

Frailty, the determinants of health and the new evidence base

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Frailty, a consequence of cumulative decline in many physiological systems during a lifetime, is a state of vulnerability to poor resolution of homeostasis after a stressor event.¹ A popular operationalization sees frailty in relation to *deficits* (i.e., symptoms, signs, diseases, and disabilities) that accumulate with age.² At a given point in time, a person's health may be quantified as a *frailty index* (FI), which is the ratio of the deficits present in the person to the total number of deficits considered.³ The FI predicts mortality independently of and more strongly than chronological age.⁴

Analogous to the theory of *damage and repair* (which asserts that the surviving fraction of cells in a mutagen-treated population is proportional to the number of potentially lethal lesions that are not removed by any repair process),⁵ the average number of deficits present in an individual is conceptualized as the product of the average intensity of the environmental *stresses* and the average *recovery time*.⁶ Therefore, it is thought that by minimizing "hits" (stresses) and maximizing "post-hit recovery rates," individuals will accumulate fewer and less severe deficits, thereby benefiting their life expectancy.⁶

In humans, the causes of premature mortality are rooted in demographic, medical, lifestyle, and psychosocial factors, and the same variety applies to the nature of the "hits" (and recovery opportunities) that individuals take (and have) during their lives. Indeed, Thomas McKeown's⁷ *determinants of health* framework can be applied to "hit" and recovery processes: On the one hand, *hits* can be caused by the environment (eg, being struck by lightning), individual behaviors (eg, smoking), genetic susceptibility (eg, to sepsis⁸), and health care-related events (eg, iatrogenic); on the other hand, recovery processes can be facilitated by nurturing environments, health-promoting behaviors, genetic prorecovery factors (eg, to neural injury⁹), and effective healthcare interventions. Thus, the determinants of health are *double-edged swords* within the "hit" and recovery model of frailty.

Although it has been argued that Geriatric Medicine should be defined by frailty,¹⁰ in many countries, access to Geriatric Medicine

services is restricted to those above a certain age (typically 65 years or above). In a small minority of people, the accumulation of deficits has accelerated to a lethal point before the age of 65 and so they never present to geriatricians. The majority of people who turn 65 have a low FI and are not comfortable with being labeled as "geriatric" patients. As these patients age toward their 70s, 80s, 90s, and 100s, their FI trajectories diversify, and increasingly, age alone loses the ability to predict where people are on the fitness-frailty spectrum.¹¹ Thus, the specialty of Geriatric Medicine cannot and should not be defined by age alone.

It is thought that 0.7 is the highest limit of accumulation of deficits in humans, beyond which survival is not biologically possible.¹² In the European population, the mean FI value at the age of 65 is 0.12 (50% confidence interval: 0.04-0.19),¹³ and in developed countries, community-dwelling older people will accumulate deficits, *on average*, at about 3% per year.¹⁴ At the *individual level*, the path toward longevity is like a car journey where the number of "accidents" experienced by the driver depends on the "road conditions" (environment), the prudence of the driver (behavior), the car make (genetics: Rolls Royce vs Ford Fiesta), and the state of car maintenance (health care). This analogy also provides for interactions and double-edged effects.

As complex and unpredictable as the journey toward longevity is, reaching a very old age without perishing is, in itself, a survival achievement. Very old persons who have accumulated health deficits over time but managed to survive are, indeed, *tough and frail*,¹⁵ and they may well say *I may be frail but I ain't no failure*.¹⁶ Some of these survivors were just "lucky"; many others had very adverse road conditions along their journeys, but drove with *prudence*; and some of them had the advantage to drive high-quality engines. Others drove basic quality machinery, but they maintained it well. The end result of this *life wisdom* and *resilience* is frailty in old age (ie, taking "hits" without dying). Perhaps another metaphorical expression would be that they are the walking wounded of the battle of living. Because

people who become frail have generally been prudent, we should make every effort to know their values and wishes when it comes to how we should deal with their disability and dependency, and respect their wishes even when they can no longer express them.

Frail older people are often excluded from clinical trials, so day-to-day treatment clinical decisions are commonly based on the evidence extrapolated from more robust patient groups with fewer physiological deficits. Extrapolating the existing evidence to the frail population may result in lack of effectiveness, and even harm. However, the emerging evidence base for the frail is not only about *avoiding potentially harmful interventions*, but also about *proactively intervening*. The most notable example of the latter is the *Cochrane systematic review* on Comprehensive Geriatric Assessment (CGA) for older adults admitted to hospital.¹⁷ This review showed that CGA (a multidimensional, interdisciplinary diagnostic process to determine the medical, psychological, and functional capabilities of a frail elderly person in order to develop a coordinated and integrated plan for treatment and long-term follow-up) increases a patient's likelihood of being alive and in their own home at up to 12 months. It is therefore of great importance to routinely identify (with routine frailty screening early during the hospital admission) those who will benefit the most from inpatient CGA.¹⁸ Routine screening for frailty, cognitive impairment, and acute illness severity in hospitals may aid the development of acute care pathways for older adults.^{19,20}

With a high degree of probability, there is presently no other area of medicine where such an exciting evidence gap has emerged concerning a sizeable and growing sector of the population, with simultaneous potential to improve patient outcomes, reduce health-care expenditure in ineffective (and potentially harmful) interventions, and help focus resources on new, proactive, and effective models of specialist geriatric care. This complexity and *double-edged evidence gathering* demand an even greater degree of involvement at the individual patient level, which is diametrically opposed from a "nihilistic" approach. As the evidence base for the frail unravels, we must ensure that we avoid purely negative stereotyping (ie, it is just as wrong to be "frailist" as it is to be ageist, racist, or sexist).

At present, endless opportunities exist to revisit evidence and generate new specialist Geriatric Medicine knowledge for the frail. Indeed, new promising horizons are to follow the incorporation of frailty into clinical practice and clinical research. This will help personalize Geriatric Medicine interventions to the benefit of patients and society: On the one hand, we will learn to avoid unnecessary "hits" for patients or, when a "hit" is deemed necessary, we will tailor its intensity to the individual vulnerability and state of repair mechanisms; on the other hand, we will learn to offer proactive interventions based on CGA, promotion of recovery time, and enhancement of repair mechanisms. The Golden Era of evidence-based Geriatric Medicine has just started.

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