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## Frailty and Multimorbidity: Different Ways of Thinking About Geriatrics

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### ABSTRACT

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The terms *multimorbidity* and *frailty* are increasingly used in the medical literature to measure the risk profile of an older individual in order to support clinical decisions and design ad hoc interventions. The construct of multimorbidity was initially developed and used in nongeriatric settings. It generates a monodimensional nosological risk profile, grounding its roots in the somewhat inadequate framework of disease. On the other hand, *frailty* is a geriatric concept that implies a more exhaustive and comprehensive assessment of the individual and his/her environment, facilitating the implementation of multidimensional and tailored interventions. This article aims to promote among geriatricians the use of terms that may better enhance their background and provide more value to their unrivaled expertise in caring for biologically aged persons.

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The terms *multimorbidity* and *frailty* are increasingly used in the medical literature and among health care professionals. Although capturing different aspects of the individual's health status, they are sometimes used interchangeably. In particular, the words *multimorbidity* and *frailty* are used to measure the risk profile of an older individual in order to support clinical decisions and design ad hoc interventions. This article aims to describe the similarities and differences underlying the two constructs with the aim of promoting terminology standardization in the field of geriatrics.

### The Concept of Multimorbidity

*Multimorbidity* is usually defined as the coexistence of two or more chronic diseases in the same individual.<sup>1</sup> It may be viewed as an evolution of the *comorbidity concept*, which refers to “the existence or occurrence of any distinct additional entity during the clinical course of a patient who has the index disease under study.”<sup>2</sup> It is readily evident that, as opposed to comorbidity, multimorbidity is a patient-centered entity, in which no index disease is pre-defined. The

difference is not trivial because it suggests the adoption of inherently different clinical approaches. To make it simple, whereas comorbidity paves the way for a disease-centered model of care in which a specific clinical condition is prioritized over the others, multimorbidity implies a more holistic evaluation of the individual's clinical complexity, in which all co-occurring conditions are attributed the same dignity.

Shifting the attention from single diseases to the resultant of multiple conditions marks an important step forward in the evolution of care, making it more respondent to the medical needs of an aging and multimorbid society. At the same time, because multimorbidity increases with age, it may be used as a marker of biological aging to support the required adaptations to models of care.<sup>3</sup> It was conceptualized to capture in an integrated way the continuous exposure to age-related chronic conditions.

Yet, some major limitations remain. First, there is no standard definition of *multimorbidity* or consensus about the conditions to be considered in its computation. Moreover, clinical conditions are equally weighted in multimorbidity, suggesting that the relationship between the number of diseases and the risk of negative health-related outcomes might follow a linear trend. As also explained in the recent *World Report on Ageing and Health* by the World Health Organization,<sup>4</sup> this is not the case. In fact, the impact of multimorbidity on the individual's risk profile can be substantially greater than the mere sum of the singular effects that are expected from the computed conditions. The

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nonlinear pattern followed by multimorbidity with age has also been described from a biological perspective by Fabbri and colleagues<sup>5</sup> in the InCHIANTI study. Their analyses showed that the accumulation of diseases accelerates later in life, and this phenomenon is enhanced by the patient's underlying inflammatory status. In other words, 1 plus 1 rarely equals 2 in the clinical setting; it rather results in something ranging between 2 and a lot!

### The Concept of Frailty

An international panel of experts defined frailty as “a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death.”<sup>6</sup> Frailty is a multidimensional condition. The impairment of different biological functions (eg, physical function, cognitive function, psychological function) defines different manifestations of frailty, all of which are valid and legitimate.

Although the theoretical definition of *frailty* is largely agreed upon, there is great controversy and multiple ambiguities concerning the practical translation of the concept in a unique operational instrument. The dispute regarding instruments has led to a loss of focus on the condition of interest, by paying more attention to the tools for its assessment (which is aberrant). As a result, it often seems as though the choice of instrument for measuring frailty is more important than the frailty condition itself.<sup>7</sup>

Leaving aside the instruments for assessing frailty and just examining the theoretical framework of this geriatric condition, it is easily realized that frailty was conceptualized for capturing the “chronological age-independent” biological status of the older person. The term *frailty* was conceived to measure the balance between the entropic forces acting against the organism and its homeostatic reserves.<sup>8</sup> In other words, without specifically looking at diseases (either alone or combined in the context of multimorbidity), the term *frailty* captures the biological decline of the aging individual and his/her risk profile for negative health-related outcomes.<sup>9</sup>

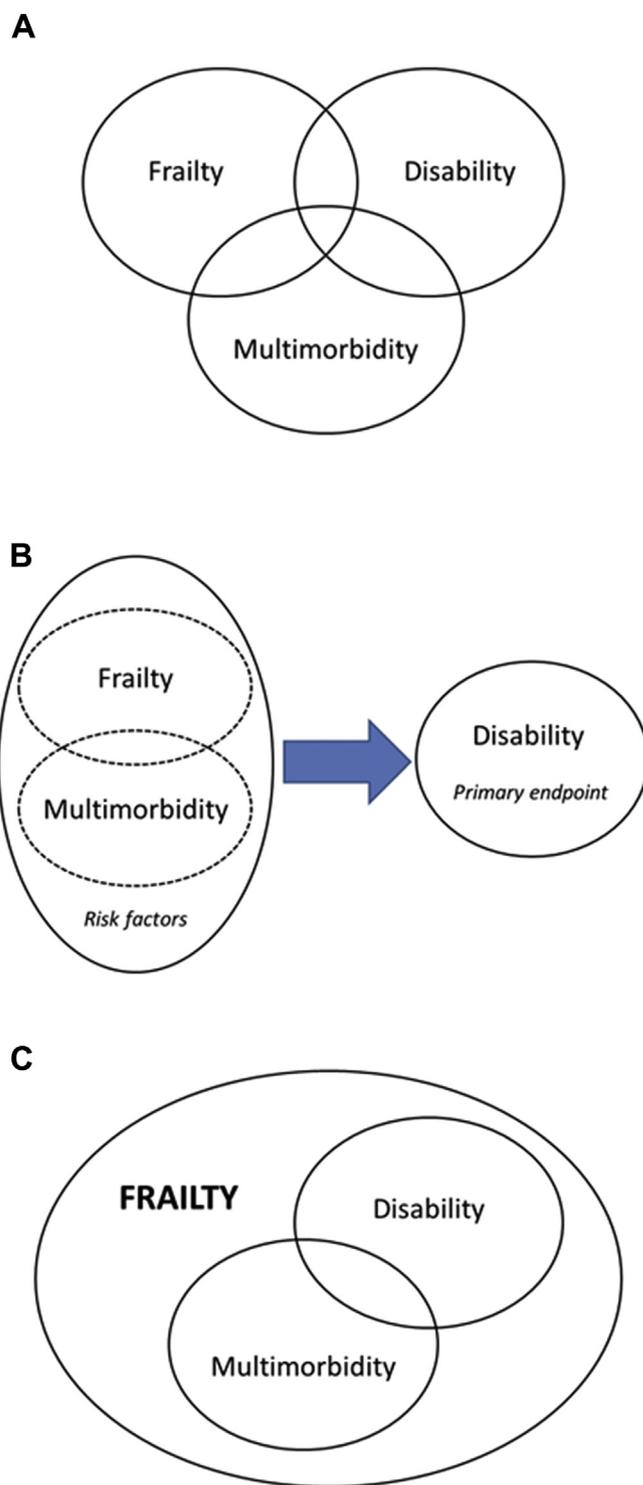
### The Relationship Between Frailty and Multimorbidity

In a seminal article published in 2004, Fried and colleagues presented a Venn diagram showing the relationship between frailty (measured according to the phenotype model), disability (defined as limitation in one or more activities of daily living), and multimorbidity (computed as two chronic conditions or more).<sup>10</sup> Figure 1A shows an overlapping and possible partial coexistence of the three concepts, which were considered independent at the same level and potentially mutually interacting. Interestingly, this model does not automatically exclude the possibility that a person may simultaneously be frail, multimorbid, and disabled.

Over the years, frailty has been repeatedly indicated as a target condition of special interest for interventions against the age-related disability process.

Accordingly, frailty has often been framed as a “pre-disability condition,”<sup>11–13</sup> in which disability served as the primary outcome of interest (Figure 1B). This is also a legitimate and valid choice, in which the objective of the intervention (ie, prevention of disability) leads to a potential selection of the overall population exposed to enhanced vulnerability. In other words, a methodological choice is applied over a biological concept in order to correctly implement a clinical/research action.

If frailty is more broadly considered as a condition of public health interest,<sup>14</sup> however, the scenario changes substantially. In fact, if frailty is conservatively considered as a condition of extreme vulnerability to stressors exposing the organism at increased risk of negative outcomes, the concepts of multimorbidity (but even disability) may become secondary (Figure 1C).



**Fig. 1.** Different theoretical ways of considering the relationships between frailty, multimorbidity, and disability in the elderly. (A) Phenotype model: Frailty, multimorbidity, and disability are three independent and mutually interacting conditions of similar weight. (B) Pre-disability model: Frailty and multimorbidity are two related risk conditions for incident disability. (C) Model for adapted care: Frailty is the umbrella for adapted (geriatric) interventions, which include multimorbidity and disability as possible targets.

Envisioning frailty as the crossroad between usual and adapted care implicitly transforms this condition in the actual foundations of geriatric medicine and the keystone for reshaping our obsolete health care systems (still based on the anachronistic criterion of “age” to

define a person as “old”). It is noteworthy that frailty includes the concept of multimorbidity (because it is partially determined by the pathological disruption of systems and functions<sup>15,16</sup>) and has been designed to support preventive actions against functional loss.<sup>17</sup> Noticeably, frailty can be measured through the use of geriatric instruments originally developed to assess the health status and care needs of geriatric inpatients.<sup>18,19</sup>

Of course, the elevation of frailty to such a higher status implies that adopting tools able to capture multidimensional risk profiles should be prioritized. Only in this way it will then be possible to adequately sustain models of care based on comprehensive assessment and multidisciplinary intervention plans. In this article, we do not recommend specific instruments to avoid so that our discussion might be reduced to promoting one tool over the other. It is important, however, to mention that such multidimensional tools for assessing frailty already exist, and that the World Health Organization is currently planning consistent actions in the same direction (eg, the recently proposed concept of intrinsic capacity).<sup>20</sup>

In the absence of a gold standard, the three types of frailty depicted in the Venn diagram (Figure 1) are all valid. In fact, they answer to different needs and objectives that are (1) to frame a clinical condition (Figure 1A), (2) to support a preventive action (Figure 1B), and (3) to feed a public health model of care (Figure 1C). It might be necessary to find and use different terms for indicating the individual models of frailty.

### The Issues Regarding Diseases (and Multimorbidity)

Why might multimorbidity inadequately serve in geriatric care? Which are the weaknesses intrinsic to the concept of multimorbidity? What is wrong with the concept of “disease”?

A disease is usually defined by a committee of experts. A panel defines clinically relevant thresholds for a biological (continuous) parameter in order to distinguish “normality” from “pathology.” It is clear that every clinical definition is somehow arbitrary, simply because it is based on the available knowledge and diagnostic limitations.

Anna Tosteson described a meeting she attended concerning the defining criteria of osteopenia and osteoporosis.<sup>21</sup> After long and exhausting days of discussions, it was difficult for the experts to come up with an indisputable threshold. The position of the cut-point defining low bone density was quite challenging. Then, since “... Ultimately, it was just a matter of, well ... it has to be drawn somewhere ... [...], someone literally stood up, drew a line through a graph depicting diminishing bone density and decreed: ‘Every woman on one side of this line has a disease ...’ ” Such an anecdote may seem to delegitimize the definition of diseases (osteoporosis in this case) and cast a shadow on the complex process of defining clinical conditions. The problem is that nature works with biological phenomena that follow continuous patterns and trajectories. In clinics, we need thresholds and categorical variables to guide choices and plan interventions. It is thus legitimate to work with approximation, creating categories where they do not exist. It is important, however, how many arbitrary, arguable (but still needed) decisions are hidden behind the definition of a disease. Although accepting the construct of “disease” (otherwise, medicine could not exist), it is still worth mentioning how many issues surround this paradigm and its derivatives (especially multimorbidity). In particular, the definition of a nosological condition is closely related to:

- Current knowledge of the condition of interest. The defining thresholds are dynamic and evolve as the increasing knowledge of the condition of interest improves. For example, simply think about the evolution of criteria defining hypertension (and driving treatment decisions).<sup>22</sup>
- Characteristics and availability of diagnostic instruments. The technological advancements are increasing our capacity to detect subtle biological anomalies. As a result, today, the diagnosis of many clinical conditions is increasingly anticipated at their earliest stages. The access to diagnostic instruments is spreading as well. The recent exponential worldwide increase of incident thyroid cancer (especially in South Korea<sup>23</sup>) is paradigmatic in this context. The implementation of an instrumental and systematic screening has boosted the number of diagnoses, causing overdiagnosis and overtreatment.
- Priorities in the formulation of the diagnosis. When diagnostic criteria are defined, the committee of experts always tries to balance the diagnostic accuracy with the feasibility of clinical implementation. In the clinical setting, easy-to-conduct, readily available, inexpensive instruments that are not time consuming are needed to categorize the different biological phenomena of an individual. Thus, trade-offs are quite common. For example, it is clear that body mass index cannot measure obesity and remains a mere measure of size. Given the urgent need of introducing the notion of excessive weight in the clinical setting, however, adopting a below-standard measure has been accepted as a pivotal parameter.<sup>24</sup>
- Access to health services. It is obvious that the diagnosis of a condition requires a physician able to judge the clinical manifestation and the eventual biological abnormalities. In low- and medium-income countries and in specific populations (eg, older persons), access to care may be limited for different reasons, consequently affecting the possibility of making diagnoses. Thus, it is not surprising that people living in wealthy regions usually show higher multimorbidity than those residing in the poorest areas.<sup>3</sup>

All these issues affecting the construct of a disease implicitly threaten the sustainability of the “multimorbidity” concept. Multimorbidity also houses other problems in its construct. As mentioned previously, the multimorbidity construct implies that every condition similarly weighs in determining the risk profile. This approach completely ignores the fact that diseases are not stand-alone entities, but rather develop unpredictable synergies. In addition, when multiple conditions exist, the clinical picture of each may be confounded by the superimposition of signs and symptoms of the others, making it challenging (and often impossible) to identify any single disease. This is especially true in older adults in whom clinical conditions frequently show atypical presentations also in the absence of concomitant illnesses. Moreover, it is well established that the individual's risk profile (particularly if elderly) is also strongly determined by the context of where he/she lives.<sup>25</sup> Today, the World Health Organization is stressing this aspect by showing that the individual's functional ability is due to his/her intrinsic capacity as well as affected by the environment.<sup>4</sup> A parameter such as multimorbidity focused only on a single (ie, nosological) domain of the individual's health status may be insufficient at measuring the biological, clinical, and social complexity of older persons.

### New Paradigms to Improve Health Care Systems

The construct of multimorbidity was initially developed and used in nongeriatric settings in order to measure the increasing complexity of patients referred to clinical services. Counting diseases was identified as a possibility for defining the individual's risk profile. This was and still is a legitimate and valid choice. If not prudently and correctly used, however (as mentioned previously), it might lead to misleading and incorrect decisions. For example, the mere observation of the count of diseases may expose patients to the risk of overdiagnosis and overtreatment, especially in clinical settings/disciplines that may not be familiar with the individual's comprehensive assessment and

prioritization of person-tailored interventions. Especially in older patients, the more you search, the more you find, and it is a matter of organizing the information rather than simply compiling a list of diseases. This organization requires the implementation of a new model of care.<sup>25</sup> The condition of frailty may perfectly fit this novel approach because it contains all the criteria for being considered a public health issue.<sup>14</sup>

In a recent document by the British Geriatrics Society,<sup>26</sup> frailty is used as the target condition for addressing individuals toward an adapted approach based on comprehensive geriatric assessment. Interestingly, the recommendations do not indicate a single measure for capturing the frailty condition, but several instruments are suggested. This implicitly means that the authors of the document could easily accept the existence of heterogeneity in the definition of the frailty condition (because every instrument would lead to a different risk profile). Thus, they prioritized the model of care, probably because it is more pragmatic to create uniform care services by acting at a higher (ie, public health) level.

The transition from the disease-centered model toward a comprehensive approach underlies a cultural evolution, even within the geriatric population.<sup>27</sup> A large number of biologically old individuals would greatly benefit from geriatric care despite their relatively young age. For example, HIV-positive persons or those with Down syndrome are not geriatric if considered under the old-fashioned chronological criterion of age. However, these persons present with all the characteristics requiring the intervention of a geriatrician (eg, multiple interacting conditions, body composition modifications, polypharmacy, social issues, etc.). They are frail and, as such, should undergo a comprehensive geriatric assessment for developing a person-tailored plan of intervention. In addition, this plan of care is only partially driven by the number of diseases they may suffer from.

Last but not least, we are aware of the small number of geriatricians worldwide. This implies that, to date, geriatricians cannot manage all the older persons with a profile of increased risk for negative outcomes. Health care professionals (in particular, those working in primary care) need to be familiar with the frailty concept, especially the one conceived as a pre-disability condition. The diffusion of frailty screening tools (particularly those characterized by being multidimensional and easier to assess in the clinical setting<sup>28–31</sup>) may represent a unique opportunity for training health care professionals at a more “geriatric” approach. In fact, by soliciting the observation of often-undervalued signs/symptoms of old age (eg, fatigue, malnutrition, reduced physical performance), these instruments may precociously alert the health care professional about possible undetected conditions to consider and refer the most complex cases of frailty to the geriatrician’s attention. A model of care such as this may simultaneously sustain a proactive movement toward promoting healthy aging as well as contribute to the development of multidisciplinary services.

## Conclusions

Multimorbidity and frailty represent two different ways of looking at the complexity of older persons. The former approach of generating the risk profile is monodimensional and grounds its roots in the somewhat inadequate framework of “disease.” On the other hand, *frailty* implies a more exhaustive and comprehensive assessment of the individual and his/her environment, facilitating the implementation of tailored interventions. Geriatricians should promote their expertise by avoiding misleading messages, refrain from using terms that are not part of their background, and give more value to the unrivaled background they have in the care of biologically aged patients.

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