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Frailty and Depression: Comorbidity in the Context of Imperfect Measurement

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To the Editor

We read with great interest the recent article by Lakey and colleagues[1] regarding associations between antidepressant use, depressive symptoms, and incident frailty among older women. We believe that the clarification of connections between frailty and depression is an important topic for research and clinical attention. Their finding that antidepressant use is associated with higher incidence of frailty[2] (as defined by Fried and colleagues) independent of depression status may have significant implications for treatment of depressionand anxiety among older adults. However, we feel that the general association between frailty and depression should be interpreted in light of evidence suggesting that the strong correlation betweenthe two constructsmay be determined, to a large extent, by the criteria used in their measurement. Though the authors recognize this possibility and use a depression screening instrument that does not include items about fatigue and energy, this may not be sufficient to avoid what they call 'operational confounding.' A recent study by our group found that, even when corrected for chance agreement, Fried frailty criteria and the Diagnostic Interview Schedule, a fully-structured instrument that has been extensively validated against psychiatric interview,[3] for Major Depressionagreed in their categorization of older adults to a much greater extent than would be expected by the operational overlap of fatigue items alone. [4] Indeed, the concordance as indicated by the chance-corrected Kappa coefficients was in the "moderate" range, which is particularly notable because Kappa is generally used to indicate the amount of agreement between two raters of the *same* construct.

These findings suggest that currently available measures of frailty and depression are either poor at discriminating between the two distinctconstructs, or that theyidentify the same underlying condition. The former possibility has important implications for studies such as the one by Lakey and colleagues which examine associations between frailty and depression. If, as the authors suggest, antidepressant users have a more severe form of depression than non-users, then they may also have a higher subclinical baseline level of frailty by virtue of the measurement instruments used to identify frailty and depression. Antidepressant users would then have a lower threshold for manifesting frailty, which would explain the finding that antidepressant users have a higher risk of developing frailtyeven when not meeting criteria for depression. If, on the other hand, frailty and depression are indeed congruent conditions in later life,[5] then the search for differentiation and association between the constructs would be largely unnecessary. While analytical evidence does not support this scenario of a single underlying condition, it is easy to see why it is difficult to

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distinguish them. For instance, apart from the aforementioned definitional overlaps, depression in later life is often marked by endorsement of more vegetative symptoms (e.g., sleep difficulty, fatigue) rather than cognitive or mood symptoms. For this reason it has been suggested that in late-life mood disturbances can be conceptualized as “depression without sadness”.[6]

Clearly, it is necessary for future work to reconcile the conceptual differences between frailty and depression with the apparent lack of operational differentiation. Resolving these issues of operational and conceptual overlap will help improve measurement of both conditions and will help researchers and cliniciansbetter understand the reasons for their comorbidity.[7] Interdisciplinary research that is informed by psychiatry, gerontology, and epidemiology will be particularly important for translating findings regarding frailty into effective clinical care.[5]

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