



# Neurocognitive Frailty Index as a Predictor of Cognitive Function: An Opinion Letter

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## Introduction

### Frailty defined, and prevalence in general population

Frailty can be defined as a dynamic age-related vulnerability emanating from multidimensional loss of energy, physical status, cognitive functioning, and general health reserves. This multifaceted state of being renders an individual prone to adverse life outcome relative to individuals who are, i.e., more physically fit. In the elderly individuals, a clinically detectable syndrome, this state tends to phenotypically manifest by the presence of 3 or more of the following symptoms, including weight loss of 10 lbs in the past year, self-reported exhaustion, weakness (e.g., grip strength), slow walking speed, and low physical activity [1]. The evidence emerging from the Canadian Health Measures Study of general population (cycles 1-3; n = 10,995, age ranging between 18-79) shows that the prevalence of frailty, using two different approaches, was between 1.8-5.3% in the 18-34 age group, 4.3-5.7% in the 35-49 age group, 6.9-11.6% in the 50-64 age group, and 7.8-20.2% in the 65+ age group [2]. Additionally, a systematic review and meta-analysis of 47 studies, conducted in 2017, emerging from low-income and middle-income countries, examining the rate of prevalence of frailty in community-dwelling older adults aged  $\geq 60$  years, found a pooled prevalence of 17.4% [3]. This knowledge points at the high heterogeneity across studies on how the frailty status were obtained, and that younger adults are at higher

risk for frailty than commonly recognized as a geriatric syndrome. This in turn informs of an important window for treatment and prevention implementation, when frailty correlates with other late-life related conditions such as cognitive aging, Alzheimer's disease or Vascular dementia.

### Frailty and its implications

There are indications that frailty status can be a predictor of late-life depressive symptoms [4] risk of falls [5], bone fracture [6], disability [7], metabolic syndrome such as hypertension [8], early hospitalization [9], lower quality of life Kojima, Iliffe [10], development of Alzheimer's disease and cognitive change [11], [12] and affecting survival rate [13]. Particularly, in the current context, evidence from a meta-analysis of scarce data (population-based longitudinal studies and a cohort study) including 936 frail elderly individuals of an overall average age of 73.3 years, shows the relations between the higher risk of incident geriatric cognitive disorder in frail older adults in contrast to that of non-frails [14]. By the same token, scientific hard signs exist from the retrospective observational study of 1,584 patient's data from TREDEM Registry (Treviso Dementia) to show the link between frailty status and the presence, degree, and some localization of cerebral brain atrophy [15]. The list goes on, only to suggest that knowledge of frailty status in older adult is important and has significant ramifications.

Additionally, noteworthy that general health practitioners and nurses are at the forefront for viewing and examining frailty status in community dwelling elderly individuals, and particularly those with Mild Cognitive Impairment (MCI), i.e., the prodromal stage of AD, or the so called Mild Neurocognitive Disorder (MND) due to AD as characterized by the Diagnostic and Statistical Manual of Mental Disorder-Fifth edition (DSM-5) [16]. Thus, the use of a psychometrically sound and easy to use assessment scale by professionals become imperative.

### Frailty assessment

The assessment of frailty, and important geriatric syndrome, via an innovative yet psychometrically reliable and valid tool that can be used by primary care professionals and others is a most, in order to detect cognitive decline at a germinating stage, and potentially slow the disease progression (e.g., neurodegeneration), and optimize quality of life. Given the mechanisms, pathways, and risk factors differences across genders for developing neuropsychiatric and neurodegenerative conditions such as depression and Alzheimer Disease [17] that in turn affects cognition and their association with frailty status [18], a measure that takes into account this diversity, is crucial. To this end, norm-based measures used to assess neurocognitive functions predicting neurocognitive frailty status and providing an accurate prognostic probability by taking into account of the gender differences for developing dementia and related conditions play a significant role, not only in community settings, but also for clinical trials where treatment for cognitive decline has been in the works [19, 20].

To achieve this particular goal, we recommend the use of novel Neurocognitive Frailty Index (NFI) scale with an accompanying application, that have demonstrated validity-evidence for showing the relationship between frailty status and cognitive change overtime in elderly individuals generally [21], and those with hypertension and heart disease [22]. Presently, the on-line prototype of NFI measure is being developed for use in clinical settings to provide an evaluation of the probability of developing dementia in people over the age of 50.

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### Conflicts of Interest

The authors declare that they have no conflict of interest.

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