**Supplemental material to “Barriers and facilitators to trial participation in neurodegenerative diseases: A systematic review and meta-analysis”**

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# **Supplement 1. Search terms**

## **Search terms for PubMed**

* 1. **ALS**

(((((((((clinical trial as topic[MeSH Terms]) OR (clinical trial\*[Title/Abstract])) OR (Randomized placebo control[Title/Abstract])) OR (Randomised placebo control[Title/Abstract])) OR (Survey\*[Title/Abstract])) OR (Qualitative research[Title/Abstract])) OR (Interview\* [Title/Abstract])) OR (Questionnaire\* [Title/Abstract])) OR (Focus group\* [Title/Abstract])) OR (Participant-observation\* [Title/Abstract])) AND (((((((((((attitude to health[MeSH Terms]) OR (participate, refusal to[MeSH Terms])) OR (participat\*[Title/Abstract])) OR (patient perspective\*[Title/Abstract])) OR (patient selection\*[Title/Abstract])) OR retention [Title/Abstract])) OR (attitude\*[Title/Abstract]) OR Recruit\* [Title/Abstract] OR Enrol\* [Title/Abstract]) OR Accrual [Title/Abstract]) OR Attrition [Title/Abstract]) AND (((((((Amyotrophic Lateral Sclerosis\*[Title/Abstract]) OR (Gehrig\*[Title/Abstract])) OR (Charcot Disease[Title/Abstract])) OR (Guam disease[Title/Abstract])) OR (motor neuron disease[MeSH Terms])) OR (Amyotrophic lateral sclerosis[MeSH Terms])) OR (ALS[Title/Abstract]))

* 1. **Alzheimer’s disease**

(((((((((clinical trial as topic[MeSH Terms]) OR (clinical trial\*[Title/Abstract])) OR (Randomized placebo control[Title/Abstract])) OR (Randomised placebo control[Title/Abstract])) OR (Survey\*[Title/Abstract])) OR (Qualitative research[Title/Abstract])) OR (Interview\* [Title/Abstract])) OR (Questionnaire\* [Title/Abstract])) OR (Focus group\* [Title/Abstract])) OR (Participant-observation\* [Title/Abstract])) AND (((((((((((attitude to health[MeSH Terms]) OR (participate, refusal to[MeSH Terms])) OR (participat\*[Title/Abstract])) OR (patient perspective\*[Title/Abstract])) OR (patient selection\*[Title/Abstract])) OR retention [Title/Abstract])) OR (attitude\*[Title/Abstract]) OR Recruit\* [Title/Abstract] OR Enrol\* [Title/Abstract]) OR Accrual [Title/Abstract]) OR Attrition [Title/Abstract])AND ((((((((alzheimer disease[MeSH Terms]) OR (Alzheimer\*[Title/Abstract])) OR (senile dementia[Title/Abstract])) OR (Primary Senile Degenerative Dementia[Title/Abstract])) OR (Presenile Dementia[Title/Abstract])) OR (diffuse cortical sclerosis[Title/Abstract]))

* 1. **Huntington’s disease**

(((((((((clinical trial as topic[MeSH Terms]) OR (clinical trial\*[Title/Abstract])) OR (Randomized placebo control[Title/Abstract])) OR (Randomised placebo control[Title/Abstract])) OR (Survey\*[Title/Abstract])) OR (Qualitative research[Title/Abstract])) OR (Interview\* [Title/Abstract])) OR (Questionnaire\* [Title/Abstract])) OR (Focus group\* [Title/Abstract])) OR (Participant-observation\* [Title/Abstract]))AND (((((((((((attitude to health[MeSH Terms]) OR (participate, refusal to[MeSH Terms])) OR (participat\*[Title/Abstract])) OR (patient perspective\*[Title/Abstract])) OR (patient selection\*[Title/Abstract])) OR retention [Title/Abstract])) OR (attitude\*[Title/Abstract]) OR Recruit\* [Title/Abstract] OR Enrol\* [Title/Abstract]) OR Accrual [Title/Abstract]) OR Attrition [Title/Abstract])AND (((((huntington disease[MeSH Terms]) OR (huntington\*[Title/Abstract])) OR (Chorea\*[Title/Abstract])) OR (VEOHD[Title/Abstract])) OR (Woody Guthrie's Disease[Title/Abstract]))

* 1. **Parkinson’s disease**

(((((((((clinical trial as topic[MeSH Terms]) OR (clinical trial\*[Title/Abstract])) OR (Randomized placebo control[Title/Abstract])) OR (Randomised placebo control[Title/Abstract])) OR (Survey\*[Title/Abstract])) OR (Qualitative research[Title/Abstract])) OR (Interview\* [Title/Abstract])) OR (Questionnaire\* [Title/Abstract])) OR (Focus group\* [Title/Abstract])) OR (Participant-observation\* [Title/Abstract])) AND (((((((((((attitude to health[MeSH Terms]) OR (participate, refusal to[MeSH Terms])) OR (participat\*[Title/Abstract])) OR (patient perspective\*[Title/Abstract])) OR (patient selection\*[Title/Abstract])) OR retention [Title/Abstract])) OR (attitude\*[Title/Abstract]) OR Recruit\* [Title/Abstract] OR Enrol\* [Title/Abstract]) OR Accrual [Title/Abstract]) OR Attrition [Title/Abstract])AND ((((((parkinson disease[MeSH Terms]) OR (Parkinson\*[Title/Abstract])) ) OR (hypokinetic rigid syndrome[Title/Abstract])) OR (paralysis agitans[Title/Abstract])) OR (shaking palsy[Title/Abstract]))

## **Search terms for EMBASE**

* 1. **Initial search (up to 2022)**
     1. **ALS**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR   
'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw) AND ('amyotrophic lateral sclerosis':ab,ti,kw OR 'amyotrophic lateral sclerosis'/exp OR 'motor neuron disease'/exp OR 'motor neuron disease':ab,ti,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2000]/sd NOT [20-01-2022]/sd

* + 1. **Alzheimer’s disease**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR 'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw) AND ('alzheimer disease'/exp OR 'Alzheimer\*':ti,ab,kw OR 'senile dementia\*':ab,ti,kw OR 'Presenile Dementia':ab,ti,kw OR 'Primary Senile Degenerative Dementia':ti,ab,kw OR 'diffuse cortical sclerosis':ti,ab,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2000]/sd NOT [20-01-2022]/sd

* + 1. **Huntington’s disease**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR 'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw)AND ('Huntington chorea'/exp OR 'Huntington\*':ti,ab,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2000]/sd NOT [20-01-2022]/sd

* + 1. **Parkinson’s disease**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR   
'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw) AND ('Parkinson disease'/exp OR 'parkinson\*':ti,ab,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2000]/sd NOT [20-01-2022]/sd

* 1. **Updated search (January 2022 – May 2023)**
     1. **ALS**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR   
'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw) AND ('amyotrophic lateral sclerosis':ab,ti,kw OR 'amyotrophic lateral sclerosis'/exp OR 'motor neuron disease'/exp OR 'motor neuron disease':ab,ti,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2022]/sd NOT [15-05-2023]/sd

* + 1. **Alzheimer’s disease**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR 'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw) AND ('alzheimer disease'/exp OR 'Alzheimer\*':ti,ab,kw OR 'senile dementia\*':ab,ti,kw OR 'Presenile Dementia':ab,ti,kw OR 'Primary Senile Degenerative Dementia':ti,ab,kw OR 'diffuse cortical sclerosis':ti,ab,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2022]/sd NOT [15-05-2023]/sd

* + 1. **Huntington’s disease**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR 'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw)AND ('Huntington chorea'/exp OR 'Huntington\*':ti,ab,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2022]/sd NOT [15-05-2023]/sd

* + 1. **Parkinson’s disease**

('clinical trial (topic)'/exp OR 'clinical trial\*':ab,ti,kw OR 'Randomized placebo control':ab,ti,kw OR 'Randomised placebo control':ab,ti,kw OR 'Survey\*':ab,ti,kw OR 'Qualitative research':ab,ti,kw OR 'Interview\*':ab,ti,kw OR 'Questionnaire\*':ab,ti,kw OR   
'Focus group\*':ab,ti,kw OR 'participant observation\*':ab,ti,kw) AND ('attitude to health'/exp OR 'refusal to participate'/exp OR 'participat\*':ab,ti,kw OR 'patient perspective\*':ab,ti,kw OR 'patient selection':ab,ti,kw OR 'retention':ab,ti,kw OR 'attitude\*':ab,ti,kw OR 'recruit\*':ab,ti,kw OR 'Attrition':ab,ti,kw OR 'enrol':ti,ab,kw OR 'Accrual':ti,ab,kw) AND ('Parkinson disease'/exp OR 'parkinson\*':ti,ab,kw) AND ([embase]/lim NOT 'conference abstract'/it) AND [01-01-2022]/sd NOT [15-05-2023]/sd

# **Supplement 2. In- and exclusion criteria**

## **2.1. Eligibility criteria for titles and abstracts**

For the initial review (up to 2022), the first 200 abstracts presented by ASReview was screened independently by two reviewers (TK and LAGvL) using the in- and exclusion criteria stated below. To determine the interrater reliability between the two reviewers, Cohen’s kappa () was calculated. A of 0.81-1.00 was required to continue with independent abstract review. Any potential disagreement was resolved with RPAvE.

**Supplemental table 1. In- and exclusion criteria for titles and abstracts.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Subject** | **Age/species** | **Article/publication type** | **Publication dates** | **Language** | **Sex** |
| **Inclusion criteria** | | | | | |
| Patients with ALS, AD, HD, or PD. | 18 years. | Studies that evaluated barriers and/or facilitators to participation in clinical trial for ALS, AD, HD and/or PD. | 2000-2023 | English, Dutch. | Male and female. |
| **Exclusion criteria** | | | | | |
| Patients with other neurodegenerative diseases, dementias, movement disorders other than ALS, AD, HD and PD. | < 18 years and species other than humans. | Grey literature, incomplete article, such as: unavailability of full text, posters, commentaries, hypothesis articles, articles that are not peer-reviewed. Reviews will also be excluded. | Before 2000 | Other languages than English and Dutch | NA |

Abbreviations: ALS = amyotrophic lateral sclerosis; AD: Alzheimer’s disease; HD = Huntington’s disease; PD = Parkinson’s disease; NA = not available.

## **2.2. Eligibility criteria for full texts**

**Supplemental table 2. Eligibility criteria for full texts**

|  |  |  |
| --- | --- | --- |
| **Content** | **Study design** | **Article type** |
| **Inclusion criteria** | | |
| The primary objective of the study was to identify barriers and/or facilitators to participation in clinical trials for ALS, AD, HD, or PD and/or strategies to overcome barriers/to improve participation of clinical trials in ALS, AD, HD or PD. | - Qualitative research, including, but not limited to: unstructured interviews, semi-structured interviews, focus-groups, open-ended questions.  - Quantitative research, including, but not limited to: surveys, structured interviews. | Complete original articles. |
| **Exclusion criteria** | | |
| Studies that did not investigate barriers and/or facilitators to participation in clinical trials for ALS, AD, HD, and PD. | - Articles that focus on ALS, AD, HD, or PD but also included patients without an official diagnosis.  - Study populations including 50% of patients with ALS, AD, HD, or PD. | Unavailability of full texts. |

Abbreviations: ALS = amyotrophic lateral sclerosis; AD = Alzheimer’s disease; HD = Huntington’s disease; PD = Parkinson’s disease.

# **Supplement 3. Critical Appraisal Skills Program (CASP) form for qualitative studies.**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Was there a clear statement of the aims of the research?** | **Is a qualitative method appropriate?** | **Was the research design appropriate to address the aims of the research?** | **Was the recruitment strategy appropriate to the aims of the research?** | **Was the data collected in a way that addressed the research issue?** | **Has the relationship between researcher and participants been adequately considered?** | **Have ethical issues been taken into consideration?** | **Was the data analysis sufficiently rigorous?** | **Is there a clear statement of findings?** | **How valuable is the research?** | **Overall assessment** |
| Sugarman, 2011 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Bardach, 2020 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Valuable | No concerns |
| Hedman, 2016 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Valuable | No concerns |
| Karlawish, 2002 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Lawrence, 2013 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Cox, 2019 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Karlawish, 2001 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Solomon, 2012 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Valuable | No concerns |
| Marquez, 2022 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Ottenhoff, 2023 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Brehaut, 2021 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Can’t tell | Yes | Yes | Valuable | Minor concerns |
| Kim, 2006 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Valuable | No concerns |
| Kim, 2012 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Olsen, 2020 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| de Melo-Martín, 2020 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Damron, 2021 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |
| Kehagia, 2022 | Yes | Yes | Yes | Yes | Yes | Can’t tell | Yes | Yes | Yes | Valuable | No concerns |

# **Supplement 4. Detailed characteristics of included studies.**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **First author, year** | **Disease** | **Responder** | **Country** | **Data collection method** | **Clinical trial scenario under study** | **N1** | **N2** | **N3** | **Aim of study** | **Age (P)** | **Ever participate? (P)** |
| Bardach, 2018 | AD | P/C | USA | Survey | Experienced clinical trials | 87 | - | - | Better understand, from the perspective of individuals engaged in clinical trials, research motivations | 72.4 | 87 |
| Bardach, 2020 | AD | P/C | USA | (Semi-)structured interview | Clinical trials in general | 33 | - | - | Explore what motivates patients who participate frequently in research, to participate | 73.6 | 33 |
| Bedlack, 2008 | ALS | HCP | USA | Survey | Experienced clinical trials | 40 | - | - | Better understand enrollment in clinical trials from an HCP perspective | - | - |
| Bedlack, 2010 | ALS | P | USA | Survey | Experienced clinical trials | 90 | - | - | To better understand enrollment in clinical trials from a patient perspective | - | - |
| Bedlack, 2010 | ALS | P | USA | Survey | Experienced clinical trials | 245 | - | - | To better understand enrollment in clinical trials from a patient perspective | 56 | - |
| Brehaut, 2021 | HD | P/C | Canada | (Semi-)structured interview | Hypothetical clinical trial | 3 | 8 | - | Describe an adaptable, behavioral-theory driven approach for designing pre-trial surveys of barriers and drivers relevant to trial participation | 37 | 7 |
| Cox, 2019 | AD | P | USA | (Semi-)structured interview | Clinical trials in general | 23 | - | - | Elucidate how patients and their study partners decide whether to enroll in a clinical trial | 78.1 | - |
| Cox, 2019 | AD | C | USA | (Semi-)structured interview | Clinical trials in general | 21 | - | - | Elucidate how patients and their study partners decide whether to enroll in a clinical trial | - | - |
| Damron, 2021 | PD | P | USA | Survey | Clinical trials in general | 101 | - | - | Investigate the perspectives of Hispanic patients regarding awareness, interest, and barriers to clinical trial participation | 67.4 | - |
| Damron, 2021 | PD | P/C/HCP | USA | (Semi-)structured interview | Clinical trials in general | 20 | 20 | 6 | Investigate the perspectives of Hispanic patients regarding awareness, interest, and barriers to clinical trial participation | 65 | - |
| DasMahapatra, 2017 | ALS | P | Several countries | Survey | Experienced clinical trials | 160 | - | - | Explore perceptions and attitudes about clinical trials | - | - |
| DasMahapatra, 2017 | PD | P | Several countries | Survey | Experienced clinical trials | 319 | - | - | Explore perceptions and attitudes about clinical trials | - | - |
| Disbrow, 2021 | AD | C | USA | Survey | Clinical trials in general | 117 | - | - | Examine knowledge of disease, resources, and research opportunities among caregivers | - | - |
| Elad, 2000 | AD | C | Israel | Survey | Experienced clinical trials | 29 | - | - | Investigate the motivation that determines the caregiver’s choice to participate in clinical trials | - | 19 |
| Gabel, 2022 | AD | P/C | USA | Survey | Experienced clinical trials | 443 | - | - | Elucidate the perceived barriers and facilitators to continued participation in longitudinal studies | - | 443 |
| Galvin, 2009 | AD | HCP | USA | Survey | Clinical trials in general | 370 | - | - | Obtain insights into physician perceptions of clinical trials | - | - |
| Goetz, 2003 | PD | P | USA | Survey | Experienced (placebo-assigned) clinical trials | 50 | - | - | Assess patients’ post-study understanding of placebo-controlled trials and placebo assignment | 63.1 | 50 |
| Hedman, 2016 | AD | P | Sweden | Focus group followed by semi-structured interview | Clinical trials in general | 13 | - | - | Assess how patients express their experience of being a research participant with respect to their sense of self | 66.2 | 9 |
| Jefferson, 2011 | AD | P | USA | Survey | Registry enrollment | 235 | - | - | Understand what motivated people to participate in clinical studies | 75.3 | - |
| Júlio, 2021 | HD | P | Several countries (most EU) | Survey | Clinical trials in general | 262 | - | - | Understand the perceptions and experiences about research participation in clinical trials | 41.2 | 121 |
| Karlawish, 2001 | AD | C | USA | (Semi-)structured interview | Phase II clinical trial | 22 | - | - | Examine how patients and caregivers decide whether to enroll in a clinical trial | - | - |
| Karlawish, 2002 | AD | P/C | USA | (Semi-)structured interview | Early phase clinical trial | 15 | 15 | - | Examine the capacity, competency, and reason of patients to enroll in an early phase clinical trial | 72.0 | - |
| Kehagia, 2022 | PD | P | UK | Semi-structured interview, focus group, and survey | Multi-center, placebo-controlled, phase II, 26-month, double-blind futility trial | 27 | - | - | Investigate the experiences of participants, care partners, and key staff to give real time feedback to an ongoing trial | - | - |
| Kehagia, 2022 | PD | C | UK | Focus group | Multi-center, placebo-controlled, phase II, 26-month, double-blind futility trial | 6 | - | - | Investigate the experiences of participants, care partners, and key staff to give real time feedback to an ongoing trial | - | - |
| Kehagia, 2022 | PD | HCP | UK | Semi-structured interview and survey | Multi-center, placebo-controlled, phase II, 26-month, double-blind futility trial | 9 | - | - | Investigate the experiences of participants, care partners, and key staff to give real time feedback to an ongoing trial | - | - |
| Khan, 2020 | PD | P | Singapore | Survey | Clinical trials, specifically trials where blood, urine/stool, CSF is collected | 105 | - | - | Identify and address barriers hindering recruitment for clinical trials | 67.5 | - |
| Kim, 2006 | PD | P | USA | (Semi-)structured interview | Hypothetical phase I gene transfer trial | 92 | - | - | Examine why some patients may be willing to volunteer for an early phase gene transfer trial | - | - |
| Kim, 2012 | PD | P | USA | (Semi-)structured interview | Phase II, brain surgical clinical trial | 71 | - | - | Compare patients who agreed and declined to participate in a clinical trial | 60.5 | - |
| Lawrence, 2013 | AD | P/C | UK | Focus groups | Hypothetical immunotherapy trial | 14 | 14 |  | Examine attitudes towards immunotherapy trial participation among family members and older adults to explain how they feel about learning their biomarker status | - | - |
| Marquez, 2022 | AD | C | USA | Focus group | Clinical trials in general | 8 | - | - | Elucidate barriers and facilitators to participating in clinical trials | - | - |
| Mastwyk, 2002 | AD | C | Australia | Survey | Experienced clinical trials | 25 | - | - | Assess why carers seek participation for their relatives in clinical trials | - | 25 |
| Mastwyk, 2005 | AD | C | Australia | Survey | Experienced clinical trials | 44 | - | - | Explore carer motivation for seeking participation for a relative in a clinical trial | - | 29 |
| Mathur, 2015 | PD | P/C | Several countries | Survey | Clinical trials in general | 240 | - | - | Establish main barriers to clinical success as perceived by patients and HCPs | - | - |
| de Melo-Martín, 2020 | PD | P | USA | Focus group | Stem cell clinical trials | 20 | - | - | Identify concerns and expectations about early-phase stem cell research | 72.7 | 11 |
| Nuño, 2017 | AD | P/C | USA | Survey | Clinical trials in general with different attributed (e.g., trial duration, procedures) | 54 | - | - | Examine whether attitudes towards trial design features differ between patient populations (CN, MCI, AD) | 71.4 | - |
| Olsen, 2020 | PD | P | USA | (Semi-)structured interview | Hypothetical early phase stem cell clinical trial | 27 | - | - | Understand how altruism and self-interest are related in PD patients’ willingness to participate in clinical trials | 74.0 | - |
| Ottenhoff, 2023 | AD | P/C | Netherlands | Survey | Clinical trials in general | 33 | 19 | - | Examine clinical trial participants’ experiences to optimize trial design | - | 52 |
| Ottenhoff, 2023 | AD | P | Netherlands | Focus group | Clinical trials in general | 4 | - | - | Examine clinical trial participants’ experiences to optimize trial design | - | 4 |
| Reijula, 2017 | PD | P/C/HCP | Finland | Survey | Clinical trials in general | 681 | - | - | Assess knowledge of, and attitudes toward, clinical trials | - | - |
| Reijula, 2018 | PD | P | Finland | Survey | Clinical trials in general | 842 | - | - | Compare knowledge of and attitudes towards clinical trials between participators and non-participators | - | 123 |
| Solomon, 2012 | AD | P | Sweden | Survey | Amyloid immunotherapy trials | 19 | - | - | Investigate practical experiences of staff, and participants in immunotherapy trials | 66.0 | 19 |
| Solomon, 2012 | AD | C | Sweden | Survey | Amyloid immunotherapy trials | 20 | - | - | Investigate practical experiences of staff, and participants in immunotherapy trials | - | 20 |
| Solomon, 2012 | AD | HCP | Sweden | (Semi-)structured interview | Amyloid immunotherapy trials | 8 | - | - | Investigate practical experiences of staff, and participants in immunotherapy trials | - | - |
| Sugarman, 2001 | AD | C | USA | (Semi-)structured interview | Different types of trials (imaging, genetic marker, standard) | 49 | - | - | Understand the decision-making process for proxies of patients | 70.4 | 49 |
| Valadas, 2011 | PD | P | Portugal | Survey | Experienced clinical trial | 91 | - | - | Assess motivators and concerns of patients concerning participation in clinical trials | 66.8 | 91 |

The type of responder is either P, C, HCP, or a combination (indicated with a slash ‘/’) of these. In case it concerns a combination of responders, if available, the sample size (N) is given for each responder type. The sample size is then given in the order of responder (e.g., responder is P/C, then N1 is the sample size of the patients, N2 is the sample size of the caregivers). In case the data can be separated between different responders, the data is taken separately and shown in a new row in the table. Age is given as the mean value of the patients (if available). If the responders were caregivers, mean age still pertained to the age of the patient. Abbreviations: AD = Alzheimer’s disease; ALS = amyotrophic lateral sclerosis; HD = Huntington’s disease; PD = Parkinson’s disease; P = patient; C = caregiver; HCP = healthcare professional; USA = United States of America; UK = United Kingdom; CN = cognitively normal; MCI = mild cognitive impairment; CSF = cerebrospinal fluid.

# **Supplement 5. Refences to the included articles.**

**Qualitative studies:**

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**Studies with qualitative and quantitative data collection methods:**

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# **Supplement 6. Heterogeneity statistics in the meta-analyses.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Univariate analysis** | | | **Moderator analysis** | | |
| **Enabler** | **# of studies** |  | **Q-statistic** | **p-value** |  | **Q-statistic** | **p-value** |
| Relationship with clinical staff | 7 | 95.32 | 187.90 | <0.001 | 59.95 | 18.62 | 0.002 |
| Information provided | 11 | 98.94 | 1374.39 | <0.001 | 98.63 | 636.18 | <0.001 |
| Placebo/sham use | 12 | 98.78 | 366.67 | <0.001 | 98.70 | 364.15 | <0.001 |
| Disruption in current medication | 2 | - | - | - | - | - | - |
| Side effects | 19 | 98.50 | 1570.33 | <0.001 | 98.09 | 1239.86 | <0.001 |
| Visiting scheme | 5 | 98.06 | 397.30 | <0.001 | 96.10 | 166.67 | <0.001 |
| Clinic reputation | 9 | 97.16 | 403.46 | <0.001 | 96.81 | 386.15 | <0.001 |
| Travel burden | 15 | 97.25 | 768.99 | <0.001 | 96.67 | 682.09 | <0.001 |
| Awareness | 4 | 94.89 | 64.74 | <0.001 | 81.41 | 43.68 | <0.001 |
| HCP recommendation | 15 | 98.07 | 695.51 | <0.001 | 96.41 | 263.05 | <0.001 |
| Home-based assessments | 2 | - | - | - | - | - | - |
| Time consumption | 17 | 96.76 | 830.37 | <0.001 | 95.72 | 595.09 | <0.001 |
| Financial compensation | 13 | 94.86 | 220.64 | <0.001 | 93.93 | 212.38 | <0.001 |
| Invasiveness | 6 | 84.39 | 47.31 | <0.001 | 64.16 | 21.36 | <0.001 |
| Assessment burden | 8 | 95.14 | 213.82 | <0.001 | 93.59 | 200.90 | <0.001 |

The Q-statistic is based on a likelihood ratio test statistic with *k*-1 degrees of freedom (*k* is number of studies).