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LETTER TO THE EDITOR

Frailty, e-health and prevention of late-onset Alzheimer disease and related disorders: it is time to take action

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To the Editor:

Alzheimer disease and related disorders (ADRD) are highly prevalent in the older population [1]. Even if age-specific incidence rates are lower than in previous decades, the number of people with ADRD is still rising [1, 2]. Around 50 million people live with ADRD worldwide [3]. This figure is expected to triple over the next decade [2, 3]. ADRD cause adverse outcomes on physical, psychological, social and economic domains for people living with these disorders, their caregivers and the society at large [1–3]. Healthcare systems in high-income countries are ill-equipped to deal with the ADRD adverse outcomes [3, 4]. The coronavirus disease 2019 (COVID-19) pandemic exacerbated this issue [5–7]. Indeed, people with ADRD are more likely expose to severe COVID-19, related disabilities and death than their non-ADRD matched counterparts [5]. Even if they are not infected by the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), they are at higher risk for worsening of neuropsychiatric symptoms due to isolation, psychosocial stressors and lack of optimal care compared to their non-ADRD counterparts [6, 7].

Disease-modifying treatments for ADRD remain elusive [8]. Recent literature including systematic reviews showed that up to 40% of late-onset ADRD may be prevented or at least delayed by addressing modifiable risk factors (MRFs) [2, 9]. The interaction of MRFs in incident ADRD is complex and challenging because of the long-time frames between intervention on MRFs and the occurrence of ADRD [9]. Because of the potential benefits of acting on MFRs, the World Health Organization (WHO) has called for immediate implementation in clinical practice of actions targeting MRFs for ADRD reduction [3]. An operative prevention of incident ADRD is based on screening people at risk and addressing their MRFs [2, 3, 9]. MRFs of ADRD are chronic morbidities [3, 9]. An effective prevention of ADRD needs to not only consider each MRF individually, but also their accumulation. A significant adverse consequence of chronic morbidity accumulation is frailty [10]. Frailty is associated with an increased risk of ADRD [11]. Frailty may be reversed and, thus, assimilated as a MRF of ADRD [10, 11]. Addressing frailty (i.e., assessing frailty level and proposing interventions to reverse it) might be a key intervention to prevent ADRD.

The association between frailty and the incidence of ADRD has been confirmed in a recent meta-analysis [11]. However, this study underscored uncertainty about this association. First, most studies used Fried's criteria which defines frailty as a strictly physical impairment, whereas psychological, cognitive and social domains also contribute to frailty and, thus, should be considered in its definition and quantification [10]. The Rockwood's deficit accumulation model considers this multidimensional aspect of frailty by counting deficits in various domains [11]. Second, although cognitive impairment, like mild cognitive impairment, is an

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important risk factor for ADRD, its place in frailty models is absent or limited [10, 11]. Fried's model does not include it, while Rockwood's model includes "poor cognition" as a deficit [10]. To counter these issues, the concept of "cognitive frailty" has been created [12]. It is defined as the simultaneous existence of both physical frailty and cognitive impairment in people free of ADRD. The effect of each component remains unclear and limiting impairment in the physical domain could restrain its predictive value for ADRD. Numerous questions are still pending about the association of frailty models and the incidence of ADRD including: is the Rockwood's model effectively associated with the incidence of ADRD? Which is the best model predicting ADRD between the Fried and Rockwood models? And how does the association between cognitive impairment in people free of ADRD and frailty state influence the incidence of ADRD?

One's frailty state may change over time in either direction, meaning a person may become more or less frail, such that frailty may successfully be reversed with timely and appropriate interventions [10, 11]. Frailty may be change through lifestyle activities like physical activity or dietary measures [12]. Changes in these behavioral lifestyle patterns may, thus, reduce the risk of ADRD [2]. Therefore, the adoption of healthy lifestyle activities represents preventive interventions for both frailty and ADRD. This adoption depends on an active participation of individuals and their empowerment. The WHO recommends the use of self-administered questionnaires (SAQs) to rate and monitor health with the goal to empower people for becoming healthier [13, 14]. The challenge in the older population is to be able to screen frailers easily and cost effectively. Electronic-health (e-Health) applications (apps) offer new opportunities for self-assessment but also empowerment and promoting healthy activities. For instance, it has demonstrated that older people may accurately assess their own health and its level of frailty via a SAQ on paper on a web platform [15, 16]. It has also shown that ludic web apps were helpful to assess cognitive disorders and that monitoring of daily activities can improve the early detection of cognitive impairments [17, 18]. These results opened care perspectives for e-health empowerment (i.e., e-health assessment performed by patients themselves) and personalized medicine (i.e., health assessment providing an accurate picture of individuals' frail state and appropriate interventions). Indeed, the results allow to propose tailored interventions (i.e., adapted to individuals' frail state) at the right time (i.e., early in the process of frailty) to the right individual (i.e., most at risk of adverse outcomes like ADRD). Among the interventions promoting healthy activities, those incorporating e-Health receive increasing attention. A systematic review on the effectiveness of e-Health solutions showed benefits of using a supportive web platform in older people as well those with ADRD and their caregivers [19]. Many older people have kept abreast of technological developments over the past years and are the new users of the internet [19, 20]. The COVID-19 pandemic accelerated this phenomenon, which opened new e-Health perspectives for ADRD prevention [20]. The benefit of mobilizing decision-making processes that use automated screening algorithms, through the collection of clinical information has been demonstrated [21]. However, there are still berries to use e-health in the older people [22–24]. For instance, its availability is limited to populations living in industrial countries [22]. The older people are not the users targeted by e-health apps and, thus, most of these apps do not take into account their needs and particularities of their health condition like frailty [23]. Furthermore, lack of instruction and guidance as well a complex device technology are reported barriers [24]. Lastly, a limited number of studies reports benefits due to methodological issues like heterogeneity among study designs and evaluation of e-health interventions [25]. Thus, a strategy associating algorithmic screening of frailty combined with tailored recommendations about healthy lifestyle activities in e-Health Apps and considering needs and feature of users may be of central importance for a personalized medicine designed to reduce incident ADRD in the older population.

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