,,

Joint Programming Neurodegenerative Disease

Joint Transnational Call for Proposals

European research projects for Pilot Studies on Preventive Strategies related to Neurodegenerative Diseases

Final Report

Please submit electronically to:
sabrina.voss@dlr.de or olaf.krueger.1@dlr.de

JPND Joint Call Secretariat
Dr. Sabrina Voss
Dr. Olaf Krüger
DLR Project Management Agency
German Aerospace Center
Health Research

I General Information

1. Acronym of the collaborative project:
MIND-AD

2. Full Title of the project:
Multimodal preventive trials for Alzheimer's Disease: towards multinational strategies

3. Project Runtime:
Please indicate the start and end date of the project, and potential extensions.

Start date: 1st January 2015
End date: 31st December 2018
Extensions: 31st December 2019 (applicable for some of the RCT sites)

4. Project Coordinator:

Partner 1

Name PI	Professor Miia Kivipelto
Institution/Department	Karolinska Institutet, Department of Neurobiology, Care Sciences and Society. Division of Clinical Geriatrics, Center for Alzheimer Research
Address	Karolinska vägen 37 A, 171 64 Stockholm
Country	Sweden
Phone	+46 (0)73 99 409 22
Email	miia.kivipelto@ki.se
Funding organisation	Vetenskapsrådet (VR)

5. Project Partners:

Partner 2

Name PI	Hilkka Soininen
Institution/Department	Institute of Clinical Medicine, Dept. of Neurology, University of Eastern Finland
Address	Yliopistonranta 1C, 70211 Kuopio
Country	Finland
Phone	00358-40-5735749
Email	hilkka.soininen@uef.fi
Funding organisation	Academy of Finland

Partner 3

Name PI	Prof. Dr. Tobias Hartmann

Institution/Department	Saarland Universität, Deutsches Institut für Demenzprävention
Address	Kirrberger Str. 100 Gebaude 90.1
Country	Germany
Phone	491726256049
Email	Tobias.hartmann@mx.uni-saarland.de
Funding organisation	BMBF

Partner 4

Name PI	Professor Sandrine Andrieu
Institution/Department	Université de Toulouse – INSERM UMR1027
Address	37 allées Jules Guesde, 31062 Toulouse
Country	France
Phone	+33 (0)5 61 14 59 32
Email	sandrine.andrieu@univ-tlse3.fr
Funding organisation	ANR

Partner 5

Name PI	Edo Richard
Institution/Department	Radbound University Medical Center
Address	Houtlaan 4, 6525 XZ Nijmegen, Netherlands
Country	The Netherlands
Phone	+31 (0)24 361 66 00
Email	Edo.Richard@radboudumc.nl
Funding organisation	The Netherlands Organisation for Health Research and Development

Partner 6

Name PI	
Institution/Department	
Address	
Country	
Phone	
Email	
Funding organisation	

External collaborators: Martin Knapp, London School of Economics and Political Science, UK; Carol Brayne, University of Cambride, UK; Patrizia Mecocci, University of Perugia, Italy; Jyrki Lötjönen, VTT Technical Research Center of Finland, Laus Broersen, Nutricia; Alzheimer Europe; Alzheimer's Disease International (ADI)

6. Amendments in the budget of the project:

Please mention any amendments in the budget of the project.

In Sweden, Professor Kivipelto applied for a no-cost extension until December 2019. This extension was approved by JPND and Swedish Research Council. She also applied for and obtained additional funding from *Alzheimerfonden and local Region Stockholm grants (ALF)*, allowing for an additional 6 months extension to the RCT.

7 Amendments in the composition of the consortia:

Please mention any amendments in the composition of the consortia during the project. Are some partners added in the consortia or did partners leave the consortia? If so, please indicate which partner left/ was added. Please also indicate the reasons and rationale for change in the composition of the consortia.

In Germany subcontracting partner (Prof. Schröder) was replaced by Prof. Pantel because the finalization date of the clinical trial had collided with his retirement.

Toulouse University hospital (CHU Toulouse) was added as a partner in order to conduct the French part of the pilot trial. Funding was transferred from Toulouse University/INSERM to CHU Toulouse, in agreement with the French funding agency (ANR).

II. Lay Abstract of the project and its achievements (200-400 words)

Please briefly summarize the project including its achievements and main conclusions in lay speech. **This abstract will be published online and may be used for the JPND webpage as well as for webpages of the JPND joint call partner organisations.**

The goal of MIND-AD project is to optimise existing infrastructures based on 5 dementia/Alzheimer's disease (AD) prevention trials, and to create a unique opportunity for rapid integration of knowledge, and harmonisation of methods and outcome measures across Europe. Its innovative approach consists of multimodal interventions, the inclusion of novel modes of delivery (e.g. computer-based cognitive training, internet-based prevention strategies, medical food with a specific nutrient combination), the inclusion of critical feed-back from the users (trial participants), and synergistic use of data from several European pioneering dementia prevention trials with over 10 000 participants.

MIND-AD$_{mini}$ trial is a 6-month, randomized, controlled, multicenter trial among individuals with prodromal AD with lifestyle and/or vascular risk factors. The four trial sites were: Sweden, Finland, Germany, and France (total N = 93). Participants were randomized into 3 trial arms: multimodal lifestyle/vascular intervention; multimodal lifestyle/vascular intervention + medical food; and control. The FINGER-based lifestyle intervention includes diet, exercise, cognitive training and vascular risk management. The primary outcome is feasibility of the multimodal intervention (recruitment rate, overall adherence to the intervention, retention rate). Secondary outcomes are adherence to intervention components and lifestyle changes. Exploratory outcomes: changes in vascular/metabolic risk factors, depressive symptoms, perceived stress, health-related quality of life, physical performance, biomarkers, participant experiences, self-reported adherence to intervention components. The MIND-AD pilot trial will provide novel results among individuals with prodromal AD, a group that is currently lacking effective interventions. It provides the first tools for further combination therapies (non-pharma + pharma) and informs larger efficacy prevention trials within EURO-FINGERS and World-Wide FINGERS (initiated by the applicant M. Kivipelto).

The MIND-AD project has provided novel and valuable results on the biological mechanisms underlying lifestyle interventions, including data from neuroimaging, blood-base biomarkers, genetics, among others. For example, data from blood-based biomarkers indicate that in prodromal AD, it is possible to estimate the treatment response already before treatment is initiated. The project results also demonstrate the cost-effectiveness of multimodal interventions. Results have also informed on the suitability of individuals / patients with prodromal AD as a target group in multi-national prevention trials.

The multi-national nature of the MIND-AD consortium provided unique data on facilitators and barriers regarding older European adults' needs, expectations, and attitudes towards participating in clinical trials and adhering to preventive interventions. Qualitative data (from participant interviews and focus groups) showed that altruism, a motivation to improve one's lifestyle and to maintain autonomy, as well as enhanced medical monitoring are factors that motivated older adults to participate in such trials.

The collective knowledge from the project also led to the contribution of evidence for the first WHO guidelines for dementia risk reduction (Prof. Kivipelto key working group member), and are setting the platform for the next generation of dementia prevention interventions.

III. Description of the project and its results

This section is for internal use by the JPND joint call partner organisations. Please also describe potential problems and highlights so we can shape our future call scheme. This information will not be published.

1. Structure of the project

1.1. Work packages of the project

Please allocate the work packages/tasks of the projects to partners involved. When referring to your partners, please use the numbering applied in section I. "General information" (e.g. "partner 1" or "P1")

WP (or the like)	**Title** (subtitles, if applicable)	**Partner N°**
1	WP1. Project coordination: month 1-36 (leader KI)	1 (KI)
2	WP2. Effects, mechanisms and mediating pathways of multimodal preventive interventions: month 1-30 (leader UEF, USAAR)	2 & 3 (UEF & Saarland)
3	WP3. Facilitators and barriers to participation in adherence to preventive interventions (ACCEPT-HATICE): month 1-30 (leader INSERM).	4 (INSERM)
4	WP4. Patients with prodromal AD as target group in prevention trials: month 1-18 (leader UEF).	2 (UEF)
5	WP5. MIND-ADMINI pilot trial, multimodal intervention in memory clinic patients: month 18-36.	1 (KI)
6	WP6. Guidelines and recommendations for AD/dementia prevention: month 24-36 (leader AMC)	6 AMC

Add lines as appropriate

1.2. Project report of goals, tasks and milestones (3 pages max)

Please describe the initially planned goals, tasks and milestones for each work package and for the overall project. Please indicate the respective partners involved by using the numbering applied in section I. General information (e.g. "partner 1" or "P1").

Overall project goals

The MIND-AD consortium combines and optimises existing infrastructures based on 5 pioneering AD/dementia prevention trials, creating an exclusive opportunity for rapid integration of knowledge, and harmonisation of methods and outcome measures across Europe. The aims were to formulate guidelines and recommendations for effective interventions in different risk groups, and for large multinational trials covering the entire spectrum of AD. The consortium investigated:

1. In at-risk community-dwelling elderly people
- Efficacy and mechanisms of different multimodal preventive interventions by synergistic use of data from the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER, Finland), Multidomain Alzheimer Preventive Trial (MAPT, France), and Prevention of Dementia by Intensive Vascular Care (PreDIVA, Netherlands)

• Facilitators of and barriers to effective prevention across Europe (ACCEPT-HATICE, ancillary study to the Healthy Aging through Internet Counselling in the Elderly (HATICE) trial).

2. In patients with prodromal AD
• Implementation and impact of new criteria for prodromal AD, used for the first time in the ongoing multinational Medical Nutrition in Prodromal Alzheimer's Disease (LipiDiDiet) trial.
• Conducting a proof-of-concept multinational pilot trial (MIND-AD$_{MINI}$) evaluating the feasibility of a multimodal preventive intervention in patients with prodromal AD (intervention based on FINGER, MAPT, PreDIVA, and LipiDiDiet). MIND-AD$_{MINI}$ represents a practical model for future large-scale multinational RCTs in prodromal AD with disease-modifying drugs in combination with vascular/lifestyle interventions.
3. Integrated preventive strategies across Europe
• Guidelines and recommendations for preventive strategies, and for multinational and multimodal prevention RCTs with community/clinic-based approaches.
• Planning larger Pan-European AD/dementia prevention trials (MIND-AD $_{MAX}$I). This new approach consists of multimodal interventions, novel modes of delivery, critical feed-back from trial participants, and synergistic use of data from several pioneering European trials d over 10 000 trial participants. The MIND-AD consortium is unique worldwide in providing extensive practical experience and expertise covering the entire spectrum of AD prevention from community to the clinic.

Goals, tasks and milestones for each work package

WP1: Coordination and management (Partner #: 1).

The goal of the coordination and management WP was to coordinate and monitor the project within time and budget constraints, and ensure that deliverables and milestones are produced as scheduled.

Deliverables: D1.1. Fully functional project website (M6); D1.2. GA meetings (2 per year) (M12, 24, 36).

WP2: Effects mechanisms and mediating pathways of multimodal preventive interventions (Partners #: 2 & 3).

The objectives of this WP were to:
- Investigate the effects of multimodal interventions on cognitive functioning, AD/dementia incidence, disability, daily life functioning, blood and imaging biomarkers
- Formulate biomarker profiles

Deliverables: D2.1. Report on multimodal intervention effects on cognition (M18), AD/dementia (M30), disability & daily life functioning (M20), and biomarkers (M20)
D2.2. Biomarker profiles for predicting cognitive decline, and for identifying at-risk elderly most likely to respond to preventive interventions (M24)

WP3. Facilitators and barriers to participation in adherence to preventive interventions (ACCEPT-HATICE): month 1-30 (Partner #: 4).

The objectives of this WP were to:
- Study the determinants of participation of European older adults in a multi-domain prevention trial
- Determine the rate of participation in an internet-based prevention trial amongst eligible

individuals; to identify facilitators and barriers to participation; to assess the level of knowledge about prevention; and to examine willingness to undergo biomarker testing to determine eligibility for preventive interventions (which may also disclose an individual's risk of AD)

Deliverables: D3.1. Report on motivations and barriers to participation and adherence in prevention RCTs (M30)
D3.2. Report on willingness to undergo biomarker testing and attitudes towards AD risk disclosure (M30)

WP4: Patients with prodromal AD as target group in prevention trials (Partner #: 2).

The objectives of this WP were to:
- Investigate how diagnostic criteria for prodromal AD are applied in different countries
- Formulate biomarker profiles for predicting cognitive decline in prodromal AD, and for identifying patients who are most likely to respond to a preventive intervention
- Assess the impact of disclosure of prodromal AD status on patients and their families
- Assess facilitators of and barriers to effective preventive interventions in patients with prodromal AD

Deliverables: D4.1. Report on implementation of diagnostic criteria for prodromal AD in different countries (M12)
D4.2. Biomarker profiles to predicting cognitive decline in prodromal AD, and for identifying patients most likely to respond to preventive interventions (M18)
D4.3. Recommendations concerning disclosure of prodromal AD status, and improving participation in prevention trials in patients with prodromal AD (M18).

WP5: MIND-AD$_{MINI}$ pilot trial, multimodal intervention in memory clinics (Partner #: 5).

The main objectives of the MIND-AD$_{MINI}$ pilot trial were to:
- Formulate a multimodal intervention protocol adjusted for memory clinic patients with prodromal AD
- Conduct a 6-month multimodal RCT in memory clinic patients with prodromal AD
- Evaluate the feasibility and adherence to the multimodal intervention (primary outcome)
- Investigate intervention effects on AD-related biomarkers and cognition (secondary/exploratory outcomes)

Deliverables: D5.1. Multimodal intervention study protocol for RCT for patients with prodromal AD (M20)
D5.2. Report on intervention feasibility, adherence and secondary outcomes (M36)

WP6. Task 6.1.2. Cost effectiveness analysis (Partner #: 6).

The objectives of this WP are to:
- Assess cost-effectiveness for different intervention types and modes of delivery
- Formulate guidelines and recommendations for practical preventive strategies (at-risk elderly people from the general population, patients with prodromal AD)
- Formulate guidelines and recommendations for multinational and multimodal prevention trials

Deliverables: D6.1. Report on cost-effectiveness for different intervention types and modes of delivery (M30)
D6.2. Guidelines and recommendations for practical preventive strategies (M36)
D6.3. Guidelines and recommendations for multinational and multimodal prevention trials (M36)

2. Delivery of the project

2.1. Major achievements of each work package and of the overall project

Overall achievements:

The major achievements are the following:

The completion of the MIND-AD$_{MINI}$ trial: a 6-month, randomized, controlled, multicenter trial among individuals with prodromal AD with lifestyle and/or vascular risk factors. The four trial sites were: Sweden, Finland, Germany, and France (total N = 93).

The MIND-AD project has provided novel and valuable results on the biological mechanisms, including data from neuroimaging, blood-base biomarkers, genetics, among others.

The project results also demonstrate the cost-effectiveness of the multimodal interventions.

Results have also informed on the suitability of individuals / patients with prodromal AD as a target group in multi-national prevention trials.

The multi-national nature of the MIND-AD consortium provided data on facilitators and barriers and older European adults' needs, expectations, and attitudes towards participating in clinical trials and adhering to preventive interventions.

MIND-AD is informing currently planned multi-national multidomain trials combining pharmacological and non-pharmacological approaches.

Achievements of each work package:

WP1: Coordination and management.

This WP has been led by Prof. M. Kivipelto (KI), with the assistance of colleagues Alina Solomon, MD, PhD (KI and UEF) and Shireen Sindi, PhD (KI) who are responsible for the scientific and clinical management of the project, as well as communication. They are also in charge of organizing the internal communication structure among the partners and external collaborators, as well as ensuring intellectual property protection and ethical implementation. At the start of the project (January 2015), a kick-off meeting was organized in Stockholm, where all participating members and partners attended, and the project goals were presented along with concrete plans. Following the kick-off meeting, a General Assembly (GA) meeting was organized every 6 months in alternating locations (e.g. Amsterdam, Paris, Stockholm). Within the first six months, a project website was developed as planned. The coordination team communicated with all project partners to follow-up on the progress and identify support in a proactive manner. In between the GA meetings, teleconferences were organized for specific project goals (e.g. biomarker analyses, conduct of the clinical trial), ensuring adequate communication, guidance and progress. An annual progress report has been submitted to JPND, summarizing project activities, achievements and outcomes during the previous year of the project. The team administrators have taken on the responsibilities regarding the financial, technical and organizational administration, with support from the Clinical Geriatrics division administrative team and the Grants Office at Karolinska Institute.

WP2: Effects mechanisms and mediating pathways of multimodal preventive intervention

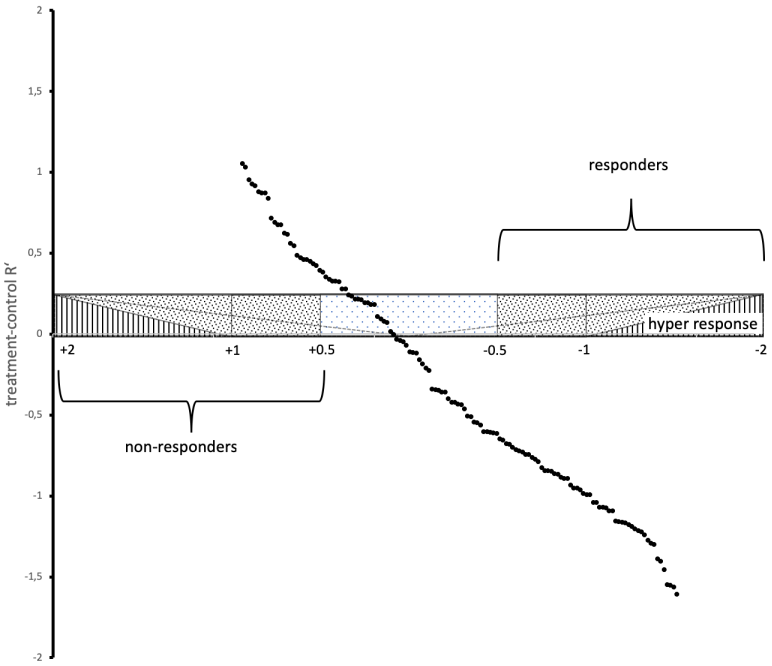
Following the main findings from the FINGER trial (Lancet 2015) showing beneficial effects on the primary cognitive outcome and several secondary outcomes, the team has been conducting more detailed analyses:
a) APOEε4 carriers versus non-carriers (manuscript published, Solomon et al. JAMA Neurol. 2018 Apr 1;75(4):462-470.). In the stratified analyses, APOE4 carriers showed clear beneficial effects supporting the earlier findings that APOE4 carriers may be more vulnerable for unhealthy lifestyle factors and suggesting that it may be a suitable target group for preventive interventions. However, APOE ε4 allele did not significantly modify the response to intervention (interaction term non-significant) and thus, the intervention can be considered beneficial regardless of genetic susceptibility to dementia.
b) Baseline telomere length (manuscript published, Sindi et al. J Alzheimers Dis. 2017;59(4):1459-1470). The cognitive benefits of the FINGER intervention were more pronounced with shorter baseline LTL, that is among higher-risk individuals.
c) Baseline C-reactive protein (CRP, manuscript published, Martiskainenet al. Ann Clin Transl Neurol. 2018;5(10):1229-1240). The data suggest that the APOE ε4 allele associates with lower levels of hs-CRP in individuals without dementia.
d) Men versus women; Younger versus older age at baseline; Lower versus higher education level; Lower versus higher baseline cognition (MMSE score) (article published Rosenberg A et al. Alzheimers Dement. 2018 Mar;14(3):263-270). None of these baseline characteristics modified the response to which was, therefore, beneficial regardless of sex, age, level of education, income status, baseline cognition, and cardiovascular risk profile. This indicates that the FINGER type of intervention may be beneficial for a large group of at risk elderly persons from general population
h) Subgroup analyses according to baseline brain MRI measures (manuscript published, Stephen et al. J Alzheimers Dis. 2017;59(2):695-705). Higher CAIDE score was related to more pronounced deep white matter lesions, lower gray matter and hippocampal volume, lower cortical thickness, and poorer cognition as well as medial temporal lobe atrophy, but not to brain amyloid load.
Health-related quality of life (manuscript published, Strandberg et al. Eur Ger Med. 2017;8(2):164-167. There was a statistically significant beneficial effect of intervention on the change in general health and physical function at 12 and 24 months.
Disability / daily functioning (manuscript published, Kulmala et al. J Am Geriatr Soc. 2019 Feb 26. doi: 10.1111/jgs.15837). The 2-year FINGER lifestyle intervention was able to maintain the daily functioning of the at-risk older population.
Dementia / longer-term cognitive decline: The extended 7-year follow-up visit of the FINGER trial was completed in the second half of 2018. New MRI scans have been conducted at the Kuopio site. The analysis related to the BioPlex measurements of 42 metabolic and inflammation-related markers in 800 FINGER participants (samples from the 2-year visit) was completed in 2018.

The following articles were also published:
Pentikäinen et al. J Alzheimers Dis. 2019 Feb 20. doi: 10.3233/JAD-180897. Over two years FINGER intervention, cardiorespiratory fitness was associated with executive functions and processing speed, and was related also to the overall cognitive function.
Martikainen et al. AJNR Am J Neuroradiol. 2019 Jan;40(1):80-85. A significant association between increases in brain β-amyloid and reductions in regional gray matter volume in individuals at increased risk of cognitive decline was found. This is consistent with a model in which increases in β-amyloid incite neurodegeneration in memory systems before cognitive impairment manifests.

Work is also ongoing on joint analyses using pooled data from the FINGER, MAPT and PreDIVA trials, e.g. intervention effects on blood pressure, blood lipids, body mass index, glucose as well as CAIDE and FINRISK risk scores, which have also been used to carry out sensitivity analysis on selected subpopulations at increased risk of CVD and cognitive impairment.

Predictive biomarkers: In this part of the work we aimed to identify commonalities in biomarker changes across the different prevention trials. Those can be separated into two generally different approaches: 1) *Baseline predictive*. The aim is to identify biomarkers which individually or as a pattern predict a) disease progression for the next 2 years for untreated trial participants/control group participants, or b) treatment response prediction, i.e. to identify who likely will respond / not respond to the treatment (heterogeneity of response).
2) *Outcome overlap*. a) one aim is to identify biomarkers which, despite utilizing a different intervention did change in a similar fashion to the intervention. This is important because it provides insight into intervention relevant mechanisms which may be used to develop more advanced interventions. B) another aim is to identify biomarkers which – already after a period of intervention – correlate with cognitive/functional performance changes which would be observable only after longer treatment duration; this is important because it would allow to stop an ineffective treatment approach early and replace it by another treatment.
No established biomarkers were previously known which would predict for an interventio of the cognitive-functional outcome. This may in part be due to the facts that treatment response in pre-clinical AD is a topic that only very recently became scientifically accessible. The critical factor in these studies is that they largely depend on that the trial actually showed a significant and sufficiently strong benefit that would be (clinically) meaningful. Most interventions in AD are not. Moreover, there are just a few prevention/early intervention trials in AD at all. In MIND-AD we have the rare opportunity that with the FINGER and LipiDiDiet trials we have two interventions which found several significant beneficial outcomes.

Baseline predictive: We identified several biomarkers which predict treatment response. This is based on the individual biomarker x treatment outcome correlations of the untreated arm participants subtracted from the correlations of the treatment arm participants. As expected, the untreated predictions, which are equivalent to the correlation between biomarker and disease progression, were less strong towards a beneficial development, as compared to the treatment arm. In the example below, a phosphatidylcholine (PC) subset of a lipidomics biomarker scan of 138 trial participants baseline subsamples correlated with CDR-SB outcome at 24 months, showed strong correlation with certain PC lipid species. In this case all biomarkers with R' below -0.5 are considered predictive for treatment response. Very strong response (below -1.0) are from trial participants predicted to would have encountered less severe disease progression without treatment and randomized to the treatment arm would have encountered an additional benefit induced by the intervention. From a baseline perspective, these would have been hyper responder. Non-responders were categorized as such if biomarker levels predicted an R' of +0.5 or higher.
Some biomarkers were previously identified as 'risk' biomarkers, i.e. biomarkers which predict dementia. In the untreated population one would expect that those biomarkers appear, because the risk reducing effect technically mimics a treatment effect in the control population. For the PC analysis of this example, according to the existing literature, arguably docosahexaenoic acid (DHA) may score as predictor. With R -0.62 DHA was among the top protective scoring PC-lipid species in the control group. DHA was not predictive in the treatment group, because treatment included DHA.



Prognostic biomarkers at baseline identify cognitive-functional response expected 2 years later *Preliminary results from MIND-AD baseline lipidomics levels predict the individual's treatment response. Each dot (black circles) represents one phosphatidylcholine species, or a specific pattern of such. Value given is: R'=correlation of baseline lipid level with CDR-SB change over 24 months, R treated – R untreated group. Lower (negative) R' values represent higher likelihood of a beneficial (cognitive/functional) response. For the responder group several biomarkers or patterns of such were identified which predict response (dark background) or very strong response (vertical lines). Analyzed subsample n=138 completer participants with baseline and 24 months data available, maximum correlation observed in treatment group R=-0.923 and untreated group R=0.734.*

Outcome overlap: Besides the expected changes in molecules increased directly by the treatment, some other changes were also very pronounced e.g. blood homocysteine (Hcy, –30%, p<0.0001) and Hcy> 11.3µM represented CDR-SB responder group (p=0.038 in ITT and p=0.005 in PP). As expected baseline Hcy also influenced outcome in total cholesterol, HDL-cholesterol. Hcy can readily be measured during routine blood clinical lab analysis. For ApoE our results with a lipid-based multinutrient intervention suggests that many differences between apoe protective and risk allele carriers may not be visible at baseline, but may only become apparent upon treatment. The strongest change in PC lipid species (besides used in the study product) was observed for PC38:0 was consistently increased in treated LipiDiDiet patients (p<0.0001) accompanied by a reduction in e.g. PC36:2 (p<0.0001). Already for PC analysis 22 lipid species with a significance level of p<0.0001 compared to control were observed.
We also observed biomarkers which overlapped between control arm and intervention arm. E.g. some PC32 lipid species appeared with similar inverse correlation (R -0.40 and -0.39) which would indicate that this lipid species is moderately indicative of slow disease progression and less predictive for treatment response.
For technical reasons FINGER analysis involved four groups (high intensity intervention with best and worst responders, and low intensity intervention with best and worst responders). We observed significant changes in LC-PUFA, separating responders from non-responders and treatment already at the lyso-lipid level. For PCaa low-intensity non-responders could be clearly separated from others, a pattern also observed for PCae, sphingomyelins and carnitines.
Importantly, we identified several biomarkers which overlapped between the FINGER and the LipiDiDiet trial, this included the expected LC-PUFA, but also saturated/monosaturated fatty

acids >PC36. This would be in line with an interpretation that despite the difference in the intervention both induce some metabolic changes which are similar and appear to be linked with a more beneficial outcome.

Classical AD biomarkers: Aß, tau and imaging biomarkers were used to validate AD as underlying disease (Soininen et al 2017). Approx. 9 out of 10 LipiDiDiet participants were found to qualify as AD according to IWG, IWG2, NIAA and NIAA2018. Several other biomarkers results (e.g. β-secretase, γ-secretase, IL1, IL6, TNFα) were in this study initially inferior to the lipidomics results and focus continued thus on the lipidomics results. Thus, data showed more promise when analyzed in combination.

Limitations: 1) The work of this project was limited to the 2-year treatment time of LipiDiDiet and Finger intervention studies. Thus, slow response, or slow or non-linear progression may not or incorrectly be monitored in this analysis. Considering the longer duration of prodromal/MCI-AD stage and the considerably longer duration of the at-risk stage of the FINGER population this is a short-moderate period. Future studies should make use of the 8-year longitudinal data which are/will become available in 2019. 2) The work in this project was limited to two intervention trials. Future work should include more trials and develop advanced approaches to integrate data from different trial sources to achieve reliable validation. 3) In this study we focused on multiple single biomarkers, in explorative ways we analyzed some biomarker patterns, which also resulted in strong predictors. Future work may specifically look at biomarker patters, including different biomarker types, including clinical data. 4) This analysis is inherently different from diagnostic biomarkers, which aim to identify a discrete aspect (to identify one disease), whereas this work aims to identify a gradual aspect (level of response in the treatment arm or level of disease progression in the control arm). Future work, especially if long-term samples and data become available, may be able to link predictive value with percentage gained in reduced disease progression. 5) This work is retrospective by design and did not address manifest dementia due to the absence of accessible non-symptomatic treatment benefits in this target group.
If addressed together this could identify generally applicable, cross trial validated biomarkers.

Conclusion: This study showed that, if a trial actually had intervention benefits, the treatment response can indeed be correlated to predictive biomarkers.
The results also indicate that it is possible, in early AD, to predict the individual's treatment response already before treatment is initiated and that treatment response may be monitored by surrogate biomarkers before a potential cognitive benefit becomes observable.
To our knowledge this is the first observation that cognitive-functional intervention benefit can be predicted based on (multiple) biomarker levels in early AD. Further work, highlighted by several limitations identified, will be needed before clinical relevance may be addressed.

WP3. Facilitators and barriers to participation in adherence to preventive interventions (ACCEPT-HATICE): month 1-30 (leader INSERM).

Within WP3, the ACCEPT-HATICE study was designed and conducted with the aims of (i) exploring older European adults' reasons for participating in an eHealth prevention trial, (ii) comparing motivations between countries, and (iii) assessing the influence of using an Internet intervention on the decision to participate. ACCEPT-HATICE was an ancillary study to the HATICE trial (an FP7-funded project), and was conducted in France, Finland and the Netherlands. The study design employed mixed methods, involving both quantitative (self-completion online questionnaire) and qualitative approaches (semi-structured face to face interviews). A total of 341 individuals completed an online self-completed questionnaire, and 46 took part in semi-structured interviews.

Results, combining both the quantitative and qualitative approaches, showed that altruism and personal benefits (wanting to improve one's lifestyle; receiving additional medical monitoring) motivated older adults to participate in the trial. Emphasizing such aspects could facilitate recruitment in future RCTs. Additional medical monitoring was particularly important when access to public health care was perceived as limited, especially in Finland. Furthermore, maintaining autonomy and preventing functional dependency emerged as a key underlying motivation amongst these young older adults. Although some trial design features influenced the decision to participate, the use of an eHealth intervention was not an important motivator.

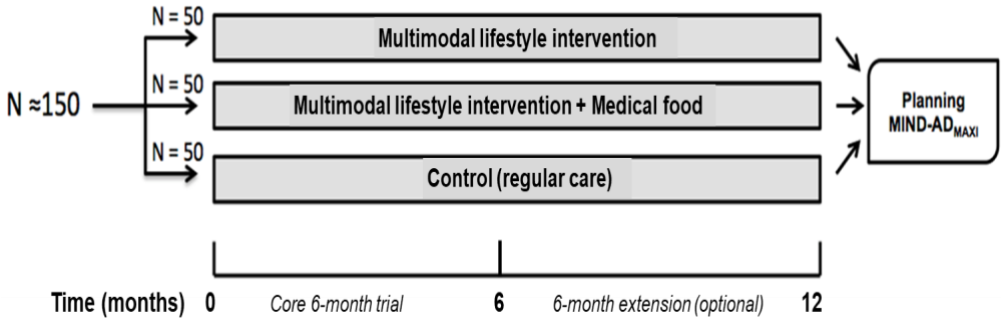
This study has been presented at five scientific conferences, and it has so far given rise to one publication (Coley N et al. J Am Med Dir Assoc. 2018; Impact factor 5.325). A second manuscript is has been published: Rosenberg, A., Coley, N., Soulier, A. et al. Experiences of dementia and attitude towards prevention: a qualitative study among older adults participating in a prevention trial. BMC Geriatr 20, 99 (2020). https://doi.org/10.1186/s12877-020-1493-4

WP4: Patients with prodromal AD as target group in prevention trials

After the publication of the main LipiDiDiet trial results in2017 showing promising results after 2 years of treatment with the medical food product (Fortasyn Connect®) in a large RCT in subjects with prodromal AD (Soininen et al. *Lancet Neurol*. 2017 Dec;16(12):965-975. Epub 2017 Oct 30), other analysis have been ongoing within the MIND-AD project to better assess the prodromal AD as a target group in prevention trials:
1) Impact of classification based on different diagnostic criteria (IWG-2, NIA-AA 2011 & 2018) on change in cognition/function and progression to dementia (Rosenberg A et a., submitted)
2) Predictors of cognitive/functional decline and progression to dementia in prodromal AD (e.g. demographics, cognitive performance, biomarkers, lifestyle-related risk factors, and comorbidity)
3) Intervention effects on exploratory outcomes (13-item ADAS-cog, MMSE, ADCS-ADL, MADRS (depressive symptoms), CSF and plasma biomarkers, fatty acid profile, nutritional and anthropometric parameters (BMI, hip-waist circumference)
4) Heterogeneity of treatment effects (baseline characteristics of trial participants as potential effect modifiers).
5) Predicting cognitive decline and response to intervention based on biomarker profiles.
6) Qualitative analysis (Kuopio) on the impact of disclosure of prodromal AD status on patients and their families, as well as facilitators of and barriers for preventive interventions in patients with prodromal AD.
The last optional extension of the LipiDiDiet trial was also completed in 2018, bringing the total trial duration up to 7 years, the longest of all AD trials to date. The following data analysis have been conducted:
I) Intervention effects on primary and secondary outcomes during 36 months (measures of cognition, function, and disease progression) showing .sustained positive effects on CDR and hippocampal volume after 3 years.[183](presentation ADPD. Lisbon, Portugal; 2019, manuscript submitted for publication) .

WP5: MIND-AD$_{MINI}$ pilot trial, multimodal intervention in memory clinics

The MIND-AD pilot trial has been carried out in the following countries: Sweden, Finland, Germany, and France. The trial has been completed in all countries, including completion of the extended 6 months follow-up in Sweden.



Accomplishments thus far include the following:

- Ethical approval: All trial sites have obtained ethical approval, and Stockholm obtain an additional approval for a 6-months extension.

- Study material and cognitive training program: Study material (was already available in Finnish based on FINGER trial) was provided to partners in Sweden, Germany and France for translation and usage in their respective trials. The cognitive training program used in MIND-AD has been modified, updated and translated into the respective languages in cooperation with the programmer and the two psychologists in Sweden.

- Teleconferences: In between the GA meetings, the teams conducting the clinical trials have maintained effective communication via general teleconferences to plan the procedures and methods for the clinical trial in consistency with other centres.

  MIND-AD added as member to the World-Wide FINGERS network. World-Wide FINGERS (WW-FINGERS) is a unique network established by Prof. Miia Kivipelto, which aims to support several countries (30+ so far) to develop intervention trials similar to FINGER and MIND-AD, while harmonizing methods, sharing experiences and adapting the interventions to local settings and cultures. MIND-AD is a core member of WW-FINGERS and as the first model of combination intervention (non-pharma + pharma approach) is used as a model for upcoming next generation of dementia prevention clinical trials.
- The trial has been completed and database closed after the final monitoring visit (April 2020). The study protocol and progress report manuscript has been finalized and several other articles under preparation.

Summary for each clinical trial site:

FINLAND

Ethical approval for the MIND-AD$_{MINI}$ trial in Kuopio was obtained in September 2017, and the first participants were randomized in November 2017. Recruitment was completed in May 2018. In total, 30 participants were randomized. 29 participants completed the trial, and one participant dropped out due to a serious adverse event (not related to the intervention). Feedback from participants was very positive, and adherence to the intervention components was in general high.

In the Kuopio site, participants had their last 6-month visits at the end of October/beginning of November 2018. In total:

- 30 participants randomised
- 45 individuals were screened
- 50 % women, mean age 72.8 years (range 61 – 84 years)
- 1 drop-out due to SAE (not related to intervention)

SWEDEN

MIND-AD$_{MINI}$ trial at the Stockholm site: Ethical approval for the MIND-AD$_{MINI}$ trial in Stockholm was obtained in January 2017, and first participants were randomized in October 2017. Ethical approval for the 6-m extension was obtained in March 2018. Charlotta Thunborg has been the trial site clinical coordinator and offered guidance to the international trial sites (Finland, France and Germany) for their trial set-up and conduct.

At the Karolinska University Hospital memory clinic, 26 participants were randomized and 25 completed the intervention. The last 6 months follow up took place in November 2018. All participants except for three agreed to participate in the 12 months extended follow up.

The first 12-month end-of-study visits took place in October 2019 and the last 12- months end-of-study visit took place in May 2019. One participant dropped out due to SAE not related to the intervention and one did not answer our invitation/calls, and one due to time restraints.

The satellite trial site (Bromma) in Stockholm was added, 10 patients were randomized.

Qualitative interviews were conducted with 8 participants twice and 9 study partners in two focus groups in total, manuscript is in preparation.

In total to date:

- 36 participants randomised
- 44 individuals were screened in total (Huddinge/ (30) Bromma (14))
- 19 participants attended the 12-m follow up in Stockholm during October 2018 to May 2019
- 50% women, mean age 72,3 years (range 60 – 82 years)
- Last 6- months end-of-study visit in Bromma: Dec 2019
- 1 drop-out in Bromma due to time restraint

GERMANY

In Germany the clinical trial was performed by AG Pantel in collaboration with Hartmann, (Homburg), Groneberg (Frankfurt), Eckert (Giessen), Hattinger (Frnakfurt), and Banzer (Frankfurt).

All testing material obtained from the central site, unless already available in German, were locally translated to German in order to keep the uniformity of the study. All activities, including blood sampling and ECG were performed at the facilities of AG Groneberg (Frankfurt). The intervention was according to central protocol. Participants underwent 2 cognitive trainings, one group excursion (group size for all activities was 8) including a museum visit and arts activity. Cognitive training was support by computer-based training at home. Dietary training sessions per group (3x) and individual (3) were performed with AG Eckert. Physical activity

sessions were performed twice weekly in collaboration with AG Banzer. MRI was performed by AG Hattinger. Intervention frequency was 4-5/week.

The trial was finalized in Germany. Data were transferred to the central study site.

In 2018 the Institute of General Practice, Goethe University Frankfurt (Germany) contributed 24 participants to the MIND-AD$_{MINI}$ trial (Prof. Pantel).

In total:

- 24 participants randomized
- 41 individuals screened
- 26 individuals pre-screened
- Mean Age 75 (24 randomized included)
- Women 15 (24 randomized included, 2 drop outs are female)
- SAE 0
- AE 0
- Drop out 2 (due to adverse events, judged to be not study related (stroke and spinalkanalstenosis)

FRANCE

The trial was conducted at a single site in Toulouse. Ethical approval for the MIND-ADmini trial in Toulouse was obtained in November 2018. The official French kick-off meeting for the trial was held on 19/12/2018.
The first participants were randomized in March 2019. In total, 3 participants were randomized. All 3 participants completed the trial (the last end-of-study visit was conducted in early November 2019). In total:
- 4 individuals were screened
- 3 were randomized (2 women and 1 man, aged 65 to 70 years old)

Recruitment rate: The team in Toulouse tried to identify the barriers that could explain the low recruitment rate at their site:

1) Competition with other clinical trials conducted in the Toulouse Clinical Research Centre (CRC). As the CRC is a national leader in participating in Alzheimer's disease clinical trials, including those with similar target populations to the MIND-ADmini trial, recruiting physicians may have preferentially directed eligible patients to more large-scale drug trials that conducted by the center rather than a pilot study.
At the start of the MIND-AD trial in Toulouse, there were 7 other clinical trials (4 phase II and 3 phase III) recruiting at the CRC at that time.

2) The CRC team considered the recruitment phase (6 months) too short to achieve the objectives. The duration of this phase was reduced due to administrative delays (e.g.: requests for clarification from the ethical committee, delays related to administrative procedures between the institution in charge the academic part of the MIND-AD project in Toulouse (the University) and the institution conducting the MIND-ADmini trial (the university hospital)).

3) The CRC teams expressed concerns about the logistics required for a pilot study.

Availability of specialized staff for the multidomain intervention: During the intervention period, the sports educator was absent for 13 weeks (sick leave and maternity leave). Given

the specialization of each multidomain team member and the fact that they didn't anticipate this type of event, they were faced with the difficulty of organizing her replacement. Over the entire study, 5 physical activity sessions had to be cancelled and 4 were replaced by a walk with the psychologist.

Overall experience: In general, the participants were very motivated, and their adherence to the different components of the intervention was high, although it differed for the different domains, and liaising with the study partner for reminders proved to be helpful.

The Toulouse CRC regularly participates in multidomain intervention studies in the general elderly population, but did not have experience of conducting such studies in subjects with prodromal AD.

The multidomain team reported that they did not encounter any particular difficulties regarding the organization or delivering the different parts of the intervention compared to other studies of the general elderly population.
The dynamics was similar, and the only real difference was that they sometimes had to communicate with the study partners regarding the study schedule to ensure that the participants would attend.

WP6. Task 6.1.2. Cost effectiveness analysis (CEA)

We have developed a decision analytic model to evaluate the cost-effectiveness of the FINGER intervention in terms of the incremental cost effectiveness ratio (ICER) with costs per gained QALY (quality adjusted life years) as outcome. The simulation starts in an "at risk state" for two arms, with and without the FINGER program. Furthermore, the effectiveness will also be expressed as the costs per avoided case of dementia and the number needed to treat (NNT) to avoid one case of dementia. The life long simulation model also presents results in terms of the years in severity states in the two simulated arms. For this model we have combined various pieces of evidence and aggregated them in a mathematical model that allows the prediction of dementia, disease progression in dementia, mortality and the costs and quality-adjusted life years associated to this of a population between 50-70 years old at risk of developing dementia. The evidence was obtained from various sources, among which the following:

- Natural progression to dementia in the general population was obtained from the EURODEM study.
- Natural disease progression between states of dementia severity and mortality in dementia states was obtained from the SveDem registry of person with dementia in Sweden.
- Natural mortality was obtained from the Statistics Sweden (SCB).
- Costs and quality of life across the various stages of dementia severity (based on published evidence and based on resource use data from Swedish datasets).
- The probability of conversion to dementia after being exposed to the FINGER intervention was obtained from the data from the participants of the FINGER study.

A manuscript is currently under review. The intervention effects and costs data come from the intervention (not literature) which is a clear strength. Importantly, the results showed that based on the assumptions in the simulations, FINGER has the potential to be a cost-effective intervention program for the dementia prevention. Especially if it is run for a long period, it

has the potential to have large societal effects. The model´s framework can easily be adapted for use on the datasets in MIND-AD.

Task 6.2 Guidelines and recommendations for practical preventive strategies
In the first two years of the project we have focused on the relationship between blood pressure and dementia (one of the risk factors with increasing evidence for dementia and clear intervention approaches). We assessed the barriers and stimulating factors of Dutch general practitioners in prescribing antihypertensive medication, the association between blood pressure variability and specific classes of antihypertensive medication and dementia and the effect of antihypertensive treatment to prevent dementia.
In 2017 we broadened our focus on methodological issues in dementia prevention trials. Long-term adherence to lifestyle interventions is difficult and an important challenge in non-pharmacological trials. We assessed the influential factors in initial and sustained engagement with the *Healthy Ageing Through Internet Counselling in the Elderly* (HATICE) trial intervention by interviewing participants. Another important methodological aspect of prevention trials is the selection of the most appropriate target population. It is suggested that it is beneficial to select a population at increased risk of dementia. We studied whether it is useful to do so using a dementia risk score with solely modifiable risk factors, within the preDIVA dataset.

Professor Kivipelto was a key member in the recently published **WHO Dementia Risk Reduction guidelines** (www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/). Along with her team, they conducted large-scale systematic reviews regarding several modifiable risk factors for dementia, evaluated the evidence from observational data and clinical trials, and offered highly valuable contributions to the working group led by the WHO. These guidelines will form the key basis for dementia risk reduction in clinical settings, in lifestyle interventions and for the wider society.

Task 6.3. Guidelines and recommendations for multinational and multimodal prevention trials

The current work in the MIND-AD project, combined with the latest developments within WW-FINGERS have identified the crucial need to develop a Master Protocol to provide harmonized guidelines and recommendations for multinational and multimodal prevention trials.
MIND-AD has enabled the preparation of the EURO-FINGERS Master Protocol: In order to support the growing number of multidomain prevention trials conducted worldwide, FINGER and MIND-AD standardized protocols will be used as starting point, allowing adaptations across the entire continuum (at-risk states to biomarker-defined preclinical/prodromal AD). Trial-specific details (e.g. target population, national adaptations of lifestyle interventions) will be described in new trial protocol Appendices. Alignment and harmonization ensures synergy, and facilitates data pooling.
Designing the first multimodal preventive intervention protocol combining lifestyle with disease-modifying drugs: The project will bridge the gap between pharma- and non-pharmaceutical interventions. The intervention protocol (based on FINGER MIND-AD), with at least one arm combining lifestyle with disease-modifying drugs for the first time. Two main intervention designs will be considered: repurposing of existing drugs with mechanisms of action relevant for AD pathophysiology (e.g. diabetes drugs); and new AD disease-modifying drugs with promising results in ongoing pharmaceutical RCTs.
Novelty: Besides novel biomarkers, this proposal uses new data from the recent 5- and 7-year FINGER extended follow-ups, and LipiDiDiet extension RCTs (total 6 years), to assess long-term sustained/increased intervention benefit. New MIND-ADmini data will also be analyzed, providing the first feasibility model for lifestyle+pharmacological intervention. This is also the first project with the evidence base for a Master protocol for the first European (and then

globally via WW-FINGERS) network of multimodal dementia precision prevention RCTs.

WP7. Results dissemination and planning MIND-ADMAXI (future larger pan-European prevention trials): month 6-36. (Leaders KI & INSERM)

From FINGER to World-Wide FINGERS: Following the so far unmatched success of the FINGER trial, and preliminary positive feed-back from MIND-AD$_{MINI}$, the applicant launched the World-Wide FINGERS (WW-FINGERS) network in July 2017 (www.alz.org/wwfingers/overview.asp). This is the first global network of multidomain dementia prevention trials and around 30 countries have already joined (e.g. in Europe, United States, China, Singapore, Japan, Australia, Latin-America). The goal is to test, adapt and optimize the FINGER intervention model to prevent dementia across the entire continuum from at-risk states to clinical and prodromal AD. This interdisciplinary network will share experiences, harmonise data, and plan joint international initiatives for dementia/cognitive impairment prevention and creates a unique opportunity for rapid knowledge dissemination and implementation. The work to date within WW-FINGERS highlighted the need to develop a 'Master Protocol' to support with planning future multidomain RCTs.

EURO-FINGERS Master Protocol Preparation: Master protocol design has never been developed for multimodal preventive interventions with non-pharmaceutical components. The FINGER and MIND-AD core standardized protocol will be used as starting point, since it has the necessary flexibility to allow adaptation into a Master protocol type of design. The Master protocol will be designed to accommodate trials across the entire continuum from at-risk states to biomarker-defined preclinical and prodromal AD. Trial-specific details (exact definition of target population, national adaptations of lifestyle intervention components to ensure feasibility without affecting efficacy, potential innovative intervention and other design elements) will be described in Appendices to the Master protocol every time a new trial will be initiated in the future. The crucial need for a Master protocol design was identified by following the start of the WW-FINGERS initiative and the growing number of trials being planned worldwide. Alignment and harmonisation across trials is crucial for reaching maximum scientific breakthrough value and to ensure synergy, harmonization, and facilitate data pooling.
Designing the first multimodal preventive intervention protocol combining lifestyle with disease-modifying drugs: Our team will bridge the gap between pharma- and non-pharmaceutical interventions. The intervention protocol will be based on FINGER and MIND-AD, with at least one arm combining lifestyle with disease-modifying drugs for the first time. Two main intervention designs will be considered: repurposing of existing drugs with mechanisms of action relevant for AD pathophysiology (e.g. diabetes drugs26); and new AD disease-modifying drugs with promising results in ongoing pharmaceutical RCTs. Funding for conducting the trial will be applied for separately from relevant national/EU sources.
Novelty: This proposal will use new data from the recent 5- and 7-year FINGER extended follow-ups, and LipiDiDiet extension RCTs (total 6 years). No other prevention RCTs currently have such crucial data for assessing longer-term effects. E.g. preliminary 3-year LipiDiDiet results suggest sustained/increased intervention benefit. New MIND-ADmini data will also be analyzed, providing the first model for designing a feasible multimodal lifestyle + disease-modifying drug intervention. This is also the first project with the evidence base for developing a Master protocol for the first European (and subsequently global by extrapolation to WW-FINGERS) network of multimodal dementia precision prevention RCTs.

This unique initiative has led the applicant (Prof. Kivipelto) and international colleagues to apply for and receive JPND funding in 2019, with the project start in 2020.

2.2. Highlights of the collaboration (scientific and structural)

Please briefly describe below highlights the consortium experienced during the project runtime with regard to (a) scientific aspects of the work plan and (b) the collaboration of the partners.

WP1: In order to manage and organize the project structure, the leading team (KI) ensured the collaboration and cooperation with all participating members. This ensured to have the Consortium Agreement signed on time, participation of all members in GA meeting, alternating the hosting of GA meetings, participation in teleconferences, providing progress information for the different progress and final reports, and ensuring that funds are allocated within the assigned budget.

WP2: This WP involved the participation of several institutes within this project. While the leaders were UEF and Saarland, collaboration was needed from KI and National Institute for Health and Welfare in Helsinki (THL) among others. FINGER samples from THL were sent to Saarland for analyses of blood-based biomarkers, as well as to the University of Perugia (external collaborator) for Bioplex analyses. Biomarker analyses were conducted by researchers at KI, UEF, Saarland (e.g. for telomere length, CSF biomarkers, neuroimaging data) with support from VTT (external collaborator, eg machine learning approach, Disease Stage Index).

WP3: involved a network of early- to mid-stage researchers (PhD students, post-docs and research assistants) from the French (WP leader), Dutch and Finnish partners. The teams involved in this WP held at least annual face-to-face meetings, and regular teleconferences / exchanges throughout the duration of the ACCEPT-HATICE study which uses data from multiple trial sites. The main publication from this WP was co-first authored by members of each team. Close collaboration with Alzheimer Europe.

WP4: While UEF was in charge of this WP, it closely collaborated with KI and Saarland. For example, the teams jointly conducted analyses on how the diagnostic criteria (IWG-2, NIA-AA 2011 & 2018) predicted conversion to dementia, as well as other demographic / biomarker predictors of cognitive decline. They also assessed the intervention effects on various biomarkers. Within this collaboration, they also partnered with investigators conducting qualitative research (e.g. at KI) to assess the impact of disclosure of prodromal AD status to patients and their families. Close collaboration with Alzheimer Europe.

WP5: The multi-center MIND-AD$_{mini}$ trial involved a collaboration between KI, Germany (Saarland and Frankfurt sites), INSERM, and UEF. Also, learnt experiences from FINGER were offered from THL. As the trial coordinating team, KI first set up the trial infrastructure, developed the trial protocol, designed all the intervention components, drafted the ethics application and hired the necessary staff members. It then closely collaborated with other sites (Finland, France, Germany) to support them with setting up their respective infrastructures, while taking into account their local available resources.

WP6: For the cost-effectiveness analyses, this was a collaboration between THL who provided the relevant FINGER costs data to KI (Collaborator Prof. Anders Wimo) who also collaborated with Ron Handel (Maastricht University, and also obtained an affiliation to KI) and Martin Knapp (external collaborator). This WP was also a collaboration between Univ. of Amsterdam who collaborated with Dutch General Practitioners to assess prescription practices of antihypertensive drugs, as well as with HATICE members (France, Finland) to understand long-term adherence to lifestyle interventions. Finally, within this WP, Prof. Kivipelto collaborated with the WHO team that conducted the work in order to develop the WHO Dementia Risk Reduction guidelines (2019) (www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/).

WP7: Considering the success of the FINGER trial, and preliminary positive feed-back from MIND-AD$_{MINI}$, the launch of the World-Wide FINGERS initiative consists of collaborations with about 30 countries, including world regions / countries such as Europe, USA, China, Singapore, Japan, Australia, Latin-America). More recently, the recently-funded Euro-FINGERS project involves a collaboration between Sweden, Finland, the Netherlands, Spain among others. Additional collaborations are expected to be added. Close collaboration with Alzheimer Europe in dissemination of the results.

2.3. Overall conclusions

The overall conclusions from the MIND-AD project are as follows:

The MIND-AD RCT, combining lifestyle intervention and medical food has been conducted in four European countries. The trial was completed in December 2019. Although analyses will be completed by autumn 2020, results to date suggest that most centers were able to recruit individuals with prodromal AD with no major challenges. The trial delivery centers have reported promising experiences to date. MIND-AD also demonstrated that it is possible to adapt a multidomain lifestyle intervention (including diet, exercise, cognitive training and vascular risk management) for this target population. Such adaptations resulted in high levels of adherence, and trial participants enjoyed and appreciated participating in the trial.

The analyses on biomarkers showed that, if a trial actually had intervention benefits, the treatment response can indeed be correlated to predictive biomarkers. The results also indicate that it is possible, in early AD, to predict the individual's treatment response already before treatment is initiated and that treatment response may be monitored by surrogate biomarkers before a potential cognitive benefit becomes observable. Results also showed positive on various neuroimaging markers, especially if the intervention is started early enough. To our knowledge this is the first observation that cognitive-functional intervention benefit can be predicted based on (multiple) biomarker levels in early AD.

With regards to prodromal AD as a target population, this population has a high conversion rate to AD in the absence of interventions. Overall the results demonstrate that this population is suitable for inclusion in multinational multidomain lifestyle interventions, and in the long-term time frame, that they can benefit from interventions that can improve synaptic function (e.g. medical food), that it is feasible to recruit them into multidomain lifestyle interventions, and if the intervention domains are well adapted, high adherence levels can be achieved.

Results on the facilitators and barriers to participation in adherence to preventive interventions showed that altruism and personal benefits (wanting to improve one's lifestyle; receiving additional medical monitoring) motivated older adults to participate in the trial. Emphasizing such aspects could facilitate recruitment in future RCTs. Additional medical monitoring was particularly important when access to public health care was perceived as limited. Furthermore, maintaining autonomy and preventing functional dependency emerged as a key motivating factor amongst these young older adults.

The cost-effectiveness analyses have shown that FINGER has the potential to be a cost-effective intervention program for the prevention of dementia. The model's framework can easily be adapted for use on the datasets in MIND-AD.

Finally, the acquired knowledge on dementia risk and protective factors, which have been included / considered in the MIND-AD trial have allowed the team to contribute to the WHO Guidelines on risk reduction of cognitive decline and dementia, and plan the Master Protocol for lifestyle interventions within the Euro-FINGERS project (recently funded by JPND).

2.4. Changes and amendments to the original work plan regarding each work package and the overall project and rationale for changes and amendments

2.5. Problems faced and their solutions (scientific and structural)

Please briefly describe problems the consortium encountered and their solutions during the project runtime with regard to scientific aspects of the work plan, and the collaboration of the partners.

Considering the complexity of the MIND-AD$_{MINI}$ trial, setting up the infrastructure took longer than expected in some sites, and therefore, the applicant applied for and received a non-cost extension approval from JPND and VR (Swedish Research Council).

The INSERM team in France had challenges with recruiting participants (e.g. due to competing trials) and with implementing the lifestyle interventions (e.g. due to staff absence). These have been described in more detail under “Delivery of the Project” section, under WP5.

2.6. End-user engagement)

Please briefly describe collaboration with end users (e.g., patients/patient groups, consumers, commercial companies and stakeholders). Has there been input from the end users? Yes/No. Please specify your answer.

We have performed qualitative interviews with participants and study partners at the Stockholm site. Sixteen interviews were performed with participants and two focus group interviews with study partner about their experiences regarding their participation in the study. Results indicate that the multimodal intervention is well tolerated by participants and according to the study partners, MIND-AD gave structure to the weekdays during a chaotic time, in connection with the prodromal AD diagnosis.
Eight participants in the Huddinge site (in Stockholm) continue to attend the gym MEDFIT twice a week for gym sessions and social company, even after the completion of the trial, indicating that they perceive benefits in this experience.

2.7. Patient and public involvement

Please briefly describe collaboration with intermediary target groups ((e.g. care providers, policymakers, professional and sector organisations) Has there been input from intermediary target groups or their representatives? Yes/No. Please specify your answer.

- Meeting with the board of the Swedish dementia association to plan future collaborations and educational seminars on the theme of multimodal healthy life style interventions.
- Collaboration and hire of gym facilities at the gym MEDFIT in Stockholm site

3. Outputs from the project

3.1. Publications

*Please indicate THE NUMBER of publications and communications in which JPND support was **acknowledged**. Please do not mention publications anterior to the start of the project.*

Number of publications and communications

Type of publication	Total N°

Peer reviewed articles	47
Books or book's chapters	2
Reviews (marked with *)	10
Articles dedicated to general public	2
Communications in scientific congresses	135
Dissertations	5
Presentations to general public audiences	59
Others	

Add lines as appropriate

List of publications and communications

Please list the publications that result from the funded project. Please group them according to the categories presented in the table above. In column 1, please underline the name of the JPND-funded partners. In column 2, please point out the project partners involved by using the numbering applied in section I General information (e.g. partner 1 or P1).

Publication (authors, title, journal, year, issue, pp.)	**Partner(s)**	**Impact**
2020		
Gadomsky L, Santos Guilherme MD, Winkler J, van der Kooij MA, Hartmann T, Grimm M, Endres K Elevated Testosterone Level and Urine Scent Marking in Male 5xFAD Alzheimer Model Mice Curr Alzheimer Res. 2020	**Saarland**	**3.3**
Reinhardt S, Schuck F, Stoye N, Hartmann T, Grimm MOW, Pflugfelder G, Endres K. Transcriptional repression of the ectodomain sheddase ADAM10 by TBX2 and potential implication for Alzheimer's disease. Cell Mol Life	**Saarland**	**6.7**
Rosenberg A, Coley N, Soulier A, Kulmala J, Soininen H, Andrieu S, Kivipelto M, Barbera M, MIND-AD and HATICE groups. Experiences of dementia and attitude towards prevention: a qualitative study among older adults participating in a prevention trial. BMC Geriatr. 2020 Mar 12;20(1):99. Doi: 10.1186/s12877-020-1493-4.	**KI**	**2.8**
Rosenberg A, Mangialasche F, Ngandu T, Solomon A, Kivipelto M. Multidomain Interventions to Prevent Cognitive Impairment, Alzheimer's Disease, and Dementia: From FINGER to World-Wide FINGERS. J Prev Alzheimers Dis. 2020;7(1):29-36. Doi: 10.14283/jpad.2019.41.	**UEF, KI ***	**---**
2019		
Kivipelto M, Ngandu, T. Good for the heart and good for the brain? The Lancet Neurology 2019 Apr;18(4):327-328.	**Ki ***	**28.8**

Kulmala J, Ngandu T, Havulinna S, Levälahti E, Lehtisalo J, Solomon A, Antikainen R, Laatikainen T, Pippola P, Peltonen M, Rauramaa R, Soininen S, Strandberg T, Tuomilehto J, Kivipelto M. The effect of multidomain lifestyle intervention on daily functioning in older people. J Am Geriatr Soc. 2019 Feb 26.	**UEF/KI/THL**	**4.4**
Pentikäinen H, Savonen K, Ngandu T, Solomon A, Komulainen P, Paajanen T, Antikainen R, Kivipelto M, Soininen H, Rauramaa R. Cardiorespiratory fitness and cognition – longitudinal associations in the FINGER study. J Alzheimers Dis. 2019 Feb 20.	**UEF/KI/THL**	**3.5**
Martikainen IK, Kemppainen N, Johansson J, Teuho J, Helin S, Liu Y, Helisalmi S, Soininen H, Parkkola R, Ngandu T, Kivipelto M, Rinne JO. Brain β-Amyloid and Atrophy in Individuals at Increased Risk of Cognitive Decline. AJNR Am J Neuroradiol. 2019 Jan;40(1):80-85.	**UEF/KI/THL**	**3.7**
Janitschke, D.; Nelke, C.; Lauer, A.A.; Regner, L.; Winkler, J.; Thiel, A.; Grimm, H.S.; Hartmann, T.; Grimm, M.O.W. Effect of Caffeine and Other Methylxanthines on Aβ-Homeostasis in SH-SY5Y Cells. *Biomolecules*2019, *9*, 689.;	**Saarland**	**4.7**
Hendrix SB, Soininen H, van Hees AMJ, Ellison N, Visser PJ, Solomon A, Attali A, Blennow K, Kivipelto M, Hartmann T. Alzheimer's Disease Composite Score: A Post-Hoc Analysis Using Data From the LipiDiDiet Trial in Prodromal Alzheimer's Disease. J Prev Alzheimers Dis 2019; 6(4):232-236	**Saarland, KI**	**---**
van Oudenhoven FM, Swinkels SHN, Hartmann T, Soininen H, van Hees AMJ, Rizopoulos D. Using joint models to disentangle intervention effect types and baseline confounding: an application within an intervention study in prodromal Alzheimer's disease with Fortasyn Connect. BMC Med Res Methodol. 2019 Jul 25;19(1):163. Doi: 10.1186/s12874-019-0791	**Saarland**	**2.5**
Grimm MOW, Lauer AA, Grösgen S, Thiel A, Lehmann J, Winkler J, Janitschke D, Herr C, Beisswenger C, Bals R, Grimm HS, Hartmann T. Profiling of Alzheimer's disease related genes in mild to moderate vitamin D hypovitaminosis. J Nutr Biochem. 2019	**Saarland**	**4.4**
Richard E, Moll van Charante EP, Hoevenaar-Blom MP, Coley N, Barbera M, van der Groep A, Meiller Y, Mangialasche F, Beishuizen CB, Jongstra S, van Middelaar T, Van Wanrooij LL, Ngandu T, Guillemont J, Brayne C, Andrieu SA#, Kivipelto M#, Soininen H#, Van Gool WA#. Healthy Ageing Through Internet Counselling in the Elderly (HATICE) – a 25ehavior25d clinical trial.[#equal contribution] Lancet Digital Health 2019;1(8):424-434	**UMC, KI, INSEMR**	**---**

Vaskivuo L, Hokkanen L, Hänninen T, Antikainen R, Bäckman L, Laatikainen T, Paajanen T, Stigsdotter-Neely A, Strandberg T, Tuomilehto J, Soininen H, Kivipelto M, Ngandu T. Self and Informant Memory Reports in FINGER: Associations with Two-Year Cognitive Change. J Alzheimers Dis. 2019;71(3):785-795.	**KI, THL**	**3.5**
Hooshmand B, Refsum H, Smith AD, Kalpouzos G, Mangialasche F, von Arnim CAF, Kåreholt I, Kivipelto M, Fratiglioni L. Association of Methionine to Homocysteine Status With Brain Magnetic Resonance Imaging Measures and Risk of Dementia. JAMA Psychiatry. 2019; Jul 24. Doi: 10.1001/jamapsychiatry.2019.1694.	**KI**	**15.9**
Coley N, Ngandu T, Lehtisalo J, Soininen H, Vellas B, Richard E, Kivipelto M, Andrieu S, van Gool P, van Charante EM, Beishuizen C. Adherence to multidomain interventions for dementia prevention: Data from the FINGER and MAPT trials. Alzheimers Dement. 2019;15(6):729-741	**INSERM; UEF; KI**	**14.4**
Coley N, Rosenberg A, van Middelaar T, Soulier A, Barbera M, Guillemont J, Steensma J, Igier V, Eskelinen M, Soininen H, van Charante EM, Richard E, Kivipelto M, Andrieu S; MIND-AD; HATICE groups. Older Adults' Reasons for Participating in an eHealth Prevention Trial: A Cross-Country, Mixed-Methods Comparison. Journal of the American Medical Directors Association. 2019;20(7):843-9.	**INSERM; UEF, KI**	**4.9**
Turunen M, Hokkanen L, Bäckman L, Stigsdotter-Neely A, Hänninen T, Paajanen T, Soininen H, Kivipelto M, Ngandu T. Computer-based cognitive training for older adults: Determinants of adherence. PloS One. 2019;14(7)	**THL, KI, UEF**	**2.8**
Lehtisalo J, Levälahti E, Lindström J, Hänninen T, Paajanen T, Peltonen M, Antikainen R, Laatikainen T, Strandberg T, Soininen H, Tuomilehto J, Kivipelto M, Ngandu T. Dietary changes and cognition over 2 years within a multidomain intervention trial—The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). Alzheimer's & Dementia. 2019;15(3):410-7.	**THL, UEF, KI**	**14.4**
Beishuizen CR, Akenine U, Barbera M, Rosenberg A, Pour MF, Richard E, Soininen H, Mangialasche F, Kivipelto M, Pols AJ, van Charante EM. Integrating nurses' experiences with supporting 26ehavior change for cardiovascular prevention into a self-management internet platform in Finland and the Netherlands: a qualitative study. BMJ open. 2019;9(6):e023480	**INSERM, KI, UEF**	**2.4**

Stephen R, Liu Y, Ngandu T, Antikainen R, Hulkkonen J, Koikkalainen J, Kemppainen N, Lötjönen J, Levälahti E, Parkkola R, Pippola P, Rinne J, Strandberg T, Tuomilehto J, Vanninen R, Kivipelto M, Soininen H, Solomon A; FINGER study group. Brain volumes and cortical thickness on MRI in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). Alzheimers Res Ther. 2019;11(1):53	**UEF, KI**	**3.6**
Kivipelto, Miia; Kulmala, Jenni; Lehtisalo, Jenni; Solomon, Alina; Lindström, Jaana; Rauramaa, Rainer; Peltonen, Markku; Laatikainen, Tiina; Havulinna, Satu; Soininen, Hilkka; Tuomilehto, Jaakko; Hänninen, Tuomo; Paajanen, Teemu; Antikainen, Riitta; Strandberg, Timo; Ngandu, Tiia. FINGER-elintapaohjelma : toimintamalli kognitiivisen toimintakyvyn tukemiseen. (FINGER lifestyle program: an action model to support cognitive functioning) Lääkärilehti 2019;4:183-186	**KI**	
Charlotta Thunborg Krister Håkansson & Miia Kivipelto En kognitiv livsstil. (A cognitive lifestyle) Äldre i Centrum	**KI**	**General public**
2018		
Kivipelto M, Mangialasche F, Ngandu T; World Wide Fingers Network. World Wide Fingers will advance dementia prevention. The Lancet Neurology. 2018 Jan;17(1):27.	**KI ***	**28.8**
Kulmala J, Ngandu T, Kivipelto M. Prevention Matters: Time for Global Action and Effective Implementation. J Alzheimers Dis. 2018;64(s1):S191-S198.	**KI ***	**3.5**
Kivipelto , Mangialasche F, Ngandu T. Lifestyle interventions to prevent cognitive impairment, dementia and Alzheimer disease. Nat Rev Neurol. 2018 Nov;14(11):653-666. doi: 10.1038/s41582-018-0070-3. Review.	**KI ***	**21.2**
Martiskainen H, Takalo M, Solomon A, Stančáková A, Marttinen M, Natunen T, Haapasalo A, Herukka SK, Kuusisto J, Soininen H, Kivipelto M, Laakso M, Hiltunen M. Decreased plasma C-reactive protein levels in APOE ε4 allele carriers. Ann Clin Transl Neurol. 2018;5(10):1229-1240	**UEF, KI , THL**	**4.6**
Solomon A, Turunen H, Ngandu T, Peltonen M, Levälahti E, Helisalmi S, Antikainen R, Bäckman L, Hänninen T, Jula A, Laatikainen T, Lehtisalo J, Lindström J, Paajanen T, Pajala S, Stigsdotter-Neely A, Strandberg T, Tuomilehto J, Soininen H, Kivipelto M. Effect of the Apolipoprotein E Genotype on Cognitive Change During a Multidomain Lifestyle Intervention: A Subgroup Analysis of a Randomized Clinical Trial. JAMA Neurol. 2018 Apr 1;75(4):462-470.	**UEF, KI, THL**	**11.5**

Rosenberg A, Ngandu T, Rusanen M, Antikainen R, Bäckman L, Havulinna S, Hänninen T, Laatikainen T, Lehtisalo J, Levälahti E, Lindström J, Paajanen T, Peltonen M, Soininen H, Stigsdotter-Neely A, Strandberg T, Tuomilehto J, Solomon A, Kivipelto M. Multidomain lifestyle intervention benefits a large elderly population at risk for cognitive decline and dementia regardless of baseline characteristics: The FINGER trial. Alzheimers Dement. 2018 Mar;14(3):263-270.	**UEF, KI/, THL**	**12.7**
Kemppainen N, Johansson J, Teuho J, Parkkola R, Joutsa J, Ngandu T, Solomon A, Stephen R, Liu Y, Hänninen T, Paajanen T, Laatikainen T, Soininen H, Jula A, Rokka J, Rissanen E, Vahlberg T, Peltoniemi J, Kivipelto M, Rinne JO. Brain amyloid load and its associations with cognition and vascular risk factors in FINGER Study. Neurology. 2018 Jan 16;90(3):e206-e213.	**UEF, KI, THL**	**8.7**
van Middelaar T, Argillander TE, Schreuder FHBM, Deinum J, Richard E, Klijn CJM, Effect of Antihypertensive Medication on Cerebral Small Vessel Disease: A Systematic Review and Meta-Analysis. STROKE 2018;49 (6):1531-1533	**UMC**	**6.0**
van Middelaar T, Ivens SD, van Peet PG, Poortvliet RKE, Richard E, Pols AJ, Moll van Charante EP, Prescribing and deprescribing antihypertensive medication in older people by Dutch general practitioners: a qualitative study. J ALZHEIMERS DIS 2018;62 (2):727-735	**UMC**	**3.5**
van Middelaar T, van Vught LA, van Gool WA, Simons EMF, van den Born BJH, Moll van Charante EP, Richard E., Blood pressure-lowering interventions to prevent dementia: a systematic review and meta-analysis. J HYPERTENS 2018;36 (9):1780-1787	**UMC**	**4.2**
Van Middelaar T, Hoevenaar-Blom MP, van Gool WA, Moll van Charante EP, van Dalen JW, Deckers K, Köhler S, Richard E, Modifiable dementia risk score to study heterogeneity in treatment effect of a dementia prevention trial: a post hoc analysis in the preDIVA trial using the LIBRA index. ALZHEIMERS RES THER 2018;10 (1):62	**UMC**	**3.6**
van Middelaar T, Beishuizen CRL, Guillemont J, Barbera M, Richard E, Moll van Charante EP; HATICE consortium. Engaging older people in an internet platform for cardiovascular risk self-management: a qualitative study among Dutch HATICE participants. BMJ Open. 2018 Jan 21;8(1):e019683.	**UMC**	**2.4**

Vaskivuo L, Hokkanen L, Hänninen T, Antikainen R, Bäckman L, Laatikainen T, Paajanen T, Stigsdotter-Neely A, Strandberg T, Tuomilehto J, Soininen H, Kivipelto M, Ngandu T. Associations between Prospective and Retrospective Subjective Memory Complaints and Neuropsychological Performance in Older Adults: The Finger Study. J Int Neuropsychol Soc. 2018 Nov;24(10):1099-1109.	**UEF, KI, THL**	**1.6**
Barbera M, Mangialasche F, Jongstra S, Guillemont J, Ngandu T, Beishuizen C, Coley N, Brayne C, Andrieu S, Richard E, Soininen H, Kivipelto M; HATICE study group. Designing an Internet-Based Multidomain Intervention for the Prevention of Cardiovascular Disease and Cognitive Impairment in Older Adults: The HATICE Trial. J Alzheimers Dis. 2018;62(2):649-663.	**UEF**	**3.5**
Håkansson K, Kivipelto M, Ngandu T. The Patient with Cognitive Impairment. In: Hachinski V (ed.) Treatable and Potentially Preventable Dementias. Cambridge University Press; 2018 Jun	**KI**	**Book chapter**
2017		
Sindi S, Ngandu T, Hovatta I, Kåreholt I, Antikainen R, Hänninen T, Levälahti E, Laatikainen T, Lindström J, Paajanen T, Peltonen M, Khalsa DS, Wolozin B, Strandberg T, Tuomilehto J, Soininen H, Kivipelto M, Solomon A; FINGER study group. Baseline Telomere Length and Effects of a Multidomain Lifestyle Intervention on Cognition: The FINGER Randomized Controlled Trial. J Alzheimers Dis. 2017;59(4):1459-1470	**UEF, KI, THL**	**3.5**
Stephen R, Liu Y, Ngandu T, Rinne JO, Kemppainen N, Parkkola R, Laatikainen T, Paajanen T, Hänninen T, Strandberg T, Antikainen R, Tuomilehto J, Keinänen Kiukaanniemi S, Vanninen R, Helisalmi S, Levälahti E, Kivipelto M, Soininen H, Solomon A. Associations of CAIDE Dementia Risk Score with MRI, PIB-PET measures, and cognition. J Alzheimers Dis. 2017;59(2):695-705.	**UEF, KI, THL**	**3.5**
Strandberg TE, Levälahti E, Ngandu T, Solomon A, Kivipelto M, FINGER Study Group. Health-related quality of life in a multidomain intervention trial to prevent cognitive decline (FINGER). Eur Ger Med. 2017;8(2):164-167.	**UEF, KI, THL**	**1.3**
Soininen H, Solomon A, Visser PJ, Hendrix SB, Blennow K, Kivipelto M, Hartmann T, LipiDiDiet clinical study group. 24-month intervention with a specific multinutrient in people with prodromal Alzheimer's disease (LipiDiDiet): a randomised, double-blind, controlled trial. Lancet Neurol. 2017 Dec;16(12):965-975.	**UEF, KI, THL**	**28.8**

Grimm MOW, Thiel A, Lauer A, Winkler J, Lehmann J, Regner L, Nelke C, Janischke D, Benoist C, Streidenberger O, Stötzel H, Endres K, Herr C, Beisswenger C, Grimm HS, Bals R, Lammert F, Hartmann T (2017) Vitamin D and its analogues decrease Amyloid-β (Aβ) formation and increase Aβ-degradation. Int J Molecular Sciences 2017, 18,	**Saarland**	**4.2**
Grimm MOW, Michaelson DM, Hartmann T (2017) Omega-3 fatty acids, lipids and apoE lipidation in Alzheimer's disease: a rationale for multi-nutrient dementia prevention. J Lipid Res. 2017	**Saarland**	**4.5**
Grimm MOW, Thiel A, Lauer A, Winkler J, Lehmann J, Regner L, Nelke C, Janischke D, Benoist C, Streidenberger O, Stötzel H, Endres K, Herr C, Beisswenger C, Grimm HS, Bals R, Lammert F, Hartmann T (2017) Vitamin D and its analogues decrease Amyloid-β (Aβ) formation and increase Aβ-degradation. Int J Molecular Sciences 2017, 18,	**Saarland**	**4.2**
Handels, R., & Wimo, A. (2019). Challenges and recommendations for the health-economic evaluation of primary prevention programmes for dementia. *Aging & mental health*, *23*(1), 53-59.	**KI**	**2.9**
Krysinska K, Sachdev P, Breitner J, Kivipelto M, Kukull W, Brodaty H. Dementia registries around the globe and their applications: A systematic review. Alzheimer's & Dementia. 2017;13(9):1031-1047	**KI**	**12.7**
Strandberg T, Kivipelto M. Healthy habits - healthy brain. Duodecim. 2017;133(2):195-200	**KI ***	**0.10**
Mangialasche F, Ngandu T, Kivipelto M Cognitive impairment – Risk Factors and Prevention Oxford Textbook of Geriatric Medicine, 3rd Ed 2017 Oxford University Press UK Jean-Pierre Michel, B. Lynn Beattie, Finbarr C. Martin, and Jeremy Walston	**KI**	**Book chapter**
Kivipelto M, Håkansson K. A Rare Success against Alzheimer's. Sci Am. 2017 Mar 14;316(4):32-37. doi: 10.1038/scientificamerican0417-32.	**KI**	**For general public**
Kulmala J, Rosenberg A, Ngandu T, Solomon A & Kivipelto M. Tutkimusnäytöstä kohti uusia käytäntöjä: Liikunta- ja elintapamuutoksilla muistisairauksia ehkäisemään. (From research to implementation: Physical activity and lifestyle modifications in dementia prevention) Liikunta & Tiede 2017; 54 (4): 17-21.	**KI ***	
2016		
Pekkala T, Hall A, Lötjönen J, Mattila J, Soininen H, Ngandu T, Laatikainen T, Kivipelto M, Solomon A. Development of a Late-Life Dementia Prediction Index with Supervised Machine Learning in the Population-Based CAIDE Study. J Alzheimers Dis. 2016;55(3):1055-1067.	**UEF/KI/THL**	**3.5**

Grimm MO, Mett J, Hartmann T. The Impact of Vitamin E and Other Fat-Soluble Vitamins on Alzheimer´s Disease. Int J Mol Sci. 2016 Oct 26;17(11). pii: E1785 review	**Saarland**	**4.183**
Brandscheid C, Schuck F, Reinhardt S, Schäfer KH, Pietrzik CU, Grimm M, Hartmann T, Schwiertz A, Endres K Altered Gut Microbiome Composition and Tryptic Activity of the 5xFAD Alzheimer's Mouse Model J Alzheimers Dis. 2016 Dec 30. doi: 10.3233/JAD-160926	**Saarland**	**3.5**
Strandberg, T. E., E. Levälahti, T. Ngandu, A. Solomon, M. Kivipelto, J. Lehtisalo, T. Laatikainen et al. "Health-related quality of life in a multidomain intervention trial to prevent cognitive decline (FINGER)." *European Geriatric Medicine* 8, no. 2 (2017): 164-167.	**KI, UEF, THL**	**1.3**
Grimm MO, Regner L , Mett J , Stahlmann CP, Schorr P , Nelke C, Streidenberger O , Stoetzel H, Winkler J, Zaidan SR, Thiel A, Endres K, Grimm HS, Volmer DA and Hartmann T. *Tocotrienol Affects Oxidative Stress, Cholesterol Homeostasis and the Amyloidogenic Pathway in Neuroblastoma Cells: Consequences for Alzheimer's Disease* Int J Mol Sci. 2016, 17, 1809; doi:10.3390/ijms17111809	**Saarland**	**4.2**
van Charante, E. P. M., Richard, E., Eurelings, L. S., van Dalen, J. W., Ligthart, S. A., Van Bussel, E. F., ... & van Gool, W. A. (2016). Effectiveness of a 6-year multidomain vascular care intervention to prevent dementia (preDIVA): a cluster-randomised controlled trial. The Lancet, 388(10046), 797-805.	**UMC**	**59.1**
Winblad B, Amouyel P, Andrieu S, Ballard C, Brayne C, Brodaty H, Cedazo-Minguez A, Dubois B, Edvardsson D, Feldman H, Fratiglioni L, Frisoni GB, Gauthier S, Georges J, Graff C, Iqbal K, Jessen F, Johansson G, Jönsson L, Kivipelto M, Knapp M, Mangialasche F, Melis R, Nordberg A, Rikkert MO, Qiu C, Sakmar TP, Scheltens P, Schneider LS, Sperling R, Tjernberg LO, Waldemar G, Wimo A, Zetterberg H. Defeating Alzheimer's disease and other dementias: a priority for European science and society. Lancet Neurol. 2016;15(5):455-532.	**KI ***	**28.8**
Kivipelto M, Ngandu, T. From Heart Health to Brain Health: Legacy of the North Karelia Project for Dementia Research. Glob Heart. 2016;11(2):235-42.	**KI ***	**3.2**
2015		
Ngandu, T., Lehtisalo, J., Solomon, A., Levälahti, E., Ahtiluoto, S., Antikainen, R., ... & Lindström, J. (2015). A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *The Lancet*, *385*(9984), 2255-2263.	**KI, UEF, THL**	**59.1**

Sindi S, Mangialasche F, Kivipelto M. Advances in the prevention of Alzheimer's Disease. F1000prime reports. 2015;7.	**KI ***	**6.0**

Conference presentations

2020	
Miia Kivipelto. Multidomain interventions to prevent cognitive impairment and Alzheimer: The Role of the Gut Microbiome (MIND-AD sub-study). The International Society for CNS Clinical Trials and Methodology (ISCTM). 19-21 February 2020 Washington, USA	**KI**
Miia Kivipelto. Plenary Lecture: World-Wide FINGERS and the next generation of clinical trials in Alzheimer´s disease. ADPD conference, 2-5 April 2020, Vienna, Austria. (Held virtually to to COVID-19 re-arrangements)	**KI**
Charlotta Thunborg ADI accepted poster, Study partners' experiences of participating in a multidomain intervention for individuals with prodromal Alzheimer's disease, Alzheimer's Disease International Conference . 2020-03-19 (postponed conference due to COVID-19, new date 2020-12-10)) Singapore	**KI**
2019	
U,Akenine,, C.Thunborg, M.Fallaphor, M.Kivipelto; **Poster at AD/PD** Experiences of participating in a non-pharmacological clinical trial MIND-AD$_{mini}$, a multimodal preventive trial for Alzheimer's disease, Lissabon Portugal	**KI**
Miia Kivipelto. Alzheimer's Association International Conference (AAIC). 17.07.2019. World Wide Fingers: A Global Collaboration for Future Generations. Lecture presented at the Alzheimer's Association International Conference (AAIC); 2019; Los Angeles, USA.	**KI**
Miia Kivipelto. Can We Prevent Some Dementias Now? Ontario, Canada. 17.10.2019. Lifestyle Changes in Decreasing Dementia Risk. Lecture presented at the symposium Can We Prevent Some Dementias Now? by The Department of Clinical Neurological Sciences, Western University; 2019; Ontario, Canada.	**KI**
Miia Kivipelto. IFA Copenhagen Summit on Cognitive Reserve, Copenhagen, Denmark. 25.10.2019. Cognitive Reserve: The Future of Ageing. Lecture presented at the IFA Copenhagen Summit on Cognitive Reserve; 2019. Copenhagen, Denmark.	**KI**
Miia Kivipelto LATAM FINGERS symposium, Buenos Aires, Argentina. 31.10.2019. Kivipelto, M. FINGER and World-Wide FINGERS. Lecture presented at the LATAM FINGERS symposium; 2019; Buenos Aires, Argentina.	**KI**
Anna Matton. Pharmaceutical company Sanofi, visit in Paris.21.02.2019. On FINGER 27-hydroxycholesterol study and myelination study	**KI**
Tiia Ngandu The 29th Alzheimer Europe Conference, Hague, the Netherland. 25.10.2019. Plenary session lecture: Multidomain lifestyle interventions to prevent cognitive impairment and dementia: From FINGER to World-Wide FINGERS	**KI, THL**
Charlotta Thunborg, Nicholas Levak, Dementia prevention- FINGER results and MIND-AD experiences Stockholm Dietary Network, 2019-05-22 Stockholm	**KI**
M. Fallahpour, U. Akenine C.Thunborg M. Kivipelto; **Poster at Occupational Science Europe conference** Experiences of participation in activities: Preliminary results of a longitudinal qualitative study focusing on prevention of cognitive decline 2019-08-30 Amsterdam Netherlands	**KI**
Charlotta Thunborg, Dementia prevention: From FINGER to MIND-AD and WW-FINGERS International Dementia day 2019-09-20 Stockholm university hospital	**KI**
Charlotta Thunborg, Better Cognitive Health, It´s never too late: MIND-AD Lidingö county national dementia day 2019-10-01, Lidingö (Stockholm)	**KI**
Charlotta Thunborg, It's never too late: Healthy lifestyle for brain health, MIND-AD for strengthen memory (and ophthalmic health) National Physiotherapy conference 2019-10-24 Stockholm, Waterfront conference Center	**KI**
Tobias Hartmann. ADPD Lissbon, dementia prevention	**Saarland**
Tobias Hartmann. CONY Madrid, value / no value in nutritional supplements	**Saarland**
Tobias Hartmann. Horizons, Birmingham, dementia prevention	**Saarland**

Shireen Sindi. Multimodal interventions and dementia prevention, at the pre-conference symposium "Reserve, Resilience and Protective Factors in AD: contribution of Molecular Imaging". European Association of Nuclear Medicine (EANM) Congress, 12-16 October 2019, Barcelona, Spain.	**KI**
Shireen Sindi. Sex Differences in Dementia: Evidence from Population-Based Studies and the Finger Lifestyle Intervention. Alzheimer's Association International Conference (AAIC), 14-18 July 2019, Los Angeles, USA.	**KI**
Sex Differences in Dementia: Evidence from Population-Based Studies and the Finger Lifestyle Intervention. International Association of Gerontology and Geriatrics (IAGG), 23-25 May 2019, Gothenburg, Sweden.	**KI**
2018	
Miia Kivipelto. Plenary Lecture (Invited Speaker) Multimodal Lifestyle Interventions. Alzheimer's Association International Conference (AAIC). 22-25 July 2018, Chicago, United States of America. (6000+ participants)	**KI**
Miia Kivipelto. Multi-domain interventions to prevent dementia: from FINGER to World-Wide FINGERS. Kuopio Alzheimer Symposium. 6-8 June 2018. Kuopio. Finland.	**KI**
Miia Kivipelto. Plenary Lecture (Invited Speaker) Multi-domain interventions to prevent cognitive impairment and dementia: From FINGER to World-Wide FINGERS. Canada Consortium of Neurodegeneration in Aging (CCNA). 30 September-3 October 2018, Montreal, Canada.	**KI**
Miia Kivipelto. Multi-domain interventions to prevent dementia: from FINGER to World-Wide FINGERS. Clinical Trials on Alzheimer's Disease (CTAD). 24-27 October 2018, Barcelona, Spain.	**KI**
Miia Kivipelto. Multidomain interventions to prevent cognitive impairment and dementia: From FINGER to World-Wide FINGERS. 2nd Stockholm-Tokyo Workshop on Sustainable Development. 28-30 October 2018, Tokyo, Japan.	**KI**
Miia Kivipelto. Plenary Lecture (Invited Speaker) Multidomain Therapy for Dementia Prevention. The 9th International Cofnerence of The International Society of Vascular Behavioural and Cognitive Disorders (VasCog 2018). 14-17 November 2018, Hong Kong, China.	**KI**
Miia Kivipelto. FINGER, MIND-China & Worldwide FINGER. Alzheimer's Association International Conference (AAIC). 18-19 December 2018, Bengaluru, India.	**KI**
Miia Kivipelto. Plenary Lecture (Invited Speaker) Multimodal Lifestyle Interventions. Alzheimer's Association International Conference (AAIC). 22-25 July 2018, Chicago, United States of America. (6000+ participants)	**KI**
Shireen Sindi. Multidomain interventions to prevent dementia. Northern Dimension Future Forum, organized by Northern Dimension Institute (NDI), 28 November 2018, Vantaa, Finland.	**KI**
Shireen Sindi. Multidomain Lifestyle Intervention, Telomere Length Change and Cognition: The FINGER Trial. International Congress of Behavioral Medicine (ICBM). 14-17 November 2018, Santiago, Chile.	**KI**
Shireen Sindi. Effective prevention strategies for dementia. Aetiology and prevention in musculoskeletal and neurodegenerative diseases. The second international Scientific Kock Symposium. 19-21 September 2018, Trelleborg, Sweden.	**KI**
Shireen Sindi. Can a multi-domain lifestyle intervention impact telomere length? (invited speaker) European Winter Conference on Brain Research (EWCBR), January 27- February 3 2018, Villars, Switzerland.	**KI**
Stephen R, Mangialasche F, Mecocci P, Ngandu T, Antikainen R, Laatikainen T, Soininen H, Kivipelto M, Solomon A. Association of CAIDE dementia risk score with inflammation and metabolic blood biomarkers in the FINGER study participants. 8th Kuopio Alzheimer Symposium, June 6-8 2018, Kuopio, Finland.	**UEF**

Rosenberg A, Coley N, van Middelaar T, Soulier A, Barbera M, Guillemont J, Steensma J, Igier V, Eskelinen M, Soininen H, Moll van Charante E, Richard E, Kivipelto M, Andrieu S for the MIND-AD and HATICE groups. Older Europeans' reasons for participating in a multinational eHealth prevention trial: a cross-country comparison using mixed methods (ACCEPT-HATICE). 8th Kuopio Alzheimer Symposium, June 6-8 2018, Kuopio, Finland.	**UEF**
Soininen H, Solomon A, Visser PJ, Hendrix S, Blennow K, Kivipelto M, Hartmann T. Reducing cognitive and functional decline in prodromal AD, the multinutrient LipiDiDiet approach (Fortasyn Connect). AAT-AD/PDTM 2018, March 15-18, Turin, Italy.	**UEF**
Soininen H. Towards personalized treatment and prevention of brain diseases. Moonshots of the 2020s, Increasing Healthy Life Years: How to make the most of the missions of Horizon Europe? 22 November 2018, Brussel, Belgium.	**UEF**
Tiia Ngandu. Innovative approaches in prevention trials for dementia and alzheimer: from finger to world-wide fingers. 24th Nordic Congress of Gerontology (NKG). 2-4 May 2018, Oslo, Norway.	**KI, THL**
Alina Solomon. Plenary Session. Scientific Progress: FINGER study. Alzheimer's Disease International. 26-29 July, Chicago, USA.	**UEF**
Solomon A. Multidomain lifestyle trials in dementia prevention. 7th Cognitive Day symposium, 11 May 2018, Ljubljana, Slovenja.	**UEF**
Solomon A. Quantifying dementia risk and prevention potential in clinical trials. 8th Kuopio Alzheimer Symposium, June 6-8 2018, Kuopio, Finland.	**UEF**
Solomon A, Levälahti E, Antikainen R, Laatikainen T, Soininen S, Kulmala J, Tuomilehto J, Kivipelto M, Ngandu T. Effects of a multidomain lifestyle intervention on overall risk for dementia: the FINGER randomized controlled trial. Alzheimer's Association International Conference, 22-26 July 2018, Chicago, USA.	**UEF**
Solomon A. Multi-domain interventions to prevent dementia: from clinical trials to implementation. Alzheimer's Association International Conference, 22-26 July 2018, Chicago, USA.	**UEF**
Solomon A. Multi-domain approach to dementia prevention: the FINGER model. Alzheimer's Europe 2018, 29-31 October, Barcelona, Spain.	**UEF**
Tobias Hartmann. Biomarker results of the LipidiDiet trial on Fortsyn Connect intervention in prodromal Alzheimer's Disease. AAT. March 2018 Torino Italy	**Saarland**
Tobias Hartmann. Nutrition for the ageing brain: Moving towards clinical appilcations- LipiDiDiet Outcomes August 2018 Madrid Spain	**Saarland**
Tobias Hartmann. Clinical Nutrition & Metabolism. Dietary Intervention In Early Alzheimer's Disease. September 2018 Madrid Spain	**Saarland**
Shireen Sindi. Multidomain interventions to prevent dementia. Northern Dimension Future Forum, organized by Northern Dimension Institute (NDI), 28 November 2018, Vantaa, Finland.	**KI**
Shireen Sindi. Multidomain Lifestyle Intervention, Telomere Length Change and Cognition: The FINGER Trial. International Congress of Behavioral Medicine (ICBM). 14-17 November 2018, Santiago, Chile.	**KI**
Shireen Sindi. Effective prevention strategies for dementia. Aetiology and prevention in musculoskeletal and neurodegenerative diseases. The second international Scientific Kock Symposium. 19-21 September 2018, Trelleborg, Sweden.	**KI**
Rosenberg A, Coley N, van Middelaar T, Soulier A, Barbera M, Guillemont J, Steensma J, Igier V, Eskelinen M, Soininen H, Moll van Charante E, Richard E, Kivipelto M, Andrieu S for the MIND-AD and HATICE groups. Older Europeans' reasons for participating in a multinational eHealth prevention trial: a cross-country comparison using mixed methods (ACCEPT-HATICE). 8th Kuopio Alzheimer Symposium, June 6-8 2018, Kuopio, Finland.	**UEF**
Stephen R, Mangialasche F, Mecocci P, Ngandu T, Antikainen R, Laatikainen T, Soininen H, Kivipelto M, Solomon A. Association of CAIDE dementia risk score with inflammation and metabolic blood biomarkers in the FINGER study participants. 8th Kuopio Alzheimer Symposium, June 6-8 2018, Kuopio, Finland.	**UEF**

2017	
Miia Kivipelto. Nutrition and prevention of dementia Miia Kivipelto. 13th Congress of the European Union Geriatric Medicine Society (EUGMS), Nice, France, September 20-22, 2017	**KI**
Miia Kivipelto. Prevention of neurodegenerative disorders - at the present and how to collaborate in the future. The Nordic Network in Dementia Diagnostics (NIDD), 26 Sept 2017.	**KI**
Miia Kivipelto. Multidomain Interventions to prevent dementia. SINO-SWEDEN Network for aging research workshop. 26 October 2017.	**KI**
Shireen Sindi. Multidomain Lifestyle Intervention, Telomere Length Change and Cognition: The FINGER Trial. Alzheimer's Association International Conference (AAIC), London, UK, July 2017.	**KI**
Shireen Sindi. Multimodal interventions and dementia prevention. (invited speaker) 1st International Conference on Cognitive Reserve in the Dementias (ResDem), November 24-25 2017, Munich, Germany	**KI**
Jenni Kulmala. Participants' experiences of multidomain lifestyle-based intervention (FINGER) to prevent cognitive decline. Finnish Gerontology Conference (Gerontologia päivät). 8 June 2017.	**KI**
Anna Matton. Multimodal interventions in Alzheimer disease. Center for Innovative Medicine (CIMED) yearly congress. 17 May 2017.	**KI**
Tessa van Middelaar. Specific classes of antihypertensive medication are associated with a reduced incidence of dementia in older patients. European Stroke Organisation Conference. 17.5.2017. Prague, Czech Republic.	**UMC**
Hilkka Soininen. 13th International Conference on Alzheimer's and Parkinson's Diseases (ADPD). March 29-April 2, Vienna, Austria. Talk title: The Lipididiet trial - effects of Fortasyn Connect in prodromal Alzheimer's disease.	**UEF**
Mariangese Barber. Adherence of older adults to the guidelines for the management of cardivascular disease risk: a European prespective. 13th International Conference on Alzheimer's and Parkinson's Diseases (ADPD). March 29-April 2, Vienna, Austria	**UEF**
Alina Solomon. IMI-AD Platform disease modelling workshop, Edinburgh, UK, 16-18 October 2017. Talk title: Multimodal prevention perspective	**UEF**
Shireen Sindi. Multidomain Lifestyle Intervention, Telomere Length Change and Cognition: The FINGER Trial. Alzheimer's Association International Conference (AAIC), London, UK, July 2017.	**KI**
Shireen Sindi. Multimodal interventions and dementia prevention. (invited speaker) 1st International Conference on Cognitive Reserve in the Dementias (ResDem), November 24-25 2017, Munich, Germany	**KI**
Alina Solomon. Nordic memory clinic conference, 25-26 September 2017, Oslo, Norway. Talk title: Risk scores in clinical use	**UEF**
Alina Solomon. Conferinta Nationala Alzheimer 2017 (National Alzheimer Conference), Bucharest, Romania, 22 - 25 February 2017. Talk title: Multi-domain approaches for prevention trials.	**UEF**
Tobias Hartmann. BIOMARKER RESULTS OF THE LIPIDIDIET TRIAL ON FORTASYN CONNECT INTERVENTION IN PRODROMAL ALZHEIMER'S DISEASE. AD/PD . 31.3.2017 Vienna, Austria	**Saarland**
Tobias Hartmann. Multinutrient Intervention in Pre-Dementia Alzheimer's Disease. Gordon Research conference on cognitive dysfunction in brain diseases. 15.6.2017 Hong Kong	**Saarland**
Tobias Hartmann Multi-nutrient intervention in prodromal Alzheimer's disease: rationale based on preclinical studies and results from the double-blind randomized controlled LipiDiDiet study. AAIC Conference 15.7.2017 London, UK	**Saarland**
Tobias Hartmann. Alzheimer's Disease Amyloid Precursor Protein (APP), a Complex Lipid Regulator and Lipid Sensor System, molecular mechanism and	**Saarland**

clinical trial results. International Conference of the Polish Society for Neuroscience, 28.8.2017 Warsaw, Poland	
Tobias Hartmann. Multi-nutrient intervention results in reduced disease progression in early Alzheimer's disease – LipiDiDiet clinical trial results23.10.2017 Food For Healthy Aging. Amsterdam, The Netherlands	**Saarland**
Tobias Hartmann. Application of the revised diagnostic criteria for the early stages of Alzheimer's disease to the LipiDiDiet study population. Clinical Trials on Alzheimer's Disease (CTAD). 4.11.2017 Boston, U.S.A.	**Saarland**
Tobias Hartmann. LipiDiDiet – Lipid Based Multi-Nutrient Intervention in Pre-Dementia Alzheimer's Disease, from Molecular Mechanisms to Disease Modifying Treatment. Düsseldorf-Jülich Symposium on Neurodegenerative Diseases. 28.11.2017	**Saarland**
Anna Lauer. Lipids and Aß Homeostasis. Lipids and Brain IV. 9 Oct. 2017, Nancy, France	**Saarland**
Heike Grimm APP-Processing, a regulatory Mechanism in Lipidhomeostasis? Implications to Alzheimer's Disease. Lipids and Brain IV. 10 Oct. 2017, Nancy, France	**Saarland**
Tessa van Middelaar. Specific classes of antihypertensive medication are associated with a reduced incidence of dementia in older patients. European Stroke Organisation Conference. 17.5.2017. Prague, Czech Republic.	**UMC**
Anna Rosenberg. Alzheimer's Association International Conference (AAIC), London, UK, July 2017. Multidomain lifestyle intervention benefits a large elderly population at risk for cognitive decline: subgroup analyses of the FINGER trial. Won the student poster competition.	**UEF**
Charlotta Thunborg. Multimodal lifestyle and nutritional intervention in prodromal Alzheiemr's disease: MIND-AD$_{MINI}$ Pilot Trial. Alzheimer's Association International Conference (AAIC), London, UK, July 2017.	**KI**
Ruth Stephen. Alzheimer's Association International Conference (AAIC), London, UK, July 2017. Impact of Baseline Brain MRI Measures on Cognitive Effects of a Multidomain Intervention: The FINGER Randomized Controlled Trial.	**UEF**
Heidi Turunen. Alzheimer's Association International Conference (AAIC), London, UK, July 2017. Associations of leucocyte telomere length with brain MRI and PIB-PET measures: the FINGER study.	**UEF**
Anette Hall. 13th International Conference on Alzheimer's and Parkinson's Diseases (ADPD). March 29-April 2, Vienna, Austria. Predicting dementia versus brain pathology in the oldest old.	**UEF**
Timo Pekkala. 13th International Conference on Alzheimer's and Parkinson's Diseases (ADPD). March 29-April 2, Vienna, Austria. Predicting brain amyloid positivity in elderly with increased risk of cognitive decline.	**UEF**
Handels R, Wimo A. Challenges and recommendations for the health-economic evaluation of primary prevention programmes for dementia. Alzheimer's Association International Conference, July 2017, London, UK.	**KI**
Tessa van Middelaar. (De)prescribing antihypertensive medication in older people by general practitioners: a qualitative study. The Dutch General Practitioners Society (NHG wetenschapsdag). 02.6.2017. Zeist, the Netherlands. (Dutch)	**UMC**
Tessa van Middelaar. Engaging older people in an Internet platform for cardiovascular risk self-management: a qualitative study. The Dutch General Practitioners Society (NHG wetenschapsdag). 02.6.2017. Zeist, the Netherlands. (Dutch)	**UMC**
Tessa van Middelaar. Lower dementia risk with different classes of antihypertensive medication in older patients. Alzheimer's association international conference. 16.7.2017. London, United Kingdom.	**UMC**
Tessa van Middelaar. Visit-to-visit blood pressure variability and the risk of dementia in older people. Alzheimer's association international conference. 16.7.2017. London, United Kingdom.	**UMC**
Coley N, Guillemont J, van Middelaar T, Barbera M, Rosenberg A, Soininen H, Igier V, Richard E, Kivipelto M, Andrieu S. ACCEPT-HATICE: a mixed methods	**INSERM**

study of facilitators and barriers to participation in an internet-based multidomain trial for the prevention of cardiovascular disease and cognitive decline in older European adults. Alzheimer's Association International Conference (AAIC), London, July 2017 (Poster presentation)	
Coley N, Guillemont J, Rosenberg A, van Middelaar T, Barbera M, Soininen H, Richard E, Kivipelto M, Andrieu S, for the MIND-AD and HATICE groups. Participation in and adherence to an internet-based multidomain trial for the prevention of cardiovascular disease and cognitive decline in French, Finnish and Dutch older adults: data from the ACCEPT –HATICE ancillary study.. 13th Congress of the European Union Geriatric Medicine Society (EUGMS), Nice, France, September 20-22, 2017 (Poster presentation).	**INSERM**
Coley N, Guillemont J, Rosenberg A, van Middelaar T, Barbera M, Soininen H, Richard E, Kivipelto M, Andrieu S, for the MIND-AD and HATICE groups. Participation in and adherence to an internet-based multidomain trial for the prevention of cardiovascular disease and cognitive decline in French, Finnish and Dutch older adults: data from the ACCEPT –HATICE ancillary study. 37th Annual Conference of the French Society for Geriatrics and Gerontology. Paris, France, November 2017 (Poster presentation).	**INSERM**
2016	
Miia Kivipelto. Prevention of dementia – What have we learned from population-based studies? May 19 2016, Demensdagerne 2016, Copenhagen, Denmark	**KI**
Miia Kivipelto. Title: Multimodal strategies to promote healthy brain aging. June 20-22, 2016, 23rd Nordic Congress of Gerontology, Tampere, Finland.	**KI**
Miia Kivipelto. Dementia Prevention, AAIC Conference /Metlife plenary session. 25 July 2016, Toronto, Canada	**KI**
Miia Kivipelto. "From innovative research to healthy aging". 15 November 2016, Nobel Forum, Stockholm, Sweden.	**KI**
Miia Kivipelto. Lifestyle intervention to prevent cognitive impairment. 16 January, 2016, MCI Symposium, Miami, USA.	**KI**
Miia Kivipelto. Is it possible to prevent Alzheimer? 9-11 March. 14 International Athens Springfield Symposium, Athens, Greece.	**KI**
Miia Kivipelto. Dementia Prevention among at Risk Persons. September 8, 2016, IPA (International Psychogeriatric Association) International Congress, San Francisco, CA, USA	**KI**
Miia Kivipelto. Advances in the prevention of vascular cognitive impairment. October 13-15, 2016, VasCog International Congress, Amsterdam, The Netherlands.	**KI**
Ruth Stephen. Structural brain changes on MRI in the FINGER trial. Poster presentation at the 2nd Congress Of The European Academy Of Neurology, May 28-31, 2016 Copenhagen, Denmark.	**UEF**
Anna Rosenberg. Influence of APOE, Age, Sex, Education and Baseline Cognition on Cognitive Intervention Effects in the FINGER trial. Poster presentation at the Alzheimer's Association International Conference (AAIC), July 24 - 28, 2016 Toronto, Canada.	**UEF**
e-Poster presentation: Nicola Coley, Juliette Guillemont, Sandra Rouquette, Alexandra Serre, Mariagnese Barbera, Anna Rosenberg, Tessa van Middelaar, Eric Moll Van Charante, Edo Richard, Valérie Igier, Sandrine Andrieu for the MIND-AD group. Participation of older adults in a randomised trial testing an internet-based lifestyle intervention for the prevention of cardiovascular disease and cognitive decline: the ACCEPT-HATICE study. eHealth Research International Congress, October 11-12 2016, Paris, France	**INSERM, UEF, KI**
Hilkka Soininen. A clinical trial investigating the effects of Fortasyn Connect (SOUVENAID) in prodromal Alzheimer's disease: Results of the LipiDiDiet study. Invited lecture at the 14th International Athens/Springfield Symposium on Advances in Alzheimer Therapy, March 9-12, 2016, Athens, Greece.	**UEF/KI/THL/USAAR**

Hilkka Soininen. New results of the LipiDiDiet study: a 24-month RCT investigating the effects of Fortasyn Connect in prodromal AD Invited lecture at the 9th Clinical Trials on Alzheimer's Disease (CTAD), December 08-10, 2016, San Diego, USA	**UEF/KI/THL/USAAR**
Hilkka Soininen. Memory and mental health. 27 October 2016, Symposium on Mental Health, University of Eastern Finland, Kuopio, Finland (oral presentation)	**UEF**
Hilkka Soininen. Impact of research and approaches to prevention at UEF. 19 October 2016, Rotary Club Meeting, Kuopio, Finland (oral presentation)	**UEF**
Alina Solomon. FINGER Study and MIND-AD. Invited lecture at the 2nd Workshop Nutrition for the Ageing Brain Functional Aspects And Strategies, 30 June-1 July 2016, Copenhagen, Denmark	**UEF/KI**
Alina Solomon. Can dementia be prevented? Invited lecture at the Nobel Forum National Symposium on dementia prevention organized by the Swedish Association for Geriatric Psychiatry, October 21, 2016, Stockholm, Sweden	**UEF/KI**
Timo Pekkala. Predicting incident dementia and amyloid deposition in population-based studies. Oral presentation at the Aging Research Center, Karolinska Institutet Seminar Series, October 18, 2016, Stockholm, Sweden	**UEF/KI/THL**
Tiia Ngandu, How to ensure old age function and quality of life – by preventing cognitive decline, 13 Jan 2016, Finnish Medical Convention, Helsinki, Finland. (oral presentation)	**THL**
Hilkka Soininen. Exercise and cognition – results of the FINGER study. 28 April 2016. Symposium “The Physiology That Unites Exercise and Cognition” – University of Eastern Finland, Kuopio Campus, Finland. (oral presentation)	**UEF/KI/THL**
Ruth Stephen. Structural brain changes on MRI in the FINGER trial. Poster presentation at the 2nd Congress Of The European Academy Of Neurology, May 28-31, 2016 Copenhagen, Denmark.	**UEF/KI/THL**
Jenni Lehtisalo. Adherence to dietary intervention among independently living individuals with elevated risk of dementia. Oral presentation; Nordic Nutrition Conference, Gothenburg, 2016.	**THL**
Francesca Mangialasche. Interventions in prodromal Alzheimer’s disease: creating an innovative research platform, May 18, 2016, Center for Innovative Medicine (CIMED) meeting, Stockholm, Sweden.	**KI**
Tiia Ngandu. Scientific evidence on prevention (plenary talk), 9 May 2016, Netherlands EU presidency conference: Living well with(out) dementia, Amsterdam, the Netherland.	**KI, THL**
Shireen Sindi. The FINGER Trial : A multi-domain intervention to prevent or postpone dementia. Lecture at the symposium Opportunities and Challenges in Cognitive Aging : New Interdisciplinary Perspective. January 2016, Heidelberg, Germany	**KI**
Anna Rosenberg. Influence of APOE, Age, Sex, Education and Baseline Cognition on Cognitive Intervention Effects in the FINGER trial. Poster presentation at the Alzheimer's Association International Conference (AAIC), July 24 - 28, 2016 Toronto, Canada.	**UEF/KI/THL**
Anna Rosenberg. Influence of age, sex, education, and baseline cognition on intervention effects on cognition in the FINGER trial. 28 April 2016. Poster presentation at Symposium “The Physiology That Unites Exercise and Cognition” – University of Eastern Finland, Kuopio Campus, Finland.	**UEF/KI/THL**
2015	
Miia Kivipelto. *Can Diet and Lifestyle Prevent Cognitive Impairment?* The New York Academy of Sciences, New York, USA. 26 March 2015	**KI**
Francesca Mangialasche. *Is there a value for non-drug interventions for dementia prevention?* 9th World Congress on Controversies in Neurology (CONy), in Budapest, Hungary. 27 March 2015.	**KI**
Shireen Sindi. *The Finnish Geriatric Study to Prevent Cognitive Impairment and Disability (FINGER study).* ADPD (Alzheimer’s Disease and Parkinson’s Disease) Conference, April 2015, Nice, France.	**KI**

Miia Kivipelto. *A multidomain two-year randomized controlled trial to prevent cognitive impairment — the FINGER study*. 7th Kuopio Alzheimer Symposium, Kuopio, Finland. 16 June 2015	**KI**
Miia Kivipelto. *The real potential to prevent Alzheimer's disease*. Canadian Academy of Health Sciences, Ottawa, Canada. 17 September 2015.	**KI**
Miia Kivipelto. *Advances in the prevention of dementia*. Horizons for Comparative and Integrative Research on Ageing and Health, Stockholm, Sweden. 7-8 October 2015.	**KI**
Shireen Sindi. *Lifestyle interventions for dementia prevention.* Horizons for Comparative and Integrative Research on Ageing and Health. Stockholm, Sweden. 7-8 October 2015.	**KI**
Miia Kivipelto. *Multi-domain approaches for prevention trials.* Nestlé International Nutrition Symposium, Lausanne, Switzerland. 23 October 2015	**KI**
Miia Kivipelto. FINGER - *A Multidomain Two-Year Randomised Trial to Prevent Cognitive Decline.* CTAD conference, Barcelona, Spain. 5-7 November 2015	**KI**
Shireen Sindi. *Multi-domain interventions to prevent cognitive impairment and dementia*. The Psychiatry and Psychotherapy in Germany : Research, Care, Inclusion (DGPPN Congress). Berlin, Germany. 26 November 2015.	**KI**
Shireen Sindi. Kan demens forebyggs? *Can dementia be prevented ?* Plenary lecture at the Demensdagene (Demetia Day). Oslo, Norway. 1-2 December 2015.	**KI**
Shireen Sindi. *The FINGER Trial : A multi-domain intervention to prevent or postpone dementia*. Lecture at the symposium Opportunities and Challenges in Cognitive Aging : New Interdisciplinary Perspective. Heidelberg, Germany. 11-13 January 2016.	**KI**
Shireen Sindi. *Multi-domain prevention in at risk groups* Symposium on risk & protective factors at the Demensdagene (Demetia Day). Oslo, Norway. 1-2 December 2015	**KI**
Mariagnese Barbera, Miia Kivipelto, Hilkka Soininen et al. *Management of vascular and lifestyle-related risk factors for Alzheimer's disease and dementia in older adults: a European perspective.* 7th Kuopio Alzheimer Symposium. 11-13 June 2015.	**UEF**
Anna Rosenberg, Shireen Sindi, Hilkka Soininen, Miia Kivipelto. *Characterization of prodromal Alzheimer's disease patients at memory clinic and in clinical trials*. 7th Kuopio Alzheimer Symposium. 11-13 June 2015.	**UEF**
Ruth Stephen, Miia Kivipelto, Hilkka Soininen, Alina Solomon et al. *Caide dementia risk score and cortical thickness on brain MRI in FINGER trial participants*. 7th Kuopio Alzheimer Symposium. 11-13 June 2015.	**UEF**
Juliette Guillement et al. *Participation des sujets âgés à une intervention de prévention via Internet: l'étude ACCEPT-HATICE [Participation of elderly in a web-based preventive intervention: the ACCEPT-HATICE study*]. 35èmes journées annuelles de la Société Française de Gériatrie et Gérontologie, Paris, France [35th Annual Conference of the French Society of Geriatrics and Gerontology]	**INSERM**

Presentations for the general public and relevant audiences:

2020

Charlotta Thunborg. Alzheimer's association (Sweden), 2020-02-07

Charlotta Thunborg. Alzheimer's association (Sweden), 2020-08-24

2019

Tobias Hartmann: Roundtable Brussels, EU.

Tobais Hartmann: Roundtable BMEL Berlin, Germany.

Tobias Hartmann: Mettlach open public, Germany.

Tobias Hartmann: Orscholz open public, Germany.

Tobias Hartmann: Neunkirchen open public, Germany.

Tobias Hartmann: Saarbrücken medical association, Germany.

Tobias Hartmann: Krems nurses, Austria.

Tobias Hartmann: Rostock pharmacies, Germany.

Charlotta Thunborg. Swedish Dementia Association 2019-03-04

Charlotta Thunborg. Swedish Dementia Association 2019-09-06

Charlotta Thunborg. Swedish Dementia Association 2020-10-04

Charlotta Thunborg. Alzheimer's association (Sweden), 2019-03-28

Charlotta Thunborg. Alzheimer's association (Sweden), 2019-04-07

Charlotta Thunborg. Alzheimer's association (Sweden), 2019-06-11

Anna Matton. Open lecture, organized by KI and Demenscentrum. Can dementia be prevented?

Jenni Kulmala. Promoting brain health. From research evidence to practical guidelines, Open lecture, Juva, Finland. Sept 2019 (members of Mikkeli Memory Association)

Jenni Kulmala. Promoting brain health. From research evidence to practical guidelines, Open lecture, Savonlinna, Finland. Sept 2019 (older adults, healthcare workers)

Jenni Kulmala. Promoting brain health. From research evidence to practical guidelines, Open lecture, Joenssu, Finland. October 2019 (South Karelian social and health care workers)

Jenni Kulmala. Promoting brain health. From research evidence to practical guidelines, Open lecture, Mikkeli, Finland. Feb 2019 (healthcare practitioners)

Jenni Kulmala. Greetings from FINGER study, Rovaniemi, Finland. April 2019 (Members of North Finland Memory Association)

Miia Kivipelto, Krister Håkansson and Charlotta Thunborg. Stockholm: International Capital of Cognitive Health among Elderly Citizens. Board meeting, Stockholm Dementia Association, Stockholm. Sept 2019

Krister Håkansson. Inspiration seminar, arranged by Stockholm City Elderly administration, Stockholm. Loneliness and Hopelessness. Emotions and Dementia Risk – how can the association be explained? Administrators of Activity Centres for elderly. Sept 2019

Krister Håkansson. Inspiration seminar, arranged by Stockholm City Elderly administration, Stockholm. Loneliness and Hopelessness. Emotions and Dementia Risk – how can the association be explained? Administrators of Activity Centres for elderly. May 2019

Krister Håkansson. ABF, open lecture. Dementia: Can it be prevented and counteracted? Sept 2019

2018

- Miia Kivipelto. World Dementia Council. G8 Dementia Summit Follow-up meeting. 5 December 2018, London, UK

- Solomon A. Hur kan man förebygga demens? De senaste rönen om livsstilsfaktorer (How can we prevent dementia? Latest research on lifestyle factors). Event organised by Alzheimerfonden for World Alzheimer's Day, 21 September 2018, Stockholm, Sweden.

- Charlotta Thunborg. Hur man förebygger och behandlar demenssjukdomar och de senaste forskningsrönen (How can we prevent dementia? Latest research on lifestyle factors). 8 May 2018, Demensföreningen, Stockholm, Sweden.

- Charlotta Thunborg. Hur man förebygger och behandlar demenssjukdomar och de senaste forskningsrönen (How can we prevent dementia? Latest research on lifestyle factors). Lecture for Swedish Alzheimer's Foundation (Seniordagarna med Alzheimerfonden), 3 November 2018, Stockholm, Sweden.

- Charlotta Thunborg. Dementia Prevention. World Alzheimer's Day at Karolinska Institute. 20 September 2018.

2017

- Miia Kivipelto. Nyckelfaktorer som kan fördröja demens. Äldreomsorgsdagarna (Elderly Care Day) 26 October 2017.

- Miia Kivipelto. Hur kan man förebygga och behandla Alzheimer? – Senaste forskningsrönen. Solstickans Foundation – Symposium on dementia. 21 November 2017.

- Shireen Sindi. Går det att förebygga demenssjukdommar? (Is it possible to prevent dementia?) Stockholms Stad: Conference for elderly care managers. 10 May 2017, Djurönäset, Värmdö, Sweden

2016

- Miia Kivipelto. Kan vi undvika att få Alzheimers sjukdom? Internationella Alzheimerdagen, Näringslivets Hus, 21 September 2016, Stockholm, Sweden

- Miia Kivipelto. 'Hur kan vi förebygga och behandla demenssjukdomar? Senaste forskningsrönen', 26 October 2016, Sollentuna, Sweden.

- Miia Kivipelto. Kan vi förebygga minnesproblem och demens? – Senaste forskningsrönen, 7 October 2016, Keynote speaker, ACT conference, Svenska Läkaresällskapet, Stockholm, Sweden.

- Miia Kivipelto. Kan demens förebyggas? 27 October 2016, ARC/Äldrecentrum open house, Aula Medica, Karolinska Institute, Stockholm, Sweden.

- Miia Kivipelto. Hur kan vi förebygga demens och förbättra framtidens äldrevård? 21 October, 2016, Aula Medica, Solna, Sweden.

- Miia Kivipelto. Åldrande och vård av äldre – framtidens möjligheter för Sverige och världen. 26 april, Swecare, Sveavägen 63, Stockholm, Sweden.

- Miia Kivipelto. The FINGER study, Presentation to policy makers 22 January, Helsinki Finland.

- Tiia Ngandu. FINGER project and ongoing European prevention programmes (HATICE, EDPI and MIND-AD), 2 Feb 2016, EU Meeting of Governmental experts on dementia, Luxemburg.

- Hilkka Soininen. Exercise and cognition – results of the FINGER study. 28 April 2016. Symposium "The Physiology That Unites Exercise and Cognition" – University of eastern Finland, Kuopio Campus, Finland

- Shireen Sindi. Dementia Prevention. Presentation to visitors from Japan: Professor Masahiro Hirose (Shimane Univeristy) and his colleagues, who would like to implement similar preventive interventions in Japan, 28 January 2016, Stockholm, Sweden.

- Shireen Sindi. Can Dementia be prevented? Lecture at the Association for English Speakers, November 2015, Stockholm, Sweden.

- Tiia Ngandu, Prevention of dementia with lifestyles, 19 May 2016, TERV-SOS, Seinäjoki, Finland.

2015

- Francesca Mangialasche. *What is good for the Heart is good for the Brain.* What is good for the Heart is good for the Brain: An Integrated Approach for Patients to Achieving 25 by 25 for NCDs". World Health Assembly Side Event Geneva Press Club (CSP), Geneva, Switzerland. 19 May 2015.

- Tiia Ngandu. Voidaanko muistisairauksia ehkäistä (*Can we prevent memory disorders*?). Tampere Summer University, Finland. 8 September 2015.

- Shireen Sindi. *Advances in research on dementia prevention.* Medical Sector seminar series, Aging Research Center, karolinska Institute. Stockholm, Sweden. 10 September 2015.

- Miia Kivipelto. Hur stimuleras vardagen för sverigefinländare med minnessjukdomar? (*How to stimulate everyday Swedish and Finnish with memory problems*?) Embassy of Finland, Stockholm, Sweden. 9 September 2015.

- Miia Kivipelto. *Can anything be done to reduce the risk of dementia?* Internationella Alzheimerdagen, Alzheimerfonden Konserthuset, Stockholm, Sweden. 21 September 2015

- Miia Kivipelto. *Prevention of Dementia.* Sandlersalen, ABF-huset, Stockholm, Sweden. 30 September 2015.

- Miia Kivipelto. *Prevention of Dementia*. Alzheimer café, Stockholm, Sweden. 1 October 2015

- Miia Kivipelto. *Multimodal intervention to prevent Alzheimer disease*. CIMED Inauguration Karolinska Institutet, Huddinge, Sweden. 7 October 2015.

- Miia Kivipelto. *Documentary on FINGER about dementia prevention*. USA TV Program. 13 October 2015.

- Miia Kivipelto. *How can we prevent dementia?.* Presentation when Miia Kivipelto was awarded the Waijlit and Eric Forsgren's prize for distinguished Alzheimer's Researchers. 17 October 2015.

- Shireen Sindi. *Current advances in the medical sector research at the Aging Research Center*. Presented at the Annual Research Day, Aging Research Center, karolinska Institute. Stockholm, Sweden.6 November 2015.

- Tiia Ngandu. Malli muistihäiriöiden ehkäisyyn (*Model for the prevention of cognitive impairment?).* Memory Conference 2015 (organized by Alzheimer Society of Finland). 19 November 2015.

- Shireen Sindi. Dementia Prevention. Presentation to visitors from Japan: Professor Masahiro Hirose (Shimane Univeristy) and his colleagues, who would like to implement similar preventive interventions in Japan, Stockholm, Sweden, 28 January 2016.

3.2. Research tools / methods / models / datasets

Please also indicate whether a laboratory centre or an organisation is to adopt the new knowledge, innovation or method or follow up the results of the project. Please mention also the name and type of the organisation and any impact arising. Please further indicate whether relevant databases have been informed and shared the results of the project (open access)? Yes/No. If yes, which databases? If no, why not?

Yes, World-Wide FINGERS is a unique platform established by Prof. Miia Kivipelto, which aims to support several countries (30+ so far) to develop intervention trials similar to FINGER and MIND-AD, while harmonizing methods, sharing experiences and adapting the interventions to local settings and cultures. In all the participating countries, local universities and / or university hospitals will adopt the FINGER intervention, while tailoring to their local culture, norms, infrastructure and settings. Updates are provided on the World-Wide FINGERs website. For more info. see (www.alz.org/wwfingers/overview.asp).

3.3. Medical products, interventions, clinical testing

Please list identity of product/intervention, stage of development/testing in clinical trial, developmental status, achievement of product

The medical food product Souvenaid, which had promising results in LipiDidiet is also used in MIND-AD.

Knowledge from MIND-AD was uses to collaborate with the EIT-Health funded MULTI-MODE project, and the FINGER-based 'Health-Swipe App' is currently under development.

Within that project, the teams collaborated to develop the Dementia Risk Tool App, to predict the risk for dementia among middle aged and older adults using easily available demographic and lifestyle information. The App is available to download for Apple and Android, free of charge.

3.4. Software, devices, technical products

(e.g., web tool, apps, software, new technology, device, etc.)

The cognitive training program used in the FINGER trial (originally developed as a collaboration with colleagues at Umeå University (Prof. Anna Stigsdotter Neely)) was further adapted and tailored for individuals with prodromal AD.

In relation to the original FINGER study, in the MIND-AD trial, the implementation of the cognitive training program was adapted for the current target group (individuals with Prodromal AD). Therefore, instead of mainly relying on individual home-based training, the participants participated in supervised individual training twice a week in groups throughout the whole intervention period. They were encouraged to practice at home, as in the original FINGER

study, but the training did not rely on whether they actually did this. The different exercises were also adapted by having a lower initial threshold of difficulty, but, as in the original FINGER study, the program automatically adjusts the level of difficulty to the level of individual performance. During pilot testing, we noticed that the initial success rate of 50% could be de-motivating, and we therefore reduced the entrance level of performance on most tasks, and we changed the success rate for progression to the next level of difficulty from 50% to 80%. Finally, in MIND-AD, we also produced a simple and pedagogical manual to facilitate home-based training between on-site sessions.

For more accurate data on physical activity and sleep, the MIND-AD trial provided actigraphs worn for several days by the participants. We have Actigraph data from, Sweden (n=36), Finland (n=30), and France (3n=). Participants wore the actigraph device for 10 days, and kept diaries to document their physical activity.

3.5. Intellectual Property and licensing

Please list type of protection (e.g., copyright, patent, trademark), and impact arising.

Number of patents and licences

Type of patent or licence	N° Submitted	N° Obtained
International patents		
EU patents		
National patents		
Licences (of exploitation/cession)		
Creation of firm (enterprise)		
Other (specify)		

Add lines as appropriate

List of patents

If details regarding patents need to be treated confidentially, please indicate as such.
In column 2, please point out the project partners involved by using the numbering applied in section I General information (e.g. partner 1 or P1)

Patent description	Partner(s) involved	Main partner (moderator)

Add lines as appropriate

3.6. Collaborations/partnerships formed during the course of the project

Please list identity of collaboration/partnership, type (e.g., financial, in kind) and outputs/impact.

Pantel (Frankfurt) – clinical trial
Groneberg (Frankfurt) – clinical trial
Eckert (Giessen) – clinical trial
Hattinger (Frankfurt) – clinical trial
Banzer (Frankfurt) – clinical trial
Ron Handels (the Netherlands) – Health economics
Lars Engstrand (Sweden) – Microbiome MIND-AD sub-study
Daniel Lundqvist (Sweden) – MEG MIND-AD sub-study

Mandana Fallah Pour (Sweden) Qualitative MIND-AD sub-study

3.7. Further funding gained as a result of the project

Please mention from where and provide relevant details.

Miia Kivipelto: FORTE (Swedish Research Council for Health, Working Life and Wellfear). Stronger 60+: Personalized implementation of the FINGER multimodal lifestyle model for healthy brain aging (4.6 milj SEK).

Miia Kivipelto: *Center for Innovative medicine (CIMED*): World Wide-FINGERS multimodal precision prevention toolbox for dementia in Alzheimer's disease, 2020-2023 (1.8 milj SEK) (PI)

Miia Kivipelto: *KI-Janssen Strategic Collaboration:* Prediction modelling, identification and validation of novel molecular signatures of dementia, 2020-2023 (19 milj SEK) (PI)

Miia Kivipelto: *JPND:* EURO-FINGERS multimodal precision prevention toolbox for dementia in Alzheimer's disease, *2020-2023 (4.6 milj SEK) (PI)*

Miia Kivipelto: *Hjärnfonden: Multimodal preventive trials for Alzheimer's Disease (MIND-AD): New Biomarkers. 2018. SEK 500 000 (PI)*

Miia Kivipelto: Academy of Finland. The MUISTIKKO model for preventing dementia and disability (2016-2018) (€299 985) (PI)

Miia Kivipelto: Swedish Research Council: Dementia prevention platform for Theme Aging: From accurate disease models and prognostic tools to effective interventions. 2018-2022 (19.2 milj SEK) (PI)

Miia Kivipelto: NIHR Imperial Biomedical Research Centre (BRC), Imperial College London, Push for Impact. Metabolic markers of cognitive change in the FINGER trial 2018-2019 (£135 000) (PI)

Miia Kivipelto: Academy of Finland. The World Wide FINGERS (WW-FINGERS) Dementia Prevention Toolbox. 2018-2020 (€250 000) (PI)

Miia Kivipelto: *Hjärnfonden: Multimodal preventive trials for Alzheimer's Disease (MIND-AD) 2015. SEK 500 000 (PI)*

Miia Kivipelto: *Alzheimerfondens Jubileumsfond:* Multimodal Preventive Trials for Alzheimer's Disease (Multi-MEMO): Developing an Innovative Swedish Research Platform, 2015 (2.5 mlj SEK) (PI)

Miia Kivipelto: Wallenberg Clinical Scholars 2016-2020 (SEK 15.000 000) (PI)

Miia Kivipelto: MetLife Foundation Major Award for Medical Research 2016 (USD 100 000) (PI)

Miia Kivipelto: Center for Innovative medicine (CIMED): Multimodal interventions in prodromal Alzheimer's disease: creating an innovative research platform, 2015-2020 (10milj SEK) (PI)

Miia Kivipelto: Alzheimerfonden: Multimodal Preventive Trials for Alzheimer's Disease (Multi-MEMO): Developing an Innovative Swedish Research Platform, 2014 (SEK 500 000) (PI)

Shireen Sindi: Karolinska Institute Foundation and Funds (KI Stiftelser och Fonder): Microbiome-Gut-Brain Axis in Prodromal Alzheimer's Disease, SEK 130,000 (2018)

Shireen Sindi: Demensförbundent (Swedish Dementia Foundation): Microbiome-Gut-Brain Axis in Prodromal Alzheimer's Disease, SEK 100,000 (2018).

Shireen Sindi: Alzheimerfonden (Swedish Alzheimer's Foundation): Microbiome-Gut-Brain Axis in Prodromal Alzheimer's Disease (AF-732931), SEK 200,000. (2018)

Charlotta Thunborg: 2017 20 000 SEK Lindhés law firm for AAIC congress travel costs

Charlotta Thunborg: 2018 10 000 SEK Lindhés law firm for travel costs Kuopio Alzheimer symposium

3.8. Policy influence

Results to be applied in policy such as use in decision making, rules applying to basic health insurance packages, use in advisory reports, use in health ministry or in policy memoranda issued by national (umbrella) organisations etc.
Please also point out the *project partners involved by using the numbering applied in section I General information (e.g. partner 1 or P1).*
Could impact be achieved (e.g., changes in healthcare provision, regulatory guidance, economic effectiveness, public atitudes etc.)

Professor Kivipelto was a key member in the recently published WHO Dementia Risk Reduction guidelines (www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/). Along with her team, they conducted large-scale systematic reviews regarding several modifiable risk factors for dementia, evaluated the evidence from observational data and clinical trials, and offered highly valuable contributions to the working group led by the WHO. These guidelines will form the key basis for dementia risk reduction in clinical settings, in lifestyle interventions and for the wider society.

3.9. Capacity and skills development – staff mobility, next destination, qualifications/recognition gained

Please list academic staff involved in the project. Please also list postdocs, PhD students, master students, undergrad students…
Furthermore, please indicate if lab visits or longer-term exchanges between partners happened based on JPND funding.

Partner #	Career stage	Academic dissertation (year, degree)	Name, Gender	Exchange from / to (country)	Duration of Exchange weeks / months
Germany	habilitation	2018	Grimm, MOW, male	Experimental Medicine	
Germany	PhD	2001	Grimm, HS, female	APP trafficking	
Germany	PhD student	pending	Lauer, A, female		

Germany	PhD student	2017	Mett, J, female	APP und Lipidhom.	
Germany	MD	2019	Lehmann, J, male	Vitamin D	
Germany	MD candidate	2019	Nelke, C, female	APP, Xanthine	
Germany	MD candidate	pending	Streidenberger, O, female		
Germany	student	pending	Stoetzel,H, female		
Germany	PhD student	pending	Stahlmann, C, male		
INSERM	Post-doc	PhD, 2010	Nicola Coley, female	From France to Finland	1 month
Sweden	PhD student	2022	Anders Rydström, male	N/A	
Sweden	PhD student	2021	Jakob Norgren, male	N/A	
Finland	PhD student	2022	Eija Pietilä, female	N/A	
Sweden	Master student	2020	Nicholas Levak, male	N/A	
Sweden	PhD student	2021	Ulrika Akenine, female	Sweden to Finland	
Sweden	Postdoctoral fellow	2019	Shireen Sindi, female	Sweden to Finland	
Finland	PhD student	2020	Ruth Stephen, female	N/A	
The Netherlands	PhD Student	2018	Tesse van Middelaar, female	N/A	
Finland	PhD Student	2022	Heidi Turunen, female	N/A	
Finland	PhD Student	2021	Elisa Neuvonen, female	N/A	
Finland	PhD Student	2020	Timo Pekkala, male	N/A	
Finland	PhD Student	2020	Anna Rosenberg, female	Finland to Sweden	
Finland	PhD Student	2022	Jenni Ikonen, female	N/A	

Add lines as appropriate

Ongoing PhD theses related to MIND-AD:

- Ruth Stephen. Analysis of structural brain changes on MRI in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). *Ongoing (2020)*

- Timo Pekkala. Modeling cognitive decline and response to preventive interventions using the Disease State Index. *(Completed April 2020)*

- Anna Rosenberg. Characterizing target populations in dementia prevention trials. Ongoing *(2020)*

- Elisa Neuvonen. The role of psychosocial factors in dementia prevention: from observational studies to a multidomain prevention trial. *Ongoing*

- Heidi Turunen. Role of APOE genotype and telomere length in interventions for preventing cognitive impairment and dementia. *Ongoing*

- Jenni Ikonen. The importance of physical activity in multi-component interventions for preventing cognitive decline. *Registration pending*

- Anders Rydström Mental stimulation and multimodal trials to prevent cognitive impairment and Alzheimer´s disease. Ongoing

- Tessa van Middelaar. Blood pressure management to prevent dementia. (*Completed. 2018)*

- Jakob Norgren. The impact of nutrition and ketone levels on cognition: From normal aging to prodromal Alzheimer's disease. Ongoing

- Ulrika Akenine. Participants‘ experiences in clinical trials. Ongoing (2020)

Exchange of researchers and PhD students between UEF, KI, UMC and Toulouse has been continuously ongoing (2015-2019), e.g. shorter visits of partner teams for data analysis and presenting and discussing preliminary results, as well as manuscript writing. Members engaging in exchange periods include: Tiia Ngandu, Alina Solomon, Shireen Sindi, Anna Rosenberg, Ulrika Akenine, Nicola Coley, among others.

PhD students from UEF have participated in courses and seminars at KI. Adj.

Ron Handels has an affiliation to the Karolinska Institutet and has performed part of the work for WP 6.1 at the Karolinska Institutet. This collaboration is intended to be continued for an undetermined time period.

3.10. List of other outcomes

These may include results to be applied in practice, such as incorporation into guidelines, protocols, standards; changes in professional practice, incorporation into manuals, training modules etc.

- *In column 2, please* specify in which field the given outcome was / will be applied.
- *In column 3, please point out the project partners involved by using the numbering applied in section I General information (e.g. partner 1 or P1).*

Outcome	Field in which the	Partner(s)

REPORT: Alzheimer's Disease International. World Alzheimer Report 2018. The state of the art of dementia research: New frontiers (See pages 23-39) https://www.alz.co.uk/research/WorldAlzheimerReport2018.pdf	Alzheimer's disease. Report for researchers, the general public and relevant stakeholders	KI
REPORT: WHO Guidelines on risk reduction of cognitive decline and dementia https://www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/	Evidence-based recommendations for researchers, the general public and relevant stakeholders	**KI**

Add lines as appropriate

4. Outreach

4.1. Public engagement activities

Please list type of engagement (presentation, media work, etc.), primary audience and any other relevant details.

Germany:
5 Presentations for Alzheimer Patient organisations (Germany)
National TV report
4 media articles

Sweden:
Presentation and collaboration with Alzheimer association Senior Fair, the largest meeting place for seniors Nov 2018

Public seminary in Gothenburg April 2019 100 p in collaboration with Alzheimer association

Two Camps for young relatives (15 p/ camp) during the summer 2019 in collaboration with Alzheimer association

Two public seminars with Dementia association in autumn 2018, two more public seminars in autumn 2019 (Sept and Oct)

Open seminars at Karolinska university Hospital on the International Alzheimer's day 21 sept 2018 and 21 sept 2019

Charlotta Thunborg/Krister Håkansson, Äldre i Centrum /May Ling. Article/ popular scientific newspaper. En kognitiv livsstil. A cognitive lifestyle.

Media appearances

- Miia Kivipelto. Vi ska tala om friskfaktorer inte bara riskfaktorer (We should talk about health factors not just risk factors). Stockholms Sjukhem

https://www.stockholmssjukhem.se/aktuellt/nyheter/2018/vi-ska-tala-om-friskfaktorer-inte-bara-riskfaktorer

- Miia Kivipelto TV4, TV-interview Kivipelto M.Tupplurar kan vara tecken på Alzheimers: ”Dålig sömn kan öka risken”. TV4, Nyhetsmorgon: Sweden; 2019.

- Miia Kivipelto TV4, Anneli Megner Arn TV-interview Kivipelto M. Tupplurar kan vara ett tidigt tecken på demens. TV4: Sweden; 2019.

- Miia Kivipelto. Så kan du träna hjärnan för att minska risken för Alzheimers (The way to train the brain to avoid Alzheimer’s). Dagens Industri. https://www.di.se/brandstudio/alzheimerfonden/sa-kan-du-trana-hjarnan-for-att-minska-risken-for-alzheimers/

- Miia Kivipelto. Kan man skydda sig mot Alzheimer? (Can you protect yourself against Alzheimer's?). Hjärnfonden. https://www.hjarnfonden.se/2018/09/kan-man-skydda-sig-mot-alzheimer/

- Miia Kivipelto. NKS tar sig an sjukvårdens viktigaste utmaning. (NKS (New Karolinska Hospital) addresses the most important challenge of the healthcare system). Svenska Dagbladet. https://www.svd.se/mirakelmedicin-ska-bromsa-demens--nks-satar-pa-aldre

- Miia Kivipelto. Suomalaistutkimus todisti, että elämäntavoilla voi vaikuttaa muistisairauksiin – Nyt aivotutkija Miia Kivipelto vie Suomen mallia maailmalle(Finnish research proved that lifestyle can affect memory diseases - Now brain researcher Miia Kivipelto takes Finland's model to the world). Helsingin Sanomat. https://www.hs.fi/kotimaa/art-2000005714662.html

- Miia Kivipelto. Alzheimer’s Disease International. Global webinars on research participation. ‘Let's Talk about Dementia Research: Global Barriers and Access to Trials’. https://www.alz.co.uk/webinars-research-participation

- Miia Kivipelto. Sky News. Interview on dementia and Alzheimer’s

- Twitter: For example:
  https://twitter.com/AlzDisInt/status/1093843443003068417
  https://twitter.com/hashtag/wwfingers
  https://twitter.com/MiiaKivipelto/status/1021626614415847424

Miia Kivipelto. (TV Interview): Aktuellt, Sweden 07-09-2017
Miia Kivipelto. (Radio Interview): Dementia prevention, YLE Pohjanmaa, Finland, 14-10-2017
Miia Kivipelto. (TV Interview): YLE Keski-Suomi, Finland 29-11-2017
Miia Kivipelt. (Newspaper): Alzheimerforskarna tvingas tänka om. 02-03-2017

Journal of Alzheimer’s disease news on telomere results (2017)
http://j-alz.com/content/telomere-length-associated-cognitive-response-lifestyle-intervention-supporting-evidence
http://ki.se/en/nvs/telomere-length-is-associated-with-the-cognitive-response-to-a-lifestyle-intervention

http://www.thehealthpilot.org/alzheimers-can-challenging-job-exercise-keep-condition-bay/
https://www.news-medical.net/news/20170829/96/Swedish.aspx
http://www.sciencenewsline.com/news/2017082817490059.html

Miia Kivipelto & Tiia Ngandu. FINGER results. Various online journals, TV channels, newspapers e.g..... (March 2015)

Miia Kivipelto. NHK Special: The Dementia Revolution: The Road to Prevention. Japan TV programme. 14 November 2015.

4.2. Materials made available to the research community and how

REPORT: Alzheimer's Disease International. World Alzheimer Report 2018. The state of the art of dementia research: New frontiers (See pages 23-39)

https://www.alz.co.uk/research/WorldAlzheimerReport2018.pdf

REPORT: WHO Guidelines on risk reduction of cognitive decline and dementia
https://www.who.int/mental_health/neurology/dementia/guidelines_risk_reduction/en/

IV. Recommendations

This section is for internal use by the JPND joint call partner organisations. Please also describe potential recommendations so we can shape our future call scheme. This information will not be published.
Describe any recommendations arising from this project.