Postprint of a Meta-Analysis on Frailty Prevalence in Older Adults with Multimorbidity

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Abstract

【摘要】**Background** As the aging problem becomes increasingly severe, the prevalence of multimorbidity in the elderly is showing a year-by-year upward trend. Multimorbidity in the elderly is a key risk factor for frailty. The occurrence of frailty increases the risk of a series of adverse health outcomes in patients with multimorbidity, while also increasing medical expenses for patients' families. Early identification of frailty prevalence in elderly patients with multimorbidity has certain guiding value for the management of chronic disease multimorbidity. **Objective** To systematically evaluate the prevalence of frailty in elderly patients with multimorbidity. **Methods** Computer searches were conducted in CNKI, VIP, CBM, Wanfang Data, PubMed, Embase, Web of Science, and The Cochrane Library for studies investigating the status of frailty in elderly patients with multimorbidity. The search period was from database inception to December 4, 2021. Data were extracted and the quality of included studies was evaluated. Meta-analysis was performed using Stata 14.0 software. **Results** A total of 25 studies were included, comprising 16,062 elderly patients with multimorbidity. Meta-analysis results showed that the prevalence of frailty and pre-frailty in elderly patients with multimorbidity was 27% [95%CI (22%, 32%)] and 48% [95%CI (44%, 51%)], respectively. Subgroup analysis results showed that the prevalence of frailty in elderly individuals with 2 or more coexisting chronic diseases was 25% [95%CI (19%, 31%)], with 3 or more was 27% [95%CI (14%, 41%)], and with 4 or more was 42% [95%CI (-2%, 87%)]; the prevalence of frailty in Oceania (52%) and Asia (31%) was higher than in Europe (17%) and South America (13%); the prevalence of frailty in elderly multimorbid patients in hospitals (26%) was higher than in community settings (23%); the prevalence of frailty screened by the Clinical Frailty Scale (CFS) in elderly multimorbid patients was 43% [95%CI (38%, 47%)], by the Fried Frailty Phenotype was 22% [95%CI (18%, 27%)], and by the FRAIL scale was 8% [95%CI (6%, 11%)]; the prevalence of frailty in survey periods 2001-2010, 2011-2015, and

2016-2020 was 21% [95%CI (13%, 29%)], 19% [95%CI (13%, 25%)], and 38% [95%CI (23%, 53%)], respectively. **Conclusion** The prevalence of frailty in elderly patients with multimorbidity is gradually increasing, with differences across varying numbers of chronic diseases, continents, assessment tools, and study settings. Therefore, relevant personnel should attach importance to early screening for frailty in patients with multimorbidity, and timely preventive measures should be taken.

Full Text

Preamble

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Abstract

Background: With population aging accelerating, the prevalence of comorbidity among older adults is rising steadily. Comorbidity represents a key risk factor for frailty, which in turn increases the risk of adverse health outcomes and imposes substantial economic burdens on patients' families. Early identification of frailty in elderly patients with comorbidity holds significant value for guiding chronic disease management.

Objective: To systematically evaluate the prevalence of frailty among elderly patients with comorbidity.

Methods: We searched databases including CNKI, VIP, CBM, WanFang, PubMed, Embase, Web of Science, and The Cochrane Library for studies investigating frailty status in elderly patients with comorbidity, from inception to December 4, 2021. Data extraction and quality assessment were performed independently by two reviewers. Meta-analysis was conducted using Stata 14.0 software.

Results: Twenty-five studies involving 16,062 elderly patients with comorbidity were included. The pooled prevalence of frailty and pre-frailty was 27% [95%CI

(22%, 32%)] and 48% [95%CI (44%, 51%)], respectively. Subgroup analyses revealed: frailty prevalence was 25% [95%CI (19%, 31%)] for those with $ $2 chronic diseases, 27% [95%CI (14%, 41%)] for $ $3 diseases, and 42% [95%CI (-2%, 87%)] for $ $4 diseases. Prevalence was higher in Oceania (52%) and Asia (31%) than in Europe (17%) and South America (13%). Hospital-based studies showed higher frailty prevalence (26%) than community-based studies (23%). Using the Clinical Frailty Scale (CFS), Fried Frailty Phenotype, and FRAIL scale, frailty prevalence was 43% [95%CI (38%, 47%)], 22% [95%CI (18%, 27%)], and 8% [95%CI (6%, 11%)], respectively. By survey period, frailty prevalence was 21% [95%CI (13%, 29%)] for 2001-2010, 19% [95%CI (13%, 25%)] for 2011-2015, and 38% [95%CI (23%, 53%)] for 2016-2020.

Conclusion: The prevalence of frailty in elderly patients with comorbidity is increasing, with substantial variation across different numbers of chronic diseases, geographic regions, assessment tools, and study settings. Healthcare professionals should prioritize early screening and preventive interventions for frailty in this population.

Keywords: frailty; elderly; comorbidity; Meta-analysis

Introduction

The global population aged 65 years and older is projected to exceed 1.5 billion by 2050 [**?**]. As life expectancy increases, the burden of chronic diseases among middle-aged and older adults accelerates. Geriatric comorbidity—defined as the coexistence of two or more chronic conditions in an older individual—has shown a gradual upward trend in recent years [**?**, **?**]. Against the backdrop of healthy aging, frailty has emerged as a focal point in geriatric research internationally. Frailty is characterized as a multisystem age-related syndrome marked by increased vulnerability to adverse health outcomes due to cumulative declines in physiological and psychological reserves [**?**]. With advancing age, comorbidity amplifies physical vulnerability, creating greater opportunities for progression from robust health to frailty [**?**]. Frailty in older adults with chronic diseases elevates the risk of multiple adverse health outcomes and serves as an independent determinant of increased healthcare expenditures [**?**, **?**]. Scholars worldwide advocate linking frailty with multimorbidity, noting that elderly patients with both conditions frequently experience cognitive impairment and psychological issues, significantly raising the probability of falls, disability, and mortality [**?**, **?**].

A previous meta-analysis reported a frailty prevalence of 16% among adults with multimorbidity, but this study encompassed a broad age range [**?**]. With population aging intensifying, elderly patients with comorbidity likely exhibit higher frailty prevalence, which varies substantially across studies ranging from 5% to 72%. Therefore, this meta-analysis synthesizes existing evidence on frailty prevalence specifically among elderly patients with comorbidity, aiming to provide a scientific basis for clinical management, prevention strategies, and health

policy development.

Methods

1.1 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Cross-sectional or cohort studies; (2) Study population aged $ $60 years with comorbidity; (3) Primary outcome: frailty prevalence in patients with comorbidity; Secondary outcomes: pre-frailty prevalence and comorbidity prevalence among frail patients.

Exclusion criteria: (1) Studies focusing on specific disease populations; (2) Studies with erroneous or non-extractable data; (3) Unavailable full texts or duplicate publications; (4) Non-Chinese or non-English publications.

1.2 Search Strategy

We systematically searched CNKI, VIP, CBM, WanFang, PubMed, Embase, Web of Science, and The Cochrane Library for studies investigating frailty status in elderly patients with comorbidity. The search combined subject headings and free-text terms. Chinese search terms included: comorbidity, coexisting diseases, frailty, frailty syndrome, weakness. English search terms included: frail*, frailty, frailty syndrome, weakness, multimorbidity, comorbidity, multiple chronic conditions, aged, old*, elder*, prevalence rate, incidence, epidemiologie. The search timeframe spanned from database inception to December 4, 2021.

1.3 Literature Screening and Data Extraction

Literature management was conducted using NoteExpress software. After deduplication, two independent reviewers screened titles, abstracts, and full texts against inclusion criteria. Data extraction was performed using Excel, capturing: first author, publication year, survey year, study type, region, age, setting, sample size, frailty assessment tool, and primary/secondary outcomes (baseline cross-sectional data for cohort studies). Discrepancies were resolved through discussion or by a third reviewer when necessary.

1.4 Quality Assessment

Quality evaluation was performed using appropriate tools for observational studies [**?**]. For cross-sectional studies, we employed the AHRQ-recommended checklist comprising 11 items scored as "yes," "no," or "unclear." Total scores of 8-11 indicated high quality, 4-7 moderate quality, and 0-3 low quality [**?**]. For cohort studies, we used the AHRQ-recommended NOS scale, which includes 3 dimensions with 8 items (total score 9), where higher scores indicate better quality. All assessments were conducted independently by two reviewers.

1.5 Statistical Analysis

Meta-analysis of single rates was performed using Stata 14.0 software, with prevalence and 95% confidence intervals (CI) as effect measures. Heterogeneity was assessed using ^{2} tests and quantified with I^2 statistics (α=0.1). When heterogeneity was absent or minimal (P$ 0.1, $I\hat{}\{2\}$$ $50%), indicating good homogeneity, a fixed-effects model was applied; otherwise, a random-effects model was used. For substantial heterogeneity, subgroup analysis was conducted to explore potential sources. Sensitivity analysis was performed to evaluate result stability, and publication bias was examined using Begg' s and Egger' s tests.

Results

2.1 Literature Screening Process

The initial search yielded 4,700 records. After deduplication and independent screening by two reviewers, 25 studies were ultimately included: 3 cohort studies [**?**, **?**, **?**] and 22 cross-sectional studies [**?**, **?**, **?**]. The screening flowchart is presented in [Figure 1: see original paper].

2.2 Characteristics of Included Studies

The 25 included studies comprised 16,062 elderly patients with comorbidity. Basic characteristics are summarized in .

2.3 Quality Assessment Results

Quality assessment was conducted separately for cross-sectional and cohort studies. Among the 22 cross-sectional studies evaluated using the AHRQ checklist, 14 were rated as high quality and 8 as moderate quality (). The 3 cohort studies assessed with the NOS scale all scored $ $7 points, indicating acceptable quality ().

2.4 Meta-Analysis Results

2.4.1 Overall Prevalence of Frailty in Comorbid Patients Random-effects meta-analysis revealed an overall frailty prevalence of 27% (see [Figure 2: see original paper]) and pre-frailty prevalence of 48% among elderly patients with comorbidity. Additionally, analyzing comorbidity prevalence among frail elderly patients across 23 studies [**?**, **?**, **?**] showed a pooled chronic comorbidity prevalence of 53%.

2.4.2 Subgroup Analysis of Frailty Prevalence Subgroup analyses were performed based on number of chronic diseases, geographic region, study setting, frailty assessment tool, and survey year. High heterogeneity across subgroups necessitated use of random-effects models ().

Number of chronic diseases: Prevalence of frailty and pre-frailty was 25% and 46% for $ $2 diseases, 27% and 45% for $ $3 diseases, and 24% and 56% for $ $5 diseases.

Geographic region: In Asia, frailty and pre-frailty prevalence was 31% and 46%; in Europe, 17% and 45%; in South America, 13% and 57%; and in Oceania, frailty prevalence was 52%.

Study setting: Community-based studies showed frailty and pre-frailty prevalence of 23% and 48%, compared to 26% and 45% in hospital-based studies.

Assessment tools: Using the Fried Frailty Phenotype, CFS, and FRAIL scale, frailty prevalence was 22%, 43%, and 8%, respectively, with corresponding pre-frailty rates of 48%, not reported, and not reported.

Survey period: Frailty prevalence was 21% for 2001-2010, 19% for 2011-2015, and 38% for 2016-2020, with pre-frailty rates of 49%, 47%, and 46%, respectively.

2.5 Publication Bias Assessment

Begg' s test (Z=0.26, P=0.797) and Egger' s test (P=0.329) indicated no significant publication bias.

2.6 Sensitivity Analysis

Simple analyses excluding either the largest [**?**] or smallest [**?**] sample yielded frailty prevalence of 28% and 26%, respectively. Leave-one-out sensitivity analysis showed prevalence ranging from 22% to 32% ([Figure 3: see original paper]). Notably, the study by Thompson et al. (2018) [**?**] using the Frailty Index (FI) demonstrated high sensitivity; its removal yielded a pooled prevalence of 24%. Overall, effect estimates remained stable, suggesting robust results.

Discussion

Frailty is an age-related clinical syndrome characterized by increased vulnerability to stressors due to loss of reserves and homeostatic dysregulation [**?**]. Research indicates that frailty is closely associated with degenerative changes across multiple physiological systems triggered by age and nutritional factors, representing a cumulative deficit effect [**?**]. Studies have linked frailty to biomarkers including interleukin-6, albumin, alanine aminotransferase (ALT), monocyte chemoattractant protein-1 (MCP-1), and macrophage inflammatory protein-1β (MIP-1β), though the precise pathogenic mechanisms remain unclear [**?**, **?**]. Clinically, frailty and geriatric comorbidity exist on a continuum, with older adults transitioning from chronic disease to multimorbidity and ultimately to frailty as part of the aging process [**?**]. Both domestic and international research confirms that poor health status increases frailty risk,

while comorbidity exacerbates exercise intolerance, medication dependency, and slowed gait, thereby precipitating frailty. Frailty and comorbidity share common features as cumulative deficit states that increase susceptibility to clinical uncertainty across four trajectories: complexity, unpredictability, ambiguity, and information scarcity. Both are associated with increased hospitalization, disability, and mortality, making management of multimorbid frail older adults particularly costly [**?**].

This meta-analysis included 25 studies of cross-sectional and cohort designs. Given their different natures, we applied appropriate quality assessment tools, yielding acceptable results. Prevalence data extracted from cohort studies used baseline cross-sectional data, permitting pooled analysis. The results demonstrated a frailty prevalence of 27% and pre-frailty prevalence of 48% among elderly patients with comorbidity, with 53% of frail elderly patients having chronic comorbidities. These findings confirm that geriatric comorbidity is a critical risk factor for frailty. Previous research indicates that comorbidity emerges during middle age and increases with age, while frailty becomes more pronounced in later life, making most frail older adults also multimorbid [**?**]. Our finding of higher comorbidity prevalence among frail elderly patients aligns with this observation. Since comorbidity is more clearly diagnosed and often precedes frailty, which is frequently overlooked, this analysis focused on frailty and pre-frailty prevalence in elderly patients with comorbidity to enhance awareness and inform management strategies.

3.1 Subgroup Analysis by Number of Chronic Diseases

Frailty and pre-frailty prevalence vary by disease count. Hanlon et al. [**?**] demonstrated that frailty prevalence generally increases with the number of chronic conditions. While our disease-count subgroups, based on varying comorbidity definitions, did not fully confirm this trend, it remains evident that more chronic diseases reduce resistance to insults, increase disease burden, and worsen physical condition, thereby accelerating frailty development. Healthcare providers should pay particular attention to older adults with numerous chronic conditions to prevent deterioration into frailty.

3.2 Subgroup Analysis by Geographic Region

Substantial regional variation exists in frailty prevalence among elderly patients with comorbidity, with Oceania (52%) and Asia (31%) showing higher rates than Europe (17%) and South America (13%). The Oceania estimate derived from a single Australian study limits comparability. Lower European and South American prevalence may reflect earlier frailty research initiation, greater public awareness, and proactive preventive interventions. Additionally, economically developed European countries like Italy and Norway offer superior healthcare that may delay frailty progression. The higher Asian prevalence, largely driven by Chinese studies, signals a concerning situation in China that warrants urgent attention to frailty screening and prevention.

3.3 Subgroup Analysis by Study Setting

Frailty prevalence differed between community (23%) and hospital (26%) settings, with hospitals showing slightly higher detection rates, likely because hospitalized patients with comorbidity have poorer health status and represent high-risk groups. Tian et al. [**?**] similarly reported higher frailty prevalence in Chinese hospital populations (22.6%) versus community settings (12.8%). Our results align with this finding and further demonstrate even higher prevalence in comorbid populations. Notably, pre-frailty detection was higher in community (48%) than hospital (45%) settings, possibly because community-dwelling older adults experience less severe comorbidity impact and maintain better overall health, resulting in more pre-frail cases. This underscores the importance of implementing frailty screening in community-based comorbidity management to identify older adults at risk of progressing to frailty who may incur high medical costs, enabling timely preventive interventions.

3.4 Subgroup Analysis by Frailty Assessment Tool

Assessment tools yielded markedly different frailty prevalence estimates: Fried Frailty Phenotype (22%), CFS (43%), and FRAIL scale (8%). The higher CFS detection rate may reflect limited reliability due to inclusion of only two studies. The Fried Frailty Phenotype, comprising unintentional weight loss, weakness, slow gait, low physical activity, and exhaustion, remains widely used despite focusing solely on physical function [**?**]. This contrasts with contemporary understanding of frailty as multisystem decline encompassing psychological and social domains. Sensitivity analysis revealed high sensitivity for the Frailty Index (FI) (45% prevalence) [**?**], suggesting FI may better identify high-risk individuals in clinical settings, though it involves more items. While frailty assessment tools are well-established internationally, China lacks instruments tailored to its aging context. Development of comprehensive, culturally adapted tools integrating physical, psychological, and social domains is needed.

3.5 Subgroup Analysis by Survey Year

Notably, frailty prevalence has increased over time, rising to 38% in 2016-2020. This likely reflects worsening population aging and rising chronic disease burden. Our pooled frailty prevalence (27%) exceeds the 16% reported by Vetrano et al. [**?**] among adults with multimorbidity, possibly because comorbidity more profoundly increases health vulnerability in older adults, compounded by rising comorbidity prevalence in recent years. Frailty remains a critical health challenge requiring urgent attention in the context of active healthy aging.

In summary, frailty and pre-frailty prevalence among elderly patients with comorbidity are 27% and 48%, respectively, with substantial variation across disease counts, regions, settings, assessment tools, and time periods. China must intensify efforts in frailty screening and intervention for this population. Research indicates that only patients experiencing severe comorbidity-related

outcomes affecting daily life require support beyond standard care [**?**]. As a prevalent yet under-recognized condition that complicates chronic disease management, frailty holds important prognostic value. Our findings reveal a more pressing pre-frailty situation in community-dwelling elderly patients with comorbidity, highlighting the importance of prevention. For relatively healthy older adults with comorbidity, community and family-based comprehensive prevention programs incorporating nutrition, physical activity, cognitive training, and psychosocial support can reverse frailty. For frail, hospitalized patients with comorbidity, healthcare providers should implement multidisciplinary interventions (nutrition, medication, exercise, psychology) within integrated healthcare networks to treat diseases while delaying frailty progression, reducing hospitalization, mortality, and fall rates, and decreasing medical expenditures.

Limitations: (1) High heterogeneity is inherent to single-rate meta-analyses; despite subgroup analyses, heterogeneity remained high, potentially affecting accuracy. (2) Cross-sectional data precluded in-depth analysis of the comorbidity-frailty relationship. (3) Few studies exclusively examined frailty prevalence in elderly patients with comorbidity, limiting stratified analysis by sex, age, and other key factors, and resulting in relatively small comorbidity sample sizes. These findings require validation through additional high-quality, large-scale, multicenter studies. Furthermore, while frailty stems from multiple chronic diseases and may predispose to comorbidity, further research should explore the causal relationship between these conditions.

Author Contributions: LIN Yang conceived and designed the study; WANG Fang supervised topic selection, feasibility, revision, quality control, and review; LIN Yang, WANG Han, and WU Rong collected data; LIN Yang, WANG Yao, XU Ziyao, and WANG Xu organized data; LIN Yang and WANG Yanding performed statistical analysis; LIN Yang drafted the manuscript and takes responsibility for the work.

Conflict of Interest: The authors declare no conflicts of interest.

References

1. IZQUIERDO M, MERCHANT R A, MORLEY J E, et al. International exercise recommendations in older adults (ICFSR): expert consensus guidelines[J]. J Nutr Health Aging, 2021, 25: 824-853. DOI: 10.1007/s12603-021-1665-8.

2. WANG M J, ZHOU X, LI Y J, et al. Prevalence rate of multiple chronic conditions in middle-aged and elderly Chinese people from 2010 to 2019: a meta-analysis[J]. Chinese General Practice, 2021, 24(16): 2085-2091. DOI: 10.12114/j.issn.1007-9572.2020.00.477.

3. NICHOLSON K, ALMIRALL J, FORTIN M. The measurement of multimorbidity[J]. Health Psychol, 2019, 38(9): 783-790. DOI:

10.1037/hea0000739.

4. THILLAINADESAN J, SCOTT I A, LE COUTEUR D G. Frailty: a multisystem ageing syndrome[J]. Age Ageing, 2020, 49(5): 758-763. DOI: 10.1093/ageing/afaa112.

5. HAJEK A, BRETTSCHNEIDER C, RÖHR S, et al. Which Factors Contribute to Frailty among the Oldest Old? Results of the Prospective AgeCoDe and AgeQualiDe Multicentre Study[J]. Gerontology, 2020, 66(5): 460-466. DOI: 10.1159/000508723.

6. CHENG M H, CHANG S F. Frailty as a Risk Factor for Falls Among Community Dwelling People: Evidence From a Meta-Analysis[J]. J Nurs Scholarsh, 2017, 49(5): 529-536. DOI: 10.1111/jnu.12322.

7. JIN H Y, LIU X, XUE Q L, et al. The Association between Frailty and Healthcare Expenditure among Chinese Older Adults[J]. J Am Med Dir Assoc, 2020, 21(6): 780-785. DOI: 10.1016/j.jamda.2020.03.008.

8. VETRANO D L, PALMER K, MARENGONI A, et al. Frailty and Multimorbidity: A Systematic Review and Meta-analysis[J]. J Gerontol A Biol Sci Med Sci, 2019, 74(5): 659-666. DOI: 10.1093/gerona/gly110.

9. XU H H, WANG Y L, YAN W. Frailty and multimorbidity in the elderly: challenges for general medical services delivered by healthcare facilities in a compact medical consortium and recommended solutions[J]. Chinese General Practice, 2021, 24(24): 3026-3031. DOI: 10.12114/j.issn.1007-9572.2021.00.509.

10. ZENG X T, LIU H, CHEN X, et al. Meta analysis series 4: quality evaluation tools for observational research[J]. Chinese Journal of Evidence-Based Cardiovascular Medicine, 2012, 4(4): 297-299. DOI: 10.3969/j.1674-4055.2012.04.004.

11. XU L, ZHANG J, SHEN S, et al. Clinical Frailty Scale and Biomarkers for Assessing Frailty in Elder Inpatients in China[J]. J Nutr Health Aging, 2021, 25(1): 77-83. DOI: 10.1007/s12603-020-1455-8.

12. CASTELLANA F, LAMPIGNANO L, BORTONE I, et al. Physical Frailty, Multimorbidity, and All-Cause Mortality in an Older Population From Southern Italy: Results from the Salus in Apulia Study[J]. J Am Med Dir Assoc, 2021, 22(3): 598-605. DOI: 10.1016/j.jamda.2020.12.026.

13. THINUAN P, SIVIROJ P, LERTTRAKARNNON P, et al. Prevalence and Potential Predictors of Frailty among Community-Dwelling Older Persons in Northern Thailand: A Cross-Sectional Study[J]. Int J Environ Res Public Health, 2020, 17(11): 4077. DOI: 10.3390/ijerph17114077.

14. LANGHOLZ P L, STRAND B H, COOK S, et al. Frailty phenotype and its association with all-cause mortality in community-dwelling Norwegian

women and men aged 70 years and older: The Tromsø Study 2001-2016[J]. Geriatr Gerontol Int, 2018, 18(8): 1200-1205. DOI: 10.1111/ggi.13447.

15. THOMPSON M Q, THEOU O, YU S, et al. Frailty prevalence and factors associated with the Frailty Phenotype and Frailty Index: Findings from the North West Adelaide Health Study[J]. Australas J Ageing, 2018, 37(2): 120-126. DOI: 10.1111/ajag.12487.

16. LEE W J, PENG L N, LIN C H, et al. The synergic effects of frailty on disability associated with urbanization, multimorbidity, and mental health: implications for public health and medical care[J]. Sci Rep, 2018, 8(1): 14125. DOI: 10.1038/s41598-018-32537-5.

17. DOS S T D, DE FREITAS C T, DIAS F A, et al. Frailty syndrome and socioeconomic and health characteristics among older adults[J]. Colomb Med (Cali), 2017, 48(3): 126-131. DOI: 10.25100/cm.v48i3.1978.

18. MERCHANT R A, CHEN M Z, TAN L, et al. Singapore Healthy Older People Everyday (HOPE) Study: Prevalence of Frailty and Associated Factors in Older Adults[J]. J Am Med Dir Assoc, 2017, 18(8): 734-739. DOI: 10.1016/j.jamda.2017.04.020.

19. PETERS L L, BOTER H, BURGERHOF J G, et al. Construct validity of the Groningen Frailty Indicator established in a large sample of home-dwelling elderly persons: Evidence of stability across age and gender[J]. Exp Gerontol, 2015, 69: 129-141. DOI: 10.1016/j.exger.2015.05.006.

20. SOUSA A C, DIAS R C, MACIEL Á C, et al. Frailty syndrome and associated factors in community-dwelling elderly in North-east Brazil[J]. Arch Gerontol Geriatr, 2012, 54(2): e95-e101. DOI: 10.1016/j.archger.2011.08.010.

21. HOECK S, FRANÇOIS G, GEERTS J, et al. Health-care and home-care utilization among frail elderly persons in Belgium[J]. Eur J Public Health, 2012, 22(5): 671-677. DOI: 10.1093/eurpub/ckr133.

22. JÜRSCHIK P, NUNIN C, BOTIGUÉ T, et al. Prevalence of frailty and factors associated with frailty in the elderly population of Lleida, Spain: the FRALLE survey[J]. Arch Gerontol Geriatr, 2012, 55(3): 625-631. DOI: 10.1016/j.archger.2012.07.002.

23. CHEN C Y, WU S C, CHEN L J, et al. The prevalence of subjective frailty and factors associated with frailty in Taiwan[J]. Arch Gerontol Geriatr, 2010, 50(1): S43-S47. DOI: 10.1016/S0167-4943(10)70012-1.

24. RIZKA A, INDRARESPATI A, DWIMARTUTIE N, et al. Frailty among Older Adults Living in Nursing Homes in Indonesia: Prevalence and Associated Factors[J]. Annals of geriatric medicine and research, 2021, 25(2): 93-97. DOI: 10.4235/agmr.21.0033.

25. HAN S J, JUNG H W, LEE J H, et al. Clinical Frailty Scale, K-FRAIL questionnaire, and clinical outcomes in an acute hospitalist unit in Korea[J]. Korean J Intern Med, 2021, 36(5): 1233-1241. DOI: 10.3904/kjim.2020.677.

26. DANON-HERSCH N, RODONDI N, SPAGNOLI J, et al. Prefrailty and chronic morbidity in the youngest old: an insight from the Lausanne cohort Lc65+[J]. J Am Geriatr Soc, 2012, 60(9): 1687-1694. DOI: 10.1111/j.1532-5415.2012.04113.x.

27. DUARTE Y, NUNES D P, ANDRADE F B, et al. Frailty in older adults in the city of São Paulo: Prevalence and associated factors[J]. Rev Bras Epidemiol, 2019, 21(02): e180021. DOI: 10.1590/1980-549720180021.supl.2.

28. MENDONÇA N, KINGSTON A, YADEGARFAR M, et al. Transitions between frailty states in the very old: the influence of socioeconomic status and multi-morbidity in the Newcastle 85+ cohort study[J]. Age Ageing, 2020, 49(6): 974-981. DOI: 10.1093/ageing/afaa054.

29. QIU L, QIU Y H. Analysis of Frailty Status and Influencing Factors of Hospitalized Patients Aged 65 Years and Above[J]. Medical Innovation of China, 2021, 18(21): 76-80. DOI: 10.3969/j.issn.1674-4985.2021.21.018.

30. FAN S Y, XU F P, PEI Z, et al. Relationship between frailty and sleep disturbances in elderly people in Guangzhou province[J]. The Journal of Practical Medicine, 2020, 36(14): 1908-1912. DOI: 10.3969/j.issn.1006-5725.2020.14.010.

31. XIAO C Y, HU Y, XU R Y, et al. Study on the status and influencing factors of frailty among rural elderly in Hunan Province[J]. China Rural Medicine and Pharmacy, 2020, 27(23): 60-62. DOI: 10.3969/j.issn.1006-5180.2020.23.036.

32. LI X F, CHEN F F, CHEN X, et al. Influencing factors of debilitating elderly inpatients[J]. Chinese Journal of Gerontology, 2019, 39(4): 970-974. DOI: 10.3969/j.issn.1005-9202.2019.04.068.

33. FANG X Y, ZHANG X Y, LIU Y, et al. Analysis of frailty status and influencing factors in elderly inpatients[J]. Chinese Journal of Gerontology, 2019, 39(2): 467-470. DOI: 10.3969/j.issn.1005-9202.2019.02.070.

34. ZHOU L H, WANG L X, YANG Y X, et al. Frail status and influencing factors in elderly inpatients with comorbidity[J]. Chinese Journal of Multiple Organ Diseases in the Elderly, 2019, 18(1): 6-11. DOI: 10.11915/j.issn.1671-5403.2019.01.002.

35. MENG L, TAN X, SHI J, et al. Distribution and influencing factors of frailty in Chinese older adults[J]. Chinese Journal of Clinical Healthcare, 2017, 20(5): 481-485. DOI: 10.3969/J.issn.1672-6790.2017.05.001.

36. WALSTON J, HADLEY E C, FERRUCCI L, et al. Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults[J]. J Am Geriatr Soc, 2006, 54(6): 991-1001. DOI: 10.1111/j.1532-5415.2006.00745.x.

37. HOWLETT S E, ROCKWOOD K. New horizons in frailty: ageing and the deficit-scaling problem[J]. Age Ageing, 2013, 42(4): 416-423. DOI: 10.1093/ageing/aft059.

38. KANE A E, SINCLAIR D A. Frailty biomarkers in humans and rodents: Current approaches and future advances[J]. Mech Ageing Dev, 2019, 180: 117-128. DOI: 10.1016/j.mad.2019.03.008.

39. LIN K X, LYU J, YU B, et al. Emerging Markers of Frailty in Older People: Recent Strides and Prospect[J]. Chinese General Practice, 2021, 24(36): 4580-4586. DOI: 10.12114/j.issn.1007-9572.2021.02.036.

40. FRANCESCHI C, GARAGNANI P, MORSIANI C, et al. The Continuum of Aging and Age-Related Diseases: Common Mechanisms but Different Rates[J]. Front Med (Lausanne), 2018, 12(5): 61. DOI: 10.3389/fmed.2018.00061.

41. TUNNARD I, YI D, ELLIS-SMITH C, et al. Preferences and priorities to manage clinical uncertainty for older people with frailty and multimorbidity: a discrete choice experiment and stakeholder consultations[J]. BMC Geriatr, 2021, 21(1): 553. DOI: 10.1186/s12877-021-02480-8.

42. MARENGONI A, ANGLEMAN S, MEINOW B, et al. Coexisting chronic conditions in the older population: Variation by health indicators[J]. Eur J Intern Med, 2016, 31: 29-34. DOI: 10.1016/j.ejim.2016.02.014.

43. HANLON P, NICHOLL B I, JANI B D, et al. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493,737 UK Biobank participants[J]. Lancet Public Health, 2018, 3(7): e323-e332. DOI: 10.1016/S2468-2667(18)30091-4.

44. TIAN P, YANG N, HAO Q K, et al. Epidemiological characteristics of frailty in Chinese elderly population: a systematic review[J]. Chinese Journal of Evidence-Based Medicine, 2019, 19(6): 656-664. DOI: 10.7507/1672-2531.201901056.

45. FRIED L P, TANGEN C M, WALSTON J, et al. Frailty in older adults: evidence for a phenotype[J]. J Gerontol A Biol Sci Med Sci, 2001, 56(3): M146-M156. DOI: 10.1093/gerona/56.3.m146.

46. KERNICK D, CHEW-GRAHAM C A, O' FLYNN N. Clinical assessment and management of multimorbidity: NICE guideline[J]. Br J Gen Pract, 2017, 67(658): 235-236. DOI: 10.3399/bjgp17X690857.