STUDY PROTOCOL

REVISED Protocol for the development of a core outcome set for evaluating mixed-diagnosis falls prevention interventions for people with Multiple Sclerosis, Parkinson's Disease and stroke [version 2; peer review: 2 approved]

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Abstract

Background: Given the high incidence of falls and their associated negative effects, the development of effective falls prevention interventions for people with Multiple Sclerosis (MS), Parkinson's Disease (PD) and stroke is a priority. Currently the implementation of condition-specific falls prevention interventions is challenging in the community due to lack of participants and resources. Given the similarities in falls risk factors across stroke, PD and MS, the design of mixed-diagnosis interventions for groups comprising of people with these three neurological conditions may solve these implementation challenges. Having a core outcome set (COS) for evaluating these interventions would enable the comparison and combination of data, thereby facilitating progress in this research area. Therefore, the aim of this research study is to develop a COS for evaluating mixed-diagnosis falls prevention interventions for people with MS, PD and stroke.

Methods: This will be a mixed-methods, international, multi-perspective Delphi consensus study with five stages. Stage one will involve the identification of potential outcomes through a systematic literature search, patient focus groups, and consultation with our stakeholder group. The second stage will be the development of the Delphi survey using the outcomes elicited from stage one. Stage three will be the prioritisation of outcomes using a two-round online Delphi survey involving patients, clinicians, researchers and policy-makers/service-planners. The fourth stage will be to identify and recommend outcome measures and definitions. The final stage will be a consensus meeting with representatives from each stakeholder

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version 2 (revision) 06 May 2022	✓ view	✓ view
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group to agree upon the final COS.

Discussion: Adoption of this COS in future trials investigating the effectiveness of mixed-diagnosis falls prevention interventions for people with MS, PD and stroke will facilitate the comparison and combination of research findings. This should translate into improved decision-making by service-planners/policy-makers and clinicians regarding the implementation of evidence-based falls prevention interventions into practice.

Keywords
Consensus methods, Core outcome set, Falls, Parkinson's Disease, Multiple Sclerosis, Stroke

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REVISED **Amendments from Version 1**

Many thanks to the reviewers for their useful feedback and suggestions. We have reflected upon this feedback and have updated the manuscript in line with this. Specifically, in this updated version we have strengthened our rationale with respect to the selection of the three neurological conditions. We are proposing the design and evaluation of mixed-diagnosis falls prevention interventions to better reflect current clinical practice and to overcome implementation challenges in the community. Given the established similarities in falls risk factors and subsequent treatment approaches across Multiple Sclerosis, Parkinson's Disease and stroke, we believe that these three conditions are the most appropriate with which to commence this mixed-diagnosis approach. Our introduction has been updated to reflect this. We have also provided additional detail on the methods for the qualitative study and the Delphi survey to enhance transparency and repeatability of this study. References 1 and 2 from the original manuscript have been deleted. Six new references have been added to this version. Figure 1 from the original submission has been replaced with a new figure, and a new table (Table 1) has been added to the updated version

Any further responses from the reviewers can be found at the end of the article

Introduction

People with neurological conditions are more likely to experience a fall than age- and gender-matched 'healthy controls'[1,2]. In Ireland, three of the most common neurological conditions with high falls rates are Multiple Sclerosis (MS), Parkinson's Disease (PD) and stroke[3]. More than 50% of people with MS and PD fall in a three-month or six-month period, respectively, while as many as 73% of people will experience a fall in their first 12 months post-stroke[4–6]. Falls have a number of physical and psychosocial effects on individuals with these neurological conditions including physical injury, fear of falling, activity curtailment, reduced independence and decreased quality of life[7–13]. In addition, the consequences of falls increase strain on healthcare systems, due to higher acute healthcare service needs, and greater requirement for home-care and/or institutional-care[8–10,14]. As a result of the high incidence of falls and the associated negative consequences, falls prevention for people with MS, PD and stroke is an important topic for research and the provision of healthcare services. However, progress in the development and evaluation of interventions to reduce falls among people with these neurological conditions has been hampered thus far by substantial variation in the outcomes assessed across studies. This heterogeneity in outcomes and/or how they are measured is repeatedly acknowledged as a limitation as it inhibits the synthesis and cross-comparison of evidence, highlighting the need for a consistent approach to evaluating the effectiveness of these falls prevention interventions[15–18].

Falls prevention intervention research for people with neurological conditions is relatively in its infancy compared to falls research among older adults, with the evidence often sparse or of low quality among individuals with neurological conditions, particularly those with small numbers of people within each diagnostic group. In recent years, there has been an increase in condition-specific falls prevention research among people with MS, PD and stroke. However, the implementation of these single-diagnosis falls prevention interventions is proving challenging in the community and primary care due to insufficient numbers of participants and resources to run separate group-based programmes[19]. While there are differences in the underlying pathophysiology of these three neurological conditions[20–23], research has identified many common physiological, psychosocial, environmental and behavioural falls risk factors across the three conditions[24–33]. Given these similarities in falls risk factors across stroke, PD and MS, the development of mixed-diagnosis multifactorial interventions for these three neurological conditions, with the scope to tailor elements such as education and exercise to the individuals' needs, is a practical solution to bridge the intervention gap. Moreover, health systems internationally, including therapy and rehabilitation services, are structured around diagnostic categories, with all three of these conditions falling under neurology. Consequently, a mixed-diagnosis intervention for these neurological conditions would align with current implementation strategies, facilitating translation into practice and the provision of services in the community.

The heterogeneity in outcomes assessed across single-diagnosis interventions is reflective of the current absence of a gold standard method to evaluate falls prevention interventions among people with these neurological conditions, as established by a search of the Core Outcome Measures in Effectiveness Trials (COMET) database. In 2005, the Prevention of Falls Network Europe (ProFaNE) published a consensus study on an outcome set for use in fall injury prevention trials among older adults[34]. However, the outcomes, definitions and outcome measures outlined in this consensus study are not routinely used in the evaluation of falls prevention interventions for people with MS, PD, and stroke, suggesting that alternative outcomes may be of higher importance to key stakeholder groups to determine if a falls prevention intervention is effective for individuals with these neurological conditions. The development of a core outcome set (COS) for evaluating falls prevention interventions among mixed-diagnosis groups comprising of people with MS, PD and stroke would mean that the outcomes assessed are more reflective of the priorities of key stakeholders.

A COS is a standardised set of outcomes that should be assessed and reported at a minimum in all trials pertaining to a specific health construct, condition or population[35]. When developing a COS, it is first necessary to gain consensus regarding 'what' to measure. When this has been completed, the second step is to determine 'how' to define and assess the outcomes that have been selected[35]. Having a COS for evaluating mixed-diagnosis falls prevention interventions among adults with MS, PD and stroke will enable the comparison and combination of data, thereby ensuring that research findings are relevant, useful and useable[36]. Consequently, the aim of this study is to develop and disseminate a COS for evaluating mixed-diagnosis falls prevention interventions for people with MS, PD and stroke.

The following are the objectives of this study:

1. To identify all potential outcomes for mixed-diagnosis falls prevention interventions for people with MS, PD and stroke through a review of the literature and focus groups with people living with these neurological conditions.

2. To achieve consensus on a COS for evaluating mixed-diagnosis falls prevention interventions for people with MS, PD and stroke using the Delphi technique and a consensus meeting.

Methods

Protocol and prospective registration

This study was prospectively registered with the COMET Initiative on the 24th September 2021 and is available online (https://www.comet-initiative.org/Studies/Details/1940). This protocol was developed and reported in adherence with the Core Outcome Set-STAndardised Protocol (COS-STAP) Items[37,38].

Scope

This COS, and the corresponding definitions and outcome measures, should apply to both clinical practice and all research where the aim is to evaluate falls prevention interventions for mixed-diagnosis groups comprising of people with MS, PD or stroke. The target population for this COS is adults (≥18 years) with MS, PD and stroke, according to a confirmed diagnostic criterion, with the ability to mobilise and stand independently (with or without the use of an aid), of any gender and disease duration. This outcome set should be applied to interventions where the aim is to reduce falls among the target population.

Participants

A purposive and iterative approach will be used to identify individuals to participate in the international Delphi survey. Survey respondents will consist of individuals from each of the following key stakeholder groups: researchers, clinicians, people living with MS, PD and stroke, and service-planners/policy-makers. While feedback between rounds will be generated based on stakeholder group, only outcomes that reach consensus for inclusion based on the combined scoring of all stakeholder groups will be included in the final COS. Therefore, to ensure that the final COS is reflective of the opinions of all relevant stakeholder groups and is not influenced by the relative proportion of stakeholders participating, we will aim to recruit a similar number of participants from each stakeholder group[39]. An additional consideration for this COS is similarity of numbers between the three conditions across stakeholder groups to increase confidence that the outcomes reflect the priorities of all three diagnostic groups. Consequently, we will also be aiming to recruit similar numbers of people with MS, PD and stroke, in addition to similar numbers of clinicians working with people with each of these conditions. There is currently an absence of robust methods to calculate the required sample size for a Delphi survey with the aim of achieving consensus on a COS, however, it is generally accepted that the more participants representing each stakeholder group, the greater the reliability and generalisability of the COS[39,40]. It has been suggested that at a minimum a panel would consist of 10 to 18 participants per stakeholder group[41]. Consequently, we will aim to recruit approximately 20 individuals from each stakeholder group in case of attrition between rounds to retain a minimum sample of 10 people per stakeholder group. Every effort will also be made to achieve a gender balance in the participants. We anticipate recruiting more females with MS and males with PD, in line with gender distribution for those conditions and therefore anticipate a gender-balanced sample overall. If an imbalance occurs, we can utilise our snowball sampling methods to recruit further people. Additionally, we will aim to recruit participants from different countries to ensure there is a wide geographic distribution.

Researchers, clinicians and policy-makers/service-planners will be recruited via their email address, which will be identified from research articles and reviews, professional body email lists, Twitter and special interest groups. Patient participants will be recruited through support groups/community services for people with PD, MS and stroke. Social media and other communications of relevant organisations will also be used. Potential participants will be provided with an information leaflet outlining the rationale, objectives and methods for the consensus, and invited to participate. The research team will follow-up with those who express interest in the study through phone call or email to address any questions that the individual may have regarding the study. Recruitment will adhere to principles of purposeful and snowball sampling. Eligibility criteria are as follows: adults (aged 18 years or over) who are able to read and write in English and are (a) living with a confirmed diagnosis of MS, PD and/or stroke; (b) researchers actively involved in falls prevention research for people with these neurological conditions and have a minimum of three peer-reviewed publications in this research field; (c) clinicians currently providing interventions to individuals with these neurological conditions; or (d) service-planners/policy-makers involved in decision-making regarding the provision of falls prevention services.

The retention of participants in Delphi surveys has proven challenging at times for COS developers. Failure to retain participants in this study has the potential to introduce attrition bias if those who do not continue to participate have differing viewpoints to those who complete all rounds of the survey[39]. Attrition bias will be assessed at each round by comparing the average score for each outcome of those who respond to the survey to those who do not, identifying any substantial differences in scoring[39]. Steps will be taken throughout the study process to maximise retention including personalised reminders, stakeholder involvement in the development of surveys to ensure the language is appropriate and understandable, and a short wait between rounds[39,42].

Design

This will be an international, multi-perspective consensus study, which will involve five stages as demonstrated in Figure 1:

1. Identification of potential outcomes through a systematic literature search, patient focus groups and consultation with our stakeholder group.

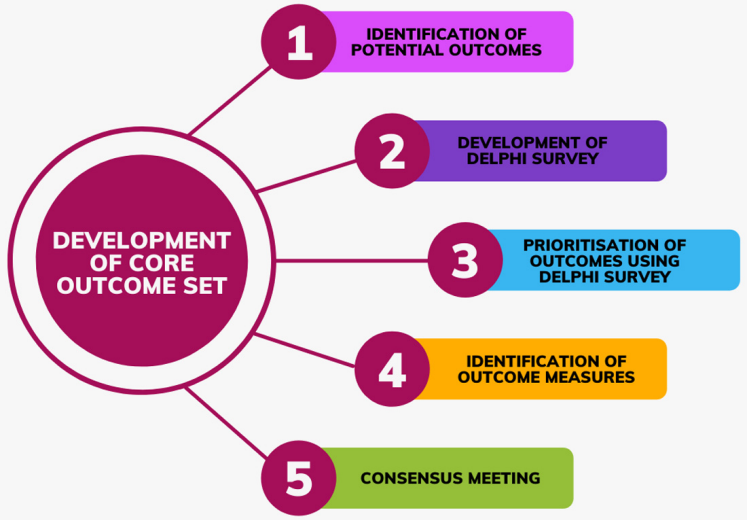

Figure 1. Flowchart of study design.

2. Development of the Delphi survey.

3. Prioritisation of outcomes using an electronic Delphi survey.

4. Identification and standardisation of outcome definitions and measures.

5. Agreement on the final COS at a consensus meeting.

Stage 1: identifying potential outcomes

Systematic search of the literature. We performed an umbrella review of systematic reviews investigating the effectiveness of falls prevention interventions for people with MS, PD and stroke[43]. This umbrella review was registered with PROSPERO (CRD42020175409) and the protocol published in an open access repository[44]. A systematic literature search was conducted using 15 electronic databases, grey literature searches and hand-screening of reference lists. Systematic reviews of randomised-controlled trials and non-randomised studies of intervention investigating the effectiveness of non-pharmacological and non-surgical interventions on falls among people with MS, PD and stroke were included. A total of 18 systematic reviews met the predefined inclusion criteria, representing 73 unique primary studies. The reported outcomes, how they were defined, the outcome measures used and time points for measurement were extracted from each systematic review. In instances where these were not reported or the details were unclear in the systematic review, the authors retrieved the original primary studies to extract this data. The outputs from this umbrella review will be used to generate the initial outcome list. All identified outcomes will be presented for rating in the Delphi survey.

Focus groups with people living with MS, PD and stroke. Outcomes collated through a review of the literature are primarily reflective of outcomes that are deemed important by researchers, potentially overlooking outcomes that are meaningful to patients[45]. Consequently, some COS developers have begun undertaking qualitative studies with patients and/or other stakeholders to ensure that a comprehensive list of outcomes, including those that are important and meaningful to all stakeholders, are considered for inclusion in the COS[39,45,46]. This study will employ a qualitative design, using focus groups to explore what outcomes for evaluating falls prevention interventions are important to people living with MS, PD and stroke. A maximum of eight people will participate in each focus group. Recently the use of 'data saturation' in reflexive thematic analysis (TA) has been criticised, and in particular predicting a data saturation point in advance to justify sample size[47]. Consequently, we will not have a pre-defined sample size but rather will make a decision regarding sample size at peer debrief sessions based on the adequacy of the collected data to address our research question[47]. Participants will include individuals aged 18 years and over who self-identify as having a confirmed diagnosis of MS, PD and/or stroke. Recruitment will adhere to the principles of purposeful maximum variation and snowball sampling[48]. To ensure that we are capturing a range of perspectives across and within diagnosis groups, we will aim to recruit a minimum of one participant with each of the characteristics outlined in Table 1. Participants will be recruited through support groups and community services for people with MS, PD and stroke across Ireland. After obtaining informed consent and prior to participation in the focus group, participants will be contacted by telephone by a member of the research team (NO'M) to collect demographic data. In light of the guidance from the World Health Organisation and Health Service Executive regarding physical distancing, these focus groups will take place using an online teleconferencing platform. Every effort will be made to overcome obstacles to participation for individuals who are interested in taking part in the study. If necessary, a member of the research team will help participants and/or their family members or carers with accessing the teleconferencing platform. In instances where an individual has difficulty verbalising responses, they will be given the opportunity to type out their answers using the chat function on the platform. Alternatively, if an individual is not comfortable using teleconferencing, they will be offered the choice to take part in a one to one telephone

Table 1. Purposive sampling criteria for participants in the qualitative study.

	Multiple Sclerosis	Parkinson's Disease	Stroke
Age	≥ 65 years < 65 years	≥ 65 years < 65 years	
Sex	Female Male	Female Male	Female Male
Mobility status	Unaided Aided	Unaided Aided	Unaided Aided
Fall in last year	Yes No	Yes No	Yes No
Disease subtype	Primary progressive Secondary progressive Relapsing remitting		

interview. Provisions will also be made to split up the telephone interview across several sessions if participants find the completion of the full interview in one session too challenging. A semi-structured topic guide consisting of open-ended questions will be used by the facilitator to direct the focus groups and telephone interviews. Focus groups and interviews will be audio-recorded, transcribed and analysed using reflexive TA. From this analysis, a list of outcomes will be generated. The data generated from this qualitative study will also be used to provide context around why the outcomes discussed are important to patients and to develop lay definitions for outcomes presented in the Delphi survey.

Consultation with stakeholder group. The lists of outcomes generated from the literature review and focus groups will be reviewed and discussed by the research team and stakeholder group to identify all distinct outcomes to be included in the Delphi survey. Given their expertise and insights into practice evidence, patient evidence and contextual factors, three key aspects of evidence-based practice and treatment decision-making[49,50], our stakeholder group will also have the opportunity to suggest additional outcomes that they think are potentially important/meaningful but are not included in the list.

Stage 2: development of the Delphi survey

The Delphi method has four fundamental features: sequential questionnaires, anonymity of participant responses, the provision of controlled feedback between questionnaire rounds, and the aggregation of participant responses to determine if and when consensus has been achieved[51]. The controlled Delphi method is favoured over less structured methods used to gain consensus, such as round-table discussions, as there is no direct contact or interactions between participants, thereby reducing the likelihood of responses being influenced by domineering individuals[51,52].

A sequential two-round electronic, international Delphi survey will be completed involving key stakeholders to develop a preliminary COS. The online software Qualtrics (Provo, UT) will be used to administer the survey. Outcomes identified in stage one will be listed in alphabetical order in the survey to avoid potential weighting[53]. This survey will be developed with input from our stakeholder group to ensure ease of completion and clarity. Following its development, the survey will be piloted and will be modified as required prior to formal circulation to participants. Each round of the survey will remain open for two weeks, with a reminder email sent out to participants three working days before closure. If participants are unfamiliar with the online software or find it challenging to use, a member of the research team will contact them to resolve any problems that they are encountering. Additionally, a member of the research team will talk to a carer or family member, with the participant's consent, to discuss how they can support the individual complete the survey. Alternatively, participants can provide their survey responses over the phone. The data obtained from each round will be analysed and presented to the participants in the next round. It is proposed that the prioritisation of outcomes will comprise of two rounds, however, the determination of the number of rounds will be a dynamic process with additional or less rounds included as appropriate[39].

Delphi survey participants will be asked to score individual outcomes using the Grading of Recommendations Assessment, Development and Evaluations (GRADE) nine-point Likert scale, with 1–3 signifying an outcome of limited importance, 4–6 an important but not critical outcome, and 7–9 indicating a critically important outcome[35,54]. The '70/15%' consensus definition will be used to determine whether consensus has been achieved[35]. Consensus that an outcome should be included in the final COS will be defined as 70% or greater of the participants scoring it as critically important (7–9) and less than 15% scoring it as having limited importance (1–3)[35]. Consensus regarding whether an outcome should be excluded from the COS will be defined as 70% or greater of the respondents scoring it as having limited importance (1–3) and less than 15% scoring it as critically important (7–9)[35]. Score distributions

outside of those outlined above will signify a lack of agreement with respect to the inclusion of an outcome in the COS[35].

Stage 3: prioritisation of outcomes

Delphi survey – round one. During round one, participants will provide their demographic data including gender, age, nationality, stakeholder group, profession and years of experience. The patient stakeholder group will be asked for specific details including neurological diagnosis, time since diagnosis, falls history and mobility status. Clinicians will be asked to provide details regarding their qualifications, which diagnostic groups they work with, how long they have been working with those groups, and what percentage of their caseload they account for. Respondents will be each provided with a unique identifier to facilitate future anonymity. Participants will be asked to rank each outcome using the nine-point Likert scale described above. Participants will also be encouraged to give the rationale for their scores (each item in the survey will have a comment box). These responses will be summarised using content analysis and these data will be provided to participants in the next round to provide context to the scores given to outcomes. Finally, participants will have the option to suggest additional outcomes for inclusion in the next round of the survey. Additional outcomes suggested in this round will be reviewed by two members of the research team to determine if they represent new outcomes[53]. All outcomes will be brought forward from round one to round two to allow participants to consider and reflect on the feedback and responses of each participant group before deciding whether to alter their responses based on this new information, or retain the original score.

Delphi survey – round two. Individuals who participated in round one of the survey will be provided with the descriptive statistics of their own and other respondents' scores from round one, in addition to a summary of the reasons that individuals gave for their scoring of each outcome. Descriptive statistics will be calculated for the panel as a whole and for each stakeholder group, with all participants being provided both sets of statistics. Participants will be asked to reflect on these summaries and statistics provided for each stakeholder group and their own scores before being asked to rescore all outcomes from round one and to score any new outcomes suggested by participants using the nine-point scoring system. If participants change their score for an outcome in round two, they will be encouraged to provide their rationale for this. Following round two of the survey, outcomes will be divided into three categories: category A (those meeting the criteria for consensus on inclusion – high agreement and high support), category B (those not achieving consensus - low agreement and mixed support) or category C (those meeting criteria for consensus on exclusion - high agreement and low support)[55]. Category A outcomes will be added to the preliminary COS. Category B outcomes will be added to a list called 'supplementary outcomes'. Category C outcomes will not be involved in any further discussions and will not be considered for inclusion in the final COS. At the end of round two of the survey, there will be a question included asking respondents if they would be interested in taking part in the virtual face-to-face consensus meeting.

Delphi survey – round three (if required). We will be applying two levels of termination criteria to the Delphi survey[56]. The first of these will be based on the degree of agreement between participants following completion of round two. If any outcomes are identified as rated 7–9 by more than 50% of participants and rated 1–3 by less than 15% of participants, then a third round of the Delphi survey will be completed. To reduce burden on participants, only outcomes deemed to have met the aforementioned criteria will be included in round three. Following completion of round three, the scores for these outcomes will be evaluated to determine if they meet the criteria for category A or if they are to remain in category B. The second level will be based on a time-related criterion, with the survey being terminated following a third round regardless of whether or not consensus on all outcomes has been achieved.

Stage 4: identification and standardisation of outcome definitions and measures

The COnsensus-based Standards for the selection of health status Measurement Instruments (COSMIN) recommends a thorough methodology for in-depth evaluation and selection of outcome instruments[57]. For the purpose of this study, we intend to take a more pragmatic approach to the identification and selection of outcome definitions and measures. For all potential core outcomes (categories A and B) identified during the Delphi study, we will identify the definitions and outcome measures that were used in the studies included in our umbrella review. In the case of an outcome that was not identified as part of our umbrella review, we will perform targeted literature searches to identify relevant outcome measures. Targeted literature searches of MEDLINE and the COSMIN database will be used to identify studies investigating the quality of the outcome measures. Our research team and stakeholder group will review the available evidence and provisionally prioritise the use of a single outcome measure after consideration and discussion of the following[58]: 1) the frequency with which the outcome measure has been used in existing research; 2) the time and resources necessary to use the outcome measure; and 3) the available data on their measurement properties as outlined in the COSMIN recommendations (validity, reliability, responsiveness and interpretability)[57]. Recommendations regarding the selection of outcome measures will be presented during the consensus meeting.

Stage 5: consensus meeting

A virtual face-to-face meeting will take place with representatives from each stakeholder group to discuss, vote and agree upon the final COS and the definitions and methods to be utilised to assess these outcomes. Approximately 16 experts involved in the Delphi survey will be invited to take part in the consensus meeting. This panel will be purposively sampled to ensure that it includes representatives from each stakeholder group and from a range of geographic locations. The meeting will commence with a presentation outlining the preliminary COS and the 'supplementary outcomes' list. This will be followed by a timed discussion between panel members and a final vote. Similar to other COSs, the definition for consensus will be at least 70% of participants voting for

the outcome to be included and a minimum of one patient representative voting for the outcome to be included in the COS[36]. Any outcomes not meeting these criteria will remain on the 'supplementary outcomes' list. Relevant arguments for or against the inclusion of an outcome will be noted along with the vote counts. Finally, recommendations regarding definitions and outcome measures will be discussed. The consensus panel will be invited to provide feedback and discuss the recommendations before finalising the selection of a single outcome measure and definition, where applicable, for every included outcome. Reasoning for all decisions will be described narratively in the final published consensus statement.

Dissemination and implementation strategy

A multi-modal approach to the dissemination of this COS will be employed. This COS will be developed and reported according to the Core Outcome Set-STAndards for Reporting (COS-STAR) guidelines[59]. The final COS will be published in a peer-reviewed journal and will be shared through national and international conference presentations, and the appropriate media channels. In addition, this study has been registered with COMET and the final COS will be published on their website. The final COS will also be disseminated through relevant professional and patient organisations to inform healthcare professionals and the public.

Ethics requirements

Ethics approval for the qualitative study has been granted by the Faculty of Education and Health Sciences Research Ethics Committee at the University of Limerick (EHSREC No: 2020_06_12). The information sheet and informed consent sheet will be reviewed with participants and informed verbal consent to participate will be obtained at entry to the study and will be re-confirmed at the start of the focus group or interview. Participants will be advised that participation in the study is voluntary and that they can withdraw at any stage without penalty. Ethics approval for the consensus study has been granted by the Faculty of Education and Health Sciences Research Ethics Committee at the University of Limerick (EHSREC No: 2021_06_12). Participants in the Delphi survey will be provided with a study information leaflet as part of the invitation. At the beginning of round one of the online survey, participants will consent to take part in the study. Participants will be given the option to withdraw without explanation from this study at any time. Participants' personal data will only be accessed by members of the research team and all survey responses will be confidential.

Stakeholder involvement

A stakeholder group has been established to guide the development of this COS. This group comprises of relevant stakeholders in Ireland, including individuals living with MS, PD and stroke, healthcare professionals, and representatives working with patient organisations. As outlined in Figure 2, this stakeholder group will provide input and feedback from the design stage through to the dissemination and implementation stages of this study.

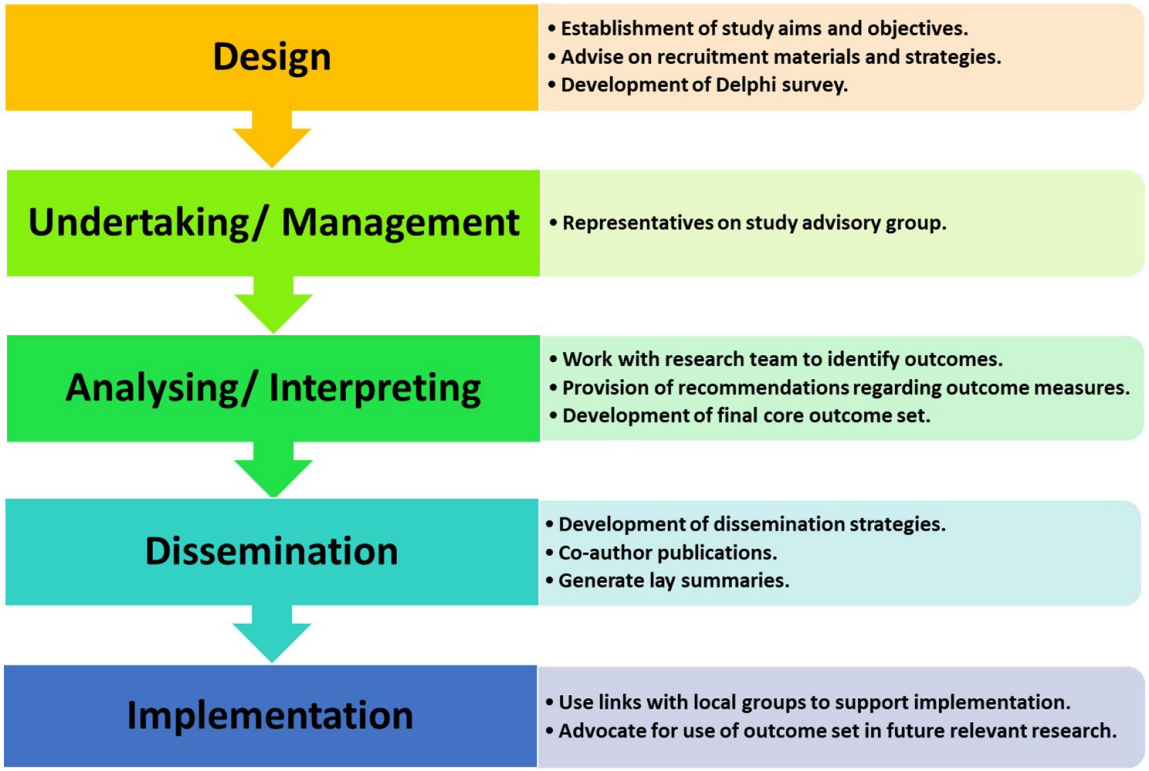

Figure 2. Overview of stakeholder involvement in study.

Discussion

This protocol outlines the design of an international, multi-perspective Delphi consensus study to develop a COS for evaluating mixed-diagnosis falls prevention interventions for people with MS, PD and stroke. To our knowledge, the Delphi technique has not been previously used to gain consensus on a COS in this subject area. Given the high frequency of falls and their associated negative consequences among individuals with these neurological conditions, falls prevention is a priority for research and the provision of services. The establishment of an international standard for the assessment of outcomes would allow for transparent and coordinated falls research for people with these neurological conditions, facilitating advancements in this research field. The successful development and implementation of a COS would enable pooling of data, the conduction of meta-analyses and the cross-comparison of findings, aiding progress in the design and provision of effective evidence-based mixed-diagnosis falls prevention interventions for people with MS, PD and stroke. Once published, researchers investigating the effectiveness of falls prevention interventions for these conditions will have a well-founded rationale for the assessment of outcomes based on input from key stakeholders, thereby reducing heterogeneity and selective reporting of outcomes. Additionally, clinicians and service-planners/policy-makers will be better placed to compare research findings to guide clinical decision-making, optimising the translation and implementation of evidence-based falls prevention interventions into practice.

Data availability

No data are associated with this article.

Reporting guidelines

Figshare: COS-STAP Checklist for 'Protocol for the development of a core outcome set for evaluating mixed-diagnosis falls prevention interventions for people with Multiple Sclerosis, Parkinson's Disease and stroke', https://doi.org/10.6084/m9.figshare.16669681.v1[38].

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Open Peer Review

Current Peer Review Status: ✔ ✔

Version 2

Reviewer Report 20 May 2022

https://doi.org/10.21956/hrbopenres.14802.r31997

✔ **Catriona McDaid**
Department of Health Sciences, York Trials Unit, University of York, York, UK
Rachel Cunningham-Burley
University of York, York, UK

Thank-you to the authors for their detailed response, clarifications and amendments. We have no further comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: applied health research, clinical trials, systematic reviews, musculoskeletal

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 10 May 2022

https://doi.org/10.21956/hrbopenres.14802.r31998

✔ **Michelle Cameron**
Department of Neurology, VA Portland Health Care System, Oregon Health & Science University, Portland, OR, USA

Thank you for addressing my concerns.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Falls and mobility in people with multiple sclerosis.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 28 February 2022

https://doi.org/10.21956/hrbopenres.14669.r31431

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Rachel Cunningham-Burley
University of York, York, UK
Catriona McDaid
Department of Health Sciences, York Trials Unit, University of York, York, UK

This clearly written paper provides an overview of the methods for the development of a core outcome set for use in the evaluation of falls prevention interventions applicable to mixed groups of people with stroke, Parkinson's Disease and Multiple Sclerosis. A pragmatic rationale is presented that it is often not feasible to implement interventions for single condition groups and these conditions share similar risk factors. It could be clearer why these specific three conditions and not a wider range of conditions. Whilst you state that there are similarities in the falls risk in these three conditions, due to a number of common factors, it would be good to substantiate this further, particularly how these risks may differ, by virtue of the underlying neurological condition, from falls risk more generally. In addition, it is implied in the introduction that there is no COS for the individual conditions – this could be clearer and how this was established, for example through a search of COMET.

The paper is scientifically sound and the methods are appropriate to answer the study objectives: the authors identify an explicit scope in terms of the population and proposed use of the COS, identify how the initial items for the Delphi will be identified (full details of the systematic review protocol are available separately), the process for undertaking the Delphi including the threshold for retention and removal of items and how they will identify relevant outcome measures. The methods mitigate against a single group dominating or unduly influencing the output from Delphi and consensus meeting. Ethical approval has been granted, though it could be clearer whether this extends to the qualitative study. The study is registered on COMET.

Some specific suggestions for clarification in the protocol or for consideration when undertaking the study:

- It is a strength of the research that focus groups are planned to obtain the views of people with the three conditions of interest, as the authors correctly point out, the items derived from existing trials are more likely to reflect healthcare professional and researcher perspectives. However, more detail on the plans for the qualitative study would be helpful. How many focus groups are planned, what size will the groups be, what sampling methods will be used to capture a range of perspectives across conditions and within groups are captured? How will people be identified for inclusion in this part of the study, how will information be sought?

- Attrition can be very high from online surveys so aiming to recruit 15 from each group at the outset may be a bit risky to achieve the planned target of the suggested 10-18 per stakeholder group throughout the study. This only allows for one-third attrition. If feasible, consideration could be given to a larger initial pool. There are plans to achieve a geographic and gender balance. It could be clearer what is meant by geographic – urban-rural and/or across countries? Balance across conditions for patients and healthcare professionals is also likely to be important in order to be confident that the COS reflects the priorities of all three disease groups. However, no plans are described regarding this. You may also wish to consider the gender balance seen among the stakeholder groups; for example, MS is three times more common in females. Related to this it could be clearer in Stage 3 whether information about which condition patient participants have and duration of diagnosis or areas of clinical expertise (or generalist) for HCP participants will be gathered as part of the demographic data.

- Given the nature of the included neurological conditions, some participants may have communication or other difficulties that may make participation challenging. Are there any plans to encourage the involvement of people who may require the support of a carer or family member to participate in the study either for health reasons, difficulties communicating or where they are not confident IT users? Will there be an option for an alternative means of completion of the rounds of surveys, other than electronically, to include those who may not have access to online technologies? Ideally, the perspectives of a wide range of patient groups would be captured. This also applies to the qualitative study.

- It is a strength that a third round will be used if necessary; however, it is not clear what would instigate the use of the third round.

- At the bottom of P5, it states that “All outcomes will be brought forward from round one to round two”. This suggests that the threshold criteria will not be applied at the end of round one – is this your intention or should the sentence refer to all newly elicited outcomes?

- It is a strength of the study that patients and the public will be involved at key stages of the study. However, given that the group also includes healthcare professionals ‘stakeholder group’ may be a more appropriate description than Patient and Public Involvement panel.

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?
Partly

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: applied health research, clinical trials, systematic reviews, musculoskeletal

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 03 May 2022

Nicola O'Malley, University of Limerick, Limerick, Ireland

Many thanks for your time spent reviewing this protocol, and for your constructive and insightful feedback and comments. We have reflected upon your feedback and revised our manuscript in line with it. Please see below a detailed point-by-point response to all comments (reviewer's comments in **bold** and authors' responses in black font).

<u>Comment 2.1:</u> This clearly written paper provides an overview of the methods for the development of a core outcome set for use in the evaluation of falls prevention interventions applicable to mixed groups of people with stroke, Parkinson's Disease and Multiple Sclerosis. A pragmatic rationale is presented that it is often not feasible to implement interventions for single condition groups and these conditions share similar risk factors. It could be clearer why these specific three conditions and not a wider range of conditions. Whilst you state that there are similarities in the falls risk in these three conditions, due to a number of common factors, it would be good to substantiate this further, particularly how these risks may differ, by virtue of the underlying neurological condition, from falls risk more generally. In addition, it is implied in the introduction that there is no COS for the individual conditions – this could be clearer and how this was established, for example through a search of COMET.

As discussed in Response 1.2, the three most common neurological conditions presenting for falls prevention interventions are MS, PD and stroke. Additionally, we have evidence to demonstrate that falls risk factors and subsequent treatment approaches have many similarities across these three conditions. Consequently, we believe that these three conditions are the most appropriate for commencing this mixed-diagnosis approach to falls prevention interventions to facilitate implementation. We have now updated our introduction to clarify the rationale for including the three neurological conditions. Additionally, we have clarified in the introduction that a search of COMET was undertaken to establish whether a COS exists.

Comment 2.2: **The paper is scientifically sound and the methods are appropriate to answer the study objectives: the authors identify an explicit scope in terms of the population and proposed use of the COS, identify how the initial items for the Delphi will be identified (full details of the systematic review protocol are available separately), the process for undertaking the Delphi including the threshold for retention and removal of items and how they will identify relevant outcome measures. The methods mitigate against a single group dominating or unduly influencing the output from Delphi and consensus meeting. Ethical approval has been granted, though it could be clearer whether this extends to the qualitative study. The study is registered on COMET.**

Ethics has been granted by the Faculty of Education and Health Sciences Research Ethics Committee at the University of Limerick for both the qualitative study and the Delphi consensus study. This has been clarified under 'Ethics requirements'.

Comment 2.3: **It is a strength of the research that focus groups are planned to obtain the views of people with the three conditions of interest, as the authors correctly point out, the items derived from existing trials are more likely to reflect healthcare professional and researcher perspectives. However, more detail on the plans for the qualitative study would be helpful. How many focus groups are planned, what size will the groups be, what sampling methods will be used to capture a range of perspectives across conditions and within groups are captured? How will people be identified for inclusion in this part of the study, how will information be sought?**

Thank you for this suggestion. Given the recent criticisms of pre-empting a data saturation point in advance to justify sample size, we will not have a pre-defined sample size but will rather make a decision regarding sample size during peer debrief sessions based on the adequacy of the collected data to answer the research question. Recruitment will adhere to the principles of purposeful maximum variation and snowball sampling to ensure we are capturing a wide range of perspectives. Participants will be recruited through support groups and community services. The methods for our qualitative study have been clarified further in the paragraph 'Focus groups with people living with MS, PD and stroke'.

Comment 2.4: **Attrition can be very high from online surveys so aiming to recruit 15 from each group at the outset may be a bit risky to achieve the planned target of the suggested 10-18 per stakeholder group throughout the study. This only allows for one-third attrition. If feasible, consideration could be given to a larger initial pool. There are plans to achieve a geographic and gender balance. It could be clearer what is meant by geographic – urban-rural and/or across countries? Balance across conditions for patients and healthcare professionals is also likely to be important in order to be confident that the COS reflects the priorities of all three disease groups. However, no plans are described regarding this. You may also wish to consider the gender balance seen among the stakeholder groups; for example, MS is three times more common in females. Related to this it could be clearer in Stage 3 whether information about which condition patient participants have and duration of diagnosis or areas of clinical expertise (or generalist) for HCP participants will be gathered as part of the**

demographic data.

Thank you for this suggestion. We will aim to recruit 20 people per stakeholder group to retain a minimum sample of 10 per stakeholder group, with equal representation of all three conditions in the patient group. Geographic balance refers to countries rather than urban/rural. We anticipate recruiting more females with MS and males with PD, in line with gender distribution for those conditions and therefore anticipate a gender-balanced sample overall. If an imbalance occurs, we can utilise our snowball sampling methods to recruit additional people. Apologies for the lack of clarification. The above detail has now all been outlined in the 'Participants' section.

Specific demographic data that will be requested from the patient stakeholder group include neurological diagnosis, time since diagnosis, falls history and mobility status. Clinicians will be asked to provide their qualifications, which diagnostic groups they work with, how long they have been working with those groups, and what percentage of their caseload they account for. This has now been clarified under 'Delphi survey – round one'.

Comment 2.5: Given the nature of the included neurological conditions, some participants may have communication or other difficulties that may make participation challenging. Are there any plans to encourage the involvement of people who may require the support of a carer or family member to participate in the study either for health reasons, difficulties communicating or where they are not confident IT users? Will there be an option for an alternative means of completion of the rounds of surveys, other than electronically, to include those who may not have access to online technologies? Ideally, the perspectives of a wide range of patient groups would be captured. This also applies to the qualitative study.

As mentioned in the methods section, our stakeholder group will be involved in the design of the survey to make it as user-friendly as possible (for example allowing participants to complete the survey across several sessions rather than in one sitting). In addition to this, we will make provisions as appropriate to facilitate participation in both the qualitative and consensus studies. Specific details regarding these provisions for the qualitative study have been added to the section 'Focus groups with people living with MS, PD and stroke', and for the consensus study under 'Stage 2: development of the Delphi survey'.

Comment 2.6: It is a strength that a third round will be used if necessary; however, it is not clear what would instigate the use of the third round.

If there are outcomes near the thresholds for consensus (rated 7-9 by more than 50% of participants and rated 1-3 by less than 15% of participants), then a third round of the Delphi survey will be completed. The survey will be terminated following a third round regardless of whether or not all outcomes have achieved consensus. This additional information has been outlined under the section 'Delphi survey – round three (if required).

Comment 2.7: At the bottom of P5, it states that "All outcomes will be brought forward from round one to round two". This suggests that the threshold criteria will not be applied at the end of round one – is this your intention or should the sentence refer to

all newly elicited outcomes?

Yes, it is our intention to bring all outcomes forward to round two. A key feature of the Delphi method is the provision of controlled feedback to participants, For that reason, we will not be applying the consensus threshold criteria at the end of round one but instead will be bringing forward all outcomes to round two to allow participants to reconsider their own responses. This has been clarified in the manuscript under 'Delphi survey – round one'.

Comment 2.8: It is a strength of the study that patients and the public will be involved at key stages of the study. However, given that the group also includes healthcare professionals 'stakeholder group' may be a more appropriate description than Patient and Public Involvement panel.

Thank you for this suggestion. The phrase 'Patient and Public Involvement panel' has been updated to 'stakeholder group' accordingly throughout this paper.

Competing Interests: No competing interests were disclosed.

Reviewer Report 06 December 2021

https://doi.org/10.21956/hrbopenres.14669.r30951

?

Michelle Cameron
Department of Neurology, VA Portland Health Care System, Oregon Health & Science University, Portland, OR, USA

This manuscript describes a protocol for developing a core outcome set (COS) for fall prevention interventions in people with multiple sclerosis (MS), Parkinson's Disease (PD), and stroke. The manuscript is well written. The language is clear. The approach is robust, with the appropriate stakeholders and iterative sequence. Thus, based on your assigned review questions, this manuscript meets the criteria of having clearly described rationale and objectives, having an appropriate study design for the research question and, providing sufficient detail to allow for replication.

However, I do have one substantial concern. I question if the research question being asked is the ideal one. Why have the authors limited the COS to people with 3 specific neurological conditions when falls are more ubiquitous? I would think a better COS for mixed-diagnosis falls prevention interventions would be diagnosis agnostic and include anyone who either has fallen often or is thought to be at high fall risk. Why would you want different outcomes related to falls in those with MS, PD and stroke compared to older adults with often multiple comorbidities contributing to their fall risk? I, therefore, suggest that the authors either broaden their target population or give

a clear rationale for why these specific 3 diagnoses and no others are included.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Falls and mobility in people with multiple sclerosis.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 03 May 2022

Nicola O'Malley, University of Limerick, Limerick, Ireland

Many thanks for your time spent reviewing this protocol, and for your constructive and insightful feedback and comments. We have reflected upon your feedback and revised our manuscript in line with it. Please see below a detailed point-by-point response to all comments (reviewer's comments in **bold** and authors' responses in black font).

Comment 1.1: This manuscript describes a protocol for developing a core outcome set (COS) for fall prevention interventions in people with multiple sclerosis (MS), Parkinson's Disease (PD), and stroke. The manuscript is well written. The language is clear. The approach is robust, with the appropriate stakeholders and iterative sequence. Thus, based on your assigned review questions, this manuscript meets the criteria of having clearly described rationale and objectives, having an appropriate study design for the research question and, providing sufficient detail to allow for replication.

Thank you for this positive feedback.

Comment 1.2: However, I do have one substantial concern. I question if the research question being asked is the ideal one. Why have the authors limited the COS to people with 3 specific neurological conditions when falls are more ubiquitous? I would think a better COS for mixed-diagnosis falls prevention interventions would be diagnosis agnostic and include anyone who either has fallen often or is thought to be at high fall

risk. Why would you want different outcomes related to falls in those with MS, PD and stroke compared to older adults with often multiple comorbidities contributing to their fall risk? I, therefore, suggest that the authors either broaden their target population or give a clear rationale for why these specific 3 diagnoses and no others are included.

Thank you for this thought-provoking comment. As you are aware, there is an existing core outcome set for fall-injury prevention interventions among older adults. Consequently, falls research for older adults can be pooled, with many systematic reviews and meta-analyses providing a solid evidence-base to support falls prevention programmes in older adults. Many people with neurological conditions are younger and therefore do not fit under that umbrella despite having high falls rates. Consequently, the focus of this core outcome set will not be on older adults to facilitate progress in falls research among other populations that are not as well researched.

Health services globally, and in Ireland, are predominantly structured around diagnostic categories/models of care, one of which is neurology. Therefore, to align with the implementation strategies within these health services, this proposed core outcome set will focus solely on falls prevention interventions for people with neurological conditions, namely MS, PD and stroke. We are proposing the design and evaluation of mixed-diagnosis interventions for people with these neurological conditions as a pragmatic approach to overcome the challenges associated with delivering single-diagnosis interventions in the community. People who have been diagnosed with stroke, PD and MS have higher rates of falls than older adults and these are the three most common conditions presenting to physiotherapists in a rehabilitation setting. We have evidence to show that many falls risk factors and subsequent intervention approaches are similar across these three conditions. As such, we believe that the combination/selection of these three conditions is the most appropriate for commencing this mixed-diagnosis approach. Our introduction has been edited to clarify our intentions in relation to the selection of the three neurological conditions.

Competing Interests: No competing interests were disclosed.