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ASSESSING FRAILTY IN OLDER ADULTS: STRATEGIES AND TOOLS FOR EFFECTIVE POLICY AND RESEARCH

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Abstract. The progressive ageing of the population, not accompanied by a corresponding increase in healthy life expectancy, brings to the forefront the study of the health of older adults from a holistic perspective. The concept of frailty aligns with this perspective, as it considers a broader condition of vulnerability involving mainly older individuals, which is much more difficult to define and measure. This article aims to provide an overview of the concept of frailty, the various definitional approaches, and, consequently, the measurement methods, while also focussing on the relationship between frailty and the two main concepts that define health: multimorbidity and disability. Following a brief overview of the types of data and their role in the study of frailty, the article concludes with an analytical approach for defining a measure of frailty.

1. Frailty in old age: From concepts to measures

1.1 The longevity paradox

Population ageing is an irreversible global trend, with every country in the world experiencing growth in both the size and proportion of older people in the population, though at different paces and speeds. According to United Nations estimates, in 2020, about 9.3% of the global population was 65 years or older. This proportion is expected to increase, reaching 16% by 2050, with a projected 1.5 billion of old population. In Europe and North America, the proportion of people 65 and older is especially high, at 19% in 2020, and is expected to exceed 25% by 2050. These figures underscore a significant challenge for social and economic policies, which must adapt to an increasingly ageing population and address its impact on healthcare, pension systems, and social inclusion (United Nations, 2020). This trend is driven primarily by two main mechanisms: advances in medicine and demographic dynamics. Over the past decades, demographic factors, particularly low and decreasing fertility rates, have altered population structures, resulting in shrinking proportions of young people and an increasing number of older individuals. At the same time, significant medical progress has driven a substantial increase in life expectancy worldwide, allowing more people to live longer lives.

However, there is a crucial distinction between lifespan – the total number of years of life– and healthspan – the number of years lived in good health. Although many people live longer, these additional years are not always characterised by good health.

Globally, life expectancy at birth reached 73.3 years in 2024, with an increase of 8.4 years since 1995 (United Nation – DESA, 2024). Further reductions in mortality are projected to result in an average longevity of around 78.2 years globally in 2050 (Vollset et al., 2024).

Healthy life expectancy (HALE, the average number of years a person can expect to live in good health) has also increased from 58.3, in 2000 to 63.7, in 2019, mainly due to declining mortality rather than reduced years lived with disability, and it has been projected to increase further to about 67.4 years in 2050 (Kyu et al., 2018; Vollset et al., 2024; Ward and Goldie, 2024; WHO, 2024). Even if both trends go in the same direction, the increase in HALE does not seem to keep pace with the increase in life expectancy.

This means that as people live longer, but not necessarily healthier, an increasing number of older individuals spend a significant proportion of their lives deprived of full health due to diseases, deficits, and disabilities. This “longevity paradox” (Fries, 1980; Garmany et al., 2021) results in heavy consequences both at the individual and at the macro level. Conditions such as reduced physiological functions, cardiovascular diseases, diabetes, and neurodegenerative disorders become more prevalent with age (Kennedy et al., 2014; Vos et al., 2017) and contribute to reduced independence, social isolation, and psychological distress, thus worsening individuals’ quality of life (Vermeiren et al., 2016). Compressing morbidity, delaying disease onset, and/or reducing disease severity, and identifying strategies to address the complex needs of an ageing population are paramount.

In this context, the study of frailty becomes crucial because it plays a significant role in these dynamics, by highlighting the vulnerability of older adults to adverse health outcomes and emphasising the need for targeted interventions to improve their overall health and quality of life (Fried et al., 2001). Frailty, characterised by a decrease in physiological reserve and a higher susceptibility to stressors, is associated with increased risks of hospitalisation, disability, and mortality (Clegg et al., 2013). Understanding frailty can lead to better screening, prevention, and management strategies, ultimately aiming to extend healthspan along with lifespan (Rockwood & Mitnitski, 2007).

1.2 Ageing and frailty

At the biological level, ageing is a process that results in a progressive and irreversible decline in physical function across all organ systems, induced by the accumulation of a wide variety of molecular and cellular damage over time, in response to a variety of endogenous and exogenous stressors (Tenchov et al., 2024). Gradual functional decline impairs the organism's intrinsic ability to defend, maintain and repair itself to function efficiently, a concept traditionally defined as homeostasis (Campisi, 2013; López-Otín et al., 2013; Tenchov et al., 2024). Homeostasis declines with age. The defence and repair mechanisms are generally good enough in early life to enable normal growth and development, but they do not provide indefinite protection in older age. This process is associated with the inability to activate and/or modulate several adaptive responses and leads to a gradual decrease in physical and mental capacity, to an increased susceptibility and vulnerability to diseases, and ultimately to death.

Even if chronological age is widely recognized as the most significant predictor and risk factor for negative health outcomes (Cesari et al., 2016; Shock et al., 1984), individuals of the same chronological age can significantly differ in their health status. As populations age, the association between chronological age and health status is increasingly heterogeneous (Kirkwood 2005; Moguilner et al., 2021; Santoni et al., 2015): some individuals are more vulnerable than others due to underlying differences in their physiological and biological resilience, in its turn influenced by multiple factors: lifestyle aspects (diet, exercise, smoking habits, stress), environmental factors such as pollution and climate change, as well as social factors (loneliness, social support, socio economic status).

The concept of frailty was first introduced in Vaupel's seminal work, whose objective was to account for the heterogeneity in mortality rates among individuals of the same chronological age, under the assumption that individuals have varying levels of susceptibility to adverse health outcomes (Vaupel, 1979). Such a susceptibility has been conceptualised as frailty: an underlying, unmeasured variable affecting population-level mortality patterns. This work laid the groundwork for the emergence of an important strand of scientific research focused on ageing and frailty. Such interest has been fuelled over time by population ageing processes, calling for the attempt to define and measure frailty, and understand its relations with adverse health outcomes at older ages. From then on, the need to identify frail individuals and predict their risk of developing negative health outcomes to find tailored interventions and care plans has been central in the ageing debate.

This article aims to provide an overview of the concept of frailty, the various definitional approaches, and, consequently, the methods of measurement, while also focusing on the relationship between frailty and the two main concepts that define health: multimorbidity and disability. Following a brief overview of the types of data and their role in the study of frailty, the article concludes with an analytical approach for defining a measure of frailty.

2. Definitions and measures of frailty

Within the epidemiological literature, frailty is considered a multidimensional, unobservable concept that encompasses physical, psychological, sensory, and social factors, making individuals vulnerable (Gobbens et al., 2010; Fried et al., 2001). The challenge of defining frailty arises from its complex nature and from the need to consider multiple facets together. Over the past 30 years, various definitions have been proposed, that reflect differing professional perspectives and areas of expertise. Initially studied and conceptualised exclusively from a physical standpoint, frailty's definition has evolved to incorporate social, psychological, and cognitive aspects, thus recognising its multidimensional nature (Rockwood et al., 2005; Clegg et al., 2013). This complexity, coupled with the difficulty of differentiating frailty from other clinical conditions such as disability and multimorbidity, makes it a debated concept. The presence of multiple facets that need to be considered together generates the challenge of determining a unique, universally accepted conceptual definition of frailty, which at the moment is still missing. In the following sections the three most recognised and widely adopted paradigms for defining and measuring frailty will be presented.

2.1 The biomedical paradigm

Definition of Frailty according to the biomedical paradigm

In the biomedical framework, frailty is defined as a biological syndrome of decreased reserve and resistance to stressors, resulting from declines in multiple physiological systems, causing vulnerability to adverse outcomes. Such a definition highlights the systemic nature of frailty and its impact on the body's ability to respond to stressors (Fried et al., 2001).

Decreased physiological reserve is a hallmark of frailty, reflecting the diminished capacity of the body's multiple systems to withstand and recover from both internal and external stressors. This decline in reserve spans critical systems, including the musculoskeletal, neuroendocrine, and immune systems, increasing the vulnerability of older adults to adverse health events. The physiological changes that accompany ageing, such as sarcopenia (loss of muscle mass), reduced mobility, and impaired balance, are central to this process. These changes significantly increase the risk of adverse outcomes, including falls, fractures, and a consequent loss of independence. Furthermore, they contribute to higher mortality rates among frail older adults (Fried et al., 2001).

The biomedical paradigm of frailty, while fundamental in geriatric research, has faced significant criticism: its focus on physiological factors is seen only as a narrow and reductionist approach that neglects other crucial dimensions of ageing. This frailty conceptualisation does not consider cognitive and psychosocial factors that, together with biological elements, are fundamental to the health and well-being of older adults. Ignoring these aspects can result in a partial and incomplete understanding of frailty, hindering the development of comprehensive intervention strategies that address the multifaceted nature of frailty (Rolfson et al., 2006).

Measures of Frailty according to the biomedical paradigm

The most widely recognised and used tool for the measurement of frailty based on the biomedical conceptualisation is the Frailty phenotype (Fried et al., 2001). The Fried Frailty Phenotype is a pivotal clinical tool based on the assessment of five elements: unintentional weight loss, exhaustion, weakness, slowness, and low physical activity.

Unintentional weight loss is defined as a loss of 10 pounds (4.5 kg) or more, or 5% or more of body weight over the past year.

Exhaustion is characterised by a persistent feeling of extreme fatigue or an inability to move on most days. This is usually measured using self-report items from the Centre for Epidemiological Studies Depression Scale (CES-D). Specific questions include the frequency with which individuals feel that everything they do requires effort or that they cannot get going. Responses indicating exhaustion on three or more days per week are considered indicative of this criterion.

Weakness is typically assessed through grip strength, a reliable proxy for overall muscle strength. Measurement is carried out using a hand dynamometer, with the highest value recorded from three attempts in each hand. The cut-off values for weakness vary according to sex and body mass index (BMI), with lower grip strength values suggesting that the individual meets the weakness criterion.

Slowness is defined by a reduced walking speed, typically measured as the time taken to walk a set distance, commonly 15 feet (4.57 metres). The time to complete this walk is recorded and the cut-off points are determined according to sex and height.

Finally, low physical activity is evaluated using self-report questionnaires, such as the Minnesota Leisure Time Activity Questionnaire. Participants report on the type and amount of physical activity they engage in, allowing for the calculation of total energy expenditure. Individuals with the lowest levels of activity, usually below a specific calorie expenditure threshold per week, are considered to meet the criterion for low physical activity.

Once the five elements have been evaluated, individuals are classified as frail if they meet three or more criteria, prefrail if they meet one or two.

Empirical studies have consistently demonstrated that frailty, measured by the Fried Frailty Phenotype, is significantly associated with an increased risk of adverse health outcomes and mortality. In the seminal study by Fried et al. (2001), frail individuals exhibited a markedly higher risk of falls, worsening mobility or disability, hospitalisation, and death compared to non-frail counterparts. Subsequent research has reinforced these findings (Bandeen-Roche et al., 2006; Kojima 2016; Clegg et al., 2013).

2.2 The cumulative deficit paradigm

Definition of Frailty according to the cumulative deficit paradigm

The cumulative deficit paradigm represents a more complex approach to the understanding of frailty in the elderly, since it takes into account not only biomedical aspects, but also cognitive, psychosocial, and geriatric factors (Rockwood, et al., 1994). According to this perspective, frailty is defined as "a state of chaotic disorganisation of physiological systems that can be estimated by assessing functional status, diseases, physical and cognitive deficits, psychosocial risk factors, and geriatric syndromes with the aim of building as complete a picture as possible of risk situations for adverse events" (Rockwood et al., 2007).

The cumulative deficit paradigm of frailty builds upon Brocklehurst's (1985) dynamic model of breakdown, which emphasises the delicate balance between assets (factors that help a person to maintain her independence in the community, namely health, functional capacity, positive attitude toward health, and other social, financial, and environmental resources) and deficits (factors that threaten independence, namely morbidity, cognitive impairments, mood disorders, chronic disease, disability, burden on caregivers) that determine an individual's capacity to maintain autonomy and independence within the community.

As people age, they experience deficits that are likely to accumulate, making them more susceptible to adverse health outcomes. A vulnerability state can be considered as the result of a precarious balance between assets and deficits. Frailty occurs when deficits outweigh positive resources, leading to noticeable functional decline and loss of autonomy. It is thus the consequence of a cumulative breakdown of multiple elements, where the concurrent decline of several factors across different systems exacerbates the overall individual functional deterioration.

Although the deficit accumulation approach to frailty has been widely adopted and provides a comprehensive framework, several limitations and challenges have been underlined in the literature. The broad and inclusive nature of the deficit accumulation approach can lead to the overdiagnosis of frailty, particularly in individuals with multiple chronic conditions, but who may still maintain functional independence (Clegg et al., 2013). Furthermore, the identification of multiple deficits can present challenges in designing and prioritising interventions. Addressing a wide range of deficits may require complex, multifaceted approaches that are difficult to implement and evaluate effectively (Rodríguez-Mañas et al., 2013).

In order to provide a robust framework for the construction of valid and reliable frailty indices, thus facilitating their application in research and clinical practice while assessing and monitoring older adults' health, a standardised and validated approach for the development of accumulation-based frailty measures has been proposed in the literature (Searle et al., 2008). This approach establishes five fundamental guidelines:

The variables included in the frailty index must be intrinsically related to an individual's health status. Each deficit should reflect a meaningful aspect of health decline that contributes to frailty.

The prevalence of each deficit should generally increase with age, acknowledging that the prevalence of certain conditions may decline in very advanced ages due to survival effects. This ensures that the index accurately reflects the age-related accumulation of health deficits.

Deficits included in the index should not reach saturation too early. Conditions or diseases that become almost universal at a certain age should be excluded, as their inclusion would diminish the index's ability to differentiate between varying levels of frailty in older populations.

The selection of variables should be balanced across different physiological systems. Over-representation of deficits related to a single system would compromise the index's validity, transforming it from a general frailty index into one that reflects the health of a specific system.

When using the frailty index repeatedly on the same individuals, it is crucial to ensure that the same variables are used consistently. This allows for reliable longitudinal assessments of frailty, ensuring that changes over time reflect true changes in health status rather than variations in the composition of the index.

The optimal number of deficits to include when constructing a frailty index typically ranges between 30 and 40. Generally, as the number of variables used increases, the precision of the frailty index estimates also improves. However, estimates become unstable when the number of deficits is too low. On the other hand, including an excessively large number of deficits does not significantly enhance the accuracy of the index.

Measures of Frailty according to the cumulative deficit paradigm

Several measures have been proposed in the literature, based on the accumulation of deficits perspective (Mitnitski et al., 2001; Romero-Ortuno, 2013; Bennett et al., 2013; Blodgett et al., 2015; Jones et al., 2004; Rolfson et al., 2006). The Frailty Index (FI) (Mitnitski et al., 2001) is one of the most widely used. In a multidimensional perspective, it encompasses a wide range of clinical signs, symptoms, disabilities, and laboratory abnormalities. Unlike phenotype-based measures, the FI does not rely on a predefined set of criteria, but instead uses a comprehensive list of potential deficits, which can number between 30 and 70 or more, depending on the availability of the data and on the study design. Each deficit is assigned a value of 1 if present and 0 if absent, with intermediate values possible for partial deficits. The elements generally taken into account can be categorised into several macro-areas: physical health, sensory impairments, respiratory and cardiovascular conditions, functional status, cognitive function, mental health, nutritional status, social and economic factors, and general symptoms like fatigue, pain, and sleep disturbances. The index is calculated by adding the values of all present deficits and dividing by the total number of deficits considered. Unlike the Frailty Phenotype, which provides a clear classification of individuals into frail, pre-frail, and robust categories, the Frailty Index (FI) does not inherently offer such distinctions. Instead, it provides a score that reflects the proportion of deficits accumulated by an individual. However, to address the need for classification similar to the biomedical approach, a two-threshold system has been proposed in the literature (Romero-Ortuno et al., 2010). This system sets specific cut-off points on the FI scale to categorise individuals into frail, pre-frail, and robust groups, thereby facilitating clinical decision-making and research comparisons. The FI is robust in its predictive validity for adverse outcomes such as mortality and hospitalisation (Mitnitski et al., 2001; Rockwood and Mitnitski, 2007; Chang et al., 2018).

2.3 The bio-psycho-social paradigm

Definition of frailty according to the bio-psycho-social paradigm

The bio-psycho-social paradigm for frailty offers a comprehensive framework that integrates biological, psychological, and social factors in understanding and addressing frailty in older adults. Unlike models that focus solely on physical or biomedical aspects, this paradigm recognises that frailty is a multidimensional syndrome influenced by a complex interplay of various determinants. Gobbens et al.

(2010) define frailty as "a dynamic state affecting an individual who experiences losses in one or more domains of human functioning (physical, psychological, and social), which are caused by the influence of a range of variables and which increase the risk of adverse outcomes”. This definition is the result of a comprehensive review of the literature and consultations with experts in the field, ensuring that this conceptualisation of frailty is evidence-based and reflective of clinical realities.

Biologically, frailty is associated with age-related changes such as sarcopenia, inflammation, and hormonal imbalances, which contribute to decreased physiological reserves and increased vulnerability to stressors. Psychologically, cognitive impairment, depression, and anxiety are critical components, as mental health significantly affects an individual’s ability to cope with and recover from illnesses and disabilities. Socially, factors such as social support, socioeconomic status, and living conditions play crucial roles in determining an individual's frailty status. Social isolation, financial hardship, and lack of access to healthcare resources can exacerbate frailty, underscoring the importance of a supportive social environment.

This holistic approach is based on the idea that interventions targeting multiple individual life domains – such as combining physical exercise with social engagement and mental health support – are more effective in mitigating frailty and protecting against adverse health outcomes than those focussing on a single aspect.

Measures of frailty according to the bio-psycho-social paradigm

Presented by Gobbens and coauthors in 2010, the Tilburg Frailty Indicator (TFI) is based on 15 items collected across three domains via a self-administered questionnaire. These domains include physical components, psychological factors, and social elements. The physical domain includes health, weight loss, difficulty walking, balance, hearing, vision, grip strength, and fatigue. The psychological domain covers memory, feeling down, anxiety, and coping. The social domain addresses living alone, social isolation, and social support.

Each item is scored 1 for the presence and 0 for the absence of the specific problem. The physical domain ranges from 0 to 8, the psychological domain from 0 to 4, and the social domain from 0 to 3. In total, there are 15 items, 11 of which are dichotomous with "yes" and "no" categories, while 4 have three categories: "yes", "sometimes", and "no", but are then dichotomized. The index value is equal to the sum of the present characteristics, ranging from 0 to 15. Individuals are considered frail if they score 5 or more. The cut-off points for physical, psychological, and social frailty are 3, 2, and 2, respectively. People can be frail on one or more domains simultaneously, while overall non-frail people can be frail with regard to one of the separate domains.

3. Frailty, disability, and multimorbidity: Three distinct concepts

The concept of frailty is relatively newer compared to the concepts of disability and multimorbidity, but together they contribute to a more comprehensive understanding of an individual's health. First, it is important to clarify that these are three distinct, but interrelated, concepts.

Multimorbidity is a term that has been increasingly used in recent years, as opposed to the term comorbidity, which was introduced over 40 years ago. Multimorbidity is broadly defined as the coexistence of two or more chronic conditions, where none necessarily dominates the others. Comorbidity, on the other hand, refers to the coexistence of medical conditions in an individual, where an index disease occurs first (Espinoza et al., 2018). Multimorbidity is often quantified by counting the number of diseases, but well-known comorbidity indices, such as the Charlson Comorbidity Index (CCI) or the Cumulative Illness Rating Scale (CIRS), are also used. The CCI includes 19 chronic diseases, selected and weighted based on their association with mortality (Charlson et al., 1987). CIRS categorises chronic conditions within different body systems and counts the number of systems affected by at least one chronic disease (Hudon et al., 2005). However, there is no consensus in the literature on the cut-off values to define multimorbidity using these measures. Consequently, the prevalence of multimorbidity varies depending on the definition and cut-off points used.

Disability refers to the condition of individuals who, due to one or more impairments, have a reduced ability to interact with their social environment compared to what is considered the norm. As a result, they may be less autonomous in carrying out daily activities and often face disadvantages in participating in social life (WHO, 2001). Disability assessment is based on the ability to perform activities, from the simplest to the most complex, and to maintain a social role. In relation to complexity and difficulty, the activities of daily living can be defined as "basic" Activities of Daily Living (ADLs) or "instrumental" Activities of Daily Living (IADLs). ADLs include fundamental functions related to self-care, such as walking, dressing, eating, hygiene, and sphincter control (Katz et al., 1963). IADLs involve more complex functions, such as shopping, managing money, cooking, maintaining a household, and using the telephone (Lawton & Brody, 1969). Independence in IADLs is crucial as it often determines whether an individual can live alone or not.

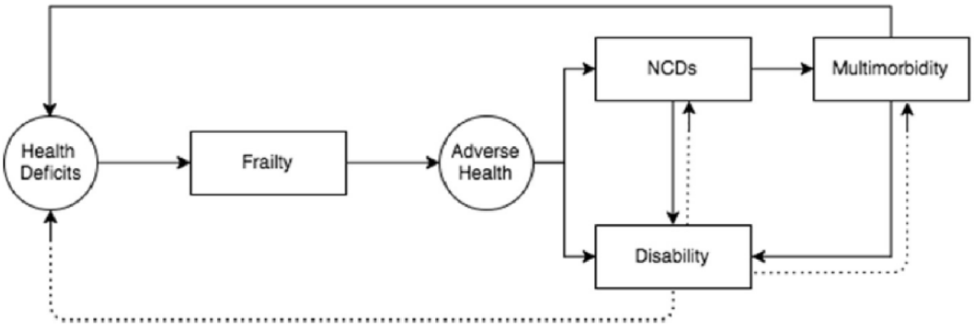
From the definitions provided (and the associated measures), it is clear that frailty, multimorbidity, and disability are distinct concepts and that individuals may experience one or more of these conditions.

Fried et al. (2004) showed that among 100 frail individuals, only 27.2% are also disabled, 67.7% have multimorbidity (Fried uses the term comorbidity, which is now recognised as multimorbidity), and 21.5% of frail individuals are both disabled and have multimorbidity. Only 2.8% of the total sample exhibits all three characteristics simultaneously. Boeckxstaens et al. (2015) observed that Fried et al. used a relatively limited measure of multimorbidity, including only nine chronic diseases, and suggested that a more comprehensive measure might reveal a closer relationship between multimorbidity and frailty. In their study, which considered 22 chronic diseases, the overlap between frailty, disability, and multimorbidity was only 2.3%. In Pivetta et al. (2020), the overlap was 5.4%, but the sample size was small (n=166) and limited to individuals aged 80 and over.

As we have seen, the overlap between frailty, multimorbidity, and disability is quite small, making it interesting to explore the relationship between these three phenomena. It is very challenging to define the relational structure linking them. Much of the literature describes disability as one of the adverse health outcomes to which frailty leads, but this does not negate the fact that disability can also exacerbate frailty. Multimorbidity, being a more nuanced and widespread concept, is even more difficult to categorise.

Villacampa-Fernández et al. (2016) propose an extremely effective relational schema.

Figure 1 - *Flowchart of the System Failure Process. Circles represent inputs/outputs, rectangles represent clinical conditions, continuous lines represent direct effects, and dotted lines represent indirect or secondary effects. NCDs = non-communicable diseases (from Villacampa-Fernández et al., 2016).*



According to this chart, frailty and multimorbidity are both predictors and outcomes of each other, as well as predictors of disability. The system failure process starts with an accumulation of health deficits that leads to a clinical state characterised by depletion of physiological reserve and redundancy, known as frailty. This frail system is more vulnerable to any stressor, thereby increasing the risk of adverse health outcomes due to an inability to recover homeostasis. By adverse health outcomes, the authors refer to the full range of possible diseases and/or impairments, with institutionalisation and mortality as the worst-case scenarios. These adverse health outcomes, in turn, increase the risk of multimorbidity and disability. The consequent multimorbidity leads to further accumulation of deficits and thus to frailty. Disability also increases the risk of deficit accumulation and frailty, although its effect is considered more indirect or secondary. Furthermore, multimorbidity directly increases the risk of disability, while disability is a consequence of chronic diseases and multimorbidity.

Several authors have attempted to understand the role of frailty, multimorbidity, and disability in the occurrence of adverse events, usually mortality, with sometimes discordant results. For example, Aarts et al. (2015) showed that frailty (as measured by Fried's phenotype), when not accompanied by disability and/or multimorbidity, does not lead to a higher risk of mortality or institutionalisation compared to non-frail individuals. Abizanda et al. (2014) demonstrated that frailty is a risk factor for mortality and/or disability in individuals younger than 80 years, but not in those aged 80 years and older. Boeckxstaens et al. (2015) found that multimorbidity is independently associated with disability but not with frailty. In a study by Ritt et al. (2017), frailty was found to be a better predictor of mortality than disability. Leme et al. (2019) showed that frail older adults, with or without multiple simultaneous chronic diseases and disabilities, had shorter survival times. These findings highlight the importance of frailty as a predictor of a shorter survival time, independently of functional status and the number of simultaneous chronic diseases. Abizanda et al. (2014) reported similar results, providing a clear explanation: “Perhaps the most important reason that could explain the exclusion of comorbidity or multimorbidity from the models is that older adults with multimorbidity are heterogeneous in terms of illness severity, frailty, functional status, mental status, geriatric syndromes, prognosis, personal priorities, and risk of adverse events even when diagnosed with the same pattern of conditions. Thus, it is not the disease but the underlying disability, biological vulnerability or frailty, age-related conditions, time to adverse event conditioned by age, and model of care that will determine the risk of adverse events. Health services and health policies for older adults should take into account age, frailty, and disability, and not only comorbidity or multimorbidity.”

Regarding the relationship between frailty and disability, it seems that in older adults under the age of 80 years, prevention, detection, and treatment of frailty should be the main focus of health policies. However, for those over 80 years of age, the focus should shift to disability, probably because frailty at that age may have already triggered detected or undetected disability, and the contribution of disability to adverse events surpasses that of frailty. Physical frailty, unlike most disabilities, can potentially be prevented or treated with specific approaches, such as exercise, protein-calorie supplementation, vitamin D, and reduced polypharmacy (Morley et al., 2013). Therefore, identifying pre-frail and frail older adults should be a clear goal for screening people older than 70 years in order to implement primary and secondary prevention to reduce incident disability.

4. Data to Measure and Analyse Frailty

The different definitions and, therefore, measures of frailty are based on significantly different content, as we discussed in Section 2. For example, the frailty phenotype defined by Fried et al. (2001) is based on concepts such as unintentional weight loss or low activity, which can only be measured through specific surveys conducted on particular groups of subjects. Similarly, Gobbens' psychosocial approach refers to specific psychological and social aspects in the construction of the Tilburg Frailty Indicator. On the other hand, the cumulative deficit perspective (Rockwood et al., 2005) uses a range of deficits that are readily available in survey or clinical data, many of which can be potentially retrieved for the entire population based on administrative data such as hospitalisation records.

In addition to the definitional aspects, different types of data are necessary depending on the research objectives.

From a public health perspective, in Italy, there is an increasing need to address and manage the challenges related to chronic diseases (which constitute a significant part of the country's health burden), to implement a population stratification process identifying homogeneous subgroups in terms of needs and characteristics (individual and socio-familial factors that may influence the individual's capacity to manage the pathology), and to create a model of integrated and personalised healthcare, targeted and personalised interventions, thus optimising the effectiveness of care and the use of healthcare resources. These needs are emphasised in the National Plan for Chronicity (NPC) (Ministry of Health, 2016) and the Sector Reform of the National Recovery and Resilience Plan (PNRR, Decree No. 77 - May 23, 2022).

From an epidemiological perspective, the objectives are quite different, as there is an interest in understanding the risk factors of frailty, assessing inequalities, comprehending causal relationships, and the role that those multiple aspects (social, economic, lifestyle, relationships, etc.) play in the risk of frailty.

We can essentially divide the types of available data for frailty analysis into two major groups: administrative data and data from surveys (sample surveys or surveys on specific subgroups of the population, such as residents of nursing homes). These two types allow us to answer different research questions. Administrative sources, typically health records held by Local Health Authorities, have complete coverage of the assisted population and therefore allow for actual population stratification, as required by the Italian legislation. These data are collected for administrative purposes, so the type of available data is limited to the information necessary for the objectives for which the data flow was created. Thus, such data generally inform on hospitalisations and their causes, used medications, exemptions, causes of death, etc. These data have total coverage and systematic updating; since they often need to meet spending objectives, they are of good quality and are available at a low or no cost. From a public health perspective and to quantify frail individuals in the population, administrative data are clearly indispensable.

However, being collected for administrative purposes, the available information is limited to what is strictly necessary to meet the treatment objectives. Everything that goes beyond administrative purposes, such as information on family networks, lifestyles, health risk factors, etc., is not included. Moreover, there are complex privacy issues that must be properly managed. As a consequence, not everyone can access this type of data.

On the contrary, data from ad-hoc surveys (whether representative of the entire population or of specific groups) have greater informational potential, as the available information spans 360 degrees and refers to lifestyles, family and social networks, support received and given, as well as health conditions and the use of health services. Clearly, the concept of frailty finds its full application in the case of ad-hoc surveys, where a substantial set of objective and subjective information can be utilised. It is possible to obtain measures that embrace different theories, both Fried's phenotype theory and the bio-psycho-social theory, and to explore comparisons between measurement tools. It is also possible to analyse associations and causal relationships between potential risk factors and frailty. From an epidemiological perspective, for a deep understanding of the phenomenon and scientific research, this is certainly the appropriate context.

Nationally, we can refer to the ISTAT health conditions[1] surveys, available to all researchers, or other valuable surveys such as the Italian Longitudinal Study on Ageing (ILSA) (Galluzzo et al., 2023) or the Passi d'Argento surveillance system[2], accessible only to the research groups involved. Internationally, we have the SHARE survey for Europe (Börsch-Supan et al., 2013) and similar surveys for other countries.

Potentially, these two approaches, which we have termed *public health approach* and *epidemiological approach,* could converge by jointly using administrative data and survey data. There are (few) extremely interesting experiences of this type. An example is the linkage between health surveys and mortality and hospitalisation data (Sebastiani et al., 2019), carried out by ISTAT with some regions. However, only

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[1] https://www.istat.it/tag/condizioni-di-salute/

[2] https://www.epicentro.iss.it/passi-argento/

restricted groups of researchers have access to this kind of data, following specific agreements between entities and in compliance with complex privacy regulations. It would be desirable to facilitate such research collaboration, bringing us closer to those European countries where health information systems are structured from the outset to allow data integration. For example, in Sweden, each individual has a personal identifier that is used for all records. However, this topic goes beyond this discussion, as it enters the complex field of personal data processing.

5. A path to measuring frailty with administrative data

The excursus presented so far clearly shows how relevant it is to measure frailty in an ageing society and how the measurement process primarily depends on the definition of frailty adopted and on the objectives pursued by proposing a frailty measure.

This section outlines our proposal for an analytical path to create a measure of frailty, based on the requirements expressed by Italian legislation (Section 4): a frailty index for the population, which makes it possible to stratify the population according to health needs and to support healthcare providers in planning service delivery.

It is important to clarify from the outset that many other frailty indexes have been proposed in the literature, some driven by similar objectives to ours and others aimed at different goals, such as those of a more etiological nature.

A brief description of the analytical path is provided in the following, with the aim of highlighting its strengths and weaknesses. The methodological details and results have already been published elsewhere (Silan et al., 2019, 2022).

Let us start with the concept of frailty used, which is linked to the objective of the investigation: from a public health perspective, where prevention and personalised healthcare are priorities, we considered that the most appropriate approach was to adopt the theory that those individuals at higher risk of adverse events are the frail ones. Proper identification and quantification of these individuals enable the healthcare system to implement more effective preventive and care measures.

In the literature, there are several proposals for "Electronic Frailty Indices" (e.g., De Luca et al. 2023; Khanna et al., 2023; Luo et al., 2022; Rebora et al., 2023; Thandi et al. 2024), which draw on Electronic Health Records, but most of them aim to predict at most two adverse events, typically mortality and hospitalisation, or mortality and disability. Furthermore, several works rely on regression models, subsequently providing indicators based on the linear combination of variables weighted by regression coefficients calculated on specific populations. The underlying assumption is that the results obtained for one population can be generalised to other contexts. Finally, many indices are based on large numbers of variables, making their actual calculation in settings such as healthcare providers very burdensome.

Based on the strengths and weaknesses of the proposals in the literature, our goal is to propose an indicator with the following characteristics:

- It should be a simple tool, based on few variables and therefore replicable and easy to calculate, as it needs to be used by healthcare providers, not by research institutes.
- It must necessarily be based on population data and not on ad-hoc surveys, to allow for the stratification of the entire population.
- It should be a tool that adapts to changes over time (and space), regenerating itself easily.
- It should be capable of capturing multiple adverse health outcomes simultaneously.

With these premises in mind, we briefly describe the analytical path, outlined in Figure 2.

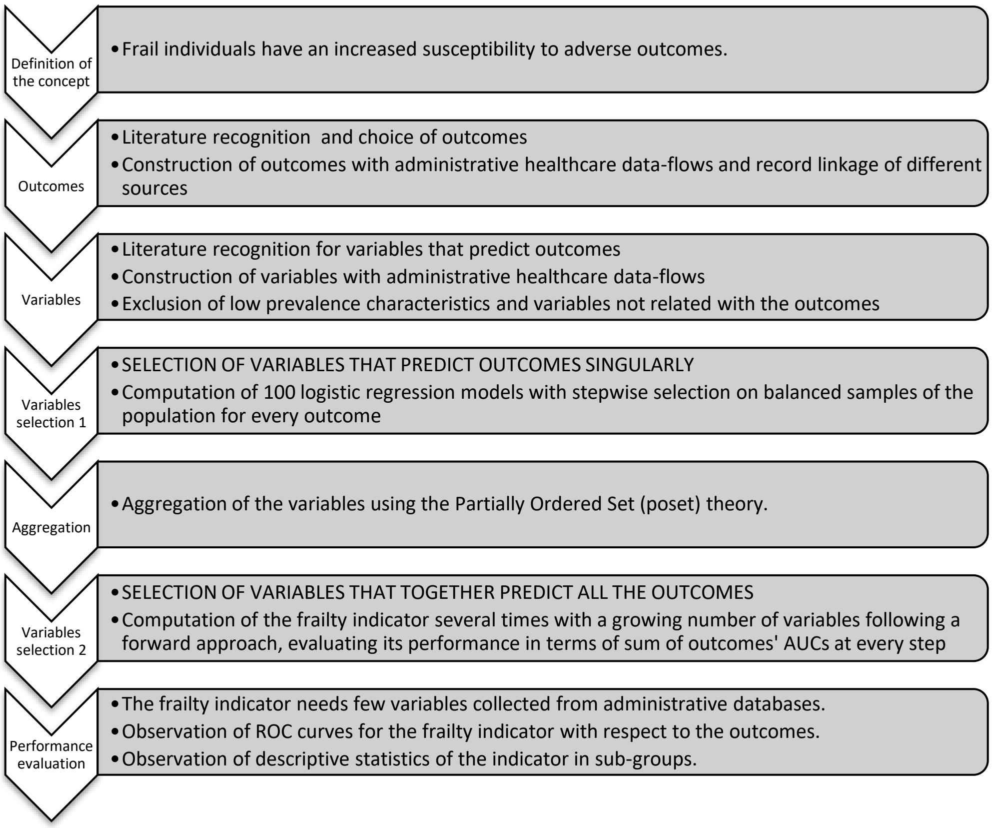
5.1 Selection of adverse health outcomes

Given the choice to identify as frail those individuals most vulnerable to adverse health outcomes, the first step is to identify these health outcomes. The choice and number of outcomes to be considered will affect the variables that compose the frailty indicator, as different outcomes are presumably associated with different explanatory variables.

Death is clearly the outcome that is always considered. Through the study of two important systematic reviews (Sternberg et al., 2011; Wallace, 2014), integrated by our additional analysis of the literature, it emerges that the most common outcomes related to frailty condition are death, disability, hospitalisation, and institutionalisation. the decline in physical performance, home care, falls/incidents, fractures, worsening mobility, worsening disability, emergency hospitalisation, dementia, comorbidities, length of hospital stay, significant use of healthcare and avoidable hospitalisation, are also considered

Clearly, many of these outcomes are strongly associated. For example, Brocco (2020), through analysis of ULSS6 Euganea data for the period 2016-17, shows how emergency hospitalisation includes avoidable hospitalisation and femoral neck fracture, since practically all hospitalisations for these two causes are urgent (99% and 98%, respectively).

Figure 2 - *Analysis path for the construction of an electronic frailty indicator.*



- Frail individuals have an increased susceptibility to adverse outcomes.

- Literature recognition and choice of outcomes
- Construction of outcomes with administrative healthcare data-flows and record linkage of different sources

- Literature recognition for variables that predict outcomes
- Construction of variables with administrative healthcare data-flows
- Exclusion of low prevalence characteristics and variables not related with the outcomes

- SELECTION OF VARIABLES THAT PREDICT OUTCOMES SINGULARLY
- Computation of 100 logistic regression models with stepwise selection on balanced samples of the population for every outcome

- Aggregation of the variables using the Partially Ordered Set (poset) theory.

- SELECTION OF VARIABLES THAT TOGETHER PREDICT ALL THE OUTCOMES
- Computation of the frailty indicator several times with a growing number of variables following a forward approach, evaluating its performance in terms of sum of outcomes' AUCs at every step

- The frailty indicator needs few variables collected from administrative databases.
- Observation of ROC curves for the frailty indicator with respect to the outcomes.
- Observation of descriptive statistics of the indicator in sub-groups.

5.2 Construction of variables from current healthcare data flows

Both health outcomes and the variables candidate to compose the frailty index are derived from administrative data related to various current healthcare data flows, such as mortality, hospital discharges, drug prescriptions, first aid, income exemptions, home care service, and medical exemptions. These flows are linked to the health registry, allowing reconstruction of health events for an individual.

The process is very complex; we highlight here the two main points of complexity.

1) Measurement of each health variable, typically a pathology, requires the preparation of complex algorithms for case identification (Canova et al., 2019;

Giraudo et al. 2023). These algorithms indicate which healthcare data flows to consider and which pathology codes to use in each flow, according to the classifications adopted in each healthcare flow.

2) The use of this type of data is subject to regulations on the processing of personal and health data for research purposes. Unless specific projects are authorized by the Data Protection Authority, some of which are included in the National Statistical Programme, the researcher can only analyse anonymised data. The path to anonymised data is complex and requires that data holders - in this case, Local Health Authorities - carry out this process. The process includes a first phase of pseudonymization, in which the tax code (the primary identifying key) is replaced with a pseudonym ID, and all direct identifiers are subsequently eliminated. Note that the pseudonymization algorithm must not be known even to those who apply it. Subsequently, each pseudonymized table is merged with the pseudonymized health registry through deterministic record linkage. Then the anonymisation process follows, consisting of two phases: 1) Generalisation of quasi-identifiers (gender, age, area of residence) to eliminate the risk of subject identification; 2) Verification of the deterministic deductibility of health data, which quantifies the number of subjects at risk of deduction. In the risk assessment phase, predetermined levels of impact for affected individuals are considered, and the acceptance of any risk of deductibility is evaluated based on the value of the deducible information; otherwise, at-risk data are removed from the dataset. Details on the anonymisation process can be found, for example, in Irti (2022).

5.3 Identification and selection of variables composing the indicator

Once the adverse health outcomes have been chosen, the next step is to select the explanatory variables for these outcomes. In fact, the predictors of health outcomes are the candidates to form the indicator.

Various approaches have been presented in the literature for variable selection. Many studies consider multivariate models, typically logistic regressions, where the outcome is defined by the presence of at least one of the selected health outcomes (e.g., mortality and hospitalisation), and variable selection is then performed using standard statistical methods such as stepwise selection, lasso, etc.

Our proposal (Silan et al., 2020, 2022) instead considers several health outcomes separately (death, fracture, emergency room access with red code, urgent hospitalisation, avoidable hospitalisation, onset of disability, onset of dementia) and aims to identify the best subset of predictive variables for all outcomes, starting from candidate variables that emerged from multivariate analyses performed for each outcome. Analyses are performed separately on each health outcome based on healthcare variables observed in the previous year (in some cases, from the previous two years). The selection procedure, rather complex, is detailed in the aforementioned article and is based on a process of resampling and repetition of analyses and selection of variables that are most often selected for each outcome.

5.4 Construction of the frailty index

Once a broad subset of variables that make up the indicator has been selected, they are aggregated using the partially ordered sets (POSET) method, which, starting from a set of dichotomous and/or ordinal variables, considers each subject's profile (i.e., the set of their characteristics based on the variables considered) and then generates a measure (average rank) based on the comparison of all profiles. For details, see Silan et al. (2020).

Using POSET, it is also possible to construct the indicator using a forward technique, adding variables one by one and stopping when the performance of the indicator worsens with the addition of more variables. The criterion we adopted was the sum of the Areas Under the ROC Curve (AUC) for the various outcomes considered. In this way, we arrive at an indicator composed of a small number of variables, fewer than 10, and, therefore, easy to calculate. The indicator shows very good performance in terms of AUC, even in different populations (according to time and space), comparable to or even better than other deficit accumulation indices that consider many more variables.

5.5 Future developments and limitations

The frailty indicator proposed by Silan et al. (2020, 2022) has many advantages (has very good performance, is based on a small number of variables, considers several outcomes simultaneously, regenerates over time, and does not rely on predefined parameters or weights) and has generated significant interest among healthcare providers and regions. Therefore, further validations are underway and easy-to-use applications are being developed.

The proposed method also has limitations: the average rank assigned by POSET technique strictly depends on the structure of the population in which it is calculated according to both variables forming the indicator and variability of observed profiles. Comparison across space or time is therefore theoretically not possible, unless the observed profiles of the populations being compared are exactly the same, which is less likely. From a methodological point of view, we are working on a proposal of confidence intervals for the average rank generated by the POSET, which are currently never proposed in the literature.

A more general limitation, not related to our proposal but to the nature of health administrative data, is related to the need to make the definitions and classification systems of all health flows as shared as possible in the various regions, something that has not yet been fully achieved. In the absence of such sharing, the risk is that territorial differences are due (at least in part) to different definition and coding systems. This is a general problem that has always plagued official statistics.

6. Discussion

This work aimed primarily to highlight the different conceptual approaches to frailty in old people, showing the process that starts from the concept, leads to the definition, and then to the measurement tool for frailty. It is evident that different definitions lead to very different measures. Additionally, different types of data allow for one definitional approach over another, resulting in the measurement of different aspects. Thus, in light of a large and general concept of frailty, which describes it as a state of increased vulnerability that makes individuals more susceptible to adverse health events, it is possible to focus more on clinical, biological, or psychosocial aspects, resulting in different measures of frailty.

The researcher, particularly the official statistician, is well aware of these dynamics, which often are the subject of extensive discussions. If we consider, for example, the measurement of health and the underlying concept, we are fully aware of how different it is to talk about self-perceived health, measured through surveys, versus "objective" health, measured through administrative health data.

What is needed is to bring order to the set of definitions and measurement tools and arrive at shared and validated indicators at the international level. The level of discussion is such that we believe that the time is ripe to address this issue.

We then presented a proposed path for the construction of frailty indicators based on administrative health data. This is an increasingly relevant issue for public health management, from a perspective of prevention and appropriate healthcare. In our country, this need has been repeatedly emphasised by regulations and represents an important objective within the PNRR Age-IT partnership, "Ageing Well in an Ageing Society" (https://ageit.eu/wp/). Beyond the methodological aspects, which are gradually resolved by research, the process is made difficult by the many constraints imposed by data privacy regulations, constraints that can only be resolved through constant and intense collaboration with local health authorities or regions, at the local level, and with the Data Protection Authority, at the national level.

Today, the regulatory framework does not allow the full potential of individual-level frailty measures to be exploited. In fact, currently, the calculation of frailty indicators is carried out on anonymised data from which it is not possible to trace back the individual. Contacting at risk individuals in order to define personalised care paths, the so-called "initiative medicine," is therefore not feasible in this context, unless explicit consent from the individual has been obtained (which is currently not possible with retrospective administrative health data), or a specific regulation permits it (which currently does not exist). In fact, initiative medicine does not fall under the processing of health data for ordinary care and prevention activities, but must be considered an "additional and autonomous processing" for which one of the two aforementioned conditions is required.

The scientific community and official statistics are actively engaged in these issues, which require a collective effort that also requires legislators not to become an obstacle to the potential of research and the provision of complete healthcare.

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