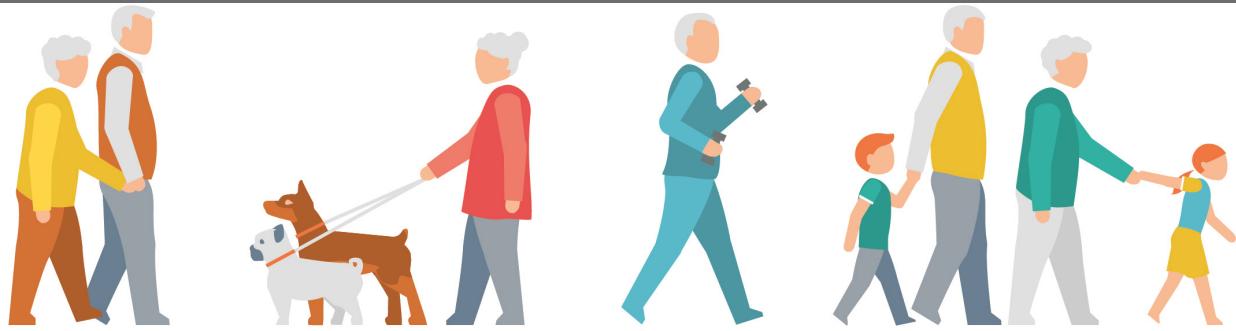


ACTIVE AGING AND DISEASE MANAGEMENT

EDITED BY: Helena Canhão, Jaime C. Branco and Giuseppe Liotta
PUBLISHED IN: Frontiers in Medicine





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ISSN 1664-8714

ISBN 978-2-88945-681-9

DOI 10.3389/978-2-88945-681-9

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ACTIVE AGING AND DISEASE MANAGEMENT

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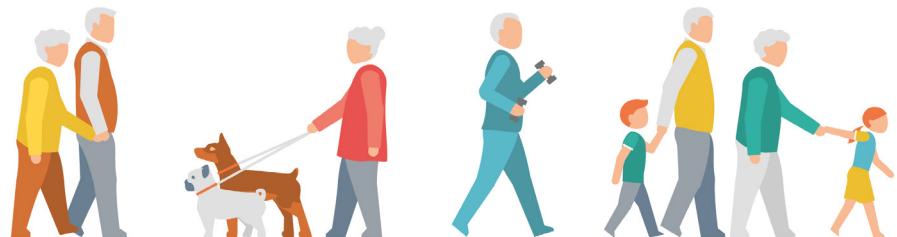


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Population aging and the associated burden of chronic diseases are one of the main challenges in public health worldwide.

This Research Topic on "Active Aging and Disease Management" provides a comprehensive overview of population aging through fourteen comprehensive papers. Chapter 1 discusses an overview of health systems in active and healthy aging,

while Chapter 2 focuses on the role of lifestyles, exercise and new technologies. Chapter 3 debates psychological and cognitive issues in aging and finally in Chapter 4, an older people self assessment is proposed and the role of communities and supporters are highlighted.

We think that real social and health care integration at community level could be the key point to deliver effective health promotion and preventive intervention. Enjoy the reading!

Citation: Canhão, H., Branco, J. C., Liotta, G., eds. (2019). Active Aging and Disease Management. Lausanne: Frontiers Media. doi: 10.3389/978-2-88945-681-9

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Editorial: Active Aging and Disease Management

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Keywords: aging, health, disease management, active, research topic

Editorial on the Research Topic

Active Aging and Disease Management

With population aging and an increasing number of older people in countries worldwide, issues such as the advancement of healthy and active aging of the individual as well as the sustainability of health care systems are of growing importance. Multimorbidity is more prevalent with advancing age, as are other factors, such as social isolation and cognitive and physical impairment. These factors result in increased mortality and a greater use of health care services by older people. Polypharmacy is a well-documented risk factor for poor health outcomes in older people, and this is particularly true for those of low income and literacy. Adequate nutrition is essential for promoting active aging, and malnutrition is a key element in many disease processes at advanced age.

All these challenging issues justify the edition of our Research Topic “Active Ageing and Disease Management” which, as we expect, can bring up some of the problems and point out good practices to tackle these health and social needs. This group of papers has in common a holistic perspective focused on health promotion and disease prevention.

This research topic gathers 14 papers from different research groups that deal with distinct aspects of active aging and disease management. Three of them are opinion articles, nine original research, one clinical trial, and one community case study.

Liotta et al. in “Active Ageing in Europe: Adding Healthy Life to Years,” emphasize the key role of the determinants of health in active and healthy aging. They recall that, in the nineteenth century, an improvement of socioeconomic conditions, environmental sanitation and nutrition started a public health revolution that ultimately allowed an increase of life expectancy from an average of 45 years old to the average of ~80 years old that we observe now at almost European countries. Strengthening the social dimension of prevention programmes and changing the lifestyles are key elements to improve quality of life and reduce the risk of loss of physical autonomy, especially among the over-75 population. Real social and health care integration at community level could be the key point to deliver effective health promotion and preventive intervention.

O’Caoimh et al. in the paper “Can the Geriatric Day Hospital Act As a Hub for Services for Older People across the Spectrum of Ageing from Active Ageing to Advanced Frailty?” discussed the potential role to be played by the Geriatric Day Hospital as a hub to manage the care of older adults with complex needs across the spectrum from active aging to pre-frailty and from established frailty to end-of-life care. To accomplish that, Day Hospitals should focus on providing innovative and proactive, preventive approaches including those that use new mobile ICT technologies to promote healthy aging, address pre-frailty and prevent or reverse frailty at an early stage, before the onset of functional decline.

Kyriazis and Kiourtzi in the opinion paper “Video Games and Other Online Activities May Improve Health in Ageing,” argued that ICTs stimulus might act as a cognitive challenge that upregulates neuronal stress response pathways, the same way as other challenges and stressors that result in “positive stress.” This upregulates neuronal health in older people and their use should be encouraged.

OPEN ACCESS

Edited and reviewed by:

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Specialty section:

This article was submitted to

Geriatric Medicine,

a section of the journal

Frontiers in Medicine

Received: 27 July 2018

Accepted: 12 September 2018

Published: 05 October 2018

Citation:

Canhao H, Branco JC and Liotta G (2018) Editorial: Active Aging and Disease Management.

Front. Med. 5:278.

doi: 10.3389/fmed.2018.00278

Original research brought up different hot topics, stressing the role played by nutrition, physical exercise, and healthy lifestyles in older people.

Fernandes et al. reported on “Food Insecurity in Older Adults: Results From the Epidemiology of Chronic Diseases Cohort Study 3” that food insecurity is associated with higher likelihood for chronic diseases, poor self-management, and lower HRQoL and should be fought with adequate policies. Tomás et al. with “Functional Capacity and Levels of Physical Activity in Ageing: A 3-Year Follow-up,” Dekker-van Weering et al. with “User Experience, Actual Use, and Effectiveness of an Information Communication Technology-Supported Home Exercise Program for Pre-Frail Older Adults” and Oliveira et al. with “Kinematic Changes during Prolonged Fast-Walking in Old and Young Adults” highlighted the benefits of physical exercise, namely walking and activities that use hands, since these specific components seem to have a major impact in functional physical condition. The second study provides evidence that a home-based exercise program is easy to use and has potential on improving quality of life and health status of physically pre-frail, older adults who live at home. The last one showed that fast walking induces changes over time on kinematics of old adults, mainly at ankle and hip, and in the coordination among the lower-limb angles that were more prominent during the swing phase of the gait and may indicate an augmented risk of falling. These findings provide a foundation for future studies in the assessment of the risk of falls in older adults associated with walking at a faster pace.

Another interesting paper from Duarte et al. “Health and Lifestyles Factors Associated With Osteoarthritis among Older Adults in Portugal,” showed the independent association of osteoarthritis with age, female gender, higher number of comorbidities, physical disability, and low levels of physical activity.

When thinking of old people taking into account their multidimensional aspects, psychological and cognitive issues have a key role. Three papers address these questions: “Active Ageing in Very Old Age and the Relevance of Psychological Aspects” from Paúl et al. “Anxiety and Depression in the Portuguese Older Adults: Prevalence and Associated Factors” by Sousa et al. and “Neuropsychological Correlates of Pre-Frailty in Neurocognitive Disorders: A Possible Role for Metacognitive Dysfunction and Mood Changes” from Amanzio et al. Psychological aspects proved to be of great relevance for active aging, and corroborate previous research that consider mental health balance as an important contributor to an optimist view of life and cognitive capacity. Prevalence of anxiety and depression among elders is around 10–12%, and health-related quality of life and physical function play an important role in depression and anxiety. In patients with neurocognitive disorders such as Alzheimer’s disease, cognitive functions can have a significant role in the pathogenic mechanisms of frailty, establishing a link between them.

The last three papers deal with three distinct but very important subjects. In “Ageing, Disability, and Informal Caregivers: A Cross-sectional Study in Portugal,” Pego and Nunes stressed the key role of informal caregivers. A significant

proportion of dependent older people lacks any kind of informal care (39.5%), which supports the argument that the current limitations of the long-term care model impose a revolution of the community care model to be addressed. The paper underlines the marked nuclearization of the family and solidarity networks mainly composed of family members. Geographical distance also is extremely relevant to the frequency of care, i.e., the closer the caregiver lives, the higher the frequency of care provided.

The results of this study show a critical situation for both groups (elderly and caregivers) and an alarming prospect in the near future due to the reduced availability of informal young caregivers to care for the older person; this is a global challenge, since many countries share the same characteristics. The community care model cannot ignore these challenges; otherwise, they drive to fail the whole care systems due to the potential increase of demand in the next years.

Gonçalves et al. developed a new tool, the “Selfie Ageing Index: An Index for the Self-assessment of Healthy and Active Ageing.” SAI measures healthy and active aging at the individual level and was designed for individuals to monitor their aging status. For this reason, it is completely based on self-assessed indicators, without requiring a health-care professional to complete it—a new approach to the community care that is particularly needed to screen large population. The SAI has the potential to put the individual at the center of the aging discussion, contributing to patient empowerment and promoting patient-centered care.

Finally, in “The Quadruple Helix-Based Innovation Model of Reference Sites for Active and Healthy Ageing in Europe: The Ageing@Coimbra Case Study,” Malva et al. reported on the innovative and successful example of Ageing@Coimbra as a Reference Site of European Innovation Partnership on Active and Healthy Ageing. It supports the adoption of bottom-up, inclusive, and holistic approaches to create regional networks and partnerships with the aim of supporting the creation and replication of good practices for Active and Healthy Ageing. It is a good example of a forum to elaborate shared policy for the older adults’ QoL, which will be spread at European level.

We believe the papers show a comprehensive vision of relevant aspects of active aging and disease management and help to increase knowledge and awareness around these themes. Enjoy the reading!

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Active Ageing in Europe: Adding Healthy Life to Years

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Keywords: active and healthy ageing, Europe, healthy life years, blue print initiative, frailty

OPEN ACCESS

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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 09 August 2017

Accepted: 12 April 2018

Published: 30 April 2018

Citation:

Liotta G, Canhao H, Cenko F, Cutini R, Vellone E, Illario M, Kardas P, Poscia A, Sousa RD, Palombi L and Marazzi MC (2018) Active Ageing in Europe: Adding Healthy Life to Years. *Front. Med.* 5:123.
doi: 10.3389/fmed.2018.00123

BACKGROUND

The European Union (EU) is a conglomerate of more than 500 million people, 19.2% (approximately 100 million) of whom are older adults (1). The ageing population is triggering dramatic demographic, epidemiological, and anthropological changes, highlighting the importance of active and healthy ageing (AHA). In Europe, the most common household type is single occupancy (33.4% of the total number of households) (2). This household type also recorded the highest increase from 2005 to 2015 (3). These findings highlight several questions from both an individual and public perspective. Who will take care of the current generation as we become older? What types of health and social organisations should we develop to preserve the quality of life of an ageing population and sustain our health care systems over the medium and long term? Supporting AHA is one answer to these questions: an AHA population is a resource that benefits all of society. Maintaining a healthy ageing population may also lower demands for health care services. In addition, in many cases, older adults in good health are able to support their fellow generation and represent a strength dedicated to the common well-being.

ACTIVE AGEING AND HEALTHY LIFE YEARS

Active ageing is a multidimensional concept affected by several factors, including physical functionality, lifestyle, urban environment, and social inclusion (4, 5). In 2015, the World Health Organisation defined active ageing as "...the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age" and healthy ageing as "...the process of developing and maintaining the functional ability that enables well-being in older age" (6). The World Health Report on ageing underlined the role of public health strategies in building and maintaining health in older adults.

An operational definition of healthy ageing is still being debated, however, and consensus has not yet been achieved. McLaughlin and colleagues, who analysed the impact of different definitions of healthy ageing, concluded that a functional definition of health, i.e., free from symptomatic diseases and disabilities, may be acceptable (7). The valuable pragmatic approach supported by these researchers, however, does not account for the social dimension of "active" ageing. This social dimension is considered to be crucial because of its impact on developing and maintaining health at all ages. For example, the role played by social isolation as a risk factor for negative events in the older adult population, such as death, is well known (8–11). A more comprehensive approach to assess the process of AHA at the population level, therefore, should take into account several domains, including health status, income security, capability, and environment (12). This concept is consistent with

the approach recently proposed by WHO, that describes healthy ageing as the result of the interaction between the physical and mental capacity of an individual (the intrinsic capacity), and the context of each individual's life (the environment) (13).

Several models have been proposed to measure AHA, however, consensus is needed to be able to implement specific actions (14, 15). The healthy life year (HLY) expectancy, which accounts for the interaction of psychophysical and socioeconomic factors during the individual's life course, could be considered a marker of AHA (16). In this view, HLY expectancy could be used as a measure to guide the development of the AHA process at the population level (17).

Although life expectancy at birth has increased by approximately 3 years over the past decade, disability-free life expectancy (i.e., the HLY expectancy) has not increased over this same time period (18). This phenomenon is not consistent across European countries, since in 12 countries out of 28 the HLY expectancy at 65 years is decreased from 2010 to 2014 (19). Moreover, the gap between life expectancy and healthy life expectancy is increasing. HLY expectancy is determined primarily by progressive impairment in performing activities of daily life (ADL), a measure of functional decline that is associated with frailty (20, 21). Frailty is associated with loss of autonomy in performing ADLs as well as health-related problems, institutionalisation, and/or hospitalisation, with negative influences on quality of life. From a public health perspective, frailty is a multidimensional issue resulting from changes in physical and mental health and functional status as well as lack of social and economic resources. There is evidence that functional decline is associated with lower psychosocial status, namely social isolation, malnutrition, and comorbidity (22–26), which are all determinants of frailty.

A number of initiatives are ongoing at the EU level to increase HLY expectancy at the population level *via* management of frailty at the community level. For example, the European Innovation Partnership on AHA gathers hundreds of public and private stakeholders from different backgrounds (e.g., academic and regulatory bodies, private entrepreneurs, non-government organisations, civil society) to brainstorm and execute innovative solutions for AHA to be exchanged and implemented across different settings within Europe (27). As another example, the Joint Action on Frailty witnesses the commitment of the European governments to set up common instruments and approaches to manage frailty in the community (28).

ACTIVE AGEING AND PREVENTION IN EUROPE

Prevention is the likely key to increasing HLY expectancy (29). For example, approximately 50% of the reduction in mortality due to cardiovascular disease is the result of prevention-based activities, such as a change in lifestyle or smoking cessation (30, 31). Unfortunately, prevention programmes that are targeted to older adults are limited and chaotic, and not implemented in the framework of programmes with measurable outcomes. The European project "Pro Health 65+," which seeks to determine effective methods for promoting a healthy lifestyle among older

individuals, experienced some difficulties in collecting information on prevention programmes targeted to the older population. In many European countries, such as Italy, the public administration provides only a generic regulatory framework for promoting and facilitating such programmes (32). Even in countries with a national plan for the elderly, gathering data about either the implementation of different programmes or their impact is difficult (33), suggesting that more effort is needed to determine the impact of prevention programmes on the quality of life and demand of care among the older adult population in Europe.

Some communities within Europe have already developed successful programmes. In Barcelona, the Institut d'Investigació en Atenció Primària (IDIAP) Jordi Gol has developed a programme working with community nurses who provides elderly community members with advice on physical activities, diet, and medication schedule and also hold memory workshops: this programme reduced the use of health care services as well as the mortality rate of individuals over 65 years old in this community (34). The University Federico II in Naples has developed a programme that provides both information and communication technology (ICT) literacy and suggestions on diet and physical activities to the elderly community with positive outcomes among the over-65 population (35). In Rome, the Community of Sant'Egidio, a catholic NGO, has been running a programme called "Long Live the Elderly!" for the past 14 years. This programme, which applies social interventions to counteract social isolation in the over-75 population, was associated with a reduction in the use of health care services, health care costs, and mortality rate among this population (36). In addition, a study from the Campania Region of Italy has shown an improvement in bone health among older individuals who adhered to a Mediterranean diet (37). Thus, interventions aimed at lifestyle changes or counteracting social isolation are associated with reduced risk of death and reduced use of hospital services among older populations in Europe.

OCCUPATIONAL PERSPECTIVE ON ACTIVE AGEING

The European Commission is strongly committed to connecting digitalization to AHA. The "Blueprint" initiative, a framework for strategic cooperation between key stakeholders (e.g., business, trade unions, research, education and training institutions, public authorities), outlined how digital innovation enabled by a functioning Digital Single Market can transform demographic changes into opportunities for Europe's economy and society (38, 39) providing also the increase of job opportunities. The Digital Single Market is a strategy of the European Commission adopted in May 2015, to ensure access to online activities for individuals and businesses under conditions of fair competition and consumer and data protection. The grey digital gap (i.e., the lower proclivity of older adults to use personal computers or to communicate *via* the Internet), however, is deep; only approximately 45% of the over-65 population across Europe use the Internet at least once per week (40), and in 19 out of 28 countries in the EU, less than 50% of older adult citizens use the Internet at least once per week. Low Internet usage is due in part to lower

education levels of older European citizens in these countries. In Portugal, for example, 77.3% of individuals over 65 years old have 4 or less years of education, and 84.5% have never used computers, videogames, or tablets (41). The “Blueprint” initiative, which aims to implement prevention programmes among European older adults, will, therefore, take significant time (e.g., 5–10 years) to implement among elderly EU citizens. It is likely that parallel efforts, aimed at health promotion and education and targeted at robust and pre-frail individuals, will be needed to maximise the impact of the “Blueprint” initiative over the next several years.

The health care market has not declined over the past 10 years despite the presence of a general economic crisis. The need for care has continued to increase as the population ages, and households are likely to invest more of their resources into this sector over the coming years. There is a window of opportunity, therefore, to implement programmes that proactively target the population at highest risk of frailty and functional decline, namely those over 75 years old. A large investment in health promotion and education that centres on strengthening health, ICT literacy, and social integration not only would serve as insurance for healthier old age and support for the sustainability of the European Health Systems, but also would offer significant occupational benefits to those who are interested in care services. Such programmes would require reorganisation of current models of care at the community level, and would also require individuals to change their view of AHA to that of a long-life approach based on health promotion and education.

CONCLUSION

This debate emphasizes the key role of the determinants of health in AHA. In nineteenth century Europe, an improvement in socioeconomic conditions was the starting point for the most revolutionary demographic and epidemiologic transition in

the contemporary age. Environmental sanitation and improved nutrition were the most important factors leading to this revolution at the population level. During this time, life expectancy increased from an average of 45 years to an average of approximately 80 years in most European countries. Europe was the first geographical area in the world to experience this success in life expectancy. Today, Europe continues to experience more advantages and more challenges with its ageing population than any other region in the world. Strengthening the social dimension of prevention programmes and changing the life styles represent key elements in improving quality of life and reducing the risk of loss of physical autonomy, especially among the over-75 population. These programmes can also provide occupational advantages across many European countries.

A strong effort is needed to improve the integration of the growing number of older adults to avoid the negative consequences of social isolation, malnutrition, and reduced physical activity. In the era of technological development and personalised medicine, environmental and nutritional factors together with healthy lifestyles represent the most powerful factors that determine the health of a population, which is encouraging because these are factors that can be influenced by health promotion and educational intervention. The current weakness of the public health approach to the promotion of AHA which threatens the quality of life of European older adults as well as the medium- and long-term sustainability of the health systems. However, Europe is well-poised to play a leading role worldwide in facing the challenges of increasing HLY expectancy by taking advantage of its assets in knowledge and innovation.

AUTHOR CONTRIBUTIONS

GL wrote the text. HC, MI, AP, and PK revised the text. FC, RC, EV, LP, MM, and RS contributed to the text with suggestions, comments, and proposals.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The reviewer AZ and handling Editor declared their shared affiliation.

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Can the Geriatric Day Hospital Act As a Hub for Services for Older People across the Spectrum of Ageing from Active Ageing to Advanced Frailty?

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Keywords: Day Hospital, frailty, pre-frailty, Comprehensive Geriatric Assessment, geriatrics, ageing

OPEN ACCESS

Edited by:

Helena Canhao,
Unidade EpiDoC, Epidemiologia de
doenças crônicas, Portugal

Reviewed by:

Antony Bayer,
Cardiff University, United Kingdom
Lisa Robinson,
Newcastle upon Tyne Hospitals NHS
Foundation Trust, United Kingdom

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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 15 August 2017

Accepted: 23 January 2018

Published: 02 March 2018

Citation:

O'Caoimh R, Kennelly S and O'Shea D (2018) Can the Geriatric Day Hospital Act As a Hub for Services for Older People across the Spectrum of Ageing from Active Ageing to Advanced Frailty? *Front. Med.* 5:23.
doi: 10.3389/fmed.2018.00023

This article examines the potential of the Geriatric Day Hospital to address the challenge of an aging society, which has begun to place an emphasis on the promotion of active and healthy aging, yet faces rising numbers of pre-frail and frail older adults with complex care needs. Can the Day Hospital model become a hub for the care of older adults across the spectrum of aging? This article explores its origins and traditional role in delivering Comprehensive Geriatric Assessment (CGA), assesses how it is currently being used to identify, triage and manage frailty, providing reablement, chronic disease management and anticipatory care planning, and discusses future models focused on the prevention, surveillance, and monitoring of frailty. It will examine how such approaches could increasingly deploy information communication technologies (ICT) using the Geriatric Day Hospital as a hub to maintain older adults in their home environment, to promote active aging, while both preventing and managing frailty.

A consequence of population aging worldwide, but particularly in the European Union (1), is high rates of frailty (2) and multi-morbidity (3) among older people. This has directed health policies toward prevention and the pursuit of active and healthy aging (4, 5) but has nevertheless resulted in increasing numbers of older patients who could benefit from specialist geriatric services, meaning that limited resources must be stretched further. A fundamental challenge now faced in the management of older adults with multiple interacting medical and social problems is how to move from a single system, unidimensional construct to a more holistic and multidimensional model of care (6) that promotes preventative approaches and reablement as well as providing long-term management and rehabilitation. In this evolving environment, established ambulatory models of care for older people with complex needs that traditionally focused on the latter such as the Geriatric Day Hospital could be leveraged to find an additional purpose, to promote active and healthy aging and manage pre-frailty, while continuing to support the care of frail older adults.

The Geriatric Day Hospital, which originated in the United Kingdom in the 1950s, is a dedicated outpatient service providing specialized, interdisciplinary, ambulatory, and usually rapid access geriatric medical, nursing, and rehabilitation care to community-dwelling older patients, whose primary strength is arguably the flexibility it offers (7). Day Hospitals represented an evolution in primary and secondary level ambulatory care models for older people with complex needs. Those attending Day Hospitals receive and benefit from CGA, individualized multi-domain assessment by a multidisciplinary team using validated scales and interventions that reduce adverse outcomes, hospital admission, and length of hospitalization (8). CGA is, however, labor intensive and economically costly; the Day Hospital rationalizes and targets this limited resource "under one roof" (9) in an effective (10) and cost-effective manner (11). A recent systematic review summarizing evidence from 16 studies comparing Geriatric Day Hospitals to non-integrated, non-comprehensive

services suggests that it is superior, reducing the risk of functional impairment, institutionalization and death, albeit the evidence remains limited, and no cost benefit has been established (9). Further, there is much heterogeneity in terms of what is offered and to whom with studies varying in their sampling strategies; the strongest evidence being for models focusing on geriatric rehabilitation and subspecialty diseases such as stroke, dementia, and heart failure (12). There is limited evidence for its use in prevention and health promotion.

The most recent change in Day Hospitals is a shift toward specialty services, clinics, and ambulatory investigations. Paralleling this change, the relatively new construct of frailty has begun to replace historical models of geriatric care and is increasingly being used in Day Hospitals to select and risk-stratify attendees. Frailty is a multi-factorial state correlating with vulnerability, disability, comorbidity, and self-reported health status with a recognized prodrome, pre-frailty (13). This construct recognizes that the stereotypical characteristics of community-dwelling older patients such as age are insufficient to identify older adults deemed most at risk of adverse healthcare outcomes and hence most in need of CGA (14). Given the current ageing demographic (1), the construct of frailty can help to identify those most likely to benefit from the Day Hospital (15). However, few studies have been conducted to examine the role of the Day Hospital in identifying frail older adults. A study using the SHARE Frailty Index to examine the prevalence of frailty among community-dwelling attendees at a University Hospital affiliated Day Hospital in Ireland found that the prevalence of frailty in this transitional care sample was high at 32% (16). In France, another observational cross sectional study applying consecutive sampling using Fried's criteria, to a similar sample referred to a single geriatric unit, found a higher prevalence of 51% (17). Levels of pre-frailty were also high in both samples at 26 and 41%, respectively. These data represent values between those in community and inpatient settings (2, 18, 19), suggesting that most attendees at Day Hospitals have high-care requirements, but also represent an ideal population to target for measures designed to tackle, prevent, and reverse frailty, including those that promote active and healthy aging at population-level.

The Geriatric Day Hospital is also increasingly being used as a coordination center to deliver integrated care (20) between acute services (emergency departments, acute medicine assessment units, and inpatient wards) (21), rehabilitation services (formal inpatient and early supported discharge teams), community services (primary care teams and general practitioners), and public health services designed to promote active and healthy aging in place, the person's own community (implementation of local, national, and transnational population-level preventative healthcare strategies). A consistent approach to identify frailty across primary, secondary, and social care, e.g., coordinated by case managers, community public health nurses, or primary care physicians can promote equity of access to CGA services (22). Identifying pre-frailty and frailty in people attending for Day Hospital assessment services may be looked on as a form of case finding and an opportunity for health promotion (23). This, in turn, allows for comprehensive proactive management of conditions that result in high levels of acute care episodes. Models that

reflect mutual goal setting in determining outcomes (e.g., Goal Attainment Scores) will be increasingly used and will provide a key element of person-centered support in the Day Hospital (20). Screening for complexity and pre-frailty also may have the additional benefit of taking on a much more proactive approach to the planning of care needs and potentially impact on transitions of care given that most of the CGA has taken place beforehand (24). In essence, the Day Hospital is a "hub" or "command center" to integrate the delivery of CGA services, subspecialty clinics, and preventative healthcare to those most in need.

The Day Hospital may be the ideal location to encourage anticipatory care planning including end-of-life care and cancer survivorship care planning, which help people think about their future health and social care needs. When aligned with CGA, the development of a person-centered care plan to promote this way of thinking about the future in a non-acute care setting enables the older person, their family members, and the multidisciplinary team to address changing needs, complexity, and requirement for support, surveillance, and monitoring from health and social care systems (24). Advanced and personalized care planning is most sustainable when incorporated into routine care in a specialized, dedicated environment where patient trajectories can be predicted and followed (25, 26). Similarly, cancer survivorship care is poorly coordinated in general practice, with little evidence for its integration into routine care (27). Older patients with chronic conditions such as dementia (20) and older cancer survivors (28), whose care needs are markedly different from younger patients could benefit from the CGA, monitoring and advanced care planning delivered in a Day Hospital setting offered in an arguably more appropriate, unhurried and timely manner than in primary or secondary care.

Interventions to target frailty transitions and potentially reverse or prevent onset of frailty may also be best delivered in a Geriatric Day Hospital. A randomized controlled trial that assessed the effectiveness of CGA and subsequent intervention in pre-frail and frail community-dwelling older adults based on the Fried's criteria found that CGA and subsequent intervention showed a favorable outcome based on frailty status and the Barthel Index of activities of daily living (29). More recently, randomized trial data have shown that targeting pre-frailty using two-staged frailty screening followed by more detailed assessment with tailored multi-factorial interventions may slow progression to frailty (30) and is acceptable to community-dwelling older adults (31). Similarly, programs that promote active and healthy aging that improve outcomes in randomized trials such as the "I am active program" (32) could be coordinated or delivered in Day Hospitals.

The use of innovative ICT solutions to improve care for older adults attending the Day Hospital may represent the next step in re-purposing the construct. There is a growing consensus that these new approaches can drive active and healthy aging (33), and it is argued that the use of ICT in ambulatory care settings (including Geriatric Day Hospitals) could be used to promote this through improved diagnostics, individualized telemedicine, and by enhancing connectivity, social engagement, and continued learning (eHealth literacy) among older adults (34). This use of "silver innovations" to support active aging and

healthcare strategies has already proven useful in community-based samples in countries ranging from the Netherlands (35) and Italy (36) to the United States (37) and Japan (38), though these innovations require educational, financial, and policy supports to succeed (38). Although the extent to which ICT can be promoted and implemented in a Day Hospital setting is unknown, its success is likely to be similar to its use in a home care setting (39). The expected shift to greater use of remote monitoring using mobile ICT health technologies is predicted to require more infrastructure (40), particularly for older adults who will require greater support to utilize these services. Traditional services like the Geriatric Day Hospital could be leveraged to this new purpose by providing a “hub” to assist and supervise this for appropriate patients rather than require the building of new and likely commercial infrastructure, which may not have the means or interest to serve this distinct and specialized group. Given that older adults attending a Geriatric Day Hospital in Ireland rated their experience with ICT as limited (41), eHealth literacy would also need to be fostered in this setting. This is echoed by evidence that a supportive environment attuned to the needs of older adults is required for them to effectively use ICT (42).

In a time of limited resources, the Geriatric Day Hospital is as important as ever. Current healthcare systems, under pressure from aging demographics, should re-examine its role and the evidence base for the care it provides, which has arguably not received

the attention and recognition that it deserves. Day Hospitals have the potential to evolve and manage the care of older adults with complex care needs across the spectrum from active aging to pre-frailty and from established frailty to end-of-life care. While they should continue to focus on providing CGA, capitalizing on the growing evidence for a frailty syndrome has helped rationalize this limited resource more appropriately (43), Day Hospitals should focus increasingly on providing innovative and proactive, preventative approaches including those that use new mobile ICT technologies to promote healthy aging, address pre-frailty and prevent or reverse frailty at an early stage, before the onset of functional decline (33). Day Hospitals can also be used to promote a system's wide integrated program of care and education for older adults and healthcare professionals. Thus, although in the future the Day Hospital is likely to remain clinically focused, given its flexibility, it should be able take on new role as a connector “hub” to link primary, secondary, social, and public healthcare; to promote the use of new ICT developments to screen, monitor, and manage the care of community-dwelling older adults; and to advance educational initiatives and eHealth literacy to encourage active and healthy aging well into the twenty-first century.

AUTHOR CONTRIBUTIONS

All the authors (ROC, SK, DOS) contributed equally to the planning and writing of the manuscript.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Video Games and Other Online Activities May Improve Health in Ageing

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Keywords: hormesis, stress response, video games, information exposure, literacy practices

INTRODUCTION

Humans are highly adaptable organisms. Our environment is now increasingly more digital, and we need to assimilate a vast amount of information, much of which requires us to act (1). This has an impact on our neuronal stress response mechanisms, which are activated in order to minimize any disturbance to our homeostasis, or more precisely to our homoeodynamic space (2). Therefore, function is dynamically maintained within healthy limits.

In this paper, we propose that by exposing ourselves to informative, co-interactive digital platforms which are defined by a variety of “Information-that-requires-action in time and on demand,” we are subjected to beneficial positive stress which upregulates neuronal function. This neuronal upregulation has a positive impact on the rest of the somatic repair processes which may reduce age-related degeneration (3). Beneficial positive stress is invoked when the information is important or significant, in the sense that it entices the organism to act, and thus adapt (i.e., reach a state which is functionally better compared to the previous one). When such information reaches the neuron, it acts as a cognitive stimulus which induces the neuron to upregulate its metabolism in order to process this new information (4). It has been argued that such exposure to novel digital information can influence our somatic repair processes through hormetic events (3). Hormesis is a widespread phenomenon in nature that is defined by a non-linear “low dose stimulation, high dose inhibition” principle. This means that exposure to a relatively weak stimulus may positively challenge the organism and upregulate the stress response. This results in health benefits, whereas an excessive, suboptimal, or prolonged exposure may result in damage and disease (5). Hormetic challenges (positive stress) may be used in order to reduce age-related dysfunction in general (6).

OPEN ACCESS

Edited by:

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Reviewed by:

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Specialty section:

This article was submitted to

Geriatric Medicine,

a section of the journal

Frontiers in Medicine

Received: 09 November 2017

Accepted: 15 January 2018

Published: 29 January 2018

Citation:

Kyriazis M and Kiourtī E (2018) Video

Games and Other Online Activities

May Improve Health in Ageing.

Front. Med. 5:8.

doi: 10.3389/fmed.2018.00008

DISCUSSION

Video Games in Later Life

There is increasingly strong evidence that online video games have beneficial cognitive effects in older adults (7). For instance, video game training improves several aspects of cognitive functioning (8), such as reaction time, memory, and attention span, as well as general cognitive control and multitasking (9). Complex 3-D video games improve hippocampal-associated memory (10) and also physical parameters, such as postural balance and muscle strength (11), particularly those games that concentrate on strategy (12). Video games may also be useful in dementia (13). One way these activities may effect health enhancement is through a hormetic mechanism. In this case, the instigation of hormesis is based on a continual state of cognitive novelty, when one operates at the “outer edge of their comfort zone,” performing mental activities that are “challenging but do-able.” In practice, this translates as an activity that provokes rather than annoys, and it is pleasantly frustrating.

Cognitive Stimulation through Video Games

In the case of online video games, we find an example which is at the intersection where digital information, human brain, and human biology interact. Many thousands of players all over the world participate in virtual online worlds and interact with a variety of video game genres. Globally, gamers play competitively and cooperatively in their communities of practice (14, 15), in a way that is beyond just entertainment. Video games are complex digi-social microcosms which are constructed by social conventions and rules that may be different from actual world rules. For example, the rules may defy the physical law of gravitation and others, such as mortality and social conventions. These microcosms are carriers of complex layers of meaning, reflecting a certain set of ideologies about society and its power relationships. These virtual microcosms induce hormetic health benefits (16). It is not just a matter of being physically able to perform an action, but it is also an opportunity to interact with new kinds of text genres that require different literacy skills than the conventional ones encountered when we passively read a book. These new text genres are very relevant not only for the individual player but also for the rest of the team because the players can use the information to initiate actions which influence the behavior of other players. Players are becoming agents who provide meaning of the text within the game (17, 18). The linguistic interactions and overall performance of the player is also relevant, because these engage the player into debates with other players and thus strengthen social bonds. These social bonds may, again, break the rules of politeness (19) and open new horizons of performative and linguistic interactions which are, perhaps, totally new for the older person. New verbal and non-verbal expressions may develop in order to help increase the pleasure of playing the game. Imagination and simulation of an experience prepare the player to tackle problems in real life situations. Thus, the elements of novelty and creativity flourish. Strategic problem-solving (20), creative thinking, overlapping goal development, involvement with digital literacy practices (21), learning of new skills, and many other cognitive skills become the fruits of such game activities (22–25). Therefore, the aging player may develop skill sets and cognitive capabilities which could be very useful, even essential, in the course of their life. Examples of action- and goal-directed simulations of embodied experience video games include multiplayer games, like World of Warcraft, League of Legends, Minecraft, and Ikariam. The brain activities involved during the course of such games enhance cognition in multiple ways and are thus considered as hormetic. In addition to these, there exist other video games which are more oriented toward literary creativity with prose and poetry, such as the video game Elegy for a Dead World (26).

Internet and Health

Being cognitively stimulated in a virtual setting is shown to have several health benefits. For instance, playing online action video games affects the plasticity of sensorimotor regions in the gray matter, and improves connectivity between neurons, particularly those involved in attention and experience (27). Use of general

video games for 1 h a day improves spatial memory, cognitive control, and complex verbal span (28). These cognitive benefits are not specific to action video games, but other active online experiences may also improve cognition. General use of the Internet has been studied in a variety of settings and initial results show health promoting effects (29) including an increase in life expectancy (30). For instance, a study in Taiwan found that internet use (broadband, wireless, or mobile) is positively associated with quality of life, self-esteem, and reduction in stress (31).

In addition, it was shown that higher levels of Internet use among older people are associated with lower levels of loneliness, improved social support and psychological well-being, and better life satisfaction (32). Web-based interventions which are specific to memory and cognition have a special role to play in cases of mild cognitive impairment and dementia (33).

How does online cognitive stimulation upregulate health? When a mildly stressful information from an online cognitive activity (i.e., information which requires a fast response and instant feedback, such as video games) reaches the neuron, it activates the neuronal stress response which facilitates adaptation to this stressful situation. Neurotransmitters and molecules involved in memory and in cognition are also involved. Such molecules include cyclic guanosine monophosphate, glutamate, leptin, and angiotensin IV. Another marker in hormesis is Heat Shock Proteins (HSP) which is expressed in cases of shock (challenge). Overexpression of HSP is neuroprotective (34).

The risk always exists that excessive use of the Internet, particularly in a way that is repetitive and non-meaningful, may lead to social isolation of the user. In this paper, we highlight the importance of the meaningfulness of information sharing, i.e., information that requires the user to act. In addition, despite concerns that use of online platforms may lead to social isolation, some researchers (35), report that it may, on the contrary, actually decrease loneliness and social isolation. However, older people may experience physical limitations such as arthritis, visual problems, etc. which may impede full use of online activities. The market needs to take into account these age-related limitations.

Cognitive Challenges May Impact on Physical Health

It is well accepted that physical exercise has cognitive benefits and that cognitive exercise has cognitive benefits [for example, Ref. (36)]. What is less well studied, but nevertheless important, is the *physical* benefits obtained through *cognitive* training. Some research exists in this respect. We know, for example, that while cognitive exercise may increase the speed of information processing (37), it can also improve certain physical health parameters in older people, including vitality, physical functioning, and bodily pain, as well as social and emotional functioning, and instrumental activities of daily living (38). This type of hormetically intense cognitive training not only improves physical functioning but its effects were found to persist for several years (39). A significant number of older people who followed a program of cognitive exercises rated their physical health and quality of life as excellent or very good (40). While clearly more research is needed in this respect, there could be some possible physical health benefits

obtained through cognitive stimulation. The hormetic health benefits of cognitive challenges can be augmented by playing online video games or similar engaging activities.

There is growing evidence that these concepts are valid within human groups in the community. D'Orsi et al. (41) have shown that internet use was significantly associated with a lower risk of 10-year mortality, controlling for sex, age, education, cognitive function, functional impairment, and diabetes. In another study, d'Orsi et al. (42), found a specific association between increased use of internet and reduction of dementia risk. Therefore, we could speculate on the potential physical effects obtained through a combination of both physical and cognitive activities, while awaiting further corroboration.

CONCLUSION

The increasing presence of online environments, such as action video games and other digital media platforms that share similar characteristics, translate into opportunities for information sharing among the users. In several instances, this information is actually quite meaningful, in the sense that it incites the recipient to act, and it can thus be considered hormetic. We have argued elsewhere (16) that such information may act as a cognitive challenge that upregulates neuronal stress response pathways, the same way as other hormetic challenges and stressors that result in "positive stress" such as physical exercise, heat or cold exposure, radiation, and medication.

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Thus, the main points of this paper are several. Cognitive challenges may act along universally encountered hormetic principles, in order to invoke the neuronal stress response. This, as a consequence, upregulates neuronal health and it is likely to result in cognitive health improvement in older people. One example of such cognitive challenge is interaction with online video games, although other challenging cognitive activities may carry similar benefits. We need to encourage increasing use of online action video games for older people.

AUTHOR CONTRIBUTIONS

Both contributors have contributed to the conception of the work; MK has discussed biologically related concepts and EK has worked on the acquisition of data and presentation of concepts relating to computer gaming. MK has drafted the work and both have revised it critically; both have agreed the corrections following peer review. Both approve the paper for publication of the content and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

FUNDING

No funding was available for this paper.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Food Insecurity in Older Adults: Results From the Epidemiology of Chronic Diseases Cohort Study 3

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OPEN ACCESS

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Specialty section:

This article was submitted to
Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 10 August 2017

Accepted: 25 June 2018

Published: 12 July 2018

Citation:

Fernandes SG, Rodrigues AM,
Nunes C, Santos O, Gregório MJ,
de Sousa RD, Dias S and Canhão H
(2018) Food Insecurity in Older Adults:
Results From the Epidemiology of
Chronic Diseases Cohort Study 3.
Front. Med. 5:203.
doi: 10.3389/fmed.2018.00203

Introduction: The public health problem of food insecurity also affects the elderly population. This study aimed to estimate the prevalence of household food insecurity and its associations with chronic disease and health-related quality of life characteristics in individuals ≥ 65 years of age living in the community in Portugal.

Methods: The data were collected from the Epidemiology of Chronic Diseases Cohort Study 3 (EpiDoC3)—Promoting Food Security Study (2015–2016), which was the third evaluation wave of the EpiDoC and represented the Portuguese adult population. Food insecurity was assessed using a psychometric scale adapted from the Brazilian Food Insecurity Scale. The data on sociodemographic variables, chronic disease, and management of chronic disease were self-reported. Health-related quality of life were assessed using the European Quality of Life Survey (version validated for the Portuguese population). Logistic regression models were used to determine crude and adjusted odds ratios (for age group, gender, region, and education). The dependent variable was the perceived level of food security.

Results: Among older adults, 23% were living in a food-insecure household. The odds of living in a food-insecure household were higher for individuals in the 70–74 years age group (odds ratio (OR) = 1.405, 95% confidence interval (CI) 1.392–1.417), females (OR = 1.545, 95% CI 1.534–1.556), those with less education (OR = 3.355, 95% CI 3.306–3.404), low income (OR = 4.150, 95% CI 4.091–4.210), and those reporting it was very difficult to live with the current income (OR = 16.665, 95% CI 16.482–16.851). The odds of having a chronic disease were also greater among individuals living in food-insecure households: diabetes mellitus (OR = 1.832, 95% CI 1.818–1.846), pulmonary diseases (OR = 1.628, 95% CI 1.606–1.651), cardiac disease (OR = 1.329, 95% CI 1.319–1.340), obesity (OR = 1.493, 95% CI 1.477–1.508), those who reduced their frequency of medical visits (OR = 4.381, 95% CI 4.334–4.428), and who stopped taking medication due to economic difficulties (OR = 5.477, 95% CI 5.422–5.532). Older adults in food-insecure households had lower health-related quality of life (OR = 0.212, 95% CI 0.210–0.214).

Conclusions: Our findings indicated that food insecurity was significantly associated with economic factors, higher values for prevalence of chronic diseases, poor management of chronic diseases, and decreased health-related quality of life in older adults living in the community.

Keywords: food insecurity, chronic diseases, quality of life, older adults, management of chronic diseases

INTRODUCTION

Populations worldwide are undergoing unprecedented changes in age demographics. In Portugal and other European countries, more than 19% of the individuals are ≥ 65 years of age (1, 2). Age is the most powerful predictor of morbidity and mortality. Multifaceted and numerous mechanisms link age to health status (1). To maximize health and well-being, healthcare systems should be responsive to the diversity and heterogeneity of the health status of older adults (1).

The increasing proportions of countries' oldest populations are associated with greater vulnerability and high-risk of development of chronic diseases and disabilities. These negative health outcomes have direct effects on access to adequate food and result in food insecurity (3). Food security is the condition where “*all people, at all times, have physical and economic access to sufficient, safe and nutritious food to meet their dietary needs and food preferences for an active and healthy life*” (4). This broad concept encompasses the availability of food and the accessibility and proper use of food. Food insecurity can affect the health and well-being of individuals (4–8). Nutrition is one of the main determinants of healthy and active aging. Consumption of nutritious food is crucial for physiological well-being and better health and quality of life (9).

The health characteristics of older adults differ from other age groups. The multidimensional phenomenon of food insecurity is also different in this population (10, 11). In older populations, food insecurity results from more than financial resource constraints. Functional impairment, not owning a home, isolation, gender, financial vulnerability, and poor health have statistically significant associations with food insecurity. These associations suggest that differences in food use between older and younger populations should be considered. These important risk factors for food insecurity tend to occur together, which results in a much higher risk for food insecurity in older populations (8, 10–13). As older populations increase in size, accurate assessments of the extension of food insecurity become more essential for public health (14). Previous studies of food insecurity have mostly examined populations of children and non-elderly adults. Little is known about the characteristics of food insecurity in older adults and associations with health outcomes (11, 15).

Abbreviations: EpiDoC3, Promoting Food Security Study; EpiDoC cohort, Epidemiology of Chronic Diseases Cohort Study; BMI, Body mass index; HRQoL, Health-related quality of life; EQ-5D-3L, European Quality of Life Survey with five dimensions and three levels; EQ VAS, thermometer scale from the EQ5D-3L questionnaire.

Approximately 23% of the global burden of disease is attributable to conditions that affect older people; the main conditions that contribute to this excessive burden are chronic diseases (16). Chronic disease can negatively affect the ability to shop for food, carry foodstuffs home, and prepare meals, which can affect older adults' food security as much as financial vulnerability (5). A poor diet also has severe effects on quality of life and health. Older adults who adopt poor dietary patterns have higher risks of malnutrition, frailty, deteriorating health conditions, and disability compared with those that consume a healthy diet (9, 12). Previous findings indicate that food insecurity is particularly prevalent among older adults (11, 12, 17) and is associated with poor health (5, 12), increased depression, disability (18), and poor quality of life (5, 19).

National and international initiatives promote active and healthy aging, but there are still opportunities for the results of this approach to be reflected in increased quality of life and health of older adults. Rethinking aging implies a true transverse commitment and reconsideration of the entire set of associated factors (20). One of the main objectives of the Healthy People 2020 Report is to “*improve the health, function, and quality of life*” (21), so understanding the associations between food insecurity, chronic diseases, and quality of life is fundamental for improvement of health policies and resulting successful promotion of active and healthy aging populations. The purpose of this study was to estimate the prevalence of household food insecurity and its associations with chronic diseases and health-related quality of life (HRQoL) factors in individuals ≥ 65 years of age living in the community.

MATERIALS AND METHODS

This observational study used a cross-sectional analysis of data from a national ongoing prospective cohort study, the Epidemiology of Chronic Diseases Cohort Study (EpiDoC). The data from this population-based study represent the Portuguese adult non-institutionalized (i.e., live in private homes) population in Portugal (Mainland, Madeira, and Azores Islands). The EpiDoC cohort began with the EpiDoC 1 study (EpiReumaPt); two subsequent evaluations have been performed using data from the same subjects [EpiDoC 2 (CoReumaPt) and EpiDoC 3 (Promoting Food Security)] studies. The sampling method used for the EpiDoc 1 study followed a cross-country random route procedure; sampling was stratified by region (North, Centre, Lisbon, Alentejo, Algarve, Madeira, and Azores) and size of locality. Data collection was performed using a computer-assisted telephone interview method. The number of interviews conducted for each stratum was proportional to

the actual distribution of the population. Census 2001 results indicated that the eligible Portuguese population ≥ 18 years old was $N = 7,719,986$. Therefore, a sample of 10,661 participants was randomly selected (random route method) (22). All 10,661 participants in the EpiDoC 1 study signed an informed consent form for follow-up, and those who provided their telephone number were included in the subsequent EpiDoC cohort follow-up evaluations (EpiDoC 2 and EpiDoC 3). In the EpiDoC 2 and EpiDoC 3 studies, all participants were contacted by telephone (23, 24). Of the 9,003 participants eligible for the EpiDoC 3 (Promoting Food Security) study, 2,366 were lost due to unsuccessful contact and 1,004 participants were lost to follow-up for other reasons; there were 5,653 participants in the third wave of the study. A total of 1,885 individuals in this Portuguese noninstitutionalised population were ≥ 65 years of age; the data from these participants were included in the analyses described in this article.

Instruments and Variables

Sociodemographic (age, gender, years of education, and health region) and socioeconomic (income and information on perception of family income) data were collected. Data on self-reported diseases (high cholesterol levels, hypertension, diabetes, gastrointestinal disease, mental disease, cardiac disease, pulmonary disease, cancer, neurological disease, hyperuricemia, and urinary disease) were also assessed. HRQoL was assessed using the European Quality of Life Survey (version validated for the Portuguese population) (25) with five dimensions and three levels (EQ-5D-3L). The EQ-5D descriptive system was converted into a single index using a formula that assigned values to each of the levels in each dimension. These value-sets were derived for use of the EQ-5D for the Portuguese population (25). A higher EQ-5D index score corresponded to a higher quality of life. Self-perception of general health status at the time of the survey was also assessed by adapting the original EQ5D-3L visual analog scale to the question “Considering a scale on which the best state of health you can imagine is 100 and the worst state of health you can imagine is 0, we would like you to tell us how good or bad it is, in your opinion, your state of health today?”.

Data on whether there was a reduction in the numbers of visits to a physician due to economic difficulties (Yes/No), whether the respondent took any medication (Yes/No), and whether the respondent stopped taking any medication due to economic difficulties (Yes/No) were also recorded. Body mass index (BMI, body weight in kilograms divided by the square of the height in meters) was calculated using the values for self-reported weight and height. The BMI values were assigned to categories according to World Health Organization criteria (26).

Food insecurity was assessed using a psychometric scale adapted from the Brazilian Food Insecurity Scale; this scale was adapted from the US Household Food Security Survey Module (27–29). This tool was used to assess the quantitative and qualitative components of food insecurity within the 3 months before the respondent answered the survey. A score ranging from 0 to 14 was obtained as an outcome of the total number of affirmative answers. Each score was used to assign the respondent to one of four categories of food insecurity (i.e., “food security,” “low food insecurity,” “moderate food insecurity,” and “severe food insecurity”; Table 1).

Statistical Analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences - IBM-SPSS for Windows 24.0®. To assure the representativeness of the sample for the 65 years and older Portuguese population, weighting coefficients were computed and used for the additional statistical analyses. The EpiDoC 3 study participants and non-participants were first compared regarding sociodemographic, socioeconomic, and health status characteristics. We then adjusted the weights based on the corresponding population stratification groups (gender, age group, and health region). Weighted proportions of food insecurity according to age group, gender, health region, years of education, income, and household income perception were calculated. Prevalence estimates for food insecurity were calculated as weighted proportions, consistent with the sample design. After the descriptive analyses were performed, each participant was assigned to the “Food Security” or “Food Insecurity” (including mild, moderate and severe food

TABLE 1 | Definitions of Food Security levels.

Food Security Level	Cut-offs	Definition
Food Security	If the household includes minors (<18 years old): 0 Household without minors (≥ 18 years): 0	Households show access at all times to enough food for an active and healthy life.
Low Food Insecurity	If the household includes minors (<18 years old): 1 - 5 Household without minors (≥ 18 years): 1 - 3	Households reports at least anxiety about lack of food to meet dietary needs. At this level, coping strategies to deal with economic and food constraints can also have an important on the reduction of diet quality.
Moderate Food Insecurity	If the household includes minors (<18 years old): 6 - 9 Household without minors (≥ 18 years): 4 - 5	Adults in the household reported food intake reduction and changes in eating patterns due to economic difficulties in accessing food.
Severe Food Insecurity	If the household includes minors (<18 years old): 10 - 14 Household without minors (≥ 18 years): 6 - 8	At this level, households without children experienced the physical sensation of hunger and households with children reported a reduction of children's food intake.

Adapted from the Brazilian Institute of Geography and Statistics. National Household Sample Survey - Food Security 2004/2009. Rio de Janeiro; 2010 (30).

insecurity) categories to evaluate the relationships between food insecurity and the other study variables. The magnitudes of the associations between the variables were calculated using binary logistic regression models. The dependent variable was food security status [“food insecurity” (event) vs. “food security”]. Independent variables were sequentially added to the model based on existing knowledge about the variables that could affect the event. Crude and adjusted odds ratios (ORs; age group, gender, health region, and years of education) and the corresponding 95% confidence intervals (CIs) were computed. EQ5D-3L and self-perception of general health status data were analyzed as continuous variables. We interpreted these variables considering that the EQ5D-3L values ranged from 0 to 1 and that the self-perception of general health status values ranged from 0 to 100. A significance level of $\alpha = 0.05$ (two-tailed) was used for all analyses.

Ethical Issues

The EpiDoC 3 study was performed according to the criteria established by the Declaration of Helsinki and revised in 2013 in Fortaleza (31). The study was reviewed and approved by the National (Portuguese) Committee for Data Protection and by the NOVA Medical School Ethics Committee. The participants gave informed signed consent to be included in all phases of the study.

RESULTS

The data were collected using telephone interviews of 1,885 Portuguese people ≥ 65 years of age living in communities in the mainland, or the Madeira or Azores islands, between July 2015 and September 2016. The sample consisted of 55.5% women and 44.5% men (mean \pm standard deviation (SD), 74.3 ± 6.8 years (range, 65–104 years). The results for the sociodemographic and socioeconomic characteristics of this older population are presented in Table 2.

Prevalence of Food Insecurity

A Cronbach's α coefficient of 0.949 was found when we analyzed only the adult household-related items of the scale. The first validation of the Household Food Insecurity Scale used a sample from the Portuguese population. It was performed by Gregorio et al. in 2015. They found a Cronbach's α coefficient of 0.865 (27).

Twenty-three percent ($n = 500$) of 65 years and older households reported being food-insecure. Of this food-insecure group, 16.3% were in the low food insecurity, 4.8% were in the moderate, and 2% were in the severe food insecurity, group (Table 3). There were apparent differences between genders and age groups (Table 4). Older females were more likely to report living in a food-insecure household (26.5%) compared with older males (18.9%) ($OR = 1.545$, 95% CI 1.534–1.556). A higher proportion (25.9%) of food insecurity was found in the households of the individuals in the 70–74 years age group ($OR = 1.405$, 95% CI 1.392–1.417). The highest proportion of severe food insecurity was also found among the individuals in the 70–74 years age group (2.9%) (Table 3).

TABLE 2 | Sociodemographic and socioeconomic characteristics of older adults.

Variables	Total n (%)
AGE (n = 1885)	
65-69 years	563 (29.4)
70-74 years	475 (27)
75-79 years	393 (19.9)
≥ 80 years	454 (23.7)
GENDER (n = 1885)	
Female	1243 (55.5)
Male	642 (44.5)
EDUCATION LEVEL (n = 1877)	
0 years of education	174 (9.7)
1 - 4 years of education	1205 (63.8)
5 – 9 years of education	267 (13.9)
10- 12 years of education	117 (6.3)
>12 years of education	114 (6.4)
HEALTH REGION (n = 1885)	
North	501 (32.2)
Centre	414 (27.1)
Lisbon	371 (23.1)
Alentejo	136 (9.6)
Algarve	78 (4.1)
Azores	183 (1.8)
Madeira	202 (2)
INCOME (n = 1384)	
$\leq 500\text{€}$	950 (64.4)
501€ until 750€	208 (15.5)
751€ until 1000€	89 (9.6)
1001€ until 1500€	84 (6.4)
$\geq 1501\text{€}$	53 (4.1)
INCOME PERCEPTION (n = 1869)	
I live comfortably with my current income	223 (12.4)
I can live with my current income	777 (41.9)
It is difficult to live with the current income	585 (30.7)
It is very difficult to live with the current income	284 (14.9)

All percentages were weighted for correcting to population representativeness.

VARIABLES ASSOCIATED WITH FOOD INSECURITY

Sociodemographic Characteristics

The results for the analysis of the sociodemographic characteristics of the sample and for the application of a binary logistic regression model for the event (food insecurity, binary variable) are presented in Table 4. The results indicated that for the sociodemographic factors related to food insecurity, females ($OR = 1.545$, 95% CI 1.534–1.556), the oldest ages (70–74 years vs. 65–69 years: $OR = 1.405$, 95% CI 1.392–1.417; 75–79 years vs. 65–69 years: $OR = 1.246$, 95% CI 1.233–1.258; ≥ 80 years vs. 65–69 years: $OR = 1.234$, 95% CI 1.222–1.246), lower levels of education (0 years of school vs. 5–9 years: $OR = 3.355$,

TABLE 3 | Food Insecurity status by age group and gender.

Variables	Total n (%)	Food Security n (%)	Low Food Insecurity n (%)	Moderate Food Insecurity n (%)	Severe Food Insecurity n (%)
AGE (n = 1885)					
65-69 years	563 (29.4)	418 (80.1)	94 (14.1)	33 (4.0)	18 (1.8)
70-74 years	475 (27)	347 (74.1)	85 (19.4)	26 (2.6)	17 (2.9)
75-79	393 (19.9)	288 (76.4)	68 (16.6)	32 (6.1)	5 (0.9)
≥80 years	454 (23.7)	332 (76.5)	80 (15.1)	30 (6.1)	12 (2.2)
GENDER (n = 1885)					
Female	1243 (55.5)	865 (73.5)	241 (17.1)	93 (6.2)	44 (3.1)
Male	642 (44.5)	520 (81.1)	86 (15.1)	28 (3.1)	8 (0.7)

All percentages were weighted for correcting to population representativeness.

TABLE 4 | Food Insecurity status: Associations with Sociodemographic Characteristics.

Variables	Total n (%)	Food Security n (%)	Food Insecurity n (%)	Crude OR (95% CI)
AGE (n = 1885)				
65-69 years	563 (29.4)	418 (80.1)	155 (19.9)	1
70-74 years	475 (27)	347 (74.1)	128 (25.9)	1.405(1.392-1.417)
75-79 years	393 (19.9)	288 (76.4)	105 (23.6)	1.246 (1.233-1.258)
≥80 years	454 (23.7)	332 (76.5)	122 (23.5)	1.234 (1.222-1.246)
GENDER (n = 1885)				
Female	1243 (55.5)	865 (73.5)	378 (26.5)	1.545 (1.534-1.556)
Male	642 (44.5)	520 (81.1)	122 (18.9)	1
EDUCATION LEVEL (n = 1877)				
0 years of education	174 (9.7)	91 (65.6)	83 (34.4)	3.355 (3.306-3.404)
1 - 4 years of education	1205 (63.8)	852 (73.8)	436 (26.2)	2.269 (2.242-2.296)
5 – 9 years of education	267 (13.9)	223 (86.5)	44 (13.5)	1
10-12 years of education	117 (6.3)	105 (89.2)	12 (10.2)	0.776 (0.760-0.793)
>12 years of education	114 (6.4)	108 (91.8)	6 (8.2)	0.572 (0.559-0.585)
HEALTH REGION (n = 1885)				
North	501 (32.2)	359 (75.6)	142 (24.4)	1
Centre	414 (27.1)	312 (76.1)	102 (23.9)	0.972 (0.964-0.980)
Lisboa	371 (23.1)	312 (81.2)	59 (18.8)	0.717 (0.710-0.724)
Alentejo	136 (9.6)	104 (78.4)	32 (21.6)	0.853 (0.842-0.864)
Algarve	78 (4.1)	57 (77.8)	21 (22.2)	0.881 (0.866-0.897)
Azores	183 (1.8)	123 (68.1)	60 (31.9)	1.451 (1.417-1.485)
Madeira	202 (2)	118 (58.8)	84 (41.2)	2.161 (2.116-2.207)

All percentages were weighted for correcting to population representativeness.

95% CI 3.306–3.404; 1–4 years vs. 5–9 years: OR = 2.269, 95% CI 2.242–2.296), living in the Azores (Azores vs. North: OR = 1.451, 95% CI 1.417–1.485) and Madeira (Madeira vs. North: OR = 2.161, 95% CI 2.116–2.207) were associated with increased odds of living in a food-insecure household.

Socioeconomic Characteristics

The results for the application of a binary logistic regression model for the event food insecurity are presented in **Table 5**. The socioeconomic characteristics were included in the model and the results were presented as crude and adjusted ORs (i.e., adjusted

by age group, gender, education level, and health region). The analysis of socioeconomic characteristics revealed that having an monthly income $\leq 500\text{€}$ (i.e., $\leq 500\text{€}$ vs. 501€ to 750€ : OR = 3.125, 95% CI 4.091–4.210) and reporting having financial difficulties (*It is difficult to live with the current income* vs. *I can live with my current income*: OR = 6.366, 95% CI 6.304–6.429) or reporting that it was very difficult to live with the current income (*It is very difficult to live with the current income* vs. *I can live with my current income*: OR = 16.665, 95% CI 16.482–16.851) were associated with increased odds of living in a food-insecure household.

TABLE 5 | Food Insecurity status: Associations with Socioeconomic Characteristics.

Variables	Total n (%)	Food Security n (%)	Food Insecurity n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
INCOME (n = 1384)					
≤ 500€	950 (64.4)	614 (67.2)	336 (32.8)	4.150 (4.091-4.210)	4.442 (4.377-4.508)
501€ until 750€	208 (15.5)	177 (89.5)	31 (10.5)	1	1
751€ until 1000€	89 (9.6)	81 (94.9)	8 (5.1)	0.457 (0.444-0.470)	0.510 (0.496-0.525)
1001€ until 1500€	84 (6.4)	78 (92.4)	6 (7.6)	0.701 (0.681-0.721)	0.978 (0.950-1.008)
≥1501€	53 (4.1)	51 (89.5)	2 (10.5)	1.000 (0.971-1.031)	1.267 (1.226-1.310)
INCOME PERCEPTION (n = 1869)					
I live comfortably with my current income	223 (12.4)	217 (94.6)	6 (5.4)	0.688 (0.675-0.702)	0.774 (0.759-0.790)
I can live with my current income	777 (41.9)	703 (92.4)	74 (7.6)	1	1
It is difficult to live with the current income	585 (30.7)	359 (65.5)	226 (34.5)	6.366 (6.304-6.429)	6.228 (6.166-6.291)
It is very difficult to live with the current income	284 (14.9)	92 (42.0)	192 (58.0)	16.665 (16.482-16.851)	15.817 (15.637-15.998)

*Adjusted Odds Ratio to gender, age, education level, and health region.

All percentages were weighted for correcting to population representativeness.

Chronic Diseases

The results for the crude and adjusted ORs (i.e., adjusted for age group, gender, education level, and health region) for the presence of household food insecurity and chronic disease are presented in **Table 6**. The results indicated that older adults living in food-insecure households had greater odds of having one or more chronic diseases ($OR = 1.161$, 95% CI 1.158–1.164). The chronic conditions were diabetes ($OR = 1.832$, 95% CI 1.818–1.846), hypercholesterolemia ($OR = 1.138$, 95% CI 1.129–1.146), pulmonary disease ($OR = 1.628$, 95% CI 1.606–1.651), cardiac disease ($OR = 1.329$, 95% CI 1.319–1.340), digestive disease ($OR = 1.259$, 95% CI 1.247–1.271), mental disease ($OR = 1.334$, 95% CI 1.322–1.347), and urinary disease ($OR = 1.566$, 95% CI 1.550–1.582). Except for the variable hypercholesterolemia ($OR_a = 0.992$, 95% CI 0.988–1.004), these associations were present before and after adjusting the model. For the variable BMI, older adults from food-insecure households had greater odds of pre-obesity (pre-obesity vs. normal weight: $OR = 1.364$, 95% CI 1.353–1.376) and obesity (obesity vs. normal weight: $OR = 1.493$, 95% CI 1.477–1.508), and lower odds of being underweight (underweight vs. normal weight: $OR = 0.572$, 95% CI 0.543–0.603), before and after adjusting for age group, gender, education level, and health region.

Management of Chronic Diseases

The results for the application of a binary logistic regression model for the event food insecurity are presented in **Table 7**. The variables related to management of chronic disease were included in the model, and the results were presented as crude and adjusted ORs (i.e., adjusted for age group, gender, education level, and health region). The results of the analysis of the difficulties experienced by older adults in the management of these chronic diseases indicated that those who reported a decrease in medical visits or who stopped taking medication due to economic reasons had a higher odds ($OR = 4.381$, 95% CI 4.334–4.428, and $OR = 5.477$, 95% CI 5.422–5.532, respectively) of living in a

food-insecure household, before and after adjustment of the model.

Health Related Quality of Life

The results for the crude ORs and adjusted ORs (i.e., adjusted for age group, gender, education level, and health region) for the presence of household food insecurity and HRQoL are presented in **Table 8**. The results indicated that before and after adjustment of the model, older adults from food-insecure households had higher odds of a lower HRQoL (EQ5D-3L score: $OR = 0.212$, 95% CI 0.210–0.214). The analysis of the self-perception of general health status (thermometer scale from the EQ5D-3L questionnaire adapted to one question) revealed that older adults who reported a better health status had lower odds of living in a food-insecure household, before and after adjusting the model ($OR = 0.976$, 95% CI 0.976–0.976).

DISCUSSION

This study aimed to estimate the prevalence of food insecurity and its association with chronic diseases and HRQoL in individuals ≥ 65 years of age living in households in the community. To our knowledge, a study with these objectives has not been published.

We found a food insecurity prevalence of 23%. Few studies of food insecurity in Portugal have been performed, and none have specifically examined the older adult population. A national study of the EpiDoc cohort revealed a food insecurity prevalence of 19.3% in the adult population (≥ 18 years) (23). The results of this current study indicated that this problem is more prevalent in the older population compared with the adult population. Other analyses adult populations found values for prevalence of food insecurity between 8.1% and 50.7% (32–34). However, comparing the results of our study and published studies should be done carefully because the methodological approaches, sources of collected data, and the times of data collection were different.

TABLE 6 | Food Insecurity status: Associations with Chronic Diseases.

Variables	Food Security n (%)	Food Insecurity n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
CHRONIC DISEASES				
Number of Chronic Diseases	Mean±SD: 1.98±1.41	Mean±SD: 2.31±1.66	1.161 (1.158-1.164)	1.128 (1.125-.130)
DIABETES MELLITUS (n = 1626)				
No	910 (79.9)	294 (20.1)	1	1
Yes	286 (68.4)	136 (31.6)	1.832 (1.818-1.846)	1.764 (1.750-1.778)
HYPERCHOLESTEROLEMIA (n = 1568)				
No	518 (77.8)	162 (22.2)	1	1
Yes	631 (75.5)	257 (24.5)	1.138 (1.129-1.146)	1.992 (0.988-1.004)
PULMONARY DISEASES (n = 1644)				
No	1130 (77.3)	405 (22.7)	1	1
Yes	76 (67.6)	33 (32.4)	1.628 (1.606-1.651)	1.611 (1.588-1.634)
CARDIAC DISEASES (n = 1619)				
No	887 (78.4)	286 (21.6)	1	1
Yes	306 (73.2)	140 (26.8)	1.329 (1.319-1.340)	1.298 (1.287-1.308)
DIGESTIVE DISEASES (n = 1640)				
No	1029 (77.6)	358 (22.4)	1	1
Yes	178 (73.4)	75 (26.6)	1.259 (1.247-1.271)	1.296 (1.283-1.309)
MENTAL DISEASES (n = 1653)				
No	967 (77.8)	343 (22.2)	1	1
Yes	246 (72.4)	97 (27.6)	1.334 (1.322-1.347)	1.245 (1.233-1.257)
ONCOLOGIC DISEASES (n = 1654)				
No	1089 (76.8)	393 (23.2)	1	1
Yes	124 (77.0)	48 (23.0)	0.988 (0.977-1.000)	1.040 (1.028-1.052)
URINARY DISEASES (n = 1621)				
No	1065 (77.9)	396 (22.1)	1	1
Yes	126 (69.2)	34 (30.8)	1.566 (1.550-1.582)	1.994 (1.972-2.016)
BODY MASS INDEX CLASSIFICATION				
BMI CLASSES** (n = 1634)				
Underweight	15 (88.7)	2 (11.3)	0.572 (0.543-0.603)	0.421 (0.400-0.443)
Normal weight	375 (81.7)	110 (18.3)	1	1
Pre-obesity	579 (76.6)	180 (23.4)	1.364 (1.353-1.376)	1.388 (1.376-1.401)
Obesity	271 (75.0)	102 (25.0)	1.493 (1.477-1.508)	1.314 (1.300-1.328)

*Adjusted Odds Ratio to gender, age, education level, and health region.

All percentages and means were weighted for correcting to population representativeness.

**BMI Classes: Underweight <18,5kg/m²; Normal weight 18,5-24,9kg/m²; Pré-obesity 25-29,9kg/m²; Obesity ≥30kg/m²

Similarly, direct comparison of the values for prevalence found in our study with estimates from other countries is not always feasible because the methods of data collection differ. However, some studies used similar methodological approaches to our study. The results of a study performed by Goldberg et al. of a sample of 2,045 older adults ≥60 years of age who were included in the National Health and Nutrition Examination Survey (NHANES, USA) 2007–2008 indicated that >9% of older adult households were food-insecure (35). Russell et al. found that of a sample of 3,509 older adults in Australia, 13% reported food insecurity (5). Other studies performed in United States and Australian populations revealed a higher prevalence of food insecurity in disadvantaged urban areas (6, 8, 36). Compared with our study, these two studies found lower values for prevalence of food insecurity. However, the differences might

be due to differences in the participants' ages (i.e., the other studies included participants <65 years of age). The differences could also be due to differences in the sources of collected data (i.e., national vs. regional samples), the socioeconomic disparities between each location (37–39), the socio-economic characteristics of the population (40) or because our sample was collected after a period of economic crisis (41). The data used for other studies were collected before the period of global economic recession (42).

Consistent with the results of previous studies, our study revealed that older adults in food-insecure households were more likely to be women, have less education, and live in households with a lower per capita income (5, 11, 12, 34, 37, 43–45). The income perception is the factor with the most robust association with food insecurity in older adults; it clearly

TABLE 7 | Food Insecurity status: Associations with Management of Chronic Diseases.

Variables	Food Security n (%)	Food Insecurity n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
REDUCTION OF MEDICAL VISITS DUE TO ECONOMIC DIFFICULTIES (n = 1883)				
No	1305 (79.4)	393 (20.6)	1	1
Yes	78 (46.9)	107 (53.1)	4.381 (4.334-4.428)	4.350 (4.301-4.398)
TAKE MEDICATION (n = 1882)				
No	103 (76.2)	36 (23.8)	-	-
Yes	1280 (77.0)	463 (23.0)		
STOP TAKING MEDICATION DUE TO ECONOMIC DIFFICULTIES (n = 1875)				
No	1297 (80.4)	372 (19.6)	1	1
Yes	80 (42.8)	126 (57.2)	5.477 (5.422-5.532)	5.152 (5.099-5.207)

*Adjusted Odds Ratio to gender, age, health region, and level of education.

All percentages were weighted for correcting to population representativeness.

TABLE 8 | Food Insecurity status: Associations with Health-related Quality of Life.

Variables	Food Security	Food Insecurity	Crude OR (95% CI)	Adjusted OR* (95% CI)
Health-Related Quality of Life - EQ5D-3L score (n = 1715)	Mean ± SD: 0.683 ± 0.318 Medium: 0.693 Minimum: -0.438 Maximum: 1	Mean ± SD: 0.511 ± 0.336 Medium: 0.536 Minimum: -0.344 Maximum: 1	0.212 (0.210-0.214)	0.251 (0.248-0.254)
Self-perception of general health status (n = 1715)	Mean ± SD: 70.06 ± 19.79 Medium: 70 Minimum: 0 Maximum: 100	Mean ± SD: 59.33 ± 22.02 Medium: 60 Minimum: 0 Maximum: 100	0.976 (0.976-0.976)	0.979 (0.978-0.979)

*Adjusted Odds Ratio to gender, age, education level, and health region.

All means were weighted for correcting to population representativeness.

represents the relationship between economic factors and food insecurity (5, 13, 46).

Our findings for the self-reported noncommunicable diseases suggested that older adults with chronic diseases (i.e., diabetes, pulmonary disease, cardiac disease, digestive disease, mental disease, and urinary disease) had increased odds of living in a food-insecure household. Other studies have also found associations between food insecurity and higher values for prevalence of diabetes (34, 47–51), pulmonary disease (51), mental disease (12, 18, 48, 52, 53), cardiac disease (48, 54, 55) and poor health outcomes (56). The higher prevalence can be explained by the results of a study that found that food insecurity requires changes in the household food supply that reduce diet quality (57). Disturbance of the nutrient and dietary patterns linked with food insecurity may clarify the higher rates of chronic illness experienced by food-insecure individuals (55, 57).

There are other putative reasons for the higher prevalence of chronic diseases in older adults from food-insecure households. For example, a review performed by Gucciardi et al. revealed that due to the cost of out-of-pocket health care expenditures such as purchase of prescribed medications and supplies, food insecurity affects compliance with the self-management recommendations

given to individuals with diabetes (50). Seligman et al. found that persons in food-insecure households may replace the consumption of healthy foods with less expensive foods that have poor nutritional value and a higher energy density. These individuals will then consume in excess of their energy needs and these intakes can be associated with the development of diabetes (49). This finding is consistent with the finding of another study of older adults (58).

The significant association between food insecurity and pulmonary disease revealed by our study is consistent with the results of studies performed in other countries that indicate that being a smoker is a predictor for reporting characteristics associated with food insecurity (5, 51).

Our study also revealed that a higher proportion of older adults from food-insecure households reported lower rates of being underweight and higher rates of pre-obesity and obesity (Table 6). The results of previous studies have been inconsistent in this area, especially in the older adult populations where this association is weak (12, 45, 55, 59–61). Consistent with our findings, some studies found that food insecurity is associated with greater BMI values (pre-obesity and obesity) in older adults (18, 62). However, other studies have not found this association

(12) or it has only been found in populations of older females but not in populations of older males (45, 61). These conflicting results may be related to the evidence that compared with direct assessment, self-reported measures of weight and height in older adults could give biased results (18, 45, 63). The aging process is accompanied by modifications in body composition (e.g., reductions in height resulting from compression of the vertebrae, loss of muscle tone, and variations in body weight). Older adults tend to report the values they maintained in adulthood (18, 45, 60, 64). Therefore, these findings suggest that the food-insecurity association with obesity reported among adults may have different characteristics in older adults.

Some studies have found that food-insecure older adults report lower investment in their health (8). Food insecurity, cost-related medication nonadherence, and a decrease in medical visits are three related problems with negative consequences and public health implications (65). Our study found that older adults who reported a decrease in medical visits or who stopped taking medication for economic reasons had 4.5 and 5.5 higher odds, respectively, of living in a food-insecure household.

Our findings suggested that those who reported that they stopped taking medication due to economic reasons had higher odds of living in a food-insecure household. In Portugal, the acquisition of medication is associated with different levels of reimbursement by the state (range, 15% to 95%). There is typically some expenditure by the elderly for medication. Elderly people who must purchase several medications may not be able to do so, especially if they have a low income. Afulani et al. assessed the association between food security and cost-related medication under use in a sample of 10,401 American older adults (National Health Interview Survey 2011–2012). Consistent with our findings, they found that older adults from food-insecure households were more likely to report cost-related medication under use than the adults living in food-secure households (66). Bangle et al. examined the relationship between cost-related medication nonadherence and food insecurity in a sample of 1,000 low-income Georgian older adult participants of the Older Americans Act Nutrition Program. They found that food-insecure participants were three times more likely to practice cost-related medication nonadherence than their counterparts (65). In a 2008 study of older Georgians, Bhargava et al. found that food-insecure individuals were more likely to report a poorer health status, had more chronic disease, and tended to have lower health care expenditures compared with their counterparts with similar health status. Taken together, these findings suggest that food-insecure older adults may be unable to meet healthcare needs and practice healthy food consumption behaviors (6). Other studies have found similar relationships between food insecurity and lack of adherence to medical treatments and drug therapies (8, 13, 34, 50).

In older adults, food insecurity and higher prevalence of chronic diseases contribute to declines in functionality and corresponding decreases in quality of life (9, 19). The relationships between nutrition and morbidity and mortality in aging are well-established, but more research on HRQoL and food insecurity in older adults is needed. Our findings indicated that older adults from food-insecure households reported a poor

HRQoL (**Table 8**). These findings are consistent with those of a study of an older Australian cohort of community-living persons ≥49 years of age; this study revealed associations between food insecurity and poor HRQoL characteristics (19). Older adults living in food-insecure households report at least some inability to obtain enough food due to economic limitations and that consequently they reduced their diet quality or variety (28, 67). Diet quality and variety are significant determinants of HRQoL in the aging population (68, 69).

Our study also found that older adults from food-insecure households self-reported a lower health status value (**Table 8**). This finding is consistent with studies that found that than compared with food-secure older adults, food-insecure older adults self-report a poor health status (5, 8, 13, 65).

Our study had some limitations. First, it was based on a cross-sectional analysis that limited the ability to explore causal relationships and establish the temporal sequence of associations. Second, the method used to control the potential effects of sociodemographic variables was based on self-reported conditions, which might contributed to underestimates of the diagnosis of chronic conditions and BMI values (12, 18, 45, 63). Third, the food insecurity scale “*evaluates the food security situation of the household members as a set and not necessarily the condition of any specific household member*” (28, 29). Thus, it was not possible to define the food insecurity status of each older adult living in the household. Despite these limitations, our findings are a valuable resource in understanding key health-related factors associated with food insecurity in older adults. They can be used during development of preventive public health strategies and policies. To our knowledge, this study is one of the first to examine the prevalence of household food insecurity and its associations with chronic diseases and HRQoL of older adults living in the community. The strengths of our study include the use of a randomly selected sample that represented the population of Portugal. The instrument used to record information on food insecurity had high internal consistency measures for this sample. Our study also examined a relationship that has been overlooked in older populations: the association between management of chronic diseases and food insecurity. The results of this study contribute to understanding the inter-related issues that affect health status and disease evolution.

CONCLUSIONS

In conclusion, our results have implications for clinical practice and public policy development. For an increasingly aging population, the greater odds of food insecurity among households of older adults and the associated factors indicates the importance of considering this problem as one of the main public health challenges.

Ensuring that older adults have enough food to meet their needs may be an important way to help them enjoy good health and remain active while aging. Food insecurity in older adults is an undesirable problem that requires additional attention. Food insecurity is associated with higher odds of chronic disease, poor self-management of chronic disease, and lower HRQoL. Because

it is determined by economic factors, food insecurity is socially and ethically unacceptable. Therefore, during a period marked by significant financial stress, implementation of strategies aimed at ensuring the food security of the aging population is needed. We suggest that other evaluation and monitoring studies should be performed and further investigation using longitudinal data are needed to determine the health consequences of food insecurity among older adults. These results would assist health professionals and policymakers to better understand the barriers to achieve improved health in this population.

ETHICS STATEMENT

EpiDoC 3 study was performed according to the principles established by the Declaration of Helsinki and revised in 2013 in Fortaleza. The study was reviewed and approved by the National Committee for Data Protection and by the NOVA Medical School

Ethics Committee. Participants provided informed consent to contribute in all phases of the study.

AUTHOR CONTRIBUTIONS

All authors contributed to this work. HC, AR, and MG performed the initial study. SF and CN analyzed the data. SF, CN, and OS interpreted the data. SF wrote the manuscript. HC, AR, and MG provided scientific support and revised the manuscript. All authors contributed to the further discussion of the manuscript. All authors read and approved the final manuscript.

FUNDING

This project was supported by a grant from the Public Health Initiatives Programme (PT06), financed by the EEA Grants Financial Mechanism 2009–2014.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Functional Capacity and Levels of Physical Activity in Aging: A 3-Year Follow-up

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OPEN ACCESS

Edited by:

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Università degli Studi di Roma Tor
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Reviewed by:

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Specialty section:

This article was submitted to
Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 11 August 2017

Accepted: 15 December 2017

Published: 09 January 2018

Citation:

Tomás MT, Galán-Mercant A,
Carnero EA and Fernandes B (2018)
*Functional Capacity and Levels
of Physical Activity in Aging:
A 3-Year Follow-up.*
Front. Med. 4:244.
doi: 10.3389/fmed.2017.00244

Over the last decades, the world elderly population has increased exponentially and this tendency will continue during the coming years; from 2000 to 2050, people over 60 will double and those over 80 will quadruple. Loss of independence occurs as people age due to mobility restrictions, frailty, and decreased functional fitness and cognitive abilities. Evidence has shown that appropriate programs and policies contribute to keep older adults healthy and independent over time. The purpose of this chapter is to report the results of our 3-year follow-up study designed to characterize functional physical fitness in a sample of Portuguese community-dwelling older adults to propose a set of functional parameters that decline the most. We studied a group of 43 elderly people, aged 60 and over. Variables assessed on the participants were anthropometric measurements, functional capacity with the Senior Fitness Test battery (muscle strength, aerobic endurance, flexibility, agility, and dynamic balance), handgrip strength, levels of physical activity, and balance. Three years after the first assessment, a second assessment of the same variables was conducted. We analyzed what were the variables that, for this group, were related with a healthier aging and the relation with different physical activity levels. Our study showed that the distance covered in 6-min walk test and handgrip strength seem to explain a great amount of variability on functional variables that have changed on this period (68% of balance, lower and upper functional strength, respectively) and the active participants showed less decrements with aging in anthropometric and functional variables than those inactive or insufficiently active ($p < 0.05$). Greater importance should be given to prescription of exercise targeting older adults and, specifically, walking and manual activities should be given more attention as components of a community exercise program.

Keywords: predictors of disability, functional capacity, physical activity levels, aging, handgrip, 6 min walk test

INTRODUCTION

Aging is a gradual, life-long process and highly variable characterized by a progressive and cumulative generalized impairment of physiological functions (1), which may be explained at least by genetic factors, multiple morbidities, and non-genetic factors (specially nutrition, lifestyle, and physical activity) (1).

Nowadays, the increase in human life expectancy and the reduction in death rates has made the number of older adults to grow. Portugal is not an exception and, the rate of older people has risen until 148.7% in 2016 (2), which makes authorities and health care professionals be concerned with the retirement impact on levels of functional limitations (3).

According to Chen and colleagues, it is important to study disability as a process over time since it is very informative on the disability process of an aging population (4). So, a comprehensive follow-up of functional impairment rates and its relationship with disability over time may be the basic strategy to find out which factors contribute to a greater or lesser risk of disability and, thus, to promote strategies to a healthier aging process.

Body composition and cardiorespiratory fitness are the most studied health-related variables of physical fitness and function. Changes in body composition with a loss of muscle mass, bone mass, water content along with musculoskeletal and neuromotor function may predispose older adults to a functional decline with risk of disability increasingly high (5). In addition, changes in cardiorespiratory function with a decrement resulting as much as 50% by the age of 70 contribute also to a higher risk of disability (6). These previous findings have been partially confirmed in longitudinal studies focused on aging and disability, where independent associations of aging were found between lower mobility and mortality (7), and survival (8), dynapenia and abdominal obesity with disability worsening (9), cardiorespiratory fitness and muscle function (10), or cognitive/mental state or/and comorbidities and chronic diseases (11–13).

Although older adults are generally less active, physical activity and exercise training have beneficial effects on neuromuscular adaptations (muscle and myofiber hypertrophy with gains in strength and power (14)) in healthy older adults, depending on clinical status and the training modality exercise training, specially endurance training improves different aspects of muscle oxygenation (15). In fact endurance and resistance training programs have proved to be effective to the positive increment in aerobic capacity and thus also in functional capacity of participants as so in cognitive function and in the reduction of the risk for chronic diseases (16, 17). However, a great variability exists in functional responses to exercise and in levels of adherence and preferences (18). Particularly, changes in body composition with a loss of muscle mass, bone mass, and water content along with musculoskeletal and neuromotor function predisposed older adults to a functional decline with risk of disability increasingly high (5).

Despite this increment in research, it remains the need to identify the best predictors for functional capacity and what is the contribution of physical activity to maintain this capacity with aging.

It was our purpose to characterize longitudinally functional physical fitness in a sample of Portuguese community-dwelling older adults and find plausible associations between functional, and anthropometric variables, and differences across physical activity levels and cardiometabolic comorbidities in this population over a 3-year period.

MATERIALS AND METHODS

Population

Participants were recruited for this longitudinal study in day care centers and senior universities and were eligible if they were older than 60 years and independent in activities of daily living (ADL). Participants were excluded if they were unable to ambulate without assistance. Body composition, functional fitness, and physical activity assessments were carried out in all participations who met the inclusion criteria at beginning of the study (M1) and 3 years later (M2).

After an explanation of the study and after a signed informed consent, in accordance with the Declaration of Helsinki, participants performed a battery of tests to assess functional physical fitness. All study procedures were approved by the institutional review boards of the participating institutions.

Body Composition

Weight and height were measured using a digital balance with a stadiometer (SECA®). Body mass index (BMI) was calculated ($BMI = \text{kg}/\text{m}^2$). An anthropometric tape was used for measuring waist (WC) and hip circumferences (HP) as markers of regional adiposity. Waist circumference was measured at the smallest circumference above the umbilicus and below the xiphoidal process (19) and hip circumference was measured at the highest circumference of the buttocks in a level horizontal plane. Ratio waist-hip was found by dividing the waist circumference (cm) by hip circumference (cm) (20, 21).

Body Composition was assessed using anthropometric measurements (height, weight, waist, and hip circumference) and BMI and waist to hip ratio (WHR) were calculated.

Whole-body skeletal muscle mass (SMM) was estimated using the following Al-Gindan et al. (22) equations:

$$\begin{aligned} SMM(\text{kg}) \text{ in male} &= 39.5 + (0.665 \text{ weight(kg)}) \\ &\quad - (0.185 \text{ WC(cm)}) - (0.418 \text{ HC(cm)}) \\ &\quad - (0.08 \text{ age (years)}), \\ r^2 &= 0.79; \text{ SEE} = 2.7 \text{ kg} : \end{aligned} \quad (1)$$

and

$$\begin{aligned} SMM(\text{kg}) \text{ in females} &= 2.89 + (0.255 \text{ weight(kg)}) \\ &\quad - (0.175 \text{ HC(cm)}) - (0.038 \text{ age(years)}) \\ &\quad + (0.118 \text{ Height(cm)}); \\ r^2 &= 0.59; \text{ SEE} = 2.1 \text{ kg} \end{aligned} \quad (2)$$

where WC, waist circumference, HC, Hip circumference.

Functional Fitness and Disability

The Senior Fitness Test battery was used to assess functional capacity. This battery consists of six items to assess lower limbs strength and flexibility, upper body strength and flexibility, agility and dynamic balance, and aerobic endurance. All the tests were performed according to guidelines and protocols for administration (6). Briefly, lower limbs strength was measured

with the 30 s chair stand test. An arm curl test was utilized for upper body strength assessment, which consists of carrying out as many forearm curls as possible within 30 s with 2.27 kg (5 lb) and 3.63 kg (8 lb) dumbbells for women and men, respectively. The chair sit-and-reach and the back scratch tests were used to assess lower and upper body flexibility, respectively. The 8-foot up and go tests were used to assess mobility. To measure aerobic endurance we used the 6-min walk test (6MWT) (23), and estimated distance walked was calculated with a validated equation (24).

$$6MWD(m) = 218 + (5.14 \text{ Height}) - (5.32 \text{ Age}) - (1.80 \text{ Weight}) + (51.31 \text{ Sex}), \quad (3)$$

where $F = 0$; $M = 1$; $r^2 = 0.66$.

Isometric strength was assessed with a handgrip test using the American Society of Hand Therapists (ASHT) protocol. It was measured at both hands (in kg; JAMAR® dynamometer). ASHT recommends a sitting position with shoulder adducted, elbow flexed at 90° for arm and wrist in neutral position and wrist between 0° to 30° of dorsal flexion (25).

Balance was assessed with the Berg Balance Scale (BBS) (26) because it is easy to use, it takes ~15–20 min to complete and is appropriate for clinical and community settings. It consists on 14 items that the subject must complete safely. Each item is scored from 0 (unable to complete the task) to 4 (independent and safe performance). Maximum score is 56 points (26).

In addition, participants completed and *ad hoc* questionnaire about comorbidities or non-communicable diseases and musculoskeletal pain conditions.

Physical Activity

Levels of physical activity (LPA) were assessed and subjects were classified in sedentary/inactive, insufficiently active or active according the classification of physical behavior (19). An active participant was considered who perform 30 min of moderate activity at least 5 days a week and/or 20 min of vigorous activity 3 days per week or a combination of both.

Statistical Analysis

For all statistical analysis, the IBM SPSS 21.0 package for Macintosh was used (SPSS Inc., IBM Company, Chicago, IL, USA). The confidence level was established with a statistically significant p -value of less than 0.05. All variables were inspected and confirmed for a non-normal distribution prior to analysis (Kolmogorov-Smirnov normality test). Basic characteristics of the participants were obtained by analyzing frequencies (%), or calculating mean and SD (mean \pm SD).

Differences of performance, body composition, and functional fitness between M1 and M2 were analyzed by Wilcoxon signed-rank test. In addition, differences by sex were carried out using a Mann-Whitney U test.

The association between comorbidities and functional variables at M1 and M2 were analyzed with Wilcoxon Signed Rank test or a Mann-Whitney U test, for comorbidities with significant impact on functional variables.

Linear regression models were performed for the clinical variables that had significant differences between two measures (differences in clinical variables were dependent variables and physical fitness and body composition as independent). Finally, a Kruskal-Wallis analysis was conducted to find differences in functional variables between physical inactive, insufficiently active and active.

RESULTS

Baseline (M1) and 3 years later (M2) characteristics of participants aged between 60 and 91 years, all Caucasian, are described in **Table 1**.

Fourteen percent had a normal BMI at M1 but this percentage was increased to 21% at M2. There were not underweight cases and the prevalence of obesity was 23.3% ($BMI > 30.0$).

Only six participants reported none disease or musculoskeletal issue. Eighty six percent reported one to four comorbidities and 58.1% present multibordity (2 or more chronic conditions): type II diabetes was present in 18.6% of all the participants, hypercholesterolemia in 32.6%, and hypertension in 74.4%. Musculoskeletal complaints were present in 74.4% of participants. Overall, 33.3% participants suffered one or more falls in the previous year (at M1). Almost all the anthropometrical and body composition characteristics changed over the 3-year follow-up period (**Table 1**). Males reduced their weight and BMI while females decreased SMM and had small although significant increment in WHR (**Table 1**).

Most our participants were sedentary or inactive (37.2%) or insufficiently active (39.5%) and only 23.3% were active at M1. These latter results were similar at M2: 39.5% were sedentary, 30.2% insufficiently active, and 30.2% were active.

Regarding physical fitness capacity, there were only a few components with significant alteration over time (**Table 2**). Males reduced flexibility with a small increase in upper limb strength (arm curl). Among females, we could observe a decrease in balance and muscle strength. No changes in functional aerobic capacity variables were verified in both sexes (**Table 2**). Although 58.3% of males and 48.4% of females presented values for the handgrip that were classified as poor (19) at M1, only 8.3% of males and 12.9% of females presented values on handgrip strength that could be classified as having sarcopenia at M2.

Balance assessed by BBS was significantly reduced only in women. Nevertheless, a change of 6 points in BBS score indicated with 95% of confidence that a genuine change in function has occurred (27) and this occurred for 18.6% of our sample (three males and five females).

Women reduced lower limbs (30 s chair stand test) strength at M2 but not mobility, although they took longer to complete the test, the decrement in mobility was not significant (8-foot-up-and-go test). BBS results informed that our participants have an increased risk of 43% of falling, 16% risk for suffering multiple falls, and 24% risk for suffering an injurious fall.

Table 3 shows the differences on functional variables between diabetic and non-diabetic groups, and participants with or without hypercholesterolemia at M1 and M2 (only for those

TABLE 1 | Variables of characterization of participants (12 males; 31 females; total $n = 43$) (mean \pm SD) or n (%) for characterization of comorbidities.

	M1	M2	<i>p</i>
Age (years)			
M	73.50 \pm 8.84	76.50 \pm 8.85	0.000
F	73.94 \pm 8.78	76.81 \pm 8.68	0.000
T	73.81 \pm 8.69	76.72 \pm 8.62	0.000
Weight (kg)^{a, b}			
M	83.76 \pm 12.93	81.67 \pm 12.37	0.031
F	65.42 \pm 7.69	64.54 \pm 7.98	NS
T	70.54 \pm 12.47	69.31 \pm 12.08	0.009
Height (m)^{a, b}			
M	1.69 \pm 0.08	1.69 \pm 0.08	NS
F	1.53 \pm 0.06	1.53 \pm 0.06	NS
T	1.58 \pm 0.09	1.57 \pm 0.09	NS
BMI			
M	29.21 \pm 4.05	28.59 \pm 3.75	0.028
F	27.99 \pm 3.36	27.69 \pm 3.46	NS
T	28.34 \pm 3.56	27.94 \pm 3.52	0.041
WHR^{a, b}			
M	0.96 \pm 0.09	0.97 \pm 0.10	NS
F	0.82 \pm 0.06	0.85 \pm 0.07	0.04
T	0.86 \pm 0.09	0.88 \pm 0.09	0.003
SMM^{a, b}			
M	26.70 \pm 6.51	24.51 \pm 6.36	NS
F	16.31 \pm 2.12	16.05 \pm 1.95	0.031
T	19.21 \pm 6.05	18.26 \pm 5.18	0.009
Diabetes type II [n (%)]			
M	4 (33.3%)		
F	4 (12.9%)		
Hypercholesterolemia [n (%)]			
M	5 (41.7%)		
F	9 (29.0%)		
Hypertension [n (%)]			
M	11 (91.7%)		
F	21 (67.7%)		
Cardiopulmonary conditions [n (%)]			
M	8 (66.7%)		
F	11 (35.5%)		
Musculoskeletal complaints [n (%)]			
M	8 (66.7%)		
F	24 (77.4%)		
Number of comorbidities [n (%)]			
0	6 (14%)		
1	12 (27.9%)		
2	16 (37.2%)		
3	7 (16.3%)		
4	2 (4.7%)		

M, male; F, female; T, total; BMI, body mass index (weight/height²); WHR, waist to hip ratio (circumference of the waist/circumference of the hip); SMM, skeletal muscle mass [according to equations in Al-Gindan et al. (22)]; M1, first moment of assessment; M2, second moment of assessment; *p* < 0.05 based on Wilcoxon signed-rank test for differences between M1 and M2, respectively, for males or females; α , β , *p* < 0.05 based on Mann–Whitney *U* test for differences between males and females on M1 and M2, respectively.

NS = Not Significant.

variables with significant differences at least in one time point). In summary, only type II diabetes and cholesterolemia conditions seemed to influence the performance in endurance capacity, Berg scale and flexibility (type diabetes), and strength (hypercholesterolemia). Longitudinal changes in endurance capacity (6MWT) were reduced in diabetic participants but not in non-diabetic ones (**Table 3**).

Anthropometrical and functional variables were statistically different across LPA and a better profile in functional capacity

TABLE 2 | Values for functional fitness variables by gender (12 males; 31 females; total $n = 43$) (mean \pm SD).

	M1	M2	<i>P</i> Wilcoxon
6MWT (m)^a			
M	480.45 \pm 98.38	479.67 \pm 120.25	NS
F	394.21 \pm 106.59	402.27 \pm 117.13	NS
T	418.28 \pm 110.37	424.38 \pm 121.81	NS
% of ED-6MWT			
M	79.97 \pm 11.99	81.51 \pm 15.38	NS
F	78.91 \pm 16.36	82.31 \pm 19.01	NS
T	79.21 \pm 15.14	82.08 \pm 17.87	NS
Chair sit-and-reach test (cm)			
M	-4.13 \pm 9.11	-9.58 \pm 11.12	NS
F	-1.31 \pm 9.42	-5.03 \pm 9.68	NS
T	-2.09 \pm 9.31	-6.30 \pm 10.18	0.015
Back scratch test (cm)			
M	-14.00 \pm 14.37	-18.83 \pm 16.41	0.041
F	-10.15 \pm 10.03	-13.47 \pm 12.89	NS
T	-11.22 \pm 11.36	-14.96 \pm 13.96	0.006
30 s chair stand test			
M	13.33 \pm 2.71	14.08 \pm 4.29	NS
F	11.35 \pm 3.68	12.80 \pm 3.80	0.008
T	11.91 \pm 3.52	13.19 \pm 3.94	0.008
Arm curl test			
M	14.58 \pm 2.78	17.17 \pm 5.41	0.029
F	13.26 \pm 4.19	14.71 \pm 4.00	0.015
T	13.63 \pm 3.86	15.40 \pm 4.51	0.001
Right handgrip (kg)^{a, b}			
M	38.58 \pm 9.34	38.58 \pm 9.98	NS
F	26.13 \pm 7.09	25.74 \pm 6.31	NS
T	29.60 \pm 9.53	29.33 \pm 9.41	NS
Left handgrip (kg)^{a, b}			
M	37.08 \pm 11.52	36.29 \pm 10.78	NS
F	23.06 \pm 5.73	23.35 \pm 5.44	NS
T	26.98 \pm 9.94	26.97 \pm 9.28	NS
8-foot up-and-go test (s)			
M	6.66 \pm 1.54	6.85 \pm 2.25	NS
F	8.27 \pm 2.89	8.47 \pm 3.76	NS
T	7.83 \pm 2.67	8.01 \pm 3.45	NS
Berg scale			
M	54.33 \pm 1.72	51.83 \pm 4.47	NS
F	52.74 \pm 3.54	49.87 \pm 6.18	0.000
T	53.19 \pm 3.20	50.42 \pm 5.77	0.000

Legend: M, male; F, female; T, total; 6MWT, 6 min walk test; % of ED-6MWT, percentage of the estimated distance on 6MWT; *p* < 0.05 based on Wilcoxon signed-rank test for differences between M1 and M2, respectively, for males or females; α , β , *p* < 0.05 based on Mann–Whitney *U* test for differences between males and females on M1 and M2, respectively.

NS = Not Significant.

and anthropometry was showed for active when compared with inactive participants (**Table 4**). Distribution of comorbidities was similar among the physical activity level groups.

Finally, the linear regression models showed the best predictors of functional tests.

The first linear regression model to the dependent variable “Berg Balance Scale” was associated with 6MWT and “Right Handgrip” adjusted to weight was significant ($F = 27.076$; $p = 0.000$; $R^2 = 0.681$, and SEE = 3.400). The contribution of each predictor to the model was significant with a standardized Beta coefficient of 0.635 ($p = 0.000$) and 0.313 ($p = 0.039$), respectively. The whole model explained 68% of the variance.

The second linear regression model to the dependent variable “30 s chair stand test” was associated with 6MWT adjusted to

weight ($F = 26.192$; $p = 0.000$; $R^2 = 0.567$, and SEE = 2.658). The contribution of the predictor to the model had standardized Beta coefficient of 0.779 ($p = 0.000$) with 57% of the variance explained by the model.

"Arm curl test" was correlated with 6MWT and "Left Handgrip" adjusted to weight ($F = 12.190$; $p = 0.000$; $R^2 = 0.484$ and SEE = 3.362). The contribution of each predictor to the model was significant with a standardized Beta coefficient of 0.406 ($p = 0.009$) and 0.416 ($p = 0.024$), respectively (the model explained 48% of the variance).

Lower flexibility ("Chair Sit-and-Reach Test") was associated with upper flexibility ("Back Scratch Test") ($F = 9.111$; $p = 0.001$; $R^2 = 0.313$, and SEE = 8.646). The contribution of the predictor to the model was significant with a standardized Beta coefficient of 0.529 ($p = 0.000$) and the model explained 31% of the variance. Regarding, upper flexibility ("Back Scratch Test") was correlated

TABLE 3 | Values for functional fitness variables related with comorbidities (12 males; 31 females; Total $n = 43$) (mean \pm SD).

	M1	M2	P Wilcoxon
Diabetes Mellitus			
6MWT (m)			
Non-diabetes ($n = 35$)	431.35 ± 113.04	442.118 ± 123.85	NS
Diabetes ($n = 8$)	361.09 ± 80.25	349.01 ± 81.07	NS
<i>U</i> Mann-Whitney	NS	0.026	
Back Scratch Test (cm)			
Non-Diabetes ($n = 35$)	-8.84 ± 10.26	-12.38 ± 13.05	0.027
Diabetes ($n = 8$)	-21.63 ± 10.51	-26.25 ± 12.82	NS
<i>U</i> Mann-Whitney	0.006	0.005	
Berg scale			
Non-Diabetes ($n = 35$)	53.54 ± 3.14	51.11 ± 5.91	0.000
Diabetes ($n = 8$)	51.63 ± 3.20	47.38 ± 4.14	NS
<i>U</i> Mann-Whitney	0.033	0.022	
Hypercholesterolemia			
Left handgrip (kg)			
Non-High Cholesterol ($n = 29$)	24.38 ± 6.09	24.22 ± 6.34	NS
High Cholesterol ($n = 14$)	32.36 ± 13.89	32.64 ± 11.28	NS
<i>U</i> Mann-Whitney	NS	0.045	

6MWT, 6 min' walk test; $p < 0.05$ based on Wilcoxon signed-rank test for differences between M1 and M2, respectively, for comorbidities; $p < 0.05$ based on Mann-Whitney test for differences between M1 and M2, respectively, for comorbidities.

NS = Not Significant.

with BBS ($F = 6.894$; $p = 0.003$; $R^2 = 0.256$, and SEE = 12.34) The contribution of the predictor to the model was significant with a standardized Beta coefficient of 0.500 ($p = 0.001$) and the model explained 26% of the variance.

Summarizing, physical function predictors, 6MWT and handgrip strength were the best predictors.

Alternative or Additional

Finally, we could not find associations between changes in functional capacity tests and Berg scale or improvement in comorbidities.

DISCUSSION

To better understand the complex nature of physical function decline among older adults, we pursued two directions. First, we evaluated and identified the progression of physical function decline over a 3-year follow-up in a sample of people older than 60 years. Our results showed differences between gender in the anthropometric and functional variables after follow-up period, and these differences could be associated with changes in body composition across the aging process which is not a new finding. The level of functional fitness decreased with age, and the decrease was more important in females. On the other hand, this prospective longitudinal study showed the association between functional variables related to the balance, risk of falls, strength, physical fitness tests, and comorbidities. Our data bring knowledge to understand the variables that suffer the worst decrease with aging and may contribute to create more efficient strategies focused in these functional variables. In this scenario, the most important finding in this study is the relevance of 6MWT as predictor of other functional capacities and the influence of type II diabetes in 6MTW performance and age-related impairment.

The specific sexual phenotype of change for body weight was not new (BMI was reduced for male participants, but not for females); this adaptation followed the sarcopenic obesity paradigm since women did not lose weight in 3 years, but they increased waist and hip circumference (regional adiposity markers), and decreased whole-body skeletal muscle mass (SMM), which may increase the risk of hip fractures in the presence of a

TABLE 4 | Kruskal-Wallis analysis for differences in anthropometrical and functional variables between physical inactive, insufficiently active and active participants.

	Inactive ($n = 17$), mean \pm SD	Insufficiently active ($n = 13$), mean \pm SD	Active ($n = 12$), mean \pm SD	p-Value
BMI (kg/m^2)	28.64 ± 3.53	27.92 ± 4.34	27.26 ± 2.79	NS
WHR	0.89 ± 0.11	0.88 ± 0.07	0.87 ± 0.10	NS
SMM (kg)	16.42 ± 4.00	19.47 ± 7.04	19.56 ± 4.08	0.032
6MWT (m)	334.12 ± 109.64	449.07 ± 86.63	525.50 ± 71.83	0.000
% of ED-6MWT (%)	72.32 ± 20.02	84.27 ± 13.53	93.54 ± 10.54	0.006
Chair sit-and-reach test (cm)	-9.65 ± 10.99	-5.65 ± 9.56	-2.57 ± 8.86	NS
Back scratch test (cm)	-22.23 ± 13.77	-8.76 ± 11.23	-11.65 ± 13.23	0.011
30 s chair stand test (repetitions)	10.88 ± 3.40	14.46 ± 3.47	14.92 ± 3.77	0.009
Arm curl test (repetitions)	12.65 ± 2.91	17.54 ± 5.12	16.85 ± 3.95	0.004
Right handgrip (kg)	23.29 ± 6.29	32.85 ± 9.90	33.69 ± 8.55	0.003
Left handgrip (kg)	21.12 ± 5.90	31.62 ± 10.92	29.96 ± 7.33	0.001
8-foot up-and-go test (s)	10.49 ± 3.96	6.59 ± 1.81	6.01 ± 1.27	0.000
Berg scale	46.29 ± 6.54	52.77 ± 3.46	53.46 ± 2.69	0.001

BMI, body mass index; WHR, waist to hip ratio; SMM, skeletal muscle mass; % of ED-6MWT, percentage of the estimated distance on 6MWT. $p < 0.05$; NS = Not Significant.

loss of balance. Previous studies (28, 29) concluded that greater abdominal obesity measured by WHR increased the risk of hip fracture considerably. The mechanism for an increased fracture risk with increasing WHR after adjusting for BMI might be mechanical instability and impaired balance induced by an increased body size in the abdominal region, leading to a fall (30). It has been suggested that carrying excess weight on the torso rather than on the hips increases the risk of falls that result in hip fracture, perhaps due to a higher center of gravity (28). This paradigm that explains a relationship between the increasing in the WHR and increment in the risk of falls was partially confirmed with our results of differences in the BBS variables, which suffered biggest significant changes (see **Table 2**). Other previous studies have investigated the relationship between obese and the risk of falls and fear of falls in older women (31–33). In general, results from our study are aligned with previous studies (34–37) and also with the study of Bird et al. (38) were balance decreased without loss of strength.

The influence of physical activity in functional capacity was confirmed in our group of age with a dose-response effect, so LPA were positively associated with performance in functional tests showing better results for those who are more active. Although only 30% of the participants accomplish physical activity guidelines (physical activity at least three times a week) the deleterious effect of PA on physical function impairment may not be related with a fixed quantity of PA, which may indicate that even low amounts of PA must promote significant benefits for physical function.

Our data highlighted that balance seems to be greatly explained by aerobic functional capacity (6MWT) and strength (handgrip). These results are in accordance with a previous study, which has shown that higher lower-limb function, balance, and mobility are associated with better walking ability and distance covered in the 6MWT by healthy older adults (39). Our study revealed that 6MWT and ha handgrip strength are also related with the BBS. Handgrip strength has been used as an outcome to measure muscle strength because it has been identified as strongly related with lower extremity muscle power, knee extension torque, and calf cross-sectional muscle area (40, 41) and could predict functional decline (42, 43). These findings reveal not only major relevance of cardiorespiratory fitness but also strength for preserving a good functional capacity. The main result from functional capacity were those related with comorbidities, although functional capacity were barely affected by group of comorbidities, so type II diabetes seemed to affect functional capacity (lower distance on 6MWT, lower flexibility, and lower balance than participants without diabetes type II). Furthermore participants with diabetes present a higher decrement on distance walked on 6MWT, which can potentiate the functional decline and risk of disability associated with aging. This topic should be object of more studies since this association may be a determinant of a frailty phenotype (44–46). In addition, we noticed that 39.5% at M1 and 35.7% of participants at M2 walked less than 400 m on 6MWT, which is a cut-off point to classify sarcopenia with limited mobility; on average, diabetic participants walked way below of this cut-off latter, representing their high susceptibility to be classified as sarcopenic obese and higher risk of frailty (47, 48). Regarding

handgrip data, values split by hypercholesterolemia group were paradoxical since hypercholesterolemia group had higher values of strength, nevertheless the proportion of males and body weight values in the group of hypercholesterolemia were higher than in the group without hypercholesterolemia (35.7 vs 24.9%), which may explain our results. Although the fact of having or not having multimorbidity [the presence of 2 or more chronic conditions (49)] may put older people in higher risk of frailty our results did not confirm this hypothesis.

Physical decline, including muscle weakness, balance dysfunction and mobility problems are related to functional decline, contributing to limit functional capacity while performing ADL and increasing the risk of falling (50, 51). Individualized intervention programs should address fall risks previously identified and they should include balance training, aerobic endurance, muscle strengthening, and flexibility (50).

Improvements in balance may rely in specific balance training programs (38) but also in other strategies. Our results may suggest that exercise prescription for older people should include also aerobic endurance and muscle training (50) as guidelines state, with recommendations to walk at least 30 min a day (52). Physical activity such as walking in different environments should be prescribed as an activity of daily living with benefits on physical capacity especially in balance and specially to those that do not meet the recommended 150 min per week of physical activity of moderate intensity and have or are at risk for chronic diseases (53), with special attention to groups of participants with comorbidities such as diabetes.

Strengths and Limitations

This was a longitudinal study that analyzed whether aging-related changes could be related with a lower decrement in functional variables such as muscle strength, flexibility, or mobility. However, the time interval was too short to found undeniable or high predictive value in variables of disability.

Although our study has a well-defined target population (day care centers and senior universities), participants were volunteers, and this could be a small bias which could be overcome by a larger sample. In addition, the small size of the sample is also a limitation that prevents a more accurate analysis of the results.

A higher time interval and a larger sample should be considered in future studies.

CONCLUSION

Results of this 3-year follow-up study confirmed the relevance of endurance and strength capacities, which may be improved across physical activity levels in combination with other body composition and physical function variables. The main relevance was the influence of type II diabetes 6MWT impairment in the second time point, which may confirm the deleterious consequences of the disease on cardiovascular capacity and sarcopenia; in addition, these results must provide construct validity of 6MWT. Finally, our results suggested that the loss of functional capacity must be more related with qualitative variables than morphological (for example, SMM) since we could not find any relationship between changes in body composition and physical function variables.

When prescribing exercise or programs for promoting health targeting this population greater attention should be given in walking activities and activities that use hands since these specific components seems to have a major impact in functional physical condition.

ETHICS STATEMENT

After an explanation of the study, participants signed an informed consent. All procedures were in accordance with the Declaration of Helsinki. All study procedures were approved by the institutional review boards of the participating institutions.

AUTHOR CONTRIBUTIONS

MTT, AG-M, EC, and BF have equally contributed to this manuscript, in designing the study. Data were collected by MTT, AG-M,

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and BF and were analyzed by all authors. Data interpretation and manuscript preparation were undertaken by MTT, AG-M, EC, and BF. All authors approved the final version of the paper.

ACKNOWLEDGMENTS

The authors wish to thank to Loures Municipality all the logistical support for the assessment of participants on two the moments.

FUNDING

This work was developed upon European Innovation Partnership for Active and Healthy Ageing (EIP-AHA) commitment without any financial support. A specific grant for supporting the publishing of knowledge was obtained from the institution of Portuguese authors (IPL/2016/SFQ2017_ESTeSL).

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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User Experience, Actual Use, and Effectiveness of an Information Communication Technology-Supported Home Exercise Program for Pre-Frail Older Adults

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OPEN ACCESS

Edited by:

Helena Canhao,
Unidade EpiDoC, Epidemiologia de
doenças crônicas, Portugal

Reviewed by:

Renato Gorga Bandeira De Mello,
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Specialty section:

This article was submitted to
Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 15 September 2017

Accepted: 07 November 2017

Published: 27 November 2017

Citation:

Dekker-van Weering M, Jansen-Kosterink S, Frazer S and Vollenbroek-Hutten M (2017) User Experience, Actual Use, and Effectiveness of an Information Communication Technology-Supported Home Exercise Program for Pre-Frail Older Adults. *Front. Med.* 4:208.
doi: 10.3389/fmed.2017.00208

Objective: The main objective of this study was to investigate the use and user experience of an Information Communication Technology-supported home exercise program when offered for independent use to pre-frail older adults. Our secondary aim was to explore whether the program improved quality of life and health status compared to a control group.

Methods: A cohort multiple randomized controlled trial is being performed. Physically pre-frail older adults (65–75 years) living independently at home were included and randomly assigned to a control group or an intervention group. The intervention group received a home exercise program (strength, balance, and flexibility exercises) for a minimal duration of 12 weeks. The control group received usual care. Primary outcomes were: use of the intervention (frequency and duration), adherence to a 3-day exercise protocol and user experience [System Usability Scale (SUS); rating 1–10]. Secondary outcomes were quality of life measured with the SF12 (Physical Component Scale and Mental Component Scale) and health status (EQ-5D), assessed before the study starts and after 12 weeks of exercising.

Results: Thirty-seven independently living older adults participated in the study. Sixteen participants were allocated to the intervention group and 21 to the control group. The average score on the SUS was 84.2 (± 13.3), almost reaching an excellent score. Participants rated the intervention with an 8.5. Eighty percent of the participants finished the 12 week exercise protocol. The adherence to the 3-day exercise protocol was 68%. Participants in the intervention group trained on average 2.2 times (± 1.3) each week. The mean duration of login for each exercise session was 24 min. The Mental Component Scale of the SF12 was significantly higher in the intervention group compared to the control group. A trend was seen in the change over time in the health status between groups.

Conclusions: This study provides evidence that a home-based exercise program is easy to use and has potential in improving quality of life and health status of pre-frail

older adults who live at home. However, further refinement of the program is required to improve adherence and maximize the benefits and potential of exercising in the home environment.

Trial Registration: Unique Identifier: NTR5304. URL: <http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=5304>.

Keywords: older adults, pre-frail, e-health, active aging, functional decline

INTRODUCTION

The number of older adults in our society rises (1) and health care professionals, including physiotherapists, are increasingly confronted with frail older adults (2). Frailty is an important predisposition for falls and associated with adverse health conditions (3). It is a major concern due to its high impact on affected individuals, their families, the health care system, and the society. As such, frailty should be treated in order to prevent the human and economic burden. The American College of Sports Medicine's position stand recommend that exercise prescription for frail people is more beneficial than any other intervention and that resistance and/or balance training should precede the aerobic training for this population (4). However, to respond to demographical changes and the economic impact of frailty, it is of utmost importance to prevent frailty and by this focus on pre-frail older adults. Pre-frailty is considered to be an intermediate stage between non-frail and frail. Fried showed that pre-frail individuals have more than twice the risk of becoming frail compared with non-frail people (5). This highlights the importance of identifying and treating individuals in the pre-frail state before they become frail.

A recent systematic review showed that physical exercise interventions are beneficial for frail older adults in terms of functionality and activities of daily living and can delay progression of functional impairment or disability (6). Of the 19 interventions included, 15 were facility-based and only 4 were home-based interventions. Of those home-based exercise programs, the involvement and time investments of physiotherapists is very high (home visits) and limiting the self-management of the older adult. This indicates that home-based exercising is still quite a new field for (pre) frail older adults, especially as a self-management program. Nowadays, there is increasing interest in the role of "self-management" interventions to support the management of long-term conditions in health service settings. Self-management support has potential to improve the efficiency of health services by reducing other forms of utilization (such as primary care or hospital use) (7). As such, home-based self-management exercising might have more potential in reducing health care costs related to demographic changes compared to facility-based exercising. In addition, home-based self-management programs offer great potential for older adults as many older adults are reluctant to or unable to attend group exercise classes (8).

One widely used home-based exercise intervention is the Otago Exercise Programme (OEP) which is a cost-effective home-based individually tailored fall prevention program delivered by physiotherapists (9–11). The program has shown to improve

participants' strength and balance evaluated in older adults aged 65–97 years old (12, 13). However, the impact of this home-based exercise program in pre-frail older adults is unknown. As such, we developed an Information Communication Technology (ICT)-supported self-management exercise program based on OEP to prevent functional decline in a high-risk group of pre-frail older adults who live at home.

A major challenge that remains in this is appropriate use of such new technologies by older adults in their daily lives as it is quite a new field for older adults. Although the use of computers and tablets is steadily rising among older adults in the Netherlands, older adults are limited in adopting new technologies (14). Many questions are still open, such as whether older adults are capable of learning how to use new technologies and whether they will actually use it independently for physical training when offered by professionals (15). For this reason, the primary aim of this study was to investigate the use and user experience of the ICT-supported self-management program when offered for independent use for older adults living at home. Our secondary aim was to explore whether the intervention improved quality of life and health status of these older adults, compared to those in a control group.

MATERIALS AND METHODS

Study Design and Randomization

The study was part of the European FP7 project PERSSILAA (which stands for Personalised ICT Supported Services for Independent Living and Active Ageing). This study was the first wave of a cohort multiple randomized controlled trial (Jansen-Kosterink et al., submitted¹). This design is introduced by Relton et al. (16) and tackles some of the problems associated with pragmatic trial design. First, a large observational cohort of pre-frail older adults is recruited and their outcomes are measured every 3 months. For each randomized controlled trial pre-frail older adults are randomly selected to the trial intervention. Each person can be randomized only once to an intervention and will stay in this intervention group for the remaining period of time. The outcomes of these randomly selected older adults (intervention group) are then compared with the outcomes of pre-frail older adults randomly not selected (control group). This process will be

¹Jansen-Kosterink S, Vollenbroek-Hutten MMR. The evaluation of an online platform for older adults to monitor and train their physical and mental capacity and develop proper eating habits: a study protocol of a cohort multiplerandomized controlled trial. Submitted to *BMC Geriatrics* (2017).

repeated each time a new release of the intervention is available and a randomized controlled trial can start. Study design and procedures were approved by the Medical Ethical Committee of Medisch Spectrum at Enschede, the Netherlands, and all participants provided written informed consent in accordance with the Declaration of Helsinki. The enrollment of participants for the first cohort of the RCT in this study started in September 2014 and ended in January 2015.

Participants and Setting

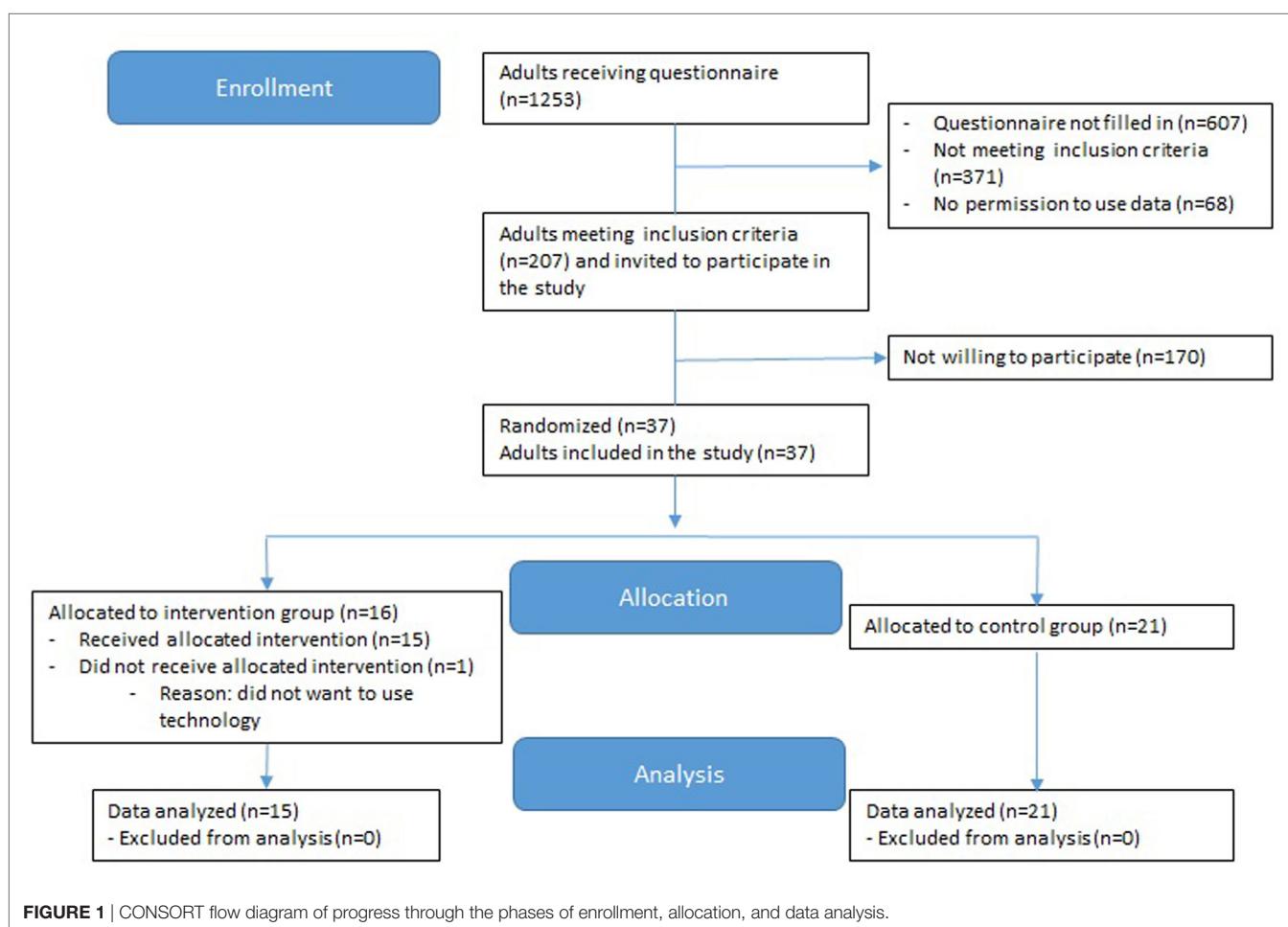
This study was conducted in the municipality of Enschede, the Netherlands. Participants were recruited through their general practitioner. They send out a questionnaire for self-screening of general health status to all their older adults between 65 and 75 years old. This self-screening instrument contained various validated questionnaires to assess the level of frailty and functional decline on the physical, cognitive, and nutrition domain. Based on this self-screening instrument, participants were marked as robust (no functional decline on any of the domains), pre-frail (functional decline on one or more domains), or frail (severe functional decline on one of the domains and professional help needed). For this study, pre-frail older adults were asked to participate. To assess the physical domain, participants completed

the SF-36 items for the physical functioning scale (PF-10) (17). A score of 60 or below on this scale indicated older adults as pre-frail. Next to this, all older adults with a score of 4 on the Groninger Frailty Indicator (GFI) are marked as pre-frail. For more information about this screening procedure, see the study by van Velsen et al. (18).

Participants were excluded if they had conditions that hamper safe execution of the exercise program or insufficient understanding of the Dutch language. Pre-frail participants who were randomly selected to the intervention, but did not fulfill the inclusion criteria for the intervention (such as having a computer with internet at home), remained in the large observational cohort. See **Figure 1** for the flow diagram of the study and allocation of participants to the control or intervention group.

Intervention

The intervention is a technology-supported self-management exercise program, which participants can perform on their own in their home setting. Through a secure login, participants log into a web portal and they can access the program. The home-based exercise program consists of a home-based exercise training that enables participants to train for 3 months. Participants can continue training after program completion. The exercise program



is based on the OEP (19), which is an individually tailored fall prevention program used worldwide for muscle strengthening and balance-training exercises of increasing intensity (13). The exercises are functional and closely related to daily activities (e.g., standing up from a chair) and are categorized in three categories: balance, strength, and flexibility. The program consists of 17 exercises each time. Each training session starts with a warming-up of five exercises and ends with a cooling down with the same four exercises. In the training session, participants perform three exercises in each category (balance, strength, and flexibility). Video and step-by-step spoken and written instruction guide the participants through the exercise (see **Figure 2**).

The use of the program was explained to the intervention group during a plenary meeting.

Participants were advised to take their own computer/tablet with them to this meeting, to make sure the program worked on their computer. During the meeting, participants received their credentials and could start training at home. If they experienced any problems with the program at home, they could call a helpdesk service and someone (SF) answered questions over the phone or would visit the participant.

Participants were advised to train three times a week for approximately 30 min at an individually chosen time, for a duration of 12 weeks. After these 12 weeks, participants could continue using the service for as long as they liked (maintenance phase). No help from physiotherapists is needed to be able to finish the program successfully. However, coaching could be

provided when asked for by the participants. When necessary, two physiotherapists could be contacted to support participants with performing exercises at home in a safe manner. When the participant was uncertain about some exercises, he could go to the physiotherapist (exercise point) in a physiotherapy practice in his neighborhood to receive additional feedback. In addition, physiotherapists could log in on the portal with their own secure account, where he has an overview of the training data (frequency of use, difficulties with exercises) of the participants. From this account, they had the possibility to adjust the program to the needs of the participant. The therapist could turn exercises on and off in case they cause any complaints or cannot be performed due to health issues.

The program progresses in four levels. Exercises are randomly and automatically chosen by the program according to the corresponding difficulty level. The first step-in level of the program consists of light and easy exercises, in order to accommodate for sedentary participants. Progression of difficulty in levels elapsed in agreement with the participant. Participants were not obliged to finish all levels during the program. Participants could see their progress in the training module which tells them at what level they are training, which week and which session. After each training session, they got an overview of the exercises performed. The participant had to indicate whether he was able to perform the exercise or not before going to the next exercise. In case he had problems performing the exercise, the question was asked what the problem was. The physiotherapist could view these remarks and adjust the program accordingly, when necessary.

Exercise 1 of 5

Head Movements



▶

00:00

00:00

!音量

暂停

Performance

- Stand up tall and look ahead
- Slowly turn your head as far as you can to the right
- Slowly turn your head as far as you can to the left

Repetitions

Repeat five times to each side

 Stop training
 Could not complete exercise
 Exercise completed

FIGURE 2 | Example of a training video in the exercise program.

Control Intervention

The control group had no access to the exercise program and received care as usual with no particular attention, referral, or treatment.

Data Collection

Questionnaires were assessed before the start of the exercise program (pretest; t0) and after 12 weeks of exercising (posttest; t1).

Outcome Measures

Demographic and clinical characteristics such as age, sex, years of education, SF36 physical functioning score, and GFI score will be collected at baseline (t0).

Primary Outcomes

The primary outcome measure is use and user experience with the intervention for those participants using the intervention, being measured at t1.

The *use of the intervention* is measured by logging data on the portal and defined in frequency and duration of log in. In addition, we calculated when participants trained during the weeks (morning, afternoon, evening) and which days of the week (weekend versus weekdays).

Adherence to the program was calculated according to completion of the training session as indicated by watching the exercise videos. For example, if a participant completed two training sessions in a week, the adherence rate was calculated as 67%.

User experience will be assessed by means of the validated System Usability Scale (SUS) (20).

This questionnaire includes 10 items which provide a global view of subjective assessment of system's usability. SUS scores have a range of 0–100. The higher the scores on the SUS, the better the acceptance of the service. A SUS score above a 68 would be considered above average and anything below 68 is below average. In addition, participants rated their satisfaction on a scale from 1 to 10, with 10 meaning most satisfied.

Secondary Outcomes

Secondary outcomes are quality of life and health status. Both will be assessed in the intervention and control group at t0 and t1.

Quality of life is measured with the 12-item Short Form questionnaire version 1 (SF-12v1) (21). The SF-12 is a generic instrument including 12 items measuring health-related quality of life (HRQoL). Six items are summed into a physical component summary (PCS) from the four domains of general health, physical function, physical role limitation, and bodily pain, and six items are summed into a mental component summary (MCS) including the four domains of role limitation, vitality, social function, and mental health. Summary scores are calculated using standard (U.S.) scoring algorithms (22). The total score for both scales ranges from 0 to 100, with a higher number indicating higher HRQoL.

Health status is measured with the EQ-5D-3L questionnaire which consists of five questions covering the following health domains: mobility, self-care, usual activity, pain, and anxiety/depression (23). Each dimension has three possible levels (i.e.,

1, 2, or 3), representing “no problems,” “some problems,” and “extreme problems,” respectively. Respondents are asked to choose one level that reflects their “own health state today” for each of the five dimensions. Once the data have been collected and a database created, a scoring function is used to assign a value (i.e., EQ-5D™ index score) to self-reported health states from a set of population-based preference weights. For the Dutch population, the possible EQ-5D™ index scores range from −0.329 (i.e., 33,333) to 1.0 (i.e., 11,111) on a scale where 0.0 = death and 1.0 = perfect health.

The second part is a 20-cm visual analog scale (EQ-VAS) that has endpoints labeled “best imaginable health state” and “worst imaginable health state” anchored at 100 and 0, respectively. Participants are asked to indicate how they rate their own health by drawing a line from an anchor box to that point on the EQ-VAS which best represents their own health on that day.

Sample Size Calculation

A power calculation based on *t*-test testing shows that at least 40 patients per group are needed (two-sided; SD 8.76; clinical relevant difference in quality of life was set on 5.5 on the SF-12 (24); alpha set at 0.05 and beta 0.2) The SD of 8.76 is derived from a study to the normative data of the SF-12 health survey (25).

Statistical Analysis

All statistical tests were performed using SPSS (SPSS 17, IBM, New York, NY, USA, version 17). The significance level was set to 0.05. Descriptive characteristics of the participants and baseline values of screening measures are reported as mean with SDs for continuous variables and frequencies for categorical data. A trend is defined as a *p* value < 0.10.

Data were checked for normality using the Shapiro-Wilk test. Paired *t*-tests (normal distributed data) or Wilcoxon-sign rank test (not normal distributed data) were used to evaluate any changes in outcome measures pre- to post-exercise and the demographic differences between the participants in the control and intervention group.

A general linear model for repeated measurements was used to analyze the effects of the intervention on the variables health status and quality of life, with time (pre and posttest) as within and intervention (control or intervention) as between factor. Data were analyzed using the intention-to-treat principle. Wilks' lambda was used to determine the statistical significance of the multivariate model. Partial eta squared was calculated to measure the effect size.

RESULTS

Thirty-seven independently living older adults participated in the study. Sixteen participants were randomly allocated to the intervention group. One of these participants dropped out of the study before the study started, because she didn't want to use technology. Twenty participants were randomly allocated to the control group and one participant didn't have a computer with internet at home and was automatically allocated to the control group.

Participants' Characteristics

Table 1 shows the characteristics of the participants included in the study. No considerable differences between both groups were noted in the baseline data for demographic and clinical measures.

User Experience

The average score on the SUS was 84.2 (± 13.3) ($n = 13$), which is above average and almost reaching an excellent score (see **Figure 3**). Participants rated the intervention with an 8.5 (± 1.0).

Problems with starting the exercise program in the home environment where mainly related to old internet browsers or no flash player being installed on the computer, which is necessary to be able to watch the exercise movies. These problems have been resolved by the helpdesk.

Use of the Intervention

Fifteen participants started using the intervention and 12 of them (80%) finished the 12-week exercise protocol. There were three drop-outs (20%) during the study. Two participants stopped using the program, because of health problems (not related to the program) and one participant dropped out because his computer didn't work during the time of the study. Of the ones finishing

the exercise protocol, 11 participants (92%) continued using the service for another 6–40 weeks [mean 25 weeks (± 16)].

Participants preferred to perform the exercises in the morning (43%) and afternoon (47%) compared to the evening (10%). Most of the training sessions were performed during weekdays (83%) compared to training sessions performed during weekend days (17%).

Three participants visited the exercise point weekly (one time a week) to receive some additional feedback about the exercises. For one participant, the therapist used the option to turn some exercises off due to (not program related) health problems (pain in shoulder). This way, this participant was able to continue using the program.

Intensity and Frequency of Training

The adherence to the 3-day exercise protocol was 68%. Participants in the intervention group trained on average 2.2 times (± 1.3) each week. The frequency of training decreased during the intervention period with a mean frequency of 2.3 (± 1.4) in the first 6 weeks and 1.9 (± 1.5) in the last 6 weeks (see **Figure 4**). The mean duration of login for each exercise session was 24 min (± 8.0) (see **Figure 5**).

Quality of Life and Health Status

Table 2 presents the results of the quality of life and health status scores. The intervention group reported greater increases over time on the MCS compared to the control group ($p = 0.016$; partial eta squared 0.178; observed power 0.694). Scores on the MCS of the SF12 were significantly higher in the intervention group pre- and posttest, whereas in the control group there were no significant changes over time. A trend was seen in the change over time in the health status (EQ5D-Index values) ($p = 0.076$). No significant differences between groups were found for the EQ-5D vas scores and the PCS of the SF12.

DISCUSSION

The objective of this study was to investigate the use and user experience of an online home-based exercise program and to determine whether the intervention improved quality of life and

TABLE 1 | Demographic and clinical characteristics.

Variables	Control ($n = 21$)	Intervention ($n = 15$)	<i>p</i>
Mean age (years, SD) [range min–max]	70.9 (3.5) [66–76]	69.2 (3.8) [65–77]	0.163
Sex	12 females 9 males	10 females 5 males	0.471
Highest education (<i>n</i>)			0.193
Elementary school	3	2	
High school	5	6	
Lower vocation school	4	—	
Vocational school	2	4	
College	1	2	
Other	5	1	
GFI score	2.9 (0.9)	3.0 (1.3)	0.692
SF36 pf score	33 (18)	43 (17)	0.105

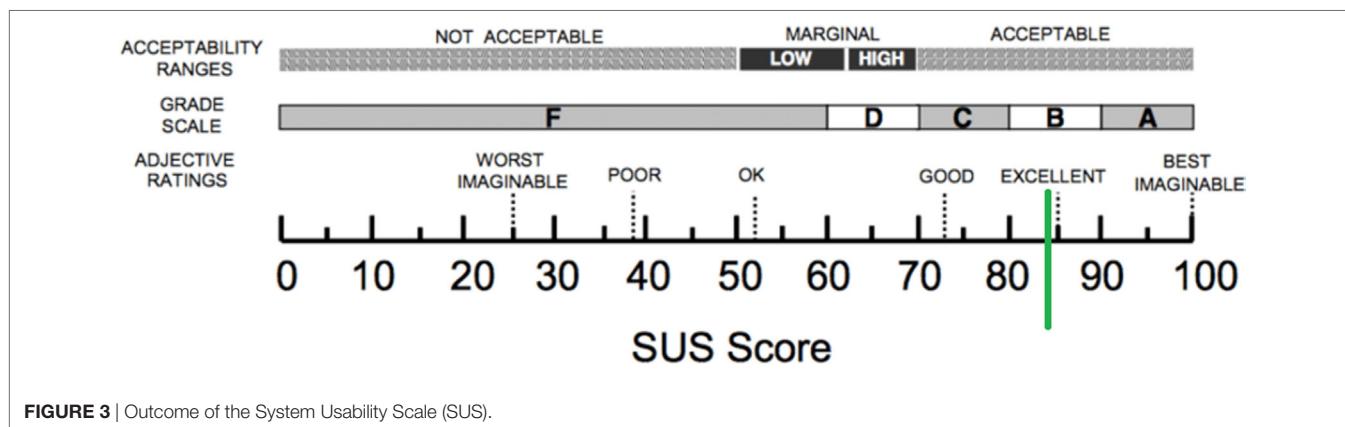
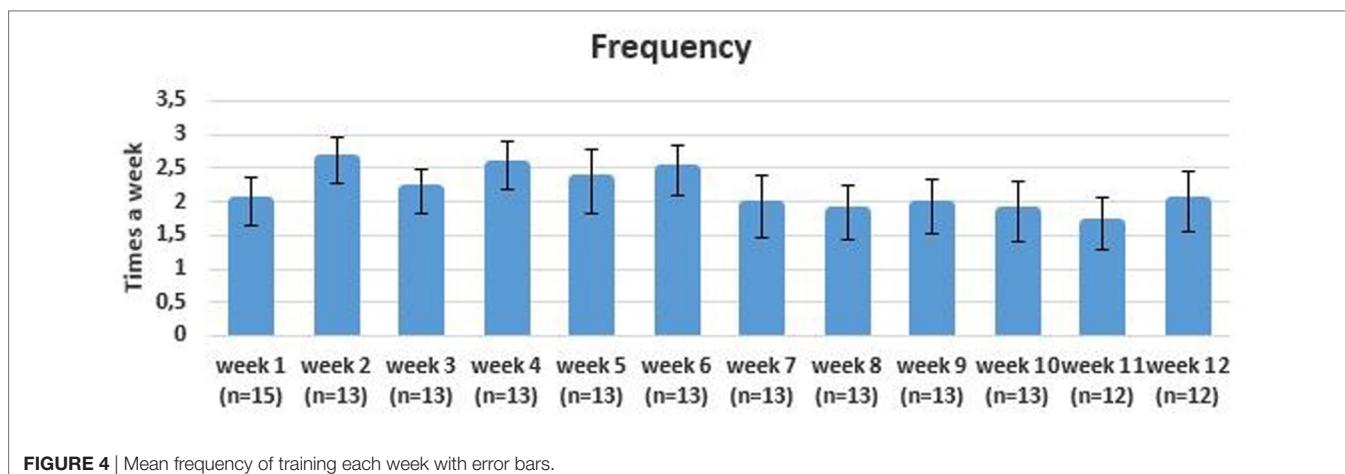
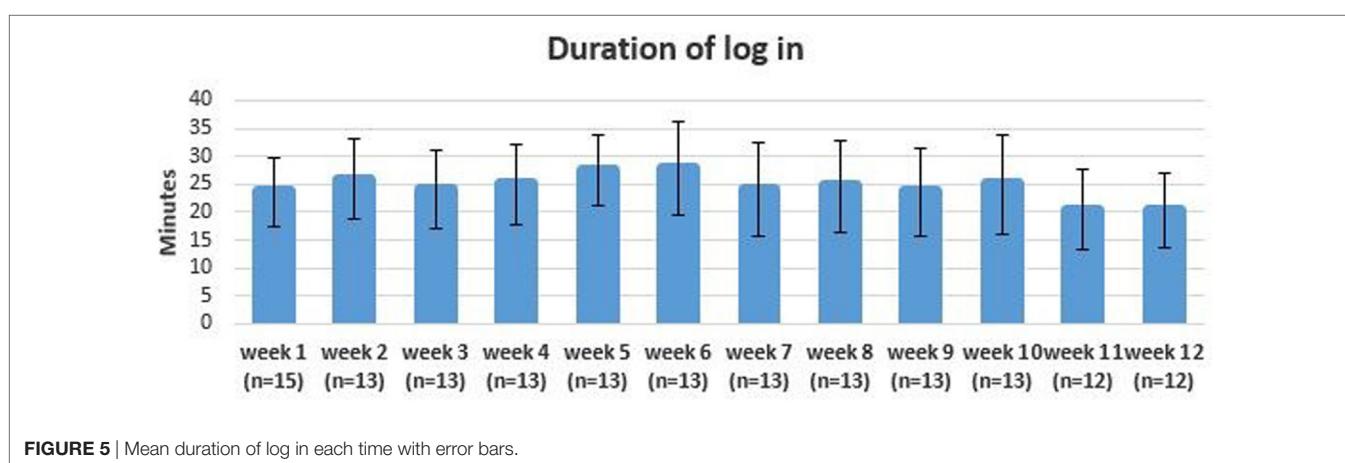


FIGURE 3 | Outcome of the System Usability Scale (SUS).

**FIGURE 4** | Mean frequency of training each week with error bars.**FIGURE 5** | Mean duration of log in each time with error bars.**TABLE 2** | Quality of life and health status scores.

Variables	Group	Baseline (t0)	After intervention (t1)	p ^a	Time × group effect ^b	Effect size ^c	Power ^d
EQ-5D-3L Index values	Control group (n = 18)	0.72 (0.19)	0.70 (0.20)	0.413	0.076	0.098	0.429
	Intervention group (n = 15)	0.73 (0.21)	0.79 (0.10)	0.173			
EQ-5D Vas	Control group (n = 19)	66.3 (13.3)	64.7 (16.8)	0.849	0.925	0.000	0.051
	Intervention group (n = 15)	67.1 (15.3)	65.9 (15.8)	0.488			
SF12 PCS	Control group (n = 18)	31.2 (7.3)	30.9 (7.5)	0.873	0.469	0.018	0.110
	Intervention group (n = 14)	35.5 (12.5)	33.4 (10.7)	0.293			
SF12 MCS	Control group (n = 18)	54.6 (7.4)	54.1 (8.9)	0.486	0.016	0.178	0.694
	Intervention group (n = 14)	51.1 (10.3)	56.0 (7.7)	0.017			

Values representing mean scores (SD).

^ap-values from paired t-test comparing the effect of the intervention on pre- and posttest outcome parameters.

^bp-value from GLM.

^cEffect size partial eta squared from GLM.

^dObserved power from GLM.

health status of physically pre-frail older adults compared to a control group.

In our study, older adults were advised to train three times a week for a period of 12 weeks. The adherence to this protocol was 68%. The drop-out rate was low (20%) and participants trained on average two times a week. We are satisfied with this adherence rate, as different studies showed that strength training on

two nonconsecutive days per week may be as effective as more frequent exercise sessions in older adults (26, 27). However, the frequency of training decreased over time with on average less than two training sessions in the last 6 weeks. Adherence to self-managed programs in older adults is an important issue in other studies as well (28, 29) and adherence rates are generally higher in supervised programs compared to non-supervised

programs (30, 31). This might reduce the effectiveness of self-management exercise programs. However, current developments in technology enable different strategies to assist in improving adherence to home-based exercise programs for older adults with minimal supervision. Different theories show that motivational strategies are important in enhancing adherence to treatment and successful motivational interventions confirm the persuasiveness of personal, individualized feedback (32). Home-based exercise programs provide an opportunity to tailor exercises to the individual needs in contrast to many group-based physical activity programs. This is an advantage that can be more elaborated in the program. Different individual parameters could be taken into account by using for example recommender techniques. Smart algorithms can be used in order to define an appropriate and more encouraging exercise program for the participant, by taking into account the exercises the participant likes, time of the day, age, and gender (33). Future research should focus on the effectiveness of these specific motivation strategies in order to increase exercise adherence for self-management programs for older adults.

Our study shows that most of the older adults were very enthusiastic about the service and didn't experience problems with the new technology when being trained beforehand. Overall, the program is well accepted and the participants are very satisfied with the program. Only three participants (20%) visited the exercise point to receive feedback about the exercises and for only one participant it was necessary to adjust the exercise program. The majority of older adults experienced no problems with the technology, which creates a future for the use of self-management interventions for older adults. A helpdesk, training before the start of the study and an exercise point during the study were helpful in our study to decrease the amount of technical and health problems. This suggests that it is important to implement such new technologies as a service and not as a stand-alone-program. Vollenbroek-Hutten et al. (34) also showed that it is important to implement new ICT services *via* a neighborhood facility instead of directly totally independent at home.

The secondary research question was whether the new intervention improves the quality of life and health status of pre-frail older adults. There is a positive result regarding HRQoL, which shows significant improvements between groups on the mental scale of the SF12. In addition, a trend was seen in improvement of health status between groups. These results are in line with a recent review investigating the aging process, which showed that health promotion interventions are beneficial in terms of improvement in quality of life and/or physical well-being (35). Although positive results, further research is necessary to investigate whether our results are related to adherence measures and if these effects hold over time compared to the control group. This would provide insight whether such ICT-supported

self-management programs have potential in preventing and/or delaying the frailty process.

Limitations

Several limitations need to be taken into consideration when interpreting our findings. The small sample size in our study was limited and as such the clinical findings need to be interpreted with caution. More research is necessary to understand the value of the results found in this study. Another limitation was that testers were not blinded to group assignment for ease of recruitment and to accommodate for time constraints. Blinding, however, is a critical methodological feature of a randomized control trial. This needs to be taken into consideration when evaluating the validity of the results.

CONCLUSION

This study provides evidence that a home-based exercise program is easy to use and has potential in improving quality of life and health status of physically pre-frail, older adults who live at home. However, further refinement of the program is required to improve adherence and maximize the benefits and potential of exercising in the home environment.

ETHICS STATEMENT

This study was approved by the Medical Ethical Committee of Medisch Spectrum at Enschede, the Netherlands. All participants gave written informed consent in accordance with the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

All authors participated in writing the manuscript, revising it critically for important intellectual content, and gave their final approval for publishing the manuscript.

ACKNOWLEDGMENTS

The authors would like to thank MC Eudokia for sending out the questionnaires for the first screening, students HBO-V of Saxion Enschede for helping older adults filling in the questionnaires and performing the second screening of the older adults and Fyon het Stadsveld for providing the exercise points for the participants of the intervention group.

FUNDING

This work was funded by the European Union within the PERSSILAA project (FP7-ICT-610359).

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Kinematic Changes during Prolonged Fast-Walking in Old and Young Adults

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OPEN ACCESS

Edited by:

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de doenças crônicas, Portugal

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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 25 July 2017

Accepted: 06 November 2017

Published: 23 November 2017

Citation:

Oliveira CF, Vieira ER,
Machado Sousa FM and
Vilas-Boas JP (2017) Kinematic
Changes during Prolonged Fast-
Walking in Old and Young Adults.
Front. Med. 4:207.

doi: 10.3389/fmed.2017.00207

Walking biomechanics is known to be influenced by speed. However, most of the research examining the effects of walking speed and gait characteristics has been conducted after a fast-walking task, neglecting the changes that may occur during the task. The aim of the present study was to determine the impact of fast-walking over time on kinematics in young and old adults. Twenty-seven young adults (26.6 ± 6.0 years) and 23 old adults (71.0 ± 5.6 years) walked at 70% of their maximum heart rate for 20 min or until exhaustion, and the effects of fast-walking on temporospatial parameters and on angular kinematics were analyzed during the activity. During the protocol, both age-groups increased step-width variability. Significant effects of time were found for the ankle and hip at toe off for the older group. For the younger group, only the ankle angle at heel strike changed over time. For both groups, fast-walking induced changes in the coordination among the lower-limb angles that were more prominent during the swing phase of the gait. In conclusion, lower-limb kinematics changes in young adults were compatible with early signs of fatigue. The increased step-width variability in older adults may indicate an augmented risk of falling. Changes in the lower-limb walking kinematics of old adults suggest that the adjustments for weight acceptance and body propulsion were restricted to the hip and ankle joints. The kinematic changes among the lower-limb joint angles during the swing phase may compromise the quality of gait. These findings provide a foundation for future studies in the assessment of the risk of falls in older adults associated with walking at a faster pace.

Keywords: active-aging, fast-walking, kinematics, falls prevention, intra-limb coordination

INTRODUCTION

The world population is aging. Approximately 14% of the European population are over the age of 65 and it is expected that this proportion will double by 2050 (1). With more than a third of older adults experiencing at least one fall per year, the consequences of falls represent a major problem for the health systems of many countries and represent huge associated costs (1). Falls often occur during walking (2) and can be a result of aging-related changes on gait (3). Gait changes observed in older adults are primarily due to reduced muscle strength and lower-limb joint range of motion as a result of physiological and neuromuscular changes (4–6). Aging-related changes in gait may be

of particular concern when walking faster than usual. Increased walking speed may magnify the effects and limitations that may occur over time, and such assessments may highlight other factors that may be associated with falls. Irrespective of the factors underlying the age-related alterations on gait, several authors have associated fast-walking with an increased risk of falling (4, 7–9).

In general, healthy older adults are more susceptible to fall in outdoors activities (10), where walking at a faster pace can be a sporadic practice among this population. According to England and Granata (11), fast-walking may influence a successful locomotion by a combination of several mechanisms, as the ability to control movement could be disrupted by the effects of fast-walking on gait kinematics and other clinical correlates of stable walking. Studies involving fast-walking activity and its association with risk of falls are crucial for understanding the strategies that may be involved in falls' prevention. However, most of the research examining the effects of fast-walking and its association with risk of falling (4, 7–9) were conducted after exposing the subjects to increased speed, neglecting changes in gait characteristics during the task. Thus, evaluating the effects of fast-walking activity over time on gait parameters may highlight potential threats that may arise while walking at a faster pace.

An individual's gait strategy can be represented by their temporospatial parameters. Therefore, assessment of the gait parameters, namely fluctuations in temporospatial gait characteristics, may provide additional insight into the motor control of gait (12). In addition, as the coordination pattern between adjacent joint angles reflects a characteristic of the motor control of organizing adjacent structures in terms of timing and position to execute a movement (13), the intra-limb coordination was analyzed to display the impact of fast-walking on the coordinative synergism among the lower-limb angles. Thus, the present study was conducted to determine the impact of walking at a faster pace on temporospatial parameters and lower-limb joint kinematics in young and old adults during the activity.

MATERIALS AND METHODS

Subjects

The participants were 27 young (26.6 ± 6.0 years) and 23 older adults (71.0 ± 5.6 years), the minimum age was 21 and 65 years for the groups of younger and older adults, respectively. Older participants were recruited from local community centers and younger adults from the local student population. Before the session, they were all screened to ensure eligibility. The exclusion criteria included any orthopedical, musculoskeletal, or cardiovascular constraints that might impair normal locomotion. All participants provided written informed consent using procedures approved by the Ethics Committee of the Faculty of Sport from the University of Porto, process number 10-2014.

Procedures

Kinematic data were captured (100 Hz) using an 8-camera motion capture system (Qualisys, QTM). Reflective markers were placed on the anterior-posterior and posterior-superior

iliac spines, bilaterally on the greater trochanter, medial and lateral femoral condyles, medial and lateral malleoli, end of the second toes, fifth metatarsal head, and calcanei. These markers were used to define the segments included in the biomechanical model (14). A standing calibration trial was recorded prior to the beginning of the task. Data were then processed using Visual 3D (C-motion, Rockville, MD, USA). Older participants wore a safety harness attached to the ceiling for safety.

Protocol

All participants completed a familiarization session on a treadmill (AMTI Inc., MA, USA) walking at their preferred walking speed for 5 min. After that, the treadmill speed was increased by 0.5 km/h every 30 s until the participants reached the speed where they reached 70% of their age-predicted maximal heart rate (HR, 220 minus age in years). The participants were instructed to walk at this intensity for 20 min or until their self-assessed exhaustion. Two examiners were accompanying closely the participant during the task. HR was measured continuously during the test with a Polar HR monitor (2010 Polar Electro Oy, FI-90440 Kempele, Finland) to ensure subjects were walking at the required intensity. In addition, perceived exertion was assessed using a modified Borg 10-point scale (15). The relative speed was kept the same for each of the participants, and constant throughout the test. During the protocol, a variation of 10% of the target HR was permitted. The participants would be asked to stop the protocol if any of the following clinical indications were met: voluntary cessation, symptoms of cardiovascular discomfort, pulmonary discomfort, or the exertion reached 90% of their maximum HR, as recommended on ACSM's guidelines for submaximal tests (16).

Dominant limb marker trajectories were collected during 30 s every minute until the end of the activity. The dominant limb was defined as the limb with which they would kick a football. Five equally distributed periods were later analyzed using Visual 3D (C-motion Inc., Rockville, MD, USA). The marker trajectories were filtered using a fourth-order low-pass Butterworth filter with a 12 Hz cut-off frequency. Gait cycle was defined by consecutive heel strikes of the dominant foot. Lower-limb angles were assigned with three rotational degrees of freedom and calculated using an XYZ Cardan sequence of rotations, which are equivalent to flexion/extension–abduction/adduction–axial rotation, respectively. Hip flexion, knee flexion, and dorsiflexion were displayed as positive displacement; whereas, hip extension, knee extension, and plantarflexion were displayed as a negative displacement.

The following parameters were assessed: sagittal angles of the hip, knee, and ankle at heel strike and toe off, cadence (number of steps per minute), stride length (distance between two successive right heel strikes), stride time (duration in seconds of a stride), step width (medio-lateral distance between heel position during heel strike of the left and right limbs). Sagittal joint angles at the ankle, knee and hip for each individual were time normalized to 100% of the gait cycle. Hip–knee–ankle sagittal angle plots were used as visual representatives of intra-limb joint coordination.

The relative position between the adjacent joints was displayed along the gait cycle for the first and last stage of the protocol. Mean and SD of all kinematic data from approximately 30 strides were calculated on an individual level and were then averaged across participants for each group at every stage. Gait variability was assessed using SD for the angular kinematic data, and coefficient of variation $CV = \frac{SD}{Mean} \times 100\%$ for all temporospatial parameters.

Data Analysis

Student's *t*-test was used to identify between-group differences in fast-walking task-speed and demographics. Analyses of differences within- and between-group were assessed by repeated measures ANOVA. If the assumption of sphericity was failed, a Greenhouse-Geisser correction was used. All statistical procedures were performed using SPSS 25 (IBM, NY, USA) and a significance level of 0.05 was used.

TABLE 1 | Characteristics of study's participants.

Characteristics	Young adults (<i>n</i> = 27)	Old adults (<i>n</i> = 23)
Age (years)*	26.6 ± 6.0	71.1 ± 5.6
Height (m)*	1.72 ± 0.11	1.63 ± 0.10
Body mass (kg)	68.0 ± 15.5	69.9 ± 10.2
Fast-walking speed (m/s)*	1.91 ± 0.20	1.22 ± 0.31

Values are displayed as mean ± SD.

*Significant difference (*p* < 0.05) between age-groups using independent sample *t*-tests.

RESULTS

Young and older adults achieved 70% at their maximum HR at significantly different velocities (*P* = 0.01). Old adults were not different from young adults in body mass but were shorter in height than the younger counterpart. Descriptive characteristics can be seen in **Table 1**.

Since gait strategies are directly influenced by the walking speed, both groups had different cadence, stride length, stride time, and step-width mean values. During the activity, both age-groups showed slight, but significant increase of stride length. Young and old adults kept the mean values of the step-width throughout the protocol. The stride time increased only for the group of older adults. Levels of variability (assessed by the coefficient of variation) were higher in the elderly group for the stride length and the stride time (see **Figure 1**). In both age-groups, statistically significant main effects of time were found only for the step-width coefficient of variation (*P* = 0.03).

Between-group comparisons of joint angular kinematics showed differences for the mean values for the ankle, knee (at heel strike), and hip (at toe off). Significant effects of time were found for the ankle and hip at toe off for the older group. For the younger group, only the ankle angle at heel strike changed over time. Older adults had higher lower-limb angular variability at heel strike for the ankle and knee than the younger adults. No time effects were found for the lower-limb joint angle's variability. Time and group differences of the sagittal angles at the heel strike and toe off are presented in **Table 2**, and can be seen in **Figure 2**.

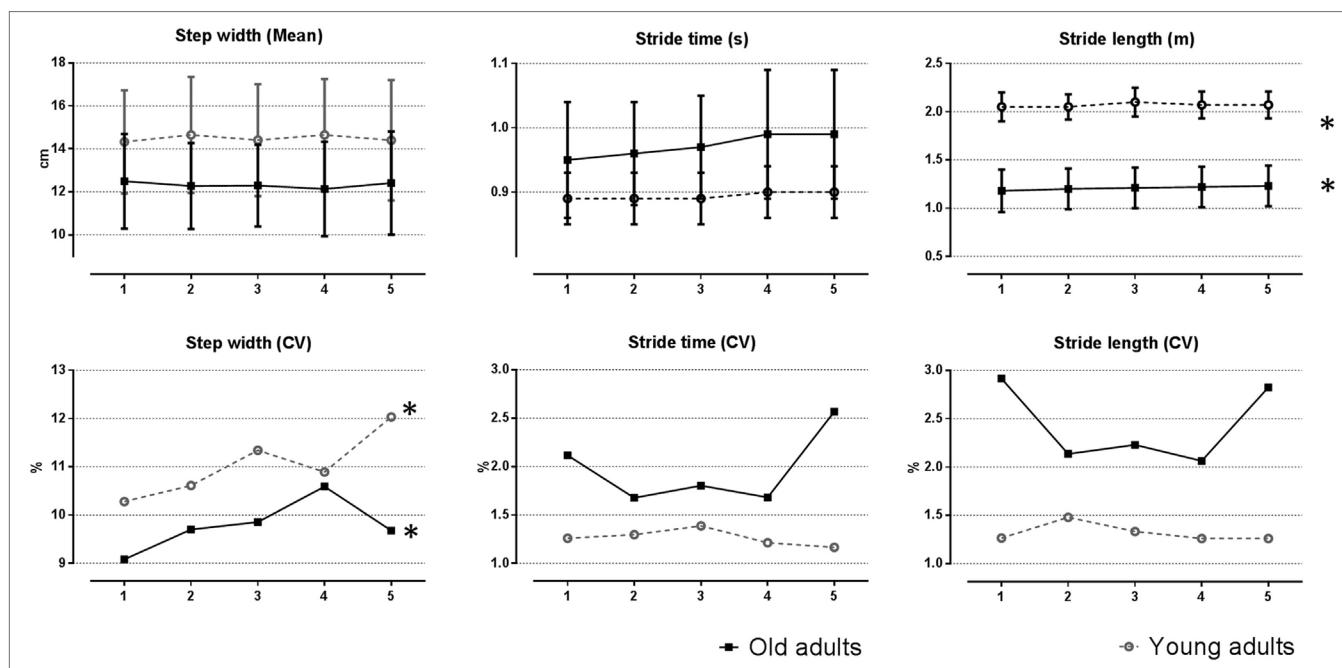


FIGURE 1 | Temporospatial parameters during fast-walking activity at the top. The mean and SD for each subject were subsequently averaged across subjects within the age-group. At the bottom, differences in the coefficient of variation revealed the differences in temporospatial variability along the task. *Indicates statistically significant time effect.

TABLE 2 | Means and SDs for gait variables across all the time points during fast-walking activity.

Variable	Group	Time points					P ANOVA		
		T1	T2	T3	T4	T5	Group	Time	Interaction
Temporospatial parameters									
Cadence	OA	61.4 ± 0.8	62.2 ± 0.9	61.3 ± 0.8	60.2 ± 0.9	58.2 ± 0.9	0.001	0.004	0.518
	YA	65.4 ± 0.8	63.8 ± 0.9	63.2 ± 0.8	62.2 ± 0.8	61.2 ± 0.7			
Stride time (s)	OA	0.95 ± 0.09	0.96 ± 0.08	0.97 ± 0.08	0.99 ± 0.10	0.99 ± 0.10	0.022	0.001	0.020
	YA	0.89 ± 0.04	0.89 ± 0.04	0.89 ± 0.04	0.90 ± 0.04	0.90 ± 0.04			
Step width (cm)	OA	12.5 ± 2.2	12.2 ± 2.0	12.2 ± 1.9	12.1 ± 2.2	12.2 ± 2.4	0.002	0.613	0.226
	YA	14.3 ± 2.4	14.6 ± 2.7	14.4 ± 2.6	14.6 ± 2.6	14.1 ± 2.8			
Stride length (m)	OA	1.18 ± 0.22	1.2 ± 0.21	1.21 ± 0.21	1.22 ± 0.21	1.23 ± 0.21	0.001	0.001	0.172
	YA	2.05 ± 0.15	2.05 ± 0.13	2.1 ± 0.15	2.07 ± 14	2.07 ± 0.14			
Stride length (CV)	OA	2.9 ± 2.6	2.1 ± 1.3	2.2 ± 1.3	2.1 ± 1.2	2.9 ± 3.8	0.012	0.341	0.174
	YA	1.3 ± 0.4	1.5 ± 1.0	1.3 ± 0.7	1.3 ± 0.3	1.3 ± 0.3			
Stride time (CV)	OA	2.1 ± 1.8	1.7 ± 0.8	1.8 ± 1.2	1.7 ± 0.9	2.5 ± 1.4	0.007	0.377	0.178
	YA	1.2 ± 0.4	1.3 ± 0.5	1.4 ± 1.0	1.2 ± 0.4	1.2 ± 0.3			
Step width (CV)	OA	9.6 ± 3.2	10.1 ± 3.6	10.4 ± 2.9	11.2 ± 3.8	11.6 ± 7.9	0.319	0.031	0.402
	YA	11.5 ± 8.0	11.9 ± 8.7	12.6 ± 8.9	12.2 ± 8.5	13.2 ± 10.2			
Angular kinematics									
Differences in the mean values along the activity									
Ankle angular position at HS	OA	-2.9 ± 5.5	-2.9 ± 5.0	-2.9 ± 4.6	-3.4 ± 4.8	-3.4 ± 5.0	0.001	0.032	0.034
	YA	3.5 ± 4.0	2.6 ± 5.0	1.3 ± 4.6	1.7 ± 4.0	1.9 ± 4.2			
Ankle angular position at TO	OA	-9.8 ± 6.0	-11.4 ± 6.4	-11.9 ± 6.4	-11.8 ± 7.0	-12 ± 6.5	0.001	0.021	0.041
	YA	-20.9 ± 10	-20.1 ± 11	-21.4 ± 10	-21.3 ± 10	-21.4 ± 10			
Knee angular position at HS	OA	4.0 ± 6.0	3.6 ± 6.6	2.9 ± 6.9	2.2 ± 6.5	1.7 ± 7.0	0.001	0.126	0.101
	YA	-3.0 ± 3.4	-2.3 ± 3.4	-2.3 ± 3.2	-2.3 ± 3.4	-2.1 ± 3.2			
Knee angular position at TO	OA	40.1 ± 6.7	40.8 ± 6.4	40.4 ± 6.5	40.4 ± 7.1	40.4 ± 7.2	0.127	0.548	0.374
	YA	37.1 ± 4.0	38.4 ± 4.1	38.0 ± 4.5	38.3 ± 4.4	38.4 ± 4.1			
Hip angle position at HS	OA	35.1 ± 7.6	35.9 ± 9.3	35.3 ± 9.4	35.1 ± 8.9	32.9 ± 10.8	0.103	0.279	0.246
	YA	31.4 ± 5.8	31.9 ± 6.2	31.4 ± 6.6	31.4 ± 6.0	31.7 ± 6.1			
Hip angle position at TO	OA	2.8 ± 9.9	2.7 ± 9.5	1.9 ± 9.8	1.4 ± 9.1	0.8 ± 9.4	0.00	0.017	0.032
	YA	-8.4 ± 6.8	-7.1 ± 7.3	-7.4 ± 6.9	-9.0 ± 7.1	-8.1 ± 6.4			
Differences in the SD along the activity									
Ankle angular position at HS	OA	1.5 ± 0.8	1.4 ± 0.7	1.3 ± 0.9	1.5 ± 1.2	1.5 ± 1.2	0.013	0.657	0.706
	YA	0.9 ± 0.3	1.1 ± 0.9	1.0 ± 0.4	1.0 ± 0.4	1.2 ± 0.7			
Ankle angular position at TO	OA	1.8 ± 0.9	1.6 ± 0.8	1.4 ± 0.7	1.6 ± 0.7	1.6 ± 0.8	0.946	0.562	0.089
	YA	1.5 ± 0.5	1.7 ± 0.8	1.7 ± 0.6	1.6 ± 0.9	1.5 ± 0.6			
Knee angular position at HS	OA	2.4 ± 1.3	2.1 ± 1.1	2.1 ± 1.3	2.4 ± 2.3	2.4 ± 2.0	0.012	0.939	0.326
	YA	1.2 ± 0.7	1.7 ± 1.2	1.7 ± 1.2	1.5 ± 1.0	1.5 ± 1.0			
Knee angular position at TO	OA	2.1 ± 0.7	2.1 ± 1.1	2 ± 1.1	2.1 ± 1.0	2.1 ± 1.1	0.159	0.533	0.684
	YA	1.8 ± 0.7	2.2 ± 2.0	1.7 ± 0.6	1.8 ± 0.9	1.7 ± 0.6			
Hip angle position at HS	OA	3.2 ± 3.8	1.5 ± 0.9	2.0 ± 1.5	2.9 ± 3.4	2.0 ± 2.8	0.078	0.303	0.005
	YA	0.9 ± 0.3	1.7 ± 1.9	1.7 ± 1.1	1.8 ± 1.1	1.8 ± 1.4			
Hip angle position at TO	OA	2.5 ± 1.6	2.2 ± 1.4	2.4 ± 2.0	2.6 ± 2.1	2.5 ± 2.4	0.667	0.344	0.366
	YA	1.6 ± 0.8	2.9 ± 4.4	2.1 ± 1.5	2.0 ± 2.1	2.5 ± 2.1			

Values are presented as mean ± SD, bold indicates $p < 0.05$. OA, old adults; YA, young adults; CV, coefficient of variation; HS, heel strike; TO, toe off.

The intra-limb trajectories representing the coordination among adjacent angles were displayed for the first (blue line) and last stage (red line) of the protocol, as can be seen in Figure 3. For both age-groups, visual inspection of the trajectories revealed that the differences between the intra-limb trajectories were more evident during the swing phase, especially for the old group.

DISCUSSION

The objective of this study was to explore the continuous acute effect of a sustained fast-walking along the activity on the gait parameters in healthy young and old adults. We searched for supplementary information regarding potential risks induced by

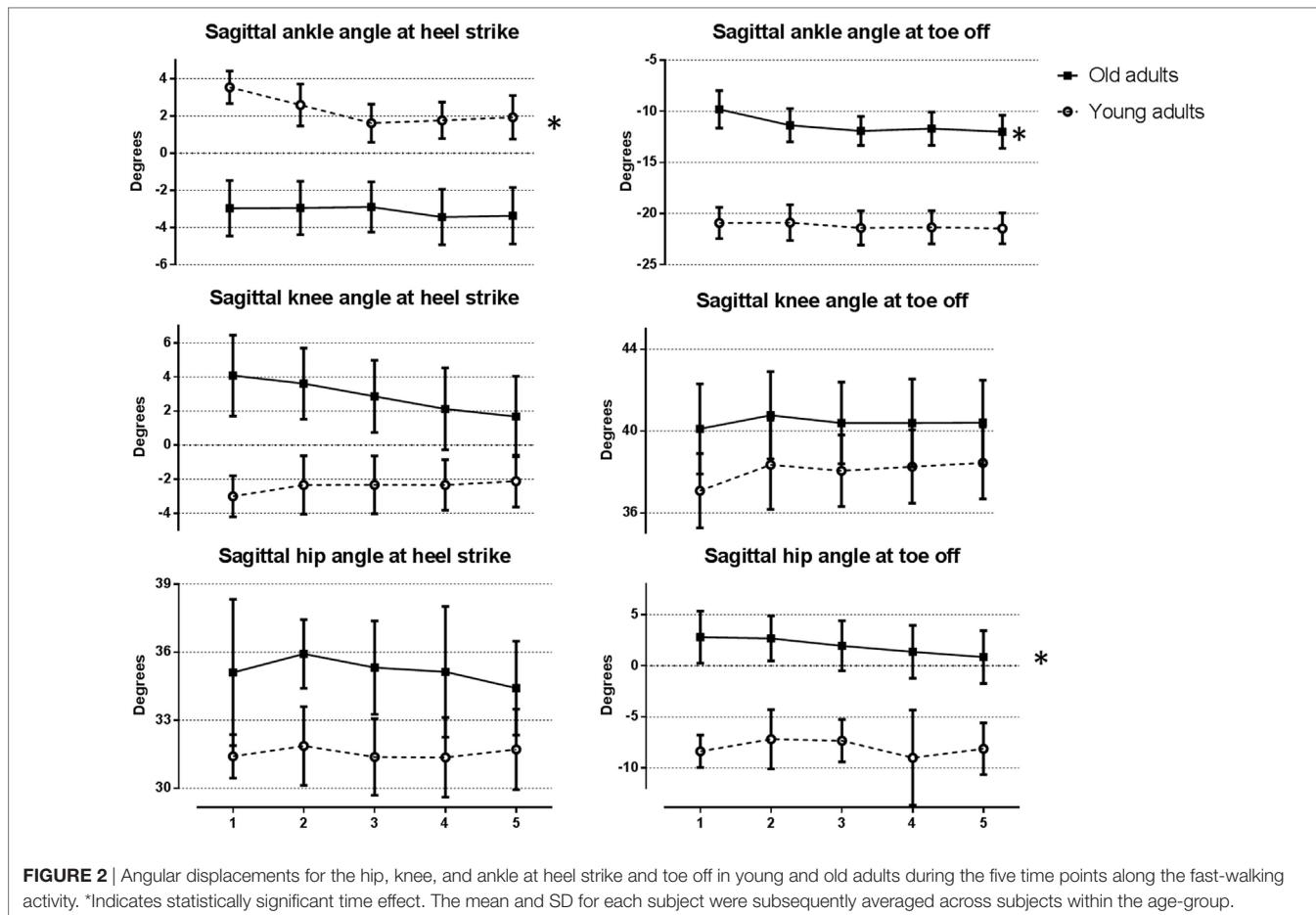


FIGURE 2 | Angular displacements for the hip, knee, and ankle at heel strike and toe off in young and old adults during the five time points along the fast-walking activity. *Indicates statistically significant time effect. The mean and SD for each subject were subsequently averaged across subjects within the age-group.

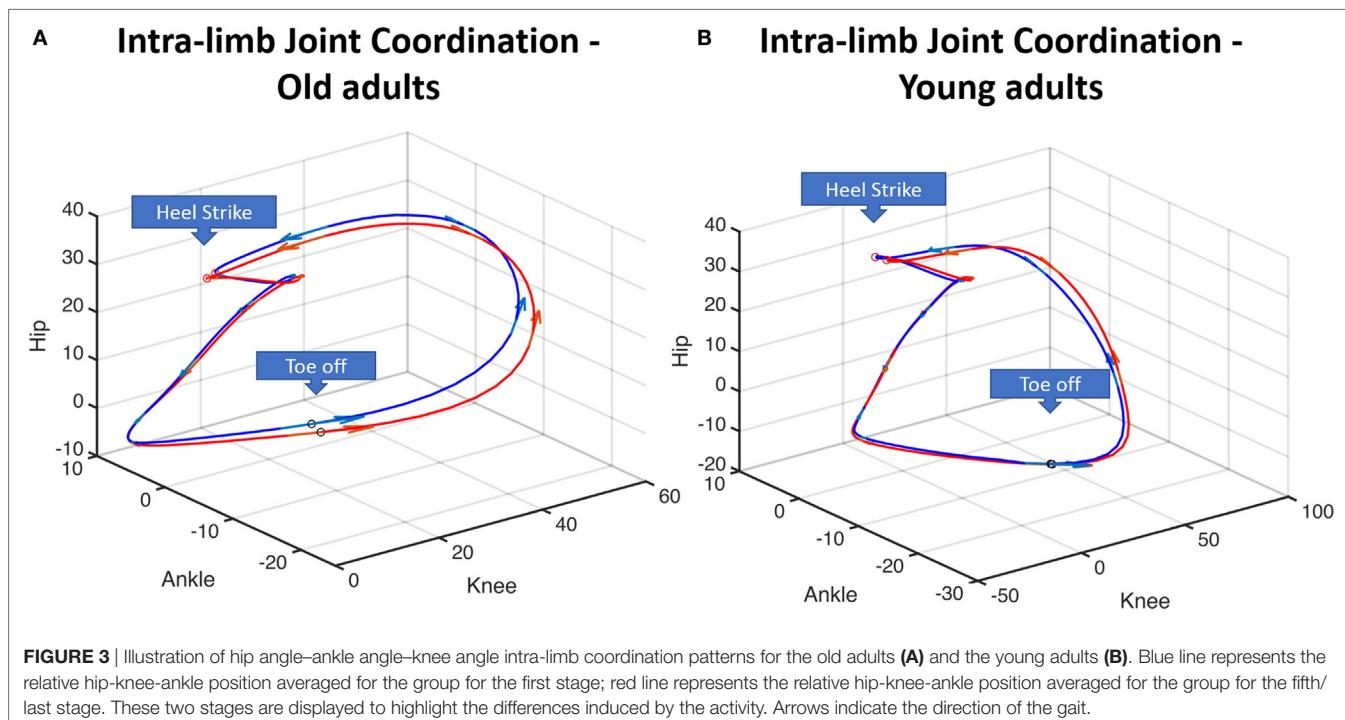


FIGURE 3 | Illustration of hip angle–ankle angle–knee angle intra-limb coordination patterns for the old adults (A) and the young adults (B). Blue line represents the relative hip-knee-ankle position averaged for the group for the first stage; red line represents the relative hip-knee-ankle position averaged for the group for the fifth/last stage. These two stages are displayed to highlight the differences induced by the activity. Arrows indicate the direction of the gait.

a more demanding activity than walking at a freely chosen speed as in daily life activities.

Along the activity, both age-groups changed their gait strategy by having fewer, but longer strides. Even though such strategy may minimize the energy cost of walking (17), it may also increase the risk of injury at the knee (18). Stride length and stride time variability were greater in old adults when compared to young participants herein. Similar findings were reported by Kang and Dingwell (19). Literature regarding age-related differences in gait variability (defined here as fluctuations in temporospatial gait characteristics) and its relationship with walking speed are contradictory. Because older adults typically walk slower, increased gait variability in healthy older adults was considered to be related to their slow walking speed. However, previous studies have suggested that age-related changes in variability rather than be a manifestation of walking speed is more likely to reflect an underlying impairment of the motor system (19–21). With respect to changes in temporospatial variability, the most relevant finding here was the effect of fast-walking on step-width variability in both age-groups. Increased step-width variability has been suggested to be a necessary adaptation to maintain lateral stability. The control of lateral foot displacement is regulated by somatosensory, visual, and vestibular input (22). Such an increase in step-width variability may be explained by the reduction of sensory information induced by the activity (23), which is congruent with the negative effects found on postural control and balance induced by a similar walking protocol of previous studies (24, 25). Thus, during fast-walking, for both groups, the increased step-width variability could be a signal of incipient lateral instability, and loss of balance (26, 27). In addition, previous studies have associated the increment in step-width variability to increased risk of falls in old adults (2, 28).

Fast-walking resulted in significant changes on the lower-limb kinematics of both age-groups. Toward the end of the practice, older adults were initiating the swing phase with additional ankle plantarflexion, and a less extended hip while no changes were observed at the knee. Thus, the necessary adjustments that may have taken place for weight acceptance and body propulsion during the activity were restricted to the hip and ankle joints in old adults. A reduction in hip extension may imply a functional tightness that would be preventing the hip to fully extend at the toe-off (29). The increased ankle plantarflexion seems to be a compensatory mechanism to the reduction in hip extension since they managed to keep and even increase the stride length (30). These findings suggest that the relative contribution of the ankle plantarflexion for propelling the body forward has increased during the activity. Meanwhile, young adults manifested early signs of muscle fatigue, as we can see through their progressive reduction of the ankle dorsiflexion at landing (31). Old adults displayed higher variability for the ankle and knee angular position at heel contact, but levels of kinematic variability did not change throughout the protocol. However, in the present study, analyses regarding variability of angular kinematics were restricted to two events of the gait cycle. Further study on progressive effects of fast-walking activity should assess kinematical variability throughout the gait cycle to provide a complete understanding of the effects of fast-walking.

As we could observe from the intra-limb coordination trajectories, both groups displayed different patterns along the gait cycle. In interpreting this finding, one must consider that this difference may be associated with differences in the walking speed between groups and not exclusively to the age-related differences in walking pattern. The intra-limb joint coordination reflects a characteristic of the motor control of organizing adjacent structures in terms of timing and position to execute a movement (13, 32–34). Several studies have studied this outcome to obtain complementary information into gait control across different neuromuscular disorders (32, 34, 35). Changes in the state of intra-limb joint coordination may emerge due to alteration on any component of the motor system, as those caused by fatigue (33), or yet, alterations on muscle co-activation (34). The shift between the first and the fifth (last) intra-limb coordination trajectories reflect the effect of the activity on the related positions among the joint angles throughout the gait cycle and was more evident during the swing phase. Differences in the coordination among the lower-limb adjacent joints may influence the swing foot trajectory (36), which, in turn, may affect gait parameters related to the risk of falls by tripping and slipping.

Some limitations of this study were the absence of kinetic analyses and the use of a treadmill, which may decrease gait variability (37). However, the use of a treadmill allowed us to analyze continuous gait cycles. To the best of our knowledge, this study was the first to describe alterations on gait during sustained faster pace walking. Our findings revealed that old adults progressively changed their kinematics at hip and ankle during the task. Meanwhile, young adults showed incipient signs of fatigue at the ankle joint. Both age-groups changed their gait strategy by reducing cadence and increasing stride length and increased the variability of step-width. Walking at faster pace had no effect on angular kinematics variability assessed at the heel strike and toe off. However, further analyses should verify the effect of fast-walking throughout the gait cycle. In addition, the differences found in intra-limb coordination trajectories revealed that changes were more prominent during the swing phase. Which, in turn, reveals that the changes were phase dependent within the gait cycle. When walking at their typical pace, healthy active elderly subjects with increased step-width variability have more chances to fall (2, 28). Lower-limb kinematics during walking are strictly associated with the safe performance of two important events during the swing phase of gait, the minimum toe clearance, and the heel contact velocity (36, 38). Both gait events are directly linked to the risk of falls by tripping, and slipping, respectively (3, 36). Therefore, the changes induced after a certain period walking faster than usual, shown here, may compromise the quality of gait increasing the risk of falls. Future work should investigate kinematic changes throughout the gait cycle, particularly at the swing phase. The findings reported herein are important for addressing potential risks associated with walking at a faster pace.

ETHICS STATEMENT

All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the

Ethics Committee of the Faculty of Sport from the University of Porto, process number 10-2014.

AUTHOR CONTRIBUTIONS

CO, principal author, is responsible for the concept, design and intellectual content of the work, data process analysis, and interpretation. EV contributed with the intellectual content of the work, drafting ideas and reviewed analysis, and the final version. FS contributed with the data acquisition, drafting the work, and final revision. JV-B substantially contributed to the

analysis and interpretation of the data and critically improved the content of the work. All the authors approved the final version of the manuscript, and declare to have no conflict of interest associated with this work, as well declare to be accountable for all aspects of it.

FUNDING

This publication was made by possible by Grant number 1637-13-4 by coordination for the improvement of higher education personnel within the Ministry of Education Brazil.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Health and Lifestyles Factors Associated With Osteoarthritis among Older Adults in Portugal

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OPEN ACCESS

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Specialty section:

This article was submitted
to Rheumatology,
a section of the journal
Frontiers in Medicine

Received: 02 August 2017

Accepted: 24 October 2017

Published: 08 November 2017

Citation:

Duarte N, Rodrigues AM,
Branco JDC, Canhão H, Hughes SL
and Paúl C (2017) Health and
Lifestyles Factors Associated With
Osteoarthritis among Older Adults in
Portugal.
Front. Med. 4:192.

doi: 10.3389/fmed.2017.00192

Objective: This study aimed to identify independent associations of sociodemographic, functionality, physical activity, physical and mental health, and osteoarthritis (OA), among older adults.

Methods: A sample of 1,645 older adults (50+ years) observed by rheumatologists, from EpiReumaPt, a population-based study was analyzed. A structured interview included sociodemographic data, chronic non-communicable disease, and physical activity. Functional ability was assessed by the Health Assessment Questionnaire Disability Index; depression and anxiety were assessed by Hospital Anxiety and Depression Scale. OA (knee OA and/or hip OA and/or hand OA) was defined after medical evaluation by rheumatologists according to expert opinion combined with the fulfillment of the American College of Rheumatology classification criteria.

Results: 1,059 participants (64.9%) met the OA classification criteria. Statistically significant differences were found between persons with and without OA in all sociodemographic variables, non-communicable diseases, functional status, physical activity, depression, and anxiety. In the unadjusted logistic regression models, all variables were associated with OA. The final adjusted model explained 32% of the variance. Those who are female with higher age, have more than five comorbidities, and lower levels of function and physical activity were more likely to meet the criteria for a diagnosis of OA.

Discussion: We have analyzed data from a population-based study and found that a diagnosis of OA was independently associated with age, female gender, higher number of comorbidities, physical disability, and low levels of physical activity. These results reinforce the usefulness of the development of a multidimensional assessment to design and test effective interventions for this population.

Keywords: predictors, rheumatic disease, aging, disability, comorbidity, women

INTRODUCTION

Osteoarthritis (OA) is the most prevalent rheumatic disease in the general population (1), and its prevalence is known to increase gradually with age (2). The World Health Organization (WHO) Scientific Group on Rheumatic Diseases estimates that 10% of the world's population 60 years or older has significant clinical problems that can be attributed to OA (3).

Osteoarthritis is a major contributor to functional impairment and loss of independence in older persons causing difficulties in maintaining their activities of daily living (4). Data from the *Global Burden of Disease Project* identify the common causes of years of healthy life lost due to disability in people older than 60 years and identify OA as one of the 10 most relevant causes of disability in this population (5).

Because of the high prevalence of this disease and its impact on independence and quality of life among patients, researchers have been studying factors associated with OA prevalence. Sociodemographic variables, such as age and gender, have been the most studied factors, but studies have also analyzed the association of OA with comorbidities [e.g., Ref. (6, 7)], psychological factors (8, 9), and physical activity (10, 11).

Currently, few studies have compared people with and without OA, furthermore, most studies have analyzed associated factors separately and the comparative contribution of each variable is unknown.

The objectives of this study are (1) to compare people with and without OA with respect to sociodemographic characteristics, functionality, physical activity, non-communicable chronic diseases, and presence of anxiety and depression symptoms; and (2) to identify independent associations between sociodemographic characteristics, functionality, physical activity, physical health and psychological symptoms, and OA.

MATERIALS AND METHODS

Sample

Data from EpiReumaPt project, which is a national, cross-sectional, and population-based study, were used (12). This study population comprised adults (≥ 18 years old) living in the community, in the Portugal mainland and islands (Azores and Madeira). Exclusion criteria were resident of an institution, and inability to speak Portuguese or to complete the assessment protocol. Participants were selected through a process of multi-stage random sampling. The sample was stratified by region and population size.

EpiReumaPt involved a three-stage approach. The first stage included the selection of potential participant household/families using a random selection process. In each household, the adult with the most recent birthday was recruited and completed a structured interview (sociodemographic, socioeconomic, anxiety and depression symptoms, lifestyle habits, chronic non-communicable diseases, health resources utilization data), and a screening for rheumatic diseases. In the second stage, all participants who screened positive for at least one rheumatic disease plus 20% of participants with no rheumatic symptoms were invited to be assessed by a rheumatologist. In the last phase,

a team of three experienced rheumatologists revised all the clinical, laboratory, and imaging data and confirmed the diagnoses using validated criteria (12). Details of the EpiReumaPt methodology have been published previously (12–14).

In this study, the sample consisted of adults 50+ years old who participated in the second phase of EpiReumaPt study and were evaluated by a rheumatologist to confirm the presence or absence of OA (knee OA and/or hip OA and/or hand OA). OA was defined by rheumatologists according to expert opinion combined with the fulfillment of the American College of Rheumatology classification criteria for knee OA, hip OA, and hand OA, as described earlier (15–17).

Sociodemographic data, physical function, anxiety and depression symptoms, lifestyle (e.g., physical activity), and chronic non-communicable diseases were collected during the first stage of the EpiReumaPt project.

Measurements

Sociodemographic data included age, gender, marital status, education, and work status. Marital status was categorized in three categories: without partner (single and divorced people), married, and widower. Work status was categorized as employed full time, part-time, not currently employed (domestic employed, unemployed, and students), and retired.

Number of current chronic non-communicable diseases was assessed using a comprehensive list which included the following 14 diseases: high blood pressure, high cholesterol, heart disease, diabetes mellitus, chronic lung disease, problems in the digestive tract, renal colic, neurological disease, allergies, mental or psychiatric illness, cancer, thyroid and parathyroid problems, hypogonadism, hyperuricemia, and other rheumatic diseases (OA was excluded from this list).

The Health Assessment Questionnaire Disability Index [HAQ-DI; (18)] was used to assess level of functional ability. HAQ-DI measures difficulties with the performance of 20 daily activities retrospectively over the preceding week with four possible responses: no difficulty (0 points), some difficulty (1 point), much difficulty (2 points), and unable to do (3 points). The 20 activities are classified into 8 categories with 2 or 3 activities each: dressing and grooming, arising eating, walking, personal hygiene, reaching, gripping, and usual activities (i.e., shopping, doing chores, getting in and out of a car) (18, 19). The score for each category is the single response within the category with the highest score (greater difficulty). The total score is computed as the mean of the eight category scores. As in previous studies, we did not correct HAQ-DI scores for use of assistive devices (19, 20).

To assess physical activity, participants were asked about the amount of time (minutes) per week they dedicated to physical activity. Answers were categorized as <150 or ≥ 150 min, based on the physical activity recommendations of the WHO (21) for older adults.

Depression and anxiety were assessed by Hospital Anxiety and Depression Scale [HADS; (22, 23)]. The HADS is a short instrument with two subscales that both have seven items that assess presence of clinical anxiety and depression. The scale has a maximum score of 21 for both anxiety and depression

subscales. People with scores between 0 and 7 are considered normal, scores between 8 and 10 are borderline, and a score ≥ 11 indicates a mood disorder. In data analysis, anxiety and depression were considered as dichotomous variables (i.e., a participant with a score ≥ 11 on either subscale was considered depressed or anxious).

Ethical Issue

EpiReumaPt was approved by the National Committee for Data Protection and by NOVA Medical School Ethics Committee. All participants provided informed consent, and the study was performed according to the principles established by the Declaration of Helsinki.

Statistical Analysis

Participants ($N = 1,645$) were divided in two groups: group 1 ($n = 1,059$) consisted of participants meeting the OA diagnostic criteria; and group 2 ($n = 586$) consisted of participants without OA diagnosis or others rheumatic diseases. There were no missing data except for physical activity ($n = 485$).

Descriptive analysis was used to describe the main characteristics of the sample, using frequencies (absolute and relative) or means and SDs, depending on the type of the variable. The comparison of groups defined by the presence/absence of OA (group 1: with OA and group 2: without OA) was performed using independent samples *t*-test for continuous variables and Chi-square test for categorical variables. Univariate logistic regression models, with presence of OA as the outcome, were performed to identify a set of factors that could predict OA presence, including sociodemographic characteristics, comorbidities, functional status, physical activity, depression, and anxiety. The final multivariable model with backward elimination included variables with *p*-values <0.05 . Odds ratios (ORs) and 95% confidence intervals were used to assess the results. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS, version 24, IBM), and $\alpha = 0.05$ was used to determine significance level.

RESULTS

Characteristics of the Sample

The sample comprised 1,645 participants. The mean age of the sample was 65.3 years ($SD = 9.3$) and 63.2% ($n = 1,040$) were women. Most of the participants were married ($n = 1097$, 66.7%) and had 4 years of education ($n = 847$, 54.5%). Regarding work status, the majority were retired ($n = 1050$, 63.8%). With respect to number of self-reported chronic non-communicable diseases, most participants reported 0–2 ($n = 720$, 43.8%) and 3–4 ($n = 540$, 32.8%) chronic diseases. Hypertension ($n = 857$, 52.1%) and high cholesterol ($n = 805$, 48.9%) were the most frequently reported diseases. Among rheumatic diseases, osteoporosis was the most frequently self-reported disease ($n = 190$, 11.6%). With respect to functional status, the mean score of HAQ-DI for the total sample was 0.55 ($SD = 0.65$) out of 3, indicating low levels of limitations. The majority of the sample met the ≥ 150 min of physical exercises per week ($n = 306$; 63.1%). Depressive symptoms were found in

10.6% ($n = 174$) and anxiety was found in 13.8% ($n = 227$) of the total sample.

Sample consisted of 1,059 adults with OA diagnosis (64.4%) and 586 without OA diagnosis (35.6%). Among people with OA, 12.5% ($n = 132$) were classified as having hip OA, 44.7% ($n = 473$) hand OA, and 68.6% knee OA ($n = 726$). Among persons with an OA diagnosis, 36.6% ($n = 388$) reported the presence of other rheumatic diseases. In this sample, the additional rheumatic diseases most commonly reported were osteoporosis ($n = 190$, 11.6%) and rheumatoid arthritis ($n = 91$, 5.5%).

Statistically significant differences were found between groups (with and without OA) in all sociodemographic variables (i.e., age, gender, marital status, education, and work status), non-communicable diseases, functional status, physical activity, depression, and anxiety (Table 1). Participants with OA were older (mean = 67.1, $SD = 9.1$) than participants without OA (mean = 62.1, $SD = 8.9$). The proportion of women with OA ($n = 774$, 73.1%) was higher than among persons without OA ($n = 266$; 45.4%). More participants with OA were

TABLE 1 | Sociodemographic and health description of the sample and comparison of groups [with and without osteoarthritis (OA) diagnosis].

	Total ($n = 1,645$)	With OA ($n = 1,059$)	Without OA ($n = 586$)	<i>p</i>
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	
Age (years)^a	65.3 (9.3)	67.1 (9.1)	62.1 (8.9)	<0.001
Gender				
Male	605 (36.8)	285 (26.9)	320 (54.6)	<0.001
Female	1,040 (63.2)	774 (73.1)	266 (45.4)	
Marital status				
Without partner	214 (13.0)	124 (11.7)	90 (15.4)	<0.001
Married	1,097 (66.7)	666 (63.5)	425 (72.5)	
Widower	334 (20.3)	263 (24.8)	71 (12.1)	
Education				
0–3 years	242 (14.7)	194 (18.3)	48 (8.2)	<0.001
4 years	847 (54.5)	580 (54.8)	267 (45.6)	
5–9 years	274 (16.7)	140 (13.2)	134 (22.9)	
10+ years	282 (17.1)	145 (13.7)	137 (23.4)	
Work status				
Full time employed	295 (17.9)	119 (11.2)	176 (30.0)	<0.001
Partial time employed	52 (3.2)	33 (3.1)	19 (3.2)	
Without labor activity	248 (15.1)	158 (14.9)	90 (15.4)	
Retired	1,050 (63.8)	749 (70.9)	301 (51.4)	
Non-communicable diseases				
0–2	720 (43.8)	355 (33.5)	365 (62.3)	<0.001
3–4	540 (32.8)	367 (34.7)	173 (29.5)	
5 or +	385 (23.4)	337 (31.8)	48 (8.2)	
Physical disability^a (HAQ)	0.55 (0.65)	0.70 (0.67)	0.28 (0.53)	<0.001
Physical activity per week (n = 485)				
<150 min	179 (36.9)	115 (43.2)	64 (29.2)	0.001
≥ 150 min	306 (63.1)	151 (56.8)	155 (70.8)	
Depressive symptoms				
Present	174 (10.6)	143 (13.5)	31 (5.3)	<0.001
Non-present	1,471 (89.4)	916 (86.5)	555 (94.7)	
Anxiety symptoms				
Present	227 (13.8)	172 (16.2)	55 (9.4)	<0.001
Non-present	1,418 (86.2)	887 (83.8)	531 (90.6)	

^aMean (SD).

married ($n = 666$, 63.5%), in comparison to persons without OA ($n = 425$, 72.5%). Widowers were the second most common category represented, 263 (24.8%) in participants with OA compared to 71 (12.1%) in those without OA. Regarding work status, the majority of participants in both groups were retired (persons with OA: $n = 749$, 70.7%; persons without OA: $n = 301$, 51.4%). Among participants with OA, the second most frequent category was “without labor activity” ($n = 158$, 14.9%), whereas for persons without OA, the second most common category was “full time employed” ($n = 176$, 30.0%). Most persons with OA reported presence 3–4 non-communicable diseases ($n = 367$, 34.7%), compared to 0–2 non-communicable diseases ($n = 365$, 62.3%) among persons without OA. Individuals with OA were significantly less active (56.8% met the recommendation of ≥ 150 min of physical activity per week) than those without OA (70.8% met the recommendation of ≥ 150 min of physical activity per week). With respect to functional status, participants with OA showed significantly higher levels of functional limitations (mean = 0.70, SD = 0.67) than persons without OA (mean = 0.28, SD = 0.58). Percentage of depressive symptoms was also higher among individuals with OA ($n = 143$, 13.5%) compared to participants without OA ($n = 93$; 8.7%). Similar

results were found for anxiety, persons with OA showed a higher percentage of anxiety symptoms ($n = 172$, 13.8%) than people without OA ($n = 55$, 9.4%).

Multivariate Predictors of OA

Using OA as the outcome, unadjusted logistic regression models found that all of the variables shown in **Table 1** were associated with presence of this chronic disease (**Table 2**). The final adjusted model contains only significant variables, and the non-significant variables were excluded, one by one, from the model. The variables were removed in the following sequence: marital status ($p = 0.387$), work status ($p = 0.216$), depression ($p = 0.512$), and anxiety ($p = 0.066$). In the final adjusted model, age, gender, number of comorbidities, physical disability, and physical activity remained statistically significant and the model explained 32% of the variance. People who were older (OR = 1.048, $p < 0.001$) and female (OR = 3.192, $p < 0.001$) were more likely to have OA. People with more than five comorbidities were more likely to report OA than people with 0–2 comorbidities (OR = 4.484, $p < 0.001$). Functional disability was also associated with OA. Specifically, persons with higher levels functional disability were more likely to report OA than those with lower levels of disability

TABLE 2 | Associations of potential explanatory variables with osteoarthritis (OA).

	N	Cases of OA	Odds ratio (OR)	Unadjusted		Adjusted		
				95% confidence intervals (CI 95%)	p	OR	CI 95%	p
Age	1,645	67.1 (9.1)	1.063	1.051–1.076	<0.001	1.048	1.021–1.076	<0.001
Gender					<0.001			<0.001
Male	605	285 (26.9%)	1	—	—	1	—	—
Female	1,040	774 (73.1%)	3.269	2.643–4.038	<0.001	3.192	2.040–4.994	<0.001
Marital status					<0.001			—
Without partner	214	124 (11.7%)	1	—	—			
Married	1,097	672 (63.5%)	1.148	0.852–1.545	0.364			
Widower	334	263 (24.8%)	2.689	1.844–3.921	<0.001			
Education					<0.001			0.037
≥10 years	282	145 (13.7%)	1	—	—	1	—	—
5–9 years	274	140 (13.2%)	0.975	0.708–1.377	0.939	0.583	0.321–1.059	0.076
4 years	847	580 (54.8%)	2.052	1.559–2.702	<0.001	1.182	0.715–1.956	0.515
0–3 years	242	194 (18.3%)	3.819	2.578–5.656	<0.001	0.503	0.192–1.313	0.160
Work status					<0.001			—
Full time employed	295	119 (11.2%)	1	—	—			
Partial time employed	52	33 (3.1%)	2.569	1.395–4.730	0.002			
Without labor activity	248	158 (14.9%)	2.596	1.833–3.677	<0.001			
Retired	1,050	749 (70.9%)	3.814	2.814–4.813	<0.001			
Comorbidities					<0.001			<0.001
0–2	720	355 (33.5%)	1	—	—	1	—	—
3–4	540	367 (34.7%)	2.181	1.729–2.752	<0.001	2.850	1.801–4.511	<0.001
5 or more	385	337 (31.8%)	7.219	5.160–10.099	<0.001	4.484	2.348–8.561	<0.001
Physical disability (HAQ)	1,645	0.70 (0.67) ^a	3.871	3.081–4.865	<0.001	1.926	1.186–3.126	<0.001
Physical activity per week					0.002			0.027
≥150 min	306	151 (56.8%)	1	—	—	1	—	—
<150 min	179	115 (43.2%)	1.844	1.263–2.694	0.002	1.630	1.056–2.516	0.027
Depression					<0.001			—
No	1,471	916 (86.5%)	1	—	—			
Yes	174	143 (13.5%)	2.795	1.869–4.179	<0.001			
Anxiety					<0.001			—
No	1,418	887 (83.8%)	1	—	—			
Yes	227	143 (16.2%)	1.872	1.357–2.584	<0.001			

^aMean (SD).

(OR = 1.926, $p < 0.001$). Physical activity was also associated with OA persons; people with lower levels of physical activity were more likely to report OA than those with higher levels of physical activity (OR = 1.630, $p = 0.027$).

DISCUSSION

The results from this study showed a positive association between older age, female gender, comorbidities (higher number of non-communicable diseases), disability, physical activity level, and presence of OA; findings that are consistent with previous results reported in the literature on OA. According to *A National Public Health Agenda for Osteoarthritis* (24), OA prevalence increases substantially at age 45. Also, the *World Health Organization World Report on Ageing and Health* (25) showed a higher rate of knee and hip OA in people above 65 years and in females. Women reported higher percentage of OA than men; these results highlight the importance of considering gender differences among people with OA. We developed an exploratory analysis of this same sample, and the results showed that women had lower levels of education, more non-communicable diseases, higher levels of disability, and depressive and anxiety symptoms than men. These results indicate that interventions that seek to improve function among persons with OA should consider the profile of the largely female population of persons with OA to maximize adherence to and impact of interventions in this population.

Other sociodemographic variables tested: marital status, and work status, lost their significance in the adjusted model, probably because people with OA and with low levels of education are mostly women ($n = 554$, 52.3%) and had higher levels of physical activity ($n = 73$, 15.1%), furthermore, retired people was the oldest group (mean age = 70.9, SD = 7.4) and had the highest level of disability (mean = 0.77, SD = 0.69). Prior studies have analyzed the impact of sociodemographic characteristics in OA, for example, Cleveland et al. (26) explored the relationship between functional status/disability and sociodemographic status in people with OA and found that persons with lower education, non-homeowners, or lower income were more likely to have increased disability.

Persons with OA seem to have a higher number of others non-communicable diseases. This result is consistent with a systematic review on multimorbidity which showed that depression, hypertension, diabetes, arthritis, asthma, and OA were prone to be comorbid with other conditions (7).

We found a positive relationship between physical disability and OA. The mean disability score, in this study among persons with OA, was 0.70, higher than the mean score that was reported for a general population (0.49) (19), but very similar to the mean reported in a population with OA (0.80) (19). The same authors have stated referred that HAQ-DI scores of 0–1 are generally considered to represent mild to moderate difficulty functioning. According to the WHO (27), among people with OA, 80% had mobility disability and 25% were unable to perform activities of daily living independently. On the one hand, OA appears to have a high impact in disability; on the other hand, low levels of functioning promote sedentary behavior which is a risk factor

for OA as well as for weight gain, general de-conditioning, and possibly the onset of other chronic conditions.

Our results showed that 56.8% of people with OA met the physical activity recommendations. This percentage is lower than the level of physical activity performed by people without OA, suggesting that the presence of OA can be a barrier to physical activity participation. The *National Food, Nutrition and Physical Activity Survey Report* (28) found low levels of physical activity in the general Portuguese population. In this national report, only 36% of young adults (15–21 years), 27% of adults, and 22% of older adults (65–84 years) met the actual recommendations for physical activity. This issue is particularly important for adults with OA, because this group is physically inactive and at risk of disability due to joint limitations (4). Several studies confirm the importance of physical activity for arthritis and have shown that increased physical activity is associated with improved disability in people with arthritis and in OA symptomatology relief (4, 25, 29). International organizations recognize regular physical activity as one of the most important non-pharmacological therapies for OA (30–32).

One study that explored the physical activity levels in knee OA patients concluded that only 41% of patients reported sufficient levels of physical activity (33). Badley and Ansari (10) concluded that physical inactivity accounted for an estimated 21% of disability attributed to arthritis and randomized clinical trials demonstrated that structured physical activity can reduce the risk of developing disability in people with OA (34).

In this study, symptoms of depressive and anxiety symptoms were higher in people with OA than in people without OA. However, in the adjusted model, these two variables ceased to be significant. According to Eurostats (35), in 2014, 7.1% of the population of EU-28 reported having chronic depression. Portugal with 11.9% was top ranked in the share of total population reporting chronic depression. Stubbs et al. (9) concluded that in Europe there is a prevalence of 19.9% of depressive symptoms in people with OA, lower than the prevalence found in studies conducted in USA (23.1%). Few studies have analyzed the symptoms of anxiety among OA patients, as most of the studies focused in the rheumatic disease in general [e.g., Ref. (36)].

Despite the results, study of psychological morbidity continued among people with OA remains important because it can affect the diagnosis and the adherence to treatment (36–38). Depressive symptoms appear to act as a potential barrier to physical activity and social participation for people with OA (9).

This study has some limitations, namely, the cross-sectional nature of the data; and the missing information about the time of duration of OA and pain, which could help us to understand the relationship between specific variables like physical activity and disability. Physical activity was assessed in a reduced number of participants which could limit the interpretation of the results. Those without a physical activity assessment could be more inactive than those who filled all the evaluation. The prevalence of OA is overestimated in this sample when compared with the Portuguese population (50+ years). This aspect is related to the general objectives of EpiReumaPt that focus on people with rheumatic diseases and with the criteria for sample selection in this study. The amount of variance in OA explained by the model

was low (32%), which limits the interpretation of the results. The variance explained could be improved by the inclusion of other biological variables, such as body mass index and muscle strength. Other limitations of the EpiReumaPt initiative were reported by Branco et al. (12). The main strengths of the study are first the large national population-based sample and second, the fact that the OA diagnosis was made by rheumatologists who are experts in performing these evaluations. A final strength of the dataset and design is that it enabled a systematized comparison of the characteristics of person with and without OA using a large number of sociodemographic, disease, and functional status variables.

In this paper, we have analyzed older adults (+50) from a population-based study and found that a diagnosis of OA was independently associated with age, female gender, higher number of comorbidities, physical disability, and low levels of physical activity. These results reinforce the need to develop multidimensional assessments to design and evaluate effective interventions for this population.

ETHICS STATEMENT

EpiReumaPt was approved by the National Committee for Data Protection and by NOVA Medical School Ethics Committee. All participants provided informed consent, and the study was performed according to the principles established by the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

ND contributed to the conception, design, analysis, and interpretation of data for the work. She agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. AR, JB, HC, and SH revised the work

critically for important intellectual content and approved the final version to be published. CP contributed to the design, analysis, and interpretation of the data for the work; revised the work critically for important intellectual content; and approved the final version to be published.

ACKNOWLEDGMENTS

The EpiReumaPt Study Group would like to acknowledge the invaluable help of Henrique de Barros, MD PhD; João Eurico da Fonseca, MD PhD; José António Pereira da Silva, MD PhD; Francisco George, MD; Rui André, MD; Luís Maurício, MD; Faculdade de Medicina da Universidade de Coimbra, Faculdade de Medicina da Universidade de Lisboa, Faculdade de Medicina da Universidade do Porto, Liga Portuguesa Contra as Doenças Reumáticas, Associações de Doentes com Doença Reumática, Administrações Regionais de Saúde (Norte, Centro, Lisboa e Vale do Tejo, Alentejo e Algarve), Governo Regional da Madeira, Governo Regional dos Açores, Associação Nacional de Freguesias, Associação Nacional dos Municípios Portugueses, Câmara Municipal de Lisboa.

FUNDING

EpiReumaPt was endorsed by the Alto Patrocínio da Presidência da República and was supported by a Grant from Directorate-General of Health. The project was also sponsored by Fundação Calouste Gulbenkian, Fundação Champalimaud, Fundação AstraZeneca, Abbvie, Merck Sharp & Dohme, Pfizer, Roche, Servier, Bial, D3A Medical Systems, Happybrands, Centro de Medicina Laboratorial Germano de Sousa, Clínica Médica da Praia da Vitória, CAL-Clínica, Galp Energia, Açoreana Seguros, and individual support of rheumatologists. The work was supported by a doctoral fellowship of the Portuguese Foundation for Science and Technology (Reference: SFRH/BD/111533/2015).

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Conflict of Interest Statement: All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication. No previous data have been reported before. All co-authors confirm the full control of all primary data and we agree to allow the journal to review their data if requested.

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Active Aging in Very Old Age and the Relevance of Psychological Aspects

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Background: Active aging encompasses a socially and individually designed mix of different domains that range from personal and familial, to social and professional. In being a key policy concept often focused on the young-old individuals, efforts in studying its dimensions in advanced ages have seldom been made. Nevertheless, there is a recognized need to promote adequate responses to the growing number of individuals reaching advanced ages and to recognize their specific dependability on health-related aspects, services attendance, social interactions, or on psychological characteristics for what it means to “age actively.”

OPEN ACCESS

Edited by:

Helena Canhão,
Unidade EpiDoc, Portugal

Reviewed by:

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Universidade de Lisboa, Portugal
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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 25 August 2017

Accepted: 10 October 2017

Published: 30 October 2017

Citation:

Paúl C, Teixeira L and Ribeiro O (2017) Active Aging in Very Old Age and the Relevance of Psychological Aspects. *Front. Med.* 4:181.
doi: 10.3389/fmed.2017.00181

Objective and methods: This study provides a secondary analysis of data and follows the preceding work on the operationalization of the World Health Organization's (WHO) active aging model by means of an assessment protocol to measure which variables, within the model's determinants, contribute the most for an active aging process (1). Authors used the achieved model (composed by six factors: health, psychological component, cognitive performance, social relationships, biological component, and personality) and performed multi-group analysis of structural invariance to examine hypothetical differences between age groups (<75 years vs. ≥75 years) and to contrast obtained findings with the originally achieved model for the total sample (1,322 individuals aged 55 +).

Results: The structural covariances for the two age groups were statistically different. The comparison of components between age groups revealed a major relevance of the psychological component for the older age group.

Conclusion: These findings reinforce the importance of psychological functioning in active aging in oldest old, and the need for further research on specific psychological features underlying the subjective meaning of active aging in more advanced ages.

Keywords: active aging, World Health Organization, confirmatory factor analysis, health, psychological determinants

INTRODUCTION

The concept of Active Aging is defined as “...the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age” (2). In being of incontestable importance as a fundamental policy concept in Europe, efforts to increase its empirical evidence in terms of operative definition and criteria have received growing attention worldwide over the last years [e.g., Ref. (3–5)].

The active aging model as presented by the World Health Organization (WHO) (2) encompasses six groups of determinants, each one including several features: (1) availability and use of health and social services (e.g., health promotion and prevention; continuous care); (2) behavioral determinants (e.g., exercise and physical activity; drinking and smoking habits; feeding; medication); (3) personal determinants (biology and genetics, and psychological characteristics); (4) physical environment (e.g., safety houses, low pollution levels); (5) social determinants (e.g., education, social care), and (6) economic determinants (e.g., wage, social security). This group is complemented by two crosscutting determinants—gender and culture. According to this model, the key elements of active aging are (1) autonomy, which is the perceived ability to control, cope with, and make decisions about how one lives on a day-to-day basis, according to personal rules and preferences; (2) independence, which refers to the ability one has to perform functions related to daily living, i.e., the capability of living in the community with no and/or little help from others; (3) quality of life; and (4) healthy life expectancy, which refers to how long people can expect to live in the absence of disabilities. The main pillars of the model are participation, health, and security. More recently, a fourth pillar has been added to the model: lifelong learning (6).

Presently, active aging appears mostly as an outcome of several determinants that are expected to help professionals and researchers to recognize particular profiles that are more at risk or, on the contrary, are more favorable to age actively. Since the majority of definitions of active aging are narrow and primarily concerned with the young-old [cf. (7)], the need for further investigating the concept's operationalization in the old-old has been increasingly recognized (8), for instance, building on and expanding the classic WHO's definition of active aging, proposed a set of principles as the basis for a wide-ranging strategy on active aging that incorporate, among others, the need for encompassing all older people, including those who are frail and dependent, i.e., those who are more likely to be older and experiencing sizeable losses in cognitive and physical potential. On this specific matter (9), in an Age UK report entitled *Improving later life: Understanding the oldest old* had already stressed the importance of fully integrating the older population into an active aging strategy that includes both prevention at earlier stages of the life course as well as into old age, and fast remedial action when autonomy is threatened.

By enlighten the active aging model in the oldest old (75+), this paper aims to test the statistical significance of observed differences in the structural weights of health, psychological component, cognitive performance, social relationships, biological component, and personality factors, across age groups.

MATERIALS AND METHODS

Data Collection

This study was conducted in several Portuguese regions, including mainland territory and the Azores and Madeira islands, and is part of a large Portuguese project on active aging entitled “DIA: From Incapacity to Activity—The Challenge of Ageing” that included a cross-sectional survey of community-dwelling

individuals aged 55 years old and over. Participants were recruited randomly through announcements in local media, local agencies (e.g., seniors clubs) and NGO's, and also recurring to the snowball method through which effective participants indicated other potential subjects who were in similar conditions. Trained researchers conducted the interviews and followed a structured questionnaire that included question on demographic, psychological, and social aspects. All interviews took place in local community facilities (e.g., parish hall) or at the participants' homes.

Measures

Different groups of determinants of active aging were assessed by means of an extensive protocol that was developed considering literature review of most common tests used in Gerontology and Geriatrics, and following previous experience with the European Survey of Aging Protocol [ESAP (10)]. Along with socio demographic characteristics (gender, age, education, and income), information was obtained on cognitive functioning by means of the Mini-Mental State Examination [MMSE (11, 12)], social network (family, friends, confidants) was assessed with the Lubben Social Network Scale [LSNS (13)], psychological distress was measured with the General Health Questionnaire [GHQ-12 (14)], optimism was assessed with the Life Orientation Test-Revised [LOT-R (15, 16)], personality (neuroticism, extraversion, openness to experience) was evaluated with the NEO Personality Inventory (17), happiness was assessed with a single question retrieved from QBE/F (18) and environment domain of quality of life measured with World Health Organization Quality of Life-BREF [WHOQOL-BREF (19, 20)]. Bio-behavioral measures included pulmonary function and grip strength, which were calculated using a standard “Mini Peak-Flow Meter” (Datasprir Peak-10, Sibumed) and an electronic dynamometer (Grip-D, TAKEI Scientific Instruments Co., Ltd.), respectively. Finally, health status and physical condition were assessed by self-report indicators of health condition (determined by a standard health-rating item: “In general, how would you rate your health?”), illness (sum of self-reported health problems), sleep problems, subjective physical activity (determined by the item: “In general, how would you rate your physical condition?”), ADL, and loneliness. A detailed description of the assessment protocol (*Protocol of Assessment of Active Aging—P3A*) comprising all instruments used for each of the WHO's active aging model determinants can be found elsewhere (1, 21). **Table 1** presents the variables used and its correspondent coding.

Ethical Procedure

The study was submitted to the ethical commission of UNIFAI/ICBAS-UPORTO. All the participants signed the informed consent form that was developed according the Declaration of Helsinki.

Statistical Analysis

Invariance Analysis Methods

Confirmatory factor analysis (CFA) models of factorial invariance enable one to test explicitly the structure of a model or its individual parameters for equivalence across subgroups or

TABLE 1 | Definition of variables.

Variable	Coding
Subjective health	1 = Very good; 2 = Good; 3 = Reasonable; 4 = Poor; 5 = Very poor
Sleep problems	0 = No; 1 = Yes
Subjective physical activity	1 = Very good; 2 = Good; 3 = Reasonable; 4 = Poor; 5 = Very poor
ADL	0 = With difficulties; 1 = Without difficulties
Illness	0 = None; 1 = 1 illness; 2 = 2 illness; 3 = illness; 4 = 4 or more illness
Psychological distress ^a	1 = <9; 2 = [9,12]; 3 = [12,16]; 4 = ≥16
Happiness	1 = Nothing; 2 = 2; 3 = 3; 4 = Very
Optimism ^a	1 = <11; 2 = [11,13]; 3 = [13,15]; 4 = ≥15
Quality of life ^a	1 = <24; 2 = [24,26]; 3 = [26,29]; 4 = ≥29
Loneliness	0 = Yes; 1 = No
Cognitive impairment ^a	1 = <25; 2 = [25,28]; 3 = [28,30]; 4 = ≥30
Income	1 = ≤386€; 2 = 386–772€; 3 = 772–1158€; 4 = > 1,158€
Education level	1 = No formal; 2 = Primary; 3 = 5–8 years; 4 = 9–12 years; 5 = University
Peak Flow ^a	1 = <180; 2 = [180,250]; 3 = [250,340]; 4 = ≥340
Grip Strength ^a	1 = <18.3; 2 = [18.3,22.9]; 3 = [22.9,29.0]; 4 = ≥29.0
Family ^a	1 = <9; 2 = [9,11]; 3 = [11,13]; 4 = ≥13
Friends ^a	1 = <5; 2 = [5,8]; 3 = [8,10]; 4 = ≥10
Confidants ^a	1 = <4; 2 = [4,7]; 3 = [7,9]; 4 = ≥9
Neuroticism ^a	1 = <30; 2 = [30,34]; 3 = [34,37]; 4 = ≥37
Extraversion ^a	1 = <39; 2 = [39,41]; 3 = [41,44]; 4 = ≥44
Openness to Experience ^a	1 = <35; 2 = [35,37]; 3 = [37,40]; 4 = ≥40

^aQuartiles.

conditions (22). Two primary models were tested: Model 1 was the baseline model with all parameters allowed to vary across groups and resulted in the first chi-square value for comparison with Model 2, which imposed the equality of factor loadings constraint across groups. The difference in the Model 2 and Model 1 chi-squares was used to evaluate overall invariance. Groups were defined regard to age: group 1: <75 years and group 2: ≥75 years. To ensure that statistically significant results were not due to model misfit, a variety of fit indexes were examined, including the chi-square goodness-of-fit test, comparative fit index (CFI), and goodness-of-fit index (GFI).

Exploratory and CFA

In the case of a significant result in the invariance analysis, the factor structure of P3A for the age group 75+ was examined by exploratory factor analysis (EFA) and CFA, using the same methodology as described in the previous work [cf. (1)]. In the EFA, a principal-components extraction with Varimax rotation was used. In the CFA, satisfaction scores for each dimension were obtained using factor score regressions. A nested models approach to test alternatives to the full model was used to obtain the final model. Goodness-of-fit criterion was used to evaluate the model fit.

A significant level of 0.05 was used in all analysis, conducted using SPSS 20 and AMOS 19 for Windows.

TABLE 2 | Sample characteristics (total and subgroups).

	Total (N = 1,321)	≥75 years (N = 427)
	n (%)	n (%)
Gender		
Male	382 (28.9)	129 (30.3)
Female	939 (71.1)	297 (69.7)
Age		
Mean (SD)	70.4 (8.7)	80.3 (4.6)
Marital status		
Married	729 (55.7)	152 (36.1)
Widow(er)	400 (30.6)	206 (48.9)
Single	114 (8.7)	44 (10.5)
Divorced	65 (4.9)	19 (4.5)
Education		
Illiterate	249 (19.1)	122 (29.3)
4 years education	722 (55.3)	239 (57.3)
5–8 years education	80 (6.1)	27 (6.5)
9–12 years education	153 (11.7)	17 (4.1)
High education	101 (7.7)	12 (2.9)

RESULTS

Sample Characteristics

The sample comprised 1,322 persons with an average age of 70.4 years (SD 8.7 years; age range 55–101 years old). Most participants were women (71.1%; n = 939). More than half of the participants were married/partnered (55.7%; n = 729), 30.6% (n = 400) were widowed, 8.7% (n = 114) were single, and 5.0% (n = 65) were divorced. Almost a quarter of the sample (24.7%) lived alone. As for the educational level, 55.3% attended primary school (4 years schooling), 19.1% never attended school, 17.8% had completed high school, and only a minority presented a trade qualification or university degree (7.7%). Almost half of the participants (49.6%) earned per month the equivalent or less than the minimum national wage (around 400 Euros). **Table 2** presents the sample characteristics (total and subgroups).

Multigroup Analysis of Structural Invariance

To test the invariance across age groups, we conducted a multigroup analysis of structural invariance. The Model 1 (baseline model—equal pattern) had CFI and GFI of 0.890 and 0.921, respectively. The respective baseline chi-square was 825.022 with 348 df (**Table 3**). In the Model 2, each item-factor loading was forced to be equal across the two age groups. Model 2 had CFI and GFI of 0.878 and 0.916, respectively. The chi-square for Model 2 is 891.526 with 363 df (**Table 3**). The Model 2 was nested within Model 1 [the set of parameters estimated in the more restrictive model (Model 2) was a subset of the parameters estimated in the less restrictive model (Model 1)]. Thus, the chi-square difference between Model 2 and Model 1 provided a test of the pre-condition for testing the invariance of structural weights. The model appeared not to be invariant across subgroups ($p < 0.001$), suggesting different structure for different age groups. All following analyses were performed only for people with 75 or more years ($N = 269$).

TABLE 3 | Structural invariance analysis.

No.	Model	χ^2	df	p	CFI	GFI	$\Delta\chi^2$	Δdf	p
1	Unconstrained	825.022	348	<0.001	0.890	0.921			
2	Measurement weights	891.526	363	<0.001	0.878	0.916	66.504	15	<0.001

χ^2 , Chi-square test; df, degree of freedom; p, p-value; CFI, comparative fit index; GFI, goodness-of-fit index.

TABLE 4 | Factor Structure of P3A for people aged 75 or more years: exploratory factor analysis.

Questions	Component					
	1	2	3	4	5	6
Psychological distress	-0.540	0.413	-0.221	-0.072	-0.116	0.166
Happiness	0.614	-0.259	0.111	-0.189	0.265	-0.084
Optimism	0.708	-0.069	-0.011	0.037	-0.016	0.095
Neuroticism	-0.664	0.015	-0.157	-0.225	0.143	-0.017
Quality of life	0.649	-0.145	0.219	0.044	-0.002	0.121
Loneliness	0.519	-0.032	0.048	0.180	0.249	-0.303
Subjective health	-0.368	0.702	-0.163	-0.056	-0.063	0.042
Subjective physical condition	-0.255	0.761	-0.071	-0.089	-0.031	-0.055
ADL	-0.034	-0.720	0.215	-0.036	0.026	-0.048
Illness	0.064	0.446	0.222	-0.270	0.065	0.353
Cognitive impairment	0.255	0.030	0.691	0.150	0.102	-0.111
Income	0.056	-0.143	0.711	0.104	0.097	-0.028
Education level	0.137	-0.151	0.804	0.052	-0.097	0.009
Peak flow	0.134	0.006	0.303	0.657	-0.007	0.010
Handgrip	0.102	-0.128	0.064	0.799	0.103	0.005
Social relationship—family	0.025	-0.068	0.105	-0.161	0.782	-0.101
Social relationship—friends	0.070	-0.347	-0.059	0.245	0.294	0.139
Social relationship—confidants	0.044	-0.018	-0.002	0.257	0.687	0.099
Extraversion	0.266	-0.393	-0.111	-0.251	0.063	0.414
Openness to experience	0.005	-0.084	-0.077	0.040	0.107	0.725
Sleep problems	-0.100	0.359	-0.013	0.118	-0.220	0.593
% of variance explained	12.9	12.0	9.6	7.4	6.9	6.6

Bold-italic indicates to show in which factor each item present higher factor loading, without significant level associated.

Exploratory Factor Analysis

The factor structure was examined by principal-components extraction with Varimax rotation for the sub-sample with 75+ years ($n = 269$). The Bartlett Sphericity test ($p < 0.001$) and the Kaiser–Meyer–Olkin (KMO = 0.798) test indicate that factor analysis seemed to be highly adjusted to this analysis. Six distinct factors, presented in **Table 4**, were revealed explaining 55.5% of total variance. The final structure was Factor 1 (psychological component): six variables load heavily of this factor (psychological distress, happiness, optimism, neuroticism, quality of life—environment, and loneliness), which account for 12.9% of the total variance; Factor 2 (health component): this factor comprises four variables (subjective health, subjective physical condition, ADL, and illness) and explained 12.0% of total variance; Factor 3 (cognitive performance): three questions have their highest loadings on this factor (cognitive impairment, income, and education

level) and explained 9.6% of total variance; Factor 4 (biological component): this factor comprises only two variables (peak flow and grip strength) and explained 7.4% of total variance; Factor 5 (social relationship component): three variables have their highest loadings on this factor (family, friends, and confidence), accounting for 6.9% of total variance; and Factor 6 (personality component): the last factor contains only two variables (extraversion and openness to experience) and explained 6.6% of total variance.

When comparing to the six-factor structure model for P3A originally obtained for the pooled sample ($n = 925$) which explained 54.6% of the total variance [cf. (1)], the achieved model for this age group reveals that the “psychological component” is the main factor associated with active aging, followed by “health component,” and that these previously occupied reverse positions (health component was in first place and explained 11.6% of total variance, followed second by the psychological component which explained 11.2% of total variance). All the other factors in the original model maintained a similar order to the current one (cognitive performance explained 10.6% of total variance; biological component explained 7.7% of total variance; social relationships explained 6.6% of total variance; and personality explained 6.6% of total variance).

Confirmatory Factor Analysis

We analyzed the full six-factor model for the 21 variables derived from the EFA (**Table 4**). For the final model, we used a nested models approach to test alternatives to the full model, eliminating of item “sleep problems.” The Confirmatory Factor analyses structure describes adequately the six factors reinforcing the adequacy of the proposed model. The goodness-of-fit indices suggest that the structure can be adequately described by the six correlated factors that are graphically presented in **Figure 1** [$\chi^2(155) = 226.700$, $p < 0.001$; CFI = 0.928 and GFI = 0.924; covariance and error estimates were omitted of the figure]. Although the personality component was not significant, it was decided to keep the same model in order to preserve the original structure of the model.

DISCUSSION

In overall, this study’s main finding points to the prominence of the psychological component in defining active aging in the oldest age group as it adds evidence to the particular value of psychological functioning (namely absence of psychological distress, presence of happiness and optimism, low neuroticism, good quality of life, and low loneliness) in allowing an active involvement with life. The comparison of components between age groups revealed its major relevance on the achieved model for

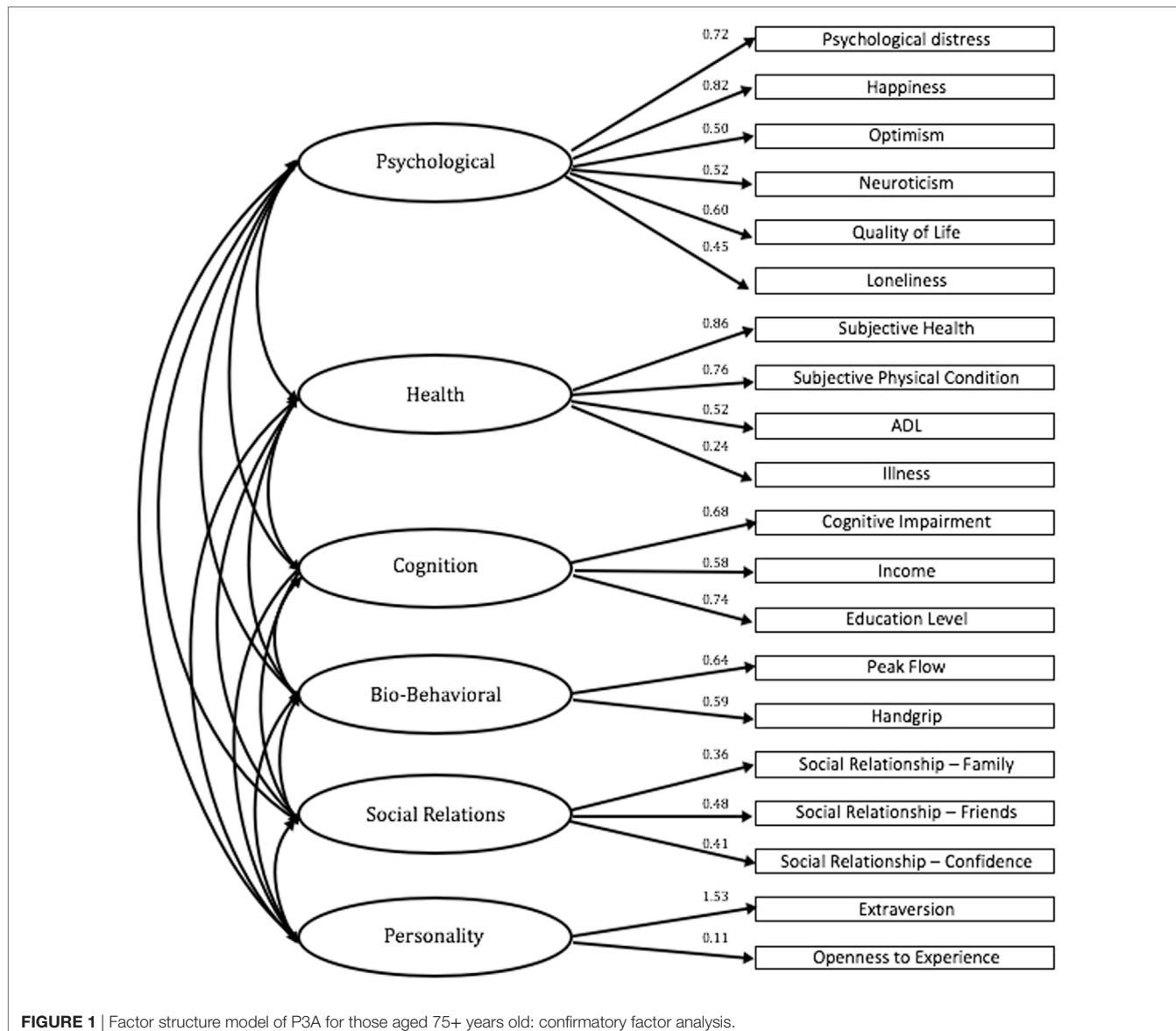


FIGURE 1 | Factor structure model of P3A for those aged 75+ years old: confirmatory factor analysis.

the 75+ group as it now explains 12.9% of total variance, followed by the health component that explains 12% of total variance. In the originally achieved model for the total sample [cf. (1)], the health component occupied first place in the factor structure model for P3A and explained 11.6% of total variance, whereas the psychological component, occupying second place, explained 11.2% of the total variance.

This observed change in the relative load of these two factors reinforces the notion that rather than health problems that most older people face, the differentiating aspect between those individuals who are aging actively from those who do not may be rooted in psychological characteristics and strengths. Traditionally, the majority of definitions of “successful aging” are based on the absence of disability with lesser inclusion of psychological variables (23). However, it is not surprising the relevance of psychological variables later in life and in predicting

quality of life in older adults by maximizing one’s self-efficacy and resilience (24) as they are involved in emotional regulation and related to health by multiple pathways: at physiological level through immune system and at emotional level through experiences and generation of psychological resources and eliciting social support to deal with adversity, and finally at motivation level through health-relevant behaviors (25). Furthermore “the ability to maintain an awareness of our positive emotions in the face of life inevitable difficulties, including challenges to health, may be a hidden key to resilience as we age.” (26).

There is an aging paradox referring to the stability or increase of affective wellbeing across adulthood while, at the same time, cognition or physical health decline (27). In fact, there is a wide consensus that older people are generally more focused on emotional issues and report more positive emotions than the younger ones [e.g., Ref. (27–29)]. This psychological capacity

(e.g., happiness, optimism, quality of life and less distress, neuroticism, or loneliness) may be what makes the difference between those aging actively and those less active, in times when having health-related issues is the norm, more than the exception. Regardless of still being to some extent autonomous while living in the community, old people may gradually lose their adaptation potential. Active aging discourses that pay a strong emphasis on health and independence, or understand the concept in terms of occupation and “youthful activities” should incorporate a more psychological rooted perspective. By acknowledging the important contributions of psychology in the conceptualization of Active Aging (30), the concept can be encapsulated as being “engaged in life” in more advanced ages and potentially incorporate spiritual and philosophical dimensions (31, 32), which are acknowledged to be of particular relevance in very old ages.

The main contributions of the present paper stress the importance of paying particular attention to the oldest group of people (75+) and emphasize the role of psychological variables in the active aging. The “subjective nature” of the concept of active aging has been already acknowledged by several researchers, including Bowling (33) who found that more than a third of respondents in her study rated themselves as aging “very actively,” and almost a half as “fairly actively.” People based their judgment on: having/maintaining physical health and functioning (43%); keeping leisure and social activities (34%) as well as maintaining mental activity (18%), and social relationships (15%). The subjective meaning of the words “active ageing” was: physical activity; autonomy, interest in life, being able to cope with challenges, and stay aware of the world (34). People seem, therefore, to mix physical, mental, and social factors, and the ability of deciding by their own. By questioning the deterministic view of the WHO model, this study puts an emphasis on the need for introducing, a psychosocial perspective, and take into consideration the pro-active attitude that people claim.

In sum, people should stay engaged with society and at the same time adopt a healthy life style to guarantee the best physical condition. However, the key aspect of the active aging model derives from the balance between individual and social responsibility in aging well as both contribute to aging outcomes. Active aging can only be achieved in contexts that are both supportive and “age friendly,” that value individual choices, and that, in

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overall, assure an easy access to a wide-ranging set of services according to specific perceived needs (35).

CONCLUSION

Based on the present data, psychological aspects proved to be of great relevance for active aging, and corroborate previous research that considers mental health balance as an optimist view of life and cognitive capacity [e.g., Ref. (36, 37)]. It is possible to conclude that although being very important, objective and subjective health seem not to be the main aspects of active aging. Health issues are common at advanced ages and psychological status matters to cope with them. Psychological variables may contribute to more positive attitudes toward health and facilitate functionality, balancing objective measures with subjective ones as supported in the literature [e.g., Ref. (1, 24, 33, 34, 38)]. We advocate greater attention to psychological aspects to foster active aging either by intervening in psychological distress or training coping strategies that help people to keep engaged with life despite the presence of health problems. As the ultimate objective of studying and intervening in very old age is to optimize the aging process and quality of life, this association should be explored in future research as (5) suggested by focusing on the individual and examining the contributions of active aging to life satisfaction and the possible predictive value of coping styles to active aging.

ETHICS STATEMENT

The study was submitted to the ethical commission of UNIFAI/ICBAS-UPORTO. All the participants signed the informed consent form that was developed according the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

CP was responsible for the study conception and design; CP and OR supervised data collection; LT performed the data analysis; CP, LT, and OR wrote the manuscript.

ACKNOWLEDGMENTS

This paper draws from a research project supported by the Foundation for Science and Technology (FCT), Portugal (Grant POCTI/PSI/56505/2004).

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Anxiety and Depression in the Portuguese Older Adults: Prevalence and Associated Factors

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OPEN ACCESS

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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 02 August 2017

Accepted: 26 October 2017

Published: 20 November 2017

Citation:

Sousa RD, Rodrigues AM,
Gregório MJ, Branco JC,
Gouveia MJ, Canhão H and Dias SS
(2017) Anxiety and Depression
in the Portuguese Older Adults:
Prevalence and Associated Factors.
Front. Med. 4:196.
doi: 10.3389/fmed.2017.00196

Anxiety and depression in the elderly individuals have been studied around the world, and some authors consider them among the most serious problems faced by modern societies. With recent economic crisis—very important in Southern European countries—isolation, loneliness, and exclusion of the active society, mental problems are probably raising and associated with distinct factors. In this cross-sectional analysis, nested in a longitudinal population-based cohort study, we analyze anxiety and depression prevalence, and their related factors, in a representative cohort of Portuguese seniors. We used data retrieved from second wave of follow-up of EpiDoC Cohort—EpiDoC 2 study, which is composed by 10,661 adults, representative of adult Portuguese population. This study included all ≥ 65 years old EpiDoC 2 study participants, who responded to Hospital Anxiety and Depression Scale (HADS), $n = 1,680$. Sociodemographic, lifestyles, self-reported non-communicable diseases, health-related quality of life (EQ-5D-3D), physical function (HAQ), and health resources consumption data were collected. Anxiety and depression were assessed with HADS. Anxiety and depression prevalence were estimated. Multivariable logistic regression was used to assess anxiety and depression score determinants. The estimated prevalence of anxiety among Portuguese elderly is 9.6% and depression is 11.8%. Seniors with anxiety and seniors with depression have a higher probability to self-report higher levels of physical disability (OR = 3.10; 95% CI 2.12–4.52; OR = 3.08, 95% CI 2.29–4.14, respectively) and lower levels of quality of life (OR = 0.03, 95% CI 0.01–0.09; OR = 0.03, 95% CI 0.01–0.06, respectively). Female gender (OR = 2.77, 95% CI 1.53–5.00), low educational level (OR = 2.30, 95% CI 1.22–4.36), allergic (OR = 2.02, 95% CI 1.14–3.55), and rheumatic disease (OR = 2.92, 95% CI 1.74–4.90) were significantly and independently associated with the presence of anxiety symptoms. Physical inactivity (OR = 1.64, 95% CI 1.11–2.42) and low educational level (OR = 2.40, 95% CI 1.41–4.09) were significantly and independently associated with depression symptoms. Subjects that reported to drink alcohol daily or occasionally were negatively associated with depression symptoms. Anxiety and depression are

frequent among Portuguese elderly. These prevalence rates suggest that preventing mental illness in senior population is a crucial need. A well-designed prevention strategy might have an effective action in raising the well-being of elderly.

Keywords: older, anxiety, depression, non-communicable chronic diseases, lifestyles, quality of life, function

INTRODUCTION

Our world is now old and aging. Aging population is a long-term trend in Portugal, Europe, and around the World. According to United Nations data from 2015, the number of people over 65 has increased considerably in the largest regions of the world, and this aging is expected to accelerate in the coming decades (1). The same data point out that, in 2015, 1 in 8 people in the world were 60 years or older, totaling 901 million elderly people. A 176 million of these elderly people live in Europe.

In Portugal, the number of people over 65 years of age doubled in relation to the 1970s and, by 2015, was already over two million, with the population over 80 years old increasing fivefold. In concrete terms, there were 836,058 people aged 65 and over in Portugal in 1971. In 1977, they surpassed one million and, in 2012, two million. In 2015, they were 2,122,996 (2).

Although the epidemiological investigation has begun to converge regarding the estimation of the prevalence of anxiety and depression in elderly populations, there are still quite a few discrepancies (3). The sampling procedures diverge greatly: some studies use representative samples from the respective country, and others use samples of convenience. In addition, there is considerable instability in age cutoffs considered for the definition of the elderly or older adult. On the other hand, there is much variation in the operationalization of anxiety and depression, partly due to the use of different evaluation instruments. In fact, some authors consider that anxiety and depression are among the most serious problems faced by modern societies is depression among the elderly (4). Although depression is fairly common in the last years of life (5), there is great variation in its prevalence in studies worldwide (9–33%) (6).

Factors associated with aging, such as social isolation, reduced autonomy, financial insecurity, and poor health, cause an increase in the prevalence of these disorders (7).

Some studies point to psychosocial risk factors for anxiety disorders and late-onset depression: female gender, cognitive dysfunction, chronic illness, poor health perception, functional limitations, personality traits such as neuroticism and weak coping strategies (8, 9). Specifically, for anxiety disorder: not having children, low income, and experiencing traumatic events (10).

Given the social and economic context of our country, generating relevant evidence on anxiety and depressive symptoms in the Portuguese elderly population, and understanding them from a point of view that goes beyond the mental illness itself, by approaching the possible associated factors, is crucial. Data on elderly mental health and associated factors could be useful to address therapeutic programs and better planning of health care.

Therefore, to comprehend models of anxiety and depression independently in the Portuguese senior population, this study

aims to: (1) determine the prevalence of anxiety and depression symptoms and (2) identify relevant associations between the symptoms of anxiety and depression and chronic self-reported non-communicable diseases, lifestyles, and sociodemographic characteristics.

MATERIALS AND METHODS

Sample

To analyze the older adult Portuguese population in terms of symptoms of anxiety and depression, their association with non-communicable chronic diseases, function, lifestyles, and quality of life we used data from the second wave of follow-up for EpiDoC Cohort—EpiDoC 2 (CoReumaPt) study—done by computer-assisted telephone interviews (CATIs).

The EpiDoC 2 evaluation consisted on a structured questionnaire, applied through phone call interviews to 10,153 eligible participants of EpiDoC 1 (EpiReumaPt) (11–13), a large population-based sample, who consented to be contacted again for follow-up. The study population comprised adults (≥ 18 years old) living in the community, in Portugal Mainland and Islands (Azores and Madeira). Exclusion criteria were as follows: being resident in institutions and individuals unable to speak Portuguese or to complete the assessment protocol. Participants were selected through a process of multistage random sampling. The sample was stratified by region and population size.

EpiDoC 2 (CoReumaPt) included 7,591 participants, representative of the adult Portuguese population. This study included 1,680 seniors (65 and more years old) of the EpiDoC 2 study, who responded to Hospital Anxiety and Depression Scale (HADS) (Figure 1).

Data Collection

Data collection was performed from March 26th 2013 to July 27th 2015. A trained research assistants' team was responsible for collecting the follow-up data from these subjects, by randomly call all the individuals. When a contact was not available, they would hold more attempts in different moments (morning, afternoon, evening, and weekends) to perform six attempts. The last contact had to have at least 1 month of interval from the previous one. Only then the contact would be abandoned. Rescheduling of the telephonic interviews to a more convenient moment was also an option. The interview was telephonically performed with the assistance of a CATI system.

Data were collected in a standardized form, and database access was protected by unique username and password, for each research team member, according to Portuguese Law of data collection (14).

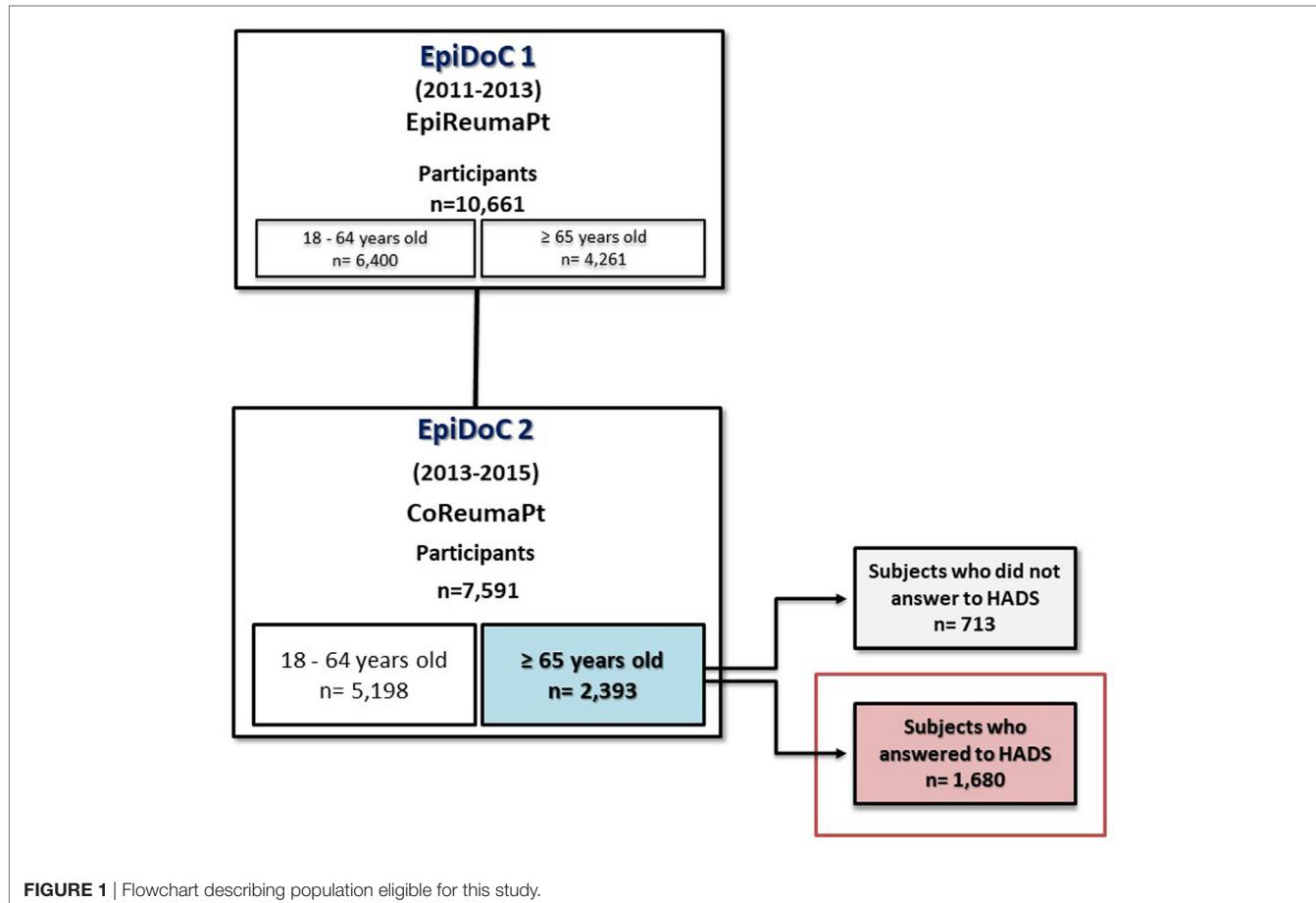


FIGURE 1 | Flowchart describing population eligible for this study.

Measurements, Assessment, and Instruments

Case Definition

To evaluate symptoms of anxiety and depression in EpiDoC 2 study, the HADS Portuguese validated version was applied (15). The HADS was originally developed by Zigmond and Snaith (16) as a screening tool to apprehend clinically significant states of anxiety and depression in a non-psychiatric hospital setting. Individual anxiety and depression scores were calculated by summation of the appropriate seven items and thus can range from 0 to 21, with higher scores indicating higher levels of anxiety or depression, respectively. In both subscales, a score between 0 and 7 is “normal,” between 8 and 10 “mild,” between 11 and 14 “moderate,” and between 15 and 21 “severe” (idem). Presence of anxiety and depression symptoms was defined when HADS scale was ≥ 11 , since Snaith suggested a score ≥ 11 was indicative of “caseness” to a mood disorder (17). We also used the HADS scale as a continuous outcome in the final analyses.

Sociodemographic and Socioeconomic Characteristics

Information on sociodemographic (sex, age, years of education, household composition, and NUT II), as well as socioeconomic variables (household income), was collected in the first

wave—EpiDoC 1 study. Subjects were asked in the EpiDoC 2 study interview whether there have been changes.

Health Characteristics

In EpiDoC 1 study, individuals were asked if they had been previously diagnosed with some chronic disease (high cholesterol level, high blood pressure, rheumatic disease, allergy, gastrointestinal disease, cardiac disease, diabetes, thyroid and parathyroid disease, urolithiasis, pulmonary disease, hyperuricemia, cancer, neurologic disease, and hypogonadism), and this information was updated in the EpiDoC 2 study interview.

Self-reported height and weight were collected in EpiDoC 2. Based on these data, body mass index (BMI, weight/height², in kg/m²) was calculated and categorized according to the World Health Organization classification in four categories: underweight (BMI < 18.5 kg/m²), normal (BMI between 18.5 and 24.9 kg/m²), overweight (BMI between 25 and 29.9 kg/m²), and obesity (BMI ≥ 30 kg/m²) (18).

Health-related quality of life was assessed using the Portuguese validated version of European Quality of Life questionnaire (EQ-5D-3L) (19, 20).

Function was evaluated based on the Portuguese version of Health Assessment Questionnaire (HAQ) (21, 22).

To assess health-care resources consumption, “number of medical appointments in the previous 12 months” and

"hospitalization in the previous 12 months (yes/no)" was asked to participants.

Lifestyle Characteristics

In EpiDoC 2 study, questions concerning lifestyle habits included frequency of alcohol intake (daily, occasionally, and never), smoking habits (current smoker, past smoker, and never smoked), sleep habits (number of hours of sleep per day, categorized in <6 and ≥6 h/day). Physical activity level was classified based on the question related to the reported weekly frequency of physical activity. A frequency of once a week or more was considered "yes" to regular physical exercise.

Statistical Analysis

Sample Weights

EpiDoC was designed to obtain a representative sample of the Portuguese population (13). To guarantee its representativeness, weighted proportions have, for this matter, been computed and are described elsewhere (13).

To maintain the representativeness of the sample in relation to the Portuguese population (Mainland and Islands) in the second wave, extrapolation weights were again computed and used in further statistical analysis. These were obtained by calibrating the extrapolation weights originally designed for the EpiDoC 1 study sample. We first compared the participants and non-participants of EpiDoC 2 study, concerning their sociodemographic, socio-economic and rheumatic disease screening, and health status characteristics. Then, we decided to adjust weights based on the stratification by seven NUTII regions [Norte, Centro, Lisboa, Alentejo, Algarve, and islands (Azores and Madeira)], gender (male and female), age categories (18–35, 36–55, 56–65, ≥8–35, 36–55 years old for NUTII Norte, Centro, and Lisboa; 18–65, 66+ for NUTII Alentejo, Algarve, and islands), and rheumatic disease screening (positive/negative).

Analysis and Statistical Software

Descriptive data for each categorical variable were presented as the absolute frequency and the correspondent proportion, weighted. The same adjustment has been done for the mean and SD for each continuous variable. Continuous variables were compared using Student's *t*-test or ANOVA, and nominal variables were compared using chi-square test.

To assess the determinants of anxiety and depression symptoms, we first performed univariate analysis to approach relations between independent variables (non-communicable chronic diseases, lifestyles, and sociodemographic characteristics) and outcomes (presence of anxiety and depression symptoms). When univariate analyses resulted in *p*-value < 0.1, those variables were included into the multivariable logistic regression models. Multivariable models were constructed using a forward selection method. The following independent variables were tested: age, gender, NUTS II, education level (0–4 vs ≥5 years), BMI (underweight, normal, overweight, and obese), alcohol intake (never, daily, and occasionally), current smoking, physical activity (yes/no), and chronic non-communicable diseases—high blood pressure, diabetes, high cholesterol level, pulmonary disease, cardiac

disease, neurologic disease, allergies, neoplastic disease, thyroid disease, hyperuricemia, and rheumatic disease. Age, gender, and NUTS II were forced to stay in the model. The goodness of fit of the final multivariable regression model for the outcome anxiety has *p* = 0.287, and the goodness of fit of the final multivariable regression model for the outcome depression has *p* = 0.4.

Significance level was set at 0.05. All analyses were weighted and executed using STATA IC version 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX, USA: StataCorp LP).

Ethical Issues and Data Protection

EpiDoC 1 study was performed following the principles established by the Declaration of Helsinki (23) and revised in 2013 in Fortaleza. The study was reviewed and approved by the National Committee for Data Protection (Comissão Nacional de Proteção de Dados) and by the NOVA Medical School Ethics Committee. The participants provided informed consent to contribute in all phases of the study.

The EpiDoC 2 study was also approved by National Committee for Data Protection (in accordance with the Portuguese law number 67/98, October 26th, regarding protection of personal data) and was submitted to the same Ethics Committee. The study was conducted in accordance with the applicable laws and regulations including, but not limited to, the Guideline for Good Clinical Practice and the ethical principles stated in the Declaration of Helsinki (23).

Participants' confidentiality is safeguarded by the nonexistence of identifiers on the database (only unique ID participants' codes). Their names and contacts are stored separately from study data transmitted to the coordinating center. Thus, all data are kept anonymously and securely by the EpiDoC 2 study authorized staff. During EpiDoC 1 study, informed consent was also signed by those accepting to participate in the EpiDoC 2 study. There will be absolutely no disclosure of individual health information to the general public.

RESULTS

Our population of interest included 1,680 participants over 64 years old, 908 (54%) of those were females. Forty four percent were 75 years old or more. With respect to educational level, almost two-thirds of participants (*n* = 1,259; 76.03%) had less or equal to 4 years of education.

Most people with 65 years of age and more reported to live on a household income of less than 1,000€ per month; 35.8% reported the lowest income level of 500€/month. Moreover, elderly tend to live in households composed by only one (25.53%) or two persons (55.89%).

With respect to health-related characteristics, the observed mean number of non-communicable chronic diseases was 3.10 (± 2.1). The most frequently reported chronic diseases were high blood pressure (57.3%), rheumatic diseases (50.53%), and high cholesterol level (49.7%).

People 65+ years old score EQ-5D-3L on average 0.61 (± 0.77) for quality of life and 0.72 (± 0.72) in HAQ for physical function.

The high consumption of health care resources by the older age group matches the health status. The average number of appointments was 7.74 (± 8.40), and 24.16% was hospitalized in the last 12 months.

Regarding lifestyle habits, namely, in terms of alcohol intake and smoking habits, 36.43% of the individuals had reported a daily intake of alcohol beverages but only 5.39% were current smokers. Among the elderly, 43.65% of the subjects never consume alcohol and 66.35% of people aged 65 and above never smoked. Almost 60% of individuals above 65 years old do not engage in regular physical exercise, and around 70% of the Portuguese elderly sleep 6 or more hours per day.

Prevalence of Anxiety and Depression Symptoms in the Elderly

This study found 176 elderly out of 1,680 (10.48%) presenting anxiety symptoms (HADS-A ≥ 11), corresponding to a prevalence of 9.59% when weighted to Portuguese elderly population (**Table 1**). The mean score for HADS-A was 5.04 (± 3.74).

In terms of depression symptoms, figures rise to 241 (14.34% in the present sample), equivalent to a prevalence of 11.77% of the Portuguese elderly population (**Table 1**). This population had a mean score for HADS-D of 5.27 (± 4.07).

Sociodemographic, socioeconomic, lifestyle, and health-related characteristics of the Portuguese elderly population with and without anxiety symptoms are summarized in **Table 2**.

Table 3 summarizes sociodemographic, socioeconomic, lifestyle, and health-related seven characteristics of the Portuguese elderly population with and without depression symptoms.

Anxiety and Depression Symptoms and Physical Function in Seniors

Seniors with anxiety have a higher probability to have reported, even after the adjustment for sex, age, region, and number of non-communicable diseases, higher levels of physical disability (OR = 3.10; 96% CI 2.12–4.52).

Similar results were found for depression symptoms and seniors with depression have reported higher levels of physical disability (OR = 3.08, 95% CI 2.29–4.14).

TABLE 1 | Prevalence of anxiety and depression in the Portuguese senior population by age group.

	Elderly with anxiety symptoms (HADS-A ≥ 11)	Elderly with depression symptoms (HADS-D ≥ 11)
	n (%)	n (%)
Total	176 (9.59)	241 (11.77)
Age group		
65–69 y.o.	52 (12.38)	44 (7.29)
70–74 y.o.	45 (7.86)	65 (11.33)
75–79 y.o.	47 (8.99)	68 (15.16)
80–84 y.o.	20 (7.96)	42 (14.85)
≥ 85 y.o.	12 (9.56)	22 (1.68)

%, weighted percentage; HADS-A, Hospital Anxiety and Depression Scale—Anxiety subscale; HADS-D, Hospital Anxiety and Depression Scale—Depression subscale; y.o., year old.

Anxiety and Depression Symptoms and Quality of Life in the Elderly

In terms of quality of life (EQ-5D-3L score), seniors with anxiety have a higher probability to report lower levels of quality of life (OR = 0.03, 95% CI 0.01–0.09). These results were found after the adjustment for sex, age, region, and number of non-communicable diseases.

Multivariable analyses adjusting to sex, age, region, and number of non-communicable diseases also showed that seniors with depression symptoms have a higher probability to have reported lower levels of quality of life (OR = 0.03; 95% CI 0.01–0.06).

Anxiety and Depression Symptoms and Health-care Resources Consumption in the Elderly

Logistic regression adjusted to sex, age, region, and number of non-communicable diseases stressed that seniors with anxiety symptoms have a higher probability to have reported higher number of hospitalizations in the previous 12 months (OR = 2.53, 95% CI 1.37–4.67) and have reported a higher number of medical appointments in the previous 12 months.

Seniors with depression symptoms have also a higher probability to have reported higher number of hospitalizations in the previous 12 months (OR = 1.55, 95% CI 1.01–2.35). In terms of number of medical appointments in the previous 12 months, there is no significant difference between elderly with and without depressive symptoms.

Sociodemographic, Lifestyles, and Health Factors Independently Associated with Anxiety in Seniors

Multivariable logistic regression, including all previous significant independent variables, showed that being a woman (OR = 2.77, 95% CI 1.53–5.00) and have a low educational level (OR = 2.30, 95% CI 1.22–4.36) were significantly associated with anxiety symptoms. Regarding self-reported non-communicable chronic diseases, our results showed that only allergies (OR = 2.02, 95% CI 1.14–3.55) and rheumatic disease (OR = 2.92, 95% CI 1.74–4.90) were statistically significant associated with anxiety symptoms (**Table 4**).

Sociodemographic, Lifestyles, and Health Factors Independently Associated with Depression in Seniors

All previous significant independent variables were included in a multivariable logistic regression to depression symptoms. In this analysis, low educational level (OR = 2.40, 95% CI 1.41–4.09), physical inactivity (OR = 1.64, 95% CI 1.11–2.42), and alcohol intake on a daily (OR = 0.54, 95% CI 0.35–0.83) and occasionally basis (OR = 0.49, 95% CI 0.29–0.84) were protectors of depression (were associated with low risk of depression symptoms) (**Table 5**).

TABLE 2 | Sociodemographic, socioeconomic, lifestyle, and health-related characteristics of the Portuguese elderly population with and without anxiety symptoms.

Sociodemographic and socioeconomic characteristics	Elderly without anxiety symptoms (HADS-A <11)		Elderly with anxiety symptoms (HADS-A ≥11)		p-Value	Adjusted p-value		
	Mean (SD) or n (%)		Mean (SD) or n (%)					
	n = 1,504 (90.41%)	n = 176 (9.59%)						
Age* (years)								
Sex*	Female	74.24 (6.60)	73.96 (6.91)	0.059	0.131			
	Male	768 (83.85)	140 (15.15)	<0.001 [†]	<0.001 [†]			
NUTS II*	Norte	736 (95.44)	36 (4.56)					
	Centro	476 (89.88)	67 (10.12)	0.906	0.977			
	Lisboa e Vale do Tejo	378 (89.93)	49 (10.07)					
	Alentejo	291 (90.56)	23 (9.44)					
	Algarve	95 (92.11)	11 (7.89)					
	Região Autónoma dos Açores	57 (93.14)	3 (6.86)					
	Região Autónoma da Madeira	80 (93.04)	7 (6.96)					
Education level*	≤4 years of education	127 (91.03)	16 (8.97)					
	>4 years of education	1,103 (88.55)	156 (11.45)	0.001 [†]	0.002 [†]			
Household income* (€)	≤500	377 (95.98)	20 (4.02)					
	501–750	384 (89.15)	58 (10.85)	0.430	0.411			
	751–1,000	301 (91.75)	31 (8.25)					
	>1,000	152 (88.38)	16 (11.62)					
Household composition	1	275 (94.52)	16 (5.48)					
	≥2	374 (88.89)	55 (11.11)	0.388	0.900			
	1,130 (90.90)	121 (9.10)						
Anthropometric data*								
BMI	Underweight	9 (84.23)	2 (15.77)	0.806	0.723			
	Normal	397 (91.5)	47 (8.5)					
	Overweight	647 (90.2)	59 (9.8)					
	Obese	297 (91.32)	40 (8.68)					
Lifestyle characteristics								
Alcohol intake*	Never	630 (86.3)	102 (13.7)	0.002 [†]	0.054			
	Daily intake	571 (94.7)	40 (5.5)					
	Occasionally	300 (90.6)	34 (9.4)					
Smoke*	Never	300 (89.5)	145 (10.5)	0.480	0.344			
	Past	449 (91.2)	25 (8.8)					
	Present	85 (95.5)	6 (4.5)					
No regular physical exercise*		873 (91.0)	109 (9.0)	0.590	0.482			
Sleep habits (h)	<6	250 (87.7)	38 (12.3)	<0.001 [†]	0.003 [†]			
	≥6	586 (95.9)	31 (4.1)					
Quality of life and physical function**								
EQ5D (0–1)		0.66 ± 0.01	0.31 ± 0.02	<0.001 [†]	<0.001 [†]			
HAQ score (0–3)		0.63 ± 0.03	1.4 ± 0.06	<0.001 [†]	<0.001 [†]			
Number of non-communicable diseases*		2.92 ± 1.95	4.76 ± 2.33	<0.001 [†]	<0.001 [†]			
High blood pressure (Y/N)		825 (87.8)	128 (12.2)	0.011 [†]	0.021 [†]			
Diabetes (Y/N)		341 (90.8)	47 (9.2)	0.808	0.874			
High cholesterol level (Y/N)		712 (89.3)	105 (10.8)	0.489	0.908			
Pulmonary disease (Y/N)		154 (82.6)	35 (17.4)	0.080	0.028 [†]			
Cardiac disease (Y/N)		370 (87.6)	67 (12.4)	0.127	0.104			
Gastrointestinal diseases (Y/N)		380 (86.4)	72 (13.6)	0.037 [†]	0.121			
Neurologic diseases (Y/N)		106 (84.1)	22 (15.9)	0.080	0.256			
Allergies (Y/N)		313 (83.0)	57 (17.0)	0.011 [†]	0.015 [†]			
Neoplastic disease (Y/N)		128 (91.2)	15 (8.8)	0.732	0.600			
Thyroid disease (Y/N)		156 (80.9)	41 (19.1)	<0.001 [†]	0.085			
Hyperuricemia (Y/N)		193 (89.1)	27 (10.9)	0.655	0.194			
Rheumatic disease (Y/N)		685 (84.0)	125 (16.0)	<0.001 [†]	<0.001 [†]			
Health resources consumption**								
Was hospitalized since last contact		343 (85.0)	60 (15.1)	0.016 [†]	0.003 [†]			
Went to medical appointments in hospitals since last contact		7.79 ± 0.36	13.9 ± 4.4	0.150	0.043 [†]			

%, weighted percentage; NUTS II, Nomenclatura das Unidades Territoriais, level II; BMI, body mass index (kg/m^2); €, euro; HADS-A, Hospital Anxiety and Depression Scale—Anxiety subscale; HAQ, Health Assessment Questionnaire (0–3); EQ5D, European Quality of Life questionnaire five dimensions three levels (0–1).

[†]p-Value ≤ 0.05.

*p-Value was adjusted for age, sex, and region.

**p-Value was adjusted for age, sex, region, and number of non-communicable diseases.

TABLE 3 | Sociodemographic, socioeconomic, lifestyle, and health-related characteristics of the Portuguese elderly population with and without depression symptoms.

Sociodemographic and socioeconomic characteristics	Elderly without depression symptoms (HADS-D <11)		Elderly with depression symptoms (HADS-D ≥11)		p-Value	Adjusted p-value		
	Mean (SD) or n (%)		Mean (SD) or n (%)					
	n = 1,439 (88.23%)	n = 241 (11.77%)						
Age* (years)								
Sex*	Female	73.57 (6.51)	75.74 (7.23)	<0.001 [†]	0.001 [†]			
	Male	747 (84.47)	161 (15.53)	<0.001 [†]	<0.001 [†]			
NUTS II*	Norte	692 (91.64)	80 (8.36)					
	Centro	463 (87.84)	80 (12.16)	0.020 [†]	0.084			
	Lisboa e Vale do Tejo	360 (85.41)	67 (14.59)					
	Alentejo	281 (93.63)	33 (6.37)					
	Algarve	89 (87.2)	17 (12.8)					
	Região Autónoma dos Açores	50 (86.89)	10 (13.11)					
	Região Autónoma da Madeira	76 (87.77)	11 (12.23)					
Education level*	≤4 years of education	120 (85.62)	23 (14.38)					
	>4 years of education	1,046 (65.37)	213 (34.63)	<0.001 [†]	<0.001 [†]			
Household income* (€)	≤500	373 (76.84)	24 (23.16)					
	501–750	342 (80.53)	100 (19.47)	<0.001 [†]	0.007 [†]			
	751–1,000	291 (88.06)	41 (11.94)					
	>1,000	154 (96.26)	14 (3.74)					
Household composition	1	271 (93.22)	20 (6.78)					
	≥2	347 (84.05)	82 (15.95)	0.009 [†]	0.161			
Anthropometric data*								
BMI	Underweight	1,092 (89.58)	159 (10.42)					
	Normal	9 (74.53)	2 (24.47)	0.293	0.245			
	Overweight	388 (89.99)	56 (10.01)					
	Obese	620 (89.98)	86 (10.02)					
		284 (86.98)	53 (13.02)					
Lifestyle characteristics								
Alcohol intake*	Never	579 (83.2)	153 (16.8)	<0.001 [†]	0.001 [†]			
	Daily intake	553 (91.7)	58 (8.3)					
	Occasionally	304 (92.1)	30 (7.9)					
Smoke*	Never	304 (92.1)	926 (85.8)	0.001 [†]	0.154			
	Past	434 (93.0)	40 (7.0)					
	Present	78 (90.2)	13 (9.8)					
No regular physical exercise*		807 (85.0)	175 (15.0)	<0.001 [†]	0.001			
Sleep habits (h)	<6	241 (86.1)	47 (13.9)	0.008 [†]	0.048 [†]			
	≥6	528 (92.1)	59 (7.9)					
Quality of life and physical function**								
EQ5D (0–1)		0.67 ± 0.02	0.32 ± 0.02	<0.001 [†]	<0.001 [†]			
HAQ score (0–3)		0.61 ± 0.03	1.38 ± 0.59	<0.001 [†]	<0.001 [†]			
Number of non-communicable diseases		2.95 ± 1.93	4.36 ± 2.70	<0.001 [†]	<0.001 [†]			
High blood pressure (Y/N)*		804 (87.2)	149 (12.76)	0.093	0.121			
Diabetes (Y/N)*		315 (84.8)	73 (15.2)	0.039 [†]	0.022 [†]			
High cholesterol level (Y/N)*		688 (86.0)	129 (14.0)	0.013 [†]	0.056			
Pulmonary disease (Y/N)*		150 (82.9)	39 (17.1)	0.023 [†]	0.038 [†]			
Cardiac disease (Y/N)*		347 (83.6)	90 (16.5)	0.001 [†]	0.015 [†]			
Gastrointestinal diseases (Y/N)*		367 (63.6)	85 (36.4)	0.019 [†]	0.019 [†]			
Neurologic diseases (Y/N)*		102 (80.5)	26 (19.5)	0.028 [†]	0.009 [†]			
Allergies (Y/N)		312 (87.9)	58 (12.1)	0.074	0.970			
Neoplastic disease (Y/N)*		122 (87.3)	21 (12.7)	0.686	0.676			
Thyroid disease (Y/N)*		157 (80.6)	40 (19.4)	0.001 [†]	0.061			
Hyperuricemia (Y/N)*		181 (83.2)	39 (16.8)	0.010 [†]	0.009 [†]			
Rheumatic disease (Y/N)*		649 (82.9)	161 (17.1)	<0.001 [†]	<0.001 [†]			
Health resources consumption**								
Was hospitalized since last contact		334 (86.6)	69 (13.4)	0.226	0.043 [†]			
Went to medical appointments in hospitals since last contact		8,170 ± 0.634	8,961 ± 1.092	0.455	0.376			

%, weighted percentage; NUTS II, Nomenclatura das Unidades Territoriais, level II; BMI, body mass index; €, euro; HADS-D, Hospital Anxiety and Depression Scale—Depression subscale; HAQ, Health Assessment Questionnaire (0–3); EQ5D, European Quality of Life questionnaire five dimensions three levels (0–1).

[†]p-Value ≤ 0.05.

*p-Value was adjusted for age, sex, and region.

**p-Value was adjusted for age, sex, region, and number of non-communicable diseases.

TABLE 4 | Factors associated with anxiety symptoms in seniors.

	Anxiety symptoms (yes/no)					
	Univariable logistic regression			Multivariable logistic regression		
	OR	95% CI	p-Value	OR	95% CI	p-Value
Gender						
Male	Ref.					
Female	3.74	2.12–6.62	0.000	2.77	1.53–5.00	0.001
Age (years)	0.98	0.94–1.02	0.371	0.96	0.92–1.00	0.078
NUTS II						
Norte	Ref.			Ref.		
Centro	0.99	0.63–1.57	0.982	0.98	0.60–1.60	0.939
Lisboa	0.92	0.29–3.00	0.897	0.97	0.37–2.54	0.949
Alentejo	0.76	0.37–1.57	0.462	0.79	0.36–1.73	0.553
Algarve	0.65	0.18–2.42	0.525	0.93	0.23–3.78	0.918
Azores	0.66	0.28–1.58	0.356	1.14	0.41–3.18	0.796
Madeira	0.87	0.46–1.66	0.683	0.91	0.48–1.75	0.785
Live alone (Y/N)	1.25	0.75–2.07	0.389			
Level of education						
≤4 years	3.09	1.72–5.54	0.000	2.30	1.22–4.36	0.010
>4 years	Ref.					
BMI						
Underweight	Ref.					
Normal	0.50	0.10–2.45	0.390			
Overweight	0.58	0.11–3.05	0.521			
Obese	0.51	0.10–2.52	0.407			
Alcohol intake						
Never	Ref.					
Daily intake	0.35	0.20–0.62	<0.001			
Occasionally	0.65	0.33–1.30	0.224			
Smoke						
Never	Ref.					
Past	0.82	0.33–2.06	0.680			
Present	0.40	0.15–1.06	0.066			
No regular physical exercise	0.85	0.48–1.53	0.590			
High blood pressure (Y/N)	2.03	1.18–3.50	0.011			
Diabetes (Y/N)	0.94	0.56–1.58	0.808			
High cholesterol level (Y/N)	1.23	0.69–2.20	0.489			
Pulmonary disease (Y/N)	1.64	0.94–2.85	0.080			
Cardiac disease (Y/N)	1.50	0.89–2.52	0.127			
Gastrointestinal diseases (Y/N)	1.80	1.03–3.13	0.039			
Neurologic diseases (Y/N)	1.85	0.93–3.67	0.080			
Allergies (Y/N)	2.43	1.23–4.79	0.011	2.02	1.14–3.55	0.015
Neoplastic disease (Y/N)	0.89	0.46–1.72	0.732			
Thyroid disease (Y/N)	2.51	1.50–4.20	<0.001			
Hyperuricemia (Y/N)	1.13	0.65–1.98	0.655			
Rheumatic disease (Y/N)	4.36	2.65–7.16	<0.001	2.92	1.74–4.90	<0.001

HADS-A, Hospital Anxiety and Depression Scale—Anxiety subscale; OR, odds ratio; CI, confidence interval; HAQ, Health Assessment Questionnaire (0–3); EQ5D, European Quality of Life questionnaire five dimensions three levels (0–1); BMI, body mass index.

*p-Value ≤ 0.05; GoF ($p = 0.287$).

DISCUSSION

This study showed a prevalence of 9.6% of anxiety symptoms among the Portuguese with 65 or more years old. This number is lower than the ones found in international studies over Australia, European, and American countries (24). These authors referred prevalence of significant anxiety symptoms between 15 and 52% in the elderly living in the community. Almost 10 years ago, an epidemiological study in Portugal, whose data were collected between 2008 and 2009, found the prevalence of generalized anxiety disorder in people over 65 years of age at 2.6% and the prevalence of any anxiety disorders 20% for the same age group (25).

Regarding depression, the estimated prevalence is of 11.8% for the Portuguese elderly living in the community, in line with the result of 12% for Major Depressive Disorder of the National Epidemiologic Study of Mental Health (25). In the Netherlands, however, depressive symptoms had a prevalence of 24% for older adults—55 years old and older (26), and Castro-Costa et al. exposed a prevalence of depressive symptoms ranging from 33% in France, Italy, and Spain, to 18–19%, in Sweden, Denmark, Netherlands, Germany, Austria, and Switzerland in adults over 50 years old (6).

Although the presented figures may suggest that Portuguese elderly are less anxious and depressed than other peoples

TABLE 5 | Factors associated with depression symptoms in seniors.

	Depression symptoms (yes/no)					
	Univariable logistic regression			Multivariable logistic regression		
	OR	95% CI	p-Value	OR	95% CI	p-Value
Gender						
Male	Ref.					
Female	2.02	1.42–2.85	<0.001	1.30	0.87–1.94	0.207
Age	1.05	1.02–1.07	<0.001	1.02	1.00–1.05	0.064
NUTS II						
Norte	Ref.					
Centro	1.23	0.84–1.82	0.289	1.11	0.73–1.70	0.607
Lisboa	0.49	0.29–0.84	0.009	0.51	0.28–0.96	0.037
Alentejo	1.06	0.58–1.94	0.849	1.18	0.64–2.18	0.603
Algarve	1.09	0.49–2.44	0.834	0.25	0.55–2.83	0.590
Azores	1.01	0.49–2.04	0.985	0.56	0.75–3.26	0.237
Madeira	1.21	0.70–2.11	0.492	1.20	0.66–2.18	0.547
Live alone (Y/N)	1.63	1.13–2.35	0.009			
Level of education (years)						
≤4	3.57	2.16–5.92	<0.001	2.40	1.41–4.09	0.001
>4	Ref.					
BMI						
Underweight	Ref.					
Normal	0.32	0.06–1.74	0.189			
Overweight	0.33	0.06–1.72	0.186			
Obese	0.44	0.08–2.30	0.334			
Alcohol intake						
Never	Ref.					
Daily intake	0.45	0.30–0.66	<0.001	0.54	0.35–0.83	0.005
Occasionally	0.42	0.26–0.70	0.001	0.49	0.29–0.84	0.009
Smoke						
Never	Ref.					
Past	0.46	0.30–0.70	<0.001			
Present	0.66	0.30–1.44	0.300			
No regular physical exercise	2.07	1.44–2.98	<0.001	1.64	1.11–2.42	0.013
High blood pressure (Y/N)	1.35	0.95–1.92	0.094			
Diabetes (Y/N)	1.50	1.02–2.21	0.040			
High cholesterol level (Y/N)	1.53	1.09–2.14	0.014			
Pulmonary disease (Y/N)	1.71	1.07–2.73	0.024			
Cardiac disease (Y/N)	1.83	1.27–2.64	0.001			
Gastrointestinal diseases (Y/N)	1.56	1.07–2.27	0.020			
Neurologic diseases (Y/N)	1.97	1.06–3.63	0.031			
Allergies (Y/N)	1.07	0.72–1.57	0.741			
Neoplastic disease (Y/N)	1.12	0.65–1.94	0.686			
Thyroid disease (Y/N)	2.01	1.31–3.08	0.001			
Hyperuricemia (Y/N)	1.74	1.14–2.65	0.011			
Rheumatic disease (Y/N)	2.94	2.04–4.23	<0.001	2.12	1.45–3.09	<0.001

HADS-D, Hospital Anxiety and Depression Scale-Depression subscale; OR, odds ratio; CI, confidence interval; HAQ, Health Assessment Questionnaire (0–3); EQ5D, European Quality of Life questionnaire five dimensions, three levels (0–1); BMI, body mass index.

Household composition: number of people that live in the house of the participant, including himself/herself.

^ap-Value ≤ 0.05; GoF (p = 0.04056).

in Europe and around the globe, one should be very careful when comparing these numbers. There are core discrepancies regarding methods of data collection, different instruments of assessing depression and anxiety, different nosological entities considered (major depression disorder, minor depression disorder, generalized anxiety disorder vs symptoms of depression and anxiety), and finally different age groups cutoffs (≥ 50 and ≥ 55 vs ≥ 65).

As Byrne stressed differences in anxiety prevalence rates may be due to differences among populations, but also to differences in assessment tools and algorithms used for diagnosis such as

State Trait Anxiety Inventory and Anxiety Disorder Scale (27). Some studies use the hierarchical approach to diagnosis, which may lead to lower prevalence by excluding individuals with diagnostic criteria that also have criteria for diagnosing other higher disorders in the hierarchy (3).

Our study demonstrates a close relationship between physical function and anxiety and depression showing that seniors with lower physical function are more likely to report anxiety and/or depression symptoms. Lenze and collaborators performed a literature review on the association of late life depression and anxiety with physical disability. Their findings indicated that depression

was a risk factor for disability, but also in the other way, being disability a risk factor for depression (28). Brenes and colleagues studied the influence of anxiety on the progression of physical disability in a community-based observational work, concluding that, after adjusting for confounders, anxiety continued to predict the development of disability in activities of daily living (29).

In terms of quality of life, our results suggest that seniors with anxiety and/or depression are more likely to have reported lower levels of quality of life. Sivertsen and colleagues, in their review article of 74 studies, concluded the same, demonstrating that depressed older people had poor global quality of life than non-depressed individuals. They added that this association was stable over time and independently of how quality of life was measured (30). Brenes also considered anxiety in relation to quality of life, and her conclusions were similar: anxiety was significantly associated with all domains of quality of life, and as severity of anxiety symptoms increased, quality of life decreased (31). Having very low income was also related to higher depression. This is in line with what Valvanne and collaborators defended in their elderly population-based study in Finland (32). McCall and colleagues findings in USA also corroborated the conclusions that related low income to higher scores of depression (33).

To assess determinants for anxiety and depression, a multivariable logistic regression, using socioeconomic factors and chronic diseases was developed.

The results considering the outcome as a binary variable "Anxiety disorders (Yes/No)" showed that being a woman, having less than 5 years of education, having a rheumatic disease and allergies were factors highly associated to higher scores of the anxiety diagnosis in Portuguese elders. Beekman and colleagues had already pointed sex and education level out as relevant to understand anxiety in their study with LASA cohort data (34).

Although other studies found a significant higher rate of anxiety in women with 55 or more years old (35), this was not found in our population.

A global model using multivariable logistic regression was also used to capture the framework of factors related to depression in Portuguese elderly, level of education, physical inactivity, alcohol intake on a daily and occasionally basis, and rheumatic disease should be taken into account when considering depression in this population.

This is in line with the literature supporting that physical activity is associated with lower levels of depression (36). Also, several studies suggest that lower education is associated with depression (37–39).

Regarding alcohol intake, the results found denote that the daily or occasional consumption of alcoholic beverages decreases the probability of reporting depression among seniors. Although this result can be unsettling at first glance, it is important to retain that this study assessed consumption frequency, rather than type or quantity. In the literature, several studies associate alcohol misuse or alcoholism with higher levels of depression (40, 41). That is, however, a different matter.

Although literature often expresses a relationship between anxiety and/or depression and diabetes (42), pulmonary (43), and neoplastic diseases (44), these associations were not confirmed in Portuguese senior population. Our study confirms,

however, conclusions of previous studies on rheumatic diseases (11, 45, 46) stressing their important association with both anxiety and depression, as well as the relationship between allergies and anxiety, patent in the literature (47).

Interestingly, the female sex is also described in literature as an important determinant of depression (46, 48). In our study, it was strongly significant even with multivariable analyses with single factors separately, such as non-communicable chronic diseases, quality of life, or function. But within a global model including all significant variables for depression, it loses its previous relevance.

Regarding age, Alameda County Study demonstrated a raise of depression prevalence with age (49). But multivariable analyses showed that the effect of age was related to physical health problems and disability associated with aging. Several studies concluded the same way, indicating that although depression prevalence increases with age, it should be due to age-related factors than age itself (50, 51).

Study limitations should be considered when interpreting results. Being cross-sectional, this analysis does not allow to draw conclusions about the effects of causality between the variables and the chronological order of the events.

Although Breeman defended HADS being used for clinical and non-clinical population (52), the use of a specific instrument to assess anxiety and depression in this particular age group is arguable.

Despite of what has been referred, several strengths related to both internal and external validity should be pointed out. Data come from large, nationally representative sample of the Portuguese elder population followed since 2011, allowing its generalization for the age group in our country. It should also be noted that data were collected by a team of 10 interviewers who were extensively and properly trained, whose proceedings were standardized, and regular and rigorously monitored to assess quality and reduce bias.

In conclusion, key findings of this study are as follows: (1) Portuguese elderly population have prevalence of anxiety and depression around 10 and 12%, respectively; (2) anxiety and depression are associated to different factors; (3) health-related quality of life and physical function play an important role in depression and anxiety; and (4) level of education distinguishes senior in terms of anxiety and depression.

ETHICS STATEMENT

This study was carried out in accordance with the recommendations of Guidelines for Good Clinical Practice and the ethical principles stated in the Declaration of Helsinki, National Committee for Data Protection (Comissão Nacional de Proteção de Dados) and by the NOVA Medical School Ethics Committee, with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the National Committee for Data Protection (Comissão Nacional de Proteção de Dados) and by the NOVA Medical School Ethics Committee.

AUTHOR CONTRIBUTIONS

RS conducted the study and wrote the paper. AR and MGr supported the development of the study design and methodology

and reviewed the paper. JB is co-responsible for the EpiDoC Cohort and reviewed the paper. MGo and HC supported the whole development of the study and writing and reviewed the paper. SD supported the data analysis process.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Neuropsychological Correlates of Pre-Frailty in Neurocognitive Disorders: A Possible Role for Metacognitive Dysfunction and Mood Changes

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OPEN ACCESS

Edited by:

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Roma Tor Vergata, Italy

Reviewed by:

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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 03 July 2017

Accepted: 31 October 2017

Published: 15 November 2017

Citation:

Amanzio M, Palermo S, Zucca M,
Rosato R, Rubino E, Leotta D,
Bartoli M and Rainero I (2017)

Neuropsychological Correlates of
Pre-Frailty in Neurocognitive
Disorders: A Possible Role for
Metacognitive Dysfunction
and Mood Changes.
Front. Med. 4:199.

doi: 10.3389/fmed.2017.00199

Background: Recent studies have suggested that cognitive functions in patients with neurocognitive disorders have a significant role in the pathogenic mechanisms of frailty. Although pre-frailty is considered an intermediate, preclinical state, epidemiological research has begun to dislodge cognition and frailty into their specific subcomponents to understand the relationship among them. We aim to analyse the possible association between pre-frailty and neuropsychological variables to outline which factors can contribute to minor and major neurocognitive disorders.

Methods: 60 subjects complaining of different cognitive deficits underwent a deep-in-wide frailty and neuropsychological assessment. We conducted three multiple linear regression analyses adjusted for a combination of demographic measures and involving several neuropsychological-behavioural parameters selected by the literature on physical frailty.

Results: We found a significant association between frailty—as measured by the multidimensional prognostic index (MPI)—and action monitoring and monetary gain (cognitive domain), depression and disinhibition (behavioural domain). Moreover, an association between MPI and impaired awareness for instrumental activities disabilities exists.

Conclusion: We propose a novel framework for understanding frailty associated with metacognitive-executive dysfunction.

Keywords: pre-frailty, mild cognitive impairment, comprehensive geriatric assessment, Alzheimer's disease, executive dysfunction

INTRODUCTION

Frailty is a complex and heterogeneous clinical syndrome. It is described by augmented vulnerability resulting from age-related decline across several body organs and physiological systems (1, 2). Frailty leads to a decrease in the ability to remain independent and to maintain a good quality of life (3). Moreover, it increases the risk of disability and mortality (3). The frailty syndrome has principally

been explored by focussing on the physical domain, mostly relying on signs and symptoms such as muscle weakness, sedentary behaviour, slow gait speed, and weight loss (1). Frailty has also been involved in general cognitive decline and impaired global cognition (4).

Canevelli and colleagues (5) have recently emphasised some criticalities of these studies: (a) the overwhelming majority of them have assessed frailty using the criteria proposed by Fried and colleagues (1), primarily aimed at describing the physical dimension of frailty; (b) most of these researches adopted only a measure of global cognitive functioning, mostly assessed by the Mini Mental State Examination [MMSE; (6)] to assess cognition, in absence of a comprehensive neuropsychological evaluation; (c) finally, the sample populations were mainly composed of community-dwelling older adults, preventing the applicability of results to other types of patients. The limitations of those studies have also been previously reported (7).

The overall concept of examining the specific cognitive correlates of frailty is interesting and may indeed shed light on a more comprehensive model of frailty that details a specific neuropsychological profile. Interestingly, the most novel evidence comes from a small number of studies aimed at examining the association between specific cognitive functions and physical frailty (5). In particular, Canevelli and colleagues (5) pointed out a significant impairment of attention and executive functions. Importantly, literature has shown that the executive function and attention domains are related to frailty, while gait speed or grip strength are the components of frailty most strongly associated with cognition (8–20). O'Halloran and colleagues (8) recently stated that pre-frail and frail individuals seem less able than robust subjects in the "Sustained Attention to Response Task" (SART). Even if these studies represent a first important attempt to describe the association between cognitive functions and physical frailty, there is still the need to assess frailty with a multidimensional approach (21–23).

Although executive function and attention domains may be related to physical frailty, no previous studies have investigated the role of different neuropsychological domains by carrying out a multidimensional assessment of frailty. In line with this, the multidimensional prognostic index (MPI) currently represents one of the suggested methods for a comprehensive assessment of frailty (24–26).

The aim of this study is to investigate whether pre-frailty, measured through the MPI, might be influenced by cognitive-behavioural measures in individuals with minor and major neurocognitive disorders [DSM-5; (27)], from mild cognitive impairment (MCI) likely due to Alzheimer's disease (AD), to mild AD patients (28). For this reason, we conducted three multiple linear regression analyses to study: (1) the role of global cognitive functioning and specific cognitive variables (selective attention, episodic memory, language comprehension, and reasoning in the visual modality); (2) the role of metacognitive executive functions, such as response monitoring; and (3) the relationship with mood changes, quality of life, and awareness of independence for daily living instrumental activities.

MATERIALS AND METHODS

Participants

All the outpatients were enrolled at the Neurology Division of the "Città della Scienza e della Salute" Hospital and the Martini Hospital, both in Turin (Italy).

Participants were included in the study if they had: (a) minor or major neurocognitive disorders (27), such as MCI-likely due to AD and mild AD. On the other hand, participants were excluded from the study if they had: (a) dysthymia or major depressive disorder, based on DSM-5 criteria (27); (b) A MMSE score <20, given that the neuropsychological measurement is not as reliable when problems of language comprehension occur; (c) were taking medications that could substantially impact cognitive functioning. CSF diagnosis that did not provide *in vivo* evidence of Alzheimer's pathology was considered exclusion criterion.

The patients underwent a complete neurological examination and neuroradiological investigations (MRI and FDG-PET). All the patients underwent lumbar puncture with cerebrospinal fluid measurement of 1-42 beta-amyloid, phospho-Tau, and total-Tau (Innogenetics kits, Ghent, Belgium).

Assessment of Frailty

Several operational definitions have been proposed to assess frailty in the elderly (29). Although this variability might be acceptable from a public health perspective, the identification of a gold standard measure might still be important to obtain. To date, frailty is still detected using different instruments and none of them has been able to prevail as superior to the others (29).

An index originally conceived and designed in the Italian general practice setting for the evaluation of chronic multipathological conditions was initially used to screen the participants' levels of frailty (30). The scale for the Evaluation of the frailty elderly (Scheda di Valutazione dell'Anziano Fragile,¹ SVAFRA) is a "multiaxial" score, interpreted according to the principles of the complexity theory in medicine and healthcare (30). This scale is a useful tool in case of multiaxial assessment in the setting of primary care (31), especially for its ability to combine technical skills, synthesis of information, and care-management suggestions (30, 31). SVAFRA was used for the first "Cognitive survey on the frailty of elderly people in Italy," which was attended by 34 Primary Care Physicians and 521 elderly recruited in Veneto, Lazio, and Sicily (32).

According to the authors, frailty is determined by issues pertaining at least one of the following evaluative dimensions (30): physical and mental health; physical and cognitive-behavioural disabilities; patient management considering the care burden; family and socio-environmental background. For each axis, determinants can assume a value between 0 (no deficiencies) and 3 (very serious problems). The level of frailty is then classified based on a combination of these four dimensions. A synthetic value—regardless of the value previously assigned to the four determinants—can also be assigned: F0 (absence of frailty, typical

¹Frailty in the elderly evaluation sheet.

of healthy patients); F1 (pre-frailty); F2 (medium frailty); F3 (severe frailty, typical of severely ill patients); T (extreme frailty, typical of *terminally ill* patients).

Since clinicians needed an outcome instrument with sound clinimetric properties (33), frailty was assessed using a comprehensive geriatric assessment (CGA), which was considered the first-choice tool for evaluating biological, functional, cognitive, social, and clinical aspects of elderly subjects, as expressed by the Italian Society of Gerontology and Geriatrics (34, 35). The MPI was developed from a standardised CGA (26, 35, 36). It was originally conceived as a prognostic index of mortality in the short- and long-term period based on information obtained through the CGA in hospitalised (37) and outpatient settings (38). With this index, the prognostic value of negative outcomes and related severity are even higher than with the indices calculated in the single domains of the rating. The MPI is also considered suitable for assessing frailty in the elderly (34–36). Moreover, as a cumulative multidimensional index, the MPI allows professionals to develop a treatment plan (22). In 2013, the European Innovation Partnership on Active and Healthy Ageing identified 98 “good practices” involved in research to reverse or prevent frailty (24). As demonstrated by the Marco Polo Initiative, the MPI is helpful in identifying frailty elders, providing personalised interventions, avoiding drug prescriptions and adverse hospital admissions (24, 39).

The MPI includes information on clinical, functional, nutritional, and neuropsychological aspects, as well as polypharmacy, pharmacological treatment, and the social support network (22, 25, 26, 35–40). Specifically, the MPI is calculated using a mathematical algorithm that includes scores of individual profiles obtained from the eight evaluation tools that make up the CGA: 1. *activity of daily living scale* (ADL); 2. *instrumental activity of daily living scale* (iADL); 3. *short portable mental status questionnaire* (to assess cognitive status); 4. *cumulative illness rating scale—comorbidity index* (CIRS-CI, to explore comorbidity); 5. *Mini Nutritional Assessment scale* (MNA, to assess nutritional status); 6. *Exton Smith Scale* (to evaluate the risk of developing pressure sores); 7. polypharmacy; 8. social condition (22, 25, 26, 35–40).

The numerical index obtained has a value between 0.0 (lowest risk) and 1.0 (highest risk of mortality) and reports three grades of risk of severe prognosis: low risk (MPI value ≤ 0.33), moderate risk (MPI value between 0.34 and 0.66), and severe risk (MPI ≥ 0.67) (22, 26, 36, 37, 40). Importantly, the effectiveness of the MPI has recently been verified in population-based cohorts. Higher MPI risk scores were associated with more days in hospital and with fewer years of survival, across a broad and stratified age range (25, 40).

Neuropsychological Assessment

The neuropsychological evaluation involved a wide assessment of global cognitive deterioration using: the CDR (41), the Addenbrooke's Cognitive Examination-Revised version [ACE-R; (42)] and, finally, the MMSE (6). Other cognitive domains were also assessed with the use of different scales: selective attention with Attentional Matrices [AM; (43)], divided attention and cognitive shifting with the Trial Making Test [TMT; (43, 44)],

episodic memory with the Recall of a Short Story test [Babcock; (37)], reasoning in the visual modality with Coloured Progressive Matrices [CPM-36; (43)], comprehension of spoken language with the Token Test [TT; (43, 45)].

Executive functions were analysed with the metacognitive version of the Wisconsin Card Sorting Test [m-WCST; (46, 47)]. This test is aimed to assess “on-line” metacognitive monitoring and control during the execution of the test (46, 47). For each card of the test, two questions evaluated “on-line” metacognitive monitoring (“What is your degree of confidence in this answer?”) and control (“Do you want to take this response into account in your total score?”) (46–48). In the original version of Koren's protocol, the participants were assigned a dollar value for each correct response (46–48). In this study, the patients received a monetary gain of 10 cents for each correct answer and they were deprived of 10 cents for every wrong answer (49). As described in our previous work that used the same procedure (49), a set of metacognitive indices were evaluated: “(1) accuracy score (AS), the number of correct voluntary answers/number of voluntary responses; (2) free choice improvement (FCI) (accuracy—number of correct responses from forced responses)/number of cards presented; (3) global monitoring (GM), the number of correct responses—the total number of sorts required in the final score; (4) monitoring resolution (MR), the gamma correlation calculated between the confidence and correctness of the sorts in the entire test; (5) control sensitivity (CS), to what extent the control process depended on the monitoring process, indexed by the gamma correlation calculated across all sorts between the level of confidence and the decision to gamble; (6) monetary gains (MG), given by the number of correct voluntary responses—incorrect number of voluntary responses” [(49), p. 138].

We verified the subjects' level of autonomy in basic and instrumental activities of daily living (50, 51) and accordingly, their quality of life with the Quality of life scale in Alzheimer's disease (QoL-AD)—patient's subscale (52). Patients were also assessed using specific neuropsychiatric rating scales of mood changes: apathy and depression with Hamilton Depression Rating Scale [HDR-S; (53)], disinhibition and hypomania with the Disinhibition Scale and the Mania Scale [DIS-S (54); MAS (55)].

Finally, in accordance with what we did in our previous work (56), “we followed the classification of Starkstein and colleagues (57) who used principal component analysis to subdivide the Awareness of Deficit Questionnaire—Dementia scale [AQD (58)] into four domains taking into consideration the factors loading on each item. One of these factors, identified in terms of impaired awareness in instrumental activities of daily living (AQD_iADL), was designated as factor 1 by the authors. Factor 1 embraces 12 items: ‘recalling the date, orienting to new places, recalling telephone calls, remembering the location of objects at home, understanding conversation and the plot of a movie, keeping belongings in order, handling money, doing mental calculations, remembering shopping lists and appointments, performing clerical work.’ Thus it accounted for most of the variance and also rated as the earliest functional deficit in patients with cognitive impairment” [(56), p. 65]. Since disabilities in

instrumental activities of daily living were one of the descriptors of frailty used in the Canadian Study on Health and Ageing (59), we decided to take it into consideration in our analyses.

Procedures

We implemented a cross-sectional study to explore data collected from our clinical population. Patients were evaluated by performing a neuropsychological assessment during a week in hospital. The participants were assessed in three experimental sessions held 1 day apart and each lasting 1 h, with a view to preventing fatigue and lack of adherence to the tasks.

Statistical Analysis

We performed statistical analyses using SAS/STAT® 9.3 (60, 61). The *post hoc* power was determined using the formula for sample size with continuous measures through G*Power 3, which is a stand-alone power analysis tool for statistical tests commonly used in social and behavioural research (62). The achieved power with a sample size of 60 was estimated to provide a minimum of 70% power at a 5% level of significance (two-sided) to detect a medium effect ($r^2 = 0.2$).

To study whether the level of the MPI index could be associated with cognitive and behavioural measurements, we conducted three multiple linear regression analyses adjusted for age, gender, and schooling. Normality assumption distribution of linear regression model residuals was evaluated by means of the Kolmogorov–Smirnov test.

Importantly, the selection of the three models was performed in line with the results obtained in the literature on physical frailty. In particular, frailty has been previously associated with general cognitive decline, impaired global cognition, and memory (5, 8, 18). Moreover, executive function and attention domains have been consistently related to frailty (8–10, 12–20). Finally, the association between physical frailty and the performance at the SART test (8) seems to suggest that pre-frail and frail people might be impaired in response monitoring.

The final selected models considered the MPI as the dependent variable and the following as independent variables:

- Model (1) to address the role of global cognitive functioning and specific cognitive variables (selective attention, episodic memory, language comprehension, and reasoning in the visual modality): ACE-R, MA, BABCOCK, TT and CPM-36;
- Model (2) to study the role of metacognitive executive functions with m-WCST: FCI, GM, MR, and MG;
- Model (3) to investigate the relationship with mood changes, quality of life and awareness of autonomy in instrumental activities of daily living: HDR-S, MAS, DIS-S, QOL-AD, and AQD_iADL.

RESULTS

Over a 24-month period, 72 patients—complaining of different cognitive deficits and presenting for the first time at the out-dep of our clinics—were evaluated with the overall neuropsychological assessment. After a month, based on CSF analysis results, only subjects with an AD-compatible liquor were included in

the experimental sample. As a result, 12 patients were excluded, while 60 subjects were enrolled. Based on the exclusion criterion, 12 patients were excluded, while 60 subjects (M/F = 22/38; mean age \pm SD = 69.6 ± 6.8 years) were enrolled (see Table 1 for demographic and clinical data). In particular, 24 MCI due to AD patients according to the CSF analysis, were included in the study. For those patients with major neurocognitive disorders, the CSF diagnosis provided *in vivo* evidence of Alzheimer's pathology for 36 patients. The neuropsychological assessment reflected the diagnoses made by the CSF (see Table 2 and Table S1 in Supplementary Material), biomarkers and neurological exams. Fifty-six of the 60 patients obtained a CDR score of between 0 and 1 attesting a low level of cognitive impairment.

Prevalence of Frailty Status

As regard the CGA evaluation, the patients fell within the lowest MPI range, attesting a low risk of severe prognosis. Considering the SVAFRA index, 97% of all patients were classified as pre-frail, and 3% with medium frailty.

Association between Frailty and Neuropsychological Variables

After adjusting the analysis for age, gender, and schooling, the MPI index scores were influenced by MR and MONEY in model 2, and by HDR-S, DIS-S, and AQD_iADL in model 3. On the contrary, the level of pre-frailty measured through the MPI index was not influenced by global cognition, memory,

TABLE 1 | Demographic characteristics and frailty evaluation by a comprehensive geriatric assessment.

	Maximum scores	Mean \pm SD	Cutoff
Demographic characteristics			
Gender (male/female)		22/38	
Age (years)		66.62 \pm 6.80	
Schooling (years)		9.28 \pm 3.86	
Early cognitive symptoms complaints (months)		31.15 \pm 27.82	
Clinical dementia rating scale		0.78 \pm 0.44	
Multidimensional prognostic index			
Activity of daily living scale	8	5.70 \pm 0.53	\geq 4
Instrumental activity of daily living scale	6	6.63 \pm 1.55	\geq 6
Short portable mental state questionnaire	10	2.46 \pm 1.63	\leq 2
Cumulative illness rating scale—comorbidity index	13	1.43 \pm 1.42	
Mini nutritional assessment	30	21.32 \pm 3.62	\geq 24
Exton Smith Scale	20	18.80 \pm 1.47	\geq 15
Polypharmacy		4.12 \pm 2.46	
Social condition		Household	
Multidimensional prognostic index	1	0.19 \pm 0.12	
SVAFRA^a			
F1		% = 97	
F2		% = 3	

Wherever there is a normative value, the cutoff scores are given in the statistical normal direction. Cells in grey indicate the absence of a normative cutoff.

^aScheda di Valutazione dell'Anziano Fragile.

TABLE 2 | Neuropsychological and neuropsychiatric assessment synopsis.

	Maximum scores	Mean \pm SD	Cutoff
Neuropsychological assessment			
Mini-mental state examination	30	25.02 \pm 2.85	\geq 24
Addenbrooke's cognitive examination—revised version	100	69.57 \pm 12.60	\geq 82
Attentional matrices	60	30.52 \pm 9.91	\geq 31
Trial making test A	500	110.73 \pm 82.92	\leq 94
Trial making test B	500	297.18 \pm 158.12	\leq 283
Trial making test B-A		194.92 \pm 127.11	\leq 187
Babcock	16	6.22 \pm 3.72	\geq 4.75
Coloured progressive matrices-36	36	22.17 \pm 7.26	\geq 18.96
Token test	36	30.21 \pm 3.61	\geq 32.69
Wisconsin card sorting test % correct answers		52.59 \pm 15.44	\geq 37.1
Wisconsin card sorting test % perseverative errors		34.34 \pm 14.95	\leq 42.7
Wisconsin card sorting test—metacognitive version			
Accuracy score		0.03 \pm 0.11	
Free choice improvement		-1.17 \pm 4.98	
Global monitoring		-20.13 \pm 14.29	
Monitoring resolution		0.19 \pm 0.24	
Control sensitivity		-0.04 \pm 0.58	
Monetary gains		2.37 \pm 1.93	
Neuropsychiatric assessment			
Quality of life scale in Alzheimer's disease—patient module	39	17.90 \pm 8.01	
Hamilton depression rating scale	67	10.95 \pm 7.47	\leq 7
Disinhibition scale	96	9.40 \pm 6.95	\leq 16.9
Mania scale	44	2.62 \pm 3.57	\leq 15
Awareness of deficit questionnaire—dementia scale for instrumental activity domain	16	3.20 \pm 8.22	\leq 4

Wherever there is a normative value, the cutoff scores are given in the statistical normal direction. Cells in grey indicate the absence of a normative cutoff.

language comprehension, non-verbal reasoning (in model 1), or by QOL-AD (in model 3, see **Table 3**).

The normality distribution assumption of residuals in each model is fulfilled (Kolmogorov-Smirnov test > 0.05).

DISCUSSION

The aim of this study was to analyse the association among a multidimensional assessment of frailty, executive dysfunction and specific cognitive and behavioural variables using an overall neuropsychological battery. Our findings suggested that pre-frailty was associated with metacognitive executive dysfunction, in terms of action monitoring in MCI-like due to AD and AD patients. Specifically, we observed a significant association between the MPI index and MR underlying the role of MR, where patients fail to distinguish between correct and incorrect sorts. The results obtained were specific and not influenced by other cognitive functions such as global cognition, memory, language comprehension, and non-verbal reasoning, with the exception of the selective attention task that reached a near significance level. Moreover, taking the MPI scores into account, we observed an involvement of mood changes in terms of depression, apathy, and disinhibition and a reduced awareness of iADL, while the relationship with hypomania was near to the significance value.

Although we considered patients with different degrees of cognitive impairment, our sample was homogeneous in terms of the etiopathogenesis, MPI level of risk, comorbidity with physical illness, somatic complaints, laboratory tests, and the level of mood changes. Moreover, we excluded all patients with neurological diseases other than AD. Most importantly, our attempt to consider these kinds of patients in the same sample was justified by the regression analysis approach we used and by

TABLE 3 | Effect of the independent variables on the multidimensional prognostic index estimated by the univariate and multiple linear regression analyses.

Model	Independent variables	Crude estimates			Adjusted estimates		
		β	p	SE	β	p	SE
1	Addenbrooke's cognitive examination—revised version	-0.20	0.18	0.001	-0.03	0.87	0.001
	Attentional matrices	-0.36	0.02	0.002	-0.29	0.11	0.002
	Babcock	-0.05	0.75	0.005	0.09	0.60	0.006
	Token test	-0.12	0.43	0.005	-0.01	0.95	0.005
	Coloured progressive matrices-36	-0.27	0.06	0.002	-0.14	0.44	0.003
	Model significance	$R^2 = 0.2056, F = 1.42 p = 0.2137$					
2	Free choice improvement	0.07	0.60	0.003	0.03	0.84	0.003
	Global monitoring	-0.07	0.60	0.001	0.11	0.42	0.001
	Monitoring resolution	0.33	0.02	0.075	0.37	0.01	0.073
	Monetary gains	-0.21	0.14	0.009	-0.30	0.04	0.009
	Model significance	$R^2 = 0.2863, F = 2.46 p = 0.0322$					
3	Hamilton depression rating scale	0.49	<0.00	0.002	0.41	<0.00	0.002
	Mania scale	0.09	0.52	0.005	-0.25	0.07	0.005
	Disinhibition scale	0.50	<0.00	0.002	0.52	<0.00	0.003
	Quality of life scale in Alzheimer's disease	-0.21	0.17	0.002	-0.01	0.91	0.002
	AQ-D scale for instrumental activity domain	-0.14	0.35	0.002	-0.30	0.02	0.002
	Model significance	$R^2 = 0.4980, F = 5.46 p < 0.0001$					

In multivariable analyses standardised coefficients are adjusted for age, gender, and schooling. Values in bold italics showed a statistically significant association ($p < 0.05$). AQ-D, Awareness Questionnaire in Dementia.

the international guidelines on ageing that consider patients with cognitive impairment to lie on a continuum between MCI and mild AD (28, 63, 64).

Based on the results we obtained, there appear to be no straightforward associations between pre-frailty and specific aspects of neuropsychological functioning such as global cognition, long-term verbal memory, language comprehension, and non-verbal reasoning. As underlined by a review on cognitive impairment and frailty, not all cognitive domains may become impaired simultaneously (7). Although Canevelli et al. (5) have described a possible association between memory and physical frailty, other studies have found that memory does not seem to be clearly associated with frailty [i.e., Ref. (17, 65)]. As far as we are aware, no previous studies have addressed the association between frailty and language comprehension on the one hand, and frailty and non-verbal reasoning on the other (18). Moreover, we found no generalised cognitive impairment as a prerequisite of pre-frailty in our patients. Nevertheless, previously researches have reported a substantial association between frailty and cognitive deterioration (5, 7, 18, 66), although the phenotype model often used in these does not include cognitive function in its definition (1). Despite these evidences—as previously suggested by Robertson and colleagues (7)—statistical analyses of the proposed components of frailty suggest that, while energy, mobility, mood, physical activity, and strength aggregate as one concept, cognitive function does not clearly correlate with this and therefore may not be part of the frailty syndrome (67, 68). Furthermore, a study of AD patients found that 22% had no indications of frailty (69, 70). Indeed, Fougère and colleagues in their review concluded that “it seems most useful, therefore, to treat frailty and cognitive impairment as related but distinct concepts that frequently co-occur” [(71), p. 3].

Notably, the assessment of executive dysfunction should be seen as an important early predictor of cognitive frailty (9), since these problems may appear as the first cognitive changes in MCI patients (72), with concomitant iADL difficulties (73). Indeed, the early identification of executive impairments may be helpful for predicting the long-term functional outcome (74). Interestingly, O’Halloran and colleagues (8) recently stated that pre-frail and frail individuals seem to make more commission errors and omissions than robust subjects on the SART that evaluates the ability to sustain attention for a long time with a response-suppression element (75, 76). This fact suggests that they may be impaired in response monitoring, as we have demonstrated through the association between pre-frailty and action monitoring using the m-WCST. Indeed, the main predictor at this level has been MR, expressed by Koren and colleagues as the correlation between the level of confidence expected from the response and correctness of the sorts in the entire WCST (46–48). In particular, our patients have shown failure to monitor their own performance considering the errors made during task execution, in terms of low metacognitive self-awareness. Moreover, we have found an association between the MPI and monetary gain, which can be interpreted as subjects’ ability to benefit from environmental feedback, anticipate the consequences of their future actions and make decisions accordingly. In addition, we have also found pre-frailty to be associated with

an inability to report unsuccessful experiences in iADL through the Awareness Questionnaire in Dementia (AQ-D) (56). In our previous article concerning impaired awareness of deficits in AD and the role of everyday executive dysfunction (56), mood orientation changes, inhibition, self-monitoring, and set shifting appeared to be important skills for awareness of iADL (AQD_iADL) (56). According to this and considering the neural substrate, AD patients with impaired awareness showed reduced activation in the Mid Cingulate Cortex during an event-related fMRI response-inhibition paradigm, compared to subjects aware of their deficits (77).

Through our current results we hypothesise that pre-frailty may arise by a disruption of the comparator mechanisms responsible for monitoring behavioural mood changes and cognitive disturbances (56). If the executive system does not function properly, as frequently described in MCI-likely due to AD and AD patients (78), the comparator mechanism does not detect incongruities between the previous and the actual state of behaviour/performance. This phenomenon has been observed as an inability: (1) to monitor one’s own performance with reference to the impact of errors made during task execution, in terms of a reduction in metacognitive self-awareness; and (2) to relate fruitless experiences in one’s everyday living through the AQ-D.

The few studies investigating the neuropsychiatric factors (79–81) have suggested that “one mechanism underlying the link between frailty and cognition may be due to psychological factors such as mood. Indeed, mood disorders such as depression have been found to be both a risk factor for and a consequence of frailty” [(7), p. 847]. In line with this, we observed a role of HDR-S scores in pre-frailty condition. The HDR-S actually measures mood changes, in terms of apathetic behaviour and depressive mood possibly related to prefrontal dysfunctions (82). This evidence also suggests a possible role of apathy in pre-frailty conditions (83). Interestingly, apathy, disinhibition, and metacognitive executive dysfunction appear to be neurally inscribed in the same network (84–87). The results we obtained proposed the suggestive hypothesis that pre-frailty may be due to a possible dysfunction of the medial prefrontal–ventral striatal network observed throughout action-monitoring disability, mood changes, and reduced awareness of iADL. These findings ask for new neuroimaging investigations and replication in a larger group of patients.

Limitations Section

The study here presented has been carefully designed and reached its aims; however, some critical aspects have to be outlined. The first aspect regards the tools used to assess frailty, which could represent a possible confounding factor. In particular, pre-frailty is defined by adopting the SVAFRA that may not be considered appropriate for stratifying the frailty status of the older person and it has been rarely adopted for these purposes. Moreover, the MPI was originally conceived as a prognostic index of mortality in the short- and long-term period (37) and a recent international survey among clinical practitioners on the methods to assess frailty in their daily practice (29) did not include MPI as a tool to assess frailty. However, as previously expressed by Bruyère and colleagues (29), frailty is still detected using different

instruments and none of them has been able to prevail as superior to the others (29). Second, the results we obtained are not generalisable for patients with different etiopathogenesis other than AD. However, our study is a first attempt to investigate possible association between pre-frailty and neuropsychological variables in a selected patient population, on the basis of liquor examination and may be limited to identify pathogenetic mechanisms of frailty. This is a cross-sectional study aimed to evaluate a possible association between frailty and neuropsychological variables in MCI-likely due to AD and AD patients. A longitudinal study may be the most correct approach to assess for the presence of cognitive disorders many years before the development of frailty itself. Further studies will be important to better characterise this association over time and replicate these findings in a larger group of patients.

CONCLUSION

This study represents a first important attempt to extend the frailty issue to neuropsychological correlates taking in consideration a multidimensional approach. These findings suggest that the assessment of pre-frailty conditions must be achieved quantitatively by means of a multidimensional approach to clarify the nature and correlates of this multifaceted phenomenon. In particular, the impact of everyday executive dysfunction, early changes in mood and the awareness of iADL disabilities must be considered. Our results benefit from the homogeneity of the experimental sample in terms of etiopathogenetic mechanisms, disease severity (CDR) and functionality in daily life (ADL/iADL). The evaluation of pre-frailty conditions and their neuropsychological correlates is clinically relevant. Indeed, this multifaceted phenomenon has diagnostic, nosological, and prognostic implications that may affect patients' wellbeing in the continuum from MCI to AD.

AUTHOR CONTRIBUTIONS

The study is based on a concept developed by MA who wrote the paper and took part in the review and critique processes as PI. She also organised the study and participated in the statistical analyses (execution and organisation, review, and critique). SP

performed the neuropsychological assessment (execution and organisation), participated in the statistical analyses, participated in writing the paper and created the infographics. RR conducted the statistical analyses (execution), participated in interpretation of results and in writing the paper. ER performed the neurological assessment (execution) and took part in the organisation of the study and in the diagnostic phase (organisation and diagnosis). MZ and MB performed the neuropsychological assessment (execution), participated in writing the paper and in drafting the work. DL and IR supervised the neurological assessment, took part in the organisation of the study and participated in writing the paper (organisation, review, and critique). All the contributors gave their approval of this version of the manuscript to be submitted.

ACKNOWLEDGMENTS

The study was approved by the Ethics Committee “A.O.U. Città della Salute e della Scienza di Torino—A.O. Ordine Mauriziano—A.S.L. Città di Torino” as part of the core research criteria followed by the Neurological Units. All the implemented procedures ensured the safety, integrity, and privacy of patients. All subjects gave their informed written consent to participate in the study. As far as data regarding human biological samples are concerned, the cerebrospinal fluid acquisition procedures used are safe and fall within the scope of ordinary clinical-diagnostic routine practice. Finally, any critical aspects, neither with regard to the functional-neurocognitive assessment phase nor to the neuropsychological assessment could be noticed. Importantly, the study has been conducted according to the principles set forth by the Declaration of Helsinki (59th WMA General Assembly, Seoul, October 2008) and in accordance with the Medical Research Involving Human Subjects Act (WMO).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at <http://www.frontiersin.org/article/10.3389/fmed.2017.00199/full#supplementary-material>.

TABLE S1 | CSF assessment synopsis. The results of all subjects are reported.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Aging, Disability, and Informal Caregivers: A Cross-sectional Study in Portugal

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Objectives: Aging is pushing states to rethink long-term care policies in several dimensions. This study aims to characterize the reality of dependent older people regarding their demographic and health characteristics, to describe their informal carers and understand the availability of informal care.

Methods: A cross-sectional study was developed in Portugal in 2013. Descriptive statistical analyses and binary logistic analysis were conducted.

OPEN ACCESS

Edited by:

Giuseppe Liotta,
Università degli Studi di Roma Tor Vergata, Italy

Reviewed by:

William Keith Gray,
Northumbria Healthcare NHS Foundation Trust, United Kingdom
Marios Kyriazis,
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Specialty section:

This article was submitted to Geriatric Medicine, a section of the journal *Frontiers in Medicine*

Received: 04 August 2017

Accepted: 21 December 2017

Published: 16 January 2018

Citation:

Pego MA and Nunes C (2018) Aging, Disability, and Informal Caregivers: A Cross-sectional Study in Portugal. *Front. Med.* 4:255.
doi: 10.3389/fmed.2017.00255

Results: Results show that the informal long-term care sector is primarily aimed at older people with severe limitations in their activities of daily living and at the chronically ill, particularly older women. Additionally, 39.5% of dependent older persons do not have informal care and only receive informal aid in cases of extreme need.

Discussion: Results show a critical situation for both social groups (older persons and caregivers) and the prospect of an alarming situation in the near future (aging and reduced availability of informal caregivers) unless a new approach for long-term care is developed.

Keywords: informal care, dependent elderly, epidemiology, aging, Portugal

INTRODUCTION

Improvements in living conditions and the quality of health services have led to a significant increase in the proportion of older people in the population, a trend that is expected to continue over the next decades. Public health authorities face the challenge of promoting the reform of health policies that are aimed at older people, due to the progressive loss of functionality and the consequent increase in dependence for their activities of daily living (ADL), leading the older person to an increased need for long-term care. These personal care components are often provided in combination with basic medical services (medication, health monitoring, prevention, rehabilitation, or palliative care services) and, sometimes, with lower level help, namely those related with Instrumental Activities of Daily Living (IADL), such as meals, shopping, and housework (1).

At first glance, one realizes that demographic, social, and economic changes are “pushing” states to reassess long-term care policies, mainly due to the restructuring of the family leading to a reduction in the availability of informal caregivers. The atomization of families, the greater volatility of marital relations, the reduction in the average size of families, declining birth rates, and the increasing

participation of women in the labor market have substantially altered family structures and functioning (2).

Informal care is generally defined as the unpaid care provided to older and dependent people by a person with whom they have a social relationship, such as a spouse, parent, child, other relative, neighbor, friend, or other non-kin (3). In Europe, there is a multiplicity of forms of organization for long-term care, in which the North tends to have a greater provision of public services and formal care and the South favors the informal care sector provided by the family, due to the limited availability of formal resources (namely, systems of social protection for older people) and a “familiar” culture (4–10). For example, a significant proportion of long-term care is provided in this way in Spain (in 2008, 78% of care was provided by informal caregivers) and in France (in 2008, this amounted to 37%), according to Costa-Font and Courbage (11). Portugal shares the main characteristics of other Southern European countries, i.e., the family (in particular women) is the main provider of care, but differs in one key aspect: it has a high female participation rate in the labor market (9, 10, 12–14).

In a context of global aging and significant changes in family structures, it is necessary to comprehend the reality of informal care in order to understand its relevance to the care of the aging population. This study specifically contributes to the knowledge of the informal sector of care and aims to (i) describe the national reality of the dependent older person in Portugal regarding demographic, residential, and health characteristics; (ii) describe the informal carers, in terms of kinship, frequency of care, and geographical proximity between carer and older person; (iii) understand the availability of informal care. This article focuses on long-term care for the elderly in Portugal, framed in a context of significant changes in family structures and shifts in social solidarity networks. Thus, we argue that the current model of long-term care, based mainly on the informal sector, has not been able to keep up with the actual demands of the elderly in Portugal. Hence, we expect to find a significant part of the geriatric population in need of care. We also expect to find a relationship between the severity of the limitations perceived by older persons and the availability of an informal carer, i.e., only the most dependent and elderly have access to an informal caregiver.

MATERIALS AND METHODS

Data Source

This study is cross-sectional, observational, and analytical. Data are obtained from the fourth wave of the Survey of Health, Aging and Retirement in Europe (SHARE) (15), the first one that included Portugal. SHARE is the first longitudinal and cross-national research project collecting data on aging and access to the informal care sector.

In each country, data collection is based on probability household samples (drawn either by simple random selection or multistage random selection) where all people aged above 50 years and their partners were interviewed using Computer Assisted Personal Interviews. Although the sampling frame includes people living in institutions, the SHARE base sample excludes these individuals. For the Portuguese SHARE sample,

the target population was defined as all Portuguese-speaking residents, born before 1960 and their spouses/partners. For each country, the sample size originally defined was 2,000 individuals. In Portugal response rate of 60%, was expected, with an expected proportion of non-sampling units of 10%. Analysis of the width and magnitude of the 95% confidence interval (95% CI) were used in order to evaluate the uncertainty of estimates. The SHARE study (fourth wave) was subject to several ethics reviews: The Ethics Committee of the University of Mannheim, Germany, Ethics Council of the Max Planck Society and by national ethics committees or institutional review boards whenever this was required. This study was conducted in full accordance with the World Medical Association Declaration of Helsinki. Written consents from all participants involved in this study were obtained.

Study Sample

For the purpose of this study two additional restrictions were applied: (1) 65 years or older and (2) functional dependence [limited in at least one ADL or one Instrumental Activity of Daily Living (IADL)]. In order to restrict the samples according to the functional dependence of the older person, we used the Katz Index (16) to characterize the ADL, and the Lawton and Brody Scale (17) to characterize the IADL.

Table 1 presents the variables used in the analysis to characterize dependent older people and informal caregivers.

TABLE 1 | Variables used in the analysis to characterize dependent old person and informal caregivers.

Variables	Categories
Dependent old person	
Sex	Male; female
Age	65–69; 70–74; 75–79; 80–84; 85–99
No. of children	0; 1; 2; 3 ^a ; 4 ^a ; 5 ^a ; 6 or more ^a
Marital status	Married or registered partnership, living with spouse; married, separated from spouse ^a ; never married ^a ; divorced ^a ; widowed ^a
Type of building	Farm house; 1 or 2 family house; building with three or more flats
Household area	Major city ^a ; small city ^a ; village ^a ; rural area
Educational level	First level (4 years); second level ^a (6 years); third level ^a (9 years); secondary school; higher education; no education
Limitation ^b	Severely limited; limited, but not severely ^a ; not limited
Chronic illness	^a Yes; no
Informal caregivers	
Kinship	Daughters and sons (named as “children”); brother or sister; spouse; son-in-law or daughter-in-law; neighbor; other relative; housekeeper; grandchildren; friend
Gender	Male; female
Geo. proximity	Live in the same house; live in the same building; live less than 1 km away; between 1 and 5 km away; between 5 and 25 km away; between 25 and 100 km away; more than 100 and away
Frequency of care	Daily care; weekly care; monthly care; less-frequent care

^aCategories merged in multivariate analyses, especially due to small frequencies.

^bPerceived limitations on ADL—derives from the following question: “For the past six months at least, to what extent have you been limited because of a health problem in activities people usually do?”

Statistical Analysis

Descriptive statistical analyses were conducted to characterize the dependent elderly population and the informal caregivers, considering the variables presented in **Table 1**. Thereafter, binary and multivariate logistic analyses (using both methods: enter and forward LR: likelihood ratio) were used to characterize the availability of informal care (Model 1), being cared for by someone within the household, named here “inside care” (Model 2), being cared for by someone outside the household, named here “outside care” (Model 3). Considering the above variables (**Table 1**), crude, adjusted (by sex and age and by all significant variables), and corresponding confidence intervals were presented. We used SPSS statistical software with a 0.05% significance level. All models were tested and validated, namely through Hosmer and Lemeshow’s goodness-of-fit test and analyses of residuals.

RESULTS

The findings from the descriptive statistics are presented in **Table 2**, globally (276) and stratified by type of help: without informal care (109), with inside care (89), and with outside care (78). The categories that best define each profile are in bold.

Table 2 shows that women were a majority in all situations, which is as expected because the sample includes more women than men. Regarding age, it is also likely that the most elderly tend to have more informal inside care. Regarding marital status, the most striking aspect is the fact that, among those who receive outside care, the majority are widowed (56.4%). Regarding the number of children, it appears that those who receive outside care differ from the rest. Indeed, they are characterized by having three or more children. Regarding the type of accommodation there is a clear distinction between those who do not have an informal carer and live primarily in a family home (54.8%), and those who have an informal carer and live primarily in buildings with more than three flats. **Table 2** shows that among those who have no care and those who are less dependent in ADL form the majority (55.0%).

The percentage of chronically ill is considerably lower among those who do not have informal care. However, it should be noted that even those who do not receive informal care have a very high percentage of chronically ill (65.1%). Inside caregivers are mainly spouses (55.5%) and adult children (24.2%), and the remaining caregivers are neighbors, housekeepers, friends, and other relatives. Of the spouses 56.3% are male and 43.6% female, and 71.4% of the adult children caregivers are female and 62.5% of the remaining caregivers are female. **Table 3** shows that the primary outside care providers are adult children (38.6%), followed by neighbors (15.9%), friends (8.4%), housekeepers (7.5%), and other relatives (27.7%).

The majority of daily care is delivered by adult children (39.6%), other relatives (24.5%, including spouses, brothers or sisters, grandchildren, daughters or sons-in-law), neighbors (15.1%), and housekeepers (11.3%). These caregivers are predominantly female (64.8%) and live less than a mile away (78.13%).

TABLE 2 | Descriptive statistics.

Categories	All, n (%)	Without informal care, n (%)	Outside care, n (%)	Inside care, n (%)
Gender				
Male	91 (33.0)	43 (39.4)	28 (31.5)	20 (25.6)
Female	185 (67.0)	66 (60.6)	61 (68.5)	58 (74.4)
Total	276 (100)	109 (39.5)	89 (32.2)	78 (28.3)
Age				
65–69	68 (25.9)	34 (31.2)	19 (22.6)	15 (21.4)
70–74	48 (18.3)	32 (29.4)	8 (9.5)	8 (11.4)
75–79	67 (25.5)	28 (25.7)	17 (20.2)	22 (31.4)
80–84	53 (20.2)	12 (11.0)	26 (30.9)	15 (21.4)
85–99	27 (10.3)	3 (2.8)	14 (16.7)	10 (14.3)
Total	263 (100)	109 (41.4)	84 (31.9)	70 (26.6)
Number of children				
0	18 (7.7)	4 (3.7)	8 (16.7)	6 (7.8)
1	56 (23.9)	25 (22.9)	10 (20.8)	21 (27.3)
2	80 (34.2)	42 (38.5)	16 (33.3)	22 (28.6)
3	34 (14.5)	19 (17.4)	3 (6.3)	12 (15.6)
4	15 (6.4)	10 (9.2)	1 (2.1)	4 (5.2)
5	10 (4.3)	3 (2.8)	3 (6.3)	4 (5.2)
6 or more children	21 (9.0)	6 (5.5)	7 (14.6)	8 (10.4)
Total	234 (100)	109 (46.5)	48 (20.5)	77 (32.9)
Marital status				
Married ^a	175 (63.4)	84 (77.1)	66 (74.2)	25 (32.1)
Married, separated from spouse	2 (0.7)	0 (0)	0 (0)	2 (2.6)
Never married	8 (2.9)	2 (1.8)	2 (2.2)	4 (5.1)
Divorced	8 (2.9)	3 (2.8)	2 (2.2)	3 (3.8)
Widowed	83 (30.1)	20 (18.3)	19 (21.3)	44 (56.4)
Total	276 (100)	109 (39.5)	89 (32.2)	78 (28.3)
Type of building				
Farm house	12 (5.8)	6 (6.5)	1 (2.3)	5 (7)
1 or 2 family house	104 (50.0)	51 (54.8)	21 (47.7)	32 (45.1)
Building with 3 or more flats	92 (44.2)	36 (38.7)	22 (50)	34 (47.9)
Total	208 (100)	93 (44.7)	44 (21.2)	71 (34.1)
Household area				
Major city	89 (42.8)	36 (38.7)	19 (43.2)	34 (47.9)
Small city	33 (15.9)	16 (17.2)	8 (18.2)	9 (12.7)
Village	24 (11.5)	11 (11.8)	3 (6.8)	10 (14.1)
Rural area	62 (29.8)	30 (32.3)	14 (31.8)	18 (25.4)
Total	208 (100)	93 (44.7)	44 (21.2)	71 (34.1)
Educational level				
First level (4 years)	147 (53.8)	62 (56.9)	47 (53.4)	38 (50)
Second level ^a (2 years)	19 (7.0)	8 (7.3)	5 (5.7)	6 (7.9)
Third level ^a (3 years)	15 (5.5)	4 (3.7)	8 (9.1)	3 (3.9)
Secondary school	16 (5.9)	5 (4.6)	5 (5.7)	6 (7.9)
Higher education	14 (5.1)	8 (7.3)	4 (4.5)	2 (2.6)
No education	62 (22.7)	22 (20.2)	19 (21.6)	21 (27.6)
Total	273 (100)	109 (39.9)	88 (32.2)	76 (27.8)
Perceived limitations in ADL				
Severely limited	144 (52.2)	28 (25.7)	67 (75.3)	49 (62.8)
Limited, but not severely	98 (35.5)	60 (55.0)	17 (19.1)	21 (26.9)
Not limited	34 (12.3)	21 (19.3)	5 (5.6)	8 (10.3)
Total	276 (100)	109 (39.5)	89 (32.2)	78 (28.3)
Chronic illness				
Yes	216 (78.3)	71 (65.1)	77 (86.5)	68 (87.2)
No	60 (21.7)	38 (34.9)	12 (13.5)	10 (12.8)
Total	276 (100)	109 (39.5)	89 (32.2)	78 (28.3)

^aOr registered partnership, living with spouse.

TABLE 3 | Characterization of the informal caregivers—outside care.

	Daily, n (%)	Weekly, n (%)	Monthly, n (%)	Less freq., n (%)	All, n (%)
Kinship					
Spouse	1 (1.89)	1 (2.70)	0 (0)	0 (0)	2 (1.68)
Children	21 (39.62)	18 (48.65)	1 (14.29)	6 (27.27)	46 (38.66)
Brother or sister	3 (5.66)	3 (8.11)	0 (0)	2 (9.09)	8 (6.72)
Daughter-in-law or son-in-law	3 (5.66)	3 (8.11)	2 (28.57)	1 (4.55)	9 (7.56)
Neighbor	8 (15.09)	5 (13.51)	1 (14.29)	5 (22.73)	19 (15.97)
Housekeepers	6 (11.32)	2 (5.41)	0 (0)	1 (4.55)	9 (7.56)
Grandchildren	4 (7.55)	2 (5.41)	0 (0)	1 (4.55)	7 (5.88)
Friend	5 (9.43)	0 (0)	2 (28.57)	3 (13.64)	10 (8.40)
Other relative	2 (3.77)	3 (8.11)	1 (14.29)	3 (13.64)	9 (7.56)
Total	53 (100)	37 (100)	7 (100)	22 (100)	119(100)
Gender					
Male	13 (35.14)	10 (34.48)	2 (33.33)	9 (56.25)	
Female	24 (64.86)	19 (65.52)	4 (66.67)	7 (43.75)	
Total	37 (100)	29 (100)	6 (100)	16 (100)	
Geographic proximity					
In the same household	12 (37.5)	4 (13.79)	0 (0)	1 (10)	
In the same building	2 (6.25)	0 (0)	0 (0)	1 (10)	
Less than 1 km away	11 (34.38)	10 (34.48)	1 (25)	4 (40)	
Between 1 and 5 km away	2 (6.25)	1 (3.45)	0 (0)	1 (10)	
Between 5 and 25 km away	5 (15.63)	9 (31.03)	1 (25)	1 (10)	
Between 25 and 100 km away	0 (0)	5 (17.24)	2 (50)	1 (10)	
More than 100 km away	0 (0)	0 (0)	0 (0)	1 (10)	
Total	32 (100)	29 (100)	4 (100)	10 (100)	

As for weekly care, this is performed mainly by adult children (48.6%), other relatives (32.4%), and neighbors (13.5%); the caregivers are predominantly female (65.5%) and most live less than a kilometer away (48.2%). As shown in **Table 3**, as the frequency of care decreases, the distance between the caregiver and the person cared for increases. To explain and model the availability of informal carers for older persons in need of care, binary logistic models were used (Model 1—all informal care, Model 2—inside care, and Model 3—outside care). OR and CI of statistically significant variables are presented in **Table 4**.

Model 1 ($G_2 = 78,075; p < 0.001$) has an explanatory capacity of 76%, with a sensitivity of 75.6% and a specificity of 76.3%. The corresponding values for Model 2 are $G_2 = 46,145 (p < 0.001)$, 78.8%, 71.4%, and 81.6% and for Model 3 are $G_2 = 41,008 (p < 0.001)$, 63.3%, 92.4%, and 50.3%.

Model 1 presents age, marital status, and limitations perceived in ADL as significant variables. Thus, it is observed that people aged 85–99 years have a 13.1 times higher probability of being informally cared for than those aged 65–69 years old. On the other hand, an older person living without a spouse is 5.1 times more likely to be informally cared for than an older person living with a spouse. It was also shown that older persons that perceive severe restrictions in their ADL have a probability 8.8 times higher of being informally cared for than those that perceive no limitation or little limitation in their ADL.

Model 2 identifies age and limitations perceived in ADL as significant variables: people aged 85–99 years have an 8.7 times greater likelihood of being informally cared for by someone within the household than people 65–69 years old. People aged 80–84 are 5.1 times more likely to be informally cared for than those aged 65–69 years old. Those that are severely limited are 6.6

times more likely to be cared for by an inside carer than those with little or no limitations in ADL.

Model 3 identifies education, marital status, perceived limitations in ADL, and the presence of chronic disease as significant variables. An older person with a secondary level of education is 9.4 times more likely to be cared for by an outside carer than an older person with no education. An older person living without a spouse is 2.8 times more likely to have outside care than those who live with their spouse. The results also show that an older person that perceives severe limitation in ADL is 2.3 times more likely to have outside care than those who perceive little or no limitation. Finally, older people with chronic disease have a 4.8 times higher probability of having outside care than those who are not chronically ill.

DISCUSSION

The majority of the informally cared for dependent elderly live with their main caregiver (53.3%). This result is expected, because older age groups are probably more dependent and in need of more frequent care and supervision in their daily activities. Similar studies (10) have shown that in Southern Europe, the main caregivers live inside the household. On the other hand, informal care is predominantly provided by family members (79.3%) (6, 18). Originally, it is the absence of a spouse that seems to influence the use of outside care, i.e., not having the possibility of being cared for by a spouse increases the probability of having a carer from outside the household.

Regarding outside care, it is mostly provided by adult children (38.6%), something that is also mentioned in the literature (10, 19). The main caregivers living outside the household are

TABLE 4 | Model 1, 2, and 3—results from the logistic regression analyses.**Model 1—availability of informal care**

Independent variables	Crude odds ratio (95% CI; p)	Adjusted odds ratio ^a (95% CI; p)	Forward LR model, ^b odds ratio (95% CI; p)
Age			
65–69 years ^c	—	—	—
70–74 years	0.498 (0.228:1.087; p = 0.08)	—	0.461 (0.149:1.433; p = 0.181)
75–79 years	1.290 (0.644:2.585; p = 0.473)	—	1.532 (0.576:4.078; p = 0.393)
80–84 years	2.922 (1.289:6.623; p = 0.010)	—	1.437 (0.475:4.345; p = 0.520)
85–99 years	10.271 (2.847:37.050; p = 0.001)	—	13.173 (2.772:62.601; p = 0.001)
Perceived limitations in the ADL			
Little or no limitation ^c	—	—	—
Severely limited	6.429 (1.904:6.616; p = 0.001)	6.481 (3.555:11.813; p = 0.001)	8.840 (3.958:19.612; p = 0.001)
Marital status			
Married and living without a spouse ^c	—	—	—
Does not live with the spouse	2.581 (1.483:4.493; p = 0.001)	1.933 (1.025:3.646; p = 0.042)	5.100 (2.288:11.371; p = 0.001)

Model 2—availability of informal care from someone inside the household

Independent variables	Raw odds ratio (95% CI; p)	Adjusted odds ratio ^a (95% CI; p)	Forward LR model, ^b odds ratio (95% CI; p)
Age			
68–69 years ^c	—	—	—
70–74 years	0.466 (0.189:1.148; p = 0.097)	—	0.593 (0.128:2.742; p = 0.504)
75–79 years	1.156 (0.543:2.459; p = 0.707)	—	1.704 (0.490:5.921; p = 0.402)
80–84 years	3.263 (1.544:6.895; p = 0.002)	—	5.136 (1.471:17.930; p = 0.010)
85–99 years	6.200 (2.465:15.592; p = 0.001)	—	8.743 (2.236:34.180; p = 0.002)
Perceived limitations in the ADL			
Little or no limitation ^c	—	—	—
Severely limited	6.768 (3.843:11.919; p = 0.001)	6.414 (3.512:11.714; p = 0.001)	6.652 (2.236:34.180; p = 0.001)

Model 3—availability of informal care from someone outside the household

Independent variables	Raw odds ratio (95% CI; p)	Adjusted odds ratio ^a (95% CI; p)	Forward LR model, ^b odds ratio (95% CI; p)
Educational level			
No education ^c	—	—	—
First level (4 years)	0.813 (0.424:1.559; p = 0.533)	0.896 (0.453:1.772; p = 0.752)	0.945 (0.446:2.003; p = 0.883)
Second (2 years) and third level (3 years)	0.779 (0.305:1.991; p = 0.602)	0.810 (0.292:2.251; p = 0.687)	1.224 (0.39:3.846; p = 0.729)
Secondary education	1.633 (0.486:5.484; p = 0.428)	1.543 (0.412:5.781; p = 0.520)	9.436 (1.665:53.472; p = 0.011)
Higher education	0.272 (0.056:1.312; p = 0.105)	0.239 (0.046:1.232; p = 0.087)	0.253 (0.048:1.324; p = 0.104)
Perceived limitations in the ADL			
No limitation or little limitation ^c	—	—	—
Severely limited	2.923 (1.680:5.088; p = 0.001)	2.937 (1.635:5.274; p = 0.001)	2.316 (1.155:4.644; p = 0.018)
Chronic illness			
No ^c	—	—	—
Yes	3.370 (1.615:7.035; p = 0.001)	1.424 (0.745:2.722; p = 0.285)	4.779 (1.668:13.691; p = 0.004)
Marital status			
Lives with the spouse ^c	—	—	—
Does not live with the spouse	3.165 (1.799:5.567; p = 0.001)	2.940 (1.492:5.795; p = 0.002)	2.772 (1.424:5.396; p = 0.003)

^aAdjusted to gender and age.^bForward model LR, embodying all the variables under analysis.^cReference class.

female. This is shown in several reports on Europe, especially Southern Europe (4, 9, 10, 20).

The results show that the main recipients are older women limited in their ADL, chronically ill, and of advanced age. The literature shows that women have a higher life expectancy; however, the quality of life after age 65 declines substantially due to limitations in ADL and chronic illness (21).

The main caregivers among coresident caregivers are spouses (55.5%). Furthermore, geographical distance is

extremely relevant in determining the frequency of care. Caregivers that care occasionally live outside the household. This shows that there is a nuclearization of the family, supporting the argument made on changes in family structure (10, 22–24).

In addition to the characterization of informal caregivers, our study aims to highlight the limitations of the current model of care. A significant proportion (39.5%) of the dependent elderly do not receive any type of informal care. The literature highlights

the limitations of the current model of long-term care imposed by changes in family structures (10, 22–24).

Regarding the availability of inside care (all care, inside or outside), one variable is consistently identified: the limitation perceived in ADL, and the higher the limitation is perceived, the greater the availability of informal carers.

People aged 80–99 years are more likely to have inside care, and older persons aged 85–89 years are more likely to have informal care. Other authors (4, 10, 19, 25) state that it is mainly the most elderly and therefore those who are more dependent who have more access to an informal caregiver. Thus, informal caregivers predominantly help the most vulnerable, dependent and older persons.

In the first and third models, the variable living without a spouse influences the availability of an informal caregiver; this means that in the absence of a spouse, older people are more likely to be informally cared for and cared for by an outside carer. Older persons residing without a spouse receive help from non-resident caregivers. Regarding the first model, it may be the fact that the spouses also have functional limitations which prevents them from providing care to their spouses. On the other hand, it turns out that being married and living with their spouse is not decisive for obtaining help from informal caregivers. This may be related to the similar percentage of married older persons and those living with a spouse among those without informal help. This does not mean that spouses do not provide care, but the marital status does not explain the availability of informal caregivers. Other studies (10, 23) reflect the same relationship between informal care and marital status, explaining that the care from a spouse is sometimes not regarded by the older person as care, and this influences the answers of the older person.

The third model has two explanatory variables that differ from the other two models: level of education and the presence of chronic disease. Older people with chronic illness are more likely to have informal care (4, 25). Older people with secondary and postsecondary education are more likely to be cared for by someone from outside, mainly by a housekeeper (7.56%). Similar data were found in a study on the Spanish situation in which users with secondary and postsecondary education are more likely to have paid care from paid domestic workers (26).

Finally, it appears that the number of children is not decisive for receiving help from informal caregivers. It is not the amount of available resources that determines whether or not there is access to long-term care. Daatland (27) states that it is the quality of the relationship between parents and children that favors the assumption of the caregiver role by the children and not the number of children.

In general the results of this study are aligned with the literature, reinforcing the internal and external validity of this study, and adding scientific evidence (namely through the magnitude of the results) to this study of this issue. Nevertheless, we would like to emphasize that these results should be carefully interpreted and generalized due to the fact that the sample under analysis is limited. The wide range of some confidence intervals reflects the uncertainty of these results. Additionally, data collection was based on self-report questionnaires (for

instance, the perceived limitations in ADL and the presence of chronic illness variables) and participants may not have responded truthfully, either because they cannot remember (memory bias) or because they wish to present themselves in a more socially acceptable manner (social desirability bias). The absence of some relevant variables referred to in the literature (economic status, availability of formal care, health status of care giver, among others) also constitutes a limitation of this study.

CONCLUSION

Based on this study, it appears that the informal long-term care sector in Portugal is primarily aimed at older people with severe limitations in their ADL and at the chronically ill, particularly older women. The absence of a spouse tends to mean that someone from outside the household responds to the need for care. Our study also shows that there are a significant proportion of dependent older persons without any kind of informal care (39.5%), which supports the argument that the current limitations of the long-term care model are imposed by changes in family structures.

Additionally, the main informal caregivers are family members and mostly women. However, the gender gap is not as clear when the primary caregiver is the spouse. Nonetheless, women represent 68% of the dependent elderly. Regarding adult children caregivers, the majority are female (71.4%). Among the caregivers who live with the older person, spouses are the main caregivers, in contrast to caregivers who live outside the household, where the majority are adult children and other relatives. It seems that there is a marked nuclearization of the family, supporting the argument in terms of the changes in family structure. On the other hand, the solidarity networks are mainly composed of family members. Regarding geographical distance, this is extremely relevant to the frequency of care, i.e., the closer the caregiver lives, the higher the frequency of care provided.

Taken as a whole, the current model of care, based on the informal long-term care sector, leaves out a significant proportion of dependent older persons and it seems that it is only in cases of extreme need that aid arises, i.e., only the most dependent and dependent older persons are helped by the informal care sector.

The results of this study show a critical situation for both social groups (older persons and caregivers) and an alarming prospect in the near future (a continuously aging society, a scarcity of young informal caregivers, the reduced availability of informal caregivers to care for the older person), something that is a global challenge, since many countries have the same characteristics. A new approach for long-term care is urgently required, a greater provision of public services and formal care is needed, especially at community and household level rather than institutionalization, allowing the elderly to live in their own context as long as is possible and promoting and safeguarding relationships and responsibilities with (and of) informal caregivers. Complementary studies on formal care are needed to understand the full context and to carefully evaluate

different possible approaches (including elderly, caregivers and social/health services).

ETHICS STATEMENT

The SHARE study (fourth wave) was subject to several ethics reviews: The Ethics Committee of the University of Mannheim, Germany, Ethics Council of the Max Planck Society and by national ethics committees or institutional review boards whenever this was required. This study was conducted in full

accordance with the World Medical Association Declaration of Helsinki. Written consents from all participants involved in this study were obtained.

AUTHOR CONTRIBUTIONS

MP designed the research, conducted the data analyses, and wrote the first draft, and reviewed and approved the final manuscript. CN designed the research, supervised the data analyses, and reviewed and approved the final manuscript.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Selfie Aging Index: An Index for the Self-assessment of Healthy and Active Aging

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Introduction: Governments across Europe want to promote healthy and active aging, as a matter of both public health and economic sustainability. Designing policies focused on the most vulnerable groups requires information at the individual level. However, a measure of healthy and active aging at the individual level does not yet exist.

Objectives: This paper develops the *Selfie Aging Index* (SAI), an individual-level index of healthy and active aging. The SAI is developed thinking about a tool that would allow each person to take a *selfie* of her aging status. Therefore, it is based entirely on self-assessed indicators. This paper also illustrates how the SAI may look like in practice.

Methods: The SAI is based on the Biopsychosocial Assessment Model (MAB), a tool for the multidimensional assessment of older adults along three domains: biological, psychological, and social. Indicators are selected and their weights determined based on an ordered probit model that relates the MAB indicators to self-assessed health, which proxies healthy and active aging. The ordered probit model predicts the SAI based on the estimated parameters. Finally, predictions are rescaled to the 0–1 interval. Data for the SAI development come from the Study of the Aging Profiles of the Portuguese Population and the Survey of Health, Aging, and Retirement in Europe.

Results: The selected indicators are BMI, having difficulties moving around indoors and performing the activities of daily living, feeling depressed, feeling nervous, lacking energy, time awareness score, marital status, having someone to confide in, education, type of job, exercise, and smoking status. The model also determines their weights.

Conclusion: Results shed light on various factors that contribute significantly to healthy and active aging. Two examples are mental health and exercise, which deserve more attention from individuals themselves, health-care professionals, and public health policy. The SAI has the potential to put the individual at the center of the healthy and active aging discussion, contribute to patient empowerment, and promote patient-centered care. It can become a useful instrument to monitor healthy and active aging for different actors, including individuals themselves, health-care professionals, and policy makers.

Keywords: **Selfie Aging Index, healthy aging, active aging, aging index, multidimensional index, biopsychosocial assessment model, ordered probit model, self-assessed health**

I have enjoyed greatly the second blooming ... suddenly you find – at the age of 50, say – that a whole new life has opened before you.

Agatha Christie

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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 31 August 2017

Accepted: 07 December 2017

Published: 22 December 2017

Citation:

Gonçalves J, Gomes MI, Fonseca M,
Teodoro T, Barros PP and
Botelho M-A (2017) Selfie Aging
Index: An Index for
the Self-assessment of Healthy
and Active Aging.
Front. Med. 4:236.
doi: 10.3389/fmed.2017.00236

INTRODUCTION

In 2016, people aged 55 and over (55+) accounted for 32% of the European Union's (EU) population, and people aged 65 and over (65+) for 19%. The EU countries with the oldest populations are Italy, Germany, Greece, and Portugal, where the 55+ represent 34–35% of the population and the 65+ represent 21–22% (own calculations based on Eurostat data). These numbers are expected to rise in the future, challenging EU governments to promote the healthy and active aging of their populations, as a matter of both public health and economic sustainability.

The concept of healthy and active aging was defined by the World Health Organization (WHO) as the process of optimizing opportunities for health to enhance quality of life as people age. The word “healthy” refers to physical, mental, and social well-being, while the word “active” refers to continuing participation in social, economic, cultural, spiritual, and civic affairs (1). It should be noted that some studies focus specifically on healthy aging or active aging alone. Other studies refer only to healthy aging or active aging but possibly mean both healthy and active aging.

To design policies to promote healthy and active aging, as well as to track their progress, measurement is crucial. With that in mind, the European Commission (EC) and the United Nations Economic Commission for Europe introduced the Active Aging Index (AAI) in 2012. The AAI is a multidimensional index that measures the level to which older people (55+) live independent lives, participate in the labor market and social activities as well as their capacity to actively age (2). As its name suggests, the AAI focuses specifically on active aging. It conceptualizes active aging as “the situation where people continue to participate in the formal labor market as well as engage in other unpaid productive activities and live healthy, independent, and secure lives as they age” (3). The AAI represents the first initiative to measure healthy and active aging. It has inspired the measurement of healthy and active aging around the world, which clearly shows the increasing interest in the aging phenomenon (4, 5).

The AAI provides a societal perspective of the aging phenomenon and is a useful tool for top-down policy design. However, it only allows for the comparison of average levels of active aging across countries. Designing policies focused on the most vulnerable groups requires information about the distributions of healthy and active aging within countries, as well as information about how healthy and active aging correlates with individual characteristics. To obtain such information, we need to measure healthy and active aging at the individual level. To that end, two recent studies develop individual-level indices of active aging based on the AAI conceptual framework (6, 7).

It is not clear that the AAI conceptual framework, developed to capture active aging at the aggregate level, is appropriate to measure active aging at the individual level. The four domains of the AAI are (1) employment, (2) participation in society, (3) independent, healthy, and secure living, and (4) capacity and enabling environment for active aging. At the individual level, these domains include indicators such as (1) being employed, (2) looking after grandchildren, (3) worrying about vandalism and crime, and (4) Internet use (7). Such indicators do not appear

relevant for example in a study about older people's perceptions of active aging. According to that study, individuals associate active aging with maintaining physical health and functioning, leisure and social activities, mental functioning and activity, and social relationships and contacts (8). However, this apparent discrepancy does not imply that the AAI conceptual framework is inappropriate for an individual-level index. In fact, such discrepancy may simply reflect different perspectives of older people—the “insiders”—and researchers—the “outsiders”—as has been documented [e.g., Ref. (9)].

The AAI-based individual-level indices have other potential limitations. First, the expert group who developed the AAI chose the weights of the indicators, which implies value judgments. Second, in the individual-level indices all indicators are dichotomized. Such strategy does not take full advantage of the variations in the data.

Focusing specifically on healthy aging, Lara et al. (10) provide a list of measures that capture key features of healthy aging, grouped into five domains: physiological and metabolic health, physical capability, cognitive function, social well-being, and psychological well-being (e.g., cardiovascular function, strength, episodic memory, mental health, perceived social support). Kuh et al. (11) conceptualize healthy aging within a life-course framework, distinguishing between healthy biological aging and changes in psychological and social well-being, and provide a review of objective measures of physical capability (e.g., grip strength, walking speed). To our knowledge, healthy aging has not been operationalized in any multidimensional index.

This paper develops the *Selfie Aging Index* (SAI). The SAI is based on a conceptual framework that tries to capture both healthy and active aging at the individual level. Its underlying methodology allows the weights to be determined by the variations and correlations present in the data, avoiding value judgments. The SAI is also innovative in that it may be entirely self-assessed, thinking about future applications of the SAI as a tool for older people to track their aging status. Thus, clinical indicators or measurements that require unusual tools are not considered (e.g., cardiovascular function, grip strength). Finally, this paper also illustrates how the SAI can be used in practice. To the absolute value of the SAI, which allows individuals to keep track of their aging status over time, we add a relative component that allows individuals to compare themselves to their peers.

MATERIALS AND METHODS

Conceptual Framework

The SAI is based on the Biopsychosocial Assessment Model [MAB—*Modelo de Avaliação Biopsicosocial*, registered copyright No 4065/2007 (12)]. The MAB is a tool for the multidimensional assessment of older adults. It consists of several indicators grouped into three domains, for example ability to conduct daily activities such as bathing or eating (biological domain), feelings of depression or nervousness (psychological domain), and having someone to confide in (social domain). The full list of indicators is available in Table S1 in Supplementary Material. The domains and subdomains of the MAB capture the various elements of the

conceptual definition of healthy and active aging of the WHO (see Introduction). Thus, the MAB seems suitable as a starting point to operationalize the measurement of healthy and active aging at the individual level. The MAB has been extensively validated and is currently used by the National Network of Continued Integrated Care (RNCCI—*Rede Nacional de Cuidados Continuados Integrados*) to characterize inpatients of the Portuguese healthcare system (13). Unlike previous conceptual models, the MAB does not rely on clinical indicators or measurements that require unusual tools. This is appealing when we think about potential applications of the SAI as a tool for individuals to self-assess their aging status.

Statistical Method

To construct the SAI, we need to select a subset of the MAB indicators. The original MAB includes a long list of indicators (see Table S1 in Supplementary Material), which is incompatible with a simple self-assessment tool for older adults. We also need to determine the weights for the aggregation of the indicators into a single index. Estimating an ordered probit model allows us to do both things, while avoiding value judgments in the selection of indicators and their respective weights. Indicators are selected based on their statistical significance and contribution to model fit, and the weights are determined based on correlations between the indicators. Another advantage of the ordered probit model is that it easily deals with any type of indicator, continuous or categorical. Ordered probit models have been used to construct health indices, in order to have a single continuous variable to measure health status [e.g., Ref. (14)].¹ The idea behind this method is predicting a latent variable—the SAI—based on the MAB indicators. To do this, we use self-assessed health in the left hand-side of the ordered probit model [i.e., self-assessed health works as a kind of proxy for healthy and active aging, following, for example, Ref. (15, 16)]. The MAB indicators appear as right hand-side variables. Though self-assessed health consists in individuals' ratings of their health in a scale (e.g., very bad, bad, fair, good, very good), the ordered probit model predicts a continuous variable based on the estimated parameters. The last step in computing the SAI is rescaling that predicted variable to a more intuitive 0–1 interval. This is done using the theoretical limits of the latent variable, which can be computed as the predicted values when all MAB indicators are set at their least and most favorable values. In sum, the SAI score is obtained by plugging the individual's characteristics in the ordered probit model, obtaining the prediction in the latent scale, and rescaling it to the 0–1 interval.

Data

We use data from the Study of the Aging Profiles of the Portuguese Population [EPEPP—*Estudo do Perfil de Envelhecimento da População Portuguesa* (17–19)] and the Survey of Health, Aging and Retirement in Europe (SHARE; Wave 4 (20)). The EPEPP was conducted specifically to evaluate the aging status of Portuguese older adults based on an earlier version of the MAB.

It was designed to be representative of the Portuguese population aged 55+ and covered about 2,700 individuals, interviewed in 2005–2006. The SHARE is a broader survey of European older adults that also contains most of the MAB indicators. It was designed to be representative of the 50+ population, but we only consider individuals aged 55+. The SHARE includes about 1,700 individuals aged 55+ in Portugal, interviewed in 2011.

There are some differences between the two datasets in self-assessed health and the MAB indicators. Self-assessed health has four levels in the EPEPP survey (bad/very bad, poor, fair, good/very good), and five levels in the SHARE survey (poor, fair, good, very good, excellent). In the EPEPP, health complaints are classified into complaints that affect or not mobility, complaints regarding eyesight, and complaints regarding hearing. In the SHARE, the long list of health conditions available allows for a much more detailed analysis of health complaints, including for example complaints about the musculoskeletal system or the respiratory system. A few MAB indicators are lacking in each dataset. The EPEPP does not include indicators of lack of interest or trouble sleeping, and the SHARE does not include waist measurement, variables related with falls, measures of mobility outdoors or climbing stairs, spatial awareness, or time alone in a 24-h period. Table S1 in Supplementary Material provides the link between the MAB indicators and the questions in the EPEPP and SHARE.²

Procedure

Given the differences between the EPEPP and SHARE surveys outlined above, the analyses of the two datasets are complementary. Estimating separate ordered probit models allows us to determine if the same MAB indicators appear relevant for healthy and active aging in both samples, providing external validity to our methodology. This is especially informative given that the EPEPP was conducted prior to the financial crisis and the SHARE was conducted after the crisis, i.e., the individuals in each sample faced different socioeconomic environments. Estimating separate models is the first stage in our procedure. All MAB indicators available in each survey are used. The original coding of the answers is maintained, in order to take full advantage of the information available. For example, the question "Over the past month, did you feel sad or depressed?" has four possible answers in the EPEPP survey ("No," "Little time," "Half of the time," and "Most of the time"), and two possible answers in the SHARE survey ("Yes" and "No").

In the second stage, the two datasets are combined. All MAB indicators available in both surveys are considered, except for health complaints (including complaints about the emotional status) because the corresponding questions are not posed in comparable ways (see Data and Table S1 in Supplementary Material). Combining the datasets requires recoding the answers to the questions that are posed in different ways in the two surveys. The new self-assessed health variable has three levels: poor/bad/very bad, fair, good/very good/excellent. Table S2 in

¹Ryser V-A, Weaver F, and Gonçalves J (Forthcoming). Health-related inequalities in life satisfaction among the 50+ population in Europe: evidence from SHARE. *Swiss J Sociol.*

²Co-authors of this study are involved in the EPEPP study and the SHARE project in Portugal and have thorough knowledge of the datasets.

Supplementary Material presents the new coding for all variables. Combining the datasets increases the sample size substantially, enhancing statistical power.

In the third stage, the model estimated in the combined dataset is simplified by eliminating the MAB indicators that do not contribute to improve model fit. To do this, the indicators are progressively added to the model according to their contribution to the log-likelihood (i.e., stepwise regression). With each addition, we assess the likelihood ratio test, as well as Akaike's and the Bayesian Information Criteria (AIC, BIC). We consider that an indicator does not contribute to improve model fit if the null hypothesis of the likelihood ratio test is not rejected at the 10% significance level and the value of the AIC or the BIC increases.³ The SAI is calculated based on the resulting simplified model.

Recoding the variables when combining the two datasets may introduce bias. Furthermore, the EPEPP and SHARE surveys were conducted several years apart under different socioeconomic environments, which may affect the relationships between the variables. To explore these potential issues, we estimate an ordered probit model, including interactions between the MAB indicators and a binary indicator of the observation's source (EPEPP or SHARE). Checking whether the associations between the MAB indicators and self-assessed health differ according to the source of data gives an indication of the extent of the problem. Given that one of the recoded variables is self-assessed health, we also test whether the estimated cutoffs significantly differ according to the dataset.

Validity Checks

To investigate the validity of the SAI, we assess its value as a predictor of several outcomes, namely the probability of having had a doctor visit and number of doctor visits over the previous 12 months, mental health (EURO-D depression scale), number of chronic conditions, and number of symptoms. The EURO-D depression scale varies between 0 (not depressed) and 12 (very depressed) and is essentially a count of 12 items, including for example feeling guilty about anything, having no hopes for the future, and lacking appetite. The number of chronic conditions is a count of up to ten conditions including for example hypertension, diabetes, and arthritis. The number of symptoms is a count of up to 12 symptoms including for example pain, incontinence, and fatigue. None of these outcomes is an indicator in the SAI. We regress each outcome on the SAI and evaluate the statistical significance of the associated coefficient as well as the R^2 . The probability of having a doctor visit and the number of doctor visits are available in both surveys, but the remaining outcomes are available only in the SHARE.

The SAI in Practice

In order to illustrate how the SAI may look like in practice, we calculate SAI scores for several hypothetical individuals. The absolute value of the SAI may be used by individuals to monitor

their aging status over time. To provide some context, we add a relative component that allows individuals to compare themselves to their peers. The individual SAI scores are displayed in the distribution of SAI scores of people aged ± 2 years. The larger sample size of the combined dataset allows us to have a significantly larger pool of peers for each individual in the dataset.

RESULTS

Estimation Results Using the EPEPP Sample

Results based on the EPEPP sample are presented in Table S3 in Supplementary Material. The MAB indicators with a statistically significant coefficient, at the 10% significance level or lower, are health complaints, obesity (captured by waist measurement), having fallen due to internal causes, such as fainting, having sequelae from falling that affect mobility, needing someone's help to perform the activities of daily living (ADLs), self-assessed emotional status, feeling depressed, feeling nervous, lacking energy, spending less than 8 h per day alone, having someone to confide in, exercising, and smoking status. Most of these variables have the expected associations with self-assessed health (i.e., the respective estimated coefficients have the expected signs). The remaining variables have no significant associations with self-assessed health. Looking at the magnitudes of the estimated coefficients, we can see that the variables with the largest associations with self-assessed health are complaints that do not affect mobility, self-assessed emotional status, feeling depressed most of the time, exercising more than 4 h per week, and smoking at present (coefficients larger than 0.3 in absolute value).

Estimation Results Using the SHARE Sample

Table S4 in Supplementary Material presents the results based on the SHARE sample. The MAB indicators that have a statistically significant association with self-assessed health are health complaints except for those regarding the urinary system, difficulties moving around indoors and performing the ADLs, being depressed, being nervous, having trouble sleeping, lacking energy, marital status, living with someone else, having someone to confide in, education, and exercising. All of these variables except for living with someone else have the expected associations with self-assessed health. The coefficients of the remaining variables are not statistically significant. The variables with the largest associations with self-assessed health are complaints about hearing, the circulatory system, and the musculoskeletal system, having difficulties moving around indoors, and being divorced.

Estimation Results Using the Combined Sample

Table 1 presents the results based on the combined dataset. Model 1 includes all MAB indicators available in both datasets. Model 2 excludes the indicators that do not contribute to improve the overall fit of the model. The excluded indicators are difficulties performing the instrumental activities of daily living (IADLs) and living with someone else, as well as age and gender. Including

³The likelihood ratio test is a statistical test used to compare the goodness of fit of two nested models. Under the null hypothesis, the simpler model is better, because it fits the data as well as the more complex one, but is more parsimonious. Lower values of the AIC and BIC indicate better model fit.

these variables in the model does not significantly increase the log-likelihood and the value of the AIC or the BIC increases, indicating worse fit (Table S5 in Supplementary Material).

We focus on the results of Model 2. The average marginal effects are shown in **Table 2**. For instance, on average and keeping all else constant, an obese person is seven percentage points less likely to report good, very good, or excellent health than a normal weight person. Having difficulties moving around indoors decreases the probability of reporting the highest level of health by nine percentage points. All three emotional status indicators have sizeable associations with self-assessed health. For example, feeling depressed decreases the likelihood of reporting good, very good, or excellent health by about ten percentage points. Having someone to confide in increases the probability of reporting the highest level of health by almost five percentage points. Engaging in moderate physical activities, such as going for a walk, contributes even more to the probability of reporting the highest level of

health than engaging in more vigorous activities, such as sports (about nine and six percentage points, respectively). Taking into account the sample means and proportions, presented in Table S6 in Supplementary Material, all estimated associations are sizeable. Finally, on average individuals from the SHARE sample are more likely to report the highest level of health.

Including interactions between the MAB indicators and a binary indicator of the observation's source (EPEPP or SHARE) produces the results presented in Table S7 in Supplementary Material. Out of the 20 interaction terms, only 4 are statistically significant, indicating that most associations between the MAB indicators and self-assessed health do not depend on the source of data. If allowed to differ according to the data source, the cutoffs are also not significantly different at the 5% significance level (results available upon request).

TABLE 1 | Estimation results of the ordered probit model using the combined sample.

	Model 1	Model 2
	Coefficient (SE)	Coefficient (SE)
Gender: female	-0.072 (0.048)	
Age	-0.079** (0.036)	
Age ²	0.001** (0.000)	
BMI (ref: normal weight)		
Undernourished	-0.115 (0.244)	-0.115 (0.240)
Overweight	-0.114** (0.050)	-0.106** (0.049)
Obese	-0.268*** (0.055)	-0.250*** (0.054)
Difficulties moving around indoors	-0.340*** (0.108)	-0.322*** (0.105)
Number of difficulties in the activities of daily living	-0.127*** (0.022)	-0.139*** (0.021)
Number of difficulties in the instrumental activities of daily living	-0.032 (0.023)	
Depressed	-0.363*** (0.047)	-0.365*** (0.047)
Nervous	-0.209*** (0.044)	-0.206*** (0.043)
Lack of energy	-0.345*** (0.051)	-0.349*** (0.051)
Time awareness	0.069* (0.036)	0.069** (0.037)
Marital status (ref: widowed)		
Married	0.046 (0.074)	0.014 (0.055)
Single	-0.126 (0.109)	-0.094 (0.109)
Divorced/separated	0.229** (0.111)	0.210** (0.107)
Lives with someone else	-0.076 (0.077)	
Has someone to confide in	0.163** (0.077)	0.164* (0.076)
Years of education	0.064*** (0.018)	0.065*** (0.018)
Years of education ²	-0.001 (0.001)	-0.001 (0.001)
Type of job: manual work	-0.152*** (0.045)	-0.147*** (0.044)
Vigorous physical activities	0.186*** (0.045)	0.199*** (0.045)
Moderate physical activities	0.306*** (0.044)	0.309*** (0.043)
Smoking status (ref: non-smoker)		
Former smoker	0.034 (0.055)	0.055 (0.051)
Current smoker	0.226*** (0.052)	0.241*** (0.051)
SHARE	0.408*** (0.050)	0.427*** (0.048)
Cutoff 1	-3.204** (1.268)	-0.309* (0.169)
Cutoff 2	-1.586 (1.267)	-1.303*** (1.171)
Observations	3,606	3,643
Pseudo R ²	0.138	0.135

Robust SEs in parentheses.

*, **, and *** denote statistical significance at the 10, 5, and 1% significance levels.

TABLE 2 | Marginal effects in Model 2.

	Probability of reporting		
	Poor, bad, or very bad health	Fair health	Good, very good, or excellent health
	Average marginal effect (SE)	Average marginal effect (SE)	Average marginal effect (SE)
BMI (ref: normal weight)			
Undernourished	0.029 (0.060)	0.004 (0.008)	-0.032 (0.067)
Overweight	0.027** (0.012)	0.003** (0.002)	-0.030** (0.014)
Obese	0.062*** (0.014)	0.008*** (0.002)	-0.070*** (0.015)
Difficulties moving around indoors	0.080*** (0.026)	0.010** (0.004)	-0.091*** (0.029)
Number of difficulties in the activities of daily living	0.035*** (0.005)	0.004*** (0.001)	-0.039*** (0.006)
Depressed	0.091*** (0.012)	0.012*** (0.003)	-0.103*** (0.013)
Nervous	0.051*** (0.011)	0.007*** (0.002)	-0.058*** (0.012)
Lack of energy	0.087*** (0.013)	0.011*** (0.003)	-0.098*** (0.014)
Time awareness	-0.017* (0.009)	-0.002* (0.001)	0.019* (0.010)
Marital status (ref: widowed)			
Married	-0.003 (0.014)	-0.000 (0.002)	0.004 (0.016)
Single	0.023 (0.027)	0.003 (0.004)	-0.026 (0.031)
Divorced/ separated	-0.052* (0.027)	-0.007* (0.004)	0.059* (0.030)
Has someone to confide in	-0.041** (0.019)	-0.005* (0.003)	0.046** (0.022)
Years of education	-0.016*** (0.004)	-0.002*** (0.001)	0.018*** (0.005)
Years of education ²	0.000 (0.000)	0.000 (0.000)	-0.000 (0.000)
Type of job: manual work	0.037*** (0.011)	0.005*** (0.002)	-0.041*** (0.012)
Vigorous physical activities	-0.050*** (0.011)	-0.006*** (0.002)	0.056*** (0.013)
Moderate physical activities	-0.077*** (0.011)	-0.010*** (0.002)	0.087*** (0.012)
Smoking status (ref: non-smoker)			
Former smoker	0.034 (0.055)	0.055 (0.051)	
Current smoker	0.226*** (0.052)	0.241*** (0.051)	
SHARE	0.408*** (0.050)	0.427*** (0.048)	
Cutoff 1	-3.204** (1.268)	-0.309* (0.169)	
Cutoff 2	-1.586 (1.267)	-1.303*** (1.171)	
Observations	3,606	3,643	
Pseudo R ²	0.138	0.135	

Robust standard errors in parentheses.

*, **, and *** denote statistical significance at the 10, 5, and 1% significance levels.

Calculating the SAI

Selfie Aging Index scores for all individuals in the combined dataset are calculated based on Model 2. Figure S1 in Supplementary Material shows the distributions of the SAI according to selected individual characteristics. It is important to note that the distributions are unconditional, i.e., there is no adjustment for other characteristics.

Validity Checks

Table S8 in Supplementary Material shows the results from regressions of the probability of having a doctor visit, number of doctor visits, mental health, number of chronic conditions, and number of symptoms on the SAI score. The associations between the SAI score and each outcome considered are negative, as expected. The *t*-statistics associated with the SAI coefficients are considerably high, indicating statistical significance at any conventional significance level. The *R*²s are also sizeable. These results reveal that the SAI is a strong predictor of the probability of having a doctor visit, number of doctor visits, mental health, number of chronic conditions, and number of symptoms.

DISCUSSION

Findings from the Ordered Probit Models

In general, the MAB indicators have the expected associations with self-assessed health. There are only a few exceptions. In the EPEPP model, having complaints about hearing has a positive estimated coefficient, and spending less than 8 h per day alone has a negative estimated coefficient. Spending less than 8 h per day alone may be capturing other unmeasured physical or cognitive limitations that require the person to be accompanied most of the time. Globally, the two counterintuitive signs may be due to multicollinearity. For example, hearing and vision complaints are highly correlated, and spending less than 8 h per day alone is highly correlated with needing auxiliary instruments to perform the ADLs as well as living with someone else. High correlations between included variables affect the efficiency of the estimators, which may result in unexpected estimates. Also intriguingly, former and current smokers rate their health better than those who never smoked. Smoking status may also be capturing unobserved characteristics. For instance, people aged 55+ who still smoke possibly never had any serious health condition that would induce them to quit. Former smokers may have quit in time to avoid serious health damages. In the SHARE model, living with someone else has an estimated negative association with self-assessed health. The reasons for that may be the same ones mentioned above regarding the negative estimated coefficient associated with spending less than 8 h per day alone in the EPEPP model. For example, living with someone else is highly correlated with marital status, which may introduce significant multicollinearity in the model. Finally, in the SHARE model divorced individuals tend to have higher SAI scores than married individuals. Again, this finding may be due to multicollinearity or unobserved characteristics related to both health and selection into divorce (e.g., urban or rural area of residence, traditional values such as the idea that marriage is for life).

The MAB indicators that stand out in both the EPEPP and SHARE models are health complaints, difficulties performing the ADLs, feeling depressed, feeling nervous, lacking energy, having someone to confide in, and exercising. This list includes indicators from all three domains of the MAB—biological, psychological, and social. Thus, a meaningful number of factors appear relevant in both models, providing external validity to our approach. It should be noted that lack of statistical significance of other MAB indicators may be attributable to the specific samples used or to lack of statistical power. It may also be the case that people simply do not consider some factors when asked to assess their health status. For instance, when self-evaluating their health status, people may be more likely to consider fear of falling, which is not measured here, than past falls, which is measured but not statistically significant.

Combining the two datasets allowed for improvements in statistical power, as the sample size increased substantially. It also implied two main drawbacks. First, several variables, including self-assessed health, had to be recoded. Still, our explorations suggest that this doesn't represent a significant problem. Second, we had to exclude health complaints. Health complaints appeared relevant in both the EPEPP and SHARE models. Excluding this indicator remains a drawback to be addressed in future work.

Difficulties performing the IADLs and living with someone else, as well as age and gender, were excluded from the final model based on statistical criteria. Conceptually and given our experience, there are some reasons why these variables may appear as not relevant for self-assessed health. The IADLs include tasks that some people do not have the ability to perform or are used to request help with, such as managing money and using transportation. Unlike difficulties in the ADLs, difficulties in the IADLs do not necessarily capture disability. Living with someone else may lose importance in our model because related variables, such as marital status and having someone to confide in, are included. Besides, one may argue that it is the need to live with someone else rather than living with someone else or not that is relevant for self-assessed health. Such need is determined by the individual's bad health and disability, which is captured by other variables in the model. Finally, age and gender may affect individuals' perception of their health status mainly due to external factors, e.g., social misconceptions such as the idea that older ages are necessarily associated with worse health. Once other biopsychosocial factors are taken into account, it seems plausible that age and gender should no longer play a role.

The individual SAI scores calculated based on Model 2 have the expected distributions according to most individual characteristics. A few distributions may appear intriguing because they are unadjusted for other characteristics. For example, men tend to have higher SAI scores than women. This may be partly explained by the male–female health-survival paradox—the phenomenon that women experience greater longevity but higher rates of disability and poor health than men at more advanced ages [e.g., Ref. (21)]. As seen above, once other characteristics are taken into account, there are no significant differences in self-assessed health due to gender. As discussed above, smoking status and marital status may be capturing both observed and unobserved characteristics, which may explain the higher SAI scores among

current and former smokers, as well as among divorced individuals. Finally, SAI scores tend to be higher in the SHARE sample than in the EPEPP sample. This may be partly related to the different socioeconomic environments that people faced in 2005–2006 and 2011 (before and after the financial crisis).

The SAI in Practice

If the SAI is to be a useful tool for individuals to assess their aging status, in addition to an absolute value, it should have a relative component. The absolute value allows monitoring one's aging status over time, while the relative component allows individuals to position themselves with respect to their peers. Thus, to illustrate how a tool based on the SAI might look like in practice, we consider ten hypothetical individuals, characterized in **Table 3**. The individuals' characteristics are chosen to illustrate how the

SAI changes as a result of changes in the various selected indicators. For each individual, we calculate his or her SAI score, and present it along with the distribution of the SAI among his or her peers (people aged ± 2 years in the sample) in **Figure 1**.

Consider for example Mary, a 68-year-old overweight woman. She has no difficulties moving around indoors or performing the ADLs. She is not depressed or nervous, and does not lack energy. She has a perfect score in time awareness. She is married and has someone to confide in. She has 4 years of education and had a manual job prior to retirement. She engages in moderate physical activities but not in more vigorous ones and does not smoke. Mary has a SAI score of 0.61, which puts her in the middle quintile of the distribution of the SAI among her peers (**Figure 1A**).

Take a second example, Michael, who is just like Mary except he is not in good shape emotionally. He has a SAI score of 0.44,

TABLE 3 | Characteristics of the hypothetical individuals.

Panel (A)

	Mary	James	Margaret	John	Michael
Age	68	78	78	78	68
BMI	Overweight	Overweight	Overweight	Overweight	Overweight
Difficulties moving around indoors	No	Yes	Yes	Yes	No
Number of difficulties in the activities of daily living (ADLs)	Zero	Five	Five	Five	Zero
Depressed	No	No	No	No	Yes
Nervous	No	No	No	No	Yes
Lack of energy	No	No	No	No	Yes
Time awareness	Four	Four	Four	Zero	Four
Marital status	Married	Married	Widowed	Widowed	Married
Has someone to confide in	Yes	Yes	No	No	Yes
Years of education	Four	Four	Four	Four	Four
Type of job: manual work	Yes	Yes	Yes	Yes	Yes
Vigorous physical activities	No	No	No	No	No
Moderate physical activities	Yes	No	No	No	Yes
Smoking status	Non-smoker	Non-smoker	Non-smoker	Non-smoker	Non-smoker
Database	EPEPP	EPEPP	EPEPP	EPEPP	EPEPP
Selfie Aging Index (SAI) score	0.61	0.36	0.32	0.27	0.44
Quintile (compared to individuals within ± 2 years of age)	3rd	1st	1st	1st	1st

Panel (B)

	Linda	Charles	Susan	Elisabeth	William
Age	58	58	58	68	58
BMI	Overweight	Overweight	Normal weight	Overweight	Overweight
Difficulties moving around indoors	No	No	No	No	No
Number of difficulties in the ADLs	Zero	Zero	Zero	Zero	Zero
Depressed	No	No	No	No	No
Nervous	No	No	No	No	No
Lack of energy	No	No	No	No	No
Time awareness	Four	Four	Four	Four	Four
Marital status	Married	Married	Married	Married	Married
Has someone to confide in	Yes	Yes	Yes	Yes	Yes
Years of education	Twelve	Twelve	Twelve	Four	Four
Type of job: manual work	No	No	No	Yes	Yes
Vigorous physical activities	No	No	Yes	No	No
Moderate physical activities	Yes	Yes	Yes	Yes	Yes
Smoking status	Non-smoker	Smoker	Non-smoker	Non-smoker	Non-smoker
Database	EPEPP	EPEPP	EPEPP	SHARE	EPEPP
SAI score	0.71	0.76	0.77	0.69	0.61
Quintile (compared to individuals within ± 2 years of age)	5th	5th	5th	5th	3rd

The characteristics that differ from those of Mary are in bold.

which puts him in the bottom quintile of the distribution of the SAI among his peers (**Figure 1E**). Besides comparing individuals with different characteristics, the SAI can be used to infer what

would happen if someone's characteristics changed. In this example, Michael's SAI score represents what we might expect of Mary's if her emotional status would deteriorate.

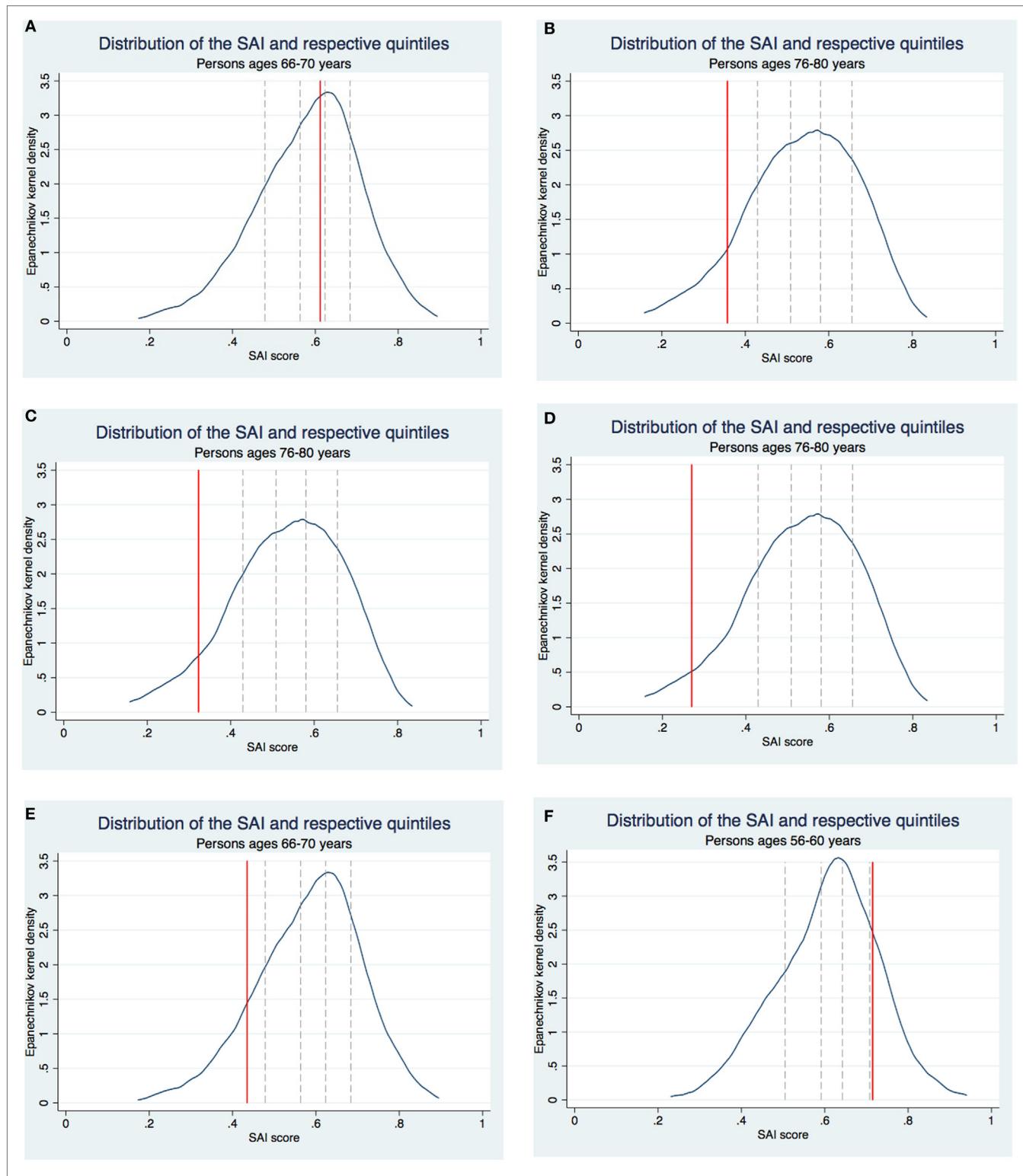


FIGURE 1 | Continued

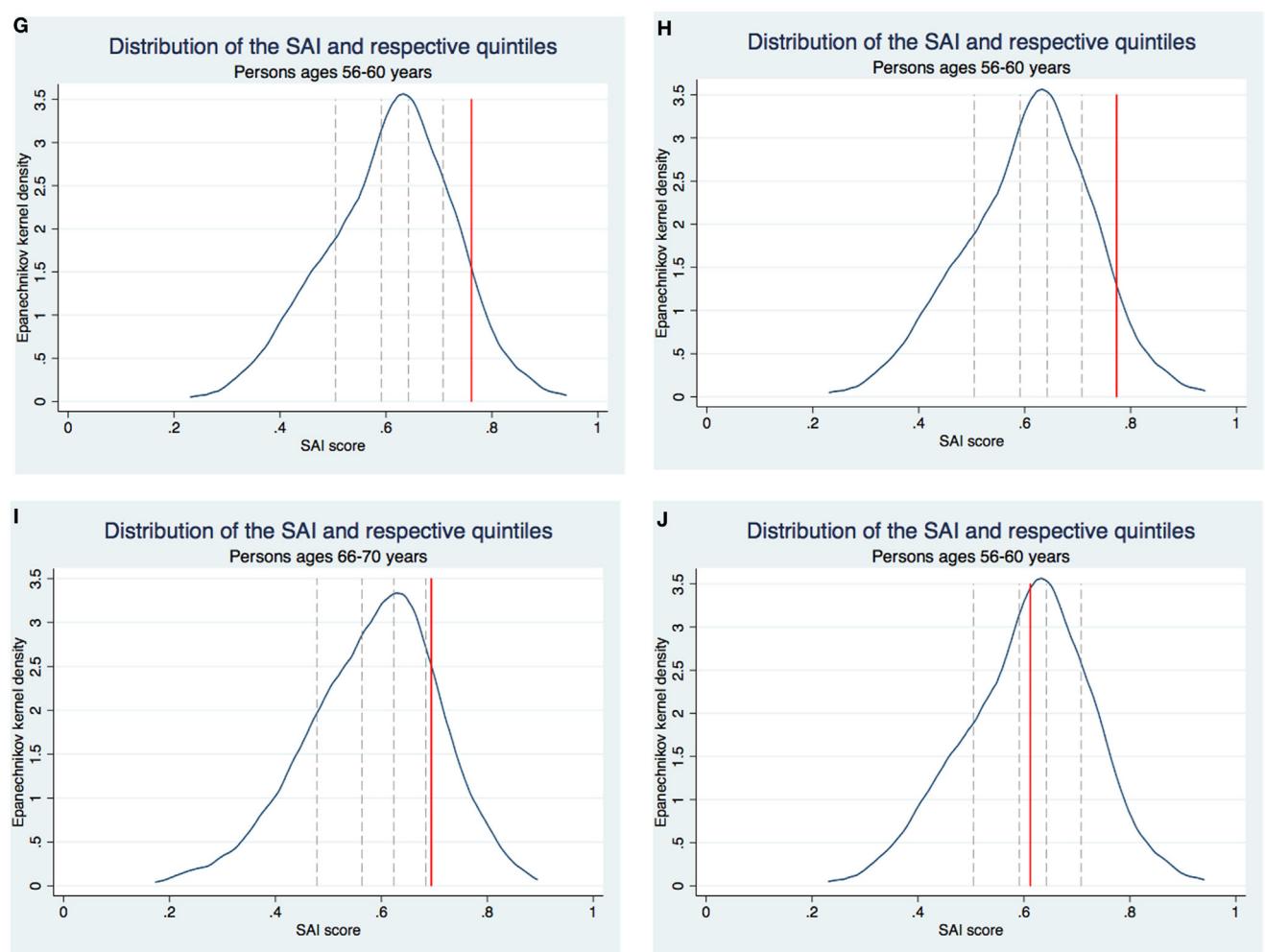


FIGURE 1 | Selfie Aging Index (SAI) scores of the hypothetical individuals. **(A)** Mary. **(B)** James. **(C)** Margaret. **(D)** John. **(E)** Michael. **(F)** Linda. **(G)** Charles. **(H)** Susan. **(I)** Elisabeth. **(J)** William.

As a final example, consider William. He has the same characteristics as Mary except he is 58 instead of 68. Given that age is not included in the SAI's calculation, William and Mary's scores are equal, but they compare themselves to different reference groups. Mary's peers are individuals aged 66–70 and William's are individuals aged 56–60. As the SAI distributions in the two age groups are very similar, in the end both William and Mary are in the middle quintile of the distributions of the SAI among their respective peers (Figures 1A,J).

CONCLUSION

Our results shed light on various factors that contribute significantly to healthy and active aging. Two examples are mental health and exercise, which deserve more attention from individuals themselves, health-care professionals, and public health policy.

This study provides several lines for future research. Other methods to construct multidimensional indices should be tested and results should be compared with the ones presented here.

Our methodology can be applied to data from other countries, to compare healthy and active aging across countries. The effectiveness of the SAI as a tool to promote healthy and active aging at the individual and aggregate levels should be investigated.

This study develops the SAI to measure healthy and active aging at the individual level. It is designed thinking about its possible implementation as a tool for individuals to monitor their aging status. For this reason, it is completely based on self-assessed indicators. The goal is that the SAI allows each person to take a *selfie* of her aging status without requiring a health-care professional to operate the camera. We illustrate how the SAI may be implemented in practice and provide it with a relative component, whereby individuals can compare themselves to their peers. The SAI also has promising applications for health-care professionals. Though it does not replace the clinical assessment of health problems, it may motivate health-care professionals to adopt a more encompassing view of individuals' health and aging status. The SAI is useful to inform the design of public health policies targeting the most vulnerable groups. In conclusion, the SAI has the potential to put the

individual at the center of the healthy and active aging discussion, contribute to patient empowerment and promote patient-centered care. It can become a useful instrument to monitor healthy and active aging for different actors, including individuals themselves, health-care professionals, and policy makers.

AUTHOR CONTRIBUTIONS

JG wrote the manuscript, and all remaining authors revised it critically.

ACKNOWLEDGMENTS

The authors appreciate the comments of participants at the annual encounter III Jornadas Científicas NOVAsaúde, the Ageing and

Independent Living (AgIL) Workshop, and the Conferência Nacional de Economia da Saúde.

FUNDING

This study was funded by NOVAsaúde and partially supported by the Portuguese Foundation for Science and Technology through the project UID/MAT/00297/2013.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at <http://www.frontiersin.org/articles/10.3389/fmed.2017.00236/full#supplementary-material>.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The Quadruple Helix-Based Innovation Model of Reference Sites for Active and Healthy Ageing in Europe: The Ageing@Coimbra Case Study

OPEN ACCESS

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Specialty section:

This article was submitted
to Geriatric Medicine,
a section of the journal
Frontiers in Medicine

Received: 02 December 2017

Accepted: 19 April 2018

Published: 08 May 2018

Citation:

Malva JO, Amado A, Rodrigues A,
Mota-Pinto A, Cardoso AF,
Teixeira AM, Todo-Bom A, Devesa A,
Ambrósio AF, Cunha AL, Gomes B,
Dantas C, Abreu C, Santana I,
Bousquet J, Apóstolo J, Santos L,
Meneses de Almeida L, Illario M,
Veríssimo R, Rodrigues V and
Veríssimo MT (2018) The Quadruple
Helix-Based Innovation Model of
Reference
Sites for Active and Healthy
Ageing in Europe: The Ageing@
Coimbra Case Study.
Front. Med. 5:132.
doi: 10.3389/fmed.2018.00132

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Challenges posed by demographic changes and population aging are key priorities for the Horizon 2020 Program of the European Commission. Aligned with the vision of the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA), the development, exchange, and large-scale adoption of innovative good practices is a key element of the responses required to ensure all European citizens remain as active and healthy as possible as they age. Urged by the need of developing scalable disruptive innovation across Europe, the European Commission and the EIP on AHA created the Reference Sites; local coalition of partners that develop good practices to support AHA. Ageing@Coimbra is an example of how this can be achieved at a regional level. The consortium comprises over 70 institutions that develop innovative practices to support AHA in Portugal. Ageing@Coimbra partners support a regional network of stakeholders that build a holistic ecosystem in health and social care, taking into consideration the specificities of the territories, living environments and cultural resources (2,243,934 inhabitants, 530,423 aged 65 or plus live in the Centre Region of Portugal). Good practices in reducing the burden of brain diseases that affect

cognition and memory impairment in older people and tackling social isolation in urban and rural areas are among the top priorities of Ageing@Coimbra. Profiting from the collaborative work of academia, business companies, civil society, and authorities, the quadruple helix of Ageing@Coimbra supports: early diagnosis of frailty and disease; care and cure; and active, assisted, and independent living. This paper describes, as a Community Case Study, the creation of a Reference Site of the EIP on AHA, Ageing@Coimbra, and its impact in Portugal. This Reference Site can motivate other regions to develop innovative formulas to federate stakeholders and networks, building consortia at regional level. This growing movement, across Europe, is inspired by the quadruple helix concept and by the replication of innovative good practices; creating new Reference Sites for the benefit of Citizens.

Keywords: ageing (aging), European commission, innovation, active and healthy aging, reference sites

INTRODUCTION

Europe faces the global challenge of population aging with strong impact in the quality of life of individuals and families, society cohesion, health, and economic resources of citizens and member states. The percentage of people aged 65 or over in the population is expected to grow from 18.4% in 2013 to 28.4% in 2060 for the average of European countries (1). The growth will be particularly evident in the oldest old (aged 80 or over), who will increase from 5.1% in 2013 to 11.8% in 2060. European projections of old-age dependency ratios (people aged 65 or over versus people aged 15–64) reveal that the current ratio of 1 person aged 65 or over per 4 working-age people will rise to a ratio of 1 person aged 65 or over to 2 working-age people in 2060 (1). This poses huge challenges for sustaining retirement and care in later life.

Portugal stands in a particular challenging position in the overall EU28 scenario. The Portuguese population is aging rapidly with an Ageing Index (people aged 65 or over per 100 people aged less than 15) of 143.9 in 2015 compared to 27 in 1960.¹ The percentage of people aged 80 years or over was 5.4% in 2013 and it is expected to grow to 16.1% in 2060, reaching the highest value of all EU28 countries (1).

Within Portugal, the population living in the Centre Region is particularly old due to the increase in life expectancy, migration of young adults and decrease in birth rate. Within the Centre Region, some areas are already facing the demographic scenarios expected for the European landscape in 2060, e.g., municipalities with Ageing Index above 700.²

Taking together, the demographic landscape of Europe, with a particularly and striking case in Portugal, urges the need of defining new strategies and implementing actions to deliver innovative and disruptive solutions. These solutions are expected to have impact at the individual, family, labor, societal, and economic dimensions to support individual health and well-being, at all ages, and deliver solutions to support health and social care sustainability. As we will elaborate bellow, the EIP on AHA movement, and the particular case of Ageing@Coimbra (as a Community

Case Study), may be inspiring for the required change management processes, delivering solutions for the challenges of aging and opening new opportunities for economic growth.

BACKGROUND AND RATIONALE

The European Innovation Partnership on Active and Healthy Ageing

The EIP on AHA³ is a coalition of European partners promoted by the European Commission to develop, implement, and replicate at large-scale innovative good practices to support AHA of European citizens.

The EIP on AHA grew from recognition that the quality of life of older people is strongly affected by life style habits across the life cycle in all ages. Many older people suffer from multiple chronic conditions that demand continuous support by medical and social care providers and limit functional independence. Ultimately, poor health in later life strongly impacts on health and economic resources, human suffering, human dignity of individuals, and families (2).

The EIP on AHA fosters collaborative work of European partners to support three main strategic pillars of AHA: (1) prevention, screening, and early diagnosis; (2) care and cure; (3) independent living and active aging. EIP on AHA partners are organized in six action groups: A1, adherence to prescription and medical plans; A2, personalized health management and prevention of falls; A3, lifespan health promotion and prevention of age-related frailty and disease; B3, replicating and tutoring integrated care for chronic diseases; C2, development of interoperable independent living solutions; D4, innovation for age-friendly buildings, cities and environments.

The main goal is to achieve a triple win for Europe: (1) Health and quality of life of European citizens; (2) Sustainable and efficient care systems; and (3) Growth and expansion of EU industry.

EIP on AHA is a wide interdisciplinary and transdisciplinary network that seeks innovative collaborative models, removing silos and developing citizen-centered processes. EIP on AHA

¹<http://www.pordata.pt/> (Accessed: April 24, 2018).

²<https://www.ine.pt/> (Accessed: April 24, 2018).

³https://ec.europa.eu/eip/ageing/home_en (Accessed: April 24, 2018).

partners joint academia, health, and social care providers, citizens and patient associations and several other stakeholder groups with innovators, entrepreneurs, and business partners. The aim is to deliver knowledge and user-based competence into innovative good practices, products, and services. Only disruptive innovation and knowledge-based added value will deliver efficient meaningful large-scale interventions to face the societal challenges, opening, at the same time, new opportunities for entrepreneurs, business activity, and job creation (3, 4).

The Reference Sites Collaborative Network

Reference Sites have been defined by the EIP on AHA as “inspirational ecosystems, delivering creative and workable solutions that improve the lives and health of older people.”⁴ Reference Sites effort is to foster and create innovative solutions and scale-up and replicate these solutions across Europe.

Reference Sites include regions, cities, integrated hospitals, or care organizations that focus on innovative and holistic approaches to support AHA. Reference Sites show diverse levels of impact and maturity toward the goal standard of regional ecosystems aligning actors across the quadruple helix: academia, authorities, business, and civil society. The impact of the activities of Reference Sites provides evidence of innovative components, and indicators are measurable in line with the Monitoring and Assessment Framework of the EIP on AHA (MAFEIP), under the dimensions “Quality of life,” “Sustainability of health-care systems,” and “Economic growth and jobs.”⁵

The first call for Reference Sites by the European Commission resulted in the award of 32 Reference Sites in 2013. The second call led to a total of 74 Reference Sites in 2016. Recently (November, 2017), the Reference Sites launched a non-profit association based in Brussels to promote synergies and collaborative work (e.g., twinning activities)—the Reference Site Collaborative Network (5).

METHODS

The Ageing@Coimbra—Creation of a Bottom-Up Innovative Quadruple Helix-Based Consortium

The Ageing@Coimbra Consortium⁶ was formally created in January 2013 as a response of the Centre Region of Portugal to the first call for Reference Sites to develop and implement innovative good practices to support AHA.

Ageing@Coimbra is an informal network of 5 founder and 65 associated partners that build a “quadruple helix”, aligning: (1) public institutions (e.g., municipalities, health and social care authorities), (2) academia (e.g., universities and research institutions), (3) industry partners (e.g., business companies, business incubators, and clusters), and (4) civil society organizations (e.g., third age universities, cultural, and civic organizations). The consortium was founded under a leadership initiative of

the University of Coimbra, the Municipality of Coimbra, the Regional Health Authority, the University of Coimbra Hospital, and the Pedro Nunes Institute (technology transfer, business incubator and business accelerator affiliated with the University of Coimbra). The Administrative Authority of the Centre Region of Portugal (“Comissão de Coordenação e Desenvolvimento Regional do Centro,” CCDRC) has been a major supporter and driver for the success of Ageing@Coimbra, actively engaging in the implementation of activities, international visibility and ownership of responsibility to include AHA in the key priorities of the Smart Specialization Strategy (RIS3) of the Center Region of Portugal. In 2017, CCDRC launched a regional competition to award three cases of good practices in three clusters: Knowledge, Health, and Life.

Ageing@Coimbra was the first EIP on AHA Reference Site in Portugal. The innovative formula and lean governance structure created an inclusive partnership with agility, rapid implementation, and growth potential. Concordantly, other regions in Portugal (e.g., Porto metropolitan area, Algarve) and regions in other European countries (e.g., Asturias in Spain, Lodz in Poland) embraced Ageing@Coimbra example to replicate the model and launched new reference sites in 2016, or they will do so in a future call expected for 2019. The same example has replication potential in other countries in Europe and globally (e.g., Northeast Brazil).

RESULTS

The Ageing@Coimbra, Consortium—Reference Site in Portugal

As an active member of EIP on AHA Action Groups, Ageing@ Coimbra participates in the collaborative activities and delivers success cases of projects and good practices.

A1 Action Group: Adherence to Medical Plans

Multimorbidity and the related prescription of multiple drugs are becoming common problems among older people, frequently associated with poor health outcomes, being inadequate and/or poor adherence to medical plans one of the relevant factors that compromise the success of treatments (6). Therefore, in agreement with the overall goals and triple win defined by the EIP on AHA, the A1 Action Group aims to contribute to the improvement of adherence to medical plans and medication at European level. Ageing@Coimbra has been actively involved in this Action Group and, since 2015, is coordinating the work and activities of one of the four strategic objectives agreed for this group's renovated Action Plan, related to the reinforcement of the multidisciplinary and integrated approach to improve adherence to prescription and to tackle inappropriate polypharmacy.

The collaborative work of Ageing@Coimbra in the A1 Action Group resulted in the successful development of the third Health Program Project SIMPATHY (Stimulating Innovative Management of Polypharmacy and Adherence in the Elderly), a project coordinated by the Scottish Government (Grant Agreement 663082)⁷ (6–8) (Figure 1).

⁴https://ec.europa.eu/eip/ageing/reference-sites_en (Accessed: April 24, 2018).

⁵<http://mafeip.eu/> (Accessed: April 24, 2018).

⁶www.ageingcoimbra.pt/en/ (Accessed: April 24, 2018).

⁷www.simpathy.eu (Accessed: April 24, 2018).

Mixed-method case studies were conducted in 9 sites, Germany, Greece, Italy, Poland, Portugal, (Spain) Catalonia, Sweden and (United Kingdom) Scotland and Northern Ireland, mapping the structures, processes, and outcomes of policies and practices at the institutional, regional, and local level.

Phase I Desk Review	Evaluating economic, political, and cultural context; Checklist of complex interventions.
Phase II Key Informant Interviews	Assessing development and implementation strategies. Participants included: Primary care and hospital pharmacists, hospital geriatricians, primary care and hospital managers, health system administrators.
Phase III Focus Groups	Validating interim report findings with focus group of primary care pharmacists, hospital and primary care geriatricians, hospital manager and health system administrator.

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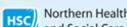
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Polypharmacy Programmes
Portuguese Case study

Public policies for polypharmacy management in the elderly



This leaflet is part of the SIMPATHY project (663082), which has received funding from the European Union's Health Programme (2014-2020).

FIGURE 1 | Flyer of SIMPATHY case study in Portugal. SIMPATHY in Portugal recognized the lack of policy guidelines for polypharmacy management across the country.

A2 Action Group: Personalized Health Management and Prevention of Falls

The relevance of the topic addressed in the A2 Action Group is supported by the Joint Declaration of the European Stakeholders Alliance for Active Ageing through Falls Prevention⁸ “falls are a major indicator of increasing frailty and loss of independence and mobility in older people.” The main objective of the A2 Action Group has been to deliver EU wide evidence-based, validated and operational programs for the prevention, early identification, and minimization of risk and management of falls in order to reduce falls and the personal, system, and societal consequences of fall-related injuries. In order to reach relevant joint achievements and goals four different areas of collaborative work are being developed: (1) implementation of an integrated and person-centered service pathway for fall prevention and management; (2) data collection for evidence-based interventions on falls; (3) awareness, information, and education, to support the training of the workforce; (4) Governance: innovation, sustainability, and scaling-up, including models for exploitation, business analysis, and strategies for falls prevention technologies take up.

The collaborative work of Ageing@Coimbra in the A2 group resulted in joint activities and collaborative work in the Prevention of Falls Network for Dissemination (ProFouND), an EC funded initiative dedicated to the dissemination and implementation of best practices in falls prevention across Europe.⁹

Also, within the scope of the A2 action group, the Project “Good practices to develop physical activity programs at work—FitWork” was developed within the framework of the ERASMUS + SPORT program aimed at developing good practices to implement physical activity programs at work attending to specific risks of workplaces (muscular-skeletal disorders and sedentary workplaces). The project is coordinated by Instituto de Biomecánica de Valencia and more information can be found at.¹⁰

A3 Action Group: Lifespan Health Promotion and Prevention of Age-Related Frailty and Disease

Reflecting a growing awareness of the need for better care and sustainable and effective health services, the A3 Action Group aims to contribute to AHA with a life-course approach, implementing the shift from reactive disease management to anticipatory care of

⁸http://www.eunaapa.org/wp-content/uploads/2015/09/Joint-Declaration_Sept-2015.pdf (Accessed: April 24, 2018).

⁹<http://profound.eu.com> (Accessed: April 24, 2018).

¹⁰www.fitwork.eu (Accessed: April 24, 2018).

functional decline through community-based prevention, early diagnosis, and screening programs, and integrated care management systems. This patient-centered approach involving social and health-care systems is based on innovative solutions that support interactions in the areas of nutrition, frailty and functional decline, cognitive decline and physical activity. It also fosters the development of networks strengthening education and training of the health workforce, citizens empowerment through health and ICT literacy, and advancing knowledge on the determinants of frailty and chronic diseases to support early detection and sustainable interventions. The joint effort of A3 partners is the improvement and alignment of services delivered to the needs of older populations and enabling caregivers' education and empowerment.

To ensure the scalability of the EIP on AHA commitments on frailty, the FOCUS project (*Frailty Management Optimization through EIPAHA Commitments and Utilization of Stakeholders' Input*) was launched (9). This project aims at a critical reduction of frailty burden in Europe by deploying knowledge and tools on frailty diagnosis/screening and management, and by supporting good practices developed in this context. The FOCUS Consortium consists of a multidisciplinary team representing Centre-North (the Netherlands) and South (Spain and Italy), East (Poland), and West (UK, Portugal) Europe, under the coordination of the University of Valencia (Grant Agreement 664367). More information can be found at <http://focus-aha.eu/home>.

B3 Action Group: Integrated Care

The B3 Action Group main goal is to provide integrated care to older people with chronic conditions through a people-centered approach, foreseeing improvements in quality of life by implementing integrated care programs to reduce unnecessary hospitalization and improve the efficiency of health care. These programs are multidisciplinary, well-coordinated, accessible, anchored in the community and home care settings, and stimulate the interplay between health and social systems, industry, academia, and health-care users in order to establish innovative responses to the challenges imposed by aging.

Within the scope of the B3 Action Group, Ageing@Coimbra and Porto4Health References Sites collaborate as the key Portuguese partners of MACVIA-Fr Reference Site in a Twinning project on the large-scale deployment of a Smartphone Application (App) to monitor and control the symptoms of allergic rhinitis (5, 10) (Figure 2).

C2 Action Group: Independent Living Solutions

The objective of the C2 Action Group is to develop interoperable independent living solutions, including guidelines for business models. This should boost the deployment of open and personalized solutions for active and independent living that are supported by global standards and new evidence on the return of investment. The C2 Action Group provides essential input to the creation of a new market for cost-effective products and services that help older people live a more active and independent

FIGURE 2 | MACVIA/ARIA allergy diary Smartphone Application (App) developed by the MACVIA-Fr Reference Site, adopted and replicated across EU and non-EU countries; 15931 users—AT 655; AU 196; BE 164; BR 2039; CA 34; CH 905; CZ 5; DE 814; DK 151; ES 736; FI 456; FR 1029; GB 962; GR 240; IT 1970; LT 394; MX 905; NL 603; PL 968; PT 2264; SE 174; TR 260 (November 22, 2017).

life. This reinforces ongoing research and innovation activities in Europe (and elsewhere), supported through public-private partnerships.

Within the scope of the C2 Action Group, in 2017, the AAL Forum, the biggest European event in the field of Technologies for AHA was organized in Coimbra, by the Pedro Nunes Institute, in partnership with the Portuguese Foundation for Science and Technology and some of the Ageing@Coimbra core partners. The theme of the Forum was “Bridging the gaps between technology solutions and aging well. What can YOU do?” Interoperable solutions were discussed as crucial to assure the value of the digital solutions, for example contributing for the integration between social and health care.

An inspirational fresh addition to this year's AAL Forum exhibition hall was the attendance of over 120 end-users above the age of 65, all eager to give their honest opinion on what they saw. Exhibitors had approximately 7 min to present and sell their AAL solution to the guests, which turned out to be more of a challenge than the majority of exhibitors expected (Figure 3). After visiting each of the exhibition stands, the group of over 65's had the hard job of picking their three favorite stands.

For the first time in the AAL Forum, the jury responsible for awarding the Exhibition Prize was constituted only by end-users above the age of 65. This activity was supported by Ageing@ Coimbra and the Administrative Authority of the Centre Region of Portugal.

Another example of the collaborative work of Ageing@ Coimbra members within the scope of C2 Action Group is well represented by the project GrowMeUp, funded under the H2020 call PHC-19-2014 “Advancing active and healthy aging with ICT: service robotics within assisted living environments”; coordinated by the University of Coimbra and including the active partnership with Caritas Coimbra as an end-user organization (Grant Agreement 643647).¹¹

¹¹www.growmeup.eu (Accessed: April 24, 2018).

D4 Action Group: Age-Friendly Environments

The D4 Action Group has its main roots on the concept of Age-Friendly Environments, as envisaged by the World Health Organization¹² (WHO), referring to physical and social environments as key determinants for health, well-being and the participation of people as they age. In that sense, the main objective of the D4 Action Group is to contribute to a more inclusive society and communities across Europe by empowering older persons through scaled up inclusive solutions.¹³ Caritas Coimbra is main coordinator of the domain 8 of this action group—connect and leverage local and regional age-friendly environments—which fosters wide participation of different stakeholders across Europe, supporting networking, transfer of experience and the upscale of good practices.

Caritas Coimbra is also a founder member and Vice-President of the European Covenant on Demographic Change, an organization that aims to gather local, regional, and national authorities as well as other stakeholders in order to cooperate and implement evidence-based solutions to support AHA.¹⁴ The Covenant comprises more than 150 members—local and regional authorities, industries, research centers/universities, civil society organizations—to link up, benefit from each other's experience and work together to promote initiatives on age-friendly environments across the EU.

The collaborative work of Ageing@Coimbra in D4 group includes the leadership of the University of Coimbra in the H2020 project Euro-Healthy (Shaping European Policies to Promote Health Equity) with a key goal to deliver a Population Health Index and a Web Geographic Information System (Web-GIS) addressing health inequity across the EU (Grant Agreement 643398) (11).¹⁵

¹²<http://www.who.int/ageing/projects/age-friendly-environments/en/> (Accessed: April 24, 2018).

¹³https://ec.europa.eu/eip/ageing/action-groups-eip-aha/d4-age-friendly-environments_en (Accessed: April 24, 2018).

¹⁴www.agefriendlyeurope.org (Accessed: April 24, 2018).

¹⁵www.euro-healthy.eu (Accessed: April 24, 2018).



FIGURE 3 | Older citizens (identified through Third Age Universities and Social Care Providers) experience and evaluate technologies at the AAL Forum 2017 (Coimbra, October 2–4, 2017). Over 120 old citizens tested, evaluated, and provided recommendations for technology developers. The identified participants and the AAL Forum organization expressed written agreement for the inclusion of these photos in the present publication.

AGEING@COIMBRA INNOVATION CLUSTERS ON BRAIN AGEING AND ON SOCIAL ISOLATION

Ageing@Coimbra Provides an Integrated Pipeline in Biomarkers for Neurodegenerative Diseases

The area of biomarkers for neurodegenerative diseases, particularly concerning Alzheimer's disease, profits from the solid basis of neuroscience research provided by CNC.IBILI. Fundamental research is transferred from bench to bedside by means of knowledge-based genetics, biochemical, imaging, and neuropsychology biomarkers of cognitive dysfunction.

Genetics and biochemical biomarkers currently used to identify risk factors and biomarkers of Alzheimer's disease include APP, tau, amyloid beta 1-42, genotyping for PSEN1, PSEN2, APP, ApoE (12).

The Faculty of Psychology of the University of Coimbra provides neuropsychology tests to screen for functional and memory competence of older adults including Adults and Older Adults Functional Assessment Inventory (IAIFA), World Health Organization Quality of Life-OLD module, Geriatric Depression Scale (GDS-15), cognitive performance (MOCA, ACE-R).

The early diagnosis pipeline is complemented with robust brain imaging tools to ensure high quality diagnosis of putative neurodegenerative conditions. The Applied Nuclear Sciences Institute (ICNAS) pipeline launches innovative cyclotron-based synthesis methods of radiotracers including PET/FDG, PET/PiB, PET/PK11195, and other radiotracers upgrading the diagnosis tools.

This integrated approach, aligning technologies and professionals/resources for a better public service results in relevant assets for Ageing@Coimbra stakeholders, creating the most valuable and reliable integrated health service in Alzheimer's diseases in Portugal; with recognized impact in the Health Cluster Portugal, the Joint Program in Neurodegenerative Diseases, and the EIT Health Knowledge Innovation Community (KIC).

The diagnostics pipeline for early detection of Alzheimer's disease contributes to better health-care management and also to liaise with patient associations (e.g., Alzheimer's disease; Alzheimer Portugal) for better social care and support to patients and care providers.

Social Isolation—Mobile Units, Continuous Integrated Care, and Healthy Food

The territory of the Center Region of Portugal offers peculiar conditions as a regional living laboratory. In the region, about 23% of residents are aged 65 or over living in diverse environments, urban versus rural, highly dense versus low-density territories. In inland areas, especially in the mountain area, low-density territories also create geographic barriers to mobility especially of frail people contributing to social isolation. On the other hand, social isolation is also a burden of older persons living alone in urban areas of the Centre Region of Portugal.

These particular conditions create a local need to develop integrated care and personalized solutions to support older people living in socially challenging conditions.

The majority of municipalities in the Region have been equipped with health mobile units to deliver primary care and social care support to frail older people living in rural isolated areas. The added value of these services is well recognized by users and professionals, showing increase demand in terms of individual requests by the citizens and attracted interest by other municipalities.

Portugal launched in 2016 a new coordination structure of the National Network for Integrated Care Units. This network provided complementary health and social care support to populations, being socially isolated frail older people the main beneficiaries. The regional network includes 3 main units for palliative care, 9 units for convalescence care, and more than 62 integrated home care teams. Ageing@Coimbra links with integrated home care teams in close collaboration with the regional health authority, the national insurance office, and municipalities.

The social support to isolated frail older people in the region is a key priority for local players, including municipalities. Several important actions support intergeneration activities to tackle social isolation, ICT literacy, polypharmacy, and adherence to therapy strategies, assisted living programs, innovative strategies to engage older citizens with meaningful activities, and an humanitarian approach in health care—both in rural and urban areas.

The regional health authority launched a program ("pão.come") to reduce the content of salt in the daily food of Portuguese citizens, in particular the amount of salt in bakery. Traditionally, Portuguese citizens use excess salt in food, specially in bakery. This fact has been associated with high-prevalence of cerebrovascular diseases (13). Interestingly, the population of the Centre Region faces a major change in the profile of cerebrovascular diseases. The number of fatalities and permanent impairment conditions has been reduced significantly. Two major driving forces can account for the success of the "pão.come" program: (1) effective reduction of salt in bread that contributes to reduce the global numbers of stroke and cerebrovascular conditions; (2) the implementation of special priority channels (green way) in hospitals for people suffering from stroke and acute cerebrovascular diseases.

A schematic representation of the innovation clusters of Ageing@Coimbra (promoting healthy brain; social isolation) is depicted in **Figure 4**.

FUNDAMENTAL AND APPLIED RESEARCH IN AGEING, CARE AND INNOVATION IN GERIATRIC MEDICINE

Fundamental and Applied Research

Research on the mechanisms of aging-related diseases is a solid and established research area at the University of Coimbra and at the Center for Neuroscience and Cell Biology of Coimbra. Research in this area delivers high-impact and highly cited publications, international collaborations, advanced training of Ph.D., and postdoctoral students as well as entrepreneurship training and new spin off companies. Highlighting the priority of aging research, in 2016, a new ERA Chair group (H2020 Widespread, Grant Agreement 669088) was appointed by the

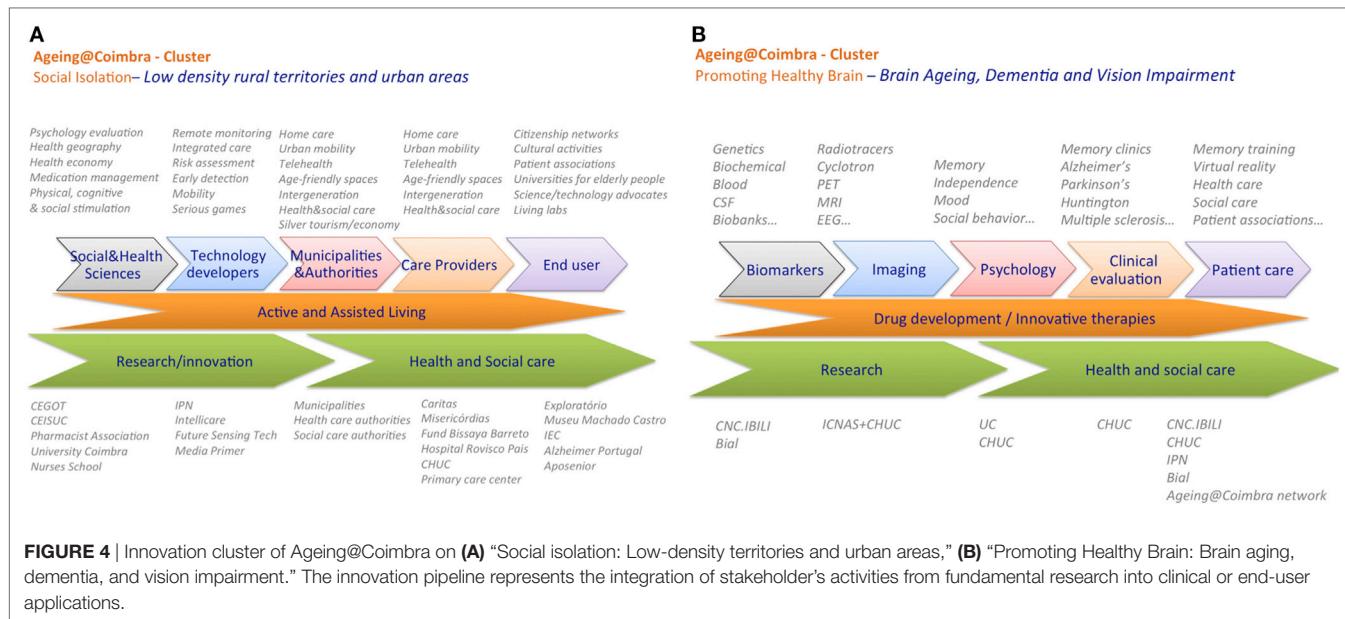


FIGURE 4 | Innovation cluster of Ageing@Coimbra on **(A)** “Social isolation: Low-density territories and urban areas,” **(B)** “Promoting Healthy Brain: Brain aging, dementia, and vision impairment.” The innovation pipeline represents the integration of stakeholder’s activities from fundamental research into clinical or end-user applications.

Faculty of Medicine of the University of Coimbra to develop a research program, advanced teaching and translational research in cardiovascular aging (14).¹⁶

EIT Health

In 2015, three founder members of Ageing@Coimbra, the University of Coimbra, University of Coimbra Hospital and Pedro Nunes Institute, were accepted, as Associated Partners, in the new KIC in Active Living and Healthy Aging from EIT Health. Together with the pharmaceutical company BIAL, they formed a cluster of Innostars, a legal entity member of EIT Health.

EIT Health is a powerful consortium of more than 140 members from academia and industry partners that develop collaborative market-driven projects to tackle societal challenges: (1) promote healthy living; (2) support active aging; (3) improve health care. Projects deliver better training of students, executives, and citizens (Campus); transform innovative ideas into products and services (Innovation Projects); and create and catapult business creation (Accelerator).¹⁷

Geriatric Medicine

The University of Coimbra Hospital offers a well-established multidisciplinary geriatric assessment service. The knowledge gathered by the clinical team supported the creation of a new clinical service entirely dedicated to AHA, including daily clinical care, a hospital residence, outpatient consultations and community health-care services. The key pillars of the new unit enclose clinical care of geriatric patients, training of new health-care professionals and research on aging and geriatrics.

The clinical unit on AHA establishes strong links with other hospital specialty services for prevalent and multimorbid conditions,

including Neurodegenerative and Psychiatric Diseases, Pneumology and Respiratory Diseases, Immunology, Cardiovascular Diseases, Diabetes, Cancer, Musculoskeletal Diseases, among others.

Geriatric Medicine profits from the institutional collaboration of the University of Coimbra Hospital and the Rehabilitation Hospital Rovisco Pais and other local Hospital units in the region. Dedicated patient-centered rehabilitation services profiting from holistic approaches and multidisciplinary care are key success factors to prevent and treat geriatric frailty, particularly orthogeriatric frailty. Long-term care and palliative care multidisciplinary services in the region offer support to patients and families affected by long-term functional dependence and end-of life care for older patients and their families, including a hospital palliative care team offering support across clinical services at the University of Coimbra Hospital and two inpatient palliative care units, at the Portuguese Cancer Institute—Coimbra and Cantanhede Hospital (the latter also offering home care support). Reinforcing this strategic area, the Calouste Gulbenkian Foundation supports a “Professorship in Palliative Care” at the Faculty of Medicine of the University of Coimbra to strengthen research and education in Palliative Care in the Centre Region.

Health Literacy and Professional Training

The training of formal caregivers (working in institutions for older people), or informal caregivers (providing non-remunerated care for older people) is extremely important, especially when taking into account the growing older population that depends on care for chronic and degenerative diseases.

The University of Coimbra, together with Ageing@Coimbra, knowing the demand for specialized caregivers’ training and the need to reach an audience with time limitations and geographically dispersed, concluded that a distance learning modality (e-learning course) was among the most appropriate responses. The Distance Learning Course, “Active and Healthy Ageing,”

¹⁶<http://erachair.uc-biotech.pt/team/> (Accessed: April 24, 2018).

¹⁷www.eithalth.eu/home (Accessed: April 24, 2018).

which is a method of active learning providing training in the basic care areas of older people, was created by a team of lecturers of the Faculty of Medicine.¹⁸

Health literacy in aging is also a priority topic in postgraduate training. The Faculty of Medicine offers a masters degree in geriatrics and gerontology, where medical doctors can learn and upgrade their knowledge in age and age-related chronic diseases. Geriatrics in Coimbra is supported by advanced teaching, clinical health care and professional training. Advanced teaching at the Faculty of Medicine of the University of Coimbra includes the Ph.D. program in health sciences, the Ph.D. program in aging and chronic diseases, the masters in geriatrics and undergraduate training in geriatrics under the scope of the masters course in medicine. Postgraduate training of health-care professionals also includes the annual course on Ageing and Geriatrics (in 2017, we celebrate its 16th Edition).

Nursing School of Coimbra promotes the implementation of the comprehensive geriatric assessment at a national level. The activities include cultural adaptation and validation of tools for use in the field of geriatrics and participation in the development of national and international web platforms to support National and European strategy to intervene on older adults' frailty and to involve stakeholders in this process. The measurable impact of work of Nursing School of Coimbra is also observable in prevention of cognitive decline in advanced age by promoting the implementation of cognitive stimulation-based practice in different health-care contexts and by enabling multidisciplinary teams to implement autonomously this practice in different regions of Portugal. In addition, Nursing School of Coimbra is also training health professionals at a national level by enabling them to achieve critical reasoning, questioning of the ongoing practices and seeking and evaluating information to support Evidence-Based Practice. Nursing School of Coimbra is also offering postgraduate programs in Geriatric Health and Ageing, Health, and Citizenship.

Social Participation

Ageing@Coimbra profits from the engagement of several institutional partners that promote the social inclusion and participation of seniors in meaningful social activities and long-life learning. These institutions include Third Age Universities, Citizenship Associations, Science Centers, Museums, among others. Together, these institutions mobilize thousands of older citizens and their families in a number of activities involving the society: including heart and cardiovascular diseases awareness; Diabetes; Brain Awareness Week; International Day of the Older Person; European Scientists Night; among others.

GOOD PRACTICES AGEING@COIMBRA, 2017

In 2017, the Regional Authority of Centre Region, in a partnership with Ageing@Coimbra, launched a call to award good practices supporting AHA and age-friendly territories in the 100 Municipalities of the Region. This initiative contributes to

(1) identify innovative good practices; (2) publicly recognize individual and institutional stakeholders; (3) disseminate knowledge to support adoption and scaling-up in other territories. The call awarded, in 2017, three categories: (1) Life+ ("Vida+"), to support healthy life styles; (2) Health+ ("Saúde+"), supporting innovative health care for older people; and (3) knowledge+ (Conhecimento+), to support research and technology applied to AHA.

We received 128 valid applications from diverse thematic and geographic origins, including 74 applications for the category "Life," 38 for "Health," and 16 applications for "Knowledge," from a total of 118 institutions. These institutions included 34 municipalities, 12 social care providers, and several citizenship associations and universities, from a total of 49 municipalities (**Figure 5**).

"Life" projects include programs for physical activity, with or without assessment of health parameters, multidimensional evaluation (clinics, social and gerontology), intergenerational dialog, therapy by arts, creation, and development of informatics platforms. The winner "Novas Primaveras," submitted by the Arts and Music Association of Pousos village, describes a program focused on therapy for older people through arts. This good practice was launched in 2004 and involves (currently) 12,711 direct and 84 indirect users from 30 Institutions, engaging users in music, dancing, theater, poetry, and other artistic expressions.

"Health" projects enclosed areas related with new mobile health units to support home care, implementation of new methodologies of health care (primary, non-formal, long-term, dementia), prevention of frailty in older people, screening and diagnosis of disease, physical and cognitive stimulation and rehabilitation,

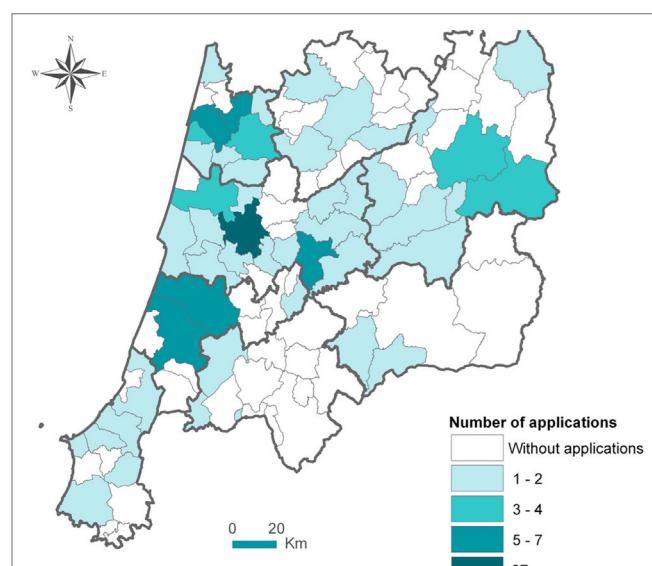


FIGURE 5 | Number of applications for the award of good practices on AHA ("Boas Práticas de Envelhecimento Ativo e Saudável da Região Centro"). The contest involved stakeholders from 49 of the 100 municipalities of Centro Region, that submitted 1 or more application, per municipality, of the total of 128 good practices (blue color scale for number of application per municipality).

¹⁸<http://www.ed.uc.pt/educ/crse?i=127> (Accessed: April 24, 2018).

monitoring of chronic diseases using ICT's, support of patients in hospital and care residence settings (arts, comedy), health literacy, and health promotion. The winner good practice described specialized care for dementia patients ("Cuidados especializados para demência") submitted by the network of care providers "União das Misericórdias Portuguesas—Unidade de Cuidados Continuados Bento XVI (Fátima)". This dementia care residence is a pilot unit established in 2013, including environmental, professional, therapeutics competences, recognized as a reference model for the care of patients with cognitive impairment and dementia. It includes 20 beds for mid-term care and rehabilitation (up to 90 days) and 30 beds for long-term care and maintenance (up to 180 days).

"Knowledge" projects include: research and application of programs and new models; application of ICT solutions; collaborative models using telehealth and teleassistance; inter-generational approaches; infrastructures; equipment and access to knowledge; multimorbidity research and care; AHA and longevity, databases and population profiling. The winner was a project submitted by the Faculty of Medicine of the University of Coimbra and the Center for Neuroscience and Cell Biology: "NoMicro Technologies." This project describes the development of a technology to support healing of chronic wounds and prevention of infection by pathogens. NoMicro Technologies is currently in a phase of preclinical proof of concept.

In conclusion, the number and quality of the applications received in the call exceeded the best expectations of the organizing committee, reflecting the growing involvement and awareness of stakeholders of the Centre Region to support AHA of citizens.

DISCUSSION

Standing on the big societal challenges created by the impact of population aging in individual's health, but also for efficiency and sustainability of the health and social care systems, the movement created by EIP on AHA addresses the individual's and societal hurdles, under a positive perspective of stimulating the economic growth and job creation.

The collaborative work developed by EIP on AHA partners, under the scope of the six active action groups or under the scope of the quadruple helix-based Reference Sites, has delivered an impressive number of ground-transforming good practices, innovation schemes, and change management process, with big societal impact and economic potential.¹⁹

EIP on AHA Reference Sites like Ageing@Coimbra have shown to be instrumental bodies for helping the European Commission in the implementation of policies, including the "Blueprint for Digital Transformation on Health and Care in an Ageing Society"²⁰ and "Boosting Innovation on Active and Healthy Ageing in the Digital Single Market."²¹ The goal of the blueprint

is to reach out in 2018 more than 50 European Regions that will invest in the implementation and/or deployment of large-scale digital solutions for health and care. EIP on AHA is one of the key champions pre-identified by the European Commission that contributed to the Blueprint and committed to deliver results. The Digital Single Market Strategy unites regions, industry, and users around a shared vision on how digital innovation can transform health and care in Europe and will create the background for the impact expected for the Blueprint policy implementation. The Reference Sites are seen as key elements and stakeholders of this transformation. Accordingly, the close interaction of EIP on AHA and Reference Sites with national/regional authorities and international organizations, including WHO, foster the impact of activities leveraged from regional to European and global dimensions (5).

The impact of Reference Sites in the European landscape is also revealed by the collaborative work under the twinning collaborative scheme, involving delivery of good practices by innovator regions/actor and adoption by twin Reference Sites. The example of the twinning project lead by MACVIA and adopted/replicated by Ageing@Coimbra, and many other Reference Sites is a good example of a successful twinning project with impact in the society (see text footnote 20).

The challenges imposed to societies by population aging and demographic changes are of paramount complexity. Innovative formulas to deliver practices and services and organization models, like those embedded in EIP on AHA Reference Sites and Ageing@Coimbra, might prove to be key elements of the change management schemes needed to deliver quality of life to citizens and sustainability of health and care systems, starting from pilot twinning schemes to large scale-up replication across Europe and Globally.

CONCLUSION

In conclusion, the innovative and successful example of Ageing@ Coimbra as a Reference Site of EIP on AHA supports the adoption of bottom-up, inclusive, and holistic approaches to create regional networks and partnerships with the aim of supporting the creation and replication of good practices for Active and Healthy Ageing. This methodology has proven to be successful in Coimbra/Centro de Portugal and other regions of Portugal, as well as in other European countries. Other examples of innovative regions embracing this model may follow and reinforce the change management objectives pursued by the EIP on AHA and the European Commission. However, important hurdles related with poor commitment of partners, oversimplification of processes in lean management structures are also difficulties that need to be constantly monitored and overcome.

Ageing@Coimbra is a growing consortium, consolidating its unique position as an aging network in the Centre Region of Portugal, with strong collaborations with other Reference Sites and international networks. Ageing@Coimbra will support the replication of good practices emerging from its stakeholder members and will twin with other European partners to foster the adoption of innovative practices and technologies for the benefit of Centre Region and European citizens.

¹⁹http://www.scale-aha.eu/fileadmin/scaleaha/documents/scaleaha_d5.4_final-studyreport.pdf (Accessed: April 24, 2018).

²⁰<https://ec.europa.eu/digital-single-market/en/blueprint-digital-transformation-health-and-care-ageing-society> (Accessed: April 24, 2018).

²¹<https://ec.europa.eu/digital-single-market/en/node/84742> (Accessed: April 24, 2018).

AUTHOR CONTRIBUTIONS

JM: concept design, writing the text, editing figures, and manuscript correction. AA: concept design, manuscript correction. AR: concept design, writing the text, editing figures, and manuscript correction. AM-P: writing the text and manuscript correction. AFC: concept design; writing the text; and manuscript correction. AT: concept design; writing the text; and manuscript correction. AT-B: editing figures and manuscript correction. AD: concept design and manuscript correction. AFA: manuscript correction. ALC: concept design; writing the text; and manuscript correction. CD: concept design; writing the text; editing figures; and manuscript correction. BG: writing the text and manuscript correction. CA: concept design; writing the text; and manuscript correction. IS: manuscript correction. JB: editing figures and manuscript correction. JA: concept design; writing the text; and manuscript correction. LS: concept design; writing the text; and manuscript correction. LA: concept design and manuscript

correction. MI: writing the text; manuscript correction. RV: manuscript correction. VR: concept design and manuscript correction. MV: concept design; writing the text; editing figures; and manuscript correction.

FUNDING

The authors acknowledge the collaboration of Dr. Armando Pereira and Dr. Inês Costa as staff members of the research management office of the Faculty of Medicine of the University of Coimbra (GGI, FMUC). The following funding sources supported projects involving Ageing@Coimbra members: Portuguese Foundation for Science and Technology (FCT-Portugal), Pest UID/NEU/04539/2013, COMPETE-FEDER POCI-01-0145-FEDER-007440; 3rd Health Program of the European Commission; Horizon 2020 (H2020) of the European Commission; Portugal 2020 (EU); Calouste Gulbenkian Foundation.

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