Frailty Defined by Deficit Accumulation and Geriatric Medicine Defined by Frailty

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KEYWORDS

• Health deficits • Frailty • Disease presentation • Frailty index
• Comprehensive geriatric assessment • Complexity

As cells age, they develop deficits as a result of the accumulation of unrepaired cellular and molecular damage. This fact is well accepted; for example, Kirkwood[1] reviewed several maintenance and repair mechanisms involved in this process of accumulation (eg, somatic mutation theory, mitochondrial theory, altered proteins theory, network theories of aging). These theories point to the complexity of the networks and the stochastic nature of the many pathways that lead to damage. The theories also make clear that various repair mechanisms exist, which means that change with aging is not always deteriorative; improvement is also possible. This multidimensionality of change also contributes to the complexity of the aging process.

As people age, they accumulate deficits that are eventually manifested as frailty, disease, or disability. An important area of inquiry involves the extent to which subcellular deficit accumulation gives rise to the deficits that are visible clinically or by test procedures. In the progression from molecular damage to cellular damage and from cellular damage to tissues and then to organs, almost all adult-onset illnesses become more common with age, even if the role of age alone causing illness remains disputed.[1] Even though all illnesses become more common as people age, most older adults are fit and do not need or receive the specialized care of geriatricians. However, those who are

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frail would benefit from such care. This article considers the nature and operationalization of frailty and the role of complexity of frailty in the practice of geriatric medicine.

DEFINING FRAILTY CONCEPTUALLY AND OPERATIONALLY

There is a fair degree of consensus that frailty is an attribute of aged people who are at an increased risk of adverse health outcomes (including death) as a consequence of a diminished ability to respond to stress.[2] The authors would add that this diminished ability to respond to stress can be conceived of as a loss of redundancy, which arises as a consequence of the accumulation of multiple deficits.[3]

Many other contributions in this issue focus on the popular definition proposed and tested in the Cardiovascular Health Study in the United States and known as the phenotypic definition of frailty.[4] That study defined frailty by the occurrence of at least 3 of the following 5 deficits in an individual: slow walking speed, impaired grip strength, a self-report of declining activity levels, unintended weight loss, or exhaustion. The approach thus classified people as frail (3 or more deficits), prefrail (1 or 2 deficits), or robust (none of the deficits present). Although items have been combined by some in an index (from 0–5), generally degrees of frailty are not graded by this approach, for which it has been criticized. The phenotypic definition, in aiming to define a clinically recognizable group of people, also defines a frailty essence and excludes characteristics (such as disability, or complex comorbidity) that can be addressed using those constructs. Although none of the individual deficits are weighted, it has been suggested that mobility slowing is the key.[5]

The phenotypic definition finds its theoretical rationale in a “cycle of frailty.” By this account, frailty gives rise to the so-called loss of physiologic reserve. The loss of reserve is itself otherwise unmeasured, so that the frailty characteristics serve as surrogates for this diminution in adaptive capacity. The phenotypic approach to frailty is the most widely studied approach, and in a variety of settings, this approach has been shown to correlate both with the risk of adverse outcomes and with many important clinical parameters.[6,7]

In addition to the phenotypic and other approaches, frailty is considered as an at-risk state caused by the age-associated accumulation of deficits.[8] A method has been proposed for how a frailty index can be derived from existing health databases by proposing criteria for deficits and procedures for counting deficits.[9] We count deficits as a whole range of health problems, which come in many forms: symptoms, signs, laboratory abnormalities, diseases, and disabilities. These features are clinically recognizable, and each represents an insult that has been insufficiently repaired and is referred to as a deficit. On average, people accumulate deficits as they age, but a challenge to understanding an essential property such as frailty is that people accumulate neither the same deficits nor the deficits at the same rate. One approach to this heterogeneity is to search for a small number of essential features that people who are at risk have in common. We have taken the opposite approach, in that we count deficits with little regard to their nature and studied instead whether the number (more particularly, the proportion) of deficits that people have defines their risk state. Our findings to now are that the number of deficits is important: the more deficits individuals accumulate, the more they are at risk of an adverse health outcome, that is, with more deficits, they are at more risk and so are more frail. In this sense, deficit accumulation is indistinguishable from the loss of physiologic reserve because it is the basis for this loss, and in systems engineering terms this loss is referred to as loss of redundancy.

As a first step, counting what is wrong needs to be standardized in some way. To date, the best way to count and standardize accumulated deficits is to combine

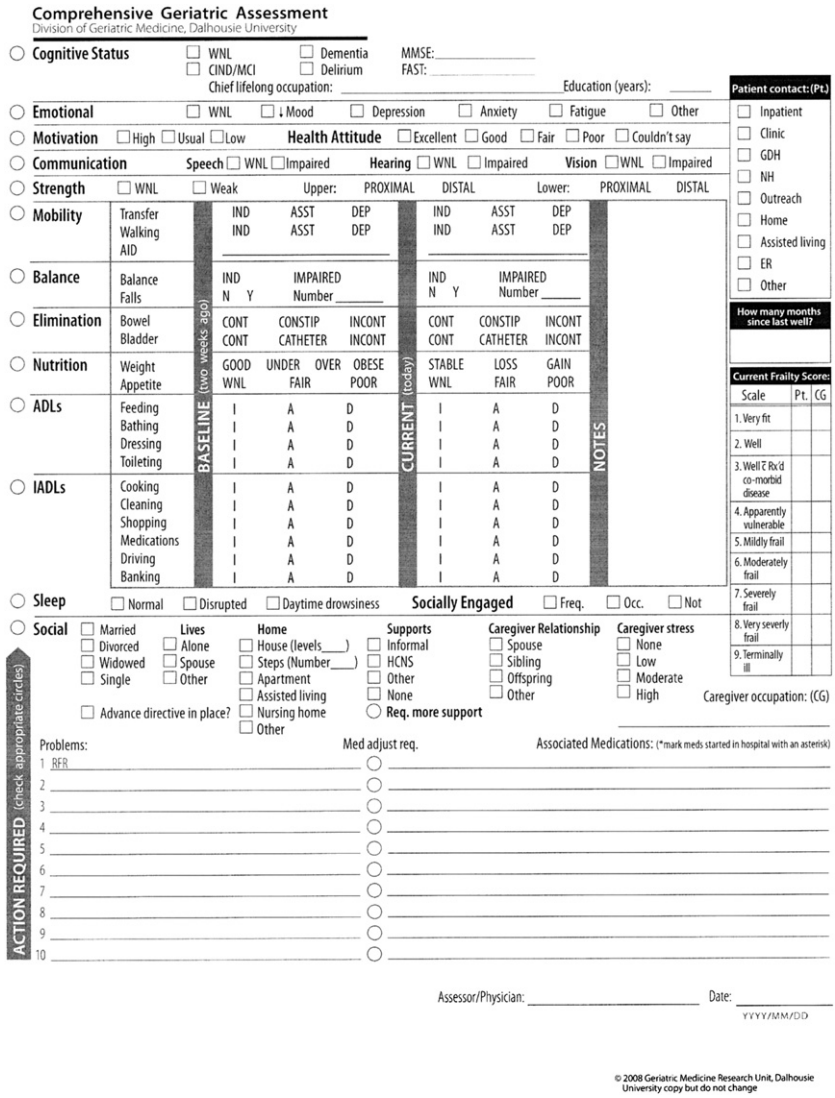
them in an index. A convenient way for geriatricians to record and count deficits is to use the information gathered as part of a routine comprehensive geriatric assessment (CGA). We refer to the frailty index so constructed[10,11] as the frailty index based on a comprehensive geriatric assessment (FI-CGA). The total number of items that can be used in a frailty index is considered to be 80, for example, assuming that the maximum number of diagnoses is 15 and the maximum number of medications is 20.

Clearly, sometimes more than these numbers can be found, but for the most part, this is a reasonable assumption. How to score the effect of medications remains under investigation. At present, the approach is to count medications as deficits: 0 to 5 medications, no deficit; 5 to 7, 1 deficit; and an additional deficit is added for every 3 medications added after 7 medications for a maximum medication deficit count of 5. The latest version of a standard 1-page form to make up the FI-CGA is presented in **Fig. 1**. This version of the CGA form also includes 10 items that can be used to make up a social vulnerability index.[12] Although the list might seem daunting to non-geriatricians, specialists can recognize elements that are key to gaining a full understanding of a patient's health.

For any individual, a frailty index score based on CGA is calculated as the number of deficits that they have, divided by the total number of deficits that were considered, for example, 80. For example, a woman with diabetes, peptic ulcer disease, osteoarthritis, hypothyroidism, osteoporosis, and obesity (5 deficits), who takes 7 medications (1 deficit); needs help with banking, shopping, and transportation (3 deficits); complains of anxiety; rates her health as only fair; and seems poorly motivated to change her health status (2 deficits) would have 11 deficits. Therefore, her frailty index score would be the 11 deficits she has, divided by the 80 deficits that were considered, that is, an FI-CGA score of $11/80 = 0.14$.

A frailty index can be generated from almost any set of health-related variables, as long as a few criteria are met.[9] The criteria for an item to be considered as a deficit are that the item needs to be acquired, age-associated, and associated with an adverse outcome and should not saturate too early. The last criterion means that the proportion of people who have the deficit should not be close to 100% because the deficit is uninformative at that point. An example would be nocturia in men. Although nocturia is age associated, interrupts sleep, and is a deficit, the problem is common, typically seen in more than 90% of men older than 75 years.

Just as the FI-CGA mixes patient self-report with physician assessment and laboratory and other measurement data, we have evaluated several samples, which have used only self-report, almost all objective data, or some combination. Strikingly, in studies with more than 33,000 people from Canada, Australia, the United States, and Sweden, deficits accumulated exponentially with age, with an average relative rate of approximately 3% per annum on a log scale (**Fig. 2**).[13] In these studies, different variables were used in different datasets and the different datasets typically used variables that were not always overlapping, that is, different variables (we did not always consider the same variables) or even the same number of variables (we constructed frailty indices using 20–130 variables) were considered in different datasets.[14–16] Across datasets, increasing values of the frailty index are highly associated with an increased risk of death (**Fig. 3**). When both frailty index and age are combined in a multivariable model, in each case, the former has better predicted mortality than the latter. This difference remained even though the items that were counted in the frailty index were not the same each time. We consider this fact to be the evidence that the idea of frailty in relation to deficit accumulation is robust. In contrast to the traditional emphasis on exact duplication of instruments from one sample to the next, it seems that at a group level if not at the individual level (for individuals it is


Comprehensive Geriatric Assessment
Division of Geriatric Medicine, Dalhousie University

Cognitive Status ☐ WNL ☐ Dementia ☐ CIND/MCI ☐ Delirium MMSE: FAST: Chief lifelong occupation: Education (years):
Emotional ☐ WNL ☐ ↓ Mood ☐ Depression ☐ Anxiety ☐ Fatigue ☐ Other
Motivation ☐ High ☐ Usual ☐ Low Health Attitude ☐ Excellent ☐ Good ☐ Fair ☐ Poor ☐ Couldn't say
Communication Speech ☐ WNL ☐ Impaired Hearing ☐ WNL ☐ Impaired Vision ☐ WNL ☐ Impaired
Strength ☐ WNL ☐ Weak Upper: PROXIMAL DISTAL Lower: PROXIMAL DISTAL

		BASELINE (two weeks ago)	CURRENT (today)	NOTES
Mobility	Transfer	IND ASST DEP	IND ASST DEP	
	Walking	IND ASST DEP	IND ASST DEP	
	AID			
Balance	Balance	IND IMPAIRED	IND IMPAIRED	
	Falls	N Y Number	N Y Number	
Elimination	Bowel	CONT CONSTIP INCONT	CONT CONSTIP INCONT	
	Bladder	CONT CATHETER INCONT	CONT CATHETER INCONT	
Nutrition	Weight	GOOD UNDER OVER OBESE	STABLE LOSS GAIN	
	Appetite	WNL FAIR POOR	WNL FAIR POOR	
ADLs	Feeding	I A D	I A D	
	Bathing	I A D	I A D	
	Dressing	I A D	I A D	
	Toileting	I A D	I A D	
IADLs	Cooking	I A D	I A D	
	Cleaning	I A D	I A D	
	Shopping	I A D	I A D	
	Medications	I A D	I A D	
	Driving	I A D	I A D	
	Banking	I A D	I A D	

Sleep ☐ Normal ☐ Disrupted ☐ Daytime drowsiness Socially Engaged ☐ Freq. ☐ Occ. ☐ Not
Social ☐ Married ☐ Divorced ☐ Widowed ☐ Single ☐ Advance directive in place? Lives ☐ Alone ☐ Spouse ☐ Other Home ☐ House (levels___) ☐ Steps (Number___) ☐ Apartment ☐ Assisted living ☐ Nursing home ☐ Other Supports ☐ Informal ☐ HCNS ☐ Other ☐ None ○ Req. more support Caregiver Relationship ☐ Spouse ☐ Sibling ☐ Offspring ☐ Other Caregiver stress ☐ None ☐ Low ☐ Moderate ☐ High Caregiver occupation: (CG)

Patient contact: (Pt.) ☐ Inpatient ☐ Clinic ☐ GDH ☐ NH ☐ Outreach ☐ Home ☐ Assisted living ☐ ER ☐ Other
How many months since last well?

Current Frailty Score:

Scale	Pt.	CG
1. Very fit		
2. Well		
3. Well ∑ Rx'd co-morbid disease		
4. Apparently vulnerable		
5. Mildly frail		
6. Moderately frail		
7. Severely frail		
8. Very severly frail		
9. Terminally ill		

ACTION REQUIRED (check appropriate circles)

Problems:	Med adjust req.	Associated Medications: (*mark meds started in hospital with an asterisk)
1 RFR	○	
2	○	
3	○	
4	○	
5	○	
6	○	
7	○	
8	○	
9	○	
10	○	

Assessor/Physician: Date: YYYY/MM/DD

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Fig. 1. FI-CGA form. (*Courtesy of* Geriatric Medicine Research Unit, Dalhousie University, Halifax, Nova Scotia.)

always important to know exactly what is wrong), the exact nature of a given deficit in relation to a person's state of health is less important than the deficit count. This approach has been confirmed by several independent studies.[17–21]

One intriguing but generally consistent finding from these analyses is that, at any given age, on average, women have more deficits than men. But if frailty is related to vulnerability risk, women are not frailer than men because for any given level of deficit accumulation, the mortality rate is higher in men than women. In other words, although women have more deficits than men, on average, they tolerate the deficits better. The biologic basis for this better toleration by women has yet to be established, but the finding is robust and implies a system effect.

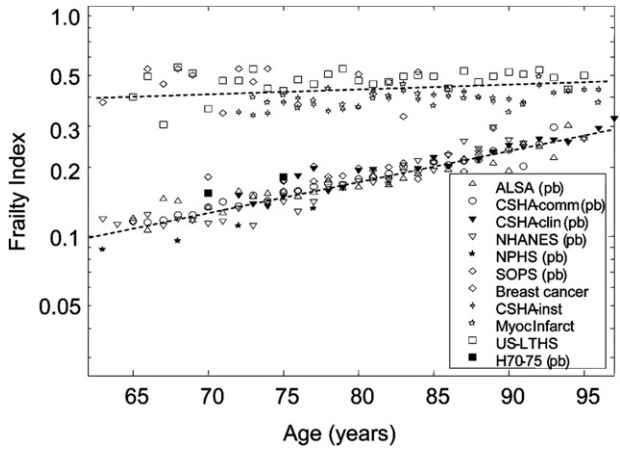

Fig. 2. The relationship between deficit accumulation and age. The lower line is the mean slope of deficit accumulation from surveys of community-dwelling people in 4 Western countries (Australia, Canada, the United States, and Sweden). The slope increases at about 0.03 per year. Note the log scale for the value of the frailty index. The upper line shows the relationship between the mean value of the frailty index and age for clinical and institutionalized samples. Note that the slope for those samples is close to 0, that is, these groups are, on average, so impaired that they cannot withstand another deficit, which is why no more deficits accumulate. (*From* Mitnitski A, Song X, Skoog I, et al. Relative fitness and frailty of elderly men and women in developed countries and their relationship with mortality. J Am Geriatr Soc 2005;53:2184–9; with permission.)

Change in the Frailty Index

It is well known that health generally does not improve with age. Deficits accumulate and this is reflected in the age-specific elevation of the trajectories of the frailty index. The trajectories can vary significantly within a group of individuals, reflecting the differences in each individual's aging rate. Individual trajectories can change in any

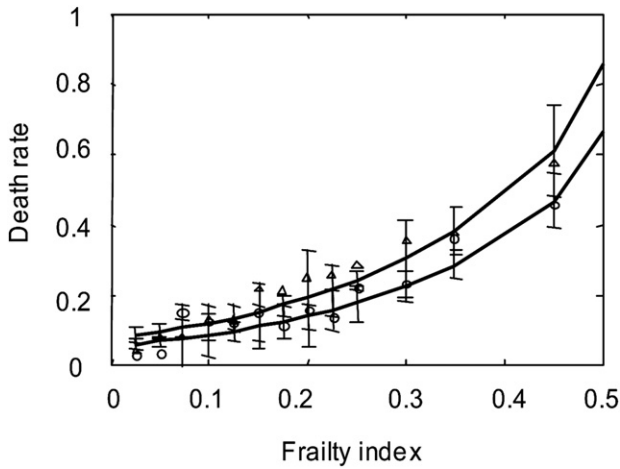

Fig. 3. The relationship between frailty index and mortality. Note that at all levels of the frailty index, deficit accumulation is more lethal for men than women. Triangles represent men and circles represent women.

direction, at least in the short term, that is, health can deteriorate or improve. Health improvement, for example, may result from lifestyle changes or medical interventions. Therefore, we have suggested a model that describes health changes in all directions: improvements, declines, and mortality.[22,23] We have developed a stochastic model of such changes considered as a Markov process and found that a relatively simple Poisson distribution can fit the data with great precision.

Our first results from the Canadian Study of Health and Aging, using the 5-year transitions, showed that transition probabilities of changes in the deficit count (which is fundamental to calculation of the frailty index) can be represented by a modified Poisson model. This model has 4 readily interpretable parameters, 2 of which represent transitions in the deficit number for those individuals who had no deficits at baseline (the so-called zero state) and the other 2 represent the incremental adjustment for these parameters proportionally to the number of deficits these individuals had at baseline. The zero state parameters are of particular importance because they indicate how the progression of health starts; in this sense, the zero state outcomes can be considered as the survival (or change in health) of the fittest. All these parameters can be easily adjusted for covariates. The model allows simultaneous estimation of the changes occurring as the individual improves, remains stable, declines, and eventually dies. Our preliminary results obtained in the Canadian Study of Health and Aging over 2 consecutive 5-year intervals were replicated in 2 different datasets: the National Population Health Survey (Canada) over 5 consecutive 2-year intervals[23] and Swedish birth cohort data (Gothenburg H-70 study).[24] In addition, this model of stochastic transitions was found to be equally applicable to cognitive changes[25,26] and was extended to address how exercise levels might affect such transitions. It was found that those who exercise regularly not only increase their survival chances but also improve or at least avoid deterioration of their cognitive functions. Finally, the same transition model was applied to social vulnerability, and the results were similar. This suggests that the model of health transitions has the power to not only predict the changes in health in any direction but also support analysis of the factors that might modify such changes.[27]

The high fit of the stochastic model of transitions supports the view that change generally happens gradually and depends on both the background and the individual state. Rapid change in the frailty index is often seen in people in the years before death. In fact, it seems that death of an individual can be better predicted based on the recent frailty index than on the review of past index values. Furthermore, review of the cumulative deficits over a long term may provide a better picture of the aging process and serve as a better predictor of death in the short term than does chronologic age. In other words, as people age, the accumulation of deficits accelerates, and this acceleration may be more useful in prediction than the individual's age. It is also clear that some people accumulate more deficits than others; for example, in the Canadian Study on Health and Aging, heavy smokers accumulated more deficits than nonsmokers.[28]

Frailty and "Biologic Age"

Given that deficit accumulation is so highly correlated with the risk of death, it is possible to view deficit accumulation as an estimate of biologic age. Consider 2 people, A and B, of the same chronologic age, for example, 78 years (**Fig. 4**). At 78 years, the mean value of the frailty index is 0.16. Person A has a frailty index value of 0.26 that is higher than the mean value by 0.1 corresponding to the mean value of the frailty index at age 93 years. In essence, person A has the life expectancy of a 93 years old; thus, although chronologically 78 years old, person A can be considered to be biologically 93 years old. By contrast, person B has a frailty index value of 0.1 that is lower than the mean value by

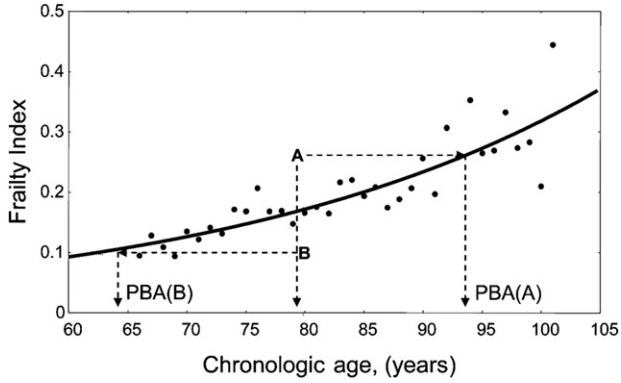

Fig. 4. Frailty and biologic age versus chronologic age.

0.06 corresponding to the mean value of the frailty index at age 63 years. In essence, person B has the life expectancy of a 63 years old; thus, although chronologically 78 years old, person B can be considered to be biologically 63 years old. Since we proposed this approach to the measurement of biologic age, 2 other groups have confirmed that the high correlation between mortality and deficit accumulation allows this approach to be considered further.[14,15,17]

Implications for Geriatric Medicine

We have proposed that frailty can be defined by deficit accumulation. One of the implications of this approach is that frailty can be considered as a complex phenomenon, and by acknowledging its complexity, we have shown that frailty has characteristic properties. Similarly, we propose that frailty can be embraced clinically, drawing on lessons from other undertakings in which complexity must be addressed. In the airline industry, for example, complexity is addressed through standard operating procedures and safety checks and identified through pattern recognition.[29] Each of these responses has so far been somewhat less formally developed in medicine. Although pattern recognition is crucial for clinical decision making, organization of information to facilitate pattern recognition is less well developed as a management strategy. As part of our strategic response to addressing the complexity of frailty, our group has focused on pattern recognition as a critical dimension of the definition and management of frailty.

Another common response to addressing the complexity of patients' needs and improving their care is the use of CGA.[30] Through assessment of general health (comorbidity), function, cognition, mood and motivation, the special senses, nutrition and medications, this tool facilitates identification of health issues and the appropriate intervention and follow-up for them. As part of a comprehensive management plan, CGA also supports continued independence and improved quality of life for an individual, in association with reduced medical costs.[31] Better patient care results from the acknowledgment of and focus on the complexity of frailty.

Other implications arise from considering the complexity of frailty. Frail elderly people can be viewed as complex systems on the brink of failure. As with other complex systems, failure generally begins with the highest-order functions. In the case of people, failure includes higher-order processing, walking upright, and planned social interaction. Failure of these high-level functions may result in delirium, falls, impaired function, and social withdrawal. These presentations have been described in the past as atypical but may in fact be typical of the frail elderly person.[32]

Although these presentations are typical in frail elderly people, there is variation in the grades of frailty and even limited changes in the number of deficits can lead to different prognoses. There is a strong correlation (0.8) between the clinical descriptions of the clinical frailty scale and the grades of the frailty index. Although some may question distinguishing between the "severe" and "very severe" frailty, there is a clear difference and those scoring at the very severe level have an accelerated risk of death. Individuals with a frailty index score greater than 0.55 have a median survival rate that is much lower than the median.

Frailty in Relation to Social Vulnerability

Social vulnerability, like frailty, has been easy to recognize clinically but has been the subject of debate over how it can best be operationalized. For example, social determinants of frailty have been discussed, and akin to the frailty index, a social vulnerability index has been proposed.[12] This index is based on social deficits drawn from a variety of indicators taken from theories such as social capital, social networks, social engagement, and social cohesion. Social vulnerability and frailty are related; greater social vulnerability is related to mortality in the elderly.

SUMMARY

Many older people are frail and have multiple diseases, disabilities, and other deficits that increase the likelihood of adverse outcomes. The complexity of their situations and variations in their deficit accumulation result in significant challenges for clinicians. The tendency is to attempt to precisely assess and provide individuals with detailed information on each deficit. In the past, providing such information has been perceived as more important than simply knowing how many deficits a person may have. However, the frailty index suggests that when deficits accumulate, it is the quantity of deficits that may be most significant in providing appropriate care. The specific details around existing deficits, or any new deficit that is identified, should not be foremost in the clinician's mind. Rather, each new deficit should be considered as part of the complex total picture.

Geriatricians have the opportunity to continuously improve the care of the elderly as more light is shed on the complexity of frailty. Acknowledging and accepting each person's "big picture" that includes a multitude of social and medical needs allow clinicians to provide more comprehensive treatment that prevents inappropriate efforts to dissect each issue and deal with it separately.

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