



Commentary

Mens sana in corpore sano: multimorbidity and mental health

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Can we escape mental illness by preventing physical diseases? While it may be too soon to tell definitely, Juvenal – an ancient Roman poet to whom the phrase “a sound mind in a sound body” is attributed – may have been right after all. Let us look at the problem through the lens of multimorbidity.

The accumulation of chronic diseases, i.e., multimorbidity, is a hallmark of the aging process and a critical challenge for our aging societies [1]. Multimorbidity affects most older people, requiring complex management and treatment regimens that burden individuals and healthcare systems alike [2]. When common mental disorders such as depression and anxiety manifest in clinically complex individuals, their combined consequences increase dramatically [3]. Co-existing chronic conditions interact with each other, influencing the development of mental disorders, especially depression, through several pathways [4]. Despite the accumulating epidemiological evidence of multimorbidity as a driver of poor mental health in late life, our understanding of how these processes unfold is still limited.

In their recent work in *The Lancet Regional Health – Europe*, Ronaldson and colleagues contributed to this research field with a relevant piece of work, that explored the association of multimorbidity and its patterns in midlife, with the development and persistence of common mental disorders such as depression and anxiety, over a 10-year follow-up [5]. Using a large sample from the UK Biobank, they reported a dose-response association between the count of somatic diseases and the risk of mental ill-health. Furthermore, the authors identified specific multimorbidity patterns, particularly the respiratory and pain/gastrointestinal diseases, that exhibited the strongest association with the risk of depression and anxiety [5].

These findings suggest that in addition to the mere presence of multiple diseases, the assortment of chronic conditions has implications for mental health as well. Indeed, specific somatic diseases tend

to cluster in the same individual because of common risk factors or due to shared pathophysiological mechanisms, which may also affect the development of mental disorders over time. For instance, vascular and inflammatory burden are commonly implicated in the pathophysiology of both chronic diseases and mental disorders. Therefore, the detection of such multimorbidity patterns, and their differential association with mental disorders, may help uncover underlying common biological pathways, which could be targets for future preventive approaches [6].

Interestingly, the authors found “undefined” multimorbidity, i.e. multiple diseases belonging to different patterns, to be nevertheless associated with increased risk of both depression and anxiety compared to the absence of multimorbidity [5]. Still, looking at the association estimates, it appears clear that the risk of mental ill health in individuals with undefined multimorbidity was lower than in those characterized by the specific patterns, such as cardiometabolic, respiratory, cerebrovascular and pain/gastrointestinal disorders. Likely, a milder type of multimorbidity, the undefined cluster may spill into other, more specific multimorbidity patterns over time, as shown in another recent study [7]. This underscores the effort required to disentangle the heterogeneity within multimorbidity that challenges researchers and clinicians alike, and warrants more research specifically dedicated to unravel how diseases cluster together.

Notably, Ronaldson and colleagues found that both depression and anxiety were predicted by multimorbidity. These findings put emphasis on how mental ill-health manifests specifically in older adults. Not only do anxiety and depressive symptoms often co-occur in late life, but many older adults also fail to fulfill conventional criteria for depression, as they are less prone to exhibit affective symptoms such as low mood. As a result, depressive syndrome in old age may end up being undetected and untreated, leading to profound consequences in terms of health trajectory [8]. Furthermore, depression and anxiety in late life are highly linked to cognitive status, as they can present as prodromes of incipient dementia. Interestingly, specific multimorbidity clusters have also been associated with increased dementia risk, which also adds another level of complexity to untangling the link between somatic and mental health in old age [9].

An important limitation of Ronaldson et al. is the reliance on self-reported diagnoses, which may have introduced some information bias, especially in consideration of the outcomes of the study. Moreover, the disease list includes conditions with different levels of aggregation, which may have affected the definition of the multimorbidity patterns. Indeed, these are common limitations of studies on

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multimorbidity. Relying on clinically assessed conditions and validated lists of diseases is warranted in this field, for the sake of comparability and generalizability across studies.

So, was Juvenal right at the end? Is preventing multimorbidity, or slowing down its progression, a feasible and effective way to combat mental disorders in late life? In order to make meaningful progress in understanding, preventing, and treating mental health disorders, researchers and clinicians need to address the complex systems from which these disorders arise [10]. Failing to account for the health heterogeneity determined by multimorbidity may hamper our ability to design effective patient-centred strategies, and ultimately provide better mental health care for older adults.

Contributors

All the authors contributed to the conception and writing of the present commentary. All the authors approved the final manuscript.

Declaration of Interests

All authors have nothing to disclose.

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