COMMENTARIES

What would make a definition of frailty successful?

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Abstract

At present, frailty is defined variably. Some consensus on a definition is likely to emerge, but the basis for a successful definition needs to be explored. Here, a classic approach to validation is proposed: a successful definition of frailty should be multifactorial but must also manage the many factors in a way that takes their interactions into account. It is likely to be correlated with disability, co-morbidity and self-rated health, and should identify a group that is vulnerable to adverse outcomes. Ideally, it should also be susceptible to animal modelling. In that frailty and age are so bound together, it is also likely that there will be some age at which virtually all people will be frail, by any definition. Apart from being valid, the success of any definition of frailty will depend on it being useful to researchers and clinicians. The need for progress on our understanding of frailty is evident, but for now, there is insufficient evidence to accept a single definition of frailty.

Keywords: *frailty, definition, disability, co-morbidity, mortality, predictive validity, consensus*

Frailty is common and especially a focus for geriatricians, but there is no consensus on its definition beyond that it arises from many factors, and is a state of vulnerability.

This paper proposes that a successful definition of frailty must also identify clinically recognisable degrees of frailty, be susceptible to animal modelling and demonstrate predictive validity as its highest standard of validation. How to define frailty should remain an active area of enquiry.

Anyone interested in research on frailty must first get to grips with what it is, and how it might be defined operationally. The current literature offers some help, but at this point allows only one non-controversial conclusion: there are many definitions of frailty [1, 2]. If that is the case, how might we proceed? For many purposes, the need to just get on with it will trump other considerations, so that once that decision is made, there are essentially two choices. One is to propose a definition, see how it relates to earlier work and, by dint of consensus, compromise or momentum, to advocate vigorously for it. There is ample precedent for this—indeed this description would seem to characterise much of the definition of cognitive disorders in the International Classification of Diseases [3] or the Diagnostic and Statistical Manual of the American Psychiatric Association [4].

A consensus group of the American Geriatrics Society has settled on defining frailty as a physiological syndrome characterised by decreased reserve and diminished resistance to stressors, resulting from cumulative decline across multiple physiological systems, and causing vulnerability to adverse outcomes [5]. For this, a phenotype of physical frailty has been proposed as the combination of weight loss, fatigue, impaired grip strength, diminished physical activity or a slow gait [6]. (On the other hand, a proposal to operationalise the definition as a clinical measure includes several features, such as cognitive, functional and social circumstances, that go well beyond just the physical aspects [7].) A related operationalisation of physical frailty narrows the definition simply to include slow gait speed [8].

Notwithstanding that consensus, another approach is to accept that a variety of definitions of frailty exist, that they can be classified, and that as research proceeds it should yield a definition clear enough so that its fit within the existing spectrum of definitions can be understood. This is the approach taken by the Canadian Initiative on Frailty and Aging, which has summarised frailty definitions as belonging to one of four classes: (i) physiological definitions; (ii) definitions based on frailty as a complex syndrome; (iii) frailty based on a balance model (which adds to the complex syndrome social elements); (iv) frailty defined on the basis of a geriatric syndrome, such as delirium and falls [1]. Given this variety, it would still seem possible to conduct legitimately useful research on frailty without necessarily measuring grip strength (this would be difficult in animal models, for example) or enquiring about decline in physical activity (in the setting, for example, of people recovering from a hip fracture).

Over time, it is likely that some definitions of frailty will be more successful than others. It is too early to know whether success will reflect the evident validity of a given definition, or whether other factors will be more important. In the interest of maximising the likelihood that the dominant definition of frailty will be valid, and that the basis for its validity can be understood, one can hypothesise about what a definition of frailty should look like. I argue that a successful definition of frailty should meet the criteria laid out in Table 1 For clarity, these are grouped by the approach to validation proposed by Streiner and Norman [9]. These criteria, of course, are in addition to the usual criteria that any relationship between entities be causal, and that any results be replicable.

Like much that we deal with in medicine ('health', for example), frailty is insubstantial, having no claim to existence in a way that is separable from that which it describes. Frailty is widely agreed to be a state that is multifactorial and that implies vulnerability, and we can use this starting point to consider how any definition of frailty might work.

Content validity

Content validity ('face validity' is a synonym) refers to whether the definition makes sense on first principles. It seems unlikely that a single cause or feature will adequately explain frailty. Rather, the consensus that frailty is multifactorial seems well founded [10, 11]. This is not to say that a single factor definition could not be the case, but rather that the onus would be on the proponent to demonstrate its validity to a high standard. Similarly, the decision to exclude factors from contributing to frailty (such as cognitive function) should be susceptible to empirical testing.

As reasonable as a multifactorial approach might seem, however, it is not without pragmatic difficulties. Any multifactorial definition faces the problem of computational tractability, inasmuch as when the number of factors to be considered increases, their interactions increase exponentially. The interactions of variables reflect that the variables are not truly independent. While classical statistical models assume independence of variables, this is often not the case in closed systems of highly inter-related components. The remedies for dependence between variables are not yet entirely satisfactory: when techniques are used to eliminate variables that are dependent, the result is often that the overall ability of the model to explain variation in the outcomes is low—in fact, while explaining 50% of the variance would often be a triumph biologically, it would also be a poor clinical standard. Clinically, we do better by taking context-specific information into account in ways that are not readily generalised by classical models. This is an even more pressing concern for any dynamic definition (i.e. any definition that includes change in various factors over time) where a set of variables would be interpreted differently in the same person if they were seen on different days as a process evolved. In consequence, frailty definitions face a tension in knowing that the definition should be multifactorial, and that the state changes over time, and in being able to take all factors into account in multivariable statistical models. Thus, a successful definition of frailty needs to be both multifactorial and computationally tractable.

Construct validity

Construct validity refers to whether the operational definition coheres with other measures of the phenomenon, related conditions and constructs, many of which themselves will be insubstantial too. Construct validity is typically measured by correlation of the new (operationalised, quantified) definition with like measures. Such like measures will include measures of disability; even though frailty is not the same as disability [8, 12], the two should not be uncorrelated. Similar considerations hold for co-morbidity and for self-rated health. Another important correlation will be age: any frailty measure should be more common as people age. Given too that women with disabilities live longer than disabled men and that frailty and disability will be correlated, then frailty is likely to be more common in women.

Criterion validity

Criterion validity exists when a new definition or test correctly classifies people according to a referent outcome. The outcome can be either an accepted test of impeccable validity (a so-called 'gold standard') or the prediction of an outcome. In the case of frailty, it is non-controversially linked with vulnerability, so one means of testing the criterion validity of a definition of frailty would be to assess its ability to predict adverse outcomes, such as death, institutionalisation, prolonged hospital stays, or common clinical sequelae, such as falls. In short, as no frailty referent yet exists, then predictive validity becomes our highest standard, and evaluating frailty definitions by their ability to demonstrate vulnerability to adverse outcomes is likely to be the most persuasive test. Some nuance in understanding predictive validity will be necessary. For example, not all people who die are frail prior to death, so correlations, though high, would not be expected to be perfect. In other words, using vulnerability to death as a test of a frailty definition is not the same as building a model of mortality prediction in elderly people,

Table 1. Criteria for a successful definition of frailty

Content validity
- includes multiple determinants
- is dynamic
- validly supercedes earlier, successful definitions
- broadly useful across contexts (e.g. clinical trials, population studies)
- computationally tractable

Construct validity
- is more common in women than in men
- is more common with age
- related to disability
- related to co-morbidity and self-rated health

Criterion validity
- predicts mortality
- predicts other adverse outcomes (delirium, falls, worse function)
- predicts an age at which everyone is frail
- scales from cellular and animal models to studies in people

which might benefit from specific measures (such as accidents during sporting events) that might be important for the very fit, but have little relevance to the frail. Similarly, given the likely differences in access, for example, some types of health services use (e.g. admission to an intensive care unit) might only have limited predictive value.

A special outcome for any frailty definition would appear to be the prediction (and then the demonstration) of an age at which virtually all people are frail. Mortality data would suggest that age 95 years is one such reasonable candidate [13]. At this age, population estimates of maximum lifespan expectancy tend to converge, and the phenomenon of 'mortality cross-overs' is common, i.e. while some factors might differentiate mortality risk below this age (e.g. race or income), individuals who live beyond age 95 are much less readily distinguishable, and some factors associated with mortality prior to that age can even become protective thereafter [13]. Again, the idea is not that absence of frailty is impossible after age 95, but rather that the burden of proof especially falls with the originators of any new definition that would claim otherwise.

A definition that otherwise meets these criteria and could give rise to an animal model would be useful, and is likely to be essential in the long term. In addition to helping define mechanisms, an animal model can more quickly close the gap between the status quo and the possibility of treatment. It need not limit opportunities to explore the contribution of cognitive or social factors as each is measurable in an animal model.

As far as I know, no existing definition meets all these criteria. Consequently, a legitimate goal of some frailty research would be to develop, validate and refine a definition of frailty. That the definition changes should not be a source of concern. For example, the definition of myocardial infarction has evolved from one that originally emphasised clinical features (such as chest pain), which we now know to be neither sensitive nor specific enough to be useful clinically, to the present approach which employs a biological marker.

These considerations of a successful definition of frailty have emphasised the need for validity, reliability and sensitivity to change. Success, however, is likely to require that the definition also be, in Feinstein's term, clinically sensible [14]. This will be a more difficult judgement, as sensibility includes not just the usual measurement properties, but also usefulness (including ease of use) and acceptability by the broad community that would use the definition. It is vital that geriatricians get to grips with frailty—arguably the care of elderly people who are frail is our chief mandate [15]. The lack of an adequate evidence base for a single definition means that the nature of frailty must be an active area of enquiry, if we are to face up to the challenges that it poses.

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Conflict of interest

I declare no financial conflict of interest.

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