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Editorial

Is accelerated biological aging the hidden link between physical frailty, social deficits, cognitive impairment and risk of incident diseases?

Over the past decades, the interplay between biological aging and age-related diseases and conditions has become a central focus of geriatric and gerontological research. According to the geroscience hypothesis, biological aging is due to specific mechanisms, such as mitochondrial dysfunction, genomic instability, impaired proteostasis, and chronic low-grade inflammation. These processes progressively lead to multisystem dysregulation across metabolic, immune, endocrine, and repair pathways and provide the biological substrate on which age-related diseases ultimately develop [1–3].

In this framework, physical frailty has been largely regarded as the clinical expression of accelerated biological aging, marking a deviation from the trajectory of normal aging [4,5].

In this issue of the Journal of Nutrition, Health and Ageing, Pei et al. [6] aimed to investigate the relationship between physical frailty, social deficits, cognitive impairment and the risk of developing 45 incident non-communicable diseases (NCDs) using the cohort of the UK Biobank. Moreover, the study explores whether accelerated biological aging mediates these associations, applying three validated indices: the Klemera–Doubal Method, PhenoAge, and Homeostatic Dysregulation.

The authors reported that impairments across each domain (physical, cognitive, and social) were independently associated with a higher risk of multiple NCDs, ranging from cardiovascular and metabolic disorders to neuropsychiatric and musculoskeletal conditions. The risk increased substantially when deficits coexisted across domains, underscoring the cumulative effect of multidimensional vulnerability. These findings are consistent with previous studies showing that the coexistence of frailty components across multiple domains confers a greater risk of adverse outcomes than single-domain deficits alone [7,8].

In the mediation analyses, accelerated biological aging explained up to 50% of the association between impairment in different domains and disease onset.

On this basis, Pei et al. proposed a conceptual model in which physical, social and cognitive impairments accelerate biological aging, thereby amplifying the risk of non-communicable diseases, a pathway summarized by the authors as "frailty → accelerated biological aging → NCDs."

As Pei and colleagues correctly acknowledge, however, causality cannot be inferred from their data. The association between physical frailty, cognitive impairment, and social deficits with biological age was evaluated only at baseline, within a cross-sectional design, which precludes establishing temporal directionality.

Moreover, although the indices used to estimate biological age have been validated, several of the underlying biomarkers (e.g., blood pressure, glucose, C-reactive protein, BMI) may also be components or consequences of these impairments themselves.

In particular, for physical frailty and cognitive impairment, current evidence more strongly supports the reverse direction of influence, that is, accelerated biological aging leading to these conditions, rather than these impairments inducing accelerated aging.

Conversely, the pathway proposed by Pei et al. appears particularly plausible for social deficits, where psychosocial stressors and reduced social participation can influence neuroendocrine, inflammatory, and metabolic pathways involved in biological aging [9–11].

From a clinical perspective, these findings highlight the importance of a comprehensive assessment that includes not only physical and cognitive, but also social dimensions. Although Pei et al. referred to social deficits rather than social frailty, as no validated instrument was used, their results highlight the broader relevance that impairments in the social dimension may have in determining health trajectories.

Social frailty has increasingly been recognized as a key determinant of health and functional decline in later life. Its prevalence among community-dwelling older adults is estimated around 20%, higher than that of physical frailty, and it is consistently associated with disability, depression, and mortality [12]. In the English Longitudinal Study of Ageing, Ragusa et al. found that social frailty, particularly poverty and living alone, was independently linked to all-cause mortality, even after adjustment for multimorbidity and depressive symptoms [13]. Similarly, Goto et al. reported that social frailty nearly doubled the risk of mortality and functional disability across longitudinal studies [14].

Emerging evidence further connects social adversity with biological aging. Kivimäki et al. demonstrated that lifelong social disadvantage was associated with proteomic signatures of accelerated immune aging linked to upregulation of NF-κB–related inflammatory pathways [15]. This convergence between social and biological mechanisms reinforces the view that social frailty is not merely psychosocial, but a state with measurable biological correlates.

Addressing social frailty, by promoting social participation, community engagement, and supportive networks, may therefore represent not only a social but also a medical intervention. Integrating validated measures of social frailty into clinical and epidemiological studies will be essential to strengthen the evidence and to support its broader implementation in research and practice.

Finally, in this study, the evidence that impairments in one or more domains are associated with a higher risk of incident non communicable diseases, was already evident before old age, strongly suggesting that a multidimensional assessment may be appropriate even before advanced age.

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Declaration of competing interest

The authors have no conflict of interest to declare.

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