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Final intervention plan to prevent cognitive, physical and social decline in the elderly

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Abstract

Finding an effective population-based strategy to prevent or delay cognitive, physical, and social decline is an increasingly salient public health priority for our aging societies.
Several guidelines to prevent cognitive and physical decline have been suggested in recent years. Taking into consideration the results of the My-AHA RCT, we suggested: 1. to implement ICT programs for early detection of frailty, 2. to plan multidimensional strategies for the prevention of frailty, 3. to actively engage older adults in prevention of cognitive, physical and social decline, 4. to validate new definitions as well as new frailty indexes that encompass all the frailty domains.

Disclaimer

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Executive summary

The purpose of this deliverable is to discus recent guidelines regarding prevention of cognitive, physical and social decline in the elderly and to discuss suggestions derived from the My-AHA randomized controlled study.

Main recommendations are:

- Due to the very large number of subjects requiring early risk detection, there is a need to implement ICT-derived instruments in order to obtain early indications regarding the frailty risks;
- A multidomain intervention is necessary to prevent and/or slow the progression from a pre-frail condition to an overt frail status, with higher compliance observed for interventions delivered in face-to-face mode than via an ICT-based platform;
- All interventions need to be strictly personalized and empowerment of older adults in preventive strategies is paramount.
- A new definition of frailty, as well as new frailty indexes, are necessary for an early diagnosis of prefrail/frail conditions as well as for develop effective prevention strategies
- Fully deployed ICT-based monitoring and interventions may not be a viable solution for older adults. Our experiences with this cohort of older adults indicate that compliance with ICT-based platforms requiring user interface is low, as is compliance with ICT-based intervention delivery. Hence, the aging cohort in our study displayed higher levels of engagement and compliance with traditional face-to-face intervention delivery but low usage of the elements of software platform requiring the end user to interface and input data. The older adults in our study showed good uptake and usage of wearable devices, indicating that automated systems for data collection and monitoring are likely to be viable for this aging cohort, with interventions being deployed through direct human interaction. It is possible that with future generations fully interactive ICT based platforms and ICT-delivered interventions involving end user interaction may be widely used by end users, however this remains speculative at this stage.

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List of abbreviations

ADL – Activity of Daily Life
HADS – Hospital Anxiety and Depression Scale
HVLT – Hopkins Verbal Learning Test
IADL – Instrumental Activity of Daily Life
ICT – Information and Communication Technology
LNSR-R - Lubben Social Network Scale, Short form
MCI – Mild Cognitive Impairment
MMSE – Mini Mental State Examination
MoCA – Montreal Cognitive Assessment
RCT – Randomized Controlled Study
Self-MNA – Self-Mini Nutritional Assessment
SPSS.26 – Statistical Package for Social Sciences – ed. 26
WHO – World Health Organization
WHOQOL-OLD - World Health Organization Quality of Life scale – OLD extension

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Appendix 1

Copy of the manuscript submitted to Alzheimer's & Dementia

1 Introduction

Healthy aging is not merely the absence of disease or disability but requires physical and mental health and ongoing social engagement. As the average E.U. life expectancy increases, recognition that public health can play a vital role in promoting healthy and successful aging in older adults has grown. In addition, actively engaging adults in prevention and wellness can serve to prevent or delay the onset of physical disabilities and cognitive decline.

As advances in public health and health care have helped to increase life expectancy, public health professionals and health care providers have the opportunity to improve the quality of life for older adults and their caregivers and reduce the burdens associated with aging.

Quality of life (QoL) in older adults has become an important concept in medical, social, and psychological research. Moreover, the evaluation of QoL in older adults is becoming increasingly important outcome measure for planning and delivery of health and social services (1). QoL is a complex concept which, according to WHO, encompasses "An individual's perception of their positions in life, in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standard and concerns" (2). Several studies have identified a link between QoL and frailty, reporting a robust inverse association between frailty/prefrailty and QoL in older adults (3). This suggests that interventions targeted at reducing frailty may have the additional benefit of improving corresponding QoL.

Numerous opportunities exist to help promote the health, well-being, and independence of older adults.

2 Prevention of cognitive decline in the elderly

Cognitive skills play a crucial role in the daily functioning of older people. Unfortunately, some of these cognitive skills (e.g., memory, problem-solving activities, or speed processing) decline in the process of aging. There are several risk factors which appear to have an impact on cognitive decline and these risk factors can be divided into modifiable and non-modifiable risk factors. The non-modifiable risk factors include age, race and ethnicity, gender, and genetics. The modifiable risk factors mainly involve diabetes, head injuries, lifestyle, and education.

Modifiable risk factors for cognitive decline have been intensively investigated in order to plan strategies for both prevention and slowing down of dementing illness. Both pharmacologic and non-pharmacologic strategies have been suggested, with inconsistent results.

At present, there is no strong evidence for the use of any pharmacologic interventions to prevent cognitive decline in healthy older adults. The non-pharmacological lifestyle intervention activities have been divided into three groups which may have a positive impact on cognitive decline: physical activities, cognitive interventions, and healthy diet. These activities may have a positive effect on the maintenance of synaptic function whose loss is usually connected with toxic forms of amyloid-β protein, which can result in the onset of aging diseases such as dementia. In addition, physical activities can contribute to the increase of vascularization, energy metabolism, and resistance against oxidative stress, which has a positive effect on cognitive functions.

Very recently, the World Health Organization (WHO) released new guidelines in order to reduce cognitive decline and dementia. The new guidelines are designed to "provide the knowledge base for healthcare providers governments, policy-makers, and other stakeholders to reduce the risk of cognitive decline and dementia through a public health approach". The rise in cognitive decline and dementia is alarming and is expected to double every 20 years, from 47 million people in 2015 to 75 million in 2030 and 131 million in 2050. This means that in the next 30 years, "the number of people with dementia is expected to triple and we need to do everything we can to reduce our risk of dementia". According to these new guidelines, physical activity should be recommended to **all adults** with normal cognition to reduce the risk for cognitive decline.

At present, there is evidence confirming the effectiveness of physical activity interventions in slowing cognitive decline. Several RCTs have investigated the role of physical exercise in preventing cognitive decline. Cassilhas and colleagues (4) investigated resistance-training protocols of moderate and high intensity compared with a placebo stretching group in a study involving 62 men over 6 months. The resistance training protocols consisted of 3 one-hour sessions per week beginning with a 10-minute warmup and then using varying resistance loads under professional supervision. The authors found a statistically significant improvement in some, but not all, tests of short-term and long-term episodic memory. The authors did not report an overall change in cognition. A second RCT compared resistance- and balance-training exercises with a flexibility and relaxation program, as well as a no-exercise control. The study, which included 152 healthy older adults who were followed for 1 year, showed no significant improvement in visual, verbal or working memory with the intervention compared with the flexibility and relaxation program, or the no-exercise control. Baker and colleagues completed a

6-month study with 28 participants comparing aerobic exercise (participants used treadmills, stationary bicycles or elliptical trainers to reach 75%–85% of their heart rate reserve) to stretching (participants carried out stretching and balancing exercises while maintaining their heart rates at or below 50% of their reserve). This study found benefits in executive function ($p = 0.04$) but not in memory in the aerobic exercise group.

Three RCT explored the role of various forms of **cognitive training ,** which can also be referred to as mental exercise, to prevent cognitive decline in the healthy older adults. Willis and colleagues (5) investigated the role of cognitive training in reasoning, speed or memory in 2802 healthy older adults. All 3 groups showed significant improvements in memory over the 5-year follow-up period, with a relatively greater effect size in the memory-trained group compared with the reasoning- or speed-training groups (effect size 0.23 v. 0.05).Smith and colleagues (6) compared a computerized cognitive training program based on brain plasticity with a general cognitive stimulation program over 8 weeks in 487 older adults. There was a significant improvement in auditory memory and attention in the treatment group compared with the control group ($p = 0.02$) with an improvement of 2.1 points (3.9 points, 95% CI 2.7 to 5.1, v. 1.8 points, 95% CI 0.6 to 3.0) on a 100-point scale; however, the overlap between the treatment and control groups indicates that the significance of the difference is unclear. Bahar and colleagues (7) assessed the impact of 10 hours of computerized visual demonstration training compared with no training in a study of 32 people over 4 weeks. They found statistically significant improvement in performance after 4 weeks in the intervention group compared with the control group ($p < 0.05$, effect size 0.81), not only in the trained perceptual task but also in untrained working memory tasks.

More recently, **diet** has been investigated as a modifiable risk factor for cognitive decline. Dietary interventions and their effects on cognition and brain functioning are less well-studied in humans in terms of randomized controlled studies, although observational studies show potential benefits for the Mediterranean-style diet to lessen the cognitive decline with aging. One interventional trial comparing a low-fat diet with supplements of either olive oil or mixed nuts also revealed benefit of the Mediterranean-style diet on cognition. In a recent systematic review and meta-analysis, Lehert and colleagues (8) examined the 12 potentially modifiable risk factors for cognitive decline in aging. They found that the greatest although small benefits were observed with a Mediterranean diet plus tai chi on global cognition and a Mediterranean diet plus olive oil and soy on memory. Overall, more randomized trials are necessary to make evidence-based recommendations about diet to influence cognitive decline in aging. Specifically, studies are needed to delineate specific nutrients that are beneficial to cognition so that recommendations can be made that have the potential to protect the brain from cognitive decline in older as well as younger adults.

Taken together these studies suggested that modifying only a single risk factor (low physical activity, low cognitive stimulation, i.e.) alone may be not enough in order to prevent cognitive decline and that only multidomain interventions may be useful to reduce the risk of cognitive decline.

3 Prevention of physical decline in the elderly

Physical activity is any bodily movement that results in increased energy expenditure, and can be achieved by a variety of leisure-time, work or transportation-related activities. Exercise refers to physical activities that are planned, structured, repetitive, and intended to improve or maintain fitness, function, and health. Ample evidence now exists that regular physical activity is key to preventing and managing major chronic diseases common to older people. Many non-communicable chronic health conditions prevalent in both developed and developing countries are associated with physical inactivity. Physical activity is also important for preserving physical function and mobility, which can then delay the onset of major disability.

It is very clear that physical inactivity is a major contributor to mortality. The WHO reported that around 3.2 million deaths each year are attributable to physical inactivity (9). Governments around the world are recognising the importance and the large impact of physical inactivity on health and health-related expenditure. This has led to the production of global and national guidelines for physical activity.

Current physical activity guidelines for older people recommend at least 150 min/week of moderate-intensity aerobic activity, with muscle-strengthening activity performed on two or more days/week. Despite the known benefits of physical activity to health and physical function in aging, the proportion of older adults meeting the recommended physical activity guidelines for aerobic activity remains low. Only one out of 4 older adults meets this standard. This low prevalence of physical activity has important implications since it is a modifiable behavior that contributes substantially to the burden of chronic disease mortality.

In the last decade, considerable evidence has emerged regarding the relative benefits of additional modes or combinations of physical activity to specific physical function outcomes (e.g., strength, gait speed, balance, activities of daily living function). These additional physical activity interventions include progressive resistance training, multicomponent exercise, dual-task training, active video gaming, tai chi, yoga, and dance. In addition, the current research has begun to address the issues of the dose-response relationship between physical activity and physical function in aging (10). Similar to studies of pharmacologic agents, it is not only important to determine if a graded relationship exists, but also to determine the shape of the relationship for specific health outcomes, in order to establish a minimal effective dose and a maximal threshold dose for safety.

In the presence of strong evidence linking physical inactivity to chronic health conditions and increased physical activity to lower mortality and morbidity in older adults, it is imperative to develop a strong commitment to improving physical activity levels in older adults. The main challenge is to find effective ways to support older adults to increase their physical activity and then to develop habitual physical activity behaviours.

4 Prevention of social decline in the elderly

Evidence from longitudinal studies suggests that one potential modifiable risk factor for decline in older adults may be participation in social activity. Social participation, which is a source of social relations and describes a person's participation in formal and informal group activities, has long been recognized as an essential component of active aging.

Social participation declines as a result of the normal aging process and negatively correlates with daily function and disability in old age. Some prior longitudinal studies of social participation in elderly persons have focused on an outcome referred to as functional disability, but the results of these studies have been contradictory.

Studies that examined the effects of social participation according to different types of groups showed that participation in several groups may have a protective effect on depression, well-being, and functional disability (11). In contrast, other studies examining the effects of participation in civic groups on all-cause mortality, cognitive function, and overall health status have not always shown a reduction in risk with participation.

Since social participation can be enhanced, clarifying what forms of participation (i.e., participation in all or specific types of social groups) are effective can provide a better understanding for increasing the healthy life years of the elderly. Social networking ties provide individuals with access to various forms of social support and social networks (e.g., access to material resources, or health-relevant information). This may enhance subjects' willingness to take an interest in health-related information through the mass media including newspapers, books, magazines, and television. In addition, stress buffering is also considered a pathway to good health.

Several studies showed that loss of a spouse, which has been classified as one of the most stressful events a person can encounter, causes functional decline in the elderly, while social interactions buffer the effects of widowhood on functional decline. As participation in various social groups increases social interactions, the elderly who participate in more groups may have more protection against functional decline. Finally, the benefits of social participation may be due to the influence of social role. An earlier study has reported that people who maintain a role in social participation experience a lower risk of depression. Participation in social groups may also provide and reinforce meaningful social roles, thereby providing a sense of value and belonging to an older adult's post-retirement life. This sense of attachment to family, friends, and community may provide a strong motivation to maintain functional capacity in later life. As participation in a diversity of social groups increases not only the number of roles, but also the opportunity to acquire meaningful social roles, the elderly who participate in more social groups can sustain stronger motivation to maintain higher-level functional capacity.

5 Recommendations from the My-AHA RCT

The My-Active and Healthy Aging RCT was a multicenter, multicultural randomized controlled trial that evaluated the effects of a multidomain ICT supported intervention on quality of life in pre-frail older subjects. This RCT deployed interventions for selected frailties (physical, cognitive, and psycho-social) and suggestions on nutrition and sleep tailored to individually determined multi-domain frailty (see detailed manuscript in appendix).

5.1 Intervention plans to prevent cognitive decline – ICT delivered

Through the ICT platforms available, the elderly has been able to perform the cognitive intervention plans assigned by using two apps: **Cognitive Platform** and **Brain HQ**.

Three intervention plans were developed for the seniors, (please refer to deliverable D5.5, for a complete description of them). All three were delivered to the participant using an ICT interface, with the participant undertaking these activities alone:

- n-back Training
- Visual spatial n–back training
- Reaction time training

One personal weekly goal can be set by the user: the number of training.

5.1.1 n-back training

"The N-back task has been designed to engage your working memory. By constantly memorizing, updating, and comparing the pictures on the screen you are practicing functions of your working memory. The task has been designed to adjust to your competency level. So, if you are doing well, it will get harder, to remain challenging. See how far you can get.

Keep an eye on your progress by comparing your results over time."

The n-back training works in conjunction with visual spatial n-back training. It has been recommended to weekly alternate between n-back training and visual-spatial n-back training.

Example:

Week 1: 3 sessions n-back training
Week 2: 3 sessions visual spatial n-back training
Week 3: 3 sessions n-back training
Week 4: 3 sessions visual spatial n-back training.

It has been asked to the elderly to perform the cognitive trainings 3 times per week equally spaced (e.g. Monday, Thursday, Saturday).

5.1.2 Visual spatial n–back training

As for n-back training.

5.1.3 Reaction time training

"This task is all about making the right choice as fast as possible. Look at the cross and then decide as fast as possible whether you can see one or two dots on the screen.

Regular practice on this task can improve your reaction time. You can keep an eye on your progress by plotting and comparing your previous results."

It has been asked to the elderly to perform 2 sessions daily.

5.1.4 Results

As already reported in other deliverables (D7.22), the adherence to these cognitive interventions was low. The graphs of the usage of the cognitive platforms show three peaks of activity timed closely around each assessment point (T6, T12 and T18) where the elderly performed the trainings following the intervention plans. However, the number of trainings performed decrease over the time, until the next assessment phase. Hence, while initial uptake is good it appears tied closely to the face-to-face assessment points, with poor maintenance of compliance with the interventions over time.

5.2 Intervention plans to prevent physical decline – face-to-face delivered

Two intervention plans have been proposed for preventing the physical decline:

- FAME (Fitness and Mobility Exercise Program)
- Otago Exercise Program

Two personal weekly goals can be set by the user: monitoring the Body Weight and Physical Activity (in terms of minutes spent in performing it).

5.2.1 FAME

A group-based face-to-face physical exercise program delivered by a trained instructor. Key elements of the FAME program revolve around improving muscle strength, balance and coordination through a series of structured supervised exercises tailored to the participants level of physical function.

Frequency of FAME activity was individually tailored for each participant based in accordance with each Phase of assessment physical function capacity assessment.

5.2.2 Otago

A home-based individual physical exercise program focusing on developing muscle strength and coordination or improvement of balance and reduction of falls risk in older adults. OTAGO comprises a series of specified exercise activities that can be tailored to accommodate the participant's level of physical function. Participants were individually trained in the program byt a trained instructor, with monthly updates to modify their individual program according to need.

As with the FAME program, the frequency of OTAGE activity was individually tailored for each participant based in accordance with each Phase of assessment physical function capacity assessment

5.3 Intervention plans to prevent social decline – face-to-face delivered

Four intervention plans were developed and implemented for preventing the social decline:

- Social activities
- Group Activities outdoor
- Meeting Point/Senior Cafès
- Activ84Health/Momoride

An app, "social Media Platform" has been tested in a subset of users, especially in the Living Lab of Siegen.

Each centre developed social activities that reflected local need and access in accordance with the participants expressed preferences. Social activities were organised and led by social activity coordinators within each centre are were a face-to-face intervention with no ICT-based interaction.

5.4 Overall results

The results of this study indicated that the interventions deployed did not significantly improve measures of physical, cognitive, social or sleep function. However, the individually tailored intervention packages were found to result in a significant protection against a decline in quality of life observed in the control group, and to significantly reduce level of depressed mood and increase nutritional status.

It is important to note that the My-AHA RCT study targeted subjects in the pre-frail stage, recruited from the general population and not from clinical settings. In addition, no subject had clinically significant cognitive or physical impairment on entry to the study. Therefore, lack of significant effects on specific cognitive and physical tests is no unsurprising. On the contrary, the significant difference observed between intervention and control individuals on a composite measure of quality of life, is of relevance.

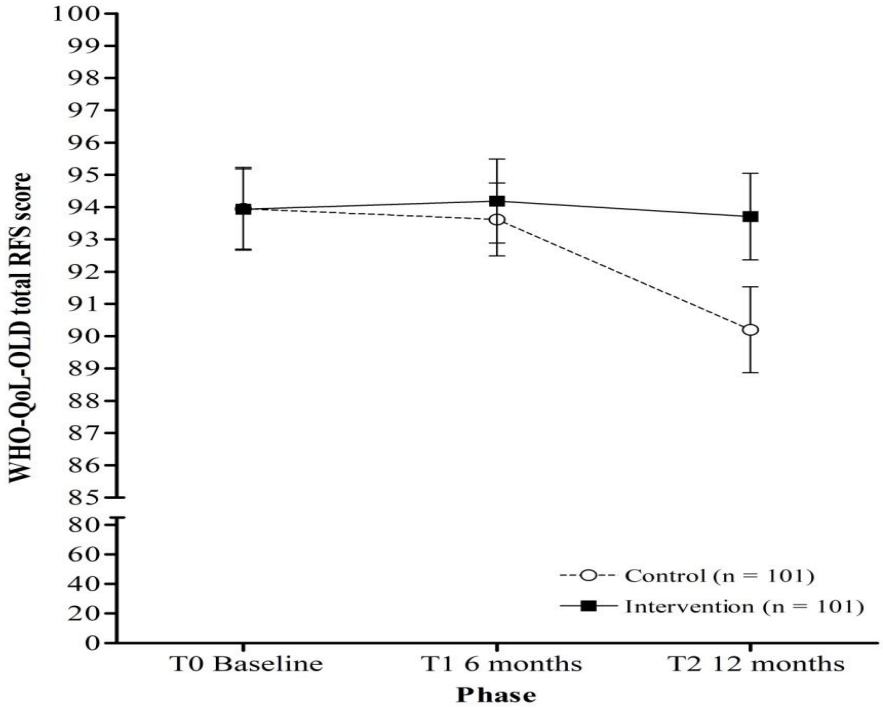

Figure 1 Group differences in WHO-QoL-OLD total RFS score across RCT phases

Figure 1 clearly shows the main result of the My-AHA study. While pre-frail subjects receiving only regular health advice showed a significant decline in quality of life, as measured by the WHO-Qol-OLD scale, subjects in the active group, monitored by the My-AHA platform showed np decline in quality of life after one year of follow-up.

In addition, **a similar effect was found regarding the mood status.** All the subjects involved in the study were not depressed, according to the HADS scale. However, subjects in the control group showed an increase in the depression scores during the study while subjects in the active group showed a significant reduction in the depressed mood scores (see figure 2).

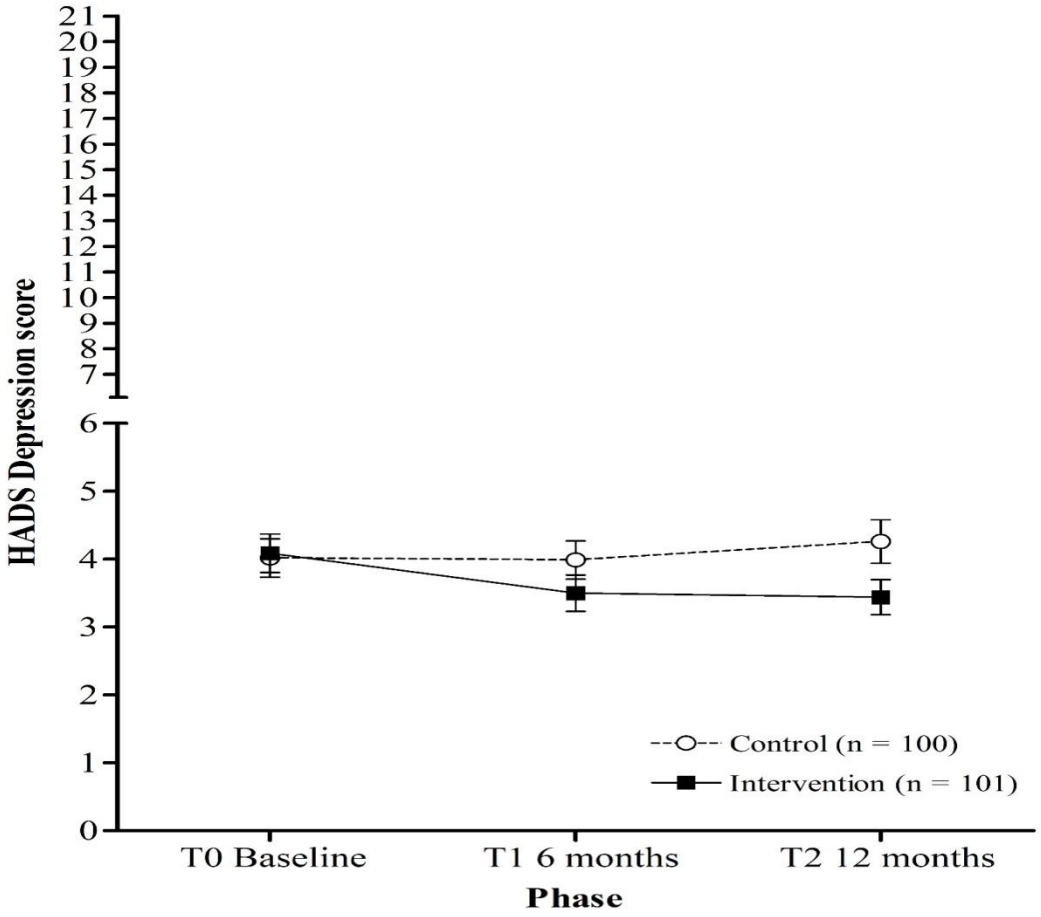

Figure 2 Group differences in HADS-Depression score across RCT phases

The extension study at 18 months, performed in a subgroup of 148 patients, provided additional data showing that also social networks (as measured by LSNSR scale), and nutrition (self MNA scale) showed an improvement through to the final phase of the study (manuscript in preparation).

Subjects involved in the My-AHA study were pre-frail. The pre-frail status, at present, has been scarcely investigated in clinical studies. Epidemiological studies suggested that, in older adults, the average prevalence of the pre-frailty status is approximately 40%, with a significant variation in different studies related to the frailty definition used (12). Identifying and treating pre-frailty may prevent or delay frailty. Evidence suggests that the pre-frail elderly may respond better to physical and nutritional interventions than already-frail people. Our study provides data suggesting that also intervention on cognitive and psychosocial frailties may be useful in preventing age-related decline in quality of life.

In conclusion, the My-AHA RCT provided evidence that multidomain interventions, targeting physical, cognitive and psychosocial frailties, with the support of an ICT platform, may prevents decline in quality of life of prefrail individuals. Additional studies are warranted in order to better investigate the neurobiological mechanisms underlying this effect.
However, several recommendations may be suggested on the basis of the results of the study:

1. There is an urgent need to **implement ICT platforms** in order to **detect** the subtle emergence of frailties in aging EU population. Prevention of cognitive, physical and social decline may be effective only if an early diagnosis is performed. A large number of studies showed, for example, that intervention on risk factors for dementia may be not effective when an overt disease is present.
    a. However, this study demonstrates a reluctance of older adults to engage with ICT-based interfaces indicating that as any detection platform requiring active engagement of the older adult with an ICT interface is likely to have low uptake. Rather, our older adults displayed ready and continued uptake and usage of wearable devices, suggesting that detection of disease markers involving automated data collection from wearable devices requiring little or no end user interface is most likely to have high rates of uptake.
    b. ICT platforms as a "background" technology receiving automatic data downloads from wearable devices monitoring diagnostic features for frailty are most likely to be widely used by older adults.

2. A **multidomain intervention** is necessary to prevent and/or slow the progression from a pre-frail condition to an over frail status. However, older adults did not engage with ICT-delivered interventions for a sufficient period of time to effect any benefit. The older adults in our study demonstrated a stronger preference for group based face-to-face interventions, indicating that deploying interventions in an ICT-based interface may not lead to sufficient uptake to effect widescale change across an aging population.

3. All interventions need to be strictly **personalized** and **empowerment** of older adults in preventive strategies is paramount.

4. A **new definition of frailty**, as well as new frailty indexes, are necessary for an early diagnosis of prefrail/frail conditions as well as for develop effective prevention strategies.

6 Conclusions

In this deliverable, after reviewing literature data regarding the proposed plans for prevention of cognitive, physical and social decline in the elderly, we propose a new strategy based on the data provided by the My-AHA study. According to this strategy a multimodal intervention plan (including physical, cognitive and social interventions) is suggested as the most useful strategy in order to prevent functional decline in the elderly. This plan needs to be strictly personalized and based on a holistic approach to subject's needs. Finally, we suggest that ICT based platform, like My-AHA, have utility in collecting data from automated sources (e.g., wearable devices) and for automated detection of disease markers (e.g., using risk algorithms) but not for the deployment of interventions as compliance with ICT-based user interfaces in older adults who have little prior experience with technologies is poor. Despite careful interface design and testing platform usability in living labs, the low rates of extended compliance with use of the myAHA platform suggests that prior lifetime experience (or lack thereof) with technologies may override any attempt to develop a user-friendly interface in this aging cohort.

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