

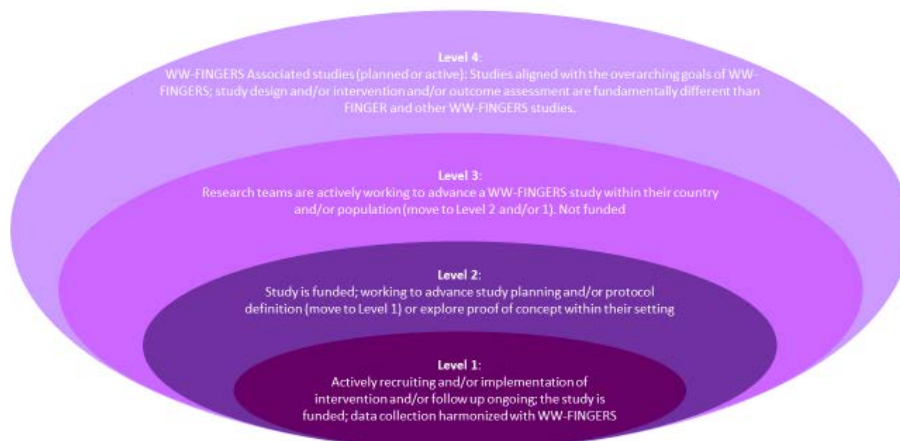


WW-FINGERS Network
AAIC In-person Meeting
Los Angeles, CA
July 12, 2019
Summary

Attendees: There were representatives from the following countries and organizations: South Korea, USA, Luxembourg, Japan, United Kingdom, Spain, Canada, Singapore, Australia, Argentina, India, World Health Organization, U.S. National Institute of Aging, U.S. National Institutes of Health

1. WW-FINGERS

Certain research gaps in research have been identified, including harmonization of methods, sparse information from low and middle-income countries, midlife versus late life risk factors and a lack of large random controlled trials. The WW-FINGERS network includes around 25 countries that have harmonize methods with the network though certain adaptations are made to the specific country. A level system has been implemented to designate the participating countries phase in their study.



WW-FINGERS is developing a master protocol but will include appendices for each countries' trial-specific details.

Future plans for the network include the inclusion of a multimodal lifestyle + pharmacological prevention intervention as well as creating a biorepository.

2. US POINTER

This is a 2-year study with the target to enroll 2000 cognitively normal, 60-79 years of age individuals who are at an increased risk for cognitive decline due to a sedentary lifestyle, poor diet, suboptimal cardiovascular health, and a 1st degree family history of significant memory impairment. A key to US POINTER is the partnership with the community and local Alzheimer's Association chapters. The recruitment to intervention timeline:

- EMR search → mailed questionnaires → telephone interview → randomization → assigned to teams → outcomes assessment

The groups are self-guided intervention versus structured intervention, there is no control group. The self-guided group will receive more support than usual standard of care. Suggestion was that countries might need to increase the dose of intensity, also US POINTER has an elaborate education curriculum to increase participant retention that can be shared to the countries in the network.

The first site at Winston-Salem, North Carolina started enrollment and recruitment. 34,000 recruitment mailings were sent out and currently there are 24 participants randomized. The study also has ancillary studies that will focus on brain imaging, sleep and the gut microbiome.

3. MIND CHINA

Prevalence of dementia is more in rural than urban areas. The goal of the study was to test whether multimodal intervention programs help cognitive and physical functioning in the rural dwelling. The study involves vascular risk interventions and a multimodal intervention. This is a cluster-randomized controlled multimodal intervention study, where a cluster is the village. Age 60-79 year olds, exclusion criteria people with dementia, who have a disability/severely impaired.

4. Singapore: SINGER

The SINGER study conducted randomized clinical trials of multiple interventions in elderly patients at risk of cognitive decline. People were enrolled in either FINGER or SINGER intervention models. For SINGER, exercise will be in an exercise facility and there was an adaptation to the diet, for example Asian type fruits. In addition, evaluations for SINGER will use pen and paper, while FINGER will be computerized. SINGER is currently in the 3rd intake and hope to finish studies next year

5. Australia Maintain Your Brain (MYB)

MYB is an internet based study with a primary outcome of decreased cognitive decline over 3 years, a secondary outcome is decreased incidence of dementia over 8 years.

Participants were recruited from *45 and Up Study* that had 267,000 people. The target of Maintain Your Brain is 8,000. There are 2 groups: internet coaching and an information group. Cognition is measured using Cogstate and Cambridge Brain Science and the domains tested are Verbal Paired Associates learning, visual memory, executive function, speed of information processing, working memory. For testing of function the Amsterdam Short Term Memory Test is being used.

The study has completed validation and most completed year 1. Invitations were sent to 96,000 and 14,000 consented which resulted in 6,236 being randomized.

6. Australia AU ARROW

AU AAROW will have 3 sites and they will incorporate the same trial design as U.S. POINTER. The primary outcome is cognition and the examples of secondary outcomes are blood and CSF biomarkers, brain amyloid imaging FDG PET, MRI. The team is currently seeking funding.

7. Europe GOIZ-ZAINDU

GOIZ-ZAINDU is in the Basque country, they will adapt the FINGER study to the area and plan to demonstrate feasibility in the general population. This study is a 1-year multi-modal intervention program including people over 60 years in age, not demented but must test below expected cognitive test performance.

8. Europe (SPAIN) PENSA

The PENSA study will evaluate the efficacy of epigallocatechin gallat (EGCG) in a randomized double blind trial. This study will include a home based cognition test and have an exercise component.

9. EURO-UK

EURO-UK studies are ready for 5- and 7-year follow-ups and will start 10 year follow up next year. There is a need to identify the right at risk target individuals. Results have found lower risk of functional decline, better health related quality of life, 60% lowered risk for multi-morbidity, 20% lower risk for hospitalization.

- MIND AD
 - This has the same format as FINGER with a target group of prodromal AD defined with biomarkers. The goal is 125 participants. 1 arm multimodal intervention and medical food.
- UK FINGER
 - APOE enrichment, complex multi-domain intervention and pharma contribution (drug repurposing approach); new technology (repeated measures, follow up).
- EURO-FINGERS: there will be a master protocol and each country will have their own section. There will also be an online registry for recruitment.

10. CANADA THUMBS UP

Canada THUMBS UP currently has partial funding with an expected project launch of January 2020 of Phase A recruitment of a trial ready cohort of 2,000, there will be 2 phases with an emphasis on people with increased risk.

11. Latin America (LATAM)

LATAM is an initiative to develop joint regional efforts for the prevention of cognitive deterioration and dementia and share, compare and harmonize data. Twenty-nine Latin countries are interested consisting of high income and upper middle income, there are currently no low and middle income countries.

Sample size is 100 elderly adults per country, 60-77 years old, at risk of cognitive deterioration (50 per group: control and intervention). The study will evaluate self-guided versus more structured intervention and will evaluate participants at 6 and 12 months.

12. INDIA

Challenges for this study include diversity of language, education and socioeconomic factors. The study in India includes an Urban cohort -Tata longitudinal study of Aging (TLSA) and Rural Cohort Srinivaspura Gaging, Neuroscience... (SANSCOG). Populations for each group are: SANSCOG n=20,000, TLSA n=10,000. Urban cohort is high in diabetes, cholesterol, homocysteine, body mass index and white matter hyperintensity.

13. JAPAN J-MINT

The J-MINT study started 2 months ago and is a multicenter open-label randomized control trial with participants aged 65-85 years who have mild cognitive dysfunction. The study excludes individuals with a MMSE score less than 24.

There is a multicomponent exercise program and also a diet component. They will use a sensitive composite score as primary outcome and measure plasma biomarkers, development of polygenic risk score, mechanism of cognitive improvement, etc.

14. South Korea: Superbrain

Study to prevent cognitive impairment and protect brain health through lifestyle intervention. Participants who have vascular and metabolic risk factors and will engage in cognitive training, social activity, exercise and nutrition.

Outcome measures are: RBANS, MMSE, CDR, motivational questionnaires, sleep questionnaire, exploratory evaluation such as the microbiome, etc. The sample size is 150 participants and the study is single blind with 2 doctor's visits and 6 nurse visits every 4 weeks. Exercise program 3 times per week, 60 minutes, implement support videos for the participants.

15. Data Sharing

The objective is to have a consensus and the main recommendation is to facilitate data sharing as early as possible where standardization, data acquisition techniques and assessments should be included. Screening and pre-randomization baseline data should be available within 12 months of study completion.

What data sharing can mean: 2 main alternatives, share the actual individual level data (files) between the partners in the network and maybe making them available for people outside of the network. It was a recommendation to identify a minimal data set (MDS) proposal, the characteristics will be simple and no room for interpretation. Anonymization can be difficult in different countries.