F.A.S.T.
Finding Alzheimer Solutions Together

Roche

# Integrating the perspectives of people living with Alzheimer's disease and their study partners into clinical trial development

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# Foreword from the F.A.S.T. Council

Alzheimer's disease is one of the biggest public health challenges of our time impacting millions of people and their families around the world. The care and support for people living with Alzheimer's disease and their care partners is extremely complex and its provision is challenging.

In this context, clinical research in Alzheimer's disease is more important than ever. However, for a variety of reasons clinical trials can be challenging for people living with Alzheimer's disease and their study partners, making recruitment and participation difficult.

Building on this insight, the Finding Alzheimer's Solutions Together Council (F.A.S.T. Council) came together to create a comprehensive guidebook that supports clinical trial design and management to encompass the needs of participants and their study partners.

This report brings the learnings from this guidebook to a wider audience. The content is aimed at researchers, industry members, patient advocacy groups, and the Alzheimer's disease community to help them:

- Better understand people living with Alzheimer's disease, their family members and care partners, as well as their journeys and the challenges traditionally faced in clinical research
- Design, set-up, recruit for, conduct and follow-up after clinical trials for Alzheimer's disease, including guidance on retention barriers and potential solutions
- Improve the way that research is carried out for Alzheimer's disease
- Increase the inclusivity of non-Alzheimer's disease trials to people living with Alzheimer's disease and their care partners

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# Acknowledgements

The Finding Alzheimer's Solutions Together (F.A.S.T.) Council and Roche would like to thank the people living with Alzheimer's disease, their care and study partners, and the global and local Alzheimer's disease patient organisations for their support in developing this report. Their insights and valuable support were crucial in developing the 'Integrating the person living with Alzheimer's (PLWA) and study partner perspective into clinical trial development' guidebook and this report. Without them, this work and the learnings gained would not have been possible.

We would also like to thank Chantal Bayard, Miriam Maylander, Priyankaa Bathia, and Susann Walda from Ipsos, a global market research consultancy, for their support in making the guidebook a reality.

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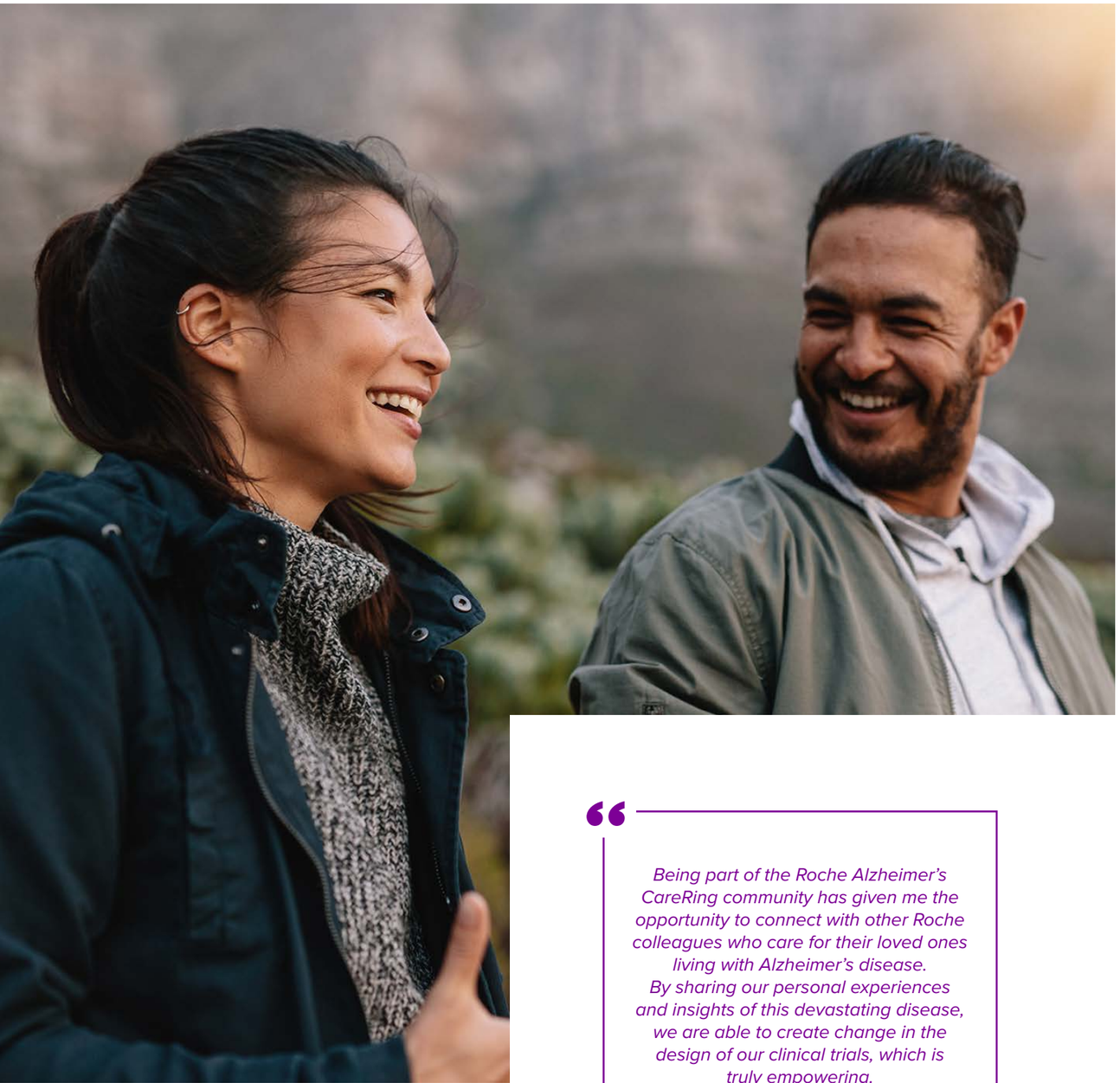


*Being part of the Roche Alzheimer's CareRing community has given me the opportunity to connect with other Roche colleagues who care for their loved ones living with Alzheimer's disease. By sharing our personal experiences and insights of this devastating disease, we are able to create change in the design of our clinical trials, which is truly empowering.*

**– Emma Dodd**, Global Medical Collaboration Lead, Roche and care partner for a person living with Alzheimer's disease

# F.A.S.T. Council members

*(Outlined in alphabetical order)*

**Alzheimer Europe,** Luxembourg
Alzheimer Europe (AE) is the European umbrella organisation of 35 national Alzheimer's associations from 32 countries. AE defines its mission as "changing perceptions, practice and policy in order to improve the lives of people affected by dementia". AE achieves this mission by providing a voice to people with dementia and their carers, making dementia a European priority, changing perceptions and combating stigma, raising awareness of brain health and prevention, strengthening the European dementia movement and supporting dementia research.

**Alzheimer's Disease International,** UK
Alzheimer's Disease International (ADI) is the international federation of Alzheimer and dementia associations around the world with 105 members globally and 25 in development. Its vision is risk reduction, timely diagnosis, care and inclusion today, and cure tomorrow. ADI believes that tackling dementia requires efforts at global, regional and local levels and works by empowering Alzheimer and dementia associations to advocate for dementia as a national priority, to raise awareness and to offer care and support for people with dementia and their care partners. Globally, ADI strives to focus attention on dementia, maintain it as a global health priority, campaign for better policy from governments and encourage investment and innovation in dementia research.

**Alzheimer's Hellas,** Greece
Founded in 1995 by care partners and medical professionals, the Greek Association of Alzheimer's Disease and Related Disorders (Alzheimer's Hellas) is a not-for-profit organisation that currently operates two Day Care Centres in Thessaloniki and has over 4.000 members. The Association's aim is to offer advice concerning the care of those living with Alzheimer's, information and services for the people affected and their families. Alzheimer's Hellas also offers mutual help to those living with Alzheimer's in order to reduce the social, economic and emotional cost deriving from the long care of people suffering from dementia. Lastly, the Association attempts to publicise the social needs of the population affected and to inform the public in order to be acquainted with the issue (or dementia).

**Alzheimer Sverige,** Sweden
Alzheimer Sverige is a national Swedish patient and care partner organisation. Their mission is to give advice and support people with Alzheimer's disease and their care partners; raise awareness about the challenges and the possibilities for those who are affected; and advocate for better healthcare for people with Alzheimer's disease.

**BrightFocus Foundation,** US
BrightFocus Foundation funds exceptional scientific research worldwide to defeat Alzheimer's disease, macular degeneration, and glaucoma; and provides expert information on these heartbreaking diseases. In 2022, BrightFocus awarded nearly $25 million in grants, with their active portfolio now including over 285 funded projects – a $75 million investment in research worldwide.

**CanAge: Canada's National Seniors Advocacy Organization,** Canada
Founded at the onset of the COVID-19 pandemic, CanAge is Canada's national seniors' advocacy organisation, working to improve the lives of older adults through advocacy, policy, and community engagement. CanAge advocates for issues affecting older people in Canada.

**Federação Brasileira das Associações de Alzheimer (Febraz),** Brazil
As a Federation, Febraz brings together four Alzheimer's Associations – ABRAZ (Associação Brasileira de Alzheimer), APAZ (Associação de Parentes e Amigos de Pessoas com Alzheimer), IAB (Instituto Alzheimer Brasil) and Instituto Não Me Esqueças. Febraz has branches in more than 23 Brazilian states and works to empower its member associations, share best practice, advocate for the rights of people living with dementia and their care partners and develop campaigns to eliminate the stigma of the disease.

**Roche,** Switzerland
Roche is a pioneer in pharmaceuticals and diagnostics, focused on advancing science to improve people's lives and is committed to working to improve the diagnosis, treatment and care of people living with Alzheimer's and dementia. Roche engaged with people living with Alzheimer's, care and study partners, global and local Alzheimer's patient organisations and healthcare professionals to understand the barriers that exist in the recruitment and retention of participants in Alzheimer's clinical trials and what could be improved to ensure the continued undertaking of clinical trials in this area. The findings of this research were used to develop a guidebook and this report, both of which were funded by Roche.

**Shanghai Jianai Charity Organization,** China
Jian Ai Charity is a nonprofit organisation headquartered in Shanghai, with a focus on the brain health of older people. Since being established in 2013, Jian Ai Charity has been an active advocate of early prevention and intervention for cognitive impairment. Primarily focusing on dementia, from 2013 to 2016, its community based initiatives covered dementia awareness and friendliness promotion, risk reduction, screening test, non pharmacological intervention, and respite care. In 2017, Jian Ai Charity strategically narrowed its focus on the early stage of disease progression – mild cognitive impairment.

# Interview with Jean Georges

**Executive Director,** Alzheimer Europe

**From the perspective of the Alzheimer's disease community, what are the current challenges when considering clinical trials and research for Alzheimer's disease?**

In Europe, it is over 20 years since the European Medicines Agency approved a medicine for Alzheimer's disease. There is, therefore, great unmet medical need in this field, and clinical trials are aiming to identify new treatment options.

Trials in the Alzheimer's field take time to fully recruit and have long durations with a high number of site visits; thus, they require a lot of commitment from people with Alzheimer's disease, as well as their study partners*. Despite the amazing commitment and dedication of industry and participants, many clinical trials to date have been unsuccessful, but the Alzheimer's disease community continues to be hopeful.

**Why is it crucial to include the voices of people living with Alzheimer's disease when designing clinical trials?**

The unique experiences of people living with Alzheimer's disease should be sought in order to identify the treatment outcomes that are most important to them. In addition, people living with Alzheimer's disease should play a key role in co-designing clinical trials to ensure that the study visits respond to their needs and do not become too burdensome. It is vital that these insights are considered from the earliest planning stage, rather than at a later stage when key decisions have already been made.

**Why is it important for Alzheimer's associations to have their voice embedded in research?**

Alzheimer's associations play an important role in updating their community about research being conducted. The more they are informed and involved in clinical trial design, the better they are able to realistically inform their communities about research progress and results and avoid raising false hopes or undue concerns.

**What should be considered when including the voice of the Alzheimer's disease community in research and clinical trial design? Are there any potential risks of which all parties should be aware?**

Collaborations between the Alzheimer's disease community and industry should always be conducted in an open and transparent fashion that respects the independence and specific roles of each of the partners. When interacting with people living with Alzheimer's disease, particular attention should be paid to supporting them and adapting consultations and interactions to their specific needs.

**What can the Clinical Trial Guidebook contribute to clinical trial design in Alzheimer's disease and dementia?**

In dialogue with the Alzheimer's disease community, including the European Working Group of People with Dementia of Alzheimer Europe, Roche identified key recommendations on how to improve the participation and input of people living with Alzheimer's disease in the design and conduct of clinical trials. It is fantastic that Roche has decided to share these learnings with other companies, researchers and associations.

*Please refer to glossary for full definition

# Interview with Ruth Croney

**Clinical Programme Leader,** Roche Early Clinical Development

**Do Alzheimer's disease clinical trials go far enough to understand the needs of people living with Alzheimer's disease and their study partners and how taking part in a trial may affect them?**

The promise of developing disease modifying treatments for Alzheimer's disease is why it is so important for those of us in the life science sector to get our approach to clinical trials right.

Clinical trials for Alzheimer's disease have historically been challenging for people living with Alzheimer's disease and their study partners. We also need to recognise that trials in Alzheimer's disease, especially in early development, often provide (very) limited treatment benefits for participants.

Given we are asking for an important commitment from both participants and their study partners, it is our duty to make sure we do everything possible to provide a positive experience before, during and after the trial.

**How do you think this report contributes to ensuring that clinical trials meet the needs of people living with Alzheimer's disease and their study partners in the future?**

We really wanted to understand what support the Alzheimer's disease community and their loved ones need to take part in clinical trials, and what barriers and challenges they face when participating in one. We first worked with the Roche CareRing Group – employees who are people living with a disease or care partners* – to gather feedback on our approach, before engaging with our partners on the F.A.S.T. Council to collect responses from numerous individuals across the world and develop a guidebook.

Our partnership approach enabled us to take a truly fresh look at the design of our clinical trials, ensuring people living with Alzheimer's disease and their study partners are at the heart of everything we do. I want to thank every person living with Alzheimer's disease, study partner and patient organisation that contributed to the development of both the clinical trials guidebook and this report.

We hope these resources are a first step in helping to deliver best practice clinical trials for people living with Alzheimer's disease and their study partners.

# Contents

# Introduction

Alzheimer's disease (AD) is a progressive neurological condition that causes brain cells to die, leading to severe memory impairment and behaviour and social challenges, with people living with Alzheimer's (PLWA) losing the ability to undertake everyday tasks and function independently.[1]

AD is the most common form of dementia, affecting around 70% of the 50 million people who have dementia worldwide and is non-discriminatory, affecting people of different ages.[1] This condition impacts not only PLWA but also their loved ones and care partners, healthcare systems and society – making AD a major global health challenge.[2,3,4]

Despite this global challenge, the medicines currently available have limited benefit as they do not slow the condition's progression, they only provide limited symptom management for PLWA.[5] It is therefore key that research continues into this condition, so that disease modifying treatments (DMTs) – that can impact the underlying disease progression – and treatments for Behavioural and Psychological Symptoms In Dementia (BPSD) (sometimes known as treatments for neuropsychiatric symptoms (NPS)) are developed for PLWA.

Even though there is an urgent need for new treatments, clinical trials in AD face many barriers, especially when it comes to participation.[6] Taking part in a clinical trial can be a challenging experience for both participants and their study partners.[6]

The F.A.S.T. Council is committed to improving the clinical trial experience for PLWA and their study partners, and in 2021 brought together PLWA, care partners, as well as global and local AD patient organisations to understand the key challenges participants may face in AD clinical trials and develop recommendations to address these.

Following these discussions, the *'Integrating the person living with Alzheimer's and study partner perspective into Alzheimer's disease clinical trial development'* guidebook was developed with support from Ipsos, a global market research consultancy. This was a first of its kind initiative between the pharmaceutical industry and the wider AD community, which provides a holistic approach to integrating the voice of PLWA and their care partners into clinical trial design and management, covering all stages of clinical trials and extending to post-trial considerations.

Recognising the wider applicability of the guidebook for the AD community, the F.A.S.T. Council has worked to develop this externally-facing report, in the hope that its findings and recommendations help improve the general understanding of clinical trials and enable wider AD clinical trial participation across the life sciences sector.

It should be noted that the recommendations outlined in this report are based on the above-mentioned feedback and may not always fully reflect the needs of every PLWA, given that living with AD is a unique journey, which depends on many factors such as the stage of the disease, the personality or circumstances of the PLWA. Therefore, we recommend that readers and clinical trial developers also consider and appreciate the needs of PLWA and their study partners on a case-by-case basis.

# Understanding the PLWA and care partner journeys

Receiving an Alzheimer's disease (AD) diagnosis can be a very difficult time for the people who receive the diagnosis, their families and their care partners, especially as they realise what this diagnosis means for them and their loved ones' future.[7]

The time from the onset of first symptoms to receiving a confirmed diagnosis can be both physically and psychologically challenging. Both the people living with AD (PLWA) and their loved ones' face fear, frustration and pain, as shown in Figure 1 and Figure 2.[7]

Participating in a clinical trial can compound on this already stressful and challenging period, making it therefore key for trials to be designed considering the needs of PLWA, their families and care partners, as well as their study partners.

To do so, we must understand the journey of PLWA from pre- to post-diagnosis, as well as the journey of their care partners, given they may also support the person during their participation in the clinical trial. From this, we can help, where possible, lessen the challenges they face and encourage them to consider participation in clinical trials as part of their treatment discussion.

The research undertaken during the development of the clinical trial guidebook helped compile both of these journeys, encompassing shared experiences and insights of PLWA and their care partners from around the world.[7]

## PLWA journey

**Enquiries about the possibility of Alzheimer's** are triggered by diminishing memory and / or family history.

> *I recently had a cognitive functioning test which gave me the diagnosis of pre-senile dementia with depressive features ...* ***Does this diagnosis foreshadow an early AD diagnosis?***

**Potential PLWA seek advice** on how to approach doctors and share their experiences / symptoms.

> *I've had* ***short term memory loss, agitation, asking people to slow down their talking at times so I can understand better.*** *I'm 61 now ... My neuro exam is on the 4th of November ...*

**PLWA adjust to the new reality,** battling with their emotions and looking for strategies that may help to maintain quality of life.

> *I was told* ***two weeks ago that I have AD,*** *it's only just sunk in ...*
>
> ***... I came to the decision that I was not going down without a fight!*** *I was going to fight for my life and my independence!*

**Disease progression makes PLWA concentrate more on managing AD,** rather than on holistic health.

> *Is agitation a part of this disease? It seems I can get angry quicker than I ever have. Is it part of early stage to: ... like being alone? ... to battle depression? ... why does eyesight get worse? ... not to care about personal hygiene such as washing your hair or taking a shower?*

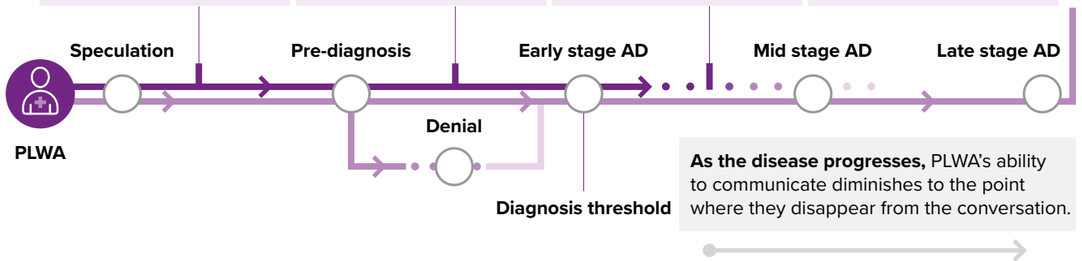



**Figure 1.** Overview of the PLWA journey from pre-diagnosis to late disease on-set.[7]

## Care partner journey

**People start worrying about relatives** (or far less commonly friends) and want information on prevention, symptoms and diagnosis. With diagnosis being a lengthy process, many rely on shared experiences – and compare notes with others in a similar position during this period.

> *... my mother and father are currently 47 and 52 years old respectively ... I want to make sure, or at* ***least lower the risks of dementia and AD.***

**Care partners go through a similar 'adjustment' process** to that of PLWA, seeking information on every aspect of life with AD.

> *Diagnosis yesterday – heartbreaking,* ***can the doctor be wrong?***

**Care partners start to focus solely on AD.** Caring for the PLWA takes its toll and care partners seek emotional support from peers.

> *It's so hard sometimes to be here watching* ***Mom slipping away down*** *this path of AD.*

**Caring for PLWA becomes too hard;** care partners seek professional care and affirmation of this decision.

> [after sending a patient to nursing home] ***Guilt*** *about not being closer, not doing enough.*

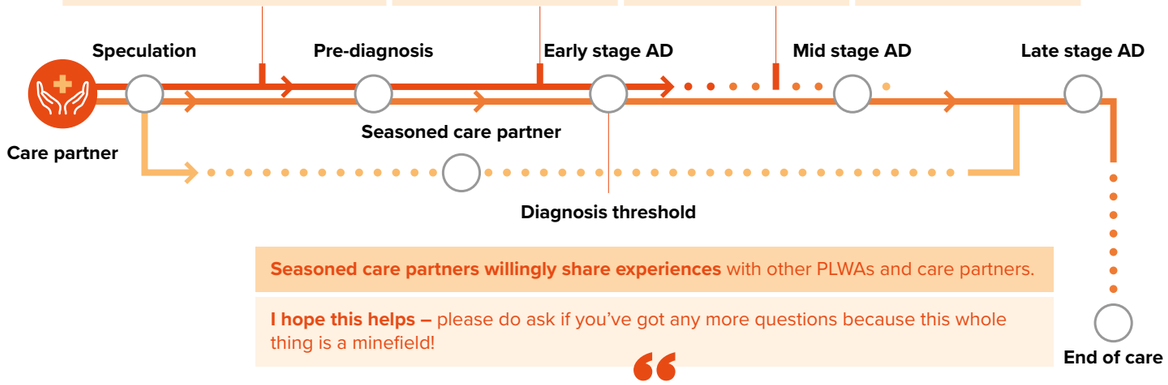



**Figure 2.** Overview of the care partner journey from pre-diagnosis to late disease on-set.[7]

# Identifying barriers facing participation in clinical trials

Historically, recruitment for, and participation in, Alzheimer's disease (AD) clinical trials has been a challenge.[6,8]

Several barriers to trial participation have been reported not only in peer reviewed papers[6,8] but also throughout the insights gathered by the F.A.S.T. Council.[7] These insights were provided by people living with AD (PLWA) and their study partners before, during and post clinical trials; healthcare professionals involved in trial management; and global and local patient organisations.

The barriers reported include:

- Lack of a study partner to support the PLWA throughout the trial and to note cognitive changes or treatment effectiveness
- The pain and fear associated with undergoing invasive procedures during a trial
- Distance to the trial centre and travel costs
- Time commitment necessary from both the participant and their study partner
- Concern over the risks to which participants may be exposed
- Participants' comorbidities
- The lack of history of positive effects in AD clinical trials
- The lack of ability to engage with underrepresented populations

Each of these barriers has been further detailed below.

## Study partner requirement

AD clinical trials usually require a study partner, a person who knows the participant and is able to provide accurate information about their daily functioning.[9] This study partner can be a spouse, a family member or a professional study partner.[10]

Their role is crucial to support the PLWA throughout their trial participation, helping to ensure the PLWA is able to complete the trial and that meaningful data can be gathered.[11,12] For example, research shows that unmarried people have a higher dropout rate (approximately 40%) from AD clinical trials than those participants who are married (27%).[13]

The role of a study partner can be extremely challenging, both physically and mentally, as they have to accompany the participant to trial visits, monitor their progress at home, prepare them for the visit and potentially manage their exhaustion after a visit.[7,12]

Given the thorough support they provide to participants and their ability to influence PLWA in their decision to participate or continue in a trial, it is key that study partners' perspectives and needs are considered when designing AD clinical trials.

## Invasive procedures

AD research may involve invasive procedures such as brain scans and lumbar punctures, not only during the trial but also as part of screening procedures for inclusion in the study.[9] These procedures can be extremely challenging for participants. For example, a PLWA may not wish to undergo an MRI or PET scan due to having to lie still for a long period of time, in a place they do not know, without someone they know present to reassure them and where it may be noisy.[7] Similarly, PLWA may have concerns about undergoing a lumbar puncture, as the procedure may be unfamiliar and may be viewed as potentially painful, if not explained in sufficient detail before the trial.[7]

Administration of study drugs can be time consuming and seen as daunting.[7,9] Participants may also have to undergo several hours of cognitive assessments.[9]

The extensive time and effort involved in participating in an AD trial can lead to PLWA dropping off the trial or deter volunteers and study partners from enrolling their loved ones into a clinical trial.[7,9]

It is thus key that PLWA and their study partners feel well-informed ahead of, and made comfortable throughout, trial visits; are supported by the same team of healthcare professionals for consistency; and are provided with information on the procedures they will undergo, including what the procedure is, how it will be conducted and why it is key for the study's success.

## Trial logistics

The logistical aspects of being part of a clinical trial may also be challenging for participant recruitment and retention.[7,9] For example, PLWA and their study partners may need to travel long distances to the trial site, which can be costly and time consuming.[9] It is therefore key for clinical trial organisers to cover travel costs and, where possible, help organise travel arrangements. For example, Roche already has an ethos in AD trials that no participant should incur out-of-pocket expenses.

Study partners and trial participants may also need to request time off work to attend trial visits, which can make participation more demanding and harder to maintain throughout the trial duration.[9] Being flexible in regard to the presence of study partners in trial visits and clearly highlighting when their presence isn't required, or when participants can be accompanied by another person rather than the study partner can help minimise this challenge.

## Time investment

The overall time investment trial participants and their study partners commit to should also be carefully considered when designing a clinical trial.

For PLWA, the time commitment includes not only the time spent on procedures and tests, but also the waiting time between procedures.[7,9] Not knowing the length of time between procedures is challenging for participants, and long waits can cause anxiety and tiredness.[7]

For study partners, this means supporting PLWA with their visits, their care at home and travel between their home and the trial site.[7] Study partners also have a key role to play in reassuring the PLWA regarding their trial visits, which also adds on to their time commitment. This can lead to study partners having to take time off work repeatedly and having to justify this to their employer.[7]

The figure below demonstrates in more detail the time commitment study partners may undergo before, during and after a trial visit. This was compiled based on experiences and information shared by study partners with the F.A.S.T. Council.[7]

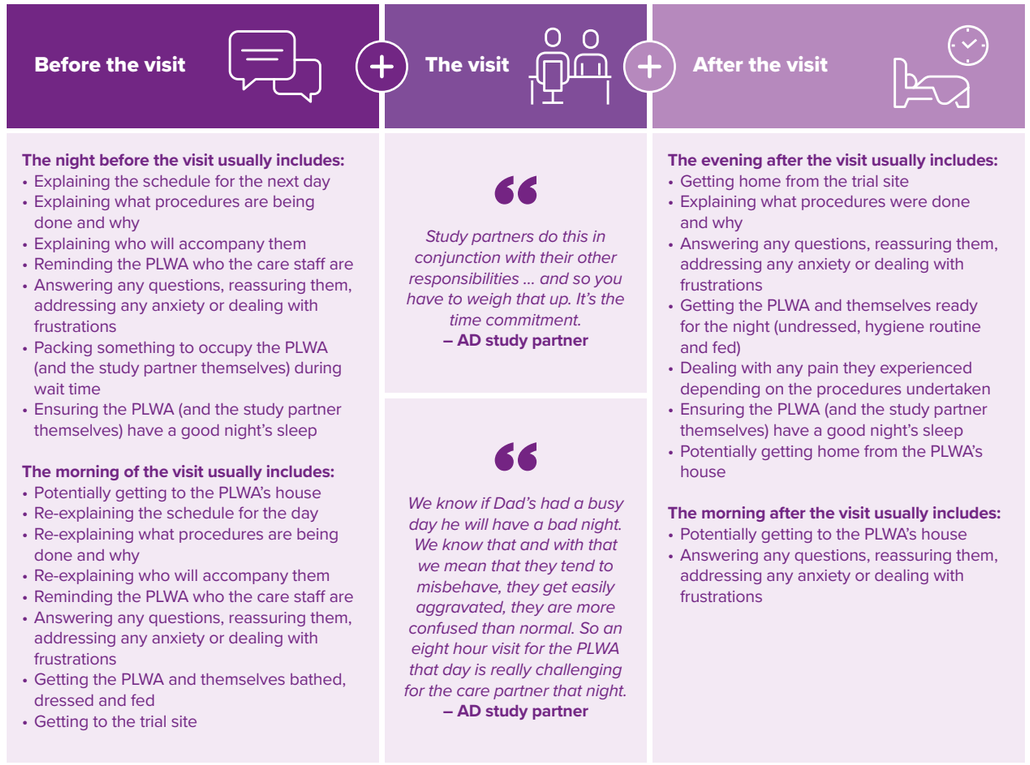



**Figure 3.** Overview of the time commitment from study partners before, during and after a clinical trial visit.[7]

## Lack of understanding of the purpose and process of trial procedures

Given the complexity and invasive nature of some of the procedures undertaken during an AD clinical trial, it can be difficult for PLWA and their study partners to understand the purpose of these procedures or how they will be run.[7] Some procedures can also be painful, so undergoing them can become stressful for both participants and study partners.[7]

To help mitigate these feelings and help both the participants and the study partners feel more comfortable with the trial's procedures, trial organisers should, before the trial starts, provide participants and study partners with an overview of each of the procedures the participant will undergo and a rationale for why they need to undergo them.

Explaining personal medical data or the trial results in person to both the participants and the study partners, in lay terms, can also help them realise what the study and their overall commitment means not only for their health, but also for their future and the future of others living with AD.

## Informed consent

This information should always be included in the Informed Consent Form, which participants and study partners are given before signing up for a trial,[14] and could also be shared within a guide with additional information on how each trial visit will be conducted.

During the Informed Consent process[14] – a process during which participants are also given information on the trial's risks and benefits, and the treatment schedules and locations – it is key that trial organisers allocate time for participants and study partners to thoroughly read the Informed Consent Form and ask any questions they may have, so that they understand the overall commitment of participating in the clinical trial.

## Fear of the unknown

PLWA can at times feel anxious or stressed when the environment or people surrounding them are different or unknown.[7] These feelings can be heightened if the participants are under additional external pressures, which can of course change from day to day. This in turn can be challenging to manage for the study partners, who themselves may face increased stress.[7]

Helping the study partner plan for the trial visits and providing them with planning tools (e.g., a calendar, a planning booklet, a PLWA booklet, or a mobile application) can help both the study partner and the participant better prepare for the visit; become more familiar with the trial site, environment and team; and ultimately feel more confident about participating in the trial.

> *Sometimes the PLWA has a bad day and is in disorder, but sometimes it may also be the care partner ... I know it from when I am stressed, then the person with Alzheimer's feels it and they get stressed too ...*
> **– AD care partner**

## Lack of trust in the medical community

Lack of trust in the medical community is sometimes intrinsically linked with a lack of understanding of the trial procedures and purpose, a lack of positive results in previous AD trials and being fearful of the unknown.[7,9] This can lead to a lack of participant enrolment in trials.[7,9]

Getting to know the PLWA and their study partner on a more personal level, can help researchers and trial organisers better understand their concerns regarding trial participation and provide them with mitigating factors. This can ultimately help improve engagement with, and participation in, the overall clinical trial, as well as ensure trial participants and their study partners are presented with a positive trial experience.[7]

Having support mechanisms in place and creating an atmosphere where both the PLWA and their study partner feel comfortable is also essential.[7] This includes developing tailored support mechanisms to meet personal information needs, such as a mobile app which details information about procedures, treatment schedules, who the care team is, etc, as well as providing them with food, beverages or entertainment during trial visits - and being flexible to accommodate their needs. For example, a 70-year-old spouse of a PLWA will likely have very different support needs than a 48-year-old employed child of a PLWA.[7]

## Lack of engagement with underrepresented populations in trials

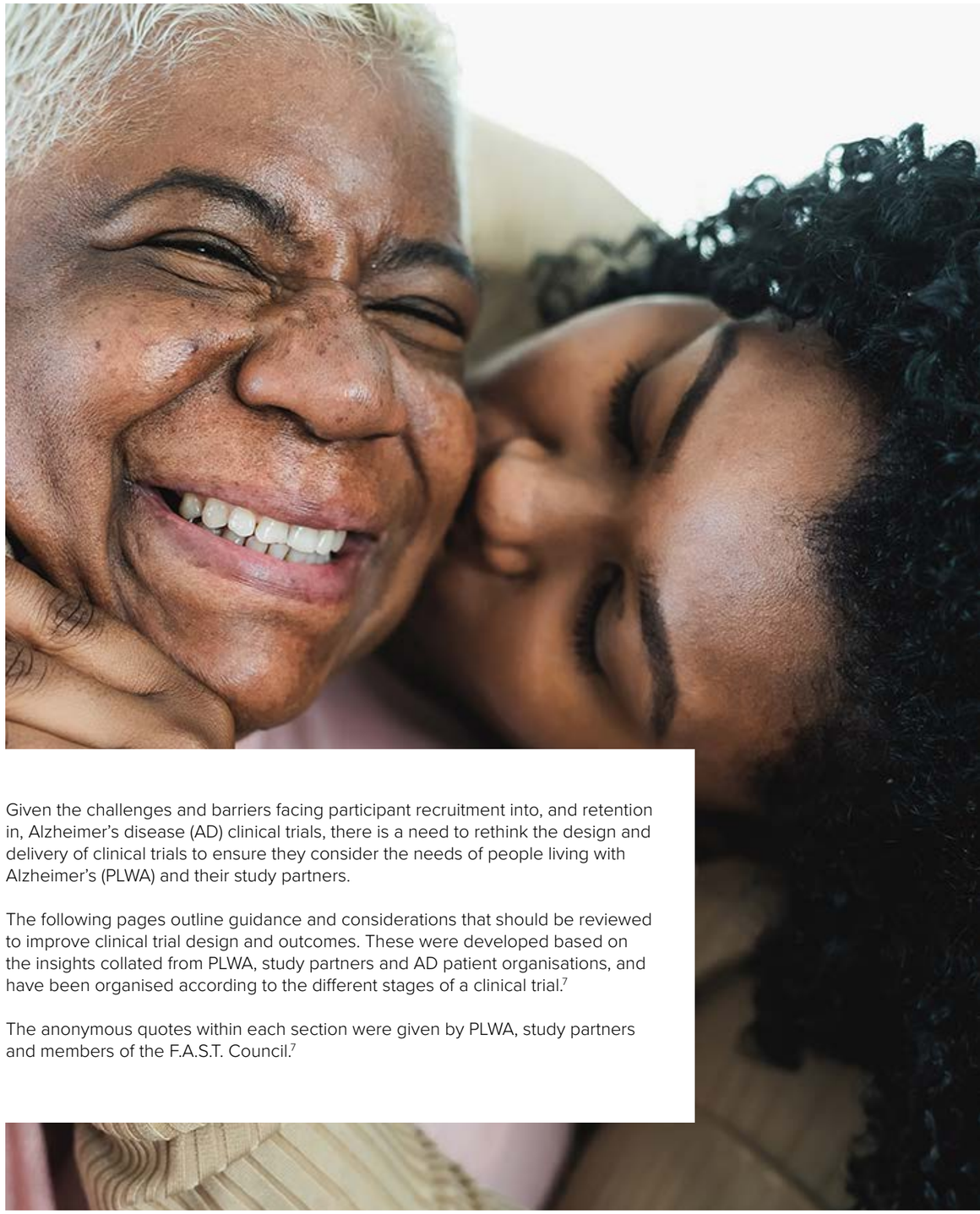
Diverse representation in clinical trials remains a challenge, with researchers struggling to engage, recruit and retain underrepresented populations.[15] These include ethnic and racial minorities, people from socioeconomically disadvantaged backgrounds, people living with disabilities, and people from the LGBQTI+ communities.[16,17] These communities often have a lack of trust in the institutions and organisations who run clinical trials for AD, making any engagement to improve recruitment more challenging.

This can have severe implications for researchers including restricting the understanding of the effectiveness of a treatment across different populations and impacting the discovery of novel medicines.[16]

It can also be detrimental for PLWA. Studies have observed that a lack of representation of people's needs, especially in underrepresented populations, can increase health disparities, reduce access to health services and exacerbate poor health outcomes.[16]



# Considerations for designing a clinical trial



Given the challenges and barriers facing participant recruitment into, and retention in, Alzheimer's disease (AD) clinical trials, there is a need to rethink the design and delivery of clinical trials to ensure they consider the needs of people living with Alzheimer's (PLWA) and their study partners.

The following pages outline guidance and considerations that should be reviewed to improve clinical trial design and outcomes. These were developed based on the insights collated from PLWA, study partners and AD patient organisations, and have been organised according to the different stages of a clinical trial.[7]

The anonymous quotes within each section were given by PLWA, study partners and members of the F.A.S.T. Council.[7]

## Before starting to design a clinical trial

> *The PLWA and their families are feeling helpless, so it is good to help them understand the disease and to simply have someone to talk to... As the disease progresses you have people, friends, family, who stop contact with these families because it is too much for them.*
> **– AD clinical trial staff**

1. Ensure that clinical trial designers and staff have an understanding of PLWA and the AD population's needs more widely. This is important for making decisions on site location, and creating eligibility criteria that is reflective of the AD population.

2. Develop a flexible approach and have the ability to adapt the trial visit schedules, when needed and possible, to the PLWA and their family's needs, as well as to the study partner's needs, given that PLWA can:

- Be psychologically extremely vulnerable
- Have different symptoms and cognitive ability, even if they are at the same stage of disease
- Be different from day to day – or hour to hour – in terms of their mood, their cognitive ability and their general ability and willingness to participate in trial procedures
- Be unpredictable
- Be combative / embarrassed as they come to terms with their disease
- Feel stigmatised

3. Be prepared to provide study partners with the tools and support they need to plan for the trial, as they carry this responsibility on top of their other daily commitments. These have been further detailed in the next sections.

## When designing a clinical trial

*General considerations*

> *I think it is very important to have a human approach. In this aspect, opening the process with the family and the PLWA in a human way is of the utmost importance because you need to gain their trust and maintain it along the whole way.*
> **– AD clinical trial staff**

4. Understand the barriers for PLWA and study partners to take part in a clinical trial and, where possible, set support mechanisms to tackle these barriers and proactively provide support to overcome them. These support mechanisms may include informational resources, detailed visit schedules and physical support during their visits.

5. Provide information upfront and be transparent about the clinical trial, so participants and study partners can fully understand the time and emotional commitment necessary for participating in the trial and the rationale for doing so. This information should be tailored to each individual given their different needs and comorbidities, and furthermore it should be culturally relevant to the site/community you are talking to. For example, the information for the study partner could provide a deeper level of detail, whilst the information for PLWA could be kept more general and easier to comprehend, by using visuals.

## When setting up a clinical trial

*Testing procedures*

6. Essential invasive procedures should be carefully selected based on trial endpoints and frequency should be adjusted according to the trial outcome measures. Consider which tests and procedures need to be done at the trial site versus the ones that could be done at home, to ensure the participants feel comfortable and at ease. For example, any blood draws that can be done at home should be offered to PLWA and their study partners, even when the nurse is different from the trial site nurse, given that the familiar surroundings can help PLWA cope better with the tests.

7. Provide clear information regarding tests and procedures included in the trial (e.g., what it is, frequency, how it is done, why the test is needed and which scientific questions it will help answer) to PLWA and study partners. Where possible, testing information should be tailored to the target audience – for example, providing a booklet for the study partner to explain the procedure to the PLWA in advance of each procedure, which could include visual aids demonstrating the procedure to the PLWA.

### *Logistics and time investment*

> *If I am there it's pretty easy. I would bring my iPad and he could watch TV while he is waiting. If he needs to move to different parts of the site, he would be comforted to know that someone he knows is with him.*
> **– AD study partner**

**8.** Understand what can be done to decrease any challenges and burdens related to travelling to the trial site, including organising visits with enough time for PLWA and their study partners to plan for their travels, covering any costs associated with said travels, and, when appropriate, setting up remote assessments (e.g. video call appointments).

**9.** Where possible, help justify participants' and study partners' absence from work. This could be achieved by providing a letter of support to their employer explaining their participation in the clinical trial and the need for them to be absent from work.

**10.** The PLWA may not always be able to cooperate, or the study partner may have other competing demands – such as caring responsibilities for young children – so be flexible and ensure appointment(s) can be rearranged for a different time/day, even if requested at the last minute.

**11.** Explain the time investment needed by trial participants and study partners (from travelling, to waiting in the hospital, to receiving the procedure), given that it may differ depending on their role and the trial stage.

**12.** Ensure participants and their study partners are comfortable during their visits (e.g., PLWA are always accompanied by someone familiar; PLWA and study partners are given snacks and drinks; PLWA are given ways to pass the time such as TV, Wi-Fi, books, and magazines). To ensure you fully accommodate their needs, you should ask the participant and the study partner for input regarding what they would like to have available during their visit.

**13.** If an overnight stay is required, please consider:

- Taking an individual approach
- Being flexible and listening to the study partner and the participant's concerns
- Giving the study partner options and letting them decide whether they stay overnight with the PLWA, in a nearby hotel, or leave the PLWA for the night
- Being aware that PLWA are often confused and may wander in the night. If the PLWA is left at the hospital without a study partner, ensure that hospital staff are trained properly to care for the PLWA. A tool such as a whiteboard could also be used to remind them where they are
- Having a trusted treatment team member on hand to accompany the PLWA throughout their stay



### *Motivating participants and defining the depth of information required*

> *A person living with Alzheimer's disease prefers routine, as does the main study partner. We as the secondary study partner can better plan with them (if there is a routine) and employers can plan for when we are going to need time off.*
> **– AD study partner**

**14.** Provide all participants and their study partners with an Informed Consent Form, which should include key information on the potential risks and benefits of the trial, the treatment schedules and locations, which procedures they will undergo and why, and the time commitment expected of them. The Informed Consent Form should be provided in lay language, and ideally in the preferred language of the PLWA and their study partner (e.g., English, Spanish etc.). Participants and their study partners should also be given time to thoroughly read the Form and ask any questions they may have, so that they understand the overall commitment of participating in the trial.

**15.** Get to know the PLWA and the study partner(s) on a personal level so you can build trust and make them feel more comfortable about their participation and involvement in the trial. Continue to invest time to build a trustful relationship throughout the trial (e.g., What are their interests? When is their birthday? How many grandchildren do they have? What is their favourite food?).

**16.** Provide study partners with a booklet or diary, that could include the following information:

- A checklist/whiteboard where the days are planned out and the activities can be ticked off as they are completed
- Picture and names of the clinical site staff
- Lists of procedures alongside explanation of each, with visual aids
- Space for them to note down any questions they may have for the clinical site staff ahead of their next visit

### *Enrolment in the trial*

**17.** Share information that is already available about the study drug (e.g., previous clinical trial results, previous safety data, mode of action, etc). This is particularly important given the history of high-profile clinical trial failures in AD and the understandable reticence to commit to clinical trials without clear evidence of benefits for some PLWA and their study partners.

**18.** Set clear expectations regarding study partner attendance to site visits from the outset.

**19.** Build a strong relationship, trust and a two-way dialogue between the clinical trial site staff involved and the participants (both PLWA and study partners). Giving participants the feeling that *"we are all partners on this journey"* is crucial – not only to recruit them, but moreover to engage and motivate participants to stay in the clinical trial until it has ended.

**20.** Have the same staff responsible for the PLWA and study partner from the start of the trial to the end, to help build a strong relationship and trust between clinical trial site staff involved and the participants (both PLWA and study partners).

## During a clinical trial

### *Supporting the PLWA*

> *A noisy area for a moment is OK but then they need to be able to go back into a room where it is quiet, and they can drink something and can focus on the silence. The nurse who looks after him can take a short walk with him outside, but you also need time for him to relax.*
> **– AD study partner**

**21.** Wherever possible, provide PLWA and study partners with:

- Food and drinks that they enjoy
- Periods of rest and relaxation, and the necessary set up for this (room, quiet area, calming music)
- Entertainment (TV, iPad, books, audiobooks, magazines)
- Support staff, such as an occupational therapist, a psychologist, and a dietician
- Any other requirements they may ask for

### *Supporting the study partner*

**22.** Provide a tool to support study partners in their role, such as a mobile application, which could include the following information:

- Calendar, to note upcoming appointments
- Travel and accommodation
- E-records
- Overview of the clinical trial's procedures
- Space for the study partner to note down any questions they may have for the clinical site staff ahead of their next trial visit
- Contact person at the trial, allowing them to ask any questions or voice concerns
- Contact to other study partners taking part in the trial, in case they would like to share their experience or learn from others
- Link to a study partners' support group

### *Strategies to keep everyone motivated*

> *I think having a 'what the future could look like' story with pictures of families so they can see it's not about them, but about the next generation. It is the study partner you need to keep motivated.*
> **– AD study partner**

**23.** If possible, create a newsletter or information outlet that could include:

- Recipes and nutrition tips
- Brain fitness and exercise: occupational therapy feature with exercises
- Helpful tips for the daily life of a study partner
- A day in the life of a family living with AD feature
- Guided relaxation/ meditation links or tips
- As far as possible and according to local guidance, consider including information on the progress of the study, such as how many people have been recruited and how many countries are participating

**24.** Thank the trial participant and their study partner when key clinical trial milestones are achieved (e.g., when the trial has been fully recruited, after their final visit or when the trial concludes) so that they feel part of every stage of the trial.

## Post-clinical trial

### *Supporting PLWA and their study partners following trial termination or completion*

**25.** Following the end of the trial, you should meet one final time with the participant and the study partner, where possible face to face and closer to their home. This meeting should be held when the trial terminates, completes or when the participant or the study partner decides to exit the trial. It should cover the following:

- Thank both the participant and the study partner for their contribution
- Ensure the participant and their study partner understand why the trial has ended or explain why they decided to exit the trial
- Ensure the staff that accompanied both the participant and their study partner throughout the trial are present for this last meeting
- Collate any feedback the participant or their study partner may have, in order to gain understanding of their trial experiences so that you can continue to learn and develop the correct and appropriate support solutions. A standardised feedback form should be developed and provided to all participants and study partners
- Where possible, offer both the PLWA, their loved ones and study partners support beyond the clinical trial (e.g., enrolment in alternative clinical trials, access to support groups, access to psychological or occupational therapy, or referral to local Alzheimer's and dementia support groups)
- If the study comes to a planned completion (rather than termination or voluntary exit), as far as possible and according to local guidance, consider including information on potential next steps to be considered for treatment (e.g., open label extension, and continued access to the medicines used in the study)

### *Sharing trial results and individual data*

**26.** Share any personal data as well as the clinical trial results with the PLWA and their study partner. When doing so consider the following:

- The person that shares this information should be a clinical trial staff member familiar with the study and with both the participant and their study partner
- Set expectations with both the participant and their study partner about what data can be shared and when, given existing compliance
- Use the follow up meeting with the PLWA and their loved ones to understand what level of information they would like to have, when it comes to their personal data and the overall trial results
- Clinical trial results should be explained personally to the PLWA, their loved ones and study partners to ensure they are interpreted correctly and they understand what the data means for their future
- Do not send clinical trial data or personal data via email or in a written form without taking the time to explain it personally
- Once this data is explained, share a summary of the clinical trial results via email or make it accessible via a dedicated and secure website

# Conclusion

Participation in clinical trials is critical to progress research into effective disease modifying treatments (DMTs) for Alzheimer's disease (AD). Although this area is still faced with several challenges, there are effective tactics that can be put into practice to make participation in AD clinical trials more accessible for people living with Alzheimer's disease (PLWA) and their study partners.

This report outlines the challenges that participants of AD clinical trials commonly face and provides recommendations on how to design and manage clinical trials so that the needs of potential trial participants and their study partners are fully considered. It also provides guidance on how to build a trusting partnership with PLWA and their study partners and raises awareness of the PLWA's perspective among study sites.

It was developed based on insights provided by PLWA, their families and study partners, healthcare professionals and AD patient organisations. This educational resource is intended for healthcare professionals, members of the scientific community, and those who are involved in the set-up, management and development of clinical trials. It can also be used to inform anyone interested in having a better understanding of this topic.

The F.A.S.T. Council is committed to supporting the journey of PLWA and their study partners, including when considering participating in clinical trials, and believes the AD community together with researchers, healthcare and long-term care professionals, and the public can continue to raise awareness of clinical research, address barriers linked with trial participation and improve the overall experience of participating in clinical trials.

We truly hope people will see this report as a positive step towards early, genuine engagement with the AD community.

# Glossary

**Alzheimer's disease (AD):** Alzheimer's disease affects the brain through a build-up of abnormal proteins called 'plaques' and 'tangles', which disrupt nerve cell functions and, over time, cause nerve cells to die.[18] The build-up of these proteins begins up to 20 years before symptoms emerge.[19] AD is the most common cause of dementia.[20] Dementia describes a set of symptoms that impact on function (activities of daily living), and may include memory loss and difficulties with thinking, problem-solving or language. AD is progressive, which means the symptoms gradually get worse over time, with the clinical presentation and severity varying from person to person.

**Care partner:** family member, friend or paid helper who regularly looks after someone with a condition.[11]

**CareRing:** CareRing is a global Roche internal community for employees that are living with a disease as well as carers. Designed to create a safe and trustful space for employees to connect, share experiences and provide support to each other.[7]

**Cerebrospinal Fluid (CSF)/lumbar puncture:** CSF is a clear fluid that surrounds the brain and spinal cord. The molecules contained in CSF can help to indicate to clinicians and researchers whether a person has dementia. To test CSF, a needle is inserted into the lower back allowing a sample of the CSF to be taken, a procedure known as lumbar puncture.[21]

**Disease modifying therapies (DMTs):** A disease modifying therapy or a disease modifying treatment slows the progress of Alzheimer's disease. In contrast, symptomatic treatments only help alleviate symptoms. No DMTs are currently licensed for Alzheimer's disease, but research is ongoing.[22]

**Finding Alzheimer's Solutions Together Council (F.A.S.T. Council):** a bi-annual council where AD patient organisations and Roche discuss areas of collaboration and work together to understand the perspectives and needs of AD. The organisation and funding of the Council is led by Roche.[7]

**Magnetic Resonance Imaging (MRI) Scan:** a scan that is used to take images of the brain. For Alzheimer's disease and dementia research the scans are important because they allow researchers to see how the brain is changing over time.[23]

**People living with Alzheimer's disease (PLWA):** someone who has been diagnosed with Alzheimer's disease.

**Positron Emission Tomography (PET) scan:** PET scans are used to measure the concentration of particular molecules in the brain.[24]

**Professional study partner:** someone, usually a paid healthcare professional or auxiliary clinician, who is involved in supporting the PLWA with their treatment monitoring and trial participation.[10]

**Study partner:** someone who is directly involved in supporting PLWA with their treatment monitoring and trial participation. This role can be undertaken by a family member or a friend.[11]

# Resources

### General language resources and community engagement and co-creation

- Council for the International Organizations of Medical Sciences (CIOMS). Report of the CIOMS Working Group. Patient involvement in the development, regulation and safe use of medicines. Available here
- Inclusion Europe. Easy to Read. Available here
- Patient Focused Medicines Development. How-to guide for patient engagement in the early discovery and preclinical phases. Available here
- Patient Focused Medicines Development. How-to guide on patient engagement in clinical trial protocol design. Available here
- Patient Focused Medicines Development. Plain language summaries (PLS) of peer-reviewed publications and conference presentations: practical 'How-To' Guide for multi-stakeholder co-creation. Available here
- TransCelerate Biopharma Inc. Study Participant Feedback Questionnaire Toolkit. Available here

### Research in Alzheimer's disease resource

- Alzheimer Europe. Discussion paper on ethical issues linked to the changing definitions/use of terms related to Alzheimer's disease. 2016. Available here
- Gove, D. et al and the European Working Group of People with Dementia. Alzheimer Europe's position on involving people with dementia in research through PPI (patient and public involvement). *Aging and Mental Health*. 2017. Available here
- Largent, EA. et al. Putting participants and study partners FIRST when clinical trials end early. *Alzheimer's & Dementia: The journal of the Alzheimer's Association*. 2022. Available here
- University of Edinburgh, College of Medicine and Veterinary Medicine. Patient and Public Involvement (PPI) for clinical impact. 2022. Available here

### List of Alzheimer Europe publications

- Alzheimer Europe. Overcoming ethical challenges affecting the involvement of people with dementia in research: recognising diversity and promoting inclusive research issues linked to restrictions of freedom of people with dementia. 2019. Available here
- Cavaller-Bellaubi, M. et al. Evaluation of patient engagement in medicine development: A multi-stakeholder framework with metrics. *Health Expectations*. 2021. Available here
- Diaz, A. et al. Conducting public involvement in dementia research: The contribution of the European Working Group of People with Dementia to the ROADMAP project. *Health Expectations*. 2021. Available here
- Faulkner, SD. et al. Optimising Multi-stakeholder Practices in Patient Engagement: A Gap Analysis to Enable Focused Evolution of Patient Engagement in the Development and Lifecycle Management of Medicines. *Therapeutic Innovation & Regulatory Science*. 2021. Available here
- Faulkner, SD. et al. Understanding multi-stakeholder needs, preferences and expectations to define effective practices and processes of patient engagement in medicine development: A mixed-methods study. *Health Expectations*. 2021. Available here
- Gove, D. et al. Alzheimer Europe's position on involving people with dementia in research through PPI (patient and public involvement). *Aging and Mental Health*. 2017. Available here
- Mank, A. et al. Identifying relevant outcomes in the progression of Alzheimer's disease; what do patients and care partners want to know about prognosis? *Alzheimer's & Dementia: Translational Research & Clinical Interventions*. 2021. Available here
- Øksnebjerg, L. et al. Towards capturing meaningful outcomes for people with dementia in psychosocial intervention research: A pan-European consultation. *Health Expectations*. 2018. Available here
- Roberts, C. et al. Our Reflections of Patient and Public Involvement in Research as Members of the European Working Group of People with Dementia. *Dementia*. 2019. Available here
- Vat, LE. et al. Evaluating the "return on patient engagement initiatives" in medicines research and development: A literature review. *Health Expectations*. 2019. Available here

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# References


1 Mayo Clinic. Alzheimer's disease. Available here [Last accessed September 2022]
2 Prince, M. et al. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement*. 2013; 9: 63-75.
3 Wong W. Economic burden of Alzheimer disease and managed care considerations. *Am J Manag Care*. 2020.
4 Etters, L. et al. Caregiver burden among dementia patient caregivers: A review of the literature. *J Am Acad Nurse Pract*. 2008; 20: 423-428.
5 Huang, LK. et al. Clinical trials of new drugs for Alzheimer disease. *J Biomed Sci*. 2020.
6 Malzbender, K. et al. Key Barriers to Clinical Trials for Alzheimer's Disease. *USC Leonard D. Schaeffer Center for Health Policy & Economics*. 2020.
7 Roche Data on File. M-GB-00009302. September 2022.
8 Weisfeld, V. et al. Public engagement and clinical trials: new models and disruptive technologies. *National Academies Press*. 2012.
9 Watson, JL. et al. Obstacles and opportunities in Alzheimer's clinical trial recruitment. *Health Aff*. 2014;33(4):574-9.
10 Largent, EA. et al. Study partners: essential collaborators in discovering treatments for Alzheimer's disease. *Alz Res Therapy*. 2018.
11 Grill, JD. et al. Effect of study partner on the conduct of Alzheimer disease clinical trials. *Neurology*. 2013;80(3):282–8.
12 Grill, JD. et al. Addressing the challenges to successful recruitment and retention in Alzheimer's disease clinical trials. *Alzheimers Res Ther*. 2010.
13 Edland, SD. et al. NIA-funded Alzheimer centers are more efficient than commercial clinical recruitment sites for conducting secondary prevention trials of dementia. *Alzheimer Dis Assoc Disord*. 2010; 24(2):159-64.
14 Sil, A. et al. Informed Consent Process: Foundation of the Researcher-participant Bond. *Indian J Dermatol*. 2017;62(4):380-386.
15 Erves, JC. et al. Needs, Priorities, and Recommendations for Engaging Underrepresented Populations in Clinical Research: A Community Perspective. *J Community Health*. 2017;42(3):472-480.
16 Bonevski, B. et al. Reaching the hard-to-reach: a systematic review of strategies for improving health and medical research with socially disadvantaged groups. *BMC Medical Research Methodology*. 2014;14(1):1–29.
17 Baird, KL. The new NIH and FDA medical research policies: targeting gender, promoting justice. *Journal of Health Politics, Policy and Law*. 1999;24(3):531–565.
18 NHS. Alzheimer's disease. 2021. Available here [Last accessed September 2022]
19 Dubois, B. et al and Proceedings of the Meeting of the International Working Group (IWG) American Alzheimer's Association. Preclinical Alzheimer's disease: Definition, natural history, and diagnostic criteria. 2016.
20 Alzheimer's Society. What is the difference between dementia and Alzheimer's disease?. 2018. Available here [Last accessed September 2022]
21 Mayo Clinic. Lumbar punction (spinal tap). Available here [Last accessed September 2022]
22 Lam, J. et al. The Potential Emergence of Disease-Modifying Treatments for Alzheimer Disease: The Role of Primary Care in Managing the Patient Journey. *The Journal of the American Board of Family Medicine*. 2019, 32 (6) 931-940.
23 Mayo Clinic. MRI. Available here [Last accessed September 2022]
24 Mayo Clinic. Positron emission tomography scan. Available here [Last accessed September 2022]










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M-XX-00010732