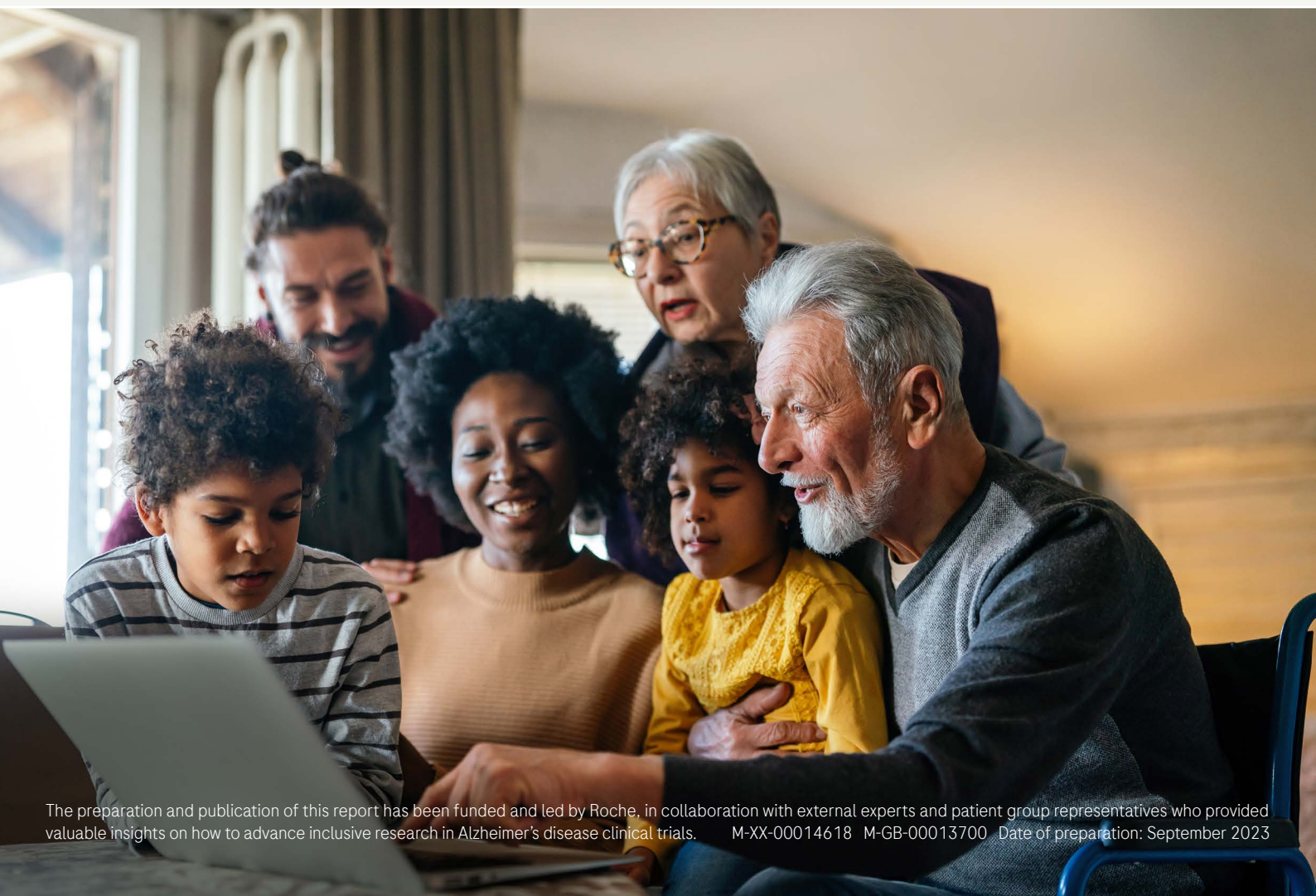


Advancing Diverse, Equitable and Inclusive Research in Alzheimer's Disease Clinical Trials



Contents

Foreword	2
Contributors	4
Executive summary	6
Diversity, equity, and inclusion in Alzheimer’s disease clinical trials	8
Roche’s approach to diversity, equity, and inclusion in Alzheimer’s disease clinical trials	12
Barriers to diversity, equity, and inclusion of Alzheimer’s disease clinical trials	14
Diversity, equity, and inclusion in Alzheimer’s disease clinical trials beyond Roche	16
Aspirations for increasing diversity, equity, and inclusion in Alzheimer’s disease clinical trials at Roche	18
Theme 1: Countries and clinical trial sites are selected in a targeted approach, with DE&I goals incorporated at the earliest stage of the study timeline	18
Theme 2: Clinical trial protocols and clinical outcome measures are informed by real-world insights and recommendations from DE&I experts	20
Theme 3: Potential barriers to clinical trial participation are reduced and engagement with local community groups is enhanced both before and throughout the clinical trial	22
Theme 4: Roche has become a consistent leader in addressing DE&I in AD	24
Adopting an agile approach to operationalise the aspirations	26
Examples of how Roche has operationalised the aspirations	28
Conclusion	29
Glossary	30
References	32

Foreword

The prevalence of Alzheimer's disease (AD) is projected to increase across the world, affecting millions of people living with AD (PLWA) and their families.¹ The majority of PLWA live in low- and middle-income countries,² despite current measurements likely underestimating the true prevalence in these regions. Within high-income countries, some ethnic minority groups are reported to be at greater risk of AD. For example, in the United States, Latino and Black Americans will make up nearly 40% of all AD diagnoses by 2030.³

Despite the global demographics of AD, the participants in AD clinical trials are predominantly recruited from high-income countries and often do not reflect the diversity of PLWA either globally or from within those countries.⁴ Factors such as sex/gender, race, ethnicity, or medical comorbidities can impact the safety and efficacy data obtained in clinical trials,⁵ underscoring the need for ensuring that the study population enrolled in the trial is as representative as possible. Consequently, it is crucial that all research in AD focuses on achieving diversity, equity, and inclusion (DE&I) when conducting clinical trials.

Roche has previously worked with international patient groups to develop recommendations for best practice in conducting clinical trials in AD, which were published in the report [Integrating the perspectives of people living with Alzheimer's disease and their study partners into clinical trial development](#). Although the recommendations contained in the report served to guide our AD clinical trials strategy in the short term, we recognised that further improvements to the way AD clinical trials are conducted, particularly in relation to DE&I, was both possible and needed.

Roche has since conducted research to further understand both the need and the challenges when aspiring for greater DE&I in AD clinical trials. We recognised that we could only truly understand the environment and thereby create tangible aspirations by working in collaboration with patient organisations, academics, and clinicians. This report contains the results of that external validation process and outlines aspirations for the field of DE&I in AD, as well as the steps we believe are required to achieve them.

It is essential that DE&I forms a central pillar of AD clinical research both now and in the future, and we hope the aspirations in this report will be embraced by other organisations involved in AD clinical trials. A lot of these recommendations are disease area agnostic and can likely be used as guidance for other disease area trials.



Contributors

The preparation and publication of this report has been funded and led by Roche, in collaboration with external experts and patient group representatives who provided valuable insights on how to advance inclusive research in Alzheimer's disease clinical trials. Roche would like to thank the contributors for their insights, as without whom, this work would not have been possible. *These experts received honoraria for their time as per local regulations and have been detailed below.*

External contributors (outlined in alphabetical order)

Malaz Boustani MD, Richard M Fairbanks Professor of Aging Research and Founding Director of both the Sandra Eskenazi Center for Brain Care Innovation and the Indiana University Center for Health Innovation and Implementation Science at Indiana University School of Medicine (US).

Sharon A. Brangman, M.D., FACP, AGSF, Distinguished Service Professor, Chair of the Department of Geriatrics and Director of the Center of Excellence for Alzheimer's Disease at Upstate Medical University (US).

Chris Butler MA PhD FRCP, Clinical Reader in Global Brain Health at Imperial College London (UK).

Temitope Farombi MD, Consultant Neurologist at Chief Tony Anenih Geriatric Centre University College Hospital (Nigeria) and visiting scholar to Northwestern University Chicago (US).

Maria Teresa Ferretti PhD, Co-founder, and former Chief Scientific Officer, at the Women's Brain Project (Switzerland), External Teacher at the Medical University of Vienna (Austria), and Faculty Member of the course for Advanced Studies of Gender Medicine at the University of Zurich (Switzerland).

Dianne Gove PhD, Director for Projects at Alzheimer Europe (Luxembourg).

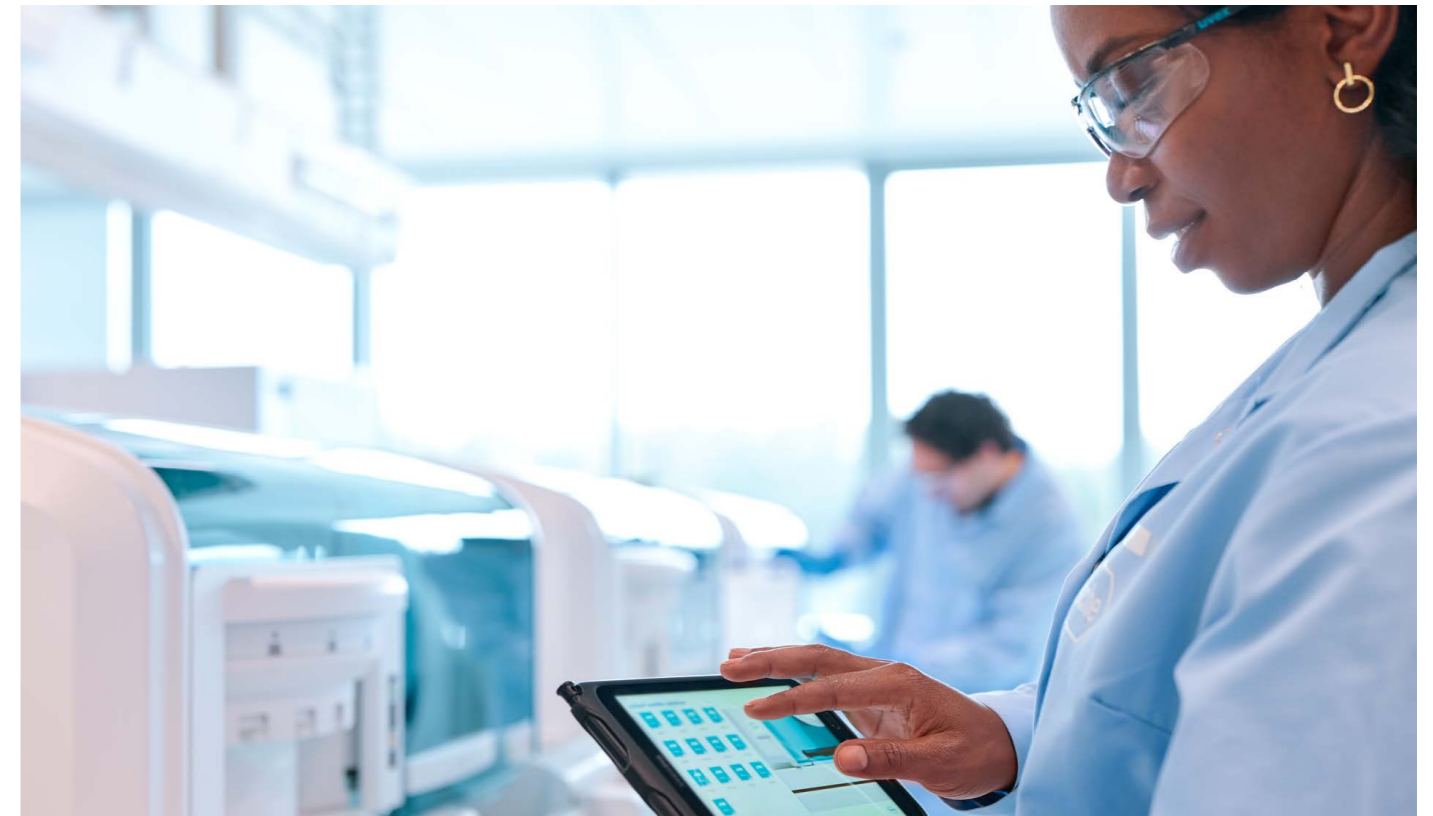
Ishtar Govia PhD, Senior Lecturer at the Epidemiology Research Unit of the Caribbean Institute for Health Research at the University of the West Indies (Jamaica), Honorary Senior Research Fellow at the Institute for Global Health at University College London (UK) and Dementia Care Management Consultant.

Agustin Ibanez PhD, Director of the Latin American Brain Health Institute at Universidad Adolfo Ibáñez (Chile), Team Leader of Predictive Brain Health Modelling Group at the Global Brain Health Institute, Trinity College Dublin (Ireland); Founder and Co-Director of Multi-Partner Consortium to Expand Dementia Research in Latin America.

Karan Jutlla PhD, Head of the Health Research Centre, and Dementia Lead at University of Wolverhampton (UK).

Charles Marshall, Cognitive Neurologist at Barts Health NHS Trust (UK) and Clinical Senior Lecturer at Queen Mary University of London Preventive Neurology Unit (UK).

Martin Knapp PhD, Professor of Health and Social Care Policy and Professorial Research Fellow in the Care Policy and Evaluation Centre at London School of Economics and Political Science (UK) and Director of the School for Social Care Research, part of the National Institute for Health Research (UK).



Jacobo Mintzer MD, Professor of Health Science, Neuroscience, Pathology, and Psychiatry at the Medical University of South Carolina (US).

Feyi Raimi-Abraham, Founder of Black Dementia Company (UK).

Marianna Tsatali PhD, Neuropsychologist at the Greek Alzheimer Association and Related Disorders (Greece), Lecturer at the Psychology Department at University of Western Macedonia (Greece), and Postdoctoral Researcher at the School of Psychology, Aristotle University of Thessaloniki (Greece).

Wendy Weidner, Head of Research and Publications at Alzheimer's Disease International (UK).

Karin Westerlund, Director at Alois Alzheimer Foundation (Sweden).

Roche contributors (outlined in alphabetical order)

We would also like to thank the following colleagues from Roche and Genentech:

Ruth Croney, Clinical Programme Leader at Roche (UK).

Emma Louise Dodd, Global Medical Collaboration Leader, Neuroscience Product Development Medical Affairs at Roche (Switzerland).

Léa Proulx, Patient Voice Partner at Roche (Switzerland).

Jannice Roeser, Global Patient Partnership Director Alzheimer's at Roche (Switzerland).

Jenee Williams, Director of Patient Advocacy Relations, Alzheimer's disease at Genentech (US).

Alexandria Wise-Brown, Principal Medical Science Director at Genentech (US).

Other contributors

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Executive summary

Alzheimer's disease (AD) is a devastating neurodegenerative condition that affects millions of people worldwide.⁶ Due to its intricate and complex mechanisms, clinical trials play a vital role in helping researchers gain deeper insights into how the disease progresses, shedding light on its underlying causes and potential intervention points.⁷ However, there are growing ethical, scientific, and equity concerns around the lack of generalisability and representation of diverse populations in these trials.⁸

AD clinical trials, including those conducted by Roche, have struggled to successfully recruit populations which adequately represent the diverse demographics and backgrounds of people living with AD (PLWA).⁸ These diverse population subgroups encompass several differentiating factors such as age, sex/gender, comorbidities, race, ethnicity, and socioeconomic disparities.⁹ These characteristics are believed to be associated with differences in safety and efficacy outcomes in clinical trials, suggesting that if groups with only a specific selection of these factors are represented in clinical trials, then the conclusions which can be drawn from the clinical trial data may have low external validity and thus generalisability.¹⁰

It should be noted that the considerations made in this report are specific to AD, and that although we recognise some clinical trials have achieved greater representation of historically underrepresented communities (for example trials investigating HIV may recruit a greater proportion from the LGBTQIA+ community), this is still not the case for AD clinical trials.

The reasons for this underrepresentation in AD clinical trials can be complex, ranging from cultural and economic barriers to some community's distrust of healthcare and research staff and organisations, as well as potentially restrictive inclusion and exclusion criteria within trial design.^{8,9}

Improvements in diversity, equity, and inclusion (DE&I) policies aimed at increasing the participation of the population subgroups that have historically not been included in AD clinical trials, are thus essential to ensuring robust clinical data that can truly translate into real-world application.⁹ This has been recognised by leading healthcare organisations such as the Food and Drug Administration, a US federal agency responsible for protecting public health, which passed a law in 2023 mandating that all future clinical trials protocols should include a "Diversity Action Plan" to outline how broad and representative study populations should be recruited by clinical trial teams.¹¹ In addition to these policies, it is also important to include the perspectives of patients, care partners, and their communities into every aspect of clinical trial design, delivery and associated decision-making processes, so that recruitment, retention and adherence can be supported.

Roche is committed to enabling these improvements and is actively working towards increasing the participation of underrepresented population subgroups in clinical trials, including those for AD. As part of our commitment, we brought together a group of patient organisations and expert academics and clinicians to further understand the need for DE&I in AD clinical trials and to brainstorm potential ways to make positive changes in this space.

This report is the culmination of this work and explores the current state of DE&I in clinical trials, examines the implications of underrepresentation, and proposes aspirations to promote greater inclusivity. It also includes an overview of how these aspirations could be operationalised and how Roche is already doing so. Some of the aspirations below will have already been met in many or all clinical trials, and some are already required by local health authorities. However, given the variation in clinical trial practice and protocols across the world, we have framed all the points as aspirations to ensure that Roche and other stakeholders involved in clinical trials are working towards these common goals globally. For ease, these aspirations have been organised under four themes, which are detailed on the next page.

Theme 1: Countries and clinical trial sites are selected in a targeted approach, with DE&I goals incorporated at the earliest stage of the study timeline

- **Aspiration 1.1:** Country and clinical trial site selection processes are better informed by the use of demographic data, geo-targeting, and expert insights and collaboration.
- **Aspiration 1.2:** Clinical trial site selection has embedded the importance of DE&I into the feasibility processes.
- **Aspiration 1.3:** Clinical trial site teams, including local representatives from the trial organiser and trial site teams, are engaged with site specific DE&I goals and each site has outlined clear methods and milestones for achieving them.
- **Aspiration 1.4:** Clinical trial site teams are, where possible, represented by individuals from underrepresented populations, including in leadership positions, and have the cultural competency to ensure their trial is diverse, equitable and inclusive.

Theme 2: Clinical trial protocols, including clinical outcome measures, are informed by real-world insights and recommendations from DE&I experts

- **Aspiration 2.1:** Diversity plans are incorporated into clinical trial protocols, including recruitment and retention strategies, and structural exclusion of particular demographic groups has been mitigated to the greatest extent possible.
- **Aspiration 2.2:** Clinical outcome measures and digital data collection tools have been cross-culturally validated before implementation into clinical trial protocols.
- **Aspiration 2.3:** Clinical trial protocols, recruitment and retention strategies, and participant-facing materials are co-created and reviewed by advisory boards comprising of PLWA, DE&I experts, patient advocacy groups, community leaders as well as other relevant stakeholders.

Theme 3: Potential barriers to clinical trial participation are reduced and engagement with local community groups is enhanced, both before and throughout the clinical trial

- **Aspiration 3.1:** Strategies to alleviate challenges faced by participants and study partners have been implemented.
- **Aspiration 3.2:** Partnerships and enhanced community engagement and outreach have been established.
- **Aspiration 3.3:** Both clinical trial site teams and local representatives from the trial organiser have had enhanced and routine training on DE&I.

Theme 4: Roche has become a consistent leader in addressing DE&I in AD

- **Aspiration 4.1:** Roche has become a partner of choice for diverse, equitable, and inclusive AD clinical trials.
- **Aspiration 4.2:** Educational efforts to support the understanding of the importance of DE&I in AD have been prioritised.
- **Aspiration 4.3:** DE&I has become a central pillar for all strategies within the AD research and development space.

Diversity, equity, and inclusion in Alzheimer's disease clinical trials

Clinical trials are vital to medical research and healthcare advancement. They rigorously test new treatments and diagnostic tests to determine their safety, efficacy, and potential benefits.¹² By providing reliable data and insights, clinical trials pave the way for evidence-based medical practices, improved patient care, and the development of innovative therapies and diagnostic tests that can save lives and enhance overall well-being.¹²

A key part of clinical trials is the recruitment process, where people are invited to participate in a trial and their eligibility is assessed based on predefined inclusion and exclusion criteria.¹² Once included in the trial, participants will be allocated to take the investigational molecule or a placebo, so that the physiological effects of the molecule under investigation may be assessed. In the past, however, clinical trial teams have had limited success in obtaining study populations that are reflective of the patient populations that novel medicines aim to treat.⁹

This lack of diversity in clinical trials has been a longstanding issue in clinical research fields.⁵ Historically, clinical trials have predominantly included relatively healthy, young, white, male participants leading to a limited understanding of how medical interventions and treatments affect other populations.⁵ This knowledge gap can have significant implications for healthcare outcomes, as individuals from other backgrounds may experience different treatment responses or side effects.⁵

Diversity, equity, and inclusion (DE&I) in clinical trials refers to the importance of ensuring that clinical trials are conducted with a diverse population that represents the true demographics of the people who have the disease in the 'real world', with equitable representation and inclusive practices.⁵ It recognises that individuals from different racial and ethnic backgrounds, sex/genders, ages, socioeconomic statuses, comorbid conditions, sensory deficits and other demographic groups may have unique biological, genetic, and environmental factors that can influence their response to investigational medical treatments.⁵

Alzheimer's disease (AD) clinical trials also face challenges in recruiting diverse populations that are representative of people living with AD (PLWA). This has been demonstrated in a systematic review of AD trials, carried out between 2001 and 2019, which found that 94.7% of trial participants were white and most trials required a minimum of 6 years of formal education for participation.¹³ On a global scale, 83% of all clinical trials take place in high-income countries, predominantly within Europe or North America,¹⁴ despite the fact that two-thirds of dementia patients worldwide reside in low- and middle-income countries.¹⁵ Similarly, an analysis between 2010 and 2021 suggests that the number of female participants in AD clinical trials is below their estimated representation in the global dementia population.¹⁶

AD is a complex age-related condition which can be caused by several socio-economic, mental, environmental, and cultural factors as well as personal biological characteristics.¹⁷ This relationship is best described through Dahlgren and Whitehead's model of the social determinants of health, in which social factors, such as food or job security, access to healthcare or educational services, language and socio-economic deprivation interact with physical attributes such as age, sex/gender or genetics, to exert an effect on health, or in this case, the risk of developing AD.¹⁸ The concept of the exposome expands on this further, showcasing how psychosocial and physical factors can interact with synthetic chemicals (e.g. pollutants) and dietary constituents to impact brain health, potentially leading to the development of AD.^{19,20} The impact of these factors on the risk of developing dementia and AD is explored further below.

AD disproportionately impacts women, with studies showing that nearly two-thirds of PLWA and over 60% of dementia care partners are women.^{1,21} Whilst some of this sex/gender disparity can be explained by the fact women live longer, we do not yet fully understand the physical factors driving this.²² Differences in genetics, modifiable risk factors (including blood pressure, rates of physical activity, chronic stress and depression), as well as hormonal changes and sex/gender discrimination have all been suggested.^{23,24} Indeed, a US study has shown that discrimination against individuals identifying as part of a sexual and gender minority group has increased the likelihood of reporting symptoms of dementia.²⁵

Moreover, race and ethnicity can also play a significant role in the prevalence of AD, with studies revealing that routinely experiencing socio-economic disparities, racism and political marginalisation can contribute to the development of chronic diseases.²⁶ For example, in the US, African Americans are twice as likely to develop AD than White Americans.²⁷ In the UK, Black and South Asian people have an increased risk of dementia when compared to White people,²⁸ while also having shorter survival post-diagnosis of AD.²⁹ These disparities are projected to become more pronounced, with a seven-fold increase in the prevalence of dementia in the UK expected among ethnic minorities, in comparison to a two-fold increase for the general population by 2050.³⁰

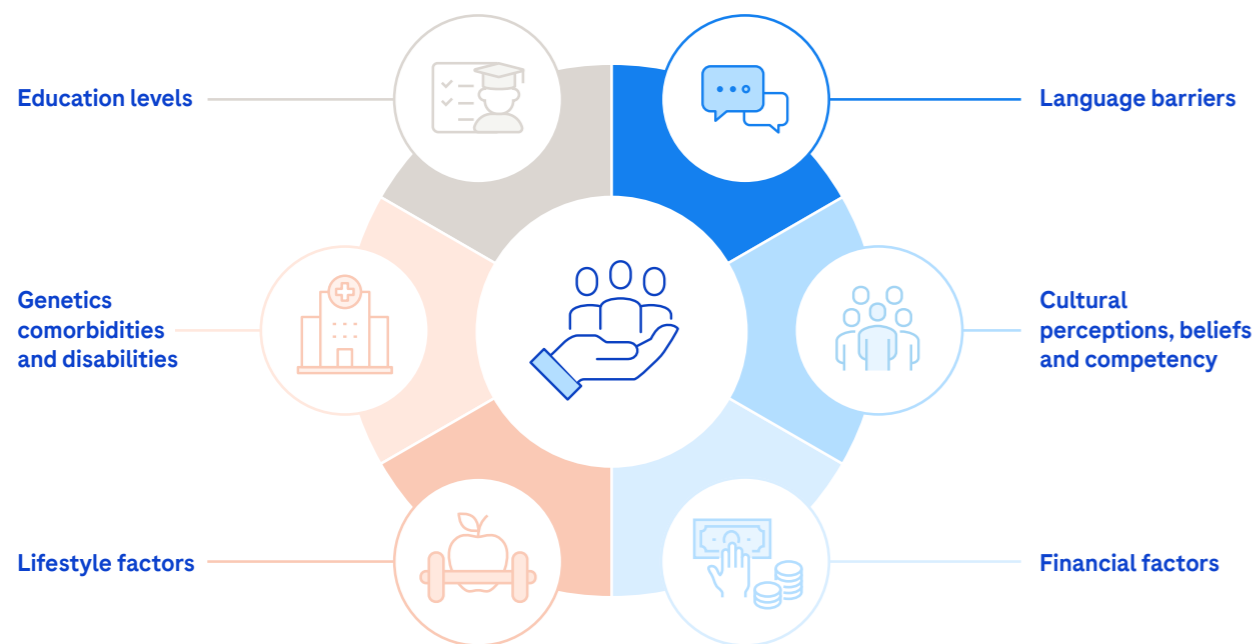


Figure 1. Biological, cultural, societal, and economic factors potentially contributing to the disparity in representation in clinical trials

It should be noted that this report has primarily included data from the US and the UK, as this is the demographic data that is publicly available. More research is needed in other countries, especially low- and middle-income countries, to truly understand the demographics and immigration patterns of PLWA globally.³¹

A person's risk of developing AD is also associated with individual biological characteristics, such as genetic biomarkers.³² For example, when the APOE ε4 gene variants are found in European and Asian individuals they are associated with a higher risk of developing AD, earlier age of onset and worse cognitive performance,³³ whereas in individuals of African ancestry, they appear protective against the disease.³⁴ In addition, these gene variants have also been shown to increase the deposition of tau proteins in the brain in women, which has been linked to a higher risk of developing AD.³⁵ There are several other genes associated either with higher or lower risk of AD – for example, approximately 50% of people with Down's syndrome have developed AD in their 60s, due to having an extra copy of the APP gene on chromosome 21.^{36,37,38} Although extremely impactful, genetic risk factors cannot alone explain the differences in AD prevalence or outcomes without a holistic understanding of wider biological, behavioural and social determinants.

Certain comorbidities, such as cardiovascular diseases, diabetes, depression, and inflammatory bowel disease, have been shown to increase the risk of developing AD.³⁹ The link with disabilities is also well established, with individuals with dual sensory loss (deaf and blindness) being at higher risk of cognitive decline.⁴⁰ However, with regards to both factors, the causal relationship between these and the risk of developing AD is still not fully understood. This lack of understanding is compounded by the fact that people with comorbidities or certain disabilities are often excluded from AD clinical trials, particularly among early phase clinical trials, which have stricter inclusion criteria due to safety endpoints.⁴¹

Finally, socioeconomic status has also been shown to be associated with higher risk of developing dementia and higher risk of dementia death. In the US, people who experience high socioeconomic deprivation during their lifetimes are significantly more likely to develop dementia compared to people with better socioeconomic status. Workers earning low wages have also been shown to experience significantly faster memory decline in older age compared to workers earning higher wages.⁴² Similar findings have been found in Latin America, where lower socio-economic status impacted cognitive processes in healthy ageing.⁴³ In Finland, research has shown that low education, occupational social class, and household income are all associated with a higher risk of dementia death.⁴⁴

The impact of these characteristics on developing dementia or AD is not yet fully understood. This underscores its importance of having a higher percentage of people with one or more of these characteristics represented in AD clinical trials. As it stands, these populations are still extremely underrepresented in studies, which can make it harder to generalise the study results given they are not fully representative of PLWA.



Roche's approach to diversity, equity, and inclusion in Alzheimer's disease clinical trials

At Roche, we recognise the importance of diversity, equity, and inclusion (DE&I) in clinical trials, especially for Alzheimer's disease (AD). We strive to conduct internally and externally valid clinical trials at different sites, to ensure our studies reflect the diverse patient population that would benefit from the diagnostic tests and therapies we develop.

In 2021 and 2022, Roche conducted two projects focused on DE&I in AD. These projects combined insights from literature reviews, Roche's clinical trial site teams and external experts to better understand DE&I in AD and build more inclusive clinical trials. The findings collated have been detailed below:

These insights were invaluable in informing our AD clinical trial approach and formed the basis of our initial discussions with the expert contributors of this report. These experts were selected to provide global perspectives on DE&I, as well as cover a diverse range of specialist roles including academics, clinicians, and patient organisation representatives. Experts were invited to provide input on the key DE&I challenges and potential solutions that could support the development of diverse, equitable and inclusive AD clinical trials. This input was collated virtually through a workshop

and follow up interviews. As outlined previously, this report details the group's findings and aspirations.

Additionally, Roche also worked with the Finding Alzheimer's Solutions Together 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 PLWA and the barriers surrounding DE&I in AD clinical trials. Together we published a report on [Integrating the perspectives of PLWA and their study partners into clinical trial development](#).

 <p>Cultural perceptions, beliefs, and competency</p>	 <p>Language barriers</p>	 <p>Education levels</p>
<ul style="list-style-type: none"> Lack of awareness from healthcare professionals of cultural perceptions and beliefs can lead to people living with AD (PLWA) feeling unsupported and misunderstood. Clinical investigators and research personnel are unaware and unprepared to support clinical trial participants with different cultural perceptions and beliefs. Groups historically not included in AD clinical trials may not have awareness of AD signs, symptoms, and management. 	<ul style="list-style-type: none"> An awareness of linguistic diversity within selected study sites is necessary among clinical investigators and research assistants when working with underrepresented populations to enhance participant recruitment and retention. Clinical trial eligibility criteria for recruitment tend to exclude individuals without written and spoken comprehension of the dominant language of the clinical trial study site. Underrepresented populations not fluent in the dominant language of the study setting may be unable to understand assessment questionnaires and tools. 	<ul style="list-style-type: none"> Lower levels of education in early life increase the risk of AD diagnosis later in life.⁴⁵ In the United States, for example, educational attainment is lower in some underrepresented groups.⁴⁶ The current cognitive assessment criteria used in AD clinical trials do not always accurately diagnose AD in older adults with low educational attainment.⁴⁷
 <p>Genetics, comorbidities, and disabilities</p>	 <p>Lifestyle factors</p>	 <p>Financial factors</p>
<ul style="list-style-type: none"> Race and chronic diseases disproportionately affect ethnic minority groups and may confer additional risk for the worsening, and onset, of AD. Lack of awareness of the proportions of comorbidities in racial and ethnic minority populations can lead to insufficient support being provided to these populations and less tailored clinical trial recruitment tactics being developed. 	<ul style="list-style-type: none"> Various lifestyle factors can contribute to the development of AD. Lack of public health interventions and campaigns, and a lack of awareness from the general public about these factors can lead to populations not trying to mitigate them. 	<ul style="list-style-type: none"> Affordability of care and lack of health insurance coverage are barriers for minority groups in some countries, regions, and populations. Access to healthcare is almost always a prerequisite to accessing clinical trials.



Barriers to diversity, equity, and inclusion in Alzheimer's disease clinical trials

There has been a persistent underrepresentation of racial, ethnic and gender minorities, as well as individuals from lower socioeconomic backgrounds and with comorbidities, in Alzheimer's disease (AD) clinical trials.⁴⁸

As highlighted previously, according to a systematic review of AD trials, 94.7% of trial participants were white and most trials required a minimum of six years of formal education for participation, even though, the majority of the population with dementia and AD are non-White people and people from lower socioeconomic backgrounds.¹³ Furthermore, a recent study outlined that on average women represented 57.9% of the individuals involved in AD trials. Although this may seem high; this proportion is significantly lower than the proportion of women in the general AD population.⁴⁹ A similar scenario is found in trials for stroke, which might suggest common and non-disease specific barriers for elderly women to participate in clinical trials.⁵⁰

While clinical trials do not represent clinical practice, this lack of diversity poses significant challenges in accurately assessing the effectiveness and safety of treatments across different population groups.¹³ It also limits our understanding of how the disease manifests and progresses in diverse individuals over time, hindering the generalisability of the research findings and potentially perpetuating health disparities.¹³ It is important to understand why this underrepresentation happens.

During the insights gathering phase of this report, our contributors identified several barriers that prevent AD clinical trials from being truly diverse, equitable, and inclusive. These have been detailed on the next page, in alphabetical order.



Cognitive assessments: Most cognitive assessments were developed for educated populations in high-income western societies, meaning they can be difficult to understand for people living with AD from different cultural backgrounds or with limited proficiency in a clinical trial site's native language.⁵¹ There is also evidence that the scales used for these assessments are generalised, and therefore may not be adapted appropriately for different sexes/genders or for people with sensory deficits.⁵² Furthermore, many cognitive assessment tools have not been validated across all global regions – for example within Asia, most studies have focused on East Asia with assessments being tailored to populations from that region and not other regions, such as South Asia.⁵³ This risks imprecise or erroneous diagnosis or screening outcomes to enter a trial, or inaccurate measurement of progress made during a trial.



Cultural and linguistic sensitivities: Clinical trials must be sensitive to cultural and linguistic differences to ensure inclusivity. Language barriers can make it challenging for individuals with limited English proficiency to understand trial procedures, risks, and benefits. Cultural beliefs and practices may also influence perceptions of research participation. One study from South Africa found that direct translations for words such as placebo and randomisation were not able to be made into local languages, creating further barriers to understanding of the study.⁵⁴



Eligibility criteria and protocol requirements: Stringent eligibility criteria may unintentionally exclude underrepresented populations from participating in AD clinical trials. These criteria often exclude people with comorbidities, particularly cardiovascular diseases, cancer, autoimmune disorders, psychiatric disorders (which are, in many countries, more common in minority communities where AD is more prevalent), or people with Down's syndrome (a group which is genetically predisposed to developing AD).⁵⁵ Criteria may also exclude people who do not have a study partner for the duration of the trial.⁴¹ Furthermore, the intensity and invasiveness of interventions and assessments as part of clinical trial protocols is likely to lead to a gradient of acceptability according to health and scientific literacy, as highlighted previously.



Lack of access: Geographical disparities in trial site locations may limit access for individuals in remote or underserved areas. The locations where the trial is advertised may also impact recruitment, especially if not frequented by underrepresented communities. Lack of transportation and financial resources can further impede participation, particularly for those from low socioeconomic backgrounds. Among the LGBTQIA+ community, concerns about being "outed" can also present a barrier to research participation.⁵⁶



Lack of awareness: Limited awareness about clinical trial opportunities and insufficient understanding of the research process among underrepresented communities can hinder participation. This lack of understanding can be caused by communities feeling like clinical trial information is not targeted at, or of interest to, them, or by the information not being understandable due to language barriers or illiteracy. Furthermore, unconscious biases from study investigators, such as assuming a person may not be compliant with the study requirements, may further limit recruitment from underrepresented groups.



Lack of diversity in the research workforce: A lack of diversity among researchers and research staff can present challenges in understanding and effectively engaging with diverse underrepresented populations. A diverse research workforce can enhance cultural competence, establish trust, and better address the unique needs and concerns of underrepresented communities.



Stigma and mistrust: Historical instances of exploitation and mistreatment of communities traditionally marginalised in medical research have led to mistrust and scepticism, which can lead to reluctance to participate in clinical trials.⁵⁷ This has been reported within US and UK literature, although it is unclear the extent to which this affects participants globally.^{58,59} Stigma can also play a role in lack of access, as dementia in some cultures is stigmatised, for example in South Africa where negative public attitudes were associated with lack of access to healthcare support.⁶⁰

Overcoming these barriers requires proactive measures that strive to create more inclusive, equitable, and representative AD clinical trials that benefit all individuals affected by the disease regardless of their background or location. The contributors of this report have proposed several aspirations, which are detailed in the *Aspirations for increasing diversity, equity, and inclusion in Alzheimer's disease clinical trials at Roche* [section](#) of this report.

Diversity, equity, and inclusion in Alzheimer's disease clinical trials beyond Roche

It is important to recognise that other major companies carrying out Alzheimer's disease (AD) research also incorporate diversity, equity, and inclusion (DE&I) into their clinical trials. These companies include, but are not limited to:

Eisai has been particularly focussed on DE&I in AD, with the Clarity AD trial recruiting 25% of US participants from Black or Hispanic backgrounds, comparable to the country's Medicare registered population.⁶¹ According to the company, this was achieved through initiatives such as the targeting of underrepresented communities when selecting sites and investigators and conducting community outreach programmes to increase clinical trial involvement.

Eli Lilly has acknowledged the underrepresentation of specific ethnic groups within their clinical trials and responded by developing three goals to guide their future work: 1) Create a robust clinical trial strategy and reach diverse populations; 2) Intentionally select a diverse range of trial sites and investigators; 3) Increase diverse representation through partnerships and collaboration.⁶²

GSK has built demographic planning into their clinical trials, so they reflect the real-world population that's affected by the diseases they are studying.⁶³ They have set a target for at least 75% of their Phase 3 trials in 2022 to include a demographics plan in their design.

Janssen set up a DE&I in Clinical Trials team that created a template to embed diversity into the clinical trial process.⁶⁴ The template covers dimensions of diversity including race, ethnicity, gender, sexual orientation, and socioeconomic factors.

Takeda has developed a strategy to create more diverse clinical trials, which includes initiatives such as partnering with community stakeholders; addressing operational barriers that impede patient access such as language and location barriers; incorporating a DE&I strategy into the clinical trial plan for all newly initiated trials; and partnering with academic institutions to collect and report on industry wide site diversity data.⁶⁵



Aspirations for increasing diversity, equity, and inclusion in Alzheimer's disease clinical trials at Roche

Addressing the challenges of diversity, equity, and inclusion (DE&I) in Alzheimer's disease (AD) clinical trials requires a comprehensive and proactive approach. The contributors of this report have provided aspirations to increase diversity and promote equitable and inclusive participation in these trials. These aspirations have been divided into four key themes and are detailed below with potential tactics:

Theme 1: Countries and clinical trial sites are selected in a targeted approach, with DE&I goals incorporated at the earliest stage of the study timeline

Aspiration 1.1: Country and clinical trial site selection processes are better informed by the use of demographic data, geo-targeting, and expert insights and collaboration

- Ensure the country and site selection process begins early for newly planned clinical trials, incorporating learnings from previously conducted trials in the therapy area.
- Incorporate the use of geo-targeted data to select countries for participation, accounting for demographic data, acknowledging intersectionality, and existing community relationships. Site selections should represent different population subgroups of interest, including those who are currently underrepresented (e.g., ethnic, racial and gender minorities; culturally diverse people; people with comorbidities or from low educational and socioeconomic backgrounds).
- Select clinical trial support vendors (e.g., participant recruitment vendors, trial planning vendors, regulatory consultants, and clinical trial software management vendors) who actively have a focus on, or are committed to, ensuring trials are diverse, equitable and inclusive.
- Prioritise sites who have established connections with local community clinics or nursing homes and with access to remote populations, as they can reach populations not normally identified by larger academic institutions or memory clinics.
- Ensure sites have access to at least the minimal required technology and internet, to support efficient data collection and participant outreach.
- Regardless of the site selected, clearly outline the limitations of the recruitment process.

Aspiration 1.2: Clinical trial site selection has embedded the importance of DE&I into the feasibility processes

- Ensure the feasibility questionnaire (a set of questions prepared by a study sponsor to identify the potential/interest of a site to run a clinical trial) collects data about the demographics of the area surrounding the study site.
- Ensure the feasibility questionnaire captures the methods of engagement with underrepresented populations used by the study site.
- Assess, through the feasibility questionnaire, the existing level of cultural competency training of clinical trial sites.

Aspiration 1.3: Clinical trial site teams are engaged with site-specific DE&I goals and each site has outlined clear methods and milestones for achieving them

- Determine site-specific needs to engage with the community to recruit and retain study participants and study partners, particularly from underrepresented populations.
- Set out DE&I goals which align with the recruitment and retention needs identified. These should be tailored to the site's resources, location, target study population and local culture.
- Define clear metrics and key performance indicators for each DE&I goal, which are measured regularly.
- Consider nominating one person from each site team to lead the site's DE&I strategy. This person should be accountable for measuring progress against the DE&I goals detailed.
- Ensure a budget is allocated to allow study sites to develop and execute engagement strategies.
- Create a panel of DE&I experts, from across the different sites involved in the study, to interact with and support the sites with the execution of site-specific strategies and tactics. If needed, they should adjust the strategies and tactics put in place.

Aspiration 1.4: Clinical trial site teams are, where possible, represented by individuals from underrepresented populations, including in leadership positions, and have the cultural competency to ensure their trial is diverse, equitable and inclusive

- Ensure, where possible, that study investigators from underrepresented populations are in clinical trial leadership positions.
- Provide cultural awareness training for trial teams (see more details under Aspiration 3.4).
- Ensure appropriate resources and staff, such as community connectors, AD champions, and patient navigators, are in place where possible.
- Consider appointing community champions to lead on engagement activities with community groups, as well as engaging cultural consultants to aid study site teams in better understanding cultural norms, beliefs, and language needs.
- Ensure each site has clinical trial coordinators and staff who can speak multiple languages, representative of the populations they are targeting, and/or employ professional interpreters. In culturally and linguistically diverse study sites, staff should be made aware of language nuances and varying cultural perceptions.



Aspiration 2.1: Diversity plans are incorporated into study protocols, including recruitment and retention, and structural exclusion of particular demographic groups has been mitigated to the greatest extent possible.

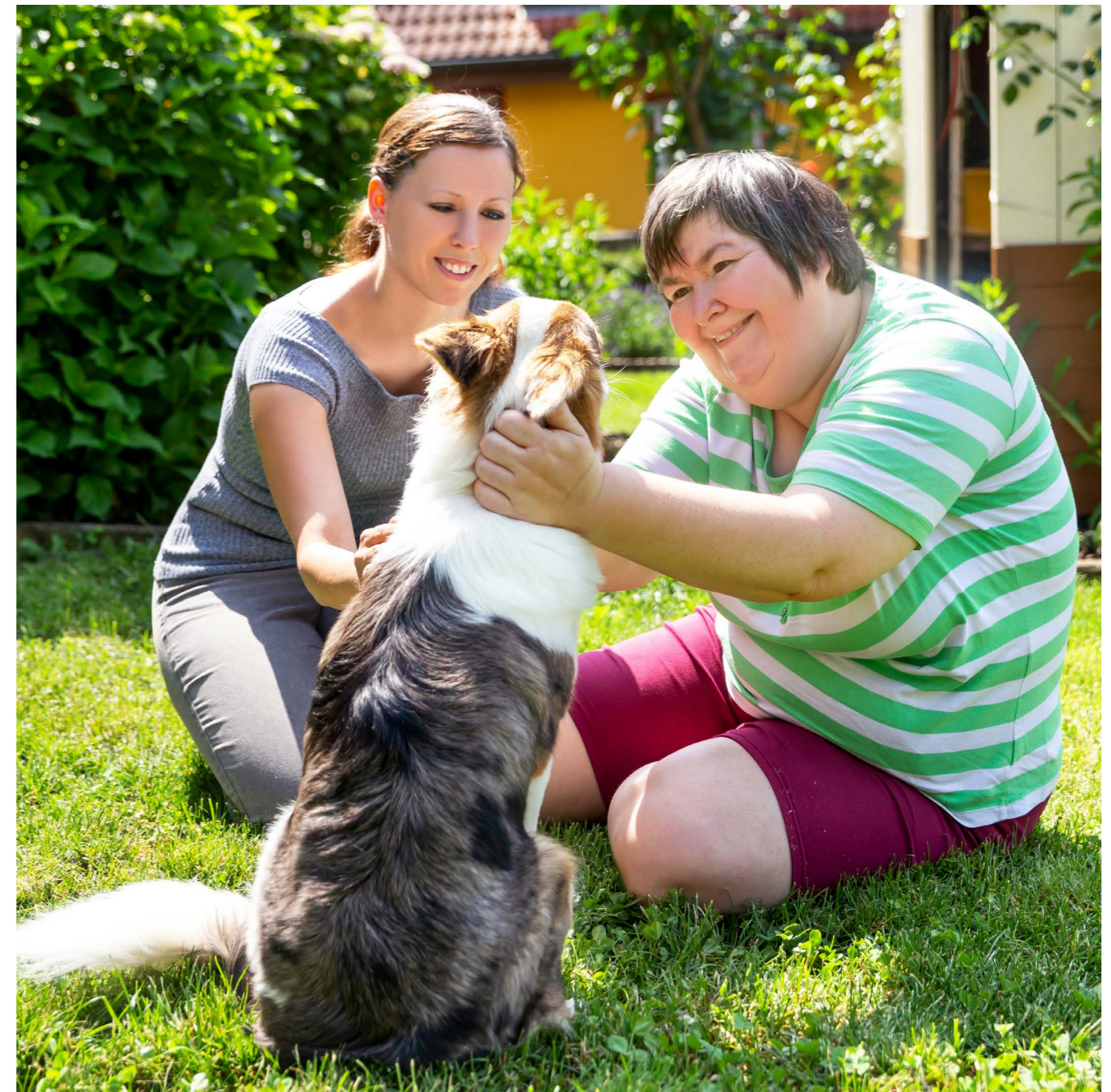
- Conduct further research to understand the disparities in retention and recruitment between different populations in previous clinical trials. Data analysed can include exclusion criteria from past and ongoing trials; rationale from PLWA who were selected for a trial but declined to participate; and predictive modelling based on multidimensional diversity data to identify additional barriers that may have been overlooked. This multidimensional diversity data should be collated from across the different stages of the clinical trial protocol and multiple indicators should be assessed, both individually and the relationship between them. Indicators can include socioeconomic status, technological aptitude if the trial requires the use of technology (e.g., mobile apps), social determinants of health, comorbidities which may have a role in contributing to AD onset, memory test thresholds and social isolation, as well as other factors that are unequally distributed amongst subgroups.
- Undertake research specifically to evaluate whether there is an ethno-racial bias in fluid and imaging markers as well as clinical/cognitive scales. Linked to the different role the APOE ε4 gene variants play in AD in different ethnicities, some studies have shown that the physical biomarkers most commonly associated with Alzheimer's disease can appear at different levels in different ethnicities,⁶⁶ potentially reducing the generalisability of test results.
- Develop a diversity plan as part of the study protocol, which outlines clear strategies and tactics to tackle the barriers identified to recruitment and retention of underrepresented groups. These should be tailored to the trial's site, target population, local culture, and available resources.
- The plan should include a set of clear metrics and key performance indicators, which are measured regularly. If the site has a DE&I lead, this person should be accountable for measuring progress against the implementation of the diversity plan.
- Ensure a budget is allocated to allow study sites to execute the diversity plan.

Aspiration 2.2: Clinical outcome measures and remote digital data collection tools have been cross-culturally validated before implementation into study protocols.

- Seek to incorporate alternative screening tools and clinical assessment scales suitable for a cross-cultural context. These should be suitable for use by individuals from traditionally underrepresented populations, including from different cultural and socio-economic backgrounds and with sensory deficits or comorbidities.
- Validate clinical assessment scales with local patient organisations and with the site's DE&I panel or with DE&I experts ahead of implementation.
- Clinical assessment scales, screening tools and methods used throughout the trial should aim to collate the highest quality data whilst ensuring the burden on participants (both the PLWA and study partners) is minimal. Usage and adoption of these scales and tools should be regularly monitored against a series of metrics and milestones, defined by the trial site, and tailored according to the site's culture, location and resources and the trial's target population.
- Consider facilitating greater access to clinical trial programmes via solutions such as a simplified schedule of clinical trial assessments, decentralised clinical trials, or use of telemedicine.
- Before telemedicine solutions are adopted, the level of technology literacy of the trial's target population should be assessed. Where appropriate, participants should be provided with phones/tablets, if they are comfortable using them, to support remote assessments. For example, this may include answering questions related to clinical care, undertaking questionnaires and cognitive tests, and monitoring treatment compliance. Training on how to use these tools should be provided before and throughout the trial. If participants are not comfortable using digital solutions, a phone line (with 24/7 support from site staff) or alternative solutions (e.g., routine support in local community clinics or routine appointments at the trial site) should be made available.
- Seek to minimise invasive investigations and when such investigations cannot be avoided, ensure the objectives of these investigations are explained to participants and study partners and that the appropriate support is provided before, during and after each procedure.

Aspiration 2.3: Clinical trial protocols, recruitment and retention strategies, and participant-facing materials are co-created and reviewed by advisory boards comprising of PLWA, DE&I experts, patient advocacy groups, community leaders as well as other relevant stakeholders.

- Co-create clinical trial inclusion/exclusion criteria with external experts, with the aim of identifying and addressing criteria that may pose a barrier to the recruitment or retention of underrepresented populations.
- Co-create assessment schedules, accounting for location, financial implications and solutions accommodating these requirements (e.g. diaries for self-reported memory problems).
- Co-create informed consent forms with DE&I experts and PLWA from various backgrounds to ensure information is easily digestible and not overwhelming for participants and study partners, and culturally appropriate.
- Consider the development of informed consent companion videos and resources to aid understanding of requirements.
- Study material content should explain why it is important that underrepresented groups have greater representation in clinical research. Imagery, language, and cultural references should align with the target population (e.g. content should be tailored to different languages, literacy levels and disabilities, such as visual impairment).



Theme 3: Potential barriers to clinical trial participation are reduced and engagement with local community groups is enhanced both before and throughout the clinical trial

Aspiration 3.1: Strategies to alleviate challenges faced by participants and study partners have been implemented

- A set of strategies should be developed to tackle the challenges faced by participants and study partners. These can be detailed in the diversity plan (Aspiration 2.1), or individually. These should be tailored to the trial's site, target population, local culture, and available resources.
- A set of clear metrics and milestones should be set, to measure progress made against the adoption of these strategies. Strategies should be adapted if successful adoption has been difficult to achieve. Some of these strategies are proposed below.
- Examine the financial burden of participating in a clinical trial for participants and study partners and consider potential up-front compensation for expenses and transport costs. Funding services, such as babysitting and pet sitting, should also be considered.
- Ensure study partner expectations, roles, and responsibilities are explained at the outset of clinical trials, including their role in data capture and importance in the consistency of care provided to the clinical trial participant. However, if study partners cannot attend site visits, others should be permitted to accompany study participants if possible as temporary substitute study partners.
- Seek to allow flexibility for scheduling participant assessments.
- Develop support materials such as study calendars, glossaries, short videos explaining the study and the clinical tests and procedures that will be undertaken, and an introduction package for participants and study partners. These study materials should include disease education and address stigmas and beliefs which may be hindering the participation of underrepresented groups. These materials must be developed in several languages and in dialect where necessary, with translation validation procedures employed as appropriate. Versions taking into account the needs of participants with sensory loss should also be developed.
- Consider the provision of support services such as in-home nursing, support groups and respite services.
- Consider developing sex/gender specific strategies to support participation in clinical trials.

Aspiration 3.2: Partnerships and enhanced community engagement and outreach have been established

- Both Roche and study sites build long-term partnerships with the disease area community, highlighting the importance of participation by people from traditionally underrepresented communities.
- Both Roche and study sites establish outreach activities to encourage clinical trial engagement and retention, including events involving community members.
- Develop partnerships with vendors who are integrated in the community and can support the development of recruitment initiatives which engage with the local community and are, where appropriate, digital to ensure they reach people in underserved communities.
- Develop a "testimonial" resource for study sites to highlight current clinical studies and past successes which include testimonials from clinical trial participants from underrepresented populations.
- Organise educational workshops, seminars, or webinars to address common misconceptions about clinical trials and engage with underrepresented communities.

Aspiration 3.3: Clinical trial site teams have increased engagement with site specific DE&I goals and have methods in place to achieve them

- Ensure the metrics and milestones set for each DE&I goal (as per Aspiration 2.1) are measured regularly to allow for seamless adoption or adaptability, where required.
- Put a strategy in place to streamline screening activities for potential clinical trial participants and introduce follow up after screening to facilitate navigation of next steps.
- Coordinate support group meetings at trial sites, for trial participants to discuss clinical trial experience and connect with others involved in the trial or in other trials.
- Ensure site teams continue to engage with Roche to discuss their progress in achieving the DE&I goals within that particular study, and that best practice sharing between sites/countries is facilitated to support learning.
- Develop raters in study sites who have the potential to increase access to typically underrepresented communities.

Aspiration 3.4: Both clinical trial site teams and internal Roche employees have had enhanced training on DE&I

- Identify, deploy and mandate effective and locally sensitive inclusive research and inherent bias training for all clinical trial sites, with recurring booster sessions throughout the duration of the clinical trial. The training should be responsive to the needs that emerge as the trial is implemented and include areas such as, but not limited to, cultural sensitivity training, education about systemic barriers and strategies to achieve a more inclusive environment.
- Ensure inclusive research training facilitates DE&I discussions with local DE&I clinical site team members.
- Develop accurate, timely, actionable, and non-judgemental feedback loops to regularly assess and update training materials to ensure they remain relevant and effective in addressing DE&I challenges.
- Foster a psychologically safe environment where clinical trial site team members feel comfortable discussing DE&I challenges and create spaces for discussion and sharing ideas for improvement.
- Ensure all team members from trial sponsors/organisers working on a clinical development programme have an enhanced understanding of the need for prioritising DE&I strategies throughout the different stages of drug development.



Theme 4: Roche has become a consistent leader in addressing DE&I in AD

Aspiration 4.1: Roche has become a partner of choice for inclusive AD clinical trials

- Establish partnerships with respected communities and groups around the world who share the common goal to advance inclusive research. Focus should be on smaller community groups at an individual country level. Regularly evaluate the effectiveness of these partnerships and seek feedback from partner organisations.
- Consider partnering with other concurrent multicentred regional research initiatives to share best practices, resources, and insights related to DE&I in AD research, creating a broader network of support and collaboration.
- Support the development and implementation of strategies that address specific challenges faced by each community, ensuring cultural sensitivity and appropriateness.
- Actively support community events and activities, demonstrating a commitment to consistently engage with these communities beyond the scope of clinical trials.

Aspiration 4.2: Educational efforts to support the understanding of the importance of DE&I in AD have been prioritised

- Partner with patient advocacy groups and DE&I experts to deliver awareness and education on inclusivity in the field of AD.
- Ensure that development of culturally appropriate education materials includes input from underrepresented communities, so that health access disparities can be addressed.
- Highlight the importance of sex/gender aspects in DE&I and how they should also be properly addressed in these educational campaigns.
- Make available information on disparities throughout the clinical trial process, in lay language or in formats that are tailored to people with sensory loss or with learning disabilities, to study participants particularly from underrepresented communities, to facilitate understanding of why clinical trial participation is important.

Aspiration 4.3: DE&I has become a central pillar for all strategies within the AD space

- Incorporate DE&I messaging into all external communications and educational materials/campaigns across AD clinical trials to facilitate the reduction of health access disparities.
- Co-create research and publications with a focus on DE&I to share knowledge and learnings with the wider research community.
- Continue to undertake an analysis of the protocols in place to ensure recruitment and retention of diverse underrepresented populations throughout and after the trial.



Adopting an agile approach to operationalise the aspirations

The previous section of this report set out a series of aspirations that, if enacted, would improve the approach to diversity, equity, and inclusion (DE&I) in Alzheimer’s disease (AD) clinical trials. However, we recognise that it will require substantial effort, investment, and commitment from the organisers of clinical trials, the site staff, as well as the wider communities of patient groups and organisations that support them, to consistently achieve these aspirations. Long-term collaboration with key stakeholders will be central to adopting these aspirations and to improving the quality of future clinical trial data – maximising our chances of discovering new and more effective treatments and diagnostics for this condition. It should, however, be noted that the DE&I challenges encountered in this field are not all unique to AD, and as such, their adoption should also be considered in the clinical trial development of other therapy areas.

To ensure these aspirations are adopted in an efficient way, we have proposed below an agile approach to operationalise them. The emerging agile science offers new approaches to design, implement, and diffuse scalable, evidence-based, and locally sensitive interventions targeting DE&I in AD clinical trials.⁶⁷ Agile science integrates insights from behavioural economics, complexity science, and network science to understand, predict, and nudge the behaviours of both an individual human and a social organisation.^{66,68,69,70,71,72} Improving DE&I in AD clinical trials requires thinking at a system level, considering the local resources, processes of care, and relationships.^{73,74,75,76,77,78,79,80,81,82,83} One of the core principles of agile innovation is to embrace failing forwards. A recognition that being wrong or not achieving the objectives of an action can in and of itself be valuable, as long as lessons are learned for the next attempt.

In this section we set out how an agile approach can be adopted to trialling, delivering, and ultimately improving DE&I in AD clinical trials. To make the quickest possible progress, we need to accept that a traditional approach to change management may not be successful. The challenges facing DE&I in clinical trials are too complex for any one organisation to be able to either know all the changes that need to be made, or to have the capacity and capability to introduce them all in one go.

In our approach to improving DE&I in our clinical trials, we have deliberately embraced this approach – bringing together a diverse cohort of experts to ideate solutions in a context that enables these to be generated rapidly. Moving forwards, Roche will ensure to take the spirit of the agile process when we are piloting and incorporating DE&I processes into our AD clinical trials. We hope that other organisers of AD clinical trials also consider the utility of this approach.

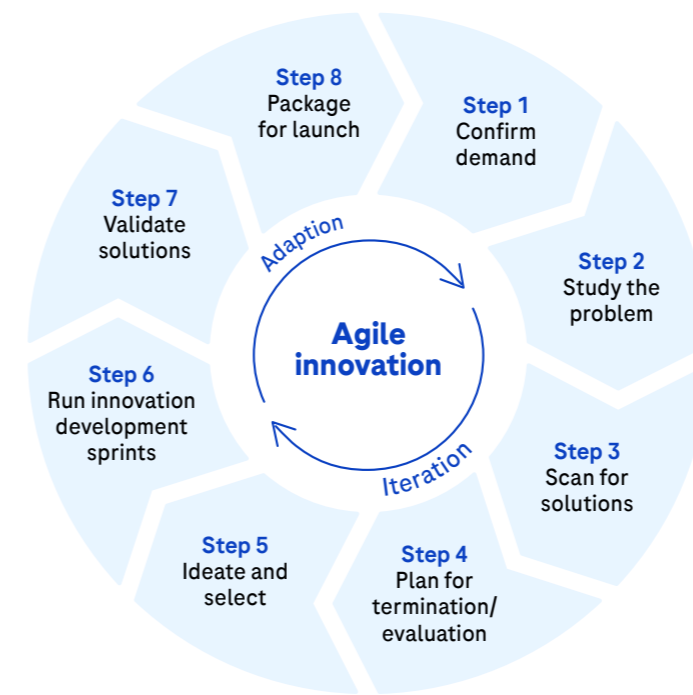


Figure 2. The eight-step agile process.⁶⁷

The eight-step agile process is set out in Figure 2. The steps, in the context of AD clinical trials are:⁶⁷



Step 1: Confirm demand. An agile project team delegates power to semi-autonomous teams in clinical trial sites and provides them with time and space to rapidly assess situations, innovate, experiment, and fail quickly and cheaply. Site staff work with representatives of the AD community such as patient advocacy groups, people living with AD, clinical trial participants (including care partners), and DE&I experts, to identify which aspirations, of those set out in the previous section, have not been met in previous clinical trials or are not being met in their ongoing clinical trial.



Step 2: Study the problem. Clinical trial organisers and site staff undertake a short analysis of why these aspirations are not being met and identify any barriers to their adoption in the trial site.



Step 3: Scan for solutions. Rather than starting from a blank piece of paper, clinical trial organisers gather existing solutions for improving DE&I in clinical trials from other sites, other disease areas, or other sponsors. The hallmark of agile is the minimally viable product (MVP), a working product made ready for immediate evaluation in iterative sprints of testing and redesigning.



Step 4: Plan for termination / evaluation. Clinical trial organisers agree to the termination criteria and evaluation plan before selecting a solution (or MVP) – this is key for delivering change in clinical trials which are complex and often long running. Rapid testing and redesigning of MVPs require a climate of psychological safety, which empowers team members to give and receive accurate, frank feedback and direction. Establishing feedback loops are thus important to this process and feedback could be collated through regular check-ins, surveys, user testing and more non-traditional methods (e.g., gossip, stories, overheard conversations).



Step 5: Ideate and select. Working with as diverse a group of stakeholders as possible from across the AD community, clinical trial organisers and site staff ideate for solutions that enable the fast adoption of the aspirations set before and that improve DE&I in clinical trials. Then select the most promising and actionable ideas. Although all aspirations should eventually be met, prioritising a few to test solutions on, can help focus resources and deliver positive change more rapidly.



Step 6: Run innovation development sprints. Develop the solution so that it is ready to be deployed. Any solution to improve DE&I deployed during a clinical trial will have to be thoroughly tested and agreed to in advance of the trial starting. It should be recognised that no solution will be perfect before it is tested and that it is better to test multiple MVP solutions quickly, than to invest significant time and resources on a solution before it has been tested.



Step 7: Validate solutions. Test the selected solutions in as efficient a way as possible. For clinical trials, this means small scale pilots and early clinical trials where the results of solutions can be evaluated quickly. The solution should be evaluated using the plan as agreed in step 4. If the solution meets the termination criteria agreed at step 4, then the process should be repeated.



Step 8: Package for launch. Solutions that are effective during testing can then be ‘packaged’ for wider launch. In a clinical trials context, this will mean publishing the methodology and results of pilots to ensure other organisers of clinical trials can adopt the same proven methods.

Examples of how Roche has operationalised the aspirations

The majority of this report has focussed on aspirations for the future of diversity, equity, and inclusion (DE&I) in Alzheimer's disease (AD) clinical trials. However, in this section we want to highlight some examples of the steps Roche has already taken to improve DE&I in either our ongoing or completed AD clinical trials. We have highlighted three examples which we hope demonstrate some of what can be achieved with dedicated focus on DE&I.

The SKYLINE 'clinical trials bus'

As part of Roche's SKYLINE clinical trial in the US, we recognised that we needed to make our trial more accessible to diverse populations.



One way we accomplished this was through the 'clinical trials bus', a mobile clinical trials centre which visited community locations. The bus succeeded in driving clinical trial recruitment in these communities who were underrepresented in SKYLINE.

The Roche rater academy

Roche has established a rater academy, which aims to offer clinical trial sites a greater ability to upskill raters. Raters are clinical trial staff members who administer rating scales to clinical trial participants.



Establishing the rater academy aims to broaden the capabilities of raters and to expand the rater workforce to include raters that are representative of the local communities where participants will be recruited from.

The co-creation of the ALUMNI AD protocol

As part of Roche's ALUMNI AD clinical trial in the US, we involved multiple stakeholders in the trial design process, including study coordinators, researchers, and therapeutic area experts. Further input from community leaders helped to strengthen relationships with the community and establish trust. Community group feedback was also obtained on informed consent forms, to assess understanding of the information provided.



Collaboration on protocol development culminated in several amendments to the protocol design, including increasing the flexibility in eligibility criteria to enable the study population to better represent real world users and providing participants with the opportunity to control comorbidities rather than excluding them.

To boost recruitment and reduce access barriers, compensation and transport support was provided. To address barriers stemming from lower health literacy, community navigators were engaged to help guide trial participants through the screening and consent process.

Furthermore, collaboration with community partners and care site staff was undertaken, to build site capacity and overcome disparities in healthcare infrastructure. This collaboration led to the standardisation of rating methodology and cultural competency training. The training also aimed to reduce mistrust of research and development within underrepresented groups.

Conclusion

This report examines the need for diversity, equity, and inclusion (DE&I) to be prioritised in the execution of Alzheimer's disease (AD) clinical trials. The lack of diversity in clinical trials hampers our ability to assess the efficacy and safety of potential treatments in various demographic groups, potentially leading to suboptimal treatment outcomes for underrepresented populations. Additionally, it perpetuates health disparities and exacerbates existing inequities in healthcare access and outcomes.

To address these challenges, it is imperative to implement multifaceted strategies within our clinical trials such as increasing outreach and engagement; providing language services; addressing cultural sensitivities, and offering transportation and financial assistance, to name a few. Moreover, the entire Alzheimer's community needs to prioritise the importance of the inclusion of diverse populations in research and funding agencies.

At Roche we are committed to ensuring these strategies are prioritised and adopted and believe it is key for the AD community to continue to work together to foster a more equitable and inclusive research landscape. We hope this report is a step in the right direction and can inspire others working in study design and execution to improve representation in clinical trials not only in AD but also in other therapy areas.



Glossary

Alzheimer's disease: Alzheimer's disease (AD) 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.⁸⁴ The build-up of these proteins begins up to 20 years before symptoms emerge.⁸⁵ AD is progressive, which means the symptoms gradually get worse over time, with the clinical presentation and severity varying from person to person. When we refer to AD in this report we are encapsulating the whole continuum from preclinical through to AD dementia, except where otherwise specified.

Care partner: family member, friend or paid helper who regularly looks after someone with a condition.⁸⁶

Clinical assessment scales: assessment tool aimed at classifying the severity of symptoms and conditions. These can include using a cognitive screening test score to screen for underlying dementia, to distinguish impairment due to dementia from normal age-related cognitive change or to monitor the effects of treatment in a clinic trial.⁸⁷

Clinical development programme: an outline of an investigational molecule's entire clinical research strategy. It outlines the clinical programme design, including development, assessment, decision points, personnel, and budgetary estimates.⁸⁸

Community champions and connectors:

Community champions are community members who volunteer to promote health and wellbeing or improve conditions in their local community.⁸⁹ In a clinical trials context they can promote participation in a trial in their community and help to connect the clinical trial team with underrepresented communities.

Diversity: practice of creating a community of people comprising of different sociodemographic factors (race, ethnicity, sex/gender, etc) and medical factors (comorbidities, genetics, physical fitness levels, etc).⁹⁰

Ethnicity: clusters of people who have common culture traits that they distinguish from those of other people. People who share a common language, geographic locale, or place of origin, religion, sense of history, traditions, values, beliefs, food habits, and so forth, are perceived, and view themselves as constituting an ethnic group.⁹¹ Ethnic groups are not permanent, inflexible entities but rather open to change and to people moving in and out of them.⁹²

Fluid markers: measures of physiological or pathogenic processes detected in biological fluids such as cerebrospinal fluid and plasma.⁹³

Genetic biomarker: a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease.⁹⁴

Gene variant: a permanent change in the DNA sequence that makes up a gene. This change may be benign, pathogenic, or of unknown significance.⁹⁵

Health equity: fair access to healthcare for people and groups, with consideration for their unique barriers or privileges.

Imaging biomarker: a biologic feature detectable in an image. In medicine, an imaging biomarker is a feature of an image relevant to a patient's diagnosis.⁹⁶

Minority: a culturally, ethnically, or racially distinct group that coexists with, but is subordinate to, a more dominant group. Minority status does not always correlate with population size.⁹⁷

Patient navigator: a person who helps guide a patient through the healthcare system. This includes help going through the screening, diagnosis, treatment, and follow-up of a medical condition.⁹⁸

Predictive modelling: mathematical process used to predict outcomes by analysing patterns in a given set of input data. It is a crucial component of predictive analytics, a type of data analytics which uses current and historical data to forecast activity, behaviour and trends.⁹⁹

Race: set of physical traits that define an individual or group of individuals as belonging to a particular social category. The definition assigned to racial groups varies dramatically across countries, cultures, and historical timeframe.⁹⁰ Race has been said to be defined in terms of biogenetic variation particularly among scientists, with another popular conception focusing more on physical features and behaviour.⁹¹ However, as races cannot be discretely defined in terms of genetic variation and often there may be more genetic variation within a defined race than between them, the idea of race has been challenged.¹⁰⁰

Rater: a person involved with clinical research who administers a rating scale to a clinical trial participant.¹⁰¹

Rater training: used within clinical trials to improve the consistency of subjective data collected from patients, caregivers/observers, and clinicians/interviewers.¹⁰²

Screen-failure data: screen failures occur when research staff put potential participants through a screening process to ensure they fit the inclusion criteria in a study, only for them to not enrol in the trial.¹⁰³

Study feasibility questionnaire: set of questions prepared by a study sponsor to identify the potential, interest, and feasibility of a site/investigator to run a clinical trial successfully.¹⁰⁴

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.⁸⁶

Underrepresented groups: populations that have been historically not included in AD clinical trials and/or that have had a low representation in AD clinical trials, when compared to their representation in PLWA. These include women; groups historically excluded due to geography; non-white ethnic groups and ethnic minorities in high-income countries; individuals with disabilities and comorbidities; sexual minority groups and groups from lower socioeconomic backgrounds. It should be noted that the factors considered to define each of these groups (e.g., race, culturally diverse backgrounds, educational and socioeconomic issues) should be considered different and independent variables that may or may not be interrelated.

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