Section 0 Header: **Preferences and Perspectives on Early Intervention Trials in Parkinson's**

Section 0 Directions: Thank you for your interest in completing this survey. This survey will gather your perspectives about early intervention clinical trials for people who are at risk for developing Parkinson's disease (PD). The survey should take about 20 to 30 minutes to complete. Please do not use your browser's back button while completing the survey, as this will cause you to lose your responses. You can save your progress at any time by scrolling to the bottom of the survey and selecting "Save answers and finish later." For security reasons, **you will be logged out 60 minutes after logging in, and any unsaved responses will be lost**. If you plan to take a break, please save your answers before leaving the survey.

Section 1 Header: **MEDICAL AND FAMILY HISTORY**

Section 1 Directions: **To start, please answer a few questions about your family and medical history.**

Q1. Do you have a first-degree blood relative (father, mother, full sibling, child) who has/had been diagnosed with Parkinson's disease?

A1. Yes
A2. No
A3. Not Sure

Question type: radio_group

Validation Message: This field is required

Q2. Do you have any problems with your sense of smell?

A1. Yes
A2. No
A3. Not Sure

Question type: radio_group

Validation Message: This field is required

Q3. Has a health provider told you that you have a sleep problem called REM sleep behavior disorder (also known as RBD)?

A1. Yes
A2. No
A3. Not Sure

Question type: radio_group

Validation Message: This field is required

Q4. Some people act out dreams while they sleep. This can include punching, flailing your arms in the air, making running movements, yelling or even falling out of bed. Have you been told you act out your dreams? Or do you suspect you may do this?

A1. Yes
A2. No

Question type: radio_group

Validation Message: This field is required

Q5. Do you carry a gene variant (e.g., LRRK2, GBA, other) related to PD?

A1. Yes
A2. No
A3. Not Sure

Question type: radio_group

Validation Message: This field is required

Q6. Have you ever been diagnosed with PD by a doctor?

A1. Yes
A2. No

Question type: radio_group

Validation Message: This field is required

Q7. How many different medical specialists (doctors other than your primary care physician) have you seen in the past 12 months to manage your health? Your best estimate is fine. Please enter a number between 0 and 20.

Question type: integer_input (restrict to 0-20)

Validation Message: Please enter a whole number between 0 and 20.

Q8. How many different prescription medications (for any medical condition) – including oral, injectable, patch, and infusion medications – have you taken in the past month? Your best estimate is fine. Please enter a number between 0 and 20.

Question type: integer_input (restrict to 0-20)

Validation Message: Please enter a whole number between 0 and 20.

Q9. Have you ever participated in a clinical trial testing an experimental treatment (e.g., drug, device, other) for any physical or mental health condition?

A1. Yes
A2. No

Logic: If Q9 = A1, show Q10

Question type: radio_group

Validation Message: This field is required

Q10. Have you ever participated in a clinical drug trial (a study in which you were randomized to receive an investigational drug or a placebo)?

A1. Yes
A2. No

Logic: If Q10 = A1, show Q11

Question type: radio_group

Validation Message: This field is required

Q11. What was the longest period that you participated in a past clinical drug trial?

A1. Less than 6 months
A2. 6-12 months
A3. 1-2 years
A4. Greater than 2 years

Question type: radio_group

Validation Message: This field is required

Section 2 Header: **PERSONAL RESEARCH INFORMATION**

Section 2 Directions: **The next set of questions is about your personal research information. PPMI shares personal research information with you, including your results from some tests: dopamine transporter imaging (DAT), alpha-synuclein seed amplification assay (SAA), University of Pennsylvania Smell Identification Test (UPSIT) and Unified Parkinson's Disease Rating Scale (UPDRS).**

Q12. Do you currently know your personal research information (your results) from any PPMI study tests?

A1. Yes
A2. No
A3. Not Sure

Logic: If Q12 = A2 or A3, show Q13
Question type: radio_group
Validation Message: This field is required

Q13. Would you be willing to learn your PPMI research information if it was used to determine whether you could join a study to help slow or stop the risk of developing PD?

A1. Yes, definitely
A2. Maybe
A3. No

Logic: If Q13 = A2 or A3, show Q14
Question type: radio_group
Validation Message: This field is required

Q14. Why might you not be interested in learning your personal research information? (Please select all that apply)

A1. There is no clear benefit (nothing will change as a result)
A2. Privacy concerns (my health data may not be protected)
A3. Fear of discrimination from insurance or employers due to test results
A4. Potential negative effects on family or close personal relationships
A5. Difficulty understanding the meaning of test results
A6. Fear of receiving unfavorable news
A7. Sense of helplessness (have no power to change anything)
A8. Increased stress and anxiety related to the results
A9. Inconsistent with my cultural, personal, or religious beliefs
A10. Some other reason

Question type: checkbox
Validation Message: This field is required

Section 3 Header: **EARLY INTERVENTION CLINICAL TRIALS**

Section 3 Directions: **Below, a general overview of early intervention clinical trials for Parkinson's will be presented**. **Please read the description carefully**. Then you will be asked a series of questions to gather your reactions about study design and the risks and benefits of participation. You will also be asked about reasons why you might be interested — or not interested — in joining a trial. Your responses will help researchers plan future studies.

Early Intervention Clinical Trials Description:

Scientists are planning to conduct **therapeutic studies**[1] to explore the ability of **experimental (new) treatments**[2] to slow or stop the onset and progression of Parkinson's disease (PD). These **early intervention trials**[3] will recruit people with **biological and clinical risk factors**[4] for the possible development of PD. **Participants will not have a diagnosis of PD at the time of study enrollment. They will have some biological and clinical signs that put them at higher risk for Parkinson's disease.**

Study drugs will be selected based on safety and scientific evidence that they could benefit people with early signs of Parkinson's. These drugs may include medications taken by mouth, intravenous (IV) infusions, and/or self-injection. Potential therapies will have been previously tested in other groups of people, including those with PD and without PD.

To speed scientific breakthroughs, some new therapies may be tested in a platform trial. This means two or more investigational drugs can be tested at the same time (in different groups of participants). Each study drug will have a matching **placebo**[5]**.** Participants will first be randomly assigned to a study treatment group, if there are multiple available (e.g., treatment A, treatment B). They will then be randomly assigned to receive either the active experimental drug or matching placebo in that study treatment group (e.g., drug A or placebo A). Depending on the number of treatment groups, the chances of receiving placebo may range from 25% to 50%.

Early intervention trials may ask participants to enroll for at least two years and maybe longer. They may ask participants to visit a clinical site often, at least four times a year. Additional (potentially monthly) visits may also be required to receive study medications.

The risks and potential side effects will depend on the specific study treatment. Generally, side effects will be mild to moderate and temporary. As is the case with all experimental treatments, new and unexpected side effects could be discovered with further study. Participants will be closely monitored for any side effects or negative reactions. Volunteers may withdraw from the study at any time.

Studies will test for any long-term impacts to disease progression. There is no guaranteed benefit to joining an early intervention trial.

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[1] **Therapeutic studies:** types of clinical studies that test how treatments work in people

[2] **Experimental treatments (also known as investigational treatments or interventions):** treatments that are being tested in clinical trials for a specific disease or condition but are not yet approved for use by regulatory bodies.

[3] **Early intervention trials:** trials testing treatments (interventions) to slow or stop disease progression in people at risk of developing Parkinson's

[4] **Parkinson's risk factors** include certain genetic mutations, dopamine loss, abnormal alpha-synuclein, ongoing smell loss, family history of disease

[5] **Placebo:** an inactive version of the study drug that looks similar to and is given the same way as the active experimental treatment being tested

Q15. Before this survey, did you know that clinical trials were being planned to test new drugs to slow or stop the onset of Parkinson's **in people at risk of developing PD**?

A1. Yes
A2. No

Question type: radio_group

Validation Message: This field is required

Q16. Based on the previous description, how interested would you be in learning more about early intervention clinical trials for Parkinson's disease?

A1. Not interested at all
A2. Slightly interested
A3. Moderately interested
A4. Very interested
A5. Extremely interested

Question type: fixed_slider

Validation Message: This field is required

Q17. Based on the previous description, how likely would you be to participate in an early intervention clinical trial for PD, if you were eligible to enroll?

A1. Not likely at all
A2. Not very likely
A3. Somewhat likely
A4. Very likely
A5. Extremely likely

Question type: fixed_slider

Validation Message: This field is required

Directions: How important might each of the following reasons for participating in an early intervention trial be to you, assuming you were eligible to enroll?

Q18. If your participation meant you might be able to slow or stop onset of PD

A1. Not important at all
A2. Slightly important
A3. Moderately important
A4. Very important
A5. Extremely important

Question type: fixed_slider
Validation Message: This field is required

Q19. If your participation meant you were helping to advance scientific knowledge about disease onset

A1. Not important at all
A2. Slightly important
A3. Moderately important
A4. Very important
A5. Extremely important

Question type: fixed_slider
Validation Message: This field is required

Q20. If your participation meant you were helping to advance new treatments for PD

A1. Not important at all
A2. Slightly important
A3. Moderately important
A4. Very important
A5. Extremely important

Question type: fixed_slider
Validation Message: This field is required

Q21. If your participation meant you could be helping your family members who might have risk factors for PD

A1. Not important at all
A2. Slightly important
A3. Moderately important
A4. Very important
A5. Extremely important

Question type: fixed_slider
Validation Message: This field is required

Q22. If your participation meant you could be helping others in the future who have risk factors for PD

A1. Not important at all
A2. Slightly important
A3. Moderately important
A4. Very important
A5. Extremely important

Question type: fixed_slider
Validation Message: This field is required

Section 4 Header: **CONSIDERATIONS FOR PARTICIPATING IN EARLY INTERVENTION CLINICAL TRIALS**

Section 4 Directions: **The next set of questions explores how different aspects of study design might impact your decision to participate in early intervention clinical trials.**

The following statements describe different factors related to **random assignment to the study drug treatment or to the placebo treatment.** Please rate how each statement would affect your decision to join an early intervention trial if you were eligible.

Q23. There are two or three drugs being tested in the study. You cannot choose which treatment you are assigned. Different study drugs may be given in different ways (like a pill, injection, or infusion) and can have different side effects. Please rate whether being **randomly assigned to a study drug treatment** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q24. You have a 25% chance of getting the placebo treatment. Please rate whether a **25% chance of getting a placebo treatment** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q25. You have a 50% chance of getting the placebo treatment. Please rate whether a **50% chance of getting a placebo treatment** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Directions: The following statements describe different factors related to **how the study medication is given.** Please rate how each statement would affect your decision to join an early intervention trial if you were eligible.

Q26. The study medication is a drug that requires self-injection. Please rate whether **receiving the study medication by self-injection** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q27. The study medication is a drug that is delivered by an intravenous (IV) infusion (medicine given in the vein). Please rate whether **receiving the study medication by IV** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q28. The study medication is a pill that can be taken by mouth. Please rate whether **receiving the study medication by a pill** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll

A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Directions: The following statements describe different factors related to **the location of study visits.** Please rate how each statement would affect your decision to join an early interventional trial if you were eligible. Consider that the trial could take two years or more. Assume that all travel costs are covered for you and a companion.

Q29. The early intervention trial is being offered at a research site that you have visited before. Please rate whether **needing to go to a study site you <u>have</u> visited before** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q30. The early intervention trial is being offered at a research site that you have not visited before. Please rate whether **needing to go to a study site you have <u>not</u> visited before** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Directions: The following statements describe different factors related to **the frequency of study visits to a local site that is within one hour from your home.** Please rate how each statement would affect your decision to join an early interventional trial if you were eligible. Assume that all travel costs are covered for you and a companion.

Q31. You are required to visit the study site 4 times a year (quarterly) for at least 2 years. Please rate whether **quarterly in-person visits** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q32. You are required to visit the study site once a month for at least 2 years. Please rate whether **monthly in-person visits** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q33. In addition to in-person visits to the study site 4 times a year (quarterly) for at least 2 years, you receive medication by IV from a qualified nurse once a month either at your home or at a local infusion center. Please rate whether **monthly infusions at home or close to home** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Directions: The following statements describe different factors related to **the convenience of study visits for a trial that could take two years or more with several study visits per year.** Please rate how each statement would affect your decision to join an early interventional trial if you were eligible.

Q34. The trial site that you go to for in-person study visits is local to you (< 1 hour away). Please rate whether **a local study site** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q35. The trial site that you go to for in-person study visits requires some travel (3+ hours one-way by any method of transportation). Please rate whether **a study site that is 3+ hours away** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q36. The trial site that you go to for in-person study visits requires an overnight stay. Please rate whether **an overnight stay** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll

A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q37. The trial site that you go to for in-person study visits requires air travel. Please rate whether **a study site that requires air travel** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Directions: Trials involving control volunteers (those without PD or PD risk factors) and people with PD have identified some common side effects of medications that may be considered for early intervention trials. These side effects include constipation, diarrhea, fatigue, headache, infusion-related reactions, sensitivity at the injection site, and swelling in legs or hands. There may also be new side effects that arise in future trials. All possible side effects may vary in terms of duration and severity.

Directions: The following statements describe different factors related to **possible side effects of study medications.** Please rate how each statement would affect your decision to join an early intervention trial if you were eligible.

Q38. You may experience **temporary** (short-term) and **mild side effects** (e.g., noticeable to you; no impact on functioning; no intervention required – like having a slight headache or mild fatigue but not needing to take any medication or lie down). Please rate whether the **possibility of experiencing <u>temporary mild side effects</u>** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q39. You may experience **chronic** (persistent) and **mild side effects** (e.g., noticeable to you; no impact on functioning; no intervention required – like having a slight headache or mild fatigue but not needing to take any medication or lie down). Please rate whether the **possibility of experiencing <u>chronic mild side effects</u>** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q40. You may experience **temporary** (short-term) and **moderate side effects** (e.g., noticeable to you; some impact on your functioning; may require an intervention – like needing to take an aspirin for a moderate headache or a nap due to fatigue). Please rate whether the **possibility of experiencing <u>temporary moderate side effects</u>** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Q41. You may experience **chronic** (persistent) and **moderate side effects** (e.g., noticeable to you; some impact on your functioning; may require an intervention – like needing to take an aspirin for a moderate headache or a nap due to fatigue). Please rate whether the **possibility of experiencing <u>chronic moderate side effects</u>** would make you more or less likely to participate in this trial.

A1. Much less likely to enroll
A2. Less likely to enroll
A3. Neutral
A4. More likely to enroll
A5. Much more likely to enroll

Question type: fixed_slider
Validation Message: This field is required

Directions: To what extent do you agree or disagree with the following expectations about participating in an early intervention clinical trial?

Q42. Participating in the trial will have little to no effect on my current or future overall health

A1. Strongly Disagree
A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree

Question type: fixed_slider
Validation Message: This field is required

Q43. Participating in the trial will have a positive impact on my current or future overall health

A1. Strongly Disagree
A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree

Question type: fixed_slider
Validation Message: This field is required

Q44. Gaining early access to study medications will benefit me long-term

A1. Strongly Disagree

A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree
Question type: fixed_slider
Validation Message: This field is required

Q45. Participating in the trial will give me priority access to new medications in the future
A1. Strongly Disagree
A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree
Question type: fixed_slider
Validation Message: This field is required

Q46. The study medications, if effective, will prevent me from developing PD
A1. Strongly Disagree
A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree
Question type: fixed_slider
Validation Message: This field is required

Q47. My health will worsen during the trial
A1. Strongly Disagree
A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree
Question type: fixed_slider
Validation Message: This field is required

Q48. The study medication will make me feel better and improve any existing symptoms
A1. Strongly Disagree
A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree
Question type: fixed_slider
Validation Message: This field is required

Q49. Participating in the trial will have little to no effect on my health if I receive a placebo
A1. Strongly Disagree
A2. Disagree
A3. Neutral
A4. Agree
A5. Strongly Agree
Question type: fixed_slider

Validation Message: This field is required

Q50. Participating in the trial will offer me a sense of hope or optimism about managing my health
- A1. Strongly Disagree
- A2. Disagree
- A3. Neutral
- A4. Agree
- A5. Strongly Agree

Question type: fixed_slider
Validation Message: This field is required

Q51. The required study visits or treatments will significantly disrupt my daily life or routines
- A1. Strongly Disagree
- A2. Disagree
- A3. Neutral
- A4. Agree
- A5. Strongly Agree

Question type: fixed_slider
Validation Message: This field is required

Q52. My family will help me decide whether to participate in the trial
- A1. Strongly Disagree
- A2. Disagree
- A3. Neutral
- A4. Agree
- A5. Strongly Agree

Question type: fixed_slider
Validation Message: This field is required

Q53. My doctors will help me decide whether to participate in the trial
- A1. Strongly Disagree
- A2. Disagree
- A3. Neutral
- A4. Agree
- A5. Strongly Agree

Question type: fixed_slider
Validation Message: This field is required

Q54. After reflecting more on early intervention trials while completing this survey, how do you think the benefits of participating in an early intervention trial compare to the risks?
- A1. The risks far outweigh the benefits
- A2. The risks somewhat outweigh the benefits
- A3. The benefits and risks seem about the same
- A4. The benefits somewhat outweigh the risks
- A5. The benefits far outweigh the risks

Question type: radio_group
Validation Message: This field is required

Q55. After reflecting more on early intervention trials while completing this survey, how likely would you be to participate in such trials, if you were eligible?

A1. Not likely at all
A2. Not very likely
A3. Somewhat likely
A4. Very likely
A5. Extremely likely

Question type: radio_group

Validation Message: This field is required

Section 5 Header: **YOUR EXPERIENCE WITH PPMI**

Section 5 Directions: **The next set of questions will ask about your experiences with your PPMI clinical site.**

Q56. How many hours does it typically take you to travel from your home to your PPMI study site? Please round to the nearest whole number between 0 and 20.

Question type: integer_input (restrict to 0-20)

Validation Message: Please round to the nearest whole number between 0 and 20.

Q57. What is your primary mode of transportation to your PPMI study site?

A1. Car
A2. Train
A3. Airplane
A4. Other

Question type: radio_group

Validation Message: This field is required

Q58. Who, if anyone, typically accompanies you to your PPMI annual visit?

A1. Spouse/partner
A2. Family member
A3. Friend
A4. Paid caregiver
A5. Unaccompanied
A6. Other

Question type: radio_group

Validation Message: This field is required

Action Buttons: SUBMIT (Do not show a “BACK” button)

Save Answers Functionality: Provide option to “save answers and finish later”