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Review Article

Aging and Multimorbidity: New Tasks, Priorities, and Frontiers for Integrated Gerontological and Clinical Research

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A B S T R A C T

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Aging is characterized by rising susceptibility to development of multiple chronic diseases and, therefore, represents the major risk factor for multimorbidity. From a gerontological perspective, the progressive accumulation of multiple diseases, which significantly accelerates at older ages, is a milestone for progressive loss of resilience and age-related multisystem homeostatic dysregulation. Because it is most likely that the same mechanisms that drive aging also drive multiple age-related chronic diseases, addressing those mechanisms may reduce the development of multimorbidity. According to this vision, studying multimorbidity may help to understand the biology of aging and, at the same time, understanding the underpinnings of aging may help to develop strategies to prevent or delay the burden of multimorbidity. As a consequence, we believe that it is time to build connections and dialogue between the clinical experience of general practitioners and geriatricians and the scientists who study aging, so as to stimulate innovative research projects to improve the management and the treatment of older patients with multiple morbidities.

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Multi-morbidity: Implications and Challenges for Medical Care and Research

The aging of the world's population and its increasing longevity during recent decades induced profound changes in the world's political and economic landscape and presented many challenges to health and social care systems. In response, medical science created new diagnostic and therapeutic tools that improved rates of long-term survival for patients affected by chronic morbidity and an increasing prevalence of multiple chronic conditions. Noteworthy for this discussion, multimorbidity, the co-occurrence of 2 or more chronic diseases in an individual patient, has become recognized as the most common chronic medical condition. That milestone marks the transition from the era of “single chronic disease medicine” to the era of “multimorbidity medicine.”¹

For centuries, medical science evolved around the nosology and pathophysiology of single diseases and devoted little to no study to

the coexistence of multiple chronic conditions in a single patient. Progressively, it has become clear that the paradigm of “1 patient–1 disease” no longer fits the medical necessities and needs of most patients, and that a more holistic, patient-centered view should be developed.^{2–4} Indeed, in recent years, the literature on multimorbidity has grown exponentially, providing clear evidence of flourishing attention from the scientific and medical world to this emerging issue. Despite this explosion of interest, there remains a dearth of evidence-based guidelines for clinical practices for treating multiple chronic conditions in patients. Worse, it is unlikely that such guidelines will be developed soon because individuals with multiple diseases are excluded from clinical trials.^{5–11}

In the literature, “multimorbidity” is usually addressed from the point of view of general practitioners (GPs).^{12,13} The relevant impact of multimorbidity in primary care is undeniable; however, the emerging importance of multimorbidity in the aging field is even more striking. In writing this report, we reviewed the existing literature and want to provide fresh insights about multimorbidity from a gerontological perspective. We conclude that it is time to build bridges between the clinical experience of GPs and geriatricians and the research of scientists who study aging. Such connections and dialogue would stimulate innovative research and other projects to

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improve the care of older patients and others who experience multiple morbidities.

One complexity in understanding multimorbidity is that diseases can coexist in the same individual for several reasons, including random chance, common risk factors or mechanisms, and iatrogenic complexities.¹⁴ Indeed, aging is the strongest risk factor for many chronic diseases. Perhaps this is because aging brings with it the chronic dysregulation of multiple organ systems. When a threshold of impairment is reached, such breakdown in regulation among several organs and tissues becomes evident to clinicians (Figure 1). From a gerontological perspective, accumulation of diseases in an older adult is a milestone for progressive loss of resilience and homeostasis. Like the tip of an iceberg, this marker constitutes a red flag for the underlying onset of accelerated aging. Thus, measures of multimorbidity can provide effective tools in clinical and research settings to identify individuals who age faster than others. Likewise, this approach to research can improve our understanding of the mechanisms of aging and help to develop effective strategies for preventing and limiting the burdens of multimorbidity in older persons.

Definition of Multimorbidity

The Lack of a Standardized Operational Approach

“Comorbidity” and “multimorbidity” are often used as interchangeable terms. However, in recent years, *comorbidity* more often describes the combined effects of additional diseases in reference to an index disease (eg, comorbidity in cancer). Meanwhile, *multimorbidity* is more often meant to describe simultaneous occurrence of 2 or more diseases that may or may not share a causal link in an individual patient.^{15–17} Such distinctions certainly help; however, methodological problems affecting the measurement and operational definition of multimorbidity still persist, while no consensus about these parameters appears to be emerging.¹⁸ Many measurement tools have appeared in the literature. They vary from complex indexes of severity, complications, treatment, and prognosis to simple counts of diagnosed diseases. Nonetheless, no consensus exists for diagnostic criteria or the types and weightings of such diseases, which encompass a few to more than 150 different conditions. Lack of consensus and standardization makes it difficult to compare findings across studies. To overcome this confusing heterogeneity and fashion a uniform approach, Fortin and colleagues¹⁸ suggested that a good

compromise is to include at least the 12 most prevalent chronic diseases that place the greatest burden in the population. Although this approach is agreeable, when assessing geriatric patients, we believe also that indices of multimorbidity should specify conditions known to be highly prevalent and strong risk factors for disability among older people. Moreover, geriatric syndromes, which most studies have omitted, should be considered in future investigations.¹⁹ Indeed, a gold standard definition for “geriatric multimorbidity” and its validation across different populations and clinical settings are high priorities for gerontological research and the design of new care systems for rapidly aging populations.

Epidemiology of Multimorbidity

The Growing Burden of Chronic Diseases

According to a recent report, nearly 80% of Medicare beneficiaries have at least 2 chronic conditions and more than 60% have at least 3 chronic conditions.²⁰ Experts estimate that 26% of the US population will be living with multiple chronic conditions by 2030.²¹ Although multimorbidity is not limited to older adults, its prevalence increases substantially with age. In a cross-sectional study that included 1.7 million patients in Scotland, Barnett and colleagues²² found that 30.4% of the population aged 45 to 64 years, 64.9% of people aged 65 to 84 years, and 81.5% of people aged 85 years or older reported at least 2 chronic conditions. Data from the representative sample included in the Italian InCHIANTI study suggested that the rise of multimorbidity with age is not linear but rather that it significantly accelerates when the elderly achieve older ages.²³

Risk Factors

Every published study describes the strong association of multimorbidity with age, and no study doubts that age is the main risk factor for prevalent and incident multimorbidity.^{22–42} Most evidence also acknowledges gender differences, notably a prevalence of multimorbidity higher among women than men.^{24,29,33,36,37,41,42} Furthermore, lower socioeconomic status and lower education are well-established risk factors for multimorbidity, an effect that is particularly evident for mental health disorders.^{22,24,29,33,34,37,41,42}

Racial and ethnic differences in the prevalence of multimorbidity remain less explored and controversial. Studying Medicare beneficiaries, DuGoff and colleagues²⁰ reported multimorbidity among

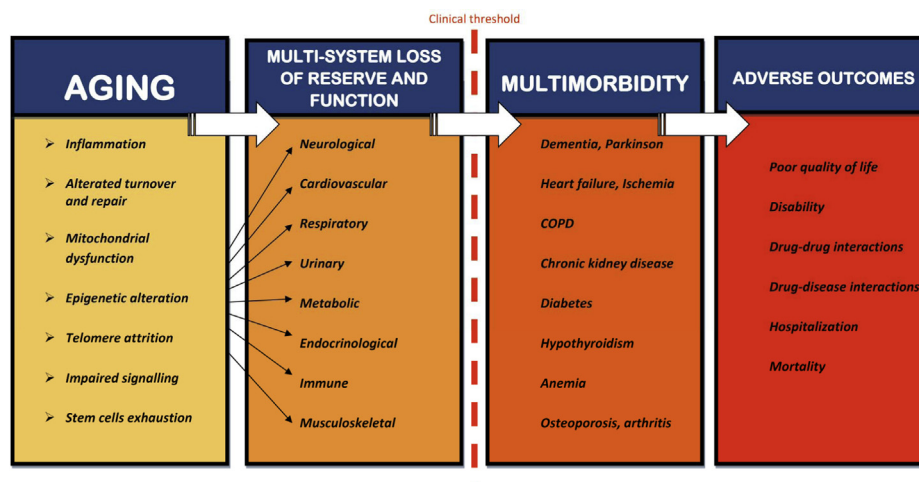


Fig. 1. The age-related multisystem loss of reserve and function, rooted in the biological determinants of the aging process, is associated with increased susceptibility for chronic diseases, which becomes clinically evident as multimorbidity when a certain threshold of impairment has been reached.

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