaMS, Elevida, FLOODLIGHT, icompanion, Konectom, Levidex, Mobilise-D, More Stamina, MS sherpa, MSReactor, MSCopilot, Neurokeys, Open MS Bioscreen, and Telemonica.[13–27] Survey respondents encompassed executive leadership

of eHealth applications (n = 5), program and operations (n = 1), product and technology (n = 2), clinical and medical teams (n = 4), as well as research and academics (n = 4). With the exception of Mobilise-D, a multicentric and international 5-year project (2019–2024) funded by the Innovative Medicines Initiative, the eHealth tools were launched in Europe (n = 12), America (n = 2) and Australia (n = 1) between 2014 and 2022 and their development was financed by private or public companies, healthcare/pharma industry, non-profit organisations or MedTech industry (Table 1). Lead developers included MedTech companies, Pharma/Biopharma companies and Academic or Healthcare organisations. Two tools explicitly reported "Conformité Européenne" (CE) marking, indicating compliance with European Union medical device regulations.[15,25]

A list of publications regarding the tools' certification and validation is provided in our Supplementary Material (Table S1).

Data are used for research in the majority of eHealth tools (n = 11), but also for self-management of people with multiple sclerosis (n = 10), monitoring by healthcare providers in real time or during clinic visits (n = 8), as well as for data reporting on behalf of people with multiple sclerosis during clinic visits (n = 6). The main goals for patient use are QOL diary functions, a multiple sclerosis symptom diary, self-measuring of neurological function and enhancement of healthcare provider–patient interaction. Target users differ among eHealth tools, with most targeting people with multiple sclerosis (n = 15), while others target caregivers (n = 6) and healthcare providers (n = 6).

General healthcare applications of the eHealth tools herein reported included support of clinical research and clinical decision making, healthcare quality management and data collection for observational studies. Regarding clinical research the tools prioritise QOL assessment, multiple sclerosis activity measuring and understanding prognosis and treatment response prediction and measurement. Data are collected remotely in fourteen tools and in the clinic in nine. The process of data collection is active, passive or through

eHealth tool	Company name	Lead developer	Other organisations involved	Financing	Country	Launch year
Amiria	Gaia	MedTech company	NA	Public/private company	Germany	2018
CogEval	Biogen Digital Health	Pharma/Biopharma	NA	Healthcare/pharma industry	United States	2018
dreaMS	RC2NB/Indivi	Academic/Healthcare organisation; MedTech company	Academic/Healthcare; MedTech company; IT company	Public/private company; Non-profit organisation; Healthcare/pharma industry; MedTech industry	Switzerland	2018
Elevida	Gaia	MedTech company	NA	Public/private company	Germany	2014
FLOODLIGHT	F. Hoffmann-LaRoche AG, Switzerland	Pharma/Biopharma	Academic/Healthcare; Pharma/Biopharma; Patient association	Healthcare/pharma industry	Switzerland	2016
icompanion	icometrix	MedTech company	NA	Public/private company	Belgium	2019
Konectom	Indivi	MedTech company	NA	Public/private company	Switzerland	2020
Levidex	GAIA	MedTech company	NA	Public/private company	Germany	2022
Mobilise-D[a] (e-SC, Clario McRoberts)[b]	IMI Consortium Mobilise-D	Pharma/Biopharma; Academic/Healthcare organisation; MedTech company	32 additional research partners including universities, hospitals, global pharmaceutical companies, and technical enterprises	Public/private company	Multicentric (16 countries)	2019
More Stamina	University of Oulu	Academic/Healthcare organisation; MedTech company	NA	Non-profit organisation; Healthcare/pharma industry; MedTech industry	Finland	2018
MS sherpa	Sherpa BV	MedTech company	MedTech company; IT company	Public/private company; Healthcare/pharma industry; MedTech industry	Netherlands	2016
MSCopilot	Ad Scientiam	MedTech company	NA	Healthcare/pharma industry; Other	France	2019
MSReactor	Monash University	Academic/Healthcare organisation	MedTech company	Non-profit organisation; Healthcare/pharma industry	Australia	2015
Neurokeys	Neurocast B.V.	MedTech company	NA	Public/private company	Netherlands	2018
Open MS Bioscreen	University of California San Francisco (UCSF) Bove Lab	Academic/Healthcare organisation	NA	Non-profit organisation	United States	2018
Telemonica	Telemonica	MedTech company	NA	Public/private company	France	2020

IT, information technology; IMI, Innovative Medicine Initiative; T, timepoint; NA, not applicable. [a]Mobilise-D recruited cohorts for various disorders. Data herein presented only regard to the Multiple Sclerosis cohorts. [b]Mobilise-D used web tools from e-Science Central, McRoberts, and Clario. Mobilise-D also distributed inertial measurement unit sensors from McRoberts and Axivity which were programmed using the MyMcRoberts platform. Mobilise-D had 1 visit (T) every 6 months for 24 months (i.e. T1-T5) starting with baseline at T1.

Table 1: **Detailed organisational information including lead developers.**

questionnaires, according to the tests used. In Mobilise-D however, data were also collected with the use of a body-worn or body-fixed inertial measurement unit. Business models include use as a research tool (n = 11) and reimbursed medical devices (n = 7), whereas 7 eHealth tools are free for people with multiple sclerosis and 2 are free for healthcare providers. In general, eHealth tools are available for public access (n = 7) or as research projects (n = 12). A detailed radial plot for the purpose of included eHealth tools is presented in Fig. 1.

A variety of tests are used for the collection of data regarding PROs. The tests' clinical domains of interest focus on movement in upper and lower extremities (including muscle strength, spasticity, hand function and dexterity), balance, sensory functions, vision, brainstem functions, bladder/bowel and sexual functions, cognition/behavior/mood, fatigue, sleep, functional capacity, activities of daily living, and QOL. The recommended frequency of tests ranges from continuous to four times a year. Table S2 provides further insights, including information about test validation.

In the Kruskal–Wallis test, the overall model demonstrated a statistically significant difference in domain-specific scores ($p = 0.0016$), confirming that certain domains were evaluated more frequently than others across eHealth tools. Post-hoc Dunn tests with Holm correction identified prioritisation in the cognition/behavior/mood domain compared with brainstem functions ($p = 0.0022$), sensory functions ($p = 0.024$), and sleep ($p = 0.030$). Descriptively, movement (total score: 50) and cognition/behavior/mood (total score: 45) remained the most frequently evaluated domains across eHealth tools, whereas domains such as vision (15), sensory functions (11), bladder/bowel/sexual functions (13), sleep (10), and brainstem functions (7) were less frequently tested (Table S3). Fig. 2 presents a radar chart illustrating each eHealth tool's main clinical domains of interest and mode of data collection.

Additional data are collected in fourteen eHealth tools (Amiria, CogEval, dreaMS, Elevida, FLOODLIGHT, icompanion, More Stamina, MSCopilot, MSReactor, Neurokeys, Open MS Bioscreen, Telemonica, Mobilise-D), such as age, gender, height, weight, body mass index and relapses. Moreover, icompanion collects data regarding type of multiple sclerosis, year of diagnosis, MRI data, type and duration of treatment, as well as physical and mental status. Open MS Bioscreen collects data regarding age of onset, multiple sclerosis type, city, education, race, employment, smoking history, and results of cerebrospinal fluid analysis. Lastly, CogEval collects data on education levels. In Mobilise-D collected data also regarded ethnicity, nutritional status, frailty, disease type, immune therapy given, comorbidities, as well as mask usage during the COVID-19 pandemic.

Adherence methods were employed in twelve eHealth tools, among which automated prompts were the most popular (n = 9), followed by gamification (n = 7), i.e., the use of game-like elements to encourage engagement.

The herein presented eHealth tools can be used with smartphones (n = 12), smartwatches or smart rings (n = 1) and tablets/computers (n = 11). In Mobilise-D body-worn or body-fixed inertial measurement unit sensors were also used (McRoberts, Axivity).

The majority are available for usage through personal digital devices, requiring internet connection, but no assistance by healthcare providers during setup or during usage. Only three eHealth tools are open-source and thirteen of them provide help desk availability (Table S4).

Managing eHealth tools involves frameworks that ensure the secure, ethical handling of patient data and compliance with applicable regulations, such as regional data-protection standards (e.g., General Data Protection Regulation [GDPR], Europe; or Health Insurance Portability and Accountability Act [HIPAA], United States). Ten eHealth tools reported having a model for sharing patient-level data with external partners. Use of an electronic informed consent and agreement to terms and conditions was reported in eight and fifteen tools, respectively. Thirteen of them have been used in virtual clinical trials/studies. More information is provided in Table S5.

Currently, eHealth tools are available as research projects (n = 13) or can be publicly accessed (n = 7) (Fig. 1). Access in the eHealth tools is secured mostly through email-password protection, two-factor authentication or log-in codes given by the study coordinators. Compliance with cybersecurity standards and regulations is also reported for some eHealth tools. Use of data encryption is clearly mentioned in ten tools and a unique identifier for each subject is used in twelve tools. Six tools report the existence of a protocol for linkage to other data sources. However, only icompanion has been integrated in an electronic medical record. Similarly, only Telemonica and MSReactor have been integrated into registry records. Further details are presented in Table S6.

Of the 16 eHealth tools, 12 are being used in 108 hospitals across 13 countries in Europe and North America (Fig. 3). Detailed information of each eHealth tool's date of last update, approximate number of downloads and users are included in Table S7. In total, approximately 33,373 downloads, 7413 people with multiple sclerosis in 44 research studies and 12,503 people with multiple sclerosis in real life use have been reported (Fig. 4).

Discussion

We herein comprehensively present the results of the landscaping exercise, performed by a dedicated PROMS working group. The eHealth tool catalogue reflects the

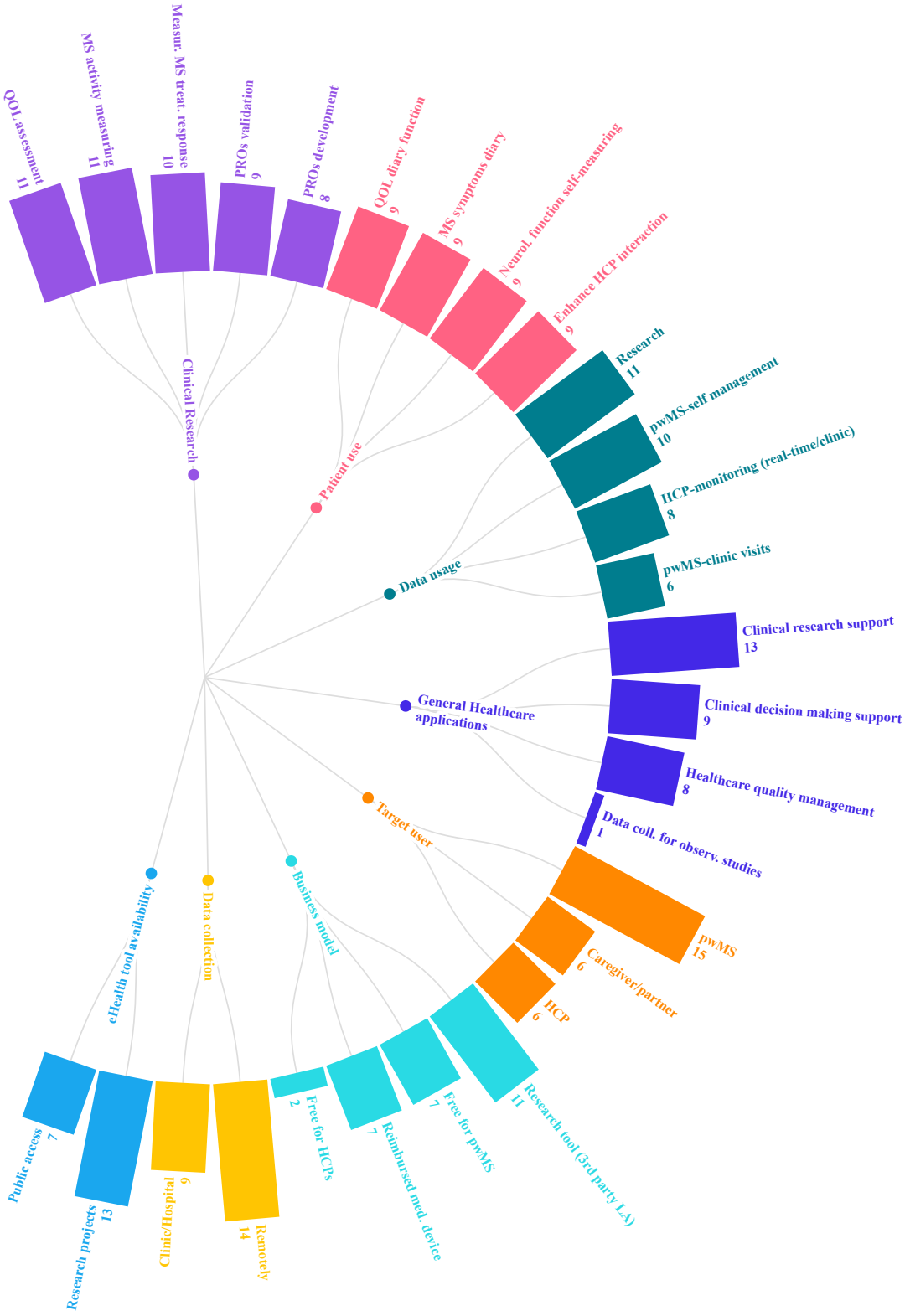

Fig. 1: Purpose of eHealth tools across functional and operational domains. Radial bar chart illustrating the distribution of purposes reported for the included eHealth tools, grouped into key domains. An interactive version of the figure can be found here: https://public.flourish.studio/visualisation/19417843/. MS, Multiple Sclerosis; pwMS, people with Multiple Sclerosis; QOL, quality of life; PROs, patient-reported outcomes; HCP, healthcare provider; LA, license agreement.

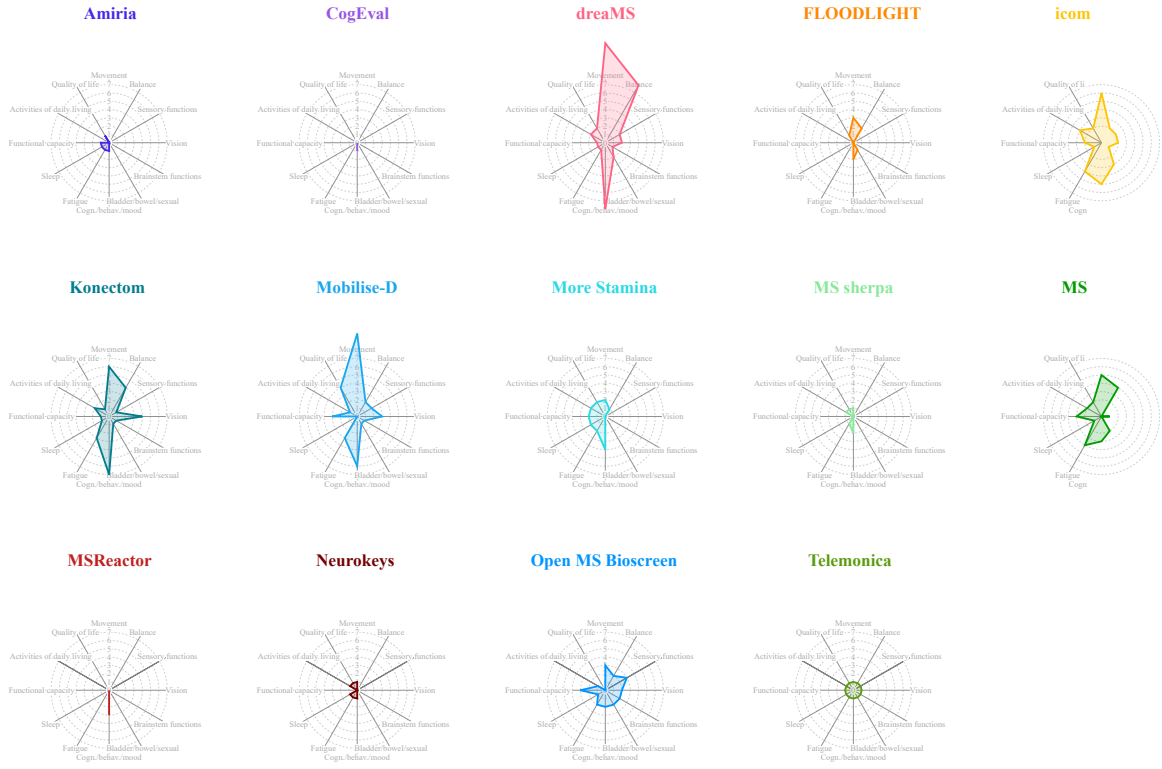

Fig. 2: Clinical domains of interest assessed by each eHealth tool. Radar plots illustrating the clinical domains evaluated across the 16 eHealth tools. Each domain (e.g., movement, balance, sensory functions) received one point for every test within the tool that assessed it, generating a domain-specific score. Colours differentiate individual tools. An interactive version of the figure can be found here: https://public.flourish.studio/visualisation/20316800/.

industry's engagement in navigating and integrating PROs in multiple sclerosis from research to care. Thanks to their compatibility with various electronic devices, eHealth tools could eventually facilitate patient participation in monitoring their health and support diverse clinical research applications. Digital PROs are being explored in clinical research focused on disease progression, prognostication and treatment response, although strong evidence for their predictive value and impact on therapeutic decisions remains to be established. Interestingly, functions associated with movement (e.g., hand function, dexterity, spasticity) and cognition/behavior/mood are evaluated more often in eHealth tools. This pattern may partly reflect current prioritisation in clinical practice, where routine assessment comprises mostly readily quantifiable motor and cognitive functions. Focussing on domains that clinicians already evaluate and that lend themselves to objective measurement may also facilitate early acceptance of digital PROs in clinical and research settings. However, it also underscores the need to expand domains of interest to gain a more comprehensive understanding of patients' overall status. Although domains such as vision, sleep, fatigue, as well as sensory, bladder/bowel/sexual and brainstem functions can be severely debilitating, they received low total scores in our analysis. This possibly indicates a need for further assessment and validation of relevant, robust, and scalable PRO measures in these areas in the future that can lead to their smooth integration in existing or novel eHealth applications and thus the creation of personalised domain-specific tools. This observation is in line with results from the recent international PROMS survey, that engaged more than 5000 people with multiple sclerosis in co-designing and piloting and identified the most prominent functional domains and interdependencies that matter to them.[28] Lastly, despite missing data in certain survey fields posing a limitation to the results herein presented, the PROMS living catalogue represents a continuum, making this paper a snapshot of an ever-evolving dataset that lays the groundwork for leveraging technological innovations to expand and refine PRO assessments across all multiple sclerosis domains.

The significance of PROs and PRO measures in detecting previously unnoticed disease progression and their potential in complementing objective clinical measures as endpoints in clinical trials is widely

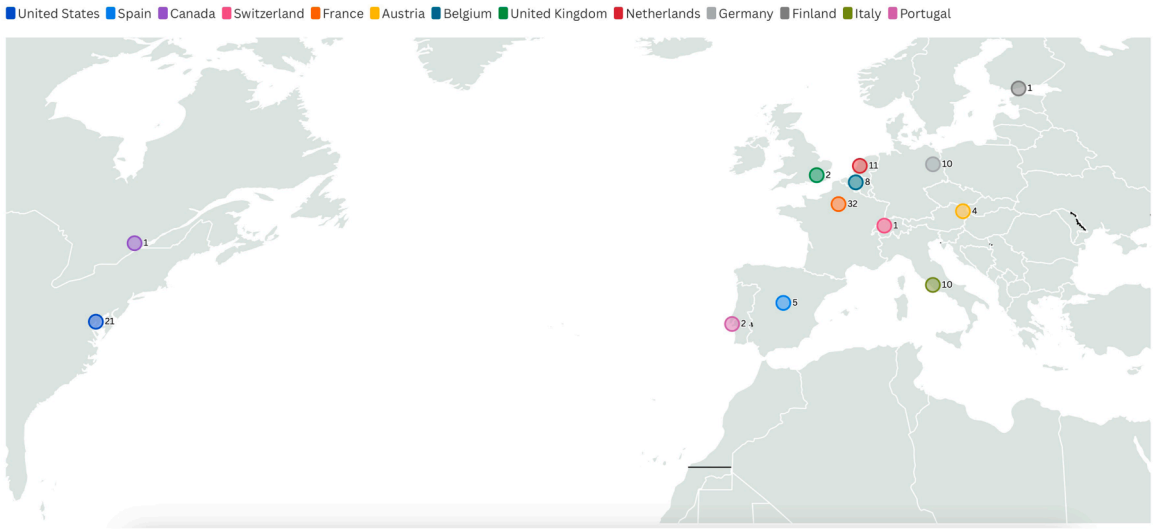

Fig. 3: Hospital use of eHealth tools. Geographic distribution of hospitals currently implementing one or more eHealth tools included in the PROMS landscape analysis. Each circle marks a different country, and the overlaid numeric label indicates the number of hospitals in that country using these tools. An interactive version of the figure can be found here: https://public.flourish.studio/visualisation/26670789/.

recognised.[7,29] Objective metrics that monitor functional domains over time could improve the transition of multiple sclerosis interventions through clinical trial phases II and III, thus enhancing access to care. Various generic (e.g., Patient-Reported Outcomes Measurement Information System [PROMIS], Quality of Life in Neurological Disorders [Neuro-QOL]) and multiple sclerosis-specific PROs (e.g., Multiple

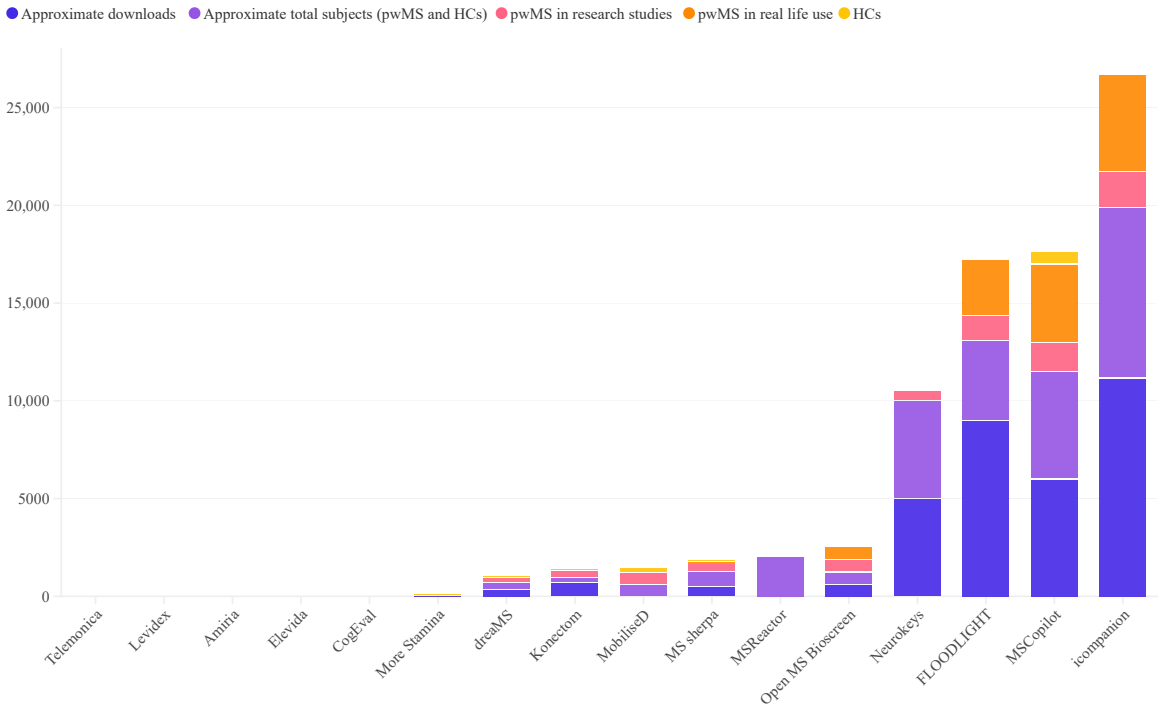

Fig. 4: Current state of eHealth tools. Stacked bar chart illustrating, for each eHealth tool, the approximate number of downloads, total subjects (pwMS and HCs), pwMS enrolled in research studies, pwMS using the tool in real-life settings, and the total number of HCs who have used the tool. An interactive version of the figure can be found here: https://public.flourish.studio/visualisation/20316965/. pwMS, people with Multiple Sclerosis; HCs, healthy controls.

Sclerosis Quality of Life scales, and Multiple Sclerosis Impact Scale-29 [MSIS-29]) assess different aspects of health and well-being, whereas the combination of PROs with clinician-assessed outcomes can enrich trial results by reflecting patients' views on treatments' efficacy and impact. Moreover, patient-centred care is highly emphasised in clinical multiple sclerosis research, with notable PROs variations in different multiple sclerosis subtypes, especially between relapsing-remitting and progressive multiple sclerosis. The effectiveness of PROs in tracking and predicting disability progression and transitions to progressive multiple sclerosis has also been highlighted, showing that subtle and nonspecific symptoms appear years before clinically detected as disability accrual.[2] At present, however, there is insufficient evidence that PRO measures, regardless of collection method, independently predict long-term disease evolution in multiple sclerosis, and their use in routine clinical practice should therefore be interpreted with caution. Moreover, wider adoption will require further standardisation across instruments and platforms, as well as clearer criteria to define and interpret clinically meaningful within-person change (improvement or worsening) over time. These limitations have important methodological implications for clinical trial design and analysis and therefore underscore the need for rigorous and reliable collection and interpretation of PRO measures in clinical trial settings, to avoid bias and misclassification. Type 2 errors, where a true effect is mistakenly considered insignificant, are critical in multiple sclerosis clinical trials as they can lead to the rejection of beneficial treatments.[3] The development and performance of PRO measures can significantly influence the occurrence of type 2 errors. New statistical methods in clinical trials, including composite endpoints and personalised priority lists for treatment outcomes, are being introduced to enhance precision and consider individual patient variations, leading to more personalised and accurate assessments of treatment efficacy.[3] Digital health platforms can potentially reduce missing information and enhance sensitivity to detect subtle changes through more frequent at-home assessments and by integrating PROs with objective sensor measurements.[7,8]

To enhance the integration of PROs with clinical metrics, recent advances in digital health tools have shown promising potential. Wearable devices and smartphone applications validated in people with multiple sclerosis offer a unique opportunity to continuously collect real-world data, beyond episodic clinical evaluations. For instance, validated algorithms can accurately monitor digital mobility outcomes like gait, cadence, and stride length in real-world settings, despite the challenges posed by slower walking speeds and shorter walking bouts, which are often seen in patients with significant gait impairments.[30] Additionally, wearable sensors generating continuous digital biomarkers can objectively monitor functions such as upper limb dexterity, sleep patterns, or fatigue levels, that complement PRO measures and enrich clinical assessment.[8] Moreover, the employment of smartphone technology has proven feasible in capturing the daily lived experiences of people with multiple sclerosis.[6] Apart from monitoring symptoms and functional abilities this approach also helps identify environmental factors, such as temperature, that may impact disease burden or worsen fatigue. Continuous smartphone-derived passive data streams, such as location and movement, can reveal subtle fluctuations and symptom triggers that could otherwise be missed.[7] However, in the fast-evolving landscape of telemedicine and wearable devices the need for rigorous technical validation and user acceptability is underscored, so that the accuracy and reliability of these tools in clinical practice is ensured.[6,7] In this regard, early feasibility studies demonstrated engagement and adherence of people with multiple sclerosis to smartphone- and sensor-based monitoring over extended periods with high user satisfaction,[15,17] indicating that people with multiple sclerosis value intuitive and minimally burdensome digital tools that can empower self-management and improve communication with healthcare providers, promoting shared decision-making and timely interventions. At the same time, exclusive reliance on digital platforms may leave behind people with multiple sclerosis who have limited internet access, lack appropriate devices, or face challenges with digital literacy. These inequalities may introduce selection bias and restrict how representative PRO data are in real-world settings, emphasising the need for accessible design and alternative modes of data collection. For this reason, digital PRO measures should complement rather than replace traditional formats, ensuring that people with multiple sclerosis who face technological barriers remain fully represented in clinical care and research.

The PROMS initiative, headed by the European Charcot Foundation and the Multiple Sclerosis International Federation (MSIF), with the Italian Multiple Sclerosis Society serving as the lead agency on behalf of the Global MSIF Movement, aims to enhance the impact of patient input on multiple sclerosis research and care. With participatory governance and a global network of stakeholders, the PROMS initiative seeks to unify views on PROs for multiple sclerosis, benefiting patients, healthcare providers and regulatory agencies.[9] Even though both the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) guidelines advocate for PROs and support their use, there are yet no specific regulatory details.[31,32] Addressing the application of PRO measures from clinical trials to everyday care requires the engagement of all stakeholders, including regulatory agencies like

the FDA and EMA, pharmaceutical companies, healthcare providers, insurance agencies, and patients for further validation, ensuring a standardised set of valid, reliable, and globally applicable multiple sclerosis-specific PROs.[1] Beyond issues of predictive validity and interpretability, digital PRO measures face persistent barriers to large-scale integration, including lack of harmonisation across data platforms, scoring systems, and domain definitions. Shared metadata standards, with a common set of definitions for symptoms and functional domains, as well as harmonised scoring scales and response options, could enhance comparability and clinical usefulness of different eHealth platforms. Furthermore, agreement on core outcome sets for multiple sclerosis, including minimum domain coverage, should be co-developed with people with multiple sclerosis, clinicians, regulators, and industry to ensure that digital PRO measures reflect priorities shared across stakeholders. PROMS, together with future initiatives in this field, can advance this alignment by fostering the multidisciplinary and multistakeholder collaboration required to establish shared, clinically meaningful digital PRO measure standards. Within this evolving landscape, regulatory engagement will also play a key role; however, while two tools reported CE marking and several have been used within clinical trials, detailed information on direct regulatory interactions or validation submissions was not captured within this landscaping exercise. A further consideration is the long-term sustainability of the organisations developing these tools. Should a platform be discontinued, responsibilities for data stewardship, patient access to historical data, and continuity of governance would need to be clearly defined, although such aspects were beyond the scope of this mapping exercise.

Common challenges for PROs in multiple sclerosis include items that may not reflect all patients' priorities, gaps in domain coverage, complexities in scoring and interpretation for clinicians, and missing responses, which are an inherent feature of real-world data. Addressing these limitations will be important to support broader clinical adoption and ensure that PRO measures remain meaningful and actionable for people with multiple sclerosis. Standardised assessments have provided evidence that existing PRO measures often lack justification for their use and sufficient psychometric quality, and generic scales may miss areas crucial to specific patient groups.[2] Involving people with multiple sclerosis in developing digital devices and standardising PROs ensures they meet user needs and enhance data collection. It is crucial to differentiate between PROs focussing on patient-reported data and patient-centric outcomes addressing specific concerns, as many PROs may overlook QOL adaptations in people with multiple sclerosis. The relative importance of different symptoms varies considerably among people with multiple sclerosis, with a uniform PRO measure set potentially failing to reflect individual priorities or capture the issues that matter most to each patient. Flexible and patient-informed approaches are needed, allowing PRO measure contents to align more closely with individual experiences of multiple sclerosis. A further challenge concerns the interpretation of change in PRO measure scores over time, as people with multiple sclerosis may differ markedly in what they consider a meaningful improvement or deterioration. Clinician-derived thresholds do not always align with patient perspectives, and a single definition of meaningful change may overlook important individual differences in disability trajectories. Employment of patient-specific baselines or individualised thresholds may aid meaningful interpretation of longitudinal PRO measure assessments.

When addressing future directions and perspectives of eHealth tools, one should not omit significant growth areas like machine learning and artificial intelligence (AI), which will shift digital health towards decision support, as well as the Internet of Things, an emerging digital health area that involves interconnected sensors interacting with patients daily.[8] Through analysis of large volumes of data from sensors and PROs, AI could predict disease exacerbations or progression, but also assist clinicians by synthesising real-world inputs offering an output of actionable and personalised clinical suggestions.[6,8] While these approaches have limitations, they benefit from being based on meaningful predefined data features and could offer tremendous capabilities regarding complex interpretation of outcomes such as PROs.

We emphasise the importance of integrating eHealth tools and PROs into routine clinical decision-making. Beyond enhancing patient engagement, these tools are increasingly recognised for their potential to detect subtle and subclinical disease changes described as smouldering progression, referring to slow, gradual worsening that occurs independently of relapses and may not be captured through conventional clinical assessments.[33] Securing reimbursement from healthcare insurance providers is crucial to ensure their widespread adoption and long-term sustainability. Institutional support is crucial for seamless management of patient-generated eHealth data and incorporation into clinical workflows or electronic medical record. We also underscore the necessity of healthcare providers being trained in the effective use of PRO measures, as well as the vital role of caregivers for the achievement of long-term patient adherence to eHealth tools.

In conclusion, the PROMS initiative exemplifies a significant advancement in integrating patient perspectives into multiple sclerosis care and research. The eHealth tools living catalogue represents a first step of a comprehensive framework for the collection and use of PROs. The identified eHealth tools facilitate remote

patient management and enhance patient independence. However, their focus on movement and cognitive domains possibly underscores the need to broaden the tools' scope to include other critical aspects for people with multiple sclerosis. While efforts to improve mapping and interoperability of existing eHealth tools are ongoing, continued stakeholder engagement is essential for ensuring eHealth tools' relevance and effectiveness. PROMS will promote inclusive engagement of people with multiple sclerosis for richer discussions to define priorities for validation of promising and valuable eHealth tools and to trace the path for further developments addressing still largely unmet needs.

Contributors

Vasilis-Spyridon Tseriotis: Data curation, Formal Analysis, Methodology, Software, Data updating/cleaning/wrangling, Statistics, Visualisation, Writing.

Liesbet M. Peeters: Conceptualisation, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing–review & editing, Visualisation, Supervision, Project administration, Part of working group, Project lead.

Lotte Geys: Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing–review & editing, Visualisation, Supervision, Project administration, First phase of contacting developers and metadata collection.

Marcus D'Souza: Methodology, Validation, Formal analysis, Investigation, Data curation, Writing–review & editing, Supervision, Project administration, Contacting developers and metadata collection.

Johan van Beek: Data curation, Investigation, Methodology, Resources, Validation, Writing—review & editing.

Ludwig Kappos: Member of working group, Conceptualisation, Contribution of data, Discussion of results, Critical review and edits of the manuscript, Approval of final version.

Valerie Block: Member of working group, Reviewing and editing the paper.

Patrick Vermersch: Member of working group, Reviewing and editing the paper.

Paola Zaratin: Conceptualisation, Methodology, Validation, Investigation, Resources, Data curation, Writing–review & editing.

Robert Hyde: Methodology, Validation, Formal analysis, Investigation, Resources, Writing–review & editing.

Letizia Leocani: Conceptualisation, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing–review & editing, Visualisation, Supervision, Co-Chair of working group, Project lead, Active role in writing and reviewing the paper.

All authors read and approved the final version of the manuscript. Vasilis-Spyridon Tseriotis, Liesbet M. Peeters and Letizia Leocani have verified the underlying data.

Data sharing statement

All data presented in the paper are publicly available online on the Multiple Sclerosis Data Alliance catalogue (https://msda.emif-catalogue.eu/).

Declaration of interests

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Liesbet M. Peeters has no conflicts of interest to disclose other then being the chair of the Multiple Sclerosis Data Alliance, which is non-for-profit organisation acting under the umbrella of the European Charcot Foundation and funded by a consortium of private partners, recently being Novartis, Janssen, Merck, Roche, Bristol-Myer-Squibb, Biogen and other.

Lotte Geys has no conflicts of interest to disclose.

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Johan van Beek is an employee of Biogen Inc.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2026.103821.

References

1 Nowinski CJ, Miller DM, Cella D. Evolution of patient-reported outcomes and their role in multiple sclerosis clinical trials. *Neurotherapeutics*. 2017;14:934–944.

2 Lerede A, Rodgers J, Middleton RM, et al. Patient-reported outcomes in multiple sclerosis: a prospective registry cohort study. *Brain Commun*. 2023;5. https://doi.org/10.1093/BRAINCOMMS/FCAD199.

3 Zaratin P, Samadzadeh S, Seferoğlu M, et al. The global patient-reported outcomes for multiple sclerosis initiative: bridging the gap between clinical research and care – updates at the 2023 plenary event. *Front Neurol*. 2024;15:1407257.

4 Gil-Perotin S, Bernad L, Reddam S, Ferrer-Pardo C, Navarro-Quevedo S, Solís-Tarazona L. Patient's perspective in clinical practice to assess and predict disability in multiple sclerosis. *Sci Rep*. 2022;12. https://doi.org/10.1038/S41598-022-23088-X.

5 Abdelhak A, Antweiler K, Kowarik MC, et al. Patient-reported outcome parameters and disability worsening in progressive multiple sclerosis. *Mult Scler Relat Disord*. 2024;81. https://doi.org/10.1016/j.msard.2023.105139.

6 Helme A, Kalra D, Brichetto G, et al. Artificial intelligence and science of patient input: a perspective from people with multiple sclerosis. *Front Immunol*. 2025;16. https://doi.org/10.3389/FIMMU.2025.1487709.

7 Heesen C, Berger T, Riemann-Lorenz K, et al. Mobile health interventions in multiple sclerosis: a systematic review. *Mult Scler*. 2023;29:1709.

8 Matthews PM, Block VJ, Leocani L. E-health and multiple sclerosis. *Curr Opin Neurol*. 2020;33:271–276.

9 Zaratin P, Vermersch P, Amato MP, et al. The agenda of the global patient reported outcomes for multiple sclerosis (PROMS) initiative: progresses and open questions. *Mult Scler Relat Disord*. 2022;61:103757.

10 Zaratin P, Bertorello D, Guglielmino R, et al. The MULTI-ACT model: the path forward for participatory and anticipatory governance in health research and care. *Health Res Policy Syst*. 2022;20:1–9.

11 Peeters LM, Parciak T, Kalra D, et al. Multiple sclerosis data alliance - A global multi-stakeholder collaboration to scale-up real world data research. *Mult Scler Relat Disord*. 2021;47. https://doi.org/10.1016/J.MSARD.2020.102634.

12 Geys L, Parciak T, Pirmani A, et al. The multiple sclerosis data alliance catalogue: enabling web-based discovery of metadata from real-world multiple sclerosis data sources. *Int J MS Care*. 2021;23:261–268.

13 Ratajska A, Zurawski J, Healy B, Glanz BI. Computerized cognitive behavioral therapy for treatment of depression in multiple sclerosis: a narrative review of current findings and future directions. *Int J MS Care*. 2019;21:113.

14 Rao SM, Losinski G, Mourany L, et al. Processing speed test: validation of a self-administered, iPad®-based tool for screening cognitive dysfunction in a clinic setting. *Mult Scler*. 2017;23:1929–1937.

15 Woelfle T, Pless S, Reyes O, et al. Reliability and acceptance of dreaMS, a software application for people with multiple sclerosis: a feasibility study. *J Neurol*. 2023;270:262–271.

16 Pöttgen J, Moss-Morris R, Wendebourg JM, et al. Randomised controlled trial of a self-guided online fatigue intervention in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2018;89:970–976.

17 Midaglia L, Mulero P, Montalban X, et al. Adherence and satisfaction of Smartphone- and smartwatch-based remote active testing and passive monitoring in people with multiple sclerosis: nonrandomized interventional feasibility study. *J Med Internet Res*. 2019;21(8):e14863. https://www.jmir.org/2019/8/e14863.

18 Van Hecke W, Costers L, Descamps A, et al. A novel digital care management platform to monitor clinical and subclinical disease activity in multiple sclerosis. *Brain Sci*. 2021;11:1171.

19 Scaramozza M, Chiesa PA, Zajac L, et al. Konectom™ cognitive processing speed test enables reliable remote, unsupervised cognitive assessment in people with multiple sclerosis: exploring the use of substitution time as a novel digital outcome measure. *Mult Scler*. 2024. https://doi.org/10.1177/13524585241259650.

20 Krause N, Riemann-Lorenz K, Rahn AC, et al. 'That would have been the perfect thing after diagnosis': development of a digital lifestyle management application in multiple sclerosis. *Ther Adv Neurol Disord*. 2022;15. https://doi.org/10.1177/17562864221118729/ASSET/IMAGES/LARGE/10.1177_17562864221118729-FIG2.JPEG.

21 Mikolaizak AS, Rochester L, Maetzler W, et al. Connecting real-world digital mobility assessment to clinical outcomes for regulatory and clinical endorsement-the Mobilise-D study protocol. *PLoS One*. 2022;17. https://doi.org/10.1371/JOURNAL.PONE.0269615.

22 Giunti G, Rivera-Romero O, Kool J, et al. Evaluation of more stamina, a Mobile app for fatigue management in persons with multiple sclerosis: protocol for a feasibility, acceptability, and usability study. *JMIR Res Protoc*. 2020;9. https://doi.org/10.2196/18196.

23 Cloosterman S, Wijnands I, Huygens S, et al. The potential impact of digital biomarkers in multiple sclerosis in the Netherlands: an early health technology assessment of MS sherpa. *Brain Sci*. 2021;11. https://doi.org/10.3390/BRAINSCI11101305.

24 Merlo D, Darby D, Kalincik T, Butzkueven H, van der Walt A. The feasibility, reliability and concurrent validity of the MSReactor computerized cognitive screening tool in multiple sclerosis. *Ther Adv Neurol Disord*. 2019;12. https://doi.org/10.1177/1756286419859183.

25 Maillart E, Labauge P, Cohen M, et al. MSCopilot, a new multiple sclerosis self-assessment digital solution: results of a comparative study versus standard tests. *Eur J Neurol*. 2020;27:429–436.

26 Schleimer E, Pearce J, Barnecut A, et al. A precision medicine tool for patients with multiple sclerosis (the Open MS BioScreen): human-centered design and development. *J Med Internet Res*. 2020;22(7):e15605. https://www.jmir.org/2020/7/e15605.

27 Lam KH, Twose J, McConchie H, et al. Smartphone-derived keystroke dynamics are sensitive to relevant changes in multiple sclerosis. *Eur J Neurol*. 2022;29:522–534.

28 Brichetto G, Helme A, Ghirotto L, et al. Frequency and impact of symptoms experienced by people with MS—results from the global PROMS Initiative survey. *Multiple Sclerosis J*. 2024;30 (3_suppl):1148–1211. https://doi.org/10.1177/13524585241269220.

29 Phillips G, Guo S, Bender R, Havrdová E, Proskorovsky I, Vollmer T. Assessing the impact of multiple sclerosis disease activity and daclizumab HYP treatment on patient-reported outcomes: results from the SELECT trial. *Mult Scler Relat Disord*. 2016;6:66–72.

30 Micó-Amigo ME, Bonci T, Paraschiv-Ionescu A, et al. Assessing real-world gait with digital technology? Validation, insights and recommendations from the Mobilise-D consortium. *J Neuroeng Rehabil*. 2023;20. https://doi.org/10.1186/S12984-023-01198-5.

31 Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes*. 2006;4. https://doi.org/10.1186/1477-7525-4-79.

32 Szende Á, Leidy NK, Revicki D. Health-related quality of life and other patient-reported outcomes in the European centralized drug regulatory process: a review of guidance documents and performed authorizations of medicinal products 1995 to 2003. *Value Health*. 2005;8:534–548.

33 Scalfari A, Traboulsee A, Oh J, et al. Smouldering-Associated worsening in multiple sclerosis: an international consensus statement on definition, biology, clinical implications, and future directions. *Ann Neurol*. 2024;96:826–845.