



The CITA GO-ON trial: A person-centered, digital, intergenerational, and cost-effective dementia prevention multi-modal intervention model to guide strategic policies facing the demographic challenges of progressive aging

Mikel Tainta¹, Javier Mikel Olaso², M. Inés Torres², Mirian Ecay-Torres¹, Nekane Balluerka², Naia Ros², Mikel Izquierdo^{3,4}, Mikel L. Sáez de Asteasu^{3,4}, Usune Etxeberria Aranburu^{5,6}, Lucía Gayoso Morandeira^{5,6}, Maider Mateo Abad^{7,8}, Oliver Ibarondo⁷, Elena Alberdi⁹, Estibaliz Capetillo-Zarate⁹, Jesus Angel Bravo Duque¹⁰, Pablo Martínez-Lage¹

¹Center for Research and Advanced Therapies, CITA-alzhéimer Foundation, Spain.

²University of the Basque Country UPV/EHU, Spain.

³Navarrabiomed, Hospital Universitario de Navarra (HUN) – Universidad Pública de Navarra (UPNA), IdiSNA, Spain.

⁴CIBER of Frailty and Healthy Aging (CIBERFES), Instituto de Salud Carlos III, Spain.

⁵Basque Culinary Center, Faculty of Gastronomic Sciences, Mondragon Unibertsitatea, Spain.

⁶BCCInnovation, Technology Center in Gastronomy, Basque Culinary Center, Spain.

⁷Biodonostia Health Research Institute, Spain.

⁸Network for Research on Chronicity, Primary Care, and Health Promotion (RICAPPS), Spain.

⁹Achucarro Basque Center for Neuroscience, Departamento de Neurociencias, Universidad del País Vasco (UPV/EHU) and CIBERNED, Spain.

¹⁰Argi Ventures s.l., Spain.

pmlage@cita-alzheimer.org, manes.torres@ehu.eus

Abstract

This paper presents a general overview of the CITA GO-ON study, a controlled and randomized trial aimed to demonstrate the efficacy and cost-effectiveness of a 2 years multi-modal intervention to control risk factors and change lifestyles in cognitively frail people at increased risk of dementia. In this framework, the applicability of a virtual agent to increase adherence and effectiveness (the “Go-ON digital coach”) will be explored.

The multidisciplinary nature of the study brings together 7 partners including non-profit organizations, universities, technological centers and companies.

Index Terms: Cognitive impairment, Dementia, Alzheimer’s disease, prevention, Healthy aging, Multidomain intervention, Randomized trial, Virtual agent, Human-machine interaction, Spoken dialogue systems.

1. Introduction

The general guidelines of the Spanish National Strategy for demographic challenge, (Council of Ministers 29 March 2019) declare the progressive aging of the population as one of the three major challenges of the demographic change.

The proportion of people over the age of 65 in Spain is expected to rise from 19.6% in 2020 to 30.1% by 2050. Unfortunately, life expectancy achievements (80.01 in males and 85.44 in women in 2020) have not been accompanied by an increase in “disability-free” life expectancy (68.0 in males and 68.0 in women in 2018)¹. Thus, the number of disabled and dependent people will increase massively over the next two or three decades. Therefore, there is an urgent need to implement effective measures in the field of active and healthy prevention and aging. Otherwise, this change in population age will result in a marked increase in the number of dependents whose care and care needs seriously threaten the sustainability of the welfare state. Alongside osteo-muscular and cardio-respiratory processes, diseases that cause dementia, such as Alzheimer’s, are the main causes of disability and dependence in older people. In Spain, the number of people with dementia is expected to significantly rise from 850,000 in 2020 to about 2 million in 2050 (3.99% of the total population). Caring for a person with dementia involves more than one family member, one of whom (usually a woman) quits her job. Preventing dementia will significantly reduce the dependency rate of retired persons/not active people.

This new era of personalized and preventive medicine has changed the way we face dementia. The concept of healthy

¹ 4.2 Esperanza de vida en buena salud <https://www.ine.es/> accessed Oct 13th 2022.

aging should emphasize that brain health, cognition and behaviour are fundamental determinants of people's quality of life. The possibility of early detecting people at risk and diagnosing pre-clinical phases, states of frailty and the early stages have oriented the efforts of the medical and scientific community to the development of intervention strategies for the prevention of dementia dependence.

In the specific case of Alzheimer's disease numerous pharmacological trials have failed to modify the course of the disease. Dependency has not been delayed. New approaches are needed in the context of primary and secondary prevention.

The pathophysiology of dementia is multifactorial and complex. The clinical expression of specific etiopathogenesis such as Alzheimer's or vascular dementia, changes depending on how different molecular and cellular mechanisms, risk factors, and risk and protection conditions of very heterogeneous nature (vascular, genetic, metabolic, inflammatory, social and personal) converge in the same brain. Preventive strategies should have a multi-factorial approach. The FINGER (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability) of the Karolinska Institute demonstrated how a multidomain intervention of risk factor control and enhancing of protective factors reduces the incidence of cognitive decline in people at high risk of dementia [1].

In 2018 CITA-alzhéimer launched the pilot study GOIZ ZAINDU [2, 3] and managed to adapt the FINGER methodology to the Basque population. In collaboration with Osakidetza and the City Council of Beasain, CITA-alzhéimer harmonized the Basque health, cultural and social environment and demonstrated a high level of acceptance and participation by users and professionals and a degree of adherence to the study similar to FINGER.

CITA GO-ON (ClinicalTrials.gov No. NCT04840030) is an on-going study that expands and modernizes the FINGER study's proposal to replicate its results in preventing cognitive decline in people at cognitively fragile risk. It is focused on the person and their empowerment and proposes a multidisciplinary approach to health and education in a personal and social context. It adds intervention on emotional aspects and adverse social situations as an essential ingredient of prevention. It incorporates the digital approach as an intervention tool that guarantees accessibility, adherence and widespread and equitable application facing the problem of the digital divide associated with age and gender. It adds an intergenerational dimension of mutual solidarity between the elderly and young to build a society that addresses its challenges in a responsible manner. It includes the application of big data analysis and artificial intelligence techniques. It explores a virtual agent as a coaching and personal assistance tool. It will result in an affordable, cost-effective, transferable service product that, on the one hand, will feed with proven data new policies and strategies to alleviate the social and economic costs of aging and provide solutions to the challenge of achieving the sustainability of the welfare state. On the other hand, it will have a potential impact on the silver economy of sectors such as leisure, food, information and

communication technologies, home automation, hospitality, culture or sport.

2. CONSORTIUM

The CITA GO-ON consortium is a multidisciplinary, collaborative team of 7 partners with proven experience in the different areas of which it is composed.

- CITA-alzhéimer Foundation, Spain (coordinator, non-profit).
- University of the Basque Country, Spain (academic)
- Public University of Navarre UPNA, Spain (academic).
- Basque Culinary Center (BCCInn), Spain (technological center).
- Biodonostia Health Research Institute, Spain (non-profit).
- Achucarro Basque Center for Neuroscience, Spain (non-profit)
- Argi Ventures S.L., Spain (company)

3. Methods

The targeted population of this efficacy trial of a 2-year multi-modal intervention are 1.000 people over 60 years at high risk of dementia but with no significant cognitive decline that could interfere in their daily living activities.

After the baseline visit, participants will be randomly assigned to the standard health advice control group (SHA, control) or the multimodal intervention group (MM-Int) on vascular risk, cognitive/physical activity, diet, psychosocial engagement, drug misuse. Random assignment will follow a proportion of 1:1 and will be based on age, sex and cognitive status (with or without mild cognitive impairment).

Study participants in both the SHA-control and MM-Int groups will receive follow-up efficacy assessments three times during the study at the baseline visit, 12-month visit, and 24-month visit.

Together with the programmed efficacy follow-up visits at 12 and 24 months, participants in the MM-Int group will receive study follow-up visits which will be conducted every 4 months by the core-research team.

4. Speech Technologies in CITA GO-ON

The project also incorporates the digital approach as an intervention tool that guarantees accessibility, adherence, and widespread and equitable application facing the problem of the digital divide associated with age and gender. In this framework, CITA GO-ON explores a virtual agent as a coaching and personal assistance tool. To this end, we are considering the conclusions of the EMPATHIC project aimed to design a Virtual Coach to improve the independent years of elderly people [4] [5] [6]. The CITA GO-ON consists of the classical modules of a Spoken Dialogue System, i.e. an ASR, a NLU, a DM, a NLG, a Virtual agent¹, and a TTS² integrated into a robust platform able to deal with 500 users who do not always have access to a high speed internet connection. The ongoing work includes the planning and development of two

¹ The avatar is provided by Institut Mines Télécom Paris

² The TTS and voices are provided by Acapella Group Belgium

different scenarios: motivational and engaging dialogues on the one hand and dialogues aimed at getting health and behavioral data on the other hand. Both scenarios have to implement different dialogue policies. Finally, the project has also to tailor the NLU to the Spanish spoken by the elderly population leaving in Gipuzkoa.

Figure 1 shows a screenshot of an interaction between a user at the upper left corner of the screen and the Virtual Agent. Subtitles are aimed at support elderly people with some hearing impairments.



Figure 1: Interaction of the user at the upper left corner on the screen and the virtual agent.

5. Acknowledgements

This work is partially funded by grant PLEC2021-008171 funded by MICIN/AEI/10.13039/501100011033 and by the European Union NextGenerationEU / PRTR, and supported by the Department of Health of the Basque Government and Fundación hna (fundacionhna.es).



6. References

1. T. Ngandu, J. Lehtisalo, A. Solomon, E. Levälähti, S. Ahtiluoto, R. Antikainen, L. Bäckman, T. Hänninen, A. Jula, T. Laatikainen, J. Lindström, F. Mangialasche, T. Paajanen, S. Pajala, M. Peltonen, R. Rauramaa, A. Stigsdotter-Neely, T. Strandberg, J. Tuomilehto, H. Soininen and M. Kivipelto. "A 2 year multidomain intervention on diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomized controlled trial," *The Lancet*, vol. 385, no. 9984, pp. 2255-2263, Jun. 2015.
2. M. Tainta, M. Ecay, A. Iriondo, A. Etanga, M. Clerigue, J. Saldias, M. de Arriba, M. Garcia-Sebastian, S. Aurtenetxe, M. Barandiaran, A. Gabilondo, J. Mar, A. Arrospide, I. Vergara, J. Mugica, F. Mangialasche, T. Ngandu, M. Kivipelto and P. Martinez-Lage. "Adopting the FINGER multimodal intervention

methodology to prevent cognitive decline in Southern Europe: The GOIZ ZAINDU pilot study," *Alzheimer's & Dementia*, vol. 17, no. S10, pp. e056022, Dec. 2021.

3. M. Ecay, M. Tainta, J. Mugica, M. Arriba, N. Ros, M. Barandiaran, A. Iriondo, M. Garcia-Sebastian, A. Estanga, S. Aurtenetxe, J. Saldias, M. Clerigue, A. Otaegui, A. Gabilondo, A. Arrospide, P. Martinez-Lage. "Cognitive results after a FINGER-like one-year randomized controlled multidomain intervention: The GOIZ ZAINDU pilot project," *Alzheimer's & Dementia*, vol. 16, no. S10, pp. e042440, Dec. 2020.
4. M. I. Torres, J. M. Olaso, C. Montenegro, R. Santana, A. Vázquez, R. Justo, J. A. Lozano, S. Schlögl, G. Chollet, N. Dugan, M. Irvine, N. Glackin, C. Pickard, A. Esposito, G. Cordasco, A. Troncone, D. Petrovska-Delacretaz, A. Mtibaa, M. A. Hmani, M. S. Korsnes, L. J. Martinussen, S. Escalera, C. Palmero Cantariño, O. Deroo, O. Gordeeva, J. Tenorio-Laranga, E. Gonzalez-Fraile, B. Fernandez-Ruanova, and A. Gonzalez-Pinto. "The EMPATHIC project: mid-term achievements". In *Proceedings of the 12th ACM International Conference on Pervasive Technologies Related to Assistive Environments (PETRA '19)*. Association for Computing Machinery, New York, NY, USA, 629–638, 2019 <https://doi.org/10.1145/3316782.3322764>
5. R. Justo, L. Ben Letaifa, C. Palmero, E. Gonzalez-Fraile, A. Torp Johansen, A. Vázquez, G. Cordasco, S. Schlögl, B. Fernández-Ruanova, M. Silva, S. Escalera, M. de Velasco, J. Tenorio-Laranga, A. Esposito, M. Komes and M.I. Torres, "Analysis of the interaction between elderly people and a simulated virtual coach." *J Ambient Intell Human Comput* **11**, 6125–6140 (2020). <https://doi.org/10.1007/s12652-020-01983-3>
6. J.K. Olaso, A. Vázquez, L. Ben Letaifa, M. De Velasco, A. Mtibaa, M.A. Hmani, D. Petrovska-Delacretaz, G. Chollet, C. Montenegro, A. López-Zorrilla, R. Justo, R. Santana, J. Teorio-Laranga, E. Gonzalez-Fraile, B. Fernández-Ruanova, G. Cordasco, A. Esposito, K. Beck, A. Torp, M.S. Komes, C. Pickard, C. Glackin, G. Cahalane, P. Buch, C. Palmero, S. Escalera, O. Gordeeva, O. Deroo, A. Fernández, D. Kyslitska, J.A. Lozano, M.I. Torres and S. Schlögl "The EMPATHIC Virtual Coach: a demo". In *Proceedings of the 2021 International Conference on Multimodal Interaction* (pp. 848-851), 2021