Alzheimer’s Association®
Leading the Way
to Treatment and Prevention

U.S. POINTER

An impact report prepared for
Sigma Kappa

June 2022
Dear Sigma Kappa,

Thank you for your generous support of the historic U.S. Study to Protect Brain Health through Lifestyle Intervention to Reduce Risk (U.S. POINTER), one of the world’s largest clinical trials designed to evaluate whether lifestyle interventions that simultaneously target many risk factors can protect cognitive function in older adults who are at increased risk for cognitive decline.

More than 6 million Americans are living with Alzheimer’s dementia today, and by 2050 this number is to increase to nearly 13 million. At present there is no drug therapy that can prevent or effectively treat Alzheimer’s for all who face it. Emerging studies continue to suggest that lifestyle interventions such as more exercise and a healthier diet may be able to help protect cognition, and scientists are eager to verify whether multiple interventions implemented together can have a significant impact.

*Thanks to leadership support from the members and families of Sigma Kappa, U.S. POINTER may potentially set the stage for development of our nation’s first accessible, scalable and sustainable program for reducing risk of cognitive decline.*

“What's particularly exciting about U.S. POINTER is that this is the first time that a study has been done in the United States that is looking at a whole recipe of things that one could change,” says epidemiologist and Northern California site co-leader Rachel Whitmer, Ph.D., University of California, Davis. “There have been studies that have looked at perhaps just blood pressure or just diet or just cognitive training. U.S. POINTER is the first time that these things have been really looked at all together.”

Progress in the trial remains steady despite the challenges presented by the COVID-19 pandemic. To date, 1,563 individuals have been enrolled and randomized in U.S. POINTER, and 85 participants have fully completed the trial. Based on clinic volume allowed (due to the pandemic), we now project reaching full enrollment of 2,000 participants by March 2023, which means all participants can be expected to have completed the two-year intervention by March 2025.
The study’s Scientific Advisory Board members, who meet three times annually to review the study’s progress, uniformly applaud this progress and acknowledge the successes that U.S. POINTER has achieved during these uncertain times. Despite delays and other challenges, the study team has continued with general recruitment, increased recruitment of underrepresented diverse populations, and pivoted several times — from in-person to virtual to in-person to virtual and now back to in-person — while maintaining the necessary study rigor.

Diversity is fundamental to ensuring that any potential findings benefit all families affected by dementia, and the study is on track in this regard. Of the study participants enrolled as of May 2022, 28.7% belong to populations that are underrepresented in research, including Black, Hispanic, Native American, Asian, Middle Eastern, other non-White and multiple race populations.

The Alzheimer’s Association is deeply committed to doing more to advance health equity, and U.S. POINTER is making a strong contribution to our commitment. We aim to break down barriers to quality care and support for all affected by dementia in all communities, especially our most vulnerable and underserved friends and neighbors.

Expressing a sentiment shared by all site leaders, neurologist and Houston site co-leader Melissa Yu, M.D., FAAN, Baylor College of Medicine, is thrilled that her city is playing a role in the worldwide effort to end dementia. “The fact that the Houston site is one little cog in this giant world of people trying to prevent Alzheimer’s disease is really exciting,” says Dr. Yu. “That is really something that I look forward to being part of.”

Thank you, Sigma Kappa, for joining with us to make dementia history through U.S. POINTER, the Women’s Alzheimer’s Research Initiative (WARI) and so much more.

Sincerely yours,

Elizabeth Harder, CFRE
Senior Donor Advisor GA, SC, NC
Alzheimer’s Association
404.728.6066 | eharder@alz.org
Researchers estimate that up to 40% of all dementia cases worldwide may be preventable by addressing modifiable factors. What’s more, new scientific evidence suggests people can take positive steps now to protect their memory and thinking. Participants in FINGER (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability) showed improvements in memory and other thinking skills after just two years of a lifestyle change that included a healthier diet, more exercise, increased intellectual and social stimulation, and better management of heart and vascular health. More recently the SPRINT MIND study showed that aggressive management of high blood pressure can reduce risk of mild cognitive impairment, a slight but measurable decline in cognitive abilities that increases a person’s risk of developing Alzheimer’s or another dementia.

With your partnership, the Alzheimer’s Association is leading a historic clinical trial to further test this emerging evidence. The U.S. Study to Protect Brain Health through Lifestyle Intervention to Reduce Risk (U.S. POINTER) is building on the last decade of scientific advances and expanding on lessons learned in FINGER to evaluate the effectiveness of lifestyle interventions in 2,000 Americans from a wide range of racial, ethnic, socioeconomic and geographic backgrounds who are at increased risk of developing memory decline and dementia. It is the first such clinical trial to be conducted in a large group of older adults across the United States.

**U.S. POINTER could set the stage for the development of our nation’s first accessible, scalable and sustainable program for reducing risk of cognitive decline.**

Study participants are being assigned randomly to one of two groups, either a self-guided lifestyle intervention group or a structured lifestyle intervention group. The two-year program for each group provides nutritional guidance, coaching for heart and vascular health, and opportunities for increased physical exercise and cognitive and social stimulation. Participants in both groups attend regular meetings with other participants to receive information about healthy lifestyle practices and strategies to adopt healthier habits.

The success of the interventions to protect or improve cognitive function are being evaluated every six months for all participants. Vascular and metabolic health, physical function, mood, quality and quantity of sleep, and quality of life also are being assessed.
Leadership, Sites and Enrollment

U.S. POINTER is being led by some of the world’s leading experts on dementia risk reduction, including:

- Laura Baker, Ph.D., Wake Forest School of Medicine
- Mark Espeland, Ph.D., Wake Forest School of Medicine
- Miia Kivipelto, M.D., Ph.D., Karolinska Institutet, Sweden, FINGER PI
- Rachel Whitmer, Ph.D., UC Davis School of Medicine
- Maria Carrillo, Ph.D., Chief Science Officer, Alzheimer’s Association
- Heather Snyder, Ph.D. Vice President, Medical & Scientific Relations, Alzheimer’s Association
- U.S. POINTER Scientific Advisory Board
- Alzheimer’s Association Chapter Leadership

U.S. POINTER comprises five sites that are recruiting and enrolling study participants and guiding them through the two-year intervention. They include:

**Western North Carolina**
- Research institution: Wake Forest School of Medicine
- Site investigators: Jeff Williamson, M.D., and Maryjo Cleveland, M.D.
- Clinical partner: Wake Forest Baptist Health
- Association chapter: Western Carolina

**Northern California**
- Research institution: UC Davis School of Medicine
- Site investigators: Rachel Whitmer, Ph.D., and Sarah Farias, Ph.D.
- Clinical partner: UC Davis Health
- Association chapter: Northern California and Northern Nevada

**Chicagoland**
- Research institutions: Advocate Health Care and Rush University Medical Center
- Site investigators: Christy Tangney, Ph.D., and Darren Gitelman, M.D.
- Clinical partners: Advocate Health Care and Rush University Medical Center
- Association chapter: Illinois

**Houston**
- Research institution: Baylor College of Medicine
- Site investigators: Valory Pavlik, Ph.D., and Melissa Yu, M.D.
- Clinical partner: Kelsey-Seybold Clinic
- Association chapter: Houston and Southeast Texas

**New England**
- Research institution: Butler Hospital
- Site investigators: Stephen Salloway, M.D., and Rena R. Wing, Ph.D.
- Clinical partners: The Miriam Hospital
- Association chapter: Massachusetts / New Hampshire

“...” — Stephen Salloway, M.D.
Site Investigator,
New England
As of June 6, 2022, 1,563 individuals are enrolled and randomized in U.S. POINTER. Eighty-five participants have fully completed the trial. Based on clinic volume allowed (due to the ongoing COVID-19 pandemic), we now project reaching full enrollment by March 2023, which means all U.S. POINTER participants can be expected to have completed the two-year intervention by March 2025.

This past winter the Alzheimer’s Association and other U.S. POINTER study leaders extended the study an additional 22 months. The new timeline accounts for research pauses at participating institutions, which delayed when studies were able to initiate recruitment and engage in community-based activities for recruitment. The leadership team feels confident that the study is on track, especially with U.S. POINTER personnel and partners returning to in-person engagement for recruitment and other study activities in accordance with guidance from the U.S. CDC.

The study’s Scientific Advisory Board members, who meet three times annually to review the study’s progress, uniformly applaud this progress and acknowledge the successes that U.S. POINTER has achieved during these uncertain times. Despite delays and other challenges, the study team has continued with general recruitment, increased recruitment of underrepresented diverse populations, and pivoted several times — from in-person to virtual to in-person to virtual and now back to in-person — while maintaining the necessary study rigor.

Each site is enrolling 400 or more adults ages 60-79 years. Eligible volunteers have medical conditions thought to increase later-life risk for cognitive decline such as mild hypertension and slightly elevated blood sugar levels. They also must have “room for improvement” in their physical and nutritional health and a first-degree relative (mother, father, brother or sister) who had or has a noticeable memory problem.

Individuals meeting the study requirements are identified through a multiprong approach that blends community-based engagement, a search of electronic medical records (EMRs), recruitment materials via mail and a telephone interview. Sites search for potential participants through grassroots efforts in their community, including leveraging the Association’s community partnerships. Each site features:

- Lead investigators who have experience conducting large-scale, nonpharmacological trials and assessing cognition in older adults;
- Extensive clinical networks and access to EMRs;
- A community partner with high-quality older-adult fitness programming;
- Clinic capacity and commitment to the study;
- Access to PET tracers and/or PET brain imaging;
- A history of engaging diverse populations; and
- A commitment to ensuring racial/ethnic diversity in the study staff.
“People are very excited to participate because of the preventative aspect,” says Houston site co-leader Melissa Yu, M.D., F.A.A.N., Baylor College of Medicine. “The participants have family members who have been affected by the disease, often a parent or an aunt or a grandparent. It's an exciting thing to be able to give them something to do to hopefully stave off the onset of the disease and change their trajectory.”

**Diversity is fundamental to ensuring that any potential findings benefit all families affected by dementia.** Of the study participants enrolled as of early June 2022, 28.7% belong to populations that are underrepresented in research, including Black, Hispanic, Native American, Asian, Middle Eastern, other non-White and multiple race populations. To achieve racial and ethnic diversity representative of the U.S. population, at least 23% of the participants must be from non-White groups (2016 U.S. Census demographics), with a strong representation of both men and women.

The Alzheimer’s Association is deeply committed to doing more to advance health equity, and U.S. POINTER is making a strong contribution to our commitment. We aim to break down barriers to quality care and support for all affected by dementia in all communities, especially our most vulnerable and underserved friends and neighbors.

Last summer, researchers at the Alzheimer’s Association International Conference® (AAIC®) — the world’s largest and most influential international meeting dedicated to advancing dementia science — shared new, evidence-based insights into why people do and do not choose to participate in clinical trials:

- Individuals are most willing to volunteer if invited to participate (85%), if they want to contribute to research (83%) or have a family member with the disease (74%).
- Black, Hispanic and American Indian respondents are significantly more likely to volunteer if asked by a person of the same race.
- According to a review of dementia clinical trials funded by the National Institute on Aging (NIA), part of the National Institutes of Health (NIH), commonly used exclusion criteria disproportionately affect Black and Hispanic individuals and may play a role in their reduced enrollment in research.

Oanh Meyer, Ph.D., M.A.S., associate adjunct professor at the Alzheimer’s Disease Center at UC Davis Health, is leading grassroots recruitment at the Northern California site. “The onus is on us, as a research team, to go into places where we can engage diverse individuals in our research,” says Dr. Meyer. “Whether it’s faith-based institutions or other community-based organizations, we need to meet people where they are.”

Dr. Meyer meets biweekly with grassroots recruiters at the other four sites. “We share ideas with one another — what’s working at your site, how are you engaging this specific population,” she says. “It has been really helpful.”
Ancillary Studies Funded by the National Institute on Aging

We have leveraged our investment and leadership to help investigators obtain four awards from the NIA that are expected to total $63.35 million for add-on studies. These awards bring the total amount invested in U.S. POINTER to more than $100 million. The studies include:

**U.S. POINTER Neuroimaging Ancillary Study**, the first large-scale investigation of how lifestyle interventions affect biological markers (biomarkers) of Alzheimer’s and other dementia in the brain.

**U.S. POINTER NeuroVascular Study (POINTER-NV)**, an investigation of how changes in blood flow and blood vessel health, resulting from a lifestyle intervention, impact cognitive health.

**U.S. POINTER-zzz Sleep Study**, an ancillary study using in-home sleep assessments to investigate whether lifestyle interventions improve chronic sleep problems and how this may benefit cognitive function.

**The POINTER-Microbiome Study**, an investigation of how a healthy lifestyle improves gut bacteria and how these changes might help protect brain function.

Hundreds of U.S. POINTER participants are enrolled in these ancillary studies.

**World Wide FINGERS**

U.S. POINTER is a member of World Wide FINGERS (www.alz.org/wwfingers/), a growing interdisciplinary network currently comprising 25 multidomain dementia prevention initiatives by researchers and other stakeholders in 30 countries.

WW-FINGERS is co-led by the Association and the FINGER research team. Members share experiences, harmonize data and plan joint international initiatives for reducing risk of cognitive impairment or dementia. Coordinating these efforts will create opportunity for rapid knowledge dissemination and implementation, potentially accelerating the development of an evidence-based model to reduce risk of cognitive decline.

The U.S. POINTER statistics team, in partnership with the FINGER statistics team, have been leading WW-FINGERS efforts to develop and disseminate guidance on intervention delivery and data considerations during the COVID-19 pandemic. This guidance is helping members and others to overcome challenges to their studies caused by the pandemic. The WW-FINGERS network has convened members to discuss strategies regarding missing data, adjusted interventions, tracking adherence and more.
In March 2021, WW-FINGERS researchers published a peer-reviewed article, “Impact of the COVID-19 pandemic on statistical design and analysis plans for multidomain intervention clinical trials: Experience from World-Wide FINGERS,” in *Alzheimer’s & Dementia: Translational Research & Clinical Interventions*. The researchers reported that, “The [WW-FINGERS] network convened a forum for researchers to discuss statistical design and analysis issues they faced during the pandemic. We report on experiences of three trials that, at various stages of conduct, altered designs and analysis plans to navigate these issues.”

They found that, “The pandemic led researchers to change recruitment plans, interrupt timelines for assessments and intervention delivery, and move to remote intervention and assessment protocols. The necessity of these changes add emphasis to the importance, in study design and analysis, of intention to treat approaches, flexibility, within-site stratification, interim power projections, and sensitivity analyses.”

U.S. POINTER researchers will join other members of WW-FINGERS this summer in a symposium at the Alzheimer’s Association International Conference 2022 in San Diego. The presentation by U.S. POINTER scientists will highlight recent data on adherence to in-person vs. virtual delivery of the study intervention. The symposium also will provide updates on the development of the WW-FINGERS network and various achievements of individual studies. Study teams from the U.S., South America, Europe, Australia, South Korea and China will participate.

**Leading the Way**

The Alzheimer’s Association has committed nearly $41.6 million to power U.S. POINTER — the most we ever have committed to one scientific study. We are pleased to share that many philanthropic partners have stepped up to help fulfill our commitment, making and pledging gifts totaling nearly $16 million to date in support of this unprecedented study.

Together, with our philanthropic partners and the U.S. POINTER family, we are making history. With chapters nationwide; numerous partnerships with health care systems and community organizations; our international research network; and a growing base of philanthropic support — we have both the will and the way to ensure the success of U.S. POINTER.

Lifestyle changes have helped drive down death rates from cancer, heart disease and other major diseases, and they could to the same for Alzheimer’s and other dementia.

*Thank you for your generous gift to ensure the success of U.S. POINTER and help realize our vision of a world without Alzheimer’s and all other dementia.*
The Alzheimer’s Association is a worldwide voluntary health organization dedicated to Alzheimer’s care, support and research.

Our mission is to lead the way to end Alzheimer’s and all other dementia — by accelerating global research, driving risk reduction and early detection, and maximizing quality care and support.

Our vision is a world without Alzheimer’s and all other dementia®.