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Expanding Cognitive Screening for Older Adults in Primary Care

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Abstract

In this piece, we raise the topic of universal cognitive screening for older adults. Dementia is the leading cause of disability, individual struggles, family challenges, and greater societal costs. We argue that universal screening for cognitive impairment among all individuals aged 65 and above has several important benefits:

(1) Early diagnosis of Alzheimer's disease and Related Dementias (ADRDs) can improve the clinical management of patients.

(2) It allows adequate time to recruit interested patients in clinical trials of novel therapeutics and to track longitudinally their cognitive and clinical status.

(3) Enable objective metrics of target engagement in response to novel treatments.

(4) Ensure earlier implementation of effective treatments during windows of opportunity that can yield the greatest improvements in patients' outcome and finally,

(5) Can offer individuals diagnosed with ADRDs a longer lead time to make important decisions about their personal and family life in the remaining time they have.

Introduction

Ensuring healthy longevity is a major challenge facing our societies. Recognizing the imperative of this challenge, the United Nations declared 2021-2030 *the Decade of Healthy Aging Initiative* [1] a global initiative to "add life to years" and "improve the lives of people, their families, and communities." To achieve this goal, addressing disability from neurological and psychiatric diseases (brain-related disability) is crucial. The WHO makes it plain: "Neurological and mental disorders are the greatest threat to human health." At present, one in four people in the world suffers a brain-related disability.

Brain disorders cause greater disability than cardiovascular diseases or cancer, and the WHO projects that by 2030 brain-related disability will account for half of the worldwide economic impact of disability. These are alarming data and yet, despite enormous efforts and large investments from the private and public sectors, progress addressing the challenge of brain-related disabilities remains elusive and aging is the single most important risk factor for brain-related disability.

In the United States (US), the older adult population has

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grown from an estimated 3 million in 1900 to 54 million in 2020 [2]. In the next 10-years, the population of older adults - defined as those 65-years and older - will grow another 17 million, to reach a total of 73 million individuals [3]. This extension of life expectancy is not unique to the US. In the next 5-years, in North America, Europe and Oceania, the older population will increase by 50%, but in Asia, South America and Africa this increase will be on the order of 200% [4]. By 2050, the global older adult population will double from what it was in 2015, from 8.5% to 16.7% of the total world population.

The extension of the human lifespan offers a wonderful opportunity for our society to harness the rich perspectives and experiences older adults have to offer. Unfortunately, to date, living longer has not meant that we live better, and the years of life gained are often associated with suffering and the need for assistance. Of the 7-years gained in life expectancy over the past two decades (from 66.8 to 73.4-years) [5] only a negligible amount, specifically 0.36-year (or about 4 months), is associated with health, the rest being burdened with disability.

Dementia is a major culprit for this lost opportunity. Dementia is the leading cause and most feared form of disability for older adults in the US [4] and Alzheimer's disease (AD) is the most common cause of dementia. Currently, 10% of people in their 60's have AD, but about half (45%) of people in their 80's will develop the disease. This means globally about 50 million lives today, and 152.8 million lives in 2050 [4]. In addition, it is worth remembering that dementia does not only affect the patients but also their spouses, children, friends, and loved ones.

Today, 16 million people in the US alone care for someone with AD or another form of dementia [6]. However, this number may rise up to 50 million by 2050 based on the projected tripling of older adults with AD because age is a major risk factor for dementia. Therefore, unless we address the risk of dementia, there is no reason to expect that more added years of life will provide individual joy or a tangible benefit to society. Rather, society faces the challenge of the long-term medical costs for those living longer, which are more than 3 times greater for those afflicted by dementia than for those without. In 2020 in the US, the annual cost for long-term care of one person with dementia was more than $52,000 [7]. Thus, added years of life with dementia increase the risk of longer disability, individual struggles, family challenges, and greater societal costs.

A common attitude is to accept these facts as the fate of human life. If so, all that is left is the hope that future therapeutic advances will bring cures. The findings of the most recent position statement on screening of cognitive impairments in older adults by the US Preventive Services Task Force (USPSTF) [8] appears to support this idea. The report concluded that screening for cognitive impairment in primary care did not improve decision-making, patient-family/caregiver's quality of life, or societal outcomes in community-dwelling older adults.

In other words, without disease-modifying treatments for Alzheimer's disease and related dementias (ADRD), there is no value in cognitive screening, because essentially, nothing can be done to prevent dementia and nothing can change the progressive disability once a dementia diagnosis is made. We wholeheartedly agree that developing disease-modifying treatments and cures for the illnesses that cause dementia is crucial. However, until we have such therapies, cognitive screening is valuable and there are many reasons why it is time that it be systematically implemented in primary care.

For starters, finding cures and disease-modifying treatments for dementia critically depends on early diagnosis of ADRDs which can also improve the clinical management of the patients [9]. When individuals are diagnosed, in many cases there is significant brain neuropathology that cannot be reversed. Early diagnosis will give investigators enough time to enroll interested patients in clinical studies, track them longitudinally, and develop objective metrics of target engagement for novel treatments.

Clear and early diagnosis will also ensure that therapies can be implemented much earlier, during windows of opportunity when the greatest improvements are possible. Beyond potentially new treatments and promising research, seemingly small lifestyle changes such as increasing physical activity, getting better sleep, eating healthier, keeping one's mind actively engaged, and nurturing social connections can monumentally impact one's cognitive trajectory.

Here we argue that the viewpoint that "presently nothing can be done" is at the very least vastly shortsighted if not simply inaccurate. Instead, screening of cognitive impairment and the resulting knowledge of a dementia diagnosis can at the very least empower individuals to make determinations about their future at a time they are healthy and most capable of doing so. Therefore, we urgently need to overcome the problem posed by the fact that over 60% of primary care physicians report not knowing how to do a proper cognitive screening, or what to do about its results if they do complete one [7].

Current cognitive screening practices

Making an AD or dementia diagnosis with high confidence, especially at earlier stages of the disease, often requires a positive biomarker test. Many have argued that broad access to blood-based biomarkers is the solution for population-level screening. However, biomarkers are not necessarily associated with the level of cognitive function, and thus are not truly predictive of disability, which is what patients most fear. Up to 33% of older individuals with a positive biomarker test do not develop dementia [10]. These marked differences in susceptibility to AD pathology, can be attributed to *cognitive reserve (CR)*, a measure of the brain's resilience against developing dementia, whereby people with larger CR can tolerate more pathological burden than others and can still maintain their function [11-14].

Because of the lack of a strong association between AD biomarkers and cognitive status, neuropsychological assessments provide critical complementary information. However, comprehensive neuropsychological batteries are

long, have limited feasibility and scalability, and are stressful for patients. Additionally, these batteries create somewhat artificial circumstances to assess the daily impact of cognitive problems. Therefore, while biomarkers and comprehensive neuropsychological evaluations are important, there remains an urgent need to improve current practices and develop more feasible cognitive screening tools that can be more readily deployed at a population level.

The results of cognitive screening can be predictive of brain-related disability when related to functional performance. For example, a recent longitudinal study that followed individuals 12-years after they were diagnosed with mild cognitive impairment shed some light on this [15]. Confirming earlier studies, individuals with *amnestic MCI* (aMCI) were twice as likely to develop dementia, when compared to *non-amnestic MCI* (naMCI).

But, interestingly, if individuals had aMCI and high frailty, they went on to develop dementia at an even faster rate than if they had low frailty. And even with naMCI, if they had high frailty, their risk of developing dementia was just as high as someone diagnosed with aMCI [15]. These findings emphasize the need to consider the entire person, not simply the performance in a given cognitive task battery, and assess the impact on the person's life and life's priorities to better predict and try to mitigate each individual's risk for brain-related disability [16]. Such studies also illustrate the value of conducting cognitive screening assessments more broadly, regardless of cognitive complaints, to identify concrete targets for therapeutic interventions that can promote an individual's health span even in the face of dementia.

Planning for the future

USPSTF's conclusion on the lack of benefit of cognitive screening appears largely based on one large-scale study conducted in response to the 2014 USPSTF evidence report summary. The main outcome measures were: health-related quality of life; health care utilization (as measured by emergency department visits and hospitalizations); advance care planning; and new ADRD recognition by physicians (primary care or specialists). Interestingly, a sub-analysis revealed that patients who screened positive and received collaborative care had significantly decreased hospital admissions compared with those not screened but with evidence of cognitive impairment.

This is consistent with previous studies showing that dementia collaborative care reduces healthcare utilization, resulting in annual cost savings ranging from $908 - $2,856 per patient [17-18]. Therefore, the conclusion seems to be that cognitive screening on its own may not be the most valuable path. Still, a sensitive cognitive screening tool enabling early diagnosis delivered with the appropriate support from a collaborative care team can be extremely impactful in helping patients and their families gain meaningful years of life in the face of the disease.

What we should do then is not give up on cognitive screening altogether, but rather develops corresponding integrated patient-centered care programs that support and address the needs of patients, their caregivers, and their families in a coordinated manner when screening detects impairments. Within an integrated collaborative care framework, early diagnosis offers an invaluable opportunity for patients to define their life goals and pursue them. It empowers patients, with appropriate support, to continue to define and enjoy their lives and those around them to take steps as early as possible to plan for and accommodate their future care needs.

In the US, only 1 in 3 adults completes any type of advanced directive for end-of-life care [19]. Knowledge of AD diagnosis can help families decide how long to continue working, planning for retirement, and health-related expenses earlier, before medical complexity increases, along with giving needs care. Becoming a caregiver, while incredibly noble, is known to seriously impact one's physical, mental, emotional, and social health [7].

So, forecasting the notion of being a caregiver of a loved one could at the very least help individuals prepare. Importantly, it can also serve as the framework for care plans and policies that can better support caregivers as well. And perhaps most importantly, more knowledge around the duration of one's healthy years can better enable the pursuit of "what really matters" at a time when one is most independent and can be fully present to enjoy that important bucket-list trip or this year's big family reunion.

Current treatments and interventions for those with ADRD

Leaving aside standard of care, including the judicious use of the few medications approved for AD, currently, there are more than 4,000 ongoing clinical trials in the US of older adults at risk for or with established cognitive decline and dementia (cognitive decline: 1,069, cognitive impairment: 1,076, dementia: 1,252, AD: 834, clinicaltrials.gov). Screening of cognitive impairment and the resulting knowledge of a dementia diagnosis can thus empower individuals to make informed decisions about their own care concerning new therapeutic alternatives, including participation in research.

Beyond potentially new treatments and promising research, let's talk about established behavioral interventions. The USPSTF evidence report summary section on therapeutics concluded that behavioral interventions such as exercise, cognitive training, rehabilitation, psycho education, and case management are effective but their effect is variable and overall small. However, the great variability in the response to such behavioral interventions does not mean that they are ineffective (and thus have less value) [20].

Such a conclusion contrasts with the compelling evidence from longitudinal trials demonstrating that a healthier lifestyle can not only decrease dementia risk by as much as 40% [21-24], but also, even in the presence of cognitive decline, a healthier lifestyle can reduce the severity of the associated disability.

For example, older adults who experience depression are at twice the risk of developing cognitive impairment [25].

There is an indication that addressing depression through behavior modifications, such as mobility, and/or medications, may reduce the risk of developing cognitive impairment [26]. Increased physical activity is also a modifiable risk factor for cognitive impairment [20,27].

When turned into habits (and that is the caveat), a healthier lifestyle can help build cognitive, physical, and emotional reserve and resilience. But, a broader implication of these aforementioned results is that committing to a healthier lifestyle is challenging and needs substantial dedication, motivation, coaching, and support. Making new lifestyle habits is difficult, particularly when multiple aspects (physical activity, sleep, nutrition, cognitive challenges, social relationships, etc.) need to be considered.

Having said that, most people are motivated to improve their brain health. In a recent survey conducted by the Global Brain Health Survey [28], 70% of respondents indicated that memory problems would be a key motivator for them to improve their lifestyle (provided that it was indeed beneficial and that the advice came from their care team). Interestingly, the number dropped to 30% if faced with the diagnosis of brain disease (after which lifestyle changes were perceived as insignificant) [28].

Importantly, willingness to actively pursue brain-healthy behaviors decreased with age. Taken together, these results highlight the imperative need for greater emphasis on prevention and implementation of personalized and behavioral interventions much earlier, and for this, proactive cognitive screening seems crucial.

Call to action

In summary, there *are* things one can do if they find they have AD or another illness that may cause dementia. Improving the trajectory of patients in a clinically meaningful way, and even investigating treatments that can achieve that crucial goal, requires early diagnosis, and, thus, we should embrace rather than dismiss cognitive screening.

The US has made it a national priority to improve early detection of ADRDs. In 2011 the US National Alzheimer's Project Act was signed into law to establish the National Plan to Address AD [29]. This Plan requires cognitive screening to be included in the Medicare Annual Wellness Visit, with the rationale that improving early diagnosis will also improve the care and treatment of older adults.

The American Academy of Neurology also recommends routine annual cognitive assessment of all adults ages 65 and older highlighting the importance of early screening for the clinical management of older adults [30]. Global efforts are also aligned; cognitive screening is a required element of the 4M's framework for Age-friendly Health Systems (what matters, medication, mentation, and mobility), and thus, annual cognitive screening is also recommended in all older adults aged 65-years and older.

Many older adults do not bring up their cognitive concerns and thus annual cognitive screening is a way to catch changes in cognition early on. A recent survey conducted by the Alzheimer's Association on current cognitive screening practices in primary care reported that while 95% of older adults want more information on their memory, only 28% received a cognitive assessment [7].

Surprisingly, despite the general increased awareness of the value of cognitive screening, only 40% of the surveyed primary care physicians are familiar with existing cognitive screening tools [7]. This lack of clarity and standardization highlights a critical need for substantial changes to existing practices to enable the broad implementation of cognitive screening in primary care.

Highly sensitive cognitive screening needs to become embedded within the current workflow of primary care providers, as brief assessments that enhance screening accuracy, increase efficiency, and improve provider and patient satisfaction. Importantly, immediately coupling cognitive screening with easy-to-access actionable recommendations, lifestyle coaching support and advanced care planning guidance for patients, and effective support for caregivers is the promising, albeit challenging way forward.

Providing key information to providers, individuals, and their families and caregivers, in ways that are useful and easy to navigate, can ease some concerns and empower patients and those who care for them to be in charge of the best decisions in the time they do have; and in parallel, it will enable cutting edge research to identify and focus on the right study participants to achieve the developments of cures and disease-modifying treatments we all await.

Conflict of Interest Statement

In this piece, we raise the topic of universal cognitive screening for older adults, and it includes academic/research ventures, as well as a private venture (Linus). Partnerships between academic/research and private ventures are valuable to address the consequences of age-related cognitive decline, as the latter have the capacity for scaling growth to meet global demands. However, this does not represent a company endorsement, and the company did not control or shape the message, and for this exact reason, we decided to disclose all relationships very clearly.

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