Review

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Frailty in older adults: A systematic review of risk factors and early intervention pathways

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SUMMARY: Frailty is an independent risk factor linked to a higher likelihood of various diseases. With limited healthcare resources worldwide — especially in developing countries — the factors that contribute to frailty need to be understood across different populations and a universal model needs to be developed. This could help reduce the burden on healthcare systems and lessen the negative health effects of frailty. This review aims to summarize current evidence on the key factors influencing frailty and its impact on disease outcomes in different countries. The goal is to facilitate the development of strategies that can help prevent or even reverse frailty. Studies were included if they examined physical frailty using validated assessment tools in older adults and explored how various factors affect its development and progression. A comprehensive search of the PubMed database was conducted from March 1 to March 31, 2024 using the keywords "vulnerability" and "influencing factors." Studies published between January 1, 2001, and March 31, 2025 were considered. A total of 1,614 articles were initially identified, with 50 studies ultimately meeting the predefined inclusion and exclusion criteria. The findings indicate that frailty is influenced by a wide range of interrelated risk and protective factors, which in turn have various effects on different disease outcomes. These interconnected factors highlight both the complexity and the potential for targeted intervention. The review provides a comprehensive understanding of the factors associated with frailty in older adults across diverse settings and underscores the urgent need to develop a robust, evidence-based frailty model to facilitate the early identification, prevention, and possibly reversal of frailty.

Keywords: frailty, influencing factor, older adults, disease, frailty model

1. Introduction

An aging population is a common phenomenon experienced by every country around the world (*1*). China has over 3.623 billion people age 65 and above, making it the country with the largest aging population in the world. Similarly, Japan has an aging rate as high as 29.1, the highest in the world (*2*). This will pose challenges to healthcare in various nations and even lead to significant difficulties in international healthcare planning.

As the population ages, the problem of frailty of the elderly has gradually come into the public's view (*3*). Prior to 2001, positing of a phenotypical operational definition of frailty by Fried *et al*. (*4*) resulted in considerable progress in understanding and exploring the pathophysiology of frailty. They defined frailty as the display of three or more of five physiological deficits (muscle weakness, low gait speed, unintentional weight loss, exhaustion, and low physical activity), and their work has attracted the attention of academic researchers focused on frailty. Frailty is a geriatric syndrome defined as the gradual reduction in functional reserve and resilience, as well as impaired adaptive capacity across multiple physiological systems, that increases the vulnerability against stressors and leads to deterioration and adverse health outcomes in the elderly (*5*), such as falls (*6*), depression (*7*), delirium (*8*), hospitalization (*9*), and even death (*10*). The demands for healthcare from frail elderly individuals continue to increase, and this will pose a tremendous burden in terms of healthcare costs (*11*).

Given that older adults are frail and the condition coexists with other age-related diseases, clinical diagnosis and screening in primary care settings is critical (*12*). Globally, an array of assessment methods has emerged to facilitate routine screening for frailty. Nevertheless, a universally recognized "gold standard" for frailty assessment remains elusive. The Fried Frailty Phenotype (FP), the FRAIL scale, and the Edmonton Frailty Scale (EFS) are among the tools used most widely (*13*). A systematic review reported on the prevalence of and factors influencing frailty in older patients with diabetes in China (*14*), and most studies have used FP and the FRAIL scale for screening. The global prevalence of hypertension among community-dwelling older adults in a study by Liu *et al.* also supports this view (*15*). However, due to the different geographical regions and the diversity of screening tools used, reaching a definitive conclusion about which tools are best is difficult.

With the increasing global focus on healthy aging, a growing group of researchers are considering frailty to be a potentially reversible condition that can be alleviated with various types of interventions. Thus, identifying factors influencing frailty could contribute to the implementation of interventions aimed at preventing or reversing frailty to reduce physical impairments and adverse health outcomes in the elderly. Many studies have reported risk factors associated with frailty. In general, in addition to age being recognized as the strongest factor related to frailty, there are still other risk factors associated with frailty that frequently appear in the literature on global aging populations, such as being female, unmarried, lack of exercise, and low income (*16-19*). Recently, an increasing number of studies have focused on psychological issues and identified psychological factors associated with frailty, such as depression and anxiety (*20,21*). These findings may provide a more comprehensive perspective for further improving measures related to the health management of older adults.

Most reviews limit their scope to specific regions or diseases when evaluating factors influencing frailty, which may lead to an overestimation or underestimation of these factors' impact on frailty. The aim of the current review is to address this gap. This paper not only systematically reviews factors associated with frailty but also summarizes frailty as an independent risk factor for various diseases. By objectively understanding the factors influencing frailty among older adults worldwide and exploring the interconnections between these factors, we can develop a universal frailty model that provides valuable guidance for healthcare professionals in preventing and managing frailty. This review aims to systematically identify and synthesize the key factors influencing frailty among older adults and to propose evidence-based pathways for early detection and intervention.

2. Research design and literature search strategy

2.1. Inclusion criteria and exclusion criteria

The inclusion criteria included: *i*) Study population: the definition of older persons may vary in different countries and regions but is usually based on age and related characteristics. This study was conducted in the Japanese context, so the median age for older adults was ≥ 65 years; *ii*) study content: assessment tools for frailty must be explicitly mentioned in the literature; *iii*) outcome indicators: prevalence of frailty and influencing factors; and *iv*) study type: retrospective, observational, prospective, cross-sectional, and longitudinal studies, with the language limited to English.

The exclusion criteria include: *i*) Only the abstract was published or the full text was not available; ii) physical frailty was not reported; and *iii*) duplicate publications.

2.2. Literature search strategy

The PubMed database was searched from March 1, 2025 to March 31, 2025. All literature published from January 1, 2001 to March 31, 2025 was included, with the language limited to English. Keywords ("vulnerability") and ("influencing factors") were used to conduct the search. Publications were identified among the literature that met the criteria. The publication selection process is shown in Figure 1.

2.3. Literature screening and data extraction

Data were extracted from each paper onto formatted spreadsheets in Excel files, including the first author and year of publication, country, type of study, sample size, age (mean or median and range), region of investigation, prevalence data, the frailty assessment tool used, and influencing factors. The second author subsequently checked for completeness again. Any disagreements were discussed until reaching a consensus.

3. Key findings based on a literature analysis

3.1. Factors influencing frailty were classified by country

A total of 1,614 publications were initially identified. After removing duplicates, 1,611 publications remained, the titles and abstracts of which were read and screened. Subsequently, the full text of 336 publications was screened. Of these, 50 papers were selected that met the eligibility criteria. Figure 1 is a flow diagram showing this process and detailing the reasons for exclusion. Of the publications included, data were collected in China (*n* = 15), the United States (*n* = 4), Japan (*n* = 4), and Spain (*n* = 4). The majority, 25 cross-sectional studies, were included in this review; 24 of the publications examined inpatients, 22 examined older adults in the community, and 4 examined outpatients.

Table 1 and Table 2 provide a summary of all included publications.

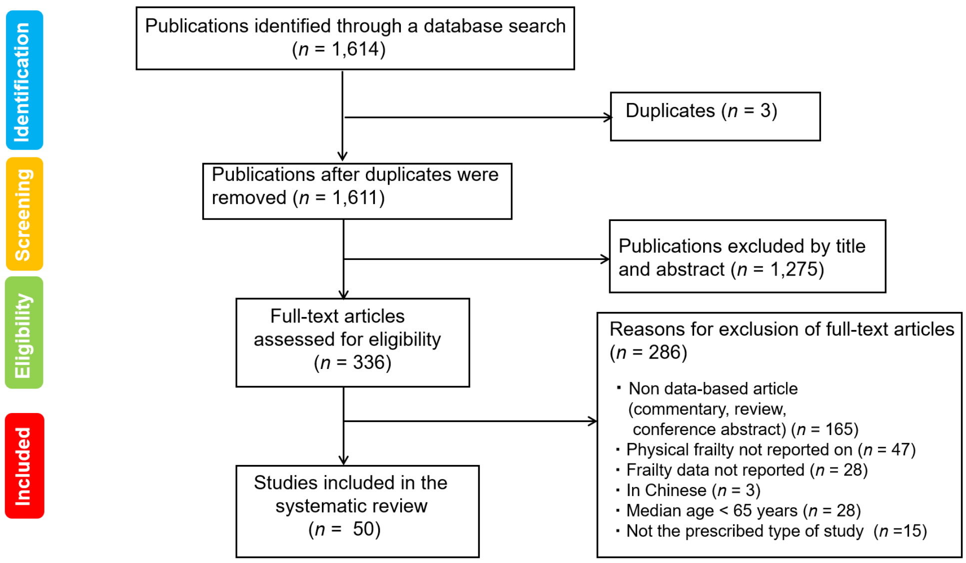

Figure 1. Flow diagram for identifying studies.

3.2. Factors influencing frailty were classified by frailty screening tool

The included studies involved a total of 11 frailty screening tools, with the FP, Frailty Index (FI), and FRAIL Scale being used most frequently. The development and refinement of instruments to assess frailty have been pivotal to advancing both frailty research and clinical use. These tools offer valuable insights into frailty from multiple perspectives, expanding from physical and psychological health to encompass functional and social domains. Despite these advances, however, the heterogeneity among frailty tools remains a significant challenge. Variations in their conceptual frameworks, scoring thresholds, and target populations contribute to inconsistencies in frailty prevalence estimates and in the strength of associations with adverse outcomes.

3.3. Factors influencing frailty were classified by type

A total of 29 studies on factors for frailty were included, and the factors associated with frailty varied across publications. This review identified 34 influencing factors. Thus, a vast number of factors affect frailty and these factors relate to our lives. Moreover, the relationships among the influencing factors are intricate and interwoven. Here, the factors influencing frailty are roughly divided into four categories for discussion (Table 1):

i) Physiological factors: age (*22-26*), sex (*17,19,20,22*), BMI (*27*), marital status (*20,28,29*), nutritional status (*25,30*), grip (*31*), muscle strength (*32*), oral health (*33*), dysphagia (*34*), disability (*16*), a history of falls (*16*), comorbidities (*25,29,35*), polypharmacy (*26*), abnormal excretion status (*24*), prealbumin (*24*), cortisol level (*36*), thyroid function (*37*), blood Gal-3 level (*38*), CRP (*19,31*), hemoglobin level (*39*), and ferritin (*26*).

ii) Psychological factors: depression (*40*), cognitive function (*16,22*), and anxiety (*20*).

iii) Socioeconomic factors: education level (*17,21,23*), economic status (*16,17,29*), and social services (*41*).

iv) Factors related to living conditions: living alone (*42,43*), smoking status (*44*), alcohol intake (*31*), exercise status (*20,23,29*), sleep status (*31,44*), activities of daily living (ADL) (*17,21*), and diet (*45,46*).

3.3.1. Physiological factors

Among the physiological factors, age was the most frequently reported, with 10 studies identifying a significant association with frailty. Next were sex and comorbidities, as show in Figure 2.

Age is a factor that was frequently found to be associated with the level of frailty and changes (*22-26)*, although the direction of the association varied by publication. Wei *et al.* (*24*) indicated that the extent of frailty differed by age group in older adults; frailty often developed at the age 86 to 90 years, though other studies reported the opposite effect. Norazman *et al.* (*19*) reported that the frailty rate in the 60-69 age group is higher than that in the age 70 and older age group, and Kim *et al.* (*22*) found that as age increases, the rate of frailty also increases. This suggests that advanced age is a risk factor for frailty in older adults. However, more research is needed to explore the trajectory of age's impact on frailty.

Another factor frequently associated with frailty is sex (*17,19,20,22*). Different studies have reported that women are more likely to be frail than men. However, a

Table 1. Frailty status and risk influencing factors in various countries

Country	Lead Author, (Year) (*Ref.*)	Type of study	Participants	Prevalence of physical frailty	Frailty Screening tools	Influencing Factors
Mexico	Sánchez-García (2014) (*17*)	Cross-sectional, longitudinal	*n* = 1,933 Median age (SD) = 70.14 (7.15) years (Older group) Community-dwelling	Frail rate =15.7%	FP	1); 2); 3); 4); 8); 13); 15); 16); 17); 18); 19); 25)
USA	Peterson (2018) (*31*)	Longitudinal	*n* = 104 Median age (SD)= 68.9 (6.7) years (Older group) Community-dwelling	Frail rate =14%	FP	6); 10); 12); 32)
UK	Ramsay (2018) (*33*)	Cross-sectional and longitudinal	*n* = 1,622 Median age (SD) = 80.5 (5.4) years (Frail) Community-dwelling	Frail rate =19%	FP	21)
	Parsons (2019) (*45*)	Prospective	*n* = 1,660 Median age (SD)= 80.5 (5.4) years (Frail) Community-dwelling	Frail rate =17.1%	FP	14)
France	Steinmeyer (2020) (*39*)	Cross-sectional	*n* = 1,829 Median age (SD) = 82.44 (6.5) years Inpatients	Frail rate =48.82%	FP	33)
Germany	Henning (2023) (*30*)	Cross-sectional	*n* = 1,271 Median age (SD)= 75.64 (5.95) years Community-dwelling	Frail rate =14.8%	FI	5)
New Zealand	Teh (2021) (*42*)	Longitudinal	*n* = 459 Median age (SD) = 85.4 (1.8) years Community-dwelling	Frail rate =16%	FP	8)
Italy	Trevisan (2016) (*28*)	Observational	*n* = 1,887 Median age (SD) = 74.2 (7.0) years Community-dwelling	Frail rate =21.9%	Fried criteria	4)
	Delli Zotti (2022) (*21*)	Cross-sectional	*n* = 1,250 Median age (IQR) = 72 years (69-77 years) Inpatients	Frail rate =27.7%	FP	13); 15); 18)

SD, standard deviation; IQR, interquartile range; FP, Fried frailty phenotype; FI, frailty index; CHS, Cardiovascular Health Study; TFI, Tilburg frailty indicator. 1) age; 2) sex; 3) body mass index (BMI); 4) marital status; 5) nutritional status; 6) grip; 7) muscle strength; 8) living alone; 9) smoking status; 10) alcohol intake; 11) exercise status; 12) sleep status; 13) activities of daily living; 14) diet; 15) education level; 16) economic status; 17) social services; 18) depression; 19) cognitive function; 20) anxiety; 21) oral health; 22) dysphagia; 23) disability; 24) a history of falls; 25) comorbidities; 26) polypharmacy; 27) abnormal excretion status; 28) prealbumin; 29) cortisol level; 30) thyroid function; 31) blood galectin-3 (Gal-3) level; 32) C-reactive protein; 33) hemoglobin level; 34) ferritin.

Table 1. Frailty status and risk influencing factors in various countries (continued)

Country	Lead Author, (Year) (*Ref.*)	Type of study	Participants	Prevalence of physical frailty	Frailty Screening tools	Influencing Factors
	Damanti (2024) (*27*)	Cross-sectional, observational	n = 320 Median age (IQR) = 72 years (69-77 years) Community-dwelling	Frail rate =21%.	FI	3)
Romania	Maştaleru (2020) (*40*)	Retrospective	n = 411 Median age (SD) = 75.85 (6.35) years Inpatients	Frail rate =73.23%	FP	18)
Japan	Nishida (2021) (*34*)	Cross-sectional	n = 320 Median age (SD) = 77.3 (6.6) years Community-dwelling	Frail rate =14.1%	CHS	22)
China	Yang (2017) (*16*)	Cross-sectional	n = 1,494 Median age (SD) = 75.52 (9.28) years Inpatients	Frail rate =18%	FP	1); 3); 16); 18); 19); 23); 24); 26)
	Wei (2018) (*24*)	Cross-sectional	n = 587 Median age (SD) = 79.8 (9.34) years Inpatients	Frail rate =33.3%	Fried questionnaire	1); 7); 27); 28)
	Wang (2021) (*46*)	Cross-sectional	n = 780 Median age (SD) = 68.85 (2.64) years Community-dwelling	Frail rate =3.85%	FP	14)
	Lv (2022) (*23*)	Prospective	n = 3,836 Median age (SD) = 73.78 (6.451) years Inpatients	Frail rate =27.2%	FRAIL Scale	1); 3); 11); 15); 25); 26)
	Guan (2022) (*37*)	Cross-sectional	n = 487 Median age (SD)= 86 (2.9) years Community-dwelling	Frail rate =22.5%	FRAIL Scale	30)
	Fang (2022) (*41*)	Cross-sectional	n = 543 Median age (SD)= 70.99 (8.26) years Community-dwelling	Frail rate =24.9%	FRAIL Scale	17)

SD, standard deviation; IQR, interquartile range; FP, Fried frailty phenotype; FI, frailty index; CHS, Cardiovascular Health Study; TFI, Tilburg frailty indicator. 1) age; 2) sex; 3) body mass index (BMI); 4) marital status; 5) nutritional status; 6) grip; 7) muscle strength; 8) living alone; 9) smoking status; 10) alcohol intake; 11) exercise status; 12) sleep status; 13) activities of daily living; 14) diet; 15) education level; 16) economic status; 17) social services; 18) depression; 19) cognitive function; 20) anxiety; 21) oral health; 22) dysphagia; 23) disability; 24) a history of falls; 25) comorbidities; 26) polypharmacy; 27) abnormal excretion status; 28) prealbumin; 29) cortisol level; 30) thyroid function; 31) blood galectin-3 (Gal-3) level; 32) C-reactive protein; 33) hemoglobin level; 34) ferritin.

Table 1. Frailty status and risk influencing factors in various countries (continued)

Country	Lead Author, (Year) (*Ref.*)	Type of study	Participants	Prevalence of physical frailty	Frailty Screening tools	Influencing Factors
	Li (2023) (*44*)	Cross-sectional	n = 3,758 Median age (SD)= 68.81 (6.26) years Community-dwelling	Frail rate =2.37%.	FRAIL Scale	5); 9); 12)
	Ji (2023) (*38*)	Cross-sectional	n = 149 Median age (SD) = 72.04 (7.05) years Community-dwelling	Frail rate =21.48%	FP	31)
	Ma (2024) (*26*)	Cross-sectional	n = 110 Median age (SD) = 72.46 (10.43) years Community-dwelling	Frail rate =48.1%	FP	1); 2); 34)
	Guo (2024) (*20*)	Cross-sectional	n = 195 Median age (SD) = 71.52 (7.59) years Community-dwelling	Frail rate =85.13%	TFI	1); 2); 4); 11); 20); 25)
	Wei (2021) (*29*)	Cross-sectional	n = 391 Median age (IQR) = 73.3 years (65-91) Inpatients	Frail rate =28.4%	FRAIL Scale	1); 4); 11); 13); 16); 18); 25)
South Korea	Kim (2022) (*22*)	Prospective	n = 1,374 Median age (SD) = 75.9 (3.85) years Community-dwelling	Frail rate =10.9%	FRAIL Scale	1); 2); 18); 19); 26)
	Han (2022) (*43*)	Cross-sectional	n = 10,041 Median age (SD) = 66.91 (5.59) years Community-dwelling	Frail rate =6.0%	FRAIL Scale	8)
Malaysia	Norazman (2020) (*35*)	Cross-sectional	n = 301 Median age (SD) = 66.91 (5.59) years Community-dwelling	Frail rate =14.6%	FP	4); 7); 25)
	Norazman (2020) (*19*)	Cross-sectional	n = 301 Median age (SD) = 67.08 (5.536) years Community-dwelling	Frail rate =15.9%	FP	1); 2); 5); 7); 16); 32)

SD, standard deviation; IQR, interquartile range; FP, Fried frailty phenotype; FI, frailty index; CHS, Cardiovascular Health Study; TFI, Tilburg frailty indicator. 1) age; 2) sex; 3) body mass index (BMI); 4) marital status; 5) nutritional status; 6) grip; 7) muscle strength; 8) living alone; 9) smoking status; 10) alcohol intake; 11) exercise status; 12) sleep status; 13) activities of daily living; 14) diet; 15) education level; 16) economic status; 17) social services; 18) depression; 19) cognitive function; 20) anxiety; 21) oral health; 22) dysphagia; 23) disability; 24) a history of falls; 25) comorbidities; 26) polypharmacy; 27) abnormal excretion status; 28) prealbumin; 29) cortisol level; 30) thyroid function; 31) blood galectin-3 (Gal-3) level; 32) C-reactive protein; 33) hemoglobin level; 34) ferritin.

Table 1. Frailty status and risk influencing factors in various countries (continued)

Country	Lead Author, (Year) (*Ref.*)	Type of study	Participants	Prevalence of physical frailty	Frailty Screening tools	Influencing Factors
Turkey	Kocyigit (2024) (*25*)	Cross-sectional	*n* = 992 Median age (SD) = 73.2 ± 7.4 Outpatients	Frail rate =13.4%	FP	1); 5); 25)
Spain	Marcos-Pérez (2019) (*36*)	Cross-sectional	*n* = 252 Median age (SD) = 79.3 ± 8.8 Community-dwelling	Frail rate =34.9%	FP	29)
Brazil	Viana (2013) (*32*)	Cross-sectional	*n* = 53 Median age (SD) = 76.72 ± 5.89 Community-dwelling	Frail rate =15.1%	FP	7)

SD, standard deviation; IQR, interquartile range; FP, Fried frailty phenotype; FI, frailty index; CHS, Cardiovascular Health Study; TFI, Tilburg frailty indicator. 1) age; 2) sex; 3) body mass index (BMI); 4) marital status; 5) nutritional status; 6) grip; 7) muscle strength; 8) living alone; 9) smoking status; 10) alcohol intake; 11) exercise status; 12) sleep status; 13) activities of daily living; 14) diet; 15) education level; 16) economic status; 17) social services; 18) depression; 19) cognitive function; 20) anxiety; 21) oral health; 22) dysphagia; 23) disability; 24) a history of falls; 25) comorbidities; 26) polypharmacy; 27) abnormal excretion status; 28) prealbumin; 29) cortisol level; 30) thyroid function; 31) blood galectin-3 (Gal-3) level; 32) C-reactive protein; 33) hemoglobin level; 34) ferritin.

point worth noting is that studies (*19,22*) have found that the frailty rate among women is 2 to 3 times higher than that among men.

In addition, comorbidities are another factor related to frailty (*25,29,35*). A number of comorbidities can lead to frailty. A descriptive analysis by Wei *et al.* (*29*) indicated differences in the number and pattern of comorbid conditions between the frail group and the robust/prefrail group. The frail group had an average of 4.4 comorbidities, with the three most frequently reported comorbid conditions being hypertension, diabetes, and arthritis. In contrast, the robust/pre-frail groups had a mean of 3.3 comorbidities, and the most frequent were hypertension, hyperlipidemia, and arthritis. These findings indicate that proper prevention or management of comorbid conditions may delay the progression to frailty in this population.

3.3.2. Psychological factors

Depression and anxiety were factors influencing frailty (*20,40*). Both anxiety and depression share an overlapping symptomology, like functional impairment and sleep disturbance, leading to an increased risk of disability (*47*), and this may also be a consequence of increasing frailty. A previous study has indicated a clear bidirectional relationship between frailty and depression in older adults (*48*), but the association with anxiety is much less frequently explored. Anxiety was the only common factor influencing physical frailty, psychological frailty, and social frailty (*20*).

In the future, we should not only focus on the physical health of older adults but also pay greater attention to their mental well-being. Whether conducted in hospitals or communities, research has demonstrated an association between cognitive function and frailty (*16,22*). Yang *et al.* (*16*) and Sánchez-García *et al.* (*17*) further found that cognitive impairment is a risk factor for frailty. The correlation between influencing factors may even lead to depression. A review found that those with coexistent frailty and cognitive impairment had higher levels of depressive symptoms than peers (*49*). Further research is needed to explore potentially modifiable psychological factors, and this could lead to the development of supportive interventions.

3.3.3. Socioeconomic factors

Some studies found a risk effect of a low level of education on the rate of frailty (*17,23*), perhaps because people with a higher level of education usually have better living conditions, are more aware of their own healthcare, and pay more attention to disease prevention.

Similarly, economic status was found to affect frailty, the studies we included focused on aspects of employment and household income. Sánchez-García *et al.* (*17*) found that not having paid work is a protective

Table 2. Frailty as importance factor of various diseases

Various diseases	Authors, (Year) (*Ref.*)	Type of study	Participants and source of research subjects	Prevalence of physical frailty	Frailty Screening tools	Main findings
Colorectal Cancer (CRC)	Nina Ommundsen *et al.* (2014) (*52*)	Prospectively	*n* = 178 Median age (IQR) = 80 years (70-94 years) Hospital (In Norway)	Frail rate = 43%	GA	Frailty Is an Independent Predictor of Survival in Older Patients With Colorectal Cancer.
The liver transplant	Sinclair M *et al.* (2017) (*63*)	Prospectively	*n* = 587 Median age (IQR) = 60 years (53-64 years) Hospital (In USA)	Frail rate = 31.6%	FI	Physical frailty is a significant predictor of hospitalisation and total hospitalised days per year.
Myocardial infarction	Alonso Salinas GL *et al.* (2017) (*55*)	Prospectively	*n* = 234 Median age (SD) = 84.4 (5.8) years (frailty) Hospital (In Spain)	Frail rate = 40.2%	FI	Frailty was an independent predictor of the combination of death or nonfatal myocardial reinfarction, or major bleeding, and an independent predictor of readmission.
Kidney transplantation	Schopmeyer L *et al.* (2018) (*58*)	Prospectively	*n* = 139 Median age (SD) = 51.8 (14.5) years Hospital (In Netherlands)	Frail rate = 16.5%	GFI	Frailty and type of transplantation are independent factors associated with an increased risk of postoperative complications.
Chronic subdural hematoma	Shimizu K *et al.* (2018) (*62*)	Retrospective	*n* = 211 Median age (SD) = 83.5 (7.1) years Hospital (In Japan)	Frail rate = 50.2%	CFS	The evaluation of the presence of frailty on admission can be an important factor in the prediction of the prognosis of chronic subdural hematoma patients.
Elective laparoscopic cholecystectomy	Mastalerz K *et al.* (2018) (*69*)	Prospectively	*n* = 144 Median age (IQR) = 76 years (70-91 years) Hospital (In Poland)	Frail rate = 44.4%	CGA	Frailty was predictors of 1-year mortality.
Abdominal aortic aneurysm (AAA)	Morisaki K *et al.* (2019) (*59*)	Retrospective	*n* = 349 Median age (SD) = 79.1 (8.7) years (frailty) Hospital (In Japan)	Frail rate = 43.1%	FI	Assessing frailty in patients with AAA is useful for determining risk factors for 5-year overall survival and postoperative complications.
Glioblastoma in geriatric	Schneider M *et al.* (2020) (*70*)	Retrospective	*n* = 110 Median age (IQR) = 72 years (65-86 years) Hospital (In Germany)	Frail score = 0.18	FI	Frail patient as significant and independent predictors of 1-year mortality in geriatric patients with surgical treatment of glioblastoma.
Coronary artery bypass grafting	Kluszczyńska M *et al.* (2021) (*56*)	A cross-sectional	*n* = 180 Age (SD) = 69.3 (6.1) years Clinic (In Poland)	Frail rate = 28.6%	TFI	Frailty syndrome was a poor predictor of rehospitalization.

SD, standard deviation; IQR, interquartile range; FP, fried frailty phenotype; FI, frailty index; CHS, cardiovascular health study; TFI, tilburg frailty indicator; CFS, Clinical Frailty Scale; GA, geriatric assessment; GFI, Groningen Frailty Indicator; CGA, Comprehensive Geriatric Assessment; FSS, Frailty Scoring System; HFRS, Hospital Frailty Risk Score; G8, The G8 geriatric screening tool.

Table 2. Frailty as importance factor of various diseases (continued)

Various diseases	Authors, (Year) (*Ref.*)	Type of study	Participants and source of research subjects	Prevalence of physical frailty	Frailty Screening tools	Main findings
Asymptomatic aortic stenosis	Ramos M *et al*. (2021) (*71*)	Observational	*n* = 104 Age (SD) = 83.3 (8.8) years Clinic (In Spain)	Frail rate = 59.6%	FP	Frailty was independent factors for mortality, conferring an unfavorable short-term prognosis.
Hemodialysis (HD)	Li Y *et al*. (2021) (*67*)	Observational; prospectively	*n* = 150 Median age (IQR) = 69 years (64-75 years) Hospital (In China)	Frail rate = 34.7%	FP	Frailty was an independent indicator of all-cause mortality and emergency visits in elderly patients with HD.
Major hepatectomy forperihilar cholangiocarcinoma (PHCC)	Hosoda K *et al*. (2022) (*62*)	Prospectively	*n* = 87 Median age (IQR) = 72 years (59-88 years) (CFS score 3-9) Hospital (In Japan)	Frail rate = 50.6%	CFS	Frailty is a predictive factor for short- and long-term outcomes in patients who have undergone major hepatectomy for PHCC.
Surgery for Metastatic Spinal Column Tumors	Elsamadicy AA *et al*. (2022) (*64*)	Retrospective	*n* = 4,346 Median age (SD) = 66.8 (9.0) years Hospital (In USA)	Frail rate = 39.2%	HFRS	Intermediate frailty was found to be an independent predictor of unplanned 30-day readmission.
Advanced Non-Small Cell Lung Cancer	Jiménez Galán R *et al*. (2023) (*53*)	Retrospective	*n* = 101 Median age = 67 years Clinic (In Spain)	Frail rate = 31.7%	FSS	Frailty as an independent predictor of over all (OS) and progression-free survival (PFS).
Ovarian cancer (OC)	Anic K *et al*. (2023) (*65*)	Retrospective; Observational	*n* = 116 Median age (SD) = 70.9 (5.9) years Hospital (In USA)	Frail rate = 50.9%	G8	Preoperative frailty assessment with the G8 Score identified elderly women with OC recording a significantly higher rate of postoperative in-hospital complications.
Small Bowel Obstruction (SBO)	Laterza V *et al*. (2023) (*68*)	Prospectively	*n* = 424 Median age (IQR) = 85 years (82-89 years) Hospital (In Italy)	Frail rate = 33.9%	CFS	The presence of severe frailty could effectively predict an increased risk of in-hospital death.
Vascular cognitive impairment (VCI)	Zheng R *et al*. (2024) (*66*)	Retrospective	*n* = 431 Median age (SD) = 71.73 (6.41) years Hospital (In China)	Frail rate = 38.5%	FI	Frailty defined by the FI was effective for predicting the risk of mortality.
Hip fracture	Wang LX *et al*. (2024) (*57*)	Observational	*n* = 427 Median age (SD) = 80.28 (8.13) years Hospital (In China)	Frail rate = 30%	FI	Frailty serves as a reliable predictor of the probability of encountering severe adverse events while hospitalized for elderly individuals with hip fractures.

SD, standard deviation; IQR, interquartile range; FP, fried frailty phenotype; FI, frailty index; CHS, cardiovascular health study; TFI, tilburg frailty indicator; CFS, Clinical Frailty Scale; GA, geriatric assessment; GFI, Groningen Frailty Indicator; CGA, Comprehensive Geriatric Assessment; FSS, Frailty Scoring System; HFRS, Hospital Frailty Risk Score; G8, The G8 geriatric screening tool.

Table 2. Frailty as importance factor of various diseases (continued)

Various diseases	Authors, (Year) (*Ref.*)	Type of study	Participants and source of research subjects	Prevalence of physical frailty	Frailty Screening tools	Main findings
Emergency laparotomy (EL)	Goh SSN *et al.* (2024) (*54*)	Retrospective	*n* = 233 Median age (SD) = 79 (7) years Hospital (In Singapore)	Frail rate = 26%	CFS	Frailty emerged as a pivotal factor influencing the postoperative trajectory of older adults undergoing EL in Singapore.
Gastric cancer	Miao X *et al.* (2024) (*61*)	A cross-sectional	*n* = 381 Median age (SD) = 69 (8.0) years Hospital (In China)	Frail rate = 70.3%	TFI	Early assessment to predict the occurrence of heterogeneous frailty trajectories is essential to improve the outcomes of elderly gastric cancer patients.

SD, standard deviation; IQR, interquartile range; FP, fried frailty phenotype; FI, frailty index; CHS, cardiovascular health study; TFI, tilburg frailty indicator; CFS, Clinical Frailty Scale; GA, geriatric assessment; GFI, Groningen Frailty Indicator; CGA, Comprehensive Geriatric Assessment; FSS, Frailty Scoring System; HFRS, Hospital Frailty Risk Score; G8, The G8 geriatric screening tool.

factor for pre-frailty but increases the likelihood of frailty. Work status is usually related to education level, and especially in advanced age. Studies by researchers such as Yang *et al.* (*16*), Wei *et al.* (*24*), and Norazman *et al*. (*19*) have demonstrated that low income is a risk factor for vulnerability.

In addition, social services were suggested to affect changes in frailty. Findings from Fang *et al.* (*41*) suggested that the older adults who were unmarried, divorced, or widowed might perceive less social support. Sánchez-García *et al.* (*17*), however, found that use of healthcare services influenced the progression of frailty. Therefore, specific types of social services should be emphasized rather than all social services.

3.3.4. Factors related to living conditions

As shown Figure 2, living alone, exercise status, and ADL were among the factors related to living conditions. An equal number of studies indicated that all three are significantly associated with frailty. In the study by Song *et al*. (*43*), objective social isolation was a factor associated with worsening of the stages of frailty. That said, frailty can also lead to social isolation (*50*). Frailty and social isolation are interrelated, forming a cause-and-effect relationship, and may even jointly influence other factors. A study found that physical frailty and social isolation were associated with falls in older adults (*51*).

A study carried out in a Mexican community (*17*) concluded that there was an association between frailty and limitations on ADL in the older adults who were part of the sample. Results of the studies included in the current review are consistent with such an association, as the association is stronger in frail people compared to pre-frail people. Limitations on ADL further impact exercise. Exercise, without a doubt, is one of the factors influencing frailty. Lack of exercise is a risk factor for frailty (*23*); therefore, regular exercise can effectively prevent its onset. The optimal timing and type of exercise are topics worth contemplating, along with whether such exercise is suitable for various groups of people.

3.4. Classify the factors influencing frailty by disease type

Frailty plays an important role in various diseases and is also an independent predictor, especially in terms of prognosis, hospitalization, postoperative complications, and mortality rates, as shown Table 2. In this review, a large number of evidence-based studies found that frailty could be a predictive factor for adverse outcomes, including prognosis (*52-54*), hospitalization or rehospitalization (*55-57*), postoperative complications (*58*), and mortality rates (*59*), which means that screening for frailty is very important in a clinical setting.

The evaluation of the presence of frailty upon admission can be an important factor in predicting the

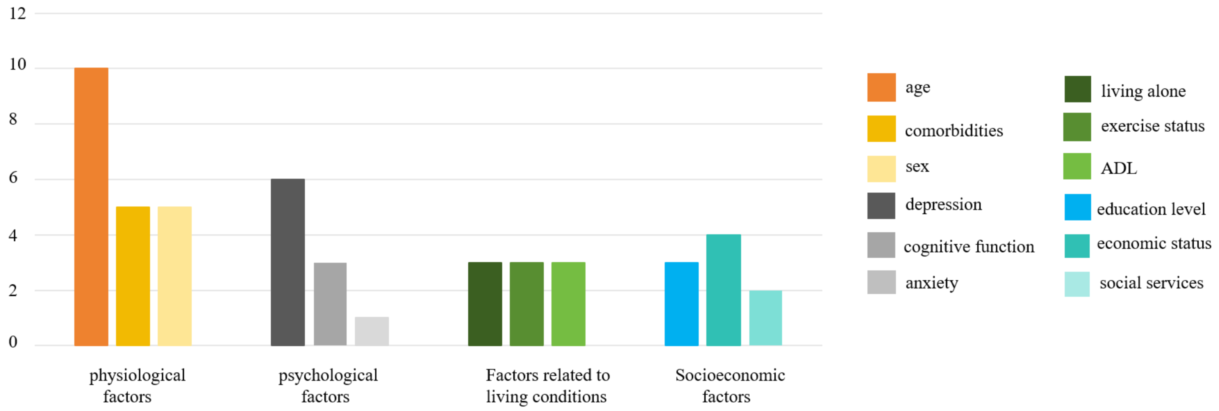

Figure 2. Top three frailty factors by category in included studies.

prognosis for patients with chronic subdural hematoma (*60*), gastric cancer (*61*), and those undergoing major hepatectomy for perihilar cholangiocarcinoma (PHCC) (*62*). Frailty was also an important predictor of hospitalization and readmissions for liver transplantation (*63*), after coronary artery bypass grafting (*56*), and metastatic surgery (*64*).

For postoperative patients, complications undoubtedly pose the greatest challenge. However, frailty is a risk factor that significantly increases the likelihood of postoperative complications, as demonstrated in studies by Schopmeyer *et al.* (*58*), Morisaki *et al.* (*59*), and Anic *et al.* (*65*). Therefore, screening for and intervening in cases of frailty in advance is essential, as this can help to further reduce the threat that postoperative complications pose to our lives.

Frailty as a predictor of mortality has widely been noted in different populations: patients with vascular cognitive impairment (*66*), patients on hemodialysis (*67*), patients with small bowel obstruction (*68*), patients undergoing elective laparoscopic cholecystectomy (*69*), geriatric patients with glioblastoma (*70*), and patients with asymptomatic aortic stenosis (*71*). Thus, independent of study design, country, and setting, frailty could be a prognostic factor for clinicians to predict mortality and frailty screening could help clinicians establish a comprehensive prognostic tool for predicting mortality in patients with various diseases and facilitate early intervention to alleviate frailty syndrome to reduce mortality rates.

Surprisingly, frailty is not only a predictor of adverse outcomes but also a significant factor in triggering cancer. Park *et al.* (*72*) established that an aged immune system promotes tumor growth, regardless of the age of the tumor or its surrounding stroma. Specifically, hematopoietic aging drives emergency myelopoiesis, and targeting IL-1R1 signaling during early tumor development to attenuate this process abrogates the protumorigenic effect of aging on tumor control. This shows that frailty can lead to changes in our bodies and even cause unforeseeable harm to our lives. This finding should prompt us to pay closer attention to the presence of frailty and encourage deeper reflection on its implications.

3.5. Multi-factor interaction and integration model

In recent years, research on frailty has shifted from examining isolated risk factors to investigating the complex interplay among multiple determinants. Increasingly, frailty is recognized not as the outcome of a single pathological process but as the dynamic result of interacting physiological, psychological, social, and lifestyle factors. Although traditional linear models are useful in identifying statistically significant predictors, they often fail to capture synergistic or antagonistic relationships between variables. To address this limitation, and as shown in Figure 2, we developed a model that better reflects the multifactorial and often non-linear nature of frailty.

As shown in Figure 4, by synthesizing findings from the literature and translating them into a practical tool for early detection and intervention, we offer a framework that enables healthcare providers and older adults to identify personalized pathways based on individual circumstances. Ultimately, these approaches may contribute to a more nuanced understanding of frailty and facilitate the development of personalized, multidisciplinary management strategies for older populations.

4. Discussion

4.1. Toward integrated models of frailty

An increasing body of evidence from studies conducted between 2001 and 2025 demonstrates a clear shift in frailty research from single-variable analyses to multifactorial and integrative modeling approaches. These models aim to capture the complex, non-linear, and often bidirectional relationships among determinants of frailty. As shown in Figure 2, frailty is

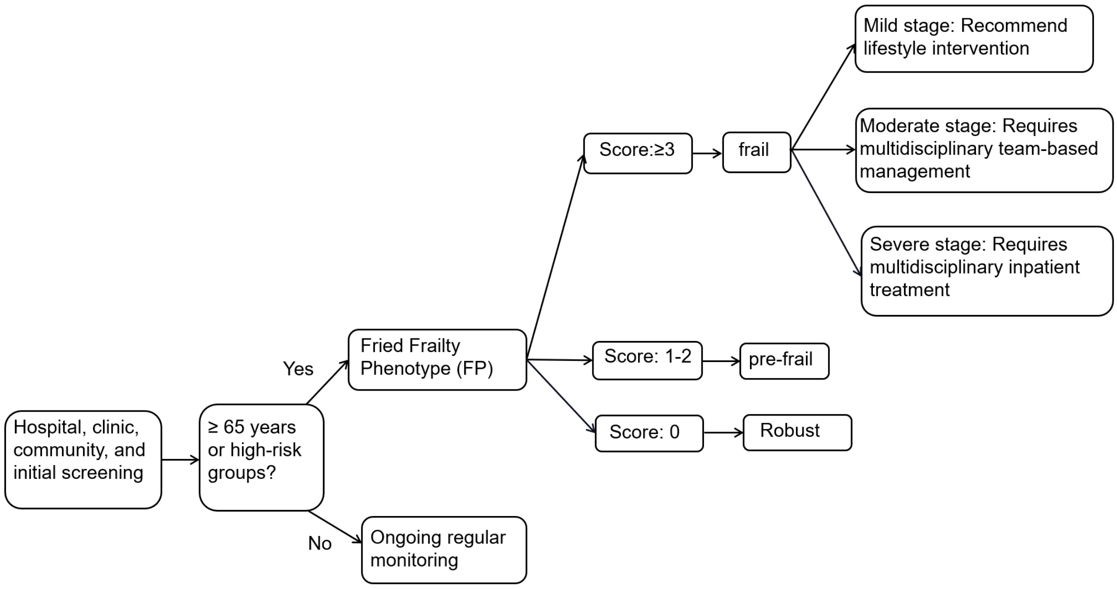

Figure 4. Model of early monitoring and intervention pathways for frailty.

a multifactorial condition influenced by physiological, psychological, behavioral, and social determinants. Notably, some studies have developed comprehensive models to elucidate how different domains interact to influence frailty progression and adverse outcomes. For example, the World Health Organization (WHO) recently published guidelines on the implementation of a new Integrated Care for Older People (ICOPE) framework, which emphasizes the integration of intrinsic capacity — including cognition, mobility, and sensory function — with environmental factors such as living conditions and access to care, forming a practical, person-centered conceptual structure (*73*). Machine learning (ML) has further enriched the understanding of frailty as a multifactorial construct. Studies using ML have proved useful in identifying individuals who became frail over time. One such study highlighted factors that may be useful in the early detection of frailty (*74*).

Importantly, there is a growing consensus on the utility of multidimensional, integrative models in both research and clinical settings. These models offer a more accurate and personalized understanding of frailty development and its implications for disease risk, care planning, and healthcare policy. Despite the promising insights yielded by interactive modeling, several challenges remain. Issues such as data heterogeneity, inconsistent variable definitions, and limited external validation hinder the generalizability of findings.

However, as shown in Figure 3, our model places greater emphasis on early screening using tools like the FP, which may be more feasible for implementation in primary care settings with limited resources. Our approach advocates for a tiered screening-to-intervention model that prioritizes early detection and scalable intervention — consistent with the emerging evidence supporting the reversibility of frailty in its initial stages. Future research should continue to integrate longitudinal datasets, real-time monitoring technologies, and advanced analytics to further refine these models.

Ultimately, such models will contribute to a more nuanced understanding of frailty and facilitate the development of personalized, multidimensional management strategies for older adults. Moreover, it can be more effectively translated into clinical and community-based screening and intervention strategies, facilitating earlier detection and management of frailty. This is particularly important given the current paucity of research in Asian populations. To address the global challenge posed by an aging population and the escalating burden of frailty on public healthcare systems, future studies should prioritize the development of a comprehensive, culturally adaptable, and globally applicable frailty model. Such a model would facilitate more equitable and effective healthcare responses across diverse regions.

4.2. The limitations of and gaps in the research

Only literature in English was included in this review, and there may be a language bias. Current studies have established a relatively consistent understanding of the determinants of frailty; however, the conclusions regarding its impact vary across different studies. Despite these mixed results, our overall findings help to elucidate the factors influencing frailty and highlight the disparity in how it affects separate groups of individuals in different ways.

In particular physiological factors seem to provide some insight into how an individual's frailty will progress over time, a finding which has important implications

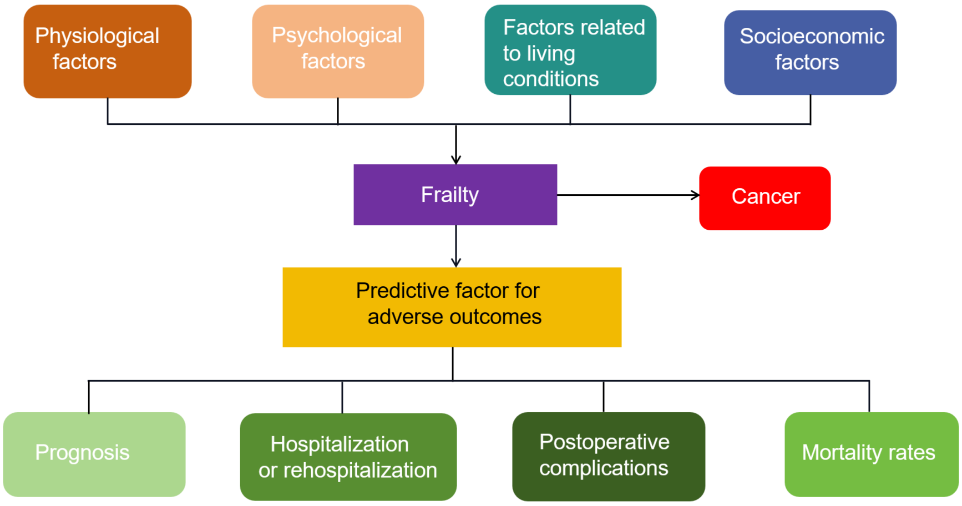

Figure 3. A multifactorial and non-linear model of frailty.

for public health policy as well as individuals and their caregivers. A major issue is the shift from viewing frailty as a static condition to understanding it as a dynamic and systemic process.

Future research should focus on developing a comprehensive yet easily interpretable frailty intervention model. A crucial first step toward achieving consistency may be the validation of a gold-standard frailty measurement tool, enabling more accurate and comparable research findings. Most studies are cross-sectional, hampering our ability to infer causal relationships. Researchers should also emphasize longitudinal studies to explore risk factors associated with frailty trajectories, as these insights may shape future strategies for frailty prevention and intervention.

4.3. Policy recommendations and future research directions

With the global acceleration of population aging, frailty — an integrated syndrome involving physiological, psychological, and social dimensions — has become a major public health issue affecting the quality of life and health outcomes of older adults. Current policies addressing frailty are mostly confined to the medical domain, lacking cross-sector collaboration and long-term integrated strategies. Based on a multilayered understanding of the factors influencing frailty, comprehensive health promotion policies should be devised. These should incorporate health management, chronic disease control, psychological support, nutritional interventions, and social participation to build an interdisciplinary and cross-sectoral frailty intervention system. Specifically, policies should promote the inclusion of frailty assessment and management in contracted primary care and encourage community healthcare centers to establish regular physical function screening, cognitive assessments, and mechanisms of monitoring nutritional status. At the same time, efforts should be made to enhance the tie between home-based and institutional care, to optimize the design of long-term care insurance systems, and to improve the quality of health management for patients with chronic conditions, and especially those with multimorbidity. In addition, social participation and promotion of mental health should be emphasized. Local governments and civil society organizations should be encouraged to enhance social connections among older adults through volunteer services, learning programs, and mutual support groups to reduce loneliness and depression. Moreover, the government should strengthen the digital infrastructure and promote the integration of frailty-related data on big data platforms to enable early detection and intervention. These measures could reduce the incidence of frailty, delay functional decline in older adults, and alleviate the socioeconomic burden.

Although existing studies have preliminarily identified several related factors — such as malnutrition, chronic inflammation, cognitive impairment, and insufficient physical activity — our understanding of the interrelationships, causal mechanisms, and dynamic progression of these factors remains limited. Future research should focus on the following areas: First, enhancing longitudinal cohort studies to explore the key pathways in the onset and progression of frailty using long-term follow-up data, and to identify reversible or modifiable nodes for intervention. Second, ML, multi-omics analysis, and systems modeling should be used to construct multifactorial models to predict frailty, enabling risk stratification and individualized assessment. Third, greater attention should be paid to specific populations, such as the very old, those living alone, and older adults in rural or ethnic minority areas, to uncover the unique risks and protective factors related to frailty. Fourth, interventional studies should promote a shift from single-dimension approaches to integrated, multidimensional interventions, investigating the synergistic effects of diet, exercise, pharmacological strategies, and psychological strategies, and their scalability and cost-effectiveness should be validated through real-world research. Fifth, interdisciplinary collaboration should be encouraged by integrating perspectives from biomedicine, behavioral science, sociology, and healthcare economics to advance the concept of "precision frailty management." Such research will provide a scientific foundation for the early identification of and precise intervention in frailty, contributing to the development of a prevention-oriented active aging strategy.

5. Conclusion

This review has found that there are many factors affecting frailty among the elderly worldwide, the most notable of which are physiological factors. When dealing with the elderly in hospitals, clinics, and communities, healthcare professionals should enhance the monitoring of physical, psychological, and social factors and implement effective interventions to reduce the incidence of frailty to some extent. Currently, research on frailty in the elderly mainly focuses on investigation of current conditions. The hope is that future studies will conduct quality research to verify methods that can better reduce frailty. Future research should also pay attention to the potential reversibility of frailty in its early stages, and healthcare policies should encourage the routine use of validated screening tools, such as the FP, in primary care and community health settings. Early identification enables timely, targeted interventions that may slow or even reverse the progression of frailty, thereby reducing long-term healthcare burdens.

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