Study Title: Prospective Case Series to Refine Standalone Cognitive Behavioral Therapy Components for Multiple Sclerosis Fatigue

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INSTRUCTIONS

- **This form is only for studies that will be reviewed by the UW IRB**. Before completing this form, check HSD's website to confirm that this should not be reviewed by an external (non-UW) IRB.
- **If you are requesting a determination** about whether the planned activity is human subjects research or qualifies for exempt status, you may skip all questions except those marked with **[DETERMINATION]** For example **1.1. [DETERMINATION]** must be answered. Do not upload consent materials for determinations in ***Zipline*** as HSD does not review or approve them.
- **Answer all questions**. If a question is not applicable to the research or if you believe you have already answered a question elsewhere in the application, state "NA" (and if applicable, refer to the question where you provided the information). If you do not answer a question, the IRB does not know whether the question was overlooked or whether it is not applicable. This may result in unnecessary "back and forth" for clarification. Use non-technical language as much as possible.
- For collaborative or multi-site research, describe only the UW activities unless you are requesting that the UW IRB provide the review and oversight for non-UW collaborators or co-investigators as well.
- You may reference other documents (such as a grant application) if they provide the requested information in non-technical language. Be sure to provide the document name, page(s), and specific sections, and upload it to ***Zipline***. Also, describe any changes that may have occurred since the document was written (for example, changes that you've made during or after the grant review process). In some cases, you may need to provide additional details in the answer space as well as referencing a document.
- **NOTE: Do not convert this Word document to PDF.** The ability to use "tracked changes" is required in order to modify your study and respond to screening requests

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1. OVERVIEW

Study Title: Prospective Case Series to Refine Standalone Cognitive Behavioral Therapy Components for Multiple Sclerosis Fatigue

1.1. [DETERMINATION] **Home institution.** Identify the institution through which the lead researcher listed on the IRB application will conduct the research. Provide any helpful explanatory information.

In general, the home institution is the institution (1) that provides the researcher's paycheck and that considers them to be a paid employee, or (2) at which the researcher is a matriculated student. Scholars, faculty, fellows, and students who are visiting the UW and who are the lead researcher: identify your home institution and describe the purpose and duration of your UW visit, as well as the UW department/center with which you are affiliated while at the UW.

Note that many UW clinical faculty members are paid employees of non-UW institutions.

*The UW IRB provides IRB review and oversight for only those researchers who meet the criteria described in the **SOP Use of the UW IRB**.*

University of Washington (UW)

1.2. [DETERMINATION] **Consultation history**. Has there been any consultation with someone at HSD about this study?

It is not necessary to obtain advance consultation. However, if advance consultation was obtained, answering this question will help ensure that the IRB is aware of and considers the advice and guidance provided in that consultation.

☒ **No**

☐ **Yes →** Briefly describe the consultation: approximate date, with whom, and method (e.g., by email, phone call, in-person meeting).

Click or tap here to enter text.

1.3. [DETERMINATION] **Similar and/or related studies**. Are there any related IRB applications that provide context for the proposed activities?

Examples of studies for which there is likely to be a related IRB application: Using samples or data collected by another study; recruiting subjects from a registry established by a colleague's research activity; conducting Phase 2 of a multi-part project or conducting a continuation of another study; serving as the data coordinating center for a multi-site study that includes a UW site.

Providing this information (if relevant) may significantly improve the efficiency and consistency of the IRB's review.

☒ **No**

☐ **Yes →** Briefly describe the other studies or applications and how they relate to the proposed activities. If the other applications were reviewed by the UW IRB, please also provide: the UW IRB number, the study title, and the lead researcher's name.

1.4. [DETERMINATION] **Externally-imposed urgency or time deadlines**. Are there any externally-imposed deadlines or urgency that affect the proposed activity?

HSD recognizes that everyone would like their IRB applications to be reviewed as quickly as possible. To ensure fairness, it is HSD policy to review applications in the order in which they are received. However, HSD will assign a higher priority to research with externally-imposed urgency that is beyond the control of the researcher. Researchers are encouraged to communicate as soon as possible with their HSD staff contact person when there is an urgent situation (in other words, before submitting the IRB application). Examples: a researcher plans to test an experimental vaccine that has just been developed for a newly emerging

epidemic; a researcher has an unexpected opportunity to collect data from students when the end of the school year is only four weeks away.

HSD may ask for documentation of the externally-imposed urgency. A higher priority should not be requested to compensate for a researcher's failure to prepare an IRB application in a timely manner. Note that IRB review requires a certain minimum amount of time; without sufficient time, the IRB may not be able to review and approve an application by a deadline.

☐ **No**

☒ **Yes →** Briefly describe the urgency or deadline as well as the reason for it.

IRB approval of this application is part of a JIT submission due 3/31 for Aim 1 of Lindsey Knowles's K23 application to the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

1.5. [DETERMINATION] **Objectives**. Using lay language, describe the purpose, specific aims, or objectives that will be met by this specific project. If hypotheses are being tested, describe them. You will be asked to describe the specific procedures in a later section.

If this application involves the use of a HUD "humanitarian" device: describe whether the use is for "on-label" clinical patient care, "off-label" clinical patient care, and/or research (collecting safety and/or effectiveness data).

First, we will develop and pilot test three telehealth cognitive behavioral therapy (CBT) components for fatigue in PwMS to maximize feasibility and acceptability. We will create treatment manuals and participant materials for the following three CBT components for PwMS and fatigue:

1. *Relaxation training* (n=7): Didactic and experiential training in one or more relaxation techniques such as diaphragmatic breathing, progressive muscle relaxation, autogenic relaxation, and guided imagery
2. *Behavioral activation* (n=7): Didactic material and practice focused on identification and reduction of avoidance behaviors (e.g., excessive rest) and increased engagement in valued and reinforcing activities (e.g., physical activity, social engagement
3. *Cognitive therapy* (n=7): Didactic material and practice focused on identifying, challenging, and modifying inaccurate and/or unhelpful patterns of thought about the self and the world (e.g., catastrophizing the meaning and consequences of fatigue) to change unwanted behavioral patterns (e.g., excessive rest)

Next, we will recruit, enroll, and randomize 21 participants. Participants will complete the baseline self-report assessment via REDCap (or by telephone, if preferred). Study staff will randomly assign them to one of three CBT intervention components noted above.

We will test each of the three components with seven fatigued PwMS (N=21) and evaluate the feasibility, acceptability, and preliminary efficacy of each component. Participants will complete the 4-session telehealth treatments by telephone or UW Zoom [Health Insurance Portability and Accountability Act (HIPAA)-compliant].

Participants will complete patient-reported outcome measures (PROMs) for pre- and post-intervention assessments via REDCap (or by telephone, if preferred). During the pre- and post-intervention assessments time periods, participants will also complete a survey consisting of four to eight questions

about their fatigue twice per day (morning and evening) for seven days via REDCap (or by telephone, if preferred). They will also complete a treatment expectancy measure after the first session via REDCap (or by telephone, if preferred). They will complete qualitative semi-structured interviews at post-intervention to contextualize quantitative data and refine the components. They will also complete a medication form by phone at the pre-treatment and post-treatment timepoints.

1.6. [DETERMINATION] **Study design**. Provide a one-sentence description of the general study design and/or type of methodology.

Your answer will help HSD in assigning applications to reviewers and in managing workload. Examples: a longitudinal observational study; a double-blind, placebo-controlled randomized study; ethnographic interviews; web scraping from a convenience sample of blogs; medical record review; coordinating center for a multi-site study.

Prospective case series

1.7. [DETERMINATION] **Intent**. Check all the descriptors that apply to your study. You must check at least one box.

This question is essential for ensuring that your application is correctly reviewed. Please read each option carefully.

Check all that apply	Descriptor
☐	Class project or other activity whose purpose is to provide an educational experience for the researcher (for example, to learn about the process or methods of doing research).
☐	Part of an institution, organization, or program's own internal operational monitoring.
☒	Improve the quality of service provided by a specific institution, organization, or program.
☒	Designed to expand the knowledge base of a scientific discipline or other scholarly field of study, and produce results that: • Are expected to apply to a larger population beyond the site of data collection or the specific subjects studied, or • Are intended to be used to develop, test, or support theories, principles, and statements of relationships, or to inform policy beyond the study.
☐	Focus directly on the specific individuals about whom the information or biospecimens are collected through oral history, journalism, biography, or historical scholarship activities, to provide an accurate and evidence-based portrayal of the individuals.
☐	A quality improvement or program improvement activity conducted to improve the implementation (delivery or quality) of an accepted practice, or to collect data about the implementation of the practice for clinical, practical, or administrative purposes. This does not include the evaluation of the efficacy of different accepted practices, or a comparison of their efficacy.

Check all that apply	Descriptor
☐	Public health surveillance activities conducted, requested, or authorized by a public health authority for the sole purpose of identifying or investigating potential public health signals or timely awareness and priority setting during a situation that threatens public health.
☐	Preliminary, exploratory or research development activities (such as pilot and feasibility studies, or reliability/validation testing of a questionnaire).
☐	Expanded access use of a drug or device not yet approved for this purpose.
☐	Use of a Humanitarian Use Device.
☐	Other. Explain:

Click or tap here to enter text.

1.8. Background, experience, and preliminary work. Answer this question **only** if the proposed activity has one or more of the following characteristics. The purpose of this question is to provide the IRB with information that is relevant to its risk/benefit analysis.

- Involves more than minimal risk (physical or non-physical)
- Is a clinical trial, or
- Involves having the subjects use a drug, biological, botanical, nutritional supplement, or medical device.

"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

1.8.a. Background. Provide the rationale and the scientific or scholarly background for the proposed activity, based on existing literature (or clinical knowledge). Describe the gaps in current knowledge that the project is intended to address.

This should be a plain language description. Do not provide scholarly citations. Limit your answer to less than one page or refer to an attached document with background information that is no more than three pages long.

Fatigue affects 80% of PwMS, and nearly half report fatigue as their most disabling symptom. The cognitive behavioral model of MS fatigue theorizes that MS disease factors trigger fatigue, but fatigue is maintained or worsened by factors like daily stress and how PwMS react cognitively, behaviorally, physiologically, and emotionally to fatigue. In-person and telehealth cognitive behavioral therapy (CBT) for fatigue targets these factors and reactions and is one of the most effective treatments for MS fatigue. However, CBT is resource intensive, as it consists of multiple components (i.e., relaxation training, behavioral activation, cognitive therapy), requiring 8-16 hour-long sessions delivered by a specialized clinician. CBT has yet to be assessed via an integrated translational model that considers all stages, from intervention development to implementation. Thus, the active components of CBT for fatigue and their mechanisms are

unclear and, despite the significant burden of MS fatigue, CBT for fatigue is not widely accessible due to various implementation barriers.

The proposed prospective case series is the first of two project aims. The overall project (Dr. Knowles's K23 research) aims to optimize CBT for fatigue to maximize efficacy and efficiency; it will advance scientific evidence on CBT's active components and facilitate implementation, thereby improving accessibility. The proposed prospective case series (K23 Aim 1) will examine the feasibility and acceptability of the telehealth CBT components (Relaxation Training, Behavioral Activation, Cognitive Therapy) for fatigue in PwMS.

1.8.b. Experience and preliminary work. Briefly describe experience or preliminary work or data (if any) that you, your team, or your collaborators/co-investigators have that supports the feasibility and/or safety of this study.

It is not necessary to summarize all the discussion that has led to the development of the study protocol. The IRB is interested only in short summaries about experiences or preliminary work that suggest the study is feasible and that risks are reasonable relative to the benefits. Examples: Your team has already conducted a Phase 1 study of an experimental drug which supports the Phase 2 study being proposed in this application; your team has already done a small pilot study showing that the reading skills intervention described in this application is feasible in an after-school program with classroom aides; your team has experience with the type of surgery that is required to implant the study device; the study coordinator is experienced in working with subjects who have significant cognitive impairment.

The study team collectively brings to this effort extensive experience in MS clinical trials and will ensure the success of this study.

Dr. Knowles is an Assistant Professor in the UW School of Medicine Department of Rehabilitation. We will run this study at UW and utilize resources within the UW Department of Rehabilitation Medicine and VAPSHCS MS Center of Excellence West (where Dr. Knowles recently completed her postdoctoral fellowship).

Dr. Knowles's distinguished K23 mentorship team includes Drs. Dawn Ehde (Primary Mentor; telehealth CBT and MS expert), Aaron Turner (MS behavioral intervention expert), Linda Collins (Multiphase Optimization Strategy expert) of New York University, and Anna Kratz (qualitative research expert) of the University of Michigan.

Dr. Ehde's team has conducted multiple trials that have demonstrated the benefits of CBT-based self-management interventions for reducing pain in PwMS.

Telehealth has considerable potential for expanding the reach of self-management interventions in people with physical disabilities. Remote technology can transcend geographical barriers and target larger populations. These approaches also have inherent scalability and are easy to centralize for public health dissemination. Remote delivery can reduce stigma and lower the threshold for treatment initiation, given that it can be used in the privacy of one's home. Telehealth approaches are also less expensive than traditional psychotherapy.

1.8.c. Subject matter expertise. Is the study a clinical trial and/or does the study involve use of a drug, biologic, botanical, nutritional supplement and/or is the study otherwise considered to be greater than minimal risk to subjects?

☒ **No** → Answering this question is optional.
☐ **Yes** → Provide the name, degree(s), and contact information (e.g., email, phone number) of someone with appropriate expertise in the subject matter described in the objectives and design of this study. The individual should be unaffiliated with the study and have no other apparent conflict of interest. The individual may be associated with the UW or external to the University. Ensure the individual is aware they may be contacted by HSD.

*Provision of this information is **required** for all clinical trials, for studies involving the use of a drug, biologic, botanical, nutritional supplement and for studies involving greater than minimal risk. For all other studies, the information is optional, though HSD reserves the right to request researcher assistance in providing a consultant if necessary to complete review of the study.*
For the consultant, the request involves a brief email or phone call with targeted questions that usually can be responded to in 30 minutes or less.

Click or tap here to enter text.

1.9. Supplements. Check all boxes that apply, to identify relevant SUPPLEMENTS that should be completed and uploaded to ***Zipline***.

This section is here instead of at the end of the form to reduce the risk of duplicating information in this IRB Protocol form that you will need to provide in these Supplements.

Check all that apply	Type of Research	Supplement Name and Link
☐	**Department of Defense** The research involves Department of Defense funding, facilities, data, or personnel.	SUPPLEMENT Department of Defense
☐	**Department of Energy** The research involves Department of Energy funding, facilities, data, or personnel.	SUPPLEMENT Department of Energy
☐	**Drug, biologic, botanical, supplement** Procedures involve the use of any drug, biologic, botanical or supplement, even if the item is not the focus of the proposed research.	SUPPLEMENT Drugs
☐	**Emergency exception to informed consent** Research that requires this special consent waiver for research involving more than minimal risk.	SUPPLEMENT Exception from Informed Consent for Emergency Research (EFIC)

Check all that apply	Type of Research	Supplement Name and Link
☐	**Genomic data sharing** Genomic data are being collected and will be deposited in an external database (such as the NIH dbGaP database) for sharing with other researchers, and the UW is being asked to provide the required certification or to ensure that the consent forms can be certified.	SUPPLEMENT Genomic Data Sharing
☐	**Medical device** Procedures involve the use of any medical device, even if the device is not the focus of the proposed research, except when the device is FDA-approved and is being used through a clinical facility in the manner for which it is approved.	SUPPLEMENT Devices
☐	**Multi-site or collaborative study** The UW IRB is being asked to review on behalf of one or more non-UW institutions in a multi-site or collaborative study.	SUPPLEMENT Multi-site or Collaborative Research
☐	**Non-UW Individual Investigators** The UW IRB is being asked to review on behalf of one or more non-UW individuals who are not affiliated with another organization for the purpose of the research.	SUPPLEMENT Non-UW Individual Investigators
☐	**Other REDCap Installation Attestation for Electronic Consent** The research will use a non-UW installation of REDCap for conducting and/or documenting informed consent.	SUPPLEMENT Other REDCap Installation
☒	None of the above.	

1.10. [DETERMINATION] **Confirm by checking the box below** that you will comply with the COVID requirements described on HSD's COVID webpage, which are based on the location of the in-person study procedures and the vaccination status of study team members and study participants.

Review the HSD website for current guidelines about which in-person research activities are allowable.

☒ **Confirmed**

2. PARTICIPANTS

2.1. [DETERMINATION] **Participants**. Describe the general characteristics of the subject populations or groups, including age range, gender, health status, and any other relevant characteristics.

Adults with MS who report at least moderate fatigue.

2.2. [DETERMINATION] **Inclusion and exclusion criteria.**

2.2.a. Inclusion criteria. Describe the specific criteria that will be used to decide who will be included in the research from among interested or potential subjects. Define any technical terms in lay language.

(1) MS diagnosis of any subtype per chart review
(2) Score 4 or higher on the Fatigue Severity Scale
(3) Are able to comply with study procedures and complete measures independently assessed via self-report
(4) All genders
(5) 18 years of age or older
(6) Able to read and speak English
(7) Has experienced fatigue for 3 or more months
(8) Are willing to maintain current fatigue treatment regimen for duration of study (although individuals who want to make a change to their fatigue treatment regimen will be considered eligible 3 months after making that change)

2.2.b. Exclusion criteria. Describe the specific criteria that will be used to decide which of the subjects who meet the inclusion criteria listed above will be excluded from the research. Define any technical terms in lay language.

(1) Score greater than 7 on the Patient Determined Disease Steps Scale
(2) Has significant cognitive impairment as indicated by 1 or more errors on the 6-item Cognitive Screener
(3) Change in disease modifying medications in the prior three months assessed via self-report (although participants will be considered eligible after the 3-month window)
(4) History of MS relapse within the last 30 days prior to screening assessed via self-report (although participants will be considered eligible after the 30-day window)
(5) Current suicidal ideation with intent or plan as indicated by a score of 1 or higher on the Patient Health Questionnaire-9 suicide item and further assessment with the Columbia-Suicide Severity Rating Scale (although individuals with suicidal ideation but no intent or plan will be considered eligible)
(6) Currently engaged in psychotherapy for fatigue assessed via self-report
(7) Current pregnancy (although participants will be considered eligible when they are no longer pregnant)
(8) Inability to read or speak English
(9) Currently participating in another research study that could impact fatigue such as intervention studies targeting mood, energy management, exercise/physical activity, and diet (although participants can be screened for eligibility again once they have completed the other research study).

2.3. [DETERMINATION] **Prisoners**. IRB approval is required in order to include prisoners in research, even when prisoners are not an intended target population.

Is the research likely to have subjects who become prisoners while participating in the study?

For example, a longitudinal study of youth with drug problems is likely to have subjects who will be prisoners at some point during the study.

☒ **No**
☐ **Yes** → If a subject becomes a prisoner while participating in the study, will any study procedures and/or data collection related to the subject be continued while the subject is a prisoner?

☐ **No**
☐ **Yes →** Describe the procedures and/or data collection that will continue with prisoner subjects.

Click or tap here to enter text.

2.4. **[DETERMINATION]** Will the proposed research recruit or obtain data from individuals that are known to be prisoners?

For records reviews: if the records do not indicate prisoner status and prisoners are not a target population, select "No". See the GUIDANCE Prisoners for the definition of "prisoner", which is not necessarily tied to the type of facility in which a person is residing.

☒ **No**
☐ **Yes →** Answer the following questions (**2.4.a.** – **2.4.d.)**

2.4.a. Describe the type of prisoners, and their locations(s).

Click or tap here to enter text.

2.4.b. One concern about prisoner research is whether the effect of participation on prisoners' general living conditions, medical care, quality of food, amenities, and/or opportunity for earnings in prison will be so great that it will make it difficult for prisoners to adequately consider the research risks. How will the chances of this be reduced?

Click or tap here to enter text.

2.4.c. Describe what will be done to make sure that (a) recruitment and subject selection procedures will be fair to all eligible prisoners and (b) prison authorities or other prisoners will not be able to arbitrarily prevent or require particular prisoners from participating.

Click or tap here to enter text.

2.4.d. If the research is funded by one of these federal departments and agencies (Health & Human Services; Energy; Defense; Homeland Security; CIA; Social Security Administration), and/or will involve prisoners in federal facilities or in state/local facilities outside of Washington State: check the box below to provide assurance that study team members will (a) not encourage or facilitate the use of a prisoner's participation in the research to influence parole or pardon decisions, and (b) clearly inform each prisoner in advance (for example, in a consent form) that participation in the research will have no effect on his or her parole or pardon.

☐ **Confirmed**

2.5. **[DETERMINATION]** **Protected populations.** IRB approval is required for the use of the subject populations listed here. Check the boxes for any of these populations that will be purposefully included. (In other words, being a part of the populations is an inclusion criterion for the study.)

The WORKSHEETS describe the criteria for approval but do not need to be completed and should not be submitted.

Check all that apply	Population	Worksheet Name and Link
☐	Fetuses in utero	WORKSHEET Pregnant Women
☐	Neonates of uncertain viability	WORKSHEET Neonates
☐	Non-viable neonates	WORKSHEET Neonates
☐	Pregnant women	WORKSHEET Pregnant Women

2.5.a. If you check any of the boxes above, use this space to provide any information that may be relevant for the IRB to consider.

N/A

2.6. [DETERMINATION] **Native Americans or non-U.S. indigenous populations**. Will Native American or non-U.S. indigenous populations be actively recruited through a tribe, tribe-focused organization, or similar community-based organization?

Indigenous people are defined in international or national legislation as having a set of specific rights based on their historical ties to a particular territory and their cultural or historical distinctiveness from other populations that are often politically dominant.

Examples: a reservation school or health clinic; recruiting during a tribal community gathering.

☒ **No**

☐ **Yes →** Name the tribe, tribal-focused organization, or similar community-based organization. The UW IRB expects that tribal/indigenous approval will be obtained before beginning the research. This may or may not involve approval from a tribal IRB. The study team and any collaborators/investigators are also responsible for identifying any tribal laws that may affect the research.

Click or tap here to enter text.

2.7. [DETERMINATION] **UW Medicine and UW Dentistry residents and fellows.** Will the research involve UW Medicine or UW Dentistry residents or fellows as study subjects?

If it will → **(1)** Describe in the Recruiting section (4.1) and Risks section (10.1) how you will ensure that residents and fellows feel free to truly make a voluntary decision about participation (i.e., no negative consequences from supervisors for saying "no") and how you will ensure that any research data will not be used in the residents' and fellows' supervisor or program evaluation of them; **AND**

(2) You must inform the UW HR Labor Relations representative who negotiates with the resident's and fellows' union about the study before beginning it. This is currently Jennifer Mallahan mallaj@uw.edu .

2.8. [DETERMINATION] **Third party subjects.** Will the research collect private identifiable information about individuals *other than* the study subjects? Common examples include: collecting medical history information or contact information about family members, friends, co-workers.

"Identifiable" means any direct or indirect identifier that, alone or in combination, would allow you or another member of the research team to readily identify the person. For example, suppose that the research is about immigration history. If subjects are asked questions about their grandparents but are not asked for names or other information that would allow easy identification of the grandparents, then private identifiable information is not being collected about the grandparents and the grandparents are not subjects.

☐ **No**

☒ **Yes →** These individuals are considered human subjects in the study. Describe them and what data will be collected about them.

We will collect collateral contact data from participants. We typically do this in case of needing other people to contact the participant during time of research.

2.9. Number of subjects. Is it possible to predict or describe the maximum number of subjects (or subject units) needed to complete the study, for each subject group?

Subject units mean units within a group. For most research studies, a group will consist of individuals. However, the unit of interest in some research is not the individual. Examples:

- *Dyads such as caregiver-and-Alzheimer's patient, or parent and child*
- *Families*
- *Other units, such as student-parent-teacher*

Subject group means categories of subjects that are meaningful for the specific study. Some research has only one subject group – for example, all UW students taking Introductory Psychology. Some common ways in which subjects are grouped include:

- *By intervention – for example, an intervention group, and a control group.*
- *By subject population or setting – for example, urban versus rural families*
- *By age – for example, children who are 6, 10, or 14 years old.*

The IRB reviews the number of subjects in the context of risks and benefits. Unless otherwise specified, if the IRB determines that the research involves no more than minimal risk: there are no restrictions on the total number of subjects that may be enrolled. If the research involves more than minimal risk: The number of enrolled subjects must be limited to the number described in this application. If it is necessary later to increase the number of subjects, submit a Modification. Exceeding the IRB-approved number (over-enrollment) will be considered non-compliance.

☐ **No →** Provide the rationale in the box below. Also, provide any other available information about the scope/size of the research. You do not need to complete the table.

Example: It may not be possible to predict the number of subjects who will complete an online survey advertised through Craigslist, but you can state that the survey will be posted for two weeks and the number who respond is the number who will be in the study.

Click or tap here to enter text.

☒ **Yes →** For each subject group, use the table below to provide the estimate of the maximum desired number of individuals (or other subject unit, such as families) who will complete the research.

Group name/description	Maximum desired number or individuals (or other subject unit) who will complete the research *Provide numbers for the site(s) reviewed by the UW IRB and for the study-wide total number; example: 20/100*
PwMS who report at least moderate fatigue	21
Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.
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Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.

3. NON-UW RESEARCH SETTINGS

Complete this section only if UW investigators and people named in the SUPPLEMENT Non-UW Individual Investigators will conduct research procedures outside of UW and Harborview

3.1. [DETERMINATION] **Research locations and rationale**. Identify the locations where the research will be conducted and include a description of the reason(s) for choosing the locations. If the research will be conducted internationally, be sure to list all the countries where the research will take place.

This is especially important when the research will occur in locations or with populations that may be vulnerable to exploitation. One of the three ethical principles the IRB must consider is Justice: ensuring that reasonable, non-exploitative, and well-considered procedures are administered fairly, with a fair distribution of costs and potential benefits.

The research will be conducted at the UW Department of Rehabilitation Medicine supported by an experienced five-person research staff who coordinate the MS rehabilitation research program.

3.2. [DETERMINATION] **Local context**. Culturally appropriate procedures and an understanding of local context are an important part of protecting subjects. Describe any site-specific cultural issues, customs, beliefs, or values that may affect the research, how it is conducted, or how consent is obtained or documented.

Examples: It would be culturally inappropriate in some international settings for a woman to be directly contacted by a male researcher; instead, the researcher may need to ask a male family member for permission before the woman can be approached. It may be appropriate to obtain permission from community leaders prior to obtaining consent from individual members of a group. In some distinct cultural groups, signing forms may not be the norm.

This federal site maintains an international list of human research standards and requirements:
http://www.hhs.gov/ohrp/international/index.html

N/A

3.3. [DETERMINATION] **Location-specific laws.** Describe any local laws that may affect the research (especially the research design and consent procedures). The most common examples are laws about:

- **Specimens** – for example, some countries will not allow biospecimens to be taken out of the country.

- **Age of consent** – laws about when an individual is considered old enough to be able to provide consent vary across states, and countries.

- **Legally authorized representative** – laws about who can serve as a legally authorized representative (and who has priority when more than one person is available) vary across states and countries.
- **Use of healthcare records** – many states have laws that are similar to the federal HIPAA law but that have additional requirements.

N/A

3.4. [DETERMINATION] **Location specific administrative or ethical requirements**. Describe local administrative or ethical requirements that affect the research.

Example: A school district may require researchers to obtain permission from the head district office as well as school principals before approaching teachers or students; a factory in China may allow researchers to interview factory workers but not allow the workers to be paid for their participation.

N/A

3.5. [DETERMINATION] **If the PI is a student: Does the research involve traveling outside of the U.S.?**

☒ **No**

☐ **Yes →** Confirm by checking the box that (1) you will register with the **UW Office of Global Affairs** before traveling; (2) you will notify your advisor when the registration is complete; and (3) you will request a UW Travel Waiver if the research involves travel to the list of countries requiring a UW Travel Waiver.

☐ **Confirmed**

4. RECRUITING AND SCREENING PARTICIPANTS

4.1. [DETERMINATION] **Recruiting and screening**. Describe how subjects will be identified, recruited, and screened. Include information about: how, when, where, and in what setting. Identify who (by position or role, not name) will approach and recruit subjects, and who will screen them for eligibility.

Note: Per UW Medicine policy, the UW Medicine eCare/MyChart system may not be used for research recruitment purposes. Additionally, researchers may not use UW Medicine's Epic Care Everywhere data for research purposes unless the clinical data is necessary for patient/participant safety activities. This means Care Everywhere data cannot be used for recruitment, data abstraction, or any research activities other than those necessary for patient/participant safety.

We will recruit participants from the UW Medicine MS Center Research Recruitment Pool, which currently has 1,300 patients who have indicated interest in participating in research. Research staff will access potential participants' names, email and mailing addresses, and telephone numbers via the Pool. UW MS Center patients have opted into this Pool and provided their contact information and consent for study staff to confirm via EPIC their MS diagnosis prior to study enrollment.

We will use procedures from past studies in which we have met our enrollment goals and retained >90% of our participants. Study staff will email interested individuals an invitation to participate in the study. Then, using the screening tool, staff will complete a telephone screening during which they will discuss the study, ask questions, and confirm eligibility. Screening questions will include:

Must be yes to qualify

1. Is the person 18 years old or older? _____
2. Is the person able to fluently converse and read in English? _____
3. Does the person currently have a diagnosis of MS? _____
    a. Confirmed via EHR _____ or
    b. Gathered via self-report and confirmed by at least one of the following. _____
        i. Person has shown after visit summary from a medical provider with MS diagnosis listed/mentioned
        ii. Person has shown note from a medical provider with MS diagnosis listed/mentioned
        iii. Person has shown photo of disease modifying therapies (DMTs) medication bottle or prescription for MS
4. Is the person able to comply with study procedures and complete measures independently assessed via self-report? _____
5. Does the person score 4 or higher on the Fatigue Severity Scale? _____
6. Has the person experienced fatigue for 3 or more months? _____
7. Is the person willing to maintain current fatigue treatment regimen for duration of study (although individuals who want to make a change to their fatigue treatment regimen will be considered eligible 3 months after making that change)? _____

Must be no to qualify

8. Does the person score 7 or higher on the Patient Determined Disease Steps Scale? _____
9. Does the person have significant cognitive impairment as indicated by 1 or more errors on the 6-item Cognitive Screener? _____
10. Did the person change disease modifying medications in the prior three months (although participants will be considered eligible after the 3-month window)? _____
11. Did the person have an MS relapse within the last 30 days prior to screening (although participants will be considered eligible after the 30-day window)? _____
12. Does the person have current suicidal ideation with intent or plan as indicated by a score of 1 or higher on the Patient Health Questionnaire-9 suicide item and further assessment with the Columbia-Suicide Severity Rating Scale (although individuals with suicidal ideation but no intent or plan will be considered eligible)? _____
13. Is the person currently engaged in psychotherapy for fatigue? _____
14. Is the person pregnant (although participants will be considered eligible when they are no longer pregnant)? _____
15. Is the person participating in another research study that could impact fatigue (although individuals can be screened for eligibility again once they have completed the other research study)? _____

<u>The PHQ-9 suicide item and Columbia-Suicide Severity Rating Scale may reveal suicide ideation. More detail is in Section 10.10.</u>

4.2. Recruitment materials.

4.2.a. What materials (if any) will be used to recruit and screen subjects?

Examples: talking points for phone or in-person conversations; video or audio presentations; websites; social media messages; written materials such as letters, flyers for posting, brochures, or printed advertisements; questionnaires filled out by potential subjects.

Info on MS Clinic provider recruitment reference sheet, recruitment script, screening form, and email. We will not post flyers in the clinic given the robust Research Center Pool.

4.2.b. Upload descriptions of each type of material (or the materials themselves) to ***Zipline***. If letters or emails will be sent to any subjects, these should include a statement about how the subject's name and contact information were obtained. No sensitive information about the person (such as a diagnosis of a medical condition) should be included in the letter. The text of these letters and emails must be uploaded to ***Zipline*** (i.e., a description will not suffice).

HSD encourages researchers to consider uploading descriptions of most recruitment and screening materials instead of the materials themselves. The goal is to provide the researchers with the flexibility to change some information on the materials without submitting a Modification for IRB approval of the changes. Examples:

- *Provide a list of talking points that will be used for phone or in-person conversations instead of a script.*
- *For the description of a flyer, include the information that it will provide the study phone number and the name of a study contact person (without providing the actual phone number or name). This means that a Modification would not be necessary if/when the study phone number or contact person changes. Also, instead of listing the inclusion/exclusion criteria, the description below might state that the flyer will list one or a few of the major inclusion/exclusion criteria.*
- *For the description of a video or a website, include a description of the possible visual elements and a list of the content (e.g., study phone number; study contact person; top three inclusion/exclusion criteria; payment of $50; study name; UW researcher).*

4.3. [DETERMINATION] **Relationship with participant population**. Do any members of the study team have an existing relationship with the study population(s)?

Example: a study team member may have a dual role with the study population such as being their clinical care provider, teacher, laboratory directory or tribal leader in addition to recruiting them for their research.

☐ **No**
☒ **Yes →** Describe the nature of the relationship.

Members of the research staff work at the UW Medicine MS Center and regularly work with MS Center patients interested in research.

4.4. Payment to participants. The IRB must evaluate subject payment for the possibility that it will unduly influence subjects to participate. Refer to **GUIDANCE Subject Payment** when designing subject payment plans. Provide the following information about your plans for paying research subjects in the text box below or note that the information can be found in the consent form.

- The total amount/value of the payment
- Schedule/timing of the payment [i.e., when will subjects receive the payment(s)]
- Purpose of the payment [e.g., reimbursement, compensation, incentive]
- Whether payment will be "pro-rated" so that participants who are unable to complete the research may still receive some part of the payment

The IRB expects the consent process or study information provided to the subjects to include all of the above-listed information about payment, including the number and amount of payments, and especially when subjects can expect to receive payment. One of the most frequent complaints received by HSD is from subjects who expected to receive cash or a check on the day that they completed a study and who were angry or disappointed when payment took 6-8 weeks to reach them.

Researchers should review current UW Financial Management requirements about when Social Security Numbers must be collected, and when research payment must be reported to the UW Tax Office and the IRS: https://finance.uw.edu/ps/how-pay/research-subjects.

If your study involves the use of Amazon's Mechanical Turk (MTurk), you must comply with the UW Procurement Services policy that no UW employee, family member, or student directly involved in the research will participate as a subject. The policy requires adding a qualifying question that asks whether the subject is a UW employee or family member, or UW student who is directly involved in the research. If they answer yes, they must be disqualified from MTurk activities.

As compensation for their time, we will offer participants $20 for the pre-intervention assessment period, $20 for the post-intervention assessment period, and $20 for completing a qualitative interview. We will pay participants only for the assessments they complete. Total possible compensation of $60 per participant.

Participants can expect to receive their checks within a month of having completed the corresponding study tasks.

4.5. [DETERMINATION] **Non-monetary compensation**. Describe any non-monetary compensation that will be provided. Example; extra credit for students; a toy for a child.

N/A

4.5.a. If class credit will be offered to students, there must be an alternate way for the students to earn the extra credit without participating in the research. If class credit will be offered, describe the alternative non-research method by which students can earn that same course credit, including who will provide the alternative (e.g., a student subject pool; the course instructor).

Click or tap here to enter text.

4.6. [DETERMINATION] **Will data or specimens be accessed or obtained for recruiting and screening procedures prior to enrollment?**

Examples: names and contact information; the information gathered from records that were screened; results of screening questionnaires or screening blood tests; Protected Health Information (PHI) from screening medical records to identify possible subjects.

☐ **No →** Skip the rest of this section; go to question **5.1.**

☒ **Yes →** Describe the data and/or specimens (including PHI) and whether it will be retained as part of the study data.

Participants' names and contact information may be accessed from various recruitment pools or referred to the study by a provider prior to enrollment. Participants will complete an initial screening to determine eligibility prior to enrollment. Before asking potential participants screening questions to determine eligibility for the study, research staff will first obtain non-written, verbal consent to ask these questions.

All participants who decline to participate yet are deemed eligible to participate will be asked to provide basic demographic information (e.g., age, sex, gender, and geographic location) to determine if any differences exist between those who enroll in the study and those who do not. Research staff will first obtain non-written, verbal consent to ask these questions.

4.7. Consent for recruiting and screening. Will consent be obtained for any of the recruiting and screening procedures? (Section 8: Consent of Adults asks about consent for the main study procedures).

"Consent" includes: consent from individuals for their own participation; parental permission; assent from children; consent from a legally authorized representative for adult individuals who are unable to provide consent.

Examples:

- *For a study in which names and contact information will be obtained from a registry: the registry should have consent from the registry participants to release their names and contact information to researchers.*
- *For a study in which possible subjects are identified by screening records: there will be no consent process.*
- *For a study in which individuals respond to an announcement and call into a study phone line: the study team person talking to the individual may obtain non-written consent to ask eligibility questions over the phone.*

☐ **No →** Skip the rest of this section; go to question **5.1.**
☒ **Yes →** Describe the consent process.

Research staff members will ask interested people a set of formalized questions to determine eligibility based on the inclusion/exclusion criteria. The research staff member staff will obtain non-written consent to ask the eligibility questions before initiating the screening process.

4.7.a. Documentation of consent. Will a written or verifiable electronic signature from the subject on a consent form be used to document consent for the recruiting and screening procedures?

☒ **No →** Describe the information that will be provided during the consent process and for which procedures.

Research staff will participate in and obtain informed consent from research participants after screening but prior to commencement of any further study procedures. Prospective participants will also be asked for consent to complete the screening questions at the start of the screening process. The informed consent process will take place over the telephone at a time deemed mutually feasible for the participant and staff member and coordinated on a case-by-case basis.

Prior to the informed consent process, research staff will email (or postal mail, if the participant prefers) a copy of an information statement for the participant to review as well as the date and time of the consent process appointment. Participants will be encouraged to read the information statement prior to the scheduled consent session and to be prepared with any questions. If the informed consent session is scheduled more than two business days in advance, research staff will call and/or email participants as a reminder. Participants will be requested to have the information statement in front of them during the consent session.

A research staff member will review each section of the information statement approved by the UW IRB, inviting discussion to ensure comprehension. Staff will be trained by study investigators to ensure competency to discuss informed consent and strategies to ensure there is no coercion.

Participants will be provided with as much time as needed to review the information statement and ask the research staff member questions about the information statement, their rights as human participants, and participation in the study. Potential participants will be fully informed of all risks and benefits prior to giving their verbal informed consent and prior to enrollment in the study.

If during the course of this contact the potential participant has questions that cannot be addressed by research staff, one of the study investigators or the research manager (depending on the nature of the questions) will follow up with the potential participant to answer the questions. Participants may take time to think about participating and render a decision at a subsequent time.

Potential participants will be asked to repeat back to research staff their understanding of the information statement material as necessary. Individuals will not be permitted to participate if there is any question as to whether a person has capacity to provide informed consent.

When all questions have been answered, research staff will ask the participant if they would like to participate in the study. The participant will then be asked to provide verbal consent to participate. The participant will not need to sign the information statement, as we will be applying for a Waiver of Documentation of Informed Consent with this IRB application.

☐ **Yes, written →** If yes and a written signature will be used to document consent:

- Upload the consent form to ***Zipline***.

☐ **Yes, electronic →** If yes and an electronic signature will be used to document consent:

- Upload the consent form to ***Zipline***.
- **If the eSignature process or method for recruiting and screening is different than for the main study procedures**, use the questions about electronic consent in Sections 8.3. and 8.4. to differentiate between recruiting/screening and main study electronic consent. **If electronic consent will be used for recruiting/screening but not main study consent**, use 8.3. and 8.4. to describe e-consent and note that it is only for recruiting/screening.

5. PROCEDURES

5.1. [DETERMINATION] **Study procedures**. Using lay language, provide a complete description of the study procedures, including the sequence, intervention, or manipulation (if any), drug dosing information (if any), blood volumes and frequency of draws (if any), use of records, time required, and setting/location. If it is available: Upload a study flow sheet or table to ***Zipline***.

*For studies comparing standards of care: It is important to accurately identify the research procedures. Review the section titled, "When to describe risks for studies evaluating medically recognized standards of care" in the **GUIDANCE Consent** and the draft guidance from the federal Office of Human Research Protections, "**Guidance on Disclosing Reasonably Foreseeable Risks in Research Evaluating Standards of Care**"; October 20, 2014.*

Information about pediatric blood volume and frequency of draws that would qualify for expedited review can be found in this **reference table** *on the Seattle Children's IRB website.*

All study activities will be completed remotely via Zoom or over the phone over the approximately 2 months. Participants will complete a baseline self-report assessment via REDCap (or by telephone, if preferred) that will take approximately 30-45 minutes to complete. At this time, they will also complete a medication collection form with research staff by phone and will be randomly assigned to one of three 4-session telehealth CBT intervention components: (1) relaxation training, (2) behavioral activation, or (3) cognitive therapy. Prior to starting their assigned intervention component, participants will complete a survey consisting of four to eight questions about their fatigue twice per day (morning and evening) for seven days via REDCap (or by telephone, if preferred). They will then complete the 4-session intervention to which they are randomly assigned in approximately 4 weeks. After completing the first intervention session, participants will complete a treatment expectancy measure via REDCap (or by telephone, if preferred). After completing the intervention, participants will complete the post-intervention self-report assessment via REDCap (or by telephone, if preferred) within one month of the last intervention session. During this time, they will also complete a medication collection form with research staff by phone and a survey consisting of four to eight questions about their fatigue twice per day (morning and evening) for seven days via REDCap (or by telephone, if preferred). Qualitative interview data will supplement the quantitative data collected in the post-intervention assessment. Study staff will conduct and audio record semi-structured interviews within one month of completing the last intervention session to query participants about feasibility, acceptability, appropriateness, and perceived efficacy of the intervention component they completed to inform potential component refinement.

5.2. [DETERMINATION] **Recordings**. Does the research involve creating audio or video recordings?

☐ **No** → Go to question **5.3.**

☒ **Yes →** Verify that you have described what will be recorded in the answer to question **5.1.**, and answer question the question below**.**

5.2.a. Before recording, will consent for being recorded be obtained from subjects and any other individuals who may be recorded?

☐ **No →** Email hsdinfo@uw.edu before submitting this application in ***Zipline***. In the email, include a brief description of the research and a note that individuals will be recorded without their advance consent.

☒ **Yes**

5.3. [DETERMINATION] **MRI scans**. Will any subjects have a Magnetic Resonance Imaging (MRI) scan as part of the study procedures?

This means scans that are performed solely for research purposes or clinical scans that are modified for research purposes (for example, using a gadolinium-based contrast agent when it is not required for clinical reasons).

☒ **No →** Go to question **5.4.**

☐ **Yes →** Answer questions **5.3.a** through **5.3.c.**

5.3.a. Describe the MRI scan(s). Specifically:

- What is the purpose of the scan(s)? *Examples: obtain research data; safety assessment associated with a research procedure.*
- Which subjects will receive an MRI scan?
- Describe the minimum and maximum number of scans per subject, and over what time period the scans will occur. *For example: all subjects will undergo two MRI scans, six months apart.*

Click or tap here to enter text.

5.3.b. MRI facility. At which facility(ies) will the MRI scans occur? Check all that apply.

☐ UWMC Radiology/Imaging Services (the UWMC clinical facility)
☐ DISC Diagnostic Imaging Sciences Center (UWMC research facility)
☐ CHN Center for Human Neuroscience MRI Center (Arts & Sciences research facility)
☐ BMIC Biomolecular Imaging Center (South Lake Union research facility)
☐ Harborview Radiology/Imaging Services (the Harborview clinical facility)
☐ Northwest Diagnostic Imaging
☐ Other: identify in the text box below:

Click or tap here to enter text.

5.3.c. Personnel. For MRI scans that will be conducted at the DISC, CHN or BMIC research facilities: Indicate who will be responsible for operating the MRI scanner by checking all that apply.

☐ MRI technician who is formally qualified
☐ Researcher who has completed scanner operator training provided by a qualified MRI operator

5.4. [DETERMINATION] **Data variables**. Describe the specific data that will be obtained (including a description of the most sensitive items). Alternatively, a list of the data variables may be uploaded to ***Zipline***.

Demographic Information and Baseline Assessment
After providing informed consent, research staff will ask the participant to provide demographic data (e.g., age, sex, gender orientation, ethnicity/race, marital status, education level, income, household size, disability compensation status, lawsuit status, employment status) for descriptive purposes. We will also ask participants to complete validated self-report questionnaires (demographics, MS disease-related variables, quality of life, and biopsychosocial symptom variables [e.g., fatigue]). We will also ask participants to complete a survey consisting of four-eight questions about their fatigue twice per day (morning and evening) for seven days (each survey should take less than 5 minutes).

Personal Contact Information
Research staff will collect the following information from participants: (1) contact information; (2) preferred telephone number to reach an individual if they have more than one line; (3) permission to leave message on mobile/landline phones; (4) permission to send a text message and, if yes, cell phone carrier; (5) best times/days to reach participant; (6) email address; (7) preferred communication method; and (8) names and contact information of people staff are allowed to contact if participant is lost to follow-up or otherwise cannot be contacted (i.e., collateral contacts).

We will gather data either from the participant directly or in the form of online self-report assessments via a password-protected database on the department's secure server.

Treatment Expectancy Assessment
Participants will complete the Credibility/Expectancy Scale after the first intervention session.

Medication collection form (pre- and post-treatment)
Participants will be asked questions about the medications they are taking (e.g., name, indication, dosage, dose units)

Post-Intervention Assessment
Participants will be asked questions about quality of life and biopsychosocial symptom variables (e.g., fatigue). We will also ask participants to complete a survey consisting of four-eight questions about their fatigue twice per day (morning and evening) for seven days (each survey should take less than 5 minutes).

Post-Intervention Qualitative Interview
Participants will complete a qualitative semi-structured interview at post-intervention to further assess and contextualize quantitative data on each component's feasibility, acceptability, appropriateness, and preliminary efficacy, for the purpose of refining the intervention components as necessary (see Study 1 List of Intervention Questions).

5.5. [DETERMINATION] **Data sources**. For all types of data that will be accessed or collected for this research: Identify whether the data are being obtained from the subjects (or subjects' specimens) or whether they are being obtained from some other source (and identify the source).

If you have already provided this information in Question 5.1, you do not need to repeat the information here.

We will gather data either from the participant directly or in the form of online surveys administered through REDCap.

5.6. [DETERMINATION] **Identifiability of data and specimens.** Answer these questions carefully and completely. This will allow HSD to accurately determine the type of review that is required and the relevant compliance requirements. Review the following definitions before answering the questions:

Access *means to view or perceive data, but not to possess or record it. See, in contrast, the definition of "obtain".*
Identifiable *means that the identity of an individual is or may be readily (1) ascertained by the researcher or any other member of the study team from specific data variables or from a combination of data variables, or (2) associated with the information.*
Direct identifiers *are direct links between a subject and data/specimens. Examples include (but are not limited to): name, date of birth, medical record number, email or IP address, pathology or surgery accession number, student number, or a collection of data that is (when taken together) identifiable.*
Indirect identifiers *are information that links between direct identifiers and data/specimens. Examples: a subject code or pseudonym.*
Key *refers to a single place where direct identifiers and indirect identifiers are linked together so that, for example, coded data can be identified as relating to a specific person. Example: a master list that contains the data code and the identifiers linked to the codes.*
Obtain *means to possess or record in any fashion (writing, electronic document, video, email, voice recording, etc.) for research purposes and to retain for any length of time. This is different from accessing, which means to view or perceive data.*

5.6.a. Will you or any members of you team have access to any direct or indirect identifiers?

☒ **Yes →** Describe which identifiers and for which data/specimens.

Research staff members will have access to the identifiers database to contact participants.

☐ **No →** Select the reason(s) why you (and all members of your team) will not have access to direct or indirect identifiers.

☐ There will be no identifiers
☐ Identifiers or the key have been (or will have been) destroyed before access.
☐ There is an agreement with the holder of the identifiers (or key) that prohibits the release of the identifiers (or key) to study team members under any circumstances.

This agreement should be available upon request from the IRB. Examples: a Data Use Agreement, Repository Gatekeeping form, or documented email.

☐ There are written policies and procedures for the repository/database/data management center that prohibit the release of the identifiers (or identifying link). This includes situations involving an Honest Broker.
☐ There are other legal requirements prohibiting the release of the identifiers or key. Describe them below.

Click or tap here to enter text.

5.6.b. Will you or any study team members obtain any direct or indirect identifiers?

☒ **Yes →** Describe which identifiers and for which data/specimens.

Research staff members will obtain first and last names, addresses, telephone numbers, and/or email addresses. For everyone we contact for recruitment purposes, we will also collect, at minimum, first and last name, and a telephone number; if available, we will also collect mailing or email addresses. The one exception is if a prospective participant contacts researchers first and only provides limited information (e.g., a participant sees a flyer in a clinic and leaves a voicemail with only her first name and telephone number).

In addition, we will retain the name, address, and telephone number of all subjects who are found ineligible or decline to avoid attempting to recruit them a second time. We will also collect information regarding the reason for ineligibility based on the inclusion and exclusion criteria.

☐ **No →** Select the reason(s) why you (and all members of your team) will not obtain direct or indirect identifiers.

☐ There will be no identifiers.
☐ Identifiers or the key have been (or will have been) destroyed before access.
☐ There will be an agreement with the holder of the identifiers (or key) that prohibits the release of the identifiers (or key under any circumstances.

This agreement should be available upon request from the IRB. Examples: a Data Use Agreement, Repository Gatekeeping form, or documented email.

☐ There are written policies and procedures for the repository/database/data management center that prohibit the release of the identifiers (or identifying link). This includes situations involving an Honest Broker.
☐ There are other legal requirements prohibiting the release of the identifiers or key. Describe them below.

Click or tap here to enter text.

5.6.c. If any identifiers will be obtained, indicate how the identifiers will be stored (and for which data). NOT: Do not describe the data security plan here, that information is requested in question **9.6**.

☒ Identifiers will be stored with the data. Describe the data to which this applies:

The research team will collect and store all study data, including participant identifiers, in REDCap which is a secure, password protected, and HIPAA compliant web-based data platform. We will (1) assign each paritpcant an ID number in REDCap to maintain confidentiality and (2) use this ID number to code/label study data. The link between the study data and a participant's identity in the form of the unique study code will only exist in REDCap. Only research staff members will know the password.

No data will be released to persons outside the research team except when required by law, e.g. freedom of information act legislation or with written permission of the subject (i.e. signed release of information form). Data will be reported in publications only in anonymous summary form.

☐ Identifiers and study data will be stored separately but a link will be maintained between the identifiers and the study data (for example, through the use of a code). Describe the data to which this applies:

Click or tap here to enter text.

☐ Identifiers and study data will be stored separately, with no link between the identifiers and the study data. Describe the data to which this applies:

Click or tap here to enter text.

5.6.d. Research collaboration. Will individuals who provide coded information or specimens for the research also collaborate on other activities for this research? If yes, identify the activities and provide the name of the collaborator's institution/organization.

Examples include but are not limited to: (1) study, interpretation, or analysis of the data that results from the coded information or specimens; and (2) authorship on presentations or manuscripts related to this work.

No

5.7. [DETERMINATION] **Protected Health Information (PHI).** Will participants' identifiable PHI be accessed, obtained, used, or disclosed for any reason (for example, to identify or screen potential subjects, to obtain study data or specimens, for study follow-up) that does not involve the creation or obtaining of a Limited Data Set?

PHI is individually identifiable healthcare record information or clinical specimens from an organization considered a "covered entity" by federal HIPAA regulations, in any form or media, whether electronic, paper, or oral. ***You must answer yes to this question if the research involves identifiable health care records (e.g., medical, dental, pharmacy, nursing, billing, etc.), identifiable healthcare information from a clinical department repository, or observations or recordings of clinical interactions.***

For information about what constitutes the UW Covered Entity, see UW Medicine Compliance Patient Information Privacy Policy 101 and diagram of the healthcare components.

☐ **No →** Skip the rest of this question; go to question **5.8**.
☒ **Yes →** Answer all of the questions below (**5.7.a.** through **5.7.f.**)

5.7.a. Describe the PHI and the reason for using it. *Be specific. For example, will any "free text" fields (such as physician notes) be accessed, obtained, or used?*

For recruitment purposes, research staff will access potential participants' names, email and mailing addresses, and telephone numbers via the UW MS Center Research Recruitment Pool. UW MS Center patients have opted into this pool and provided their

contact information and consent for study staff to confirm via EPIC their MS diagnosis prior to study enrollment.

5.7.b. Is any of the PHI located in Washington State?

☐ **No**
☒ **Yes**

5.7.c. Describe the pathway of how the PHI will be accessed or obtained, starting with the source/location and then describing the system/path/mechanism by which it will be identified, accessed, and copied for the research. *Be specific. For example: directly view records; search through a department's clinical database; submit a request to Leaf.*

Research staff will review the patient's medical records via Epic to ensure the individual has a definitive MS diagnosis before initiating the screening process.

5.7.d. For which PHI will subjects provide HIPAA authorization before the PHI is accessed, obtained and/or used?

N/A

Confirm by checking the box that UW Medicine HIPAA Authorization form maintained on the HSD website will be used to access obtain, use, or disclose any UW Medicine PHI.

☐ **Confirmed**

5.7.e. Will you obtain any HIPAA authorizations electronically (i.e., e-signature)?

☐ **No**
☐ **Yes** → Confirm by checking the box that you have read and understand the *Electronic Documentation of Consent* section of the **WORKSHEET Consent Requirements and Waivers** the **GUIDANCE Consent** *Documentation of Consent* for information regarding the use of electronic signatures and HIPAA authorizations.

☐ **Confirmed**

5.7.f. For which PHI will HIPAA authorization NOT be obtained from the subjects?

Provide the following assurances by checking the boxes.

☒ The minimum necessary amount of PHI to accomplish the purposes described in this application will be accessed, obtained and/or used.

☒ The PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted.
☒ The HIPAA "accounting for disclosures" requirement will be fulfilled, if applicable. See UW Medicine Compliance Policy #104.
☒ There will be reasonable safeguards to protect against identifying, directly or indirectly, any patient in any report of the research.

5.8. [DETERMINATION] **Genomic data sharing**. Will the research obtain or generate genomic data?

☒ **No**
☐ **Yes →** Answer the question below.

5.8.a. Will genomic data from this research be sent to a national database (for example, NIH's dbGaP database)?

☐ **No**
☐ **Yes →** Complete the **SUPPLEMENT Genomic Data Sharing** and upload it to ***Zipline***.

5.9. Whole genome sequencing. For research involving biospecimens: Will the research include whole genome sequencing?

Whole genome sequencing is sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen.

☒ **No**
☐ **Yes**

5.10. [DETERMINATION] **Cannabis (marijuana), hemp, and related compounds**. These questions are about: cannabis (any part of the plant in any form), hemp, cannabidiol (CBD), delta-8-THC, any product derived from cannabis or hemp, and related synthesized compounds. All UW research must comply with federal laws about cannabis because of conditions associated with the federal money that UW receives. Answer the questions below so that HSD can determine whether the federal laws apply to your specific situation. See the UW Guidance on Research Involving Marijuana for additional information.

5.10.a. Does your research involve any of the following? Check all that apply.
☐ Study staff will obtain or handle any of the above items
☐ Study will provide money to the participants to obtain any of the above items
☐ Study participants will use or consume any of the above items on campus or in any UW-owned or leased facility
☒ None of the above

5.10.b. If you checked any box except "None of the above", provide the following information about each cannabis and related item your research will involve: Name of the item, how you will obtain it, the source, and whether it contains ≥0.3% THC (tetrahydrocannabinol).

Click or tap here to enter text.

5.11. **Possible secondary use or sharing of information, specimens, or subject contact information.** Please consider the broadest possible future plans and whether consent will be obtained now from the subjects for future sharing or research uses (which it may not be possible to describe in detail at this time).

Many federal grants and contracts now require data or specimen sharing as a condition of funding, and many journals require data sharing as a condition of publication. "Sharing" may include (for example): informal arrangements to share banked data/specimens with other investigators; establishing a repository that will formally share with other researchers through written agreements; or sending data/specimens to a third-party repository/archive/entity such as the Social Science Open Access Repository (SSOAR), or the UCLA Ethnomusicology Archive.

Answer all of the questions below. Write **NA** in response to questions **5.11.b** through **5.11.g** if sharing is unlikely or if the only sharing will be through the NIH Genomic Data Sharing described in question **5.8**.

5.11.a Is this research funded by an NIH funding application submitted on or after January 25, 2023.

☒ **No**

☐ **Yes →** NIH Data Management and Sharing Policy applies to this research. Complete the rest of this section. If the policy applies and data will not be shared, provide the justification in response to **5.11.e** and write **NA** in response to the other questions.

5.11.b. Describe what will be stored for future use, including whether any direct or indirect (e.g., subject codes) identifiers will be stored.

All study data will be stored in de-identified form indefinitely following the closure of the IRB application. Study researchers may conduct secondary analyses of the study data in de-identified form following closure related to examining various aspects of the behavioral interventions, quality of life issues regarding individuals with MS, etc. Study data may be shared in de-identified form with outside researchers and collaborators as requested and deemed acceptable by study investigators.

5.11.c. Describe what will be shared with other researchers or with a repository/database/registry, including whether direct identifiers will be shared and (for specimens) what data will be released with the specimens. If shared through a repository, specify if it is unrestricted access (i.e., publicly accessible).

Study data may be shared in de-identified form with outside researchers and collaborators as requested and deemed acceptable by study investigators.

5.11.d. Who will oversee and/or manage the sharing?

Lindsey Knowles, UW PI

5.11.e. Describe the possible future uses, and any limitations or restrictions on future uses or users.

Examples of limitations:

- *Consent prohibits or limits the scope of sharing and use (e.g., consent states that data will be used only for cardiovascular research)*
- *Privacy or safety or research participants would be compromised (e.g., there is risk of reidentification and/or harm)*
- *Explicit federal, state, or local, or Tribal law, regulation, or policy prohibits disclosure*

- *Restrictions imposed by existing or anticipated agreements (e.g., with third party funders, partners, with repositories, medical centers providing health information under a data use agreement)*

As mentioned above, study data may be analyzed to answer both a priori and post hoc hypotheses related to various aspects of the study behavioral interventions and quality of life issues regarding individuals with MS within the context of rehabilitation medicine.

5.11.f. Consent. Will consent be obtained now from subjects for the secondary use, banking, and/or future sharing?

☐ **No**
☒ **Yes →** Be sure to include the information about this consent process in the consent form (if there is one) and in the answers to the consent question in Section 8.

5.11.g. Withdrawal. Will subjects be able to withdraw their data/specimens from secondary use, banking or sharing?

☐ **No**
☒ **Yes →** Describe how, and whether there are any limitations on withdrawal.

Example: data can be withdrawn from the repository but cannot be retrieved after they are released.

Study data cannot be withdrawn following data collection or retrieved after they are released.

5.11.h. Agreements for sharing or release. Confirm by checking the box that the sharing or release will comply with UW (and, if applicable, UW Medicine) policies that require a formal agreement with the recipient for release of data or specimens to individuals or entities other than federal databases.

Data Use Agreements or Gatekeeping forms are used for data; Material Transfer Agreements are used for specimens (or specimens plus data). Do not attach any template agreement forms; the IRB neither reviews nor approves them.

☒ **Confirmed**

5.12. Communication with subjects during the study. Describe the types of communication (if any) the research team will have with already-enrolled subjects during the study. Provide a description instead of the actual materials themselves.

Examples: email, texts, phone, or letter reminders about appointments or about returning study materials such as a questionnaire; requests to confirm contact information.

Staff will email participants notifications to complete online assessments at designated times, call to administer assessments as needed and based on participant preference, check on study progress, and, if the participant is unresponsive to email, call or send text messages.

5.13. **Future contact with subjects**. Is there a plan to retain any contact information for subjects so that they can be contacted in the future?

☐ **No**

☒ **Yes →** Describe the purpose of the future contact, and whether use of the contact information will be limited to the study team; if not, describe who else could be provided with the contact information. Describe the criteria for approving requests for information.

Examples: inform subjects about other studies; ask subjects for additional information or medical record access that is not currently part of the study proposed in this application; obtain another sample.

We would like to retain contact information so if a participant is interested in published results, we may notify them or send them information about the results.

In addition, study staff may share direct identifiers with other UW Department of Rehabilitation Medicine researchers if a participant indicates they would like to be enrolled in the department subject pool and contacted regarding future opportunities to participate in research.

5.14. Alternatives to participation. Are there any alternative procedures or treatments that might be advantageous to the subjects?

If there are no alternative procedures or treatments, select "No". Examples of advantageous alternatives: earning extra class credit in some time-equivalent way other than research participation; obtaining supportive care or a standard clinical treatment from a health care provider instead of participating in research with an experimental drug.

☒ **No**

☐ **Yes →** Describe the alternatives.

Click or tap here to enter text.

5.15. Upload to *Zipline* all data collection forms (if any) that will be directly used by or with the subjects, and any scripts/talking points that will be used to collect the data. Do not include data collection forms that will be used to abstract data from other sources (such as medical or academic records), or video recordings.

- ***Examples****: survey, questionnaires, subject logs or diaries, focus group questions.*
- ***NOTE****: Sometimes the IRB can approve the general content of surveys and other data collection instruments rather than the specific form itself. This prevents the need to submit a modification request for future minor changes that do not add new topics or increase the sensitivity of the questions. To request this general approval, use the text box below to identify the questionnaires/surveys/ etc. for which you are seeking this more general approval. Then briefly describe the scope of the topics that will be covered and the most personal and sensitive questions. The HSD staff person who screens this application will let you know whether this is sufficient or whether you will need to provide more information.*
- ***For materials that cannot be uploaded****: upload screenshots or written descriptions that are sufficient to enable the IRB to understand the types of data that will be collected and the nature of the experience for the participant. You may also provide URLs (website addresses) or written descriptions below. Examples of materials that usually cannot be uploaded: mobile apps; computer-administered test; licensed and restricted standardized tests.*
- ***For data that will be gathered in an evolving way****: This refers to data collection/questions that are not pre-determined but rather are shaped during interactions with participants in response to observations and responses made during those interactions. If this applies to the proposed research, provide a description of the process by which the data collection/questions will be established during the interactions with subjects, how the data collection/questions will be documented, the topics likely to be addressed, the most sensitive type of information likely to be gathered, and the limitations (if any) on topics that will be raised or pursued.*

Use this text box (if desired) to provide:

- Short written descriptions of materials that cannot be uploaded, such as URLs
- A description of the process that will be used for data that will be gathered in an evolving way.
- The general content of questionnaires, surveys and similar instruments for which general approval is being sought. (See the **NOTE** bullet point in the instructions above.)

See uploaded documents.

5.16. [DETERMINATION] **SARS-CoV-2 testing**. Will the subjects be tested for the SARS-CoV-2 coronavirus?

☒ **No**

☐ **Yes →** If yes:

- Name the testing lab
- Confirm that the lab and its use of this test is CLIA certified or certified by the Washington State Department of Health
- Describe whether you will return the results to the participants and, if yes, who will do it and how (including any information you would provide to subjects with positive test results).

Click or tap here to enter text.

6. CHILDREN (MINORS) AND PARENTAL PERMISSION

6.1. [DETERMINATION] **Involvement of minors**. Does the research include minors (children)?

Minor or child means someone who has not yet attained the legal age for consent for the research procedures, as described in the applicable laws of the jurisdiction in which the research will be conducted. This may or may not be the same as the definition used by funding agencies such as the National Institutes of Health.

- In Washington State the generic age of consent is 18, meaning that anyone under the age of 18 is considered a child.
- There are some procedures for which the age of consent is much lower in Washington State.
- The generic age of consent may be different in other states, and in other countries.

☒ **No →** Go to Section 8.

☐ **Yes →** Provide the age range of the minor subjects for this study and the legal age for consent in the study population(s). If there is more than one answer, explain.

Click or tap here to enter text.

☐ **Don't know →** This means is it not possible to know the age of the subjects. For example, this may be true for some research involving social media, the Internet, or a dataset that is obtained from another researcher or from a government agency. Go to Section 8.

6.2. Parental permission. Parental permission means actively obtaining the permission of the parents. This is not the same as "passive" or "opt out" permission where it is assumed that parents are allowing their children to participate because they have been provided with information about the research and have not objected or returned a form indicating they don't want their children to participate.

6.2.a. Will parental permission be obtained for:

☐ All of the research procedures → Go to question **6.2.b**.
☐ None of the research procedures → Use the table below to provide justification and skip question **6.2.b.**
☐ Some of the research procedures → Use the table below to identify the procedures for which parental permission will not be obtained.

Be sure to consider all research procedures and plans, including screening, future contact, and sharing/banking of data and specimens for future work.

Children Group[1]	Describe the procedures or data/specimen collection (if any) for which there will be NO parental permission[2]	Reason why parental permission will not be obtained	Will parents be informed about the research?[3]	
			YES	NO
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐

Table footnotes

1. *If the answer is the same for all children groups or all procedures: collapse the answer across the groups and/or procedures.*
2. *If identifiable information or biospecimens will be obtained without parent permission, any waiver granted by the IRB does not override parents' refusal to provide broad consent (for example, through the Northwest Biotrust).*
3. *Will parents be informed about the research beforehand even though active permission is not being obtained?*

6.2.b. Indicate the plan for obtaining parental permission. One or both boxes must be checked.

☐ Both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
☐ One parent, even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

This is all that is required for minimal risk research.

If both are checked explain:

Click or tap here to enter text.

6.3. Children who are wards. Will any of the children be wards of the State or any other agency, institution, or entity?

☐ **No**

☐ **Yes →** An advocate may need to be appointed for each child who is a ward. The advocate must be in addition to any other individual acting on behalf of the child as guardian or in loco parentis. The same individual can serve as advocate for all children who are wards.
Describe who will be the advocate(s). The description must address the following points:

- Background and experience
- Willingness to act in the best interests of the child for the duration of the research
- Independence of the research, research team, and any guardian organization

Click or tap here to enter text.

6.4. UW Office of the Youth Protection Coordinator. If the project involves interaction (in-person or remotely) with individuals under the age of 18, researchers must comply with UW Administrative Policy Statement 10.13 and the requirements listed at this website. This includes activities that are deemed to be Not Research or Exempt. It does not apply to third-party led research (i.e., research conducted by a non-UW PI). Information and FAQs for researchers are available.

This point is advisory only; there is no need to provide a response.

7. ASSENT OF CHILDREN (MINORS)

Go to Section 8 if your research does not involve children (minors).

When designing assent processes and forms, researchers should first review the **GUIDANCE Consent** *Protected and Vulnerable Populations* and **TIPSHEET Consent** *Assent and Legally Authorized Representative.*

7.1. Assent of children (minors). Though children do not have the legal capacity to "consent" to participate in research, they should be involved in the process if they are able to "assent" by having a study explained to them and/or by reading a simple form about the study, and then verbally expressing whether they want to participate. They may also provide a written assent if they are older. See **GUIDANCE Consent** *Protected and Vulnerable Populations* and **WORKSHEET Children** for circumstances in which a child's assent may be unnecessary or inappropriate.

7.1.a. Will assent be obtained for:

☐ All research procedures and child groups → Go to question **7.2**.
☐ None of the research procedures and child groups → Use the table below to provide justification, then skip to question **7.6.**
☐ Some of your research procedures and child groups → Use the table below to identify the procedures for which assent will not be obtained.

Be sure to consider all research procedures and plans, including screening, future contact, and sharing/banking of data and specimens for future work.

Children Group[1]	Describe the procedures or data/specimen collection (if any) for which assent will not be obtained	Reason why assent will not be obtained
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.

Children Group[1]	Describe the procedures or data/specimen collection (if any) for which assent will not be obtained	Reason why assent will not be obtained
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.

Table footnotes

1. *If the answer is the same for all children groups or all procedures, collapse your answer across the groups and/or procedures.*

7.2. Assent process. Describe how assent will be obtained, for each child group. If the research involves children of different ages, answer separately for each group. If the children are non-English speakers, include a description of how their comprehension of the information will be evaluated.

Click or tap here to enter text.

7.3. Dissent or resistance. Describe how a child's objection or resistance to participation (including non-verbal indications) will be identified during the research, and what the response will be.

Click or tap here to enter text.

7.4. E-consent. Will any electronic processes (email, websites, electronic signatures, etc.) be used to present assent information to subjects/and or to obtain documentation (signatures) of assent? If yes, describe how this will be done.

Click or tap here to enter text.

7.5. Documentation of assent. Which of the following statements describes whether documentation of assent will be obtained?

☐ None of the research procedures and child groups → Use the table below to provide justification, then go to question **7.5.b.**

☐ All of the research procedures and child groups → Go to question **7.5.a**., do not complete the table.

☐ Some of the research procedures and/or child groups → Complete the table below and then go to question **7.5.a.**

Children Group[1]	Describe the procedures or data/specimen collection (if any) for which assent will NOT be documented
Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.

Children Group[1]	Describe the procedures or data/specimen collection (if any) for which assent will NOT be documented
Click or tap here to enter text.	Click or tap here to enter text.
Click or tap here to enter text.	Click or tap here to enter text.

Table footnotes

1. *If the answer is the same for all children groups or all procedures, collapse your answer across the groups and/or procedures.*

7.5.a. Describe how assent will be documented. If the children are functionally illiterate or are not fluent in English, include a description of the documentation process for them.

Click or tap here to enter text.

7.5.b. Upload all assent materials (talking points, videos, forms, etc.) to ***Zipline***. Assent materials are not required to provide all of the standard elements of adult consent; the information should be appropriate to the age, population, and research procedures. The documents should be in Word, if possible.

7.6. Children who reach the legal age of consent during participation in longitudinal research.

When children are enrolled at a young age and continue for many years, it is best practice to re-obtain assent (or to obtain it for the first time, if it was not obtained at the beginning of their participation).

When children reach the legal age of consent, informed consent must be obtained from the now-adult subject for (1) any ongoing interactions or interventions with the subjects, or (2) the continued analysis of specimens or data for which the subject's identify is readily identifiable to the researcher, unless the IRB waives this requirement.

7.6.a. Describe the plans (if any) to re-obtain assent from children.

Click or tap here to enter text.

7.6.b. Describe the plans (if any) to obtain consent for children who reach the legal age of consent.

- If adult consent will be obtained from them, describe what will happen regarding now-adult subjects who cannot be contacted.
- If consent will not be obtained or will not be possible, explain why.

Click or tap here to enter text.

7.7. Other regulatory requirements. (This is for information only; no answer or response is required.) Researchers are responsible for determining whether their research conducted in schools, with student records, or over the Internet comply with permission, consent, and inspection requirements of the following federal regulations:

- PPRA – Protection of Pupil Rights Amendment
- FERPA – Family Education Rights and Privacy Act
- COPPA – Children's Online Privacy Protection Act

8 CONSENT OF ADULTS

When designing consent process and forms, researchers should first review the **GUIDANCE Consent** and **TIPSHEET Consent**. The topics of *A Foundation for Meaningful Consent* and *The Key Information Requirement* are particularly important for ensuring subject comprehension and voluntary participation in research. Information about parental permission can be found in the **GUIDANCE Consent** *Protected and Vulnerable Populations.*

Review the following definitions before answering the questions in this section.

TERM	DEFINITION
CONSENT	is the process of informing potential subjects about the research and asking them whether they want to participate. It does not necessarily include the signing of a consent form.
CONSENT DOCUMENTATION	refers to how a subject's decision to participate in the research is documented. This is typically obtained by having the subject sign a consent form.
CONSENT FORM	is a document signed by subjects, by which they agree to participate in the research as described in the consent form and in the consent process.
ELEMENTS OF CONSENT	are specific information that is required to be provided to subjects.

CHARACTERISTICS OF CONSENT	are the qualities of the consent process as a whole. These are:
	• Consent must be legally effective.
	• The process minimizes the possibility of coercion or undue influence.
	• Subjects or their representatives must be given sufficient opportunity to discuss and consider participation.
	• The information provided must:
	  ○ Begin with presentation of key information (for consent materials over 2,000 words).
	  ○ Be what a reasonable person would want to have.
	  ○ Be organized and presented so as to facilitate understanding.
	  ○ Be provided in sufficient detail.
	  ○ Not ask or appear to ask subjects to waive their rights.

PARENTAL PERMISSION	is the parent's active permission for the child to participate in the research. Parental permission is subject to the same requirements as consent, including written documentation of permission and required elements.

TERM	DEFINITION
SHORT FORM CONSENT	is an alternative way of obtaining written documentation of consent that is most commonly used for the unanticipated enrollment of individuals who are illiterate or whose language is one for which translated consent forms are not available.
WAIVER OF CONSENT	means there is IRB approval for not obtaining consent or for not including some of the elements of consent in the consent process. **NOTE**: if you plan to obtain identifiable information or identifiable biospecimens without consent, any waiver granted by the IRB does not override a subject's refusal to provide broad consent (for example, the Northwest Biotrust).
WAIVER OF DOCUMENTATION OF CONSENT	means that there is IRB approval for not obtaining written documentation of consent.

8.1. Groups. Identify the groups to which the answers in this section apply:

☒ **Adult** subjects
☐ **Parents** who are providing permission for their children to participate in research

→ *If you selected **PARENTS**, the word "consent" below should also be interpreted as applying to parental permission and "subjects" should also be interpreted as applying to the parents.*

8.2. The consent process and characteristics. This series of questions is about whether consent will be obtained for all procedures except recruiting and screening, and, if yes, how.

The issue of consent for recruiting and screening activities is address in question 4.7. You do not need to repeat your answer to question 4.7.

8.2.a. Are there any procedures for which consent will not be obtained?

☒ **No**
☐ **Yes** → Use the table below to identify the procedures for which consent will not be obtained. "All" is an acceptable answer for some studies.

Be sure to consider all research procedures and plans, including future contact, and sharing/banking of data and specimens for future work.

Group[1]	Describe the procedures of data/specimen collection (if any) for which there will be NO consent process	Reason why consent will not be obtained	Will subjects be provided with info about the research after they finish? (Check Yes or No)	
			YES	NO
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
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Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	☐	☐

Table footnotes

1. If the answer is the same for all groups, collapse your answer across the groups and/or procedures.

8.2.b. Describe the consent process, if consent will be obtained for any or all procedures, for any or all groups. Address groups and procedures separately if the consent processes are different.

Be sure to include:

- *The location/setting where consent will be obtained*
- *Who will obtain consent (refer to positions, roles, or titles, not names)*
- *How subjects will be provided sufficient opportunity to discuss the study with the research team and consider participation.*

Research staff will participate in and obtain informed consent from research participants after screening but prior to commencement of any further study procedures. Prospective participants will also be asked for consent to complete the screening questions at the start of the screening process. The informed consent process will take place over the telephone at a time deemed mutually feasible for the participant and staff member and coordinated on a case-by-case basis.

Prior to the informed consent process, research staff will email (or postal mail, if the participant prefers) a copy of an information statement for the participant to review as well as the date and time of the consent process appointment. Participants will be encouraged to read the information statement prior to the scheduled consent session and to be prepared with any questions. If the informed consent session is scheduled more than two business days in advance, research staff

will call and/or email participants as a reminder. Participants will be requested to have the information statement in front of them during the consent session.

A research staff member will review each section of the information statement approved by the UW IRB, inviting discussion to ensure comprehension. Staff will be trained by study investigators to ensure competency to discuss informed consent and strategies to ensure there is no coercion.

Participants will be provided with as much time as needed to review the information statement and ask the research staff member questions about the information statement, their rights as human participants, and participation in the study. Potential participants will be fully informed of all risks and benefits prior to giving their verbal informed consent and prior to enrollment in the study.

If during the course of this contact the potential participant has questions that cannot be addressed by research staff, one of the study investigators or the research manager (depending on the nature of the questions) will follow up with the potential participant to answer the questions. Participants may take time to think about participating and render a decision at a subsequent time.

Potential participants will be asked to repeat back to research staff their understanding of the information statement material as necessary. Individuals will not be permitted to participate if there is any question as to whether a person has capacity to provide informed consent.

When all questions have been answered, research staff will ask the participant if they would like to participate in the study. The participant will then be asked to provide verbal consent to participate. The participant will not need to sign the information statement, as we will be applying for a Waiver of Documentation of Informed Consent with this IRB application.

8.2.c. Comprehension. Describe the methods that will be used to ensure or test the subjects' understanding of the information during the consent process.

Staff will ask participants to give a summary of the study purpose and procedures to illustrate adequate comprehension of study procedures.

8.2.d. Influence. Does the research involve any subject groups that might find it difficult to say "no" to participation because of the setting or their relationship with someone on the study team, even if they aren't pressured to participate?

Examples: Student participants being recruited into their teacher's research; patients being recruited into their healthcare provider's research; study team members who are participants; outpatients recruited from an outpatient surgery waiting room just prior to their surgery.

☐ **No**

☒ **Yes** → Describe what will be done to reduce any effect of the setting or relationship on the participation decision.

Examples: a study coordinator will obtain consent instead of the subject's physician; the researcher will not know which subjects agreed to participate; subjects will have two days to decide after hearing about the study.

Dawn Ehde provides neuropsychological evaluations for adults with MS. It is possible that some of her patients may choose to enroll in this study, however, Dr. Ehde will not consent subjects.

Prospective subjects will be informed that they may decline to participate, and declination will not affect their medical care in any way.

8.2.e. Information provided is tailored to the needs of the subject population. Describe the basis for concluding that the information that will be provided to subjects (via written or oral methods) is what a *reasonable member* of the *subject population(s)* would want to know. If the research consent materials contain a key information section, also describe the basis for concluding that the information present in that section is that which is *most likely* to assist the selected subject population with making a decision. See **GUIDANCE Consent** *Key Information* and **EXAMPLE Key Information**.

For example: Consultation with publications about research subjects' preferences, disease-focused nonprofit groups, patient interest groups, or other researchers/study staff with experience with the specific population. It may also involve directly consulting selected members of the study population.

Consultation with publications about research subjects' preferences, disease-focused nonprofit groups, patient interest groups, or other researchers/study staff with experience with the specific population. It may also involve directly consulting selected members of the study population

8.2.f. Ongoing process, new information, and reconsent.

For research that involves multiple or continued interaction with subjects over time, describe the opportunities (if any) that will be given to subjects to ask questions or to change their minds about participating.

Throughout the course of the study, subjects may need to be notified about new information. This might take the form of a verbal or written communication or may require subjects to provide reconsent. When a modification is submitted in which subjects need to be informed about new information, describe the method and process the research team will use to provide this information.
*See **TIPSHEET Consent** Reconsent and Ongoing Subject Communication and **GUIDANCE Consent Reconsent and Ongoing Subject Communication** for details.*

Study researchers will provide contact information within each point of correspondence in case the participant has questions. In addition, study staff will remind participants during their sessions that their participation is voluntary, that they don't need to participate, and declination won't affect their medical care in any way.

8.3. **Electronic presentation of consent information**. Will any part of the consent-related information be provided electronically for some, or all of the subjects?

*This refers to the use of electronic systems and processes instead of (or in addition to) a paper consent form. For example, an emailed consent form, a passive or an interactive website, graphics, audio, video podcasts. See **GUIDANCE Consent** Electronic Consent and Documentation of Consent for information about electronic consent requirements at UW.*

☒ **No →** Skip to question **8.4.**

☐ **Yes →** Answer questions **8.3.a.** through **8.3.e.**

8.3.a. Describe the electronic consent methodology and the information that will be provided.

All information materials must be made available to the IRB. Website content should be provided as a Word document. It is considered best practice to give subjects information about multi-page/multi-screen information that will help them assess how long it will take them to complete the process. For example, telling them that it will take about 15 minutes, or that it involves reading six screens or pages.

8.3.b. Describe how the information can be navigated (if relevant).

For example, will the subject be able to proceed forward or backward within the system, or to stop and continue at a later time?

8.3.c. In a standard paper-based consent process, the subjects generally have the opportunity to go through the consent form with study staff and/or to ask study staff about any question they may have after reading the consent form. Describe what will be done, if anything, to facilitate the subject's comprehension and opportunity to ask questions when consent information is presented electronically. Include a description of any provisions to help ensure privacy and confidentiality during this process.

Examples: hyperlinks, help text, telephone calls, text messages or other type of electronic messaging, video conference, live chat with remotely located study team members.

8.3.d. What will happen if there are individuals who wish to participate but who do not have access to the consent methodology being used, or who do not wish to use it? Are there alternative ways in which they can obtain the information, or will there be some assistance available? If this is a clinical trial, these individuals cannot be excluded from the research unless there is a compelling rationale.

For example, consider individuals who lack familiarity with electronic systems, have poor eyesight or impaired motor skills, or who do not have easy email or internet access.

8.3.e. How will the research team ensure continued accessibility of consent materials and information during the study?

8.3.f. How will additional information be provided to subjects during the research, including any significant new findings (such as new risk information). If this is not an issue, explain why.

Click or tap here to enter text.

8.4. Written documentation of consent. Which of the statements below describe whether documentation of consent will be obtained? NOTE: This question does not apply to screening and recruiting procedures which have already been addressed in question **4.7**.

Documentation of consent that is obtained electronically is not considered written consent unless it is obtained by a method that allows verification of the individual's signature. In other words, saying "yes" by email is rarely considered to be written documentation of consent.

8.4.a. Is written documentation being obtained for:

☒ **None** of the research procedures → Use the following table to provide justification then go to question **8.5.**

☐ **All** of the research procedures → Do not complete the following table, go to question **8.4.b.**

☐ **Some** of the research procedures → Use the following table to identify the procedures for which written documentation of consent will not be obtained from adult subjects.

Adult subject group[1]	Describe the procedures or data/specimen collection (if any) for which there will be NO documentation of consent	Will they be provided with a written statement describing the research (optional)? (Check Yes or No)	
		YES	NO
Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	☐	☐
Click or tap here to enter text.	Click or tap here to enter text.	☐	☐

Table footnotes

1. If the answer is the same for all adult groups or all procedures, collapse the answer across the groups and/or procedures.

8.4.b. Electronic consent signature. For studies in which documentation of consent will be obtained, will subjects use an electronic method to provide their consent signature?

- *See **GUIDANCE Consent** Documentation of Consent and **INSTRUCTIONS UW E-Signature Tools** for information about options (including **REDCap** e-signature and the **DocuSign** system) and any associated requirements.*

- *FDA-regulated studies must use a system that complies with the FDA's "Part 11" requirements about electronic systems and records. Note that the UW-IT supported DocuSign e-signature system does not meet this requirement.*
- *Having subjects check a box at the beginning of an emailed or web-based questionnaire is not considered legally effective documentation of consent.*

☒ **No**

☐ **Yes** → Indicate which methodology will be used

☐ **UW ITHS REDCap** (excludes REDCap Mobile application, which is a separate software application for use with a mobile device for consent when internet service is absent or unreliable)

☐ **Other REDCap installation** → Please name the institutional version you will be using (e.g., Vanderbilt, Univ. of Cincinnati) in the following field and provide a completed **SUPPLEMENT Other REDCap Installation** with your submission.

Click or tap here to enter text.

☐ **UW DocuSign**

☐ **Other** → Please describe in the following field and provide a signed **TEMPLATE Other E-signature Attestation Letter** with your submission.

Click or tap here to enter text.

8.4.b.1. Is this method legally valid in the jurisdiction where the research will occur?

NOTE: UW ITHS REDCap (excludes REDCap Mobile application) and UW DocuSign have been vetted for compliance with Washington State and federal laws regarding electronic signatures.

☐ **No**

☐ **Yes** → What is the source of information about legal validity?

Click or tap here to enter text.

8.4.b.2. Will verification of the subject's identity be obtained if the signature is not personally witnessed by a member of the study team? Note that this is required for FDA-regulated studies.

*See the **GUIDANCE Consent** Documentation of Consent for information and examples*

☐ **No →** Provide the rationale for why this is not required or necessary to protect subjects or the integrity of the research. Also, what would be the risks to the actual subject if somebody other than the intended signatory provides the consent signature?

Click or tap here to enter text.

☐ **Yes →** Describe how subject identity will be verified, providing a non-technical description that the reviewer will understand.

Click or tap here to enter text.

8.4.b.3. How will the requirement be met to provide a copy of the consent information (consent form) to individuals who provide an e-signature?

The copy can be paper or electronic and may be provided on an electronic storage device or via email. If the electronic consent information uses hyperlinks or other websites or podcasts to convey information specifically related to the research, the information in these hyperlinks should be included in the copy provided to the subjects and the website must be maintained for the duration of the entire study.

Click or tap here to enter text.

8.4.c. Barriers to written documentation of consent. There are many possible barriers to obtaining written documentation of consent. Consider, for example, individuals who are functionally illiterate; do not read English well; or have sensory or motor impairments that may impede the ability to read and sign a consent form.

8.4.c.1. Describe the plans (if any) for obtaining written documentation of consent from potential subjects who may have difficulty with the standard documentation process (that is, reading and signing a consent form).

Examples of solutions: Translated consent forms; use of the Short Form consent process; reading the form to the person before they sign it; excluding individuals who cannot read and understand the consent form.

Consistent with UW HSD's SOP for consent documentation, if a participant is unable to read due to vision issues (common in MS patients), the study team will read the consent form in its entirety to them and have a witness (not a member of the study team) sign in addition to the participant.

8.5. Non-English-speaking or-reading adult subjects. Will the research enroll adult subjects who do not speak English or who lack fluency or literacy in English?

☒ **No**

☐ **Yes →** Describe the process that will be used to ensure that the oral and written information provided to them during the consent process and throughout the study will be in a language readily understandable to them and (for written materials such as consent forms or questionnaires) at an appropriate reading/comprehension level.

Click or tap here to enter text.

8.5.a. Interpretation. Describe how interpretation will be provided, and when. Also, describe the qualifications of the interpreter(s) - for example, background, experience, language proficiency in English and in the other language, certification, other credentials, familiarity with the research related vocabulary in English and the target language.

Click or tap here to enter text.

8.5.b. Translations. Describe how translations will be obtained for all study materials (not just consent forms). Also, describe the method for ensuring that the translations meet the UW IRB's requirement that translated documents will be linguistically accurate, at an appropriate reading level for the participant population, and culturally sensitive for the local in which they will be used.

☐ Check this box to confirm that before using them with subjects, you will upload in *Zipline* all translated consent materials that will be provided to subjects in written or electronic form (per **HSD policy**).

*If the IRB determines that your study is greater than minimal risk, or otherwise determines it is required, you will need to work with your translator to provide a **TEMPLATE Translation Attestation**. If the attestation is required, you will be informed by the IRB during the course of the review.*

Click or tap here to enter text.

8.6. **[DETERMINATION]** **Deception**. Will information be deliberately withheld, or will false information be provided, to any of the subjects?

NOTE: "Blinding" subjects to their study group/condition/arm is not considered to be deception, but not telling them ahead of time that they will be subjects to an intervention or about the purpose of the procedure(s) is deception.

☒ **No**

☐ **Yes →** Describe what information and why.

Example: it may be necessary to deceive subjects about the purpose of the study (describe why).

Click or tap here to enter text.

8.6.a. Will subjects be informed beforehand that they will be unaware of or misled regarding the nature or purposes of the research? (Note: this is not necessarily required.)

☐ **No**
☐ **Yes**

8.6.b. Will subjects be debriefed later? (Note: this is not necessarily required.)

☐ **No →** Provide your reasoning for not debriefing subjects.

Click or tap here to enter text.

☐ **Yes →** Describe how and when this will occur. Upload any debriefing materials, including talking points or a script, to ***Zipline***.

Click or tap here to enter text.

8.7. [DETERMINATION] **Cognitively impaired adults, and other adults unable to consent**. Will such individuals be included in the research?

Examples: individuals with Traumatic Brain Injury (TBI) or dementia; individuals who are unconscious, or who are significantly intoxicated.

☒ **No →** Go to question **8.8.**
☐ **Yes →** Answer the following question.

8.7.a. Rationale. Provide the rationale for including this population.

Click or tap here to enter text.

8.7.b. Capacity for consent/decision making capacity. Describe the process that will be used to determine whether a cognitively impaired individual is capable of consent decision making with respect to the research protocol and setting.

Click or tap here to enter text.

8.7.b.1. If there will be repeated interactions with the impaired subjects over a time period when cognitive capacity could increase of diminish, also describe how (if at all) decision-making capacity will be re-assessed and (if appropriate) consent obtained during that time.

Click or tap here to enter text.

8.7.c. Permission (surrogate consent). If the research will include adults who cannot consent for themselves, describe the process for obtaining permission ("surrogate-consent") from a legally authorized representative (LAR).

*For research conducted in Washington State, see **GUIDANCE Consent** Diminished and Fluctuating Consent Capacity and Use of a Legally Authorized Representative (LAR) to learn which individuals meet the state definition of "legally authorized representative".*

Click or tap here to enter text.

8.7.d. Assent. Describe whether assent will be required of all, some, or none of the subjects. If some, indicate which subjects will be required to assent and which will not (and why not). Describe any process that will be used to obtain and document assent from the subjects.

Click or tap here to enter text.

8.7.e. Dissent or resistance. Describe how a subject's objection or resistance to participation (including non-verbal) during the research will be identified, and what will occur in response.

Click or tap here to enter text.

8.8. Research use of human fetal tissue obtained from elective abortion. Federal and UW Policy specify some requirements for the consent process. If you are conducting this type of research, check the boxes to confirm these requirements will be followed.

☐ Informed consent for the donation of fetal tissue for research use will be obtained by someone other than the person who obtained the informed consent for abortion.
☐ Informed consent for the donation of fetal tissue for research use will be obtained after the informed consent for abortion.
☐ Participation in the research will not affect the method of abortion.
☐ No enticements, benefits or financial incentives will be used at any level of the process to incentivize abortion or the donation of human fetal tissue.
☐ The informed consent form for the donation of fetal tissue for use in research will be signed by both the woman and the person who obtains the informed consent.

8.9. Consent-related materials. Upload to ***Zipline*** all consent scripts/talking points, consent forms, debriefing statements, Information Statements, Short Form consent forms, parental permission forms, and any other consent related materials that will be used. Materials that will be used by a specific site should be uploaded to that site's Local Site Documents page.

- *Translations must be submitted and approved before they can be used. However, we strongly encourage you to wait to provide them until the IRB has approved the English versions.*
- *Combination forms: it may be appropriate to combine parental permission with consent if parents are subjects as well as providing permission for the participation of their children. Similarly, a consent form may be appropriately considered an assent form for older children.*
- *For materials that cannot be uploaded: upload screenshots or written descriptions that are sufficient to enable the IRB to understand the types of data that will be collected and the nature of the experience for the participants. URLs (website addresses) may also be provided, or written descriptions of websites. Examples of materials that usually cannot be uploaded: mobile apps; computer-administered text; licensed and restricted standardized tests.*

9. PRIVACY AND CONFIDENTIALITY

9.1. [DETERMINATION] **Privacy protections.** Describe the steps that will be taken, if any, to address possible privacy concerns of subjects and potential subjects.

Privacy refers to the sense of being in control of access that others have to ourselves. This can be an issue with respect to recruiting, consenting, sensitivity of the data being collected, and the method of data collection.
Examples:

- *Many subjects will feel a violation of privacy if they receive a letter asking them to participate in a study because they have ____ medical condition, when their name, contact information, and medical condition were drawn from medical records without their consent. Example: the IRB expects that "cold contact" recruitment letters will inform the subject about how their information was obtained.*
- *Recruiting subjects immediately prior to a sensitive or invasive procedure (e.g., in an outpatient surgery waiting room) will feel like an invasion of privacy to some individuals.*
- *Asking subjects about sensitive topics (e.g., details about sexual behavior) may feel like an invasion of privacy to some individuals.*

All prospective participants will be informed of how their information was obtained.

We will assign all participants a unique study code that serves as the link between the data collected for the study and participants' identity. We will keep any hard copies of participants' direct identifiers in a separate locked filing cabinet (in which only research staff will have keys) from study data. In addition, participant identifiers will be kept in a password-protected database on the department's secure server and in the password-protected REDCap. The link between the study data and a participant's identity in the form of the unique study code will only exist in the password-protected database on the department's secure server, which has restricted access, and in the password-protected REDCap databases.

Protection of qualitative data. We will use UW Zoom to record interviews with participants. We will transfer the audio files to a restricted access folder on the secure UW server with access limited to study staff. We will the delete the audio files from Zoom storage. Audio recordings will be identified by participants' unique study codes. Participants will be reminded prior to recording to avoid revealing names or other identifiable information during the recorded interviews. All interviews will be transcribed via Rev.com, a secure transcription service. The audio files will be transferred to Rev.com for secure transcription and Rev.com will transfer the redacted transcriptions files to our study staff. The transcription files will then be transferred to an unshared secure, password-protected folder on the secure UW server.

9.2. [DETERMINATION] **Identification of individuals in publications and presentations.** Will potentially identifiable information about subjects be used in publications and presentations, or is it possible that individual identities could be inferred from what is planned to be published or presented?

☒ **No**
☐ **Yes →** Will subject consent be obtained for this use?

☐ **Yes**
☐ **No →** Describe the steps that will be taken to protect subjects (or small groups of subjects) from being identifiable.

Click or tap here to enter text.

9.3. [DETERMINATION] **State mandatory reporting**. Each state has reporting laws that require some types of individuals to report some kinds of abuse, and medical conditions that are under public health surveillance. These include:

- Child abuse
- Abuse, abandonment, neglect, or financial exploitation of a vulnerable adult
- Sexual assault
- Serious physical assault
- Medical conditions subject to mandatory reporting (notification) for public health surveillance

Are you or a member of the research team likely to learn of any of the above events or circumstances while conducting the research **AND** feel obligated to report it to state authorities?

☒ **No**
☐ **Yes** → The UW IRB expects subjects to be informed of this possibility in the consent form or during the consent process, unless you provide a rationale for not doing so:

Click or tap here to enter text.

9.4. [DETERMINATION] **Records retention requirements.** Check the box below to indicate assurance that any identifiers (or links between identifiers and data/specimens) and data that are part of the research records will not be destroyed until after the end of the applicable records retention requirements (e.g., Washington State; funding agency or sponsor; Food and Drug Administration). If it is important to say something about destruction of identifiers (or links to identifiers) in the consent form, state that identifying information will be destroyed at the end of the study or after the records retention period required by state and/or federal law.

See the "Research Data" and "Personal Identifiers" sections of the following website for UW Records management for the Washington State research records retention schedules that apply in general to the UW (not involving UW Medicine data): ***http://f2.washington.edu/fm/recmgt/gs/research?title=R; https://finance.uw.edu/recmgt/gs/research?title=P.***

See the "Research Records and Data" information in Section 8 of this document for the retention schedules for UW Medicine Records: ***https://www.uwmedicine.org/recordsmanagementuwm-records-retention-schedule.pdf***

☒ **Confirm**

9.5. [DETERMINATION] **Certificates of Confidentiality.** Will a federal Certificate of Confidentiality be obtained for the research data? *NOTE: Answer "No" if the study is funded by NIH or the CDC, because most NIH-funded and CDC-funded studies automatically have a Certificate.*

☒ **No**
☐ **Yes**

9.6. [DETERMINATION] **Data and specimen security protections**. Identify the data classifications and the security protections that will be provided for all sites where data will be collected, transmitted, or stored, referring to the GUIDANCE Data and Security Protections for the minimum requirements for each data classification level. ***It is not possible to answer this question without reading this document. Data security protections should not conflict with records retention requirements.***

9.6.a. Choose the level(s) of protections that will be applied to the data and specimens. If more than one level will be used, use the text box to describe which level will apply to which data and which specimens and at which sites.

☐ **Level 1:** Very low risk of harm if disclosed
☐ **Level 2:** Some risk of minor harm if disclosed
☐ **Level 3:** Could cause risk of material harm if disclosed

☒ **Level 4:** Would likely cause serious harm to individuals if disclosed
☐ **Level 5:** Extremely sensitive; could cause severe harm to individuals if disclosed

Click or tap here to enter text.

9.6.b. Use this space to provide additional information, details, or to describe protections that do not fit into one of the levels. **HSD allows researchers to request exceptions to data security requirements, if the exception is necessary and does not significantly increase risk to participants**. If there are any protections within the level listed in 9.6.a which will not be followed, list those here, including identifying the sites where this exception will apply. For example, if you intend to store subject identifiers with study data (not permitted under requirement U9 for Risk Levels 3-5), then indicate this in the box below (e.g., "We will not adhere to requirement U9 for screening data").

The study team will store email addresses and participant initials with study data in REDCap. It is necessary to store the email address so that the study team can send survey links via email to study participants. REDCap will be set so that emails and initials will be flagged as identifiers.

10. RISK / BENEFIT ASSESSMENT

10.1. [DETERMINATION] **Anticipated risks.** Describe the anticipated risks of harm, discomforts, and hazards to the subjects and others of the research procedures.

For each harm, discomfort, or hazard:

- Describe the magnitude, probability, duration, and/or reversibility of the harm, discomfort, or hazard, AND
- Describe how the risks will be reduced or managed. Do not describe data security protections here, these are already described in question **9.6**.

- *Consider possible physical, psychological, social, legal, and economic harms, including possible negative effects on financial standing, employability, insurability, educational advancement, or reputation. For example, a breach of confidentiality might have these effects.*
- *Examples of "others": embryo, fetus, or nursing child; family members; a specific group.*
- *Ensure applicable risk information from any Investigator Brochures, Drug Package Inserts, and/or Device Manuals is included in your description.*
- *Do not include the risks of non-research procedures that are already being performed.*
- *If the study design specifies that subjects will be assigned to a specific condition or intervention, then the condition or intervention is a research procedure - even if it is a standard of care.*
- *Examples of mitigation strategies: inclusion/exclusion criteria; taking blood samples to monitor something that indicates drug toxicity.*
- *Review **GUIDANCE Consent** Identifying and Describing Reasonably Foreseeable Risks in Research for information about which risks should be described in the consent process/form.*
- *As with all questions on this application, you may refer to uploaded documents.*

General/Reaction to Assessments
Participants may experience fatigue and/or boredom while completing the assessments, qualitative interview and/or the treatment sessions.

Some participants may also experience mild anxiety, frustration, and/or stress while answering sensitive questions about fatigue and mood. As a result of answering questions about fatigue, some

participants may focus more on their fatigue, which may lead to a temporary increase in fatigue intensity.

Protections against risks: Participants will be informed during the consent process and throughout the study they do not have to discuss any topics they do not wish to during treatment or the assessment periods. In addition, participants will be informed in the consent process they are free to stop any session, assessment, or interview at any time. Participants are informed they may refuse to answer any questions that make them feel uncomfortable.

All participants will be clearly informed of their right to withdraw from the study at any point without adversely impacting their routine medical, psychiatric, or psychotherapeutic care.

All participants will be offered the opportunity to discuss any situations or experiences associated with the study procedures that they deem uncomfortable or adverse with the PI, Dr. Knowles.

Telehealth CBT intervention components for MS fatigue: Participants may experience emotional distress when participating in their assigned intervention component, potentially due to increased insight into adaptive and maladaptive behaviors contributing to fatigue management and exerting effort to change their behavior.

Multicomponent CBT consists of Relaxation Training, Behavioral Activation, and Cognitive Therapy, and as a package, CBT has been shown to be an acceptable and effective behavioral intervention for fatigue in adults with MS. Research by the UW investigative team has shown that telephone-delivered (telehealth) CBT is equally as effective as in-person CBT for reducing fatigue in MS and overcomes barriers to accessing specialized care. Last, research also demonstrates that in-person and telehealth CBT for fatigue are feasible and acceptable among patients with MS.

As individual components, Relaxation Training has been shown to reduce fatigue in adults with MS, but had a smaller effect size than multicomponent CBT. Behavioral Activation is an effective treatment for depression, but telehealth behavioral activation has not been tested as a standalone intervention for fatigue in adults with MS. Likewise, Cognitive Therapy is an effective treatment for depressive and anxiety disorders, but telehealth cognitive therapy has not been tested as a standalone intervention for fatigue in adults with MS. Given that the Relaxation Training, Behavioral Activation, and Cognitive Therapy components make up telehealth multicomponent CBT for fatigue, found to be effective and acceptable, we expect that these standalone telehealth components will be acceptable and unlikely to cause emotional distress in participants.

Loss of confidentiality: There is a small risk of loss confidentiality when human subjects provide personal information. Detailed procedures to protect participant privacy are described below.

COVID-19: Of note, this study does not contribute to risk of COVID-19 infection because all study procedures, assessments and interventions are completed remotely (by telephone and/or HIPAA-compliant videoconference). There are no necessary in-person visits and/or interpersonal contact between study staff and participants.

10.2. [DETERMINATION] **Reproductive risks**. Are there any risks of the study procedures to subjects or partner of subjects related to pregnancy, fertility, lactation or effects on a fetus or neonate?

Examples: direct teratogenic effects; possible germline effects; effects on fertility; effects on a woman's ability to continue a pregnancy; effects on future pregnancies.

☒ **No →** Go to question **10.3.**
☐ **Yes →** Answer the following questions:

10.2.a. Risks. Describe the magnitude, probability, duration and/or reversibility of the risks.

Click or tap here to enter text.

10.2.b. Steps to minimize risk. Describe the specific steps that will be taken to minimize the magnitude, probability or duration of these risks.

Examples: inform the subjects about the risks and how to minimize them; require a pregnancy test before and during the study; require subjects to use contraception; advise subjects about banking of sperm and ova.

If the use of contraception will be required, describe the allowable methods and the time period when contraception must be used.

Click or tap here to enter text.

10.2.c. Pregnancy. Describe what will be done if a subject (or a subject's partner) becomes pregnant.

For example; will subjects be required to immediately notify study staff, so that the study procedures can be discontinued or modified, or for a discussion of risks, and/or referrals or counseling?

Click or tap here to enter text.

10.3. [DETERMINATION] **MRI risk management**. A rare but serious adverse reaction called nephrogenic systemic fibrosis (NSF) has been observed in individuals with kidney disease who received gadolinium-based contrast agents (GBCAs) for the scans. Also, a few healthy individuals have a severe allergic reaction to GBCAs.

10.3.a. Use of gadolinium. Will any of the MRI scans involve the use of a gadolinium-based contrast agent (GBCA)?

☒ **No**
☐ **Yes →** Which agents will be used? *Check all that apply.*

Check all that apply	Brand Name	Generic Name	Chemical Structure
☐	Dotarem	Gadoterate meglumine	Macrocylic
☐	Eovist / Primovist	Gadoxetate disodium	Linear
☐	Gadavist	Gadobutro	Macrocyclic
☐	Magnevist	Gadpentetate dimeglumine	Linear
☐	MultiHance	Gadobenate dimeglumine	Linear
☐	Omniscan	Gadodiamide	Linear

Check all that apply	Brand Name	Generic Name	Chemical Structure
☐	OptiMARK	Gadoversetamide	Linear
☐	ProHance	Gadoteridol	Macrocyclic
☐	Other, provide name:		

Click or tap here to enter text.

10.3.a.1. The FDA has concluded that gadolinium is retained in the body and brain for a significantly longer time than previously recognized, especially for linear GBCAs. The health-related risks of this longer retention are not yet clearly established. However, the UW IRB expects researchers to provide a compelling justification for using a linear GBCA instead of a macrocyclic GBCA, to manage the risks associated with GBCAs.

Describe why it is important to use a GBCA with the MRI scan(s). Describe the dose that will be used and (if it is more than the standard clinical dose recommended by the manufacturer) why it is necessary to use a higher dose. If a linear GBCA will be used, explain why a macrocyclic GBCA cannot be used.

Click or tap here to enter text.

10.3.a.2. Information for subjects. Confirm by checking this box that subjects will be provided with the FDA-approved Patient Medication Guide for the GBCA being used in the research or that the same information will be inserted into the consent form.

☐ **Confirmed**

10.3.b. Who will (1) calculate the dose of GBCA; (2) prepare it for injection; (3) insert and remove the IV catheter; (4) administer the GBCA; and (5) monitor for any adverse effects of the GCBA? Also, what are the qualifications and training of these individual(s)?

Click or tap here to enter text.

10.3.c. Describe how the renal function of subjects will be assessed prior to MRI scans and how that information will be used to exclude subjects at risk for NSF.

Click or tap here to enter text.

10.3.d. Describe the protocol for handling a severe allergic reaction to the GBCA or any other medical event/emergency during the MRI scan, including who will be responsible for which actions.

Click or tap here to enter text.

10.4. [DETERMINATION] **Unforeseeable risks**. Are there any research procedures that may have risks that are currently unforeseeable?

Example: using a drug that hasn't been used before in this subject population.

☒ **No**

☐ **Yes →** Identify the procedures.

Click or tap here to enter text.

10.5. Subjects who will be under regional or general anesthesia. Will any research procedures occur while patients are under general or regional anesthesia, or during the 3 hours preceding general or regional anesthesia (supplied for non-research reasons)?

☒ **No**

☐ **Yes →** Check all the boxes that apply.

- ☐ Administration of any drug for research purposes
- ☐ Inserting an intra-venous (central or peripheral) or intra-arterial line for research purposes
- ☐ Obtaining samples of blood, urine, bone marrow or cerebrospinal fluid for research purposes
- ☐ Obtaining a research sample from tissue or organs that would not otherwise be removed during surgery.
- ☐ Administration of a radio-isotope for research purposes**
- ☐ Implantation of an experimental device
- ☐ Other manipulations or procedures performed solely for research purposes (e.g., experimental liver dialysis, experimental brain stimulation)

If any of the boxes are checked:

Provide the name and institutional affiliation of a physician anesthesiologist who is a member of the research team or who will serve as a safety consultant about the interactions between the research procedures and the general or regional anesthesia of the subject-patients. If the procedures will be performed at a UW Medicine facility or affiliate, the anesthesiologist must be a UW faculty member, and the Vice Chair of Clinical Research in the UW Department of Anesthesiology and Pain Medicine must be consulted in advance for feasibility, safety and billing.

Click or tap here to enter text.

*** If the box about radio-isotopes is checked, the study team is responsible for informing in advance all appropriate clinical personnel (e.g., nurses, technicians, anesthesiologists, surgeons) about the administration and use of the radio-isotope, to ensure that any personal safety issues (e.g., pregnancy) can be appropriately addressed. This is a condition of IRB approval.*

10.6. Data and Safety Monitoring. A Data and Safety Monitoring Plan (DSMP) is required for clinical trials (as defined by NIH). If required for this research, or if there is a DSMP for the research regardless of whether it is required, upload the DSMP to ***Zipline***. If it is embedded in another document being uploading (for example, a Study Protocol) use the text box below to name the document that has the DSMP. Alternatively, provide a description of the DSMP in the text box below. For guidance on developing a DSMP, see the ITHS webpage on Data and Safety Monitoring Plans.

PI Dr. Knowles will follow the full DSMP description found on page 160 of the research grant

10.7. Un-blinding. If this is a double-blinded or single-blinded study in which the participant and/or relevant study team members do not know the group to which the participant is assigned, describe the circumstances under which un-blinding would be necessary, and to whom the un-blinded information would be provided.

N/A

10.8. Withdrawal of participants. If applicable, describe the anticipated circumstances under which participants will be withdrawn from the research without their consent. Also, describe any procedures for orderly withdrawal of a participant, regardless of the reason, including whether it will involve partial withdrawal from procedures and any intervention but continued data collection or long-term follow-up.

Participants could potentially be withdrawn without consent. In the past this has been very rare. Typically happening in instances where the participant becomes unable to contact despite frequent calls from study staff. PIs also reserve the right to withdraw subjects if they feel it is in their best interest (in cases where procedures could be contributing to suicidal ideation). However, suicidal ideation is not expected to be a risk in this study.

10.9. [DETERMINATION] **Anticipated direct benefits to participants**. If there are any direct research-related benefits that some or all individual participants are likely to experience from taking part in the research, describe them below:

Do not include benefits to society or others, and do not include subject payment (if any). Examples: medical benefits such as laboratory tests (if subjects receive the results); psychological resources made available to participants; training or education that is provided.

Members of this team have run previous studies with therapeutic skills taught in the planned study support. Based on this research, we anticipate that participants will experience reductions in their daily fatigue and other benefits associated with the treatment.

In this past research, many study participants have expressed satisfaction from receiving treatment in a caring and nonjudgmental environment. Thus, participants in treatment will take away from the study new skills and knowledge regarding fatigue and how to manage it and should experience some degree of relief and increases in their quality of life.

10.10. [DETERMINATION] **Return of individual research results.**

In this section, provide your plans for the return of individual results. An "individual research result" is any information collected, generated or discovered in the course of a research study that is linked to the identity of a research participant. These may be results from screening procedures, results that are actively sought for purposes of the study, results that are discovered unintentionally, or after analysis of the collected data and/or results has been completed.

*See the **GUIDANCE Return of Individual Results** for information about results that should and should not be returned, validity of results, the Clinical Laboratory Improvement Amendment (CLIA), consent requirements and communicating results.*

10.10.a. Is it anticipated that the research will produce any individual research results that are clinically actionable?

"Clinically actionable" means that there are established therapeutic or preventive interventions or other available actions that have the potential to change the clinical course of the disease/condition or lead to an improved health outcome.

In general, every effort should be made to offer results that are clinically actionable, valid and pose life-threatening or severe health consequences if not treated or addressed quickly. Other clinically actionable results should be offered if this can be accomplished without compromising the research.

☐ **No**
☒ **Yes →** Answer the following questions (**10.10.a.1** through **10.10.a.3.**)

10.10.a.1. Describe the clinically actionable results that are anticipated and explain which results, if any, could be urgent (i.e., because they pose life-threatening or severe health consequences if not treated or addressed quickly).

Examples of urgent results include very high calcium levels, highly elevated liver function test results, positive results for reportable STDs.

Although the study poses no serious risks to participants, participants may notify research personnel about pre-existing mental health issues that have not been previously identified. Non-clinical staff will implement a suicide risk assessment protocol as follows.

a) *If a participant mentions or alludes to thoughts, intentions, plans, or behaviors related to self-directed violence (SDV) during any contact with research staff (e.g., during study consent procedures).*

b) *If a participant endorses a response > 0 on the Patient Health Questionnaire-9 (PHQ-9) item 9 during screening for eligibility, meaning the participant has thoughts of being better off dead or of hurting themselves in some way "several days," "more than half the days," or "nearly every day."*

If participants allude to thoughts about SDV (see above), non-clinical research staff will use the Columbia-Suicide Severity Rating Scale (C-SSRS) to assess suicide risk. The C-SSRS is an evidence-based, widely used suicide risk assessment tool. The C-SSRS uses a series of simple, plain-language questions to help identify whether someone is at risk for suicide and assess the severity and immediacy of that risk.

10.10.a.2. Explain which of these results will be offered to subjects.

Research staff will notify a study clinician and ask them to contact the potential participant if they determine that someone meets criteria for medium risk or greater on the C-SSRS. Staff will include the participant's contact information (first name and phone number) for the clinician to contact the participant as soon as they receive the SI referral.

10.10.a.3. Explain which results will <u>not</u> be offered to subjects and provide the rationale for not offering these results.

Reasons not to offer the results might include:

- *There are serious questions regarding validity or reliability*
- *Returning the results has the potential to cause bias*
- *There are insufficient resources to communicate the results effectively and appropriately*

- *Knowledge of the result could cause psychosocial harm to subjects*

Staff will only complete a C-SSRS for and triage those participants alluding to thoughts, intentions, plans, or behaviors related to SDV.

10.10.b. Is there a plan for offering subjects any results that are <u>not</u> clinically actionable?

Examples: non-actionable genetic results, clinical tests in the normal range, experimental and/or uncertain results.

☒ **No**

☐ **Yes →** Explain which results will be offered to subjects and provide the rationale for offering these results.

Click or tap here to enter text.

10.10.c. Describe the validity and reliability of any results that will be offered to subjects.

The IRB will consider evidence of validity such as studies demonstrating diagnostic, prognostic, or predictive value, use of confirmatory testing, and quality management systems.

N/A

10.10.d. Describe the process for communicating results to subjects and facilitating understanding of the results. In the description, include who will approach the participant with regard to the offer of results, who will communicate the result (if different), the circumstances, timing, and communication methods that will be used.

N/A

10.10.e. Describe any plans to share results with family members (e.g., in the event a subject becomes incapacitated or deceased).

N/A

10.10.f. Check the box to indicate that any plans for return of individual research results have been described in the consent document. If there are no plans to provide results to participants, this should be stated in the consent form.

See the GUIDANCE Return of Individual Results for information about consent requirements.

☒ **Confirmed**

10.11. Commercial products or patents. Is it possible that a commercial product or patent could result from this study?

☒ **No**

☐ **Yes →** Describe whether subjects might receive any remuneration/compensation and, if yes, how the amount will be determined.

Click or tap here to enter text.

11. ECONOMIC BURDEN TO PARTICIPANTS

11.1. Financial responsibility for research-related injuries. Answer this question only if the lead researcher is not a UW student, staff member, or faculty member whose primary paid appointment is at the UW.

For each institution involved in conducting the research: Describe who will be financially responsible for research-related injuries experienced by subjects, and any limitations. Describe the process (if any) by which participants may obtain treatment/compensation.

N/A

11.2. Costs to subjects. Describe any research-related costs for which subjects and/or their health insurance may be responsible (examples might include: CT scan required for research eligibility screening; co-pays; surgical costs when a subject is randomized to a specific procedure; cost of a device; travel and parking expenses that will not be reimbursed).

N/A

12. RESOURCES

12.1. [DETERMINATION] **Faculty Advisor**. (For researchers who are students or residents.) Provide the following information about the faculty advisor.

- Advisor's name
- Your relationship with your advisor (for example: graduate advisor; course instructor)
- Your plans for communication/consultation with your advisor about progress, problems, and changes.

N/A

12.2. UW Principal Investigator Qualifications. Upload a current or recent Curriculum Vitae (CV), Biosketch (as provided to federal funding agencies), or similar document to the Local Site Documents page in ***Zipline***. The purpose of this is to address the PI's qualifications to conduct the proposed research (education, experience, training, certifications, etc.).

For help with creating a CV, see http://adai.uw.edu/grants/nsf_biosketch_template.pdf and https://intranet.medicine.uw.edu/academic-hr/curriculum-vitae-cv

☒ **The CV will be uploaded.**

12.3. UW Study team qualifications. Describe the qualifications and/or training for each UW study team member to fulfill their role on the study and perform study procedures. (You may be asked about non-UW study team members during the review; they should not be described here.) You may list these individuals by name, however if you list an individual by name, you will need to modify this application if that individual is replaced. Alternatively, you can describe study roles and the qualifications and training the PI or study leadership will require for any individual who might fill that role. The IRB will use this information to assess whether risks to subjects are minimized because study activities are being conducted by properly qualified and trained individuals.

Describe: The role (or name of person), the study activities they will perform, and the qualifications or training that are relevant to performing those study activities.

Co-Investigators: Participate in weekly meetings with the study team to discuss study progress and problem-solve any issues that arise in addressing the study aims and achieving the study milestones. Collaborate in all dissemination activities. Extensive experience in research evaluating the efficacy of exercise for symptom management.

Research Manager: Provides direct supervision of the study research staff. In consultation with the study biostatistician, create and manage the study database and ensure tracking of data collection; obtain and maintain UW IRB approval; and assist with the fiscal oversight of the grant including monitoring budget expenditures and making purchase recommendations. Will have extensive experience coordinating similar research trials.

Research Study Assistant: Screen and recruit subjects for study participation; work closely with the research coordinator to maintain the study databases, including monitoring the collection of REDCap survey data and following up with participants who are late in providing assessments; ensure participants are compensated in a timely way for completing assessments; assist investigators with preparation of manuscripts and reports that result from the proposed research. Will have considerable experience working on similar research trials

Biostatistician: Provide advice and guidance with respect to data management and data analysis. Experience applying a variety of statistical methods including survival analysis, clustered data analysis, and logistic regression for clinical trials.

Click or tap here to enter text.

12.4. Study team training and communication. Describe how it will be ensured that each study team member is adequately trained and informed about the research procedures and requirements (including any changes) as well as their research-related duties and functions.

☐ There is no study team

Study team members will also be trained on the attached protocol and manual of procedures. The Site PI and study staff will talk weekly about recruitment and study procedures.

13. OTHER APPROVALS, PERMISSIONS, AND REGULATORY ISSUES

13.1. [DETERMINATION] **Approvals and permissions**. Identify any other approvals or permissions that will be obtained. For example: from a school, external site/organization, funding agency, employee union, UW Medicine clinical unit.

Do not attach the approvals and permissions unless requested by the IRB.

N/A

13.2. Financial Conflict of Interest. Does any UW member of the team have ownership or other Significant Financial Interest (SFI) with this research as defined by UW policy GIM 10?

☒ **No**

☐ **Yes →** Has the Office of Research made a determination regarding this SFI as it pertains to the proposed research?

☐ **No →** Contact the Office of Research (206.616.0804, research@uw.edu) for guidance on how to obtain the determination.

☐ **Yes →** Upload the Conflict Management Plan for every UW team member who has a FCOI with respect to the research, to ***Zipline***. If it is not yet available, use the text box to describe whether the Significant Financial Interest has been disclosed already to the UW Office of Research and include the FIDS Disclosure ID if available.

Click or tap here to enter text.