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Trajectories, Transitions, and Trends in Frailty among Older Adults: A Review

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Frailty is an age-related clinical state associated with deterioration across multiple physiological systems and a leading cause of morbidity and mortality later in life. To understand how frailty develops and what causes its progression, longitudinal data with repeated frailty measurements are required. This review summarizes evidence from longitudinal studies on frailty trajectories, transitions, and trends. We identified several consistent findings: frailty increases with aging and is a dynamic condition, and more recent generations of older adults have higher frailty levels. These findings have both clinical and public health relevance, including the provision of health-care and aged care services in the coming years. Further studies are required, particularly those conducted in low- and middle-income countries and those investigating factors associated with changes in frailty. The latter may help develop better-targeted interventions to reverse or slow the progression of frailty.

Key Words: Frail older adults, Frailty, Aging, Longitudinal studies, Trends

INTRODUCTION

The global population of older adults (60 years and over) will nearly double to 2.1 billion people by 2050 because of gains in life expectancy.[1] However, many countries are not prepared for this rapid growth in the older population.[2] Hospitals and the long-term care sector are already running at full capacity in many regions.[3] Additionally, gains in life expectancy are not translated into gains in disability-free life for many older adults; thus, in their extended years, these adults face disabilities and poor overall health.[2]

The most common condition affecting older adults in terms of both mortality and morbidity is frailty.[4,5] Frailty is defined as an age-related clinical state associated with deterioration across multiple physiological systems, particularly the musculoskeletal, cardiorespiratory, and immune systems.[5-7] Frailty is a preventable condition, and not all older adults will develop frailty during their lifetime.[8] Likewise, frailty is not a fixed state.[9,10] Rather, the condition is a dynamic entity, wherein individuals can fluctuate between states.[10] For example, a person can transition from "robust" (not frail) to either a pre-frail (the pre-cursor state of frailty) or frail state, and vice versa.[8,9] Unfortunately, frailty is common, affecting an estimated 11% of community-dwelling adults aged ≥65 years.[11] The prevalence of frailty is especially high in the oldest older adults (≥80 years),[12] those residing in low- and middle-income countries,[13] residents of long-term care facilities,[14] and populations with chronic diseases such as chronic obstructive pulmonary disease,[15] chronic kidney disease,[16] cancer,[17] and cardiovascular disease.[18] The likelihood of developing frailty is affected by inequalities in socioeconomic position.[13,19-22] The sexes show significant differences, with women typically experiencing more frailty,[23] yet with higher survival rates than men either with or without frailty.[23]

Despite the increasing awareness that frailty is preventable, longitudinal data with repeated frailty measurements are still not

widely used. This review collated longitudinal studies on frailty to inform the timelines of frailty development and progression in older adults. By examining frailty trajectories, transitions, and trends, we can identify factors that may accelerate or slow frailty development and progression.

FRAILTY MEASUREMENT

Two main conceptual models of frailty exist in the literature today: the phenotypic model first proposed by Fried et al.[24] and the accumulated deficit multidimensional frailty index (FI) described by Mitnitski et al.,[25] both of which were introduced in 2001. Fried's phenotypic model identifies frailty as the presence of three or more of five physical components: slowness (slow gait speed), shrinking (weight loss), exhaustion (self-reported), weakness (low grip strength), and low physical activity.[24] When only one or two of these physical components are present, an individual is classified as "pre-frail"; if no component is present, the individual is classified as "robust."[24]

The FI model considers frailty to be an accumulation of health deficits, wherein the more deficits individuals have, the frailer they are.[25-27] The FI is a continuous variable from 0 (no health deficits present) to 1 (all health deficits present) and is expressed as the number of deficits present divided by the total number of deficits in the list. For instance, in a list of 50 health deficits, an individual with 10 deficits has an FI score of 0.2 (10/50).[26] The maximum FI score viable for life is around 0.68.[28]

CHANGES IN FRAILTY

For many years, the field of frailty research has been dominated by studies that evaluate frailty measurements at a single time point. These studies examined the cross-sectional associations between frailty and other variables or used frailty as a predictor of adverse outcomes, particularly mortality.[5] However, longitudinal data with repeated frailty measurements are crucial to understanding how frailty develops and what causes its progression. Over the past 15 years, research on the changes in frailty has emerged, including studies on changes in frailty with aging (trajectories and transitions) as well as studies on historical changes (trends). Fig. 1 shows that the number of studies in PubMed mentioning "frailty trajectories" or "frailty changes" has progressively increased in recent years. Various study types across a wide range of populations were observed. A more detailed examination of the search results revealed two dominant research trends. First, to investigate frailty development and progression, repeated frailty measures were used in the same sample. Second, to study frailty trends, various independent samples from the same age group were used. Table 1 presents a selection of key empirical papers on trajectories, transitions, and trends in frailty among older adults,[22,29-39] which will be discussed below.

Frailty Trajectories

Various longitudinal studies have examined frailty trajectories using measurements at three or more time points, in which frailty is typically included as a continuous measure (mainly assessed with the FI).[40] Four examples of such studies are shown in Table 1. Overall, these studies provide an overview of increasing frailty levels with age. However, the rate of change and the shape of the change curve (linear or quadratic) vary across studies.[22,29-31] Jenkins et al.[30] aimed to replicate findings across five longitudinal cohort studies from Europe and the United States. The included aging cohorts had 11–20 years of follow-up. A linear model best characterized frailty progression, and frailty trajectories did not differ between men and women. Additional insights into frailty changes over the life course can be derived from the work of Raymond et al.,[31] as this study also included younger individuals. Interestingly, a turning point was observed at 65 years of age, with a faster increase in frailty levels after that age. The studies listed in Table 1 represent those on frailty trajectories in older populations. However, in the field of frailty trajectories, more specific research directions are evolving, such as work in specific patient populations (e.g., psychiatry and oncology),[41,42] latent frailty trajectories (i.e., groupings of people based on distinct frailty trajectories),[43] frailty fluctuations (i.e., within-person deviations from general frailty trajectories),[10] the order in which frailty components develop,[44] and terminal decline in frailty.[45,46]

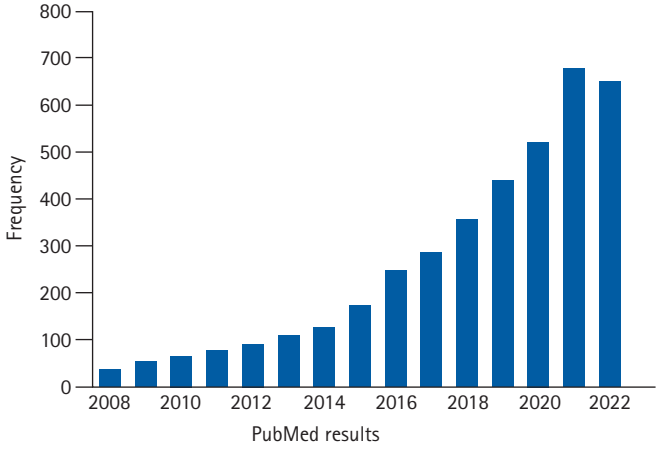

Fig. 1. Number of articles in PubMed mentioning "frailty trajectories" or "frailty changes" in the past 15 years. The year 2022 was still ongoing when the search was done (November 26, 2022).

Table 1. Selection of key empirical papers on trajectories, transitions, and trends in frailty among older adults

	Study	Year	Data	Frailty instrument	Main findings
Trajectories	Hoogendijk et al.[29]	2018	The Netherlands, the Longitudinal Aging Study Amsterdam (LASA), 17-year follow-up	Frailty index (32 items)	Linear increase in frailty with aging. Partner status impacted frailty trajectories, sex and education did not.
	Jenkins et al.[30]	2022	Five longitudinal cohorts from the USA, UK, Italy and the Netherlands, 11 to 20 years of follow-up	Frailty index (30–42 items)	Linear increase in frailty over time. No clear association between sex and frailty progression.
	Raymond et al.[31]	2020	Swedish Adoption/Twin Study of Aging (SATSA), 27-year follow-up	Frailty index (42 items)	Frailty increased non-linearly from adulthood into old age. A higher increase was observed after age 65. Deviations from normal weight were associated with frailty trajectories.
	Stolz et al.[22]	2017	10 European countries, the Survey of Health, Ageing and Retirement in Europe (SHARE), 9-year follow-up	Frailty index (40 items)	Frailty increased with aging (quadratic curve). Different measures of socioeconomic position had a different impact on frailty trajectories.
Transitions	Espinoza et al.[33]	2012	USA, San Antonio Longitudinal Study of Aging (SALSA), 7-year follow-up	Frailty phenotype	A mix of frailty transitions (worsening, improvement, no change) occurred. A lower level of education was associated with frailty worsening.
	Gill et al.[32]	2006	USA, Precipitating Events Project (PEP), 4.5-year follow-up	Frailty phenotype	During follow-up 58% of the study sample had at least one frailty transition. Frailty worsening was more common than frailty improvement.
	Lee et al.[34]	2014	China, longitudinal study, 2-year follow-up	Frailty phenotype	More than half of the sample remained in the same frailty state during follow-up. Various characteristics associated with frailty worsening were identified, such as being male.
	Romero-Ortuno et al.[35]	2021	Ireland, Irish Longitudinal Study on Ageing (TILDA), 8-year follow-up	Frailty phenotype	Frailty was shown to be dynamic. Both frailty worsening (e.g., risk of non-frail to pre-frail progression: 27%) and frailty improvement (e.g., risk of favorable transition from frail to pre-frail: 18%) were common.
Trends	Blodgett et al.[39]	2021	USA, the National Health and Nutrition Examination Survey (NHANES), 1999–2018	Frailty index (46 items)	Frailty scores were higher in more recent cohorts in middle-aged (≥ 35 years) and older adults (≥ 65 years). Frailty lethality was stable.
	Hoogendijk et al.[37]	2021	The Netherlands, the Longitudinal Aging Study Amsterdam (LASA), 1995–2016	Frailty index (32 items)	The prevalence of frailty increased among people aged 64-84 years in more recent years. The association between frailty and mortality remained the same.
	Mousa et al.[36]	2018	UK, the Cognitive Function and Ageing Studies (CFAS), 1991–2011	Frailty index (30 items)	Frailty level was higher in 2011 than in 1991 among people aged 65 and over. Its association with mortality did not change.
	Wennberg et al.[38]	2022	Sweden, the 1895–1945 birth cohorts, 1990–2020	Hospital Frailty Risk Score (HFRS)	Frailty prevalence increased in more recent birth cohorts, at all ages (75, 85 and 95 years).

Frailty Transitions

The study of frailty transitions provides another way to examine longitudinal data. To study these transitions, frailty scores must be categorized. Especially for clinical care pathways, the frailty transition approach is helpful because categorization simplifies clinical decision-making, although the classifications may sometimes be arbitrary. Understanding transitions in frailty may help to identify optimal target populations for frailty interventions. Studies have suggested targeting pre-frailty for early interventions.[47] Studies on transitions are predominantly performed using the frailty phenotype, which has clear categories (robust, pre-frail, and frail). However, theoretically, other frailty measures such as the FI may also be used for this purpose. In 2019, Kojima et al.[47] performed a systematic review of transitions between frailty states in community-dwelling older adults, which included 16 studies related to this topic. Table 1 includes four examples of studies on frailty transitions. In general, these studies showed that frailty is a dynamic condition, as all studies reported that frailty worsening and frailty

improvement were common, while large parts of the study samples remained in the same state at follow-up.[32-35] The study by Gill et al.[32] was one of the earlier studies on frailty transitions. Over 4.5 years, the participants underwent assessments every 1.5 years; among these participants, at least 58% experienced a frailty transition during follow-up. Espinoza et al.[33] examined potential predictors of frailty progression, in which fewer years of education, among other factors, was associated with frailty progression. However, only two measurements (baseline and follow-up) were performed in this study. More research over an extended time is needed to better understand the transitions in frailty later in life and the factors associated with the transitions.

Frailty Trends

Studies on frailty trends are relatively scarce as very few longitudinal cohort studies have a cohort-sequential design in which refresher samples of older adults from new generations are added to the study after several years. To our knowledge, only studies in the United States, the Netherlands, the UK, and Sweden have reported on this topic (Table 1).[36-39] All these studies focused on older adults in the same age group at different periods over a long time span, and together they cover the period from 1990 to 2020. For example, a study from the Netherlands (Longitudinal Aging Study Amsterdam [LASA]) showed that the prevalence of frailty among older adults aged 64–84 years increased from 21% in 1995–1996 to 28% in 2011–2012.[37] Other studies have shown similar results, with increasing levels of frailty or higher frailty prevalence in more recent generations of older adults aged 65 years and over.[36,38,39] Blodgett et al.[39] reported an increasing trend in frailty levels between 1999 and 2018 among middle-aged people (≥ 35 years) in the United States using data from the National Health and Nutrition Examination Survey. A study from Sweden reported that increasing frailty prevalence rates were mainly driven by increased frailty scores among individuals in the highest quartile of the frailty score.[38] Further explanations for the increasing trend in frailty among older adults are unknown and should be explored in future research. Some of the above-mentioned studies also examined trends in the association between frailty and mortality and found that this association remained stable (i.e., in subsequent generations of older adults, the association between frailty and mortality did not become weaker or stronger).[36,38,39] Altogether, the results of trend studies indicate a negative prospect for the future, as there are no signs of a decline in the excess mortality rates of frailty.

Risk Factors for Changes

Insight into risk factors for certain frailty trajectories, transitions, and trends may inform the development of better-targeted interventions to prevent or reduce frailty levels in older adults. Risk factors are not limited to lifestyle and clinical factors relevant later in life and may also involve behavioral and clinical conditions during early life stages, such as midlife and childhood.[5] A recent review of frailty trajectory studies conducted so far by Welstead et al.[40] showed that the different methodologies of these studies make it difficult to draw conclusions regarding which factors contribute to frailty progression. Some risk factors were only identified in a single study.[40] Nevertheless, factors such as low socioeconomic position and lack of physical activity likely contribute to frailty progression. This research field requires expansion, and results should be replicated using similar methodological approaches across studies and settings.

Clinical and Public Health Implications

Based on the results of studies on the trajectories, transitions, and trends in frailty among older adults, some implications for clinical practice and public health can be derived. First, the results of the studies discussed in this review emphasize the importance of early identification of frailty. Identification of frailty at an early stage of a frailty trajectory is critical to promote early interventions.[8,48] Second, regular (e.g., yearly) assessments of frailty among older adults in routine clinical care may be important to monitor frailty changes. An individual reaching a certain frailty level may require additional evidence-based clinical actions.[49] Change in frailty is a risk factor for mortality in later life,[50,51] although findings from previous studies show conflicting results.[51-53] Third, knowledge of frailty trajectories and transitions can inform the cost-effectiveness of future economic planning, which in turn, directly informs policy. Fourth, the findings from trend studies indicate the expected increased burden of frailty for healthcare systems and underscore the need for continued efforts to prevent or reduce frailty among older adults. Frailty prevalence is increasing in more recent generations of older adults, while frailty-associated mortality remains the same.[37,39] Finally, the studies presented in this review make clear the major research gaps, which limit our ability to formulate clear messages for healthcare policymakers. These gaps include the limited number of studies on risk factors for frailty trajectories, transitions, and trends and the lack of studies in low- and middle-income countries. A single study identified various risk factors for frailty progression; thus, replication of these findings is desperately needed.[40] Although most of the world's older population lives in low- and middle-income countries,[54] nearly all evidence on frailty trajectories comes from high-income countries, especially European countries and the United States. Increased efforts are needed to overcome systemic issues that make frailty research in low- and middle-income countries challenging.[5]

CONCLUSION

In the past decade, research on trajectories, transitions, and trends in frailty among older adults has emerged. The handful of publications at the beginning of the 2010s has increased in recent years to a substantial research field, with studies using data from large cohorts in various countries. Based on these studies, important clinical implications were derived. For example, frailty prevalence has increased in subsequent generations of older adults, an increase that is expected to continue.[37-39] This suggests that in clinical practice, the number of older adults presenting with frailty will increase substantially in the coming years. This imposes a high burden on already overstretched healthcare systems. Further research on frailty trajectories, transitions, and trends is needed to increase our understanding of how frailty changes over time and the factors associated with these changes. However, most studies on this topic have been conducted in high-income countries. More evidence from low- and middle-income countries, based on high-quality data collection, is required to monitor frailty globally. Simultaneously, efforts are needed to develop successful interventional programs to prevent and reduce frailty in older adults, for which data from robust clinical trials are indispensable.[6]

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, EOH, ED; Methodology, EOH; Supervision, EOH; Writing-original draft, EOH,ED; Writing-review & editing, EOH, ED.

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