

# MANAGEMENT OF FRAILTY AT INDIVIDUAL LEVEL - CLINICAL MANAGEMENT: SYSTEMATIC LITERATURE REVIEW

## MENEDŽMENT KRHKOSTI NA RAVNI POSAMEZNIKA - KLINIČNI MENEDŽMENT: SISTEMATIČNI PREGLED LITERATURE

Gregor VENINŠEK<sup>1</sup>, Branko GABROVEC<sup>2\*</sup>

<sup>1</sup>University Medical Center Ljubljana, Center for Geriatric Medicine, Zaloška 2, 1000 Ljubljana, Slovenia

<sup>2</sup>National Institute of Public Health, Health Care Center, Trubarjeva 2, 1000 Ljubljana, Slovenia

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### ABSTRACT

#### Keywords:

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**Introduction:** To deliver quality management of a frail individual, a clinician should understand the concept of frailty, be aware of its epidemiology and be able to screen for frailty and assess it when it is present, and, finally, to recommend successful interventions.

**Methodology:** A systematic literature search was conducted in the following databases: PubMed, Cochrane, Embase, Cinahl and UpToDate. The criterion in selecting the literature was that articles were published in the period from 2002 to 2017. From 67432 initial hits, 27 publications were selected.

**Results:** Useful interventions to address frailty are supplementation of vitamin D, proper nutrition, multicomponent training, home-based physiotherapy and comprehensive geriatric assessment, particularly when performed in geriatric wards.

**Conclusion:** Comprehensive geriatric assessment is an effective way to decrease frailty status especially when performed in geriatric wards. Multicomponent physical training and multidimensional interventions (physical training, nutrition, vitamin D supplementation and cognitive training) are effective measures to reduce frailty.

### IZVLEČEK

#### Ključne besede:

krhkost, geriatrija,  
geriatrične ocene,  
Joint Action  
ADVANTAGE

**Uvod:** Za kakovostno upravljanje krhkega posameznika mora klinik razumeti koncept krhkosti ter prepoznavanje in priporočanje uspešnih intervencij.

**Metode:** Za to raziskavo je bil izveden sistematičen pregled literature v naslednjih bazah: PubMed, Cochrane, Embase, Cinahl in UpToDate. Vključitveni kriterij je bil izbor literature, objavljene v zadnjih 15 letih, od leta 2002 do leta 2017. Od 67.432 zadetkov je bilo izbranih 27 publikacij.

**Rezultati:** Koristne intervencije za obravnavo krhkosti so dodajanje vitamina D, pravilna prehrana, večkomponentna telesna vadba, fizioterapija na domu in obsežna geriatrična ocena, ki se uporablja na geriatričnih oddelkih.

**Zaključki:** Če se celovita geriatrična ocena na geriatričnih oddelkih izvaja, ta povečuje možnost pacientovega preživetja in kognicije. Večkomponentna fizična vadba in večdimenzionalne intervencije, ki temeljijo na celoviti geriatrični oceni, so učinkovite pri zmanjševanju krhkosti.

\*Corresponding author: Tel. + 386 40 381 470; E-mail: [branko.gabrovec@nijz.si](mailto:branko.gabrovec@nijz.si)

## 1 INTRODUCTION

Functional capacities in healthy individuals are developed and strengthened until adulthood and slowly decline thereafter. A decline in multiple physiological systems results in frailty (1). The prevalence of frailty progresses with age and we can find 2-5% of the population with frailty in the age group between 18 and 34 (2). Determinants of frailty are gender, age, income, lifestyle, marital status and multimorbidity as the key determinant (3). Frailty is associated with incapacity and/or multimorbidity, but should not be equated with it (4). With older people frailty is a common cause condition leading to death. In the last year of life, frailty is connected to a persistent or advanced disability in basic daily activities, which is similar to an individual with organ failure (5).

Comprehensive geriatric assessment (CGA) is the most comprehensively researched model for healthcare delivery to frail older patients (6).

Frailty among older persons is a dynamic process characterised by frequent transitions between frailty states over time. Clinical management of frailty at the individual level includes prevention at the individual level, detection and management of a frail individual (7). Priorities of healthcare services and their differences between providers and recipients should be taken into account particularly in the health care of older patients and the design of healthcare policies and research (8).

Determinants of frailty have to be systematically checked to be able to recognise an individual who is at a high risk to develop frailty (3).

### 1.1 Aims and Objectives

**Aim:** To define interventions in a successful clinical management of frail people.

**Objective:** To conduct a systematic review of relevant literature for the time period from 1 January 2002 to 31 May 2017.

## 2 METHODS

### 2.1 Review Methods

Descriptive research methodology was used to review peer-reviewed medical literature. A systematic review of literature was conducted, as it enabled us to obtain data from various sources and ensured a holistic understanding of the research subject. The search for literature was conducted in the PubMed, Cochrane, Embase, Cinahl and UpToDate databases by means of several combinations of

selected search words in the English language and their synonyms, with Boolean operators AND or: Comprehensive Geriatric Assessment \*() OR Frail Disability \*() OR Frailty treatment \*() OR Frail Older adult \*() OR Frailty Screening \*() OR Frailty management \*() OR Frailty Intervention Therapy \*() OR Functional Decline \*() OR Frail Older person \*() OR Geriatric Vulnerable \*() OR Elderly Vulnerable \*() OR Frailty Scale \*(); searching in the title, key words and the abstract.

The selection criterion for articles to be included in the review was that they were published during the last 15 years. Key words were selected from a proposal of key words that was prepared by the task leader and the working group focusing on Clinical Management as part of the European Commission project 'Joint Action on Frailty Prevention - JA ADVANTAGE,' Work Package 6 - Management of Frailty at Individual Level.

In addition to language and publication time restrictions, the main inclusion factors were also peer-review scientific journals, international documents, professional guidelines, standards and research studies performed in the EU which comprehensively investigate and describe management of frailty through clinical management. The exclusion criteria were: editorials, letters, interviews, posters and no access to full text.

We have also included grey documents which were identified and proposed by the task leader and the working group focusing on Clinical Management as part of the European Commission project 'Joint Action on Frailty Prevention - JA ADVANTAGE,' Work Package 6 - Management of Frailty at Individual Level. Grey documents were identified by means of an opportunistic search, that is, a targeted or focused one, based on the information that each partner in the project Consortium could give regarding their own country. The term grey literature was used to describe information which is not published commercially or is otherwise hard to find. This includes items, such as government reports, NGO reports, theses, technical reports, white papers, etc.

### 2.2 Results of the Review

The total number of all search results was 67432. After excluding duplicates and considering inclusion criteria, the final 27 articles remained for analysis.

The process of literature review is displayed in a search table (Table 1) and in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) diagram (9), as shown in Figure 1.

Table 1. Search table.

	Key word	No. of hits	Chosen hits	Repeated chosen hits	Repeated chosen hits
PubMed	Comprehensive Geriatric Assessment	30541	12	12	4
	Frail Disability	1332	4	4	1
	Frailty treatment	3689	8	8	3
	Frail Older adult	11223	6	4	2
	Frailty Screening	3	9	3	2
	Frailty management	1491	7	7	2
	Frailty Intervention Therapy	409	9	9	2
	Functional Decline	14123	11	2	2
Cochrane	Comprehensive Geriatric Assessment	287	2	2	2
	Frail Older person	44	2	1	1
	Geriatric Vulnerable	70	1	1	1
	Elderly Vulnerable	175	1	1	1
Embase	Comprehensive Geriatric Assessment	880	2	0	0
	Frailty Scale	148	2	0	0
	Functional decline	11000	16	16	2
CINAHL	Comprehensive Geriatric Assessment	410	5	5	1
	Frailty Scale	53	0	0	0
UpToDate	Frail Older adult	795	2	0	0
	Frailty Intervention Therapy	305	13	0	0
	Frail Older person	390	6	0	0
Other sources		1			1
		67432	118		27

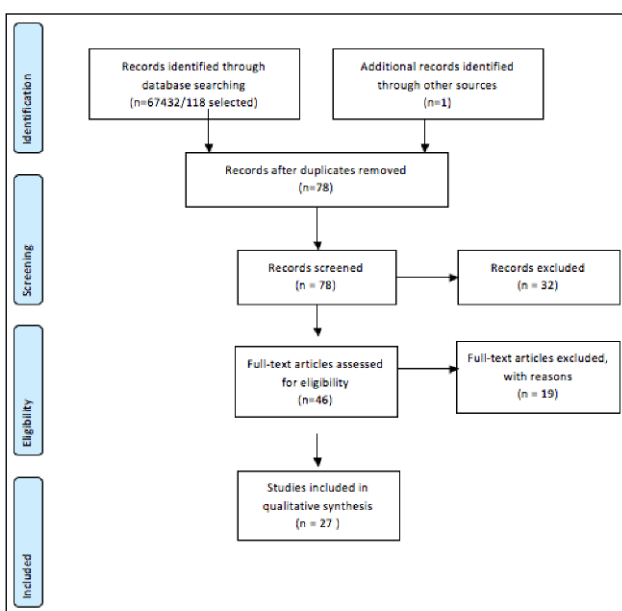


Figure 1. Flowchart of search strategy and literature selection process

### 2.3 Quality Assessment of the Review

Results of the quality assessment of systematic literature review, as shown in Table 2.

**Table 2.** Results of the quality assessment of systematic literature review.

Criteria	Yes	No	Other
1. Is the review based on a focused question that is adequately formulated and described?	X		
2. Were eligibility criteria for included and excluded studies predefined and specified?	X		
3. Did the literature search strategy use a comprehensive, systematic approach?	X		
4. Were titles, abstracts, and full-text articles dually and independently reviewed for inclusion and exclusion to minimize bias?	X		
5. Was the quality of each included study rated independently by two or more reviewers, using a standard method to appraise its internal validity?	X		
6. Were the included studies listed along with important characteristics and results of each study?	X		
7. Was publication bias assessed?	X		
8. Was heterogeneity assessed? (This question applies only to meta-analyses.)		X	

### 3 RESULTS

**Table 3.** Results of the review and literature analysis.

Author and year	Research design	Sample	Research purpose	Key findings
Kehler et al., 2017	Cross-sectional. Survey	n=7353	To examine and compare the prevalence of frailty in Canadians 18-79 years old using the Accumulation of Deficits and Fried models of frailty.	Data show that frailty is prevalent already in younger adults, has increasing prevalence with age, which varies depending on which frailty tool is used.
Gobbens et al., 2010	Cross-sectional	75 years old and older n=484	To determine which determinants predict frailty and domains of frailty.	The effect of the determinants of frailty differs across frailty domains.
Gill et al., 2006	Prospective study	70 years and older n=754	To determine the transition rates between frailty states.	Frailty is a dynamic process, characterised by frequent transitions between frailty states over time.
Fried et al., 2001	Prospective and observational study	65 years and older n=5317	To develop and operationalize a phenotype of frailty in older adults.	The study provides a potentially standardised definition for frailty.
Clegg et al., 2013	Literature review and observational study	80 years old and older	A research on how frailty develops, how it might be prevented and how it can be detected reliably.	Landmark studies have developed valid models for frailty.
Kan et al., 2008	Literature review, Expert panel	Geriatric Advisory Panel	To perform a comprehensive review of the definitions and assessment tools on frailty.	No consensus on the definition of frailty, but there was an agreement to consider frailty as a pre-disability stage.

Author and year	Research design	Sample	Research purpose	Key findings
Dent et al., 2016	Literature review	65 years old and older n=29	An overview of the definitions and measurements of frailty in research and clinical practice.	A summary of the main strengths and limitations of existing frailty measurements.
Stoicesa et al., 2016	Literature review	Reviews of six scales.	Review scales for measuring frailty.	By identifying the most time-efficient criteria, a comprehensive and clinically effective scale, a universal scale can be implemented.
Subra et al., 2012	Literature and platform review, observational study	65 years old and older n=160	The presentation of the main characteristics of the new Platform.	The Platform clinically evaluates and intervenes on frailty for the first time at the general population level.
Vellas et al., 2013	Screening tool review and observational study	65 years old and older n=442	A screening tool for frailty	The use of the GFST may help at raising awareness about the importance of identifying frailty.
Morley et al., 2013	Consensus group	Delegates from 6 major international, European, and US societies.	To create 4 major consensus points on the specific form of frailty.	Physical frailty can potentially be prevented or treated.
Sutton et al., 2016	Literature review	73 articles selected 60 years old and older	To identify existing multi-component frailty assessment tools that were developed to assess frailty.	The TFI has the most robust evidence of reliability and validity.
Ellis et al., 2011	Review of randomised controlled trials	Two reviews	To evaluate the effectiveness of CGA in the hospital.	CGA increases a patient's likelihood of being alive and in their own home.
Theou et al., 2011	Literature review	47 studies selected	To examine the effectiveness of current exercise interventions for the management of frailty.	Evidence suggests that exercise has a positive impact on some physical determinants of frailty.
Beudart et al., 2014	Literature review, Meta-analyse	30 studies selected	To summarise with a meta-analysis the effects of vitamin D supplementation.	Vitamin D supplementation has a small positive impact on muscle strength.
Bruyère et al., 2017	Literature review	No data	A review of the evidence regarding the role of vitamin D.	Several studies suggest a potential effect of vitamin D on physical frailty.
Cesari et al., 2015	Exploratory analyses	Mean age=76.8 years n=424	To explore whether a physical activity intervention can reduce prevalence and severity of frailty.	Regular PA may reduce frailty, especially in individuals at higher risk of disability.

Author and year	Research design	Sample	Research purpose	Key findings
Ng et al., 2015	Randomised controlled trial	Mean age=70 years n=151	To compare the effects of 6-month-duration interventions vs. control in reducing frailty.	Physical, nutritional, and cognitive interventional approaches were effective in reversing frailty.
Song et al., 2010	Prospective cohort study	Aged from 65 to 102 years n=2740	To evaluate the prevalence and 10-year outcomes of frailty in older adults.	The prevalence of frailty increases with age and, at any age, lessens survival.
Puts et al., 2017	Literature review	65 years old and older 14 studies selected	To review policies that are designed to prevent or reduce the level of frailty.	The best interventions and policies to prevent or reduce the level of frailty.
Turner et al., 2014	Literature review, Report	No data	To create proactive, integrated, person-centred and community-based response to frailty.	The British Geriatrics Society Fit for Frailty guideline is by consensus the best practice guidance for managing frailty.
Collard et al., 2012	Literature review	65 years old and older 21 studies selected	To systematically compare and pool the prevalence of frailty, including pre-frailty.	Different operationalization of frailty status results in widely differing prevalence between studies.
Gill et al., 2004	Randomised controlled trial	75 years old and older n=188	To determine whether a home-based physical therapy program prevents a decline in several higher-level measures of physical function.	Home-based pre-habilitation program offered modest, but consistent benefits.
Chan et al., 2012	Randomised controlled trial	65-79 years old n=117	To report interventions targeting the improvement of frailty status as an outcome.	The three-month intervention resulted in short-term frailty status improvement.
Li et al., 2010	Randomised controlled trial	65 years old and older n=310	To assess the effectiveness of CGA.	CGA showed a favourable outcome in frail and pre-frail older people.
Cameron et al., 2013	Randomized controlled trial	Mean age=83,3 years n=216	To determine whether an intervention could reduce frailty and improve mobility.	Frailty and mobility disability can be successfully treated.
Behm et al., 2016	Randomised controlled trial	80 years old and older n=459	To determine whether preventive home visits could postpone deterioration in frailty.	The results of this study show the potential of health promotion to older persons.

### 3.1 Summary of Studies Included in Review

#### 3.1.1 Definition of Frailty

Although frailty is a commonly used term to indicate older persons at an increased risk for adverse outcomes, the consensus about how to define it is lacking (17). One consensus definition quotes 'frailty as a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death' (17). Physical frailty is considered to be a consequence of a cycle of decreasing energy expenditure, negative energy balance and sarcopenia (10). It is a state of poor homeostatic reserve due to critically decreased physiological reserves and is considered as a state of pre-disability (11, 12, 26). Other components, such as cognition, mood, social circumstances, living environment, income, lifestyle, multimorbidity, disability and sensory impairment, should also be included as domains of frailty (3, 12).

#### 3.1.2 Epidemiology of Frailty

Up to 50 years of age, frailty is more prevalent when defined by Fried criteria, but after this age, it becomes more prevalent when defined as an accumulation of deficits or Frailty index (2). In general, the prevalence of frailty defined as an accumulation of deficits is 1.3-1.37 times more prevalent than when it is defined by Fried criteria (2, 27). General prevalence of frailty is 9.9% and 13.6% and of pre-frailty 44.2% and 34.5%, respectively, when defined by Fried criteria and by the broad definition (27). The prevalence of frailty increases with age, is more prevalent in women than in men, and can be as high as 39.1% in men aged 85 years or older and 45.1% in women in the same age group (24).

#### 3.1.3 Tools for Screening and Diagnosing Frailty

There are literally dozens of tools designated to assess frailty, ranging from simple to multicomponent (10-15, 18, 26). There are two principal frailty models, namely: the phenotype model (Fried model or CHS Index) and the cumulative deficit model (Frailty index) (10, 11). Among the definitions of frailty that are valid and reliable for predicting the outcome, Fried Frailty Phenotype, Frailty Index of Accumulated Deficits and Study of Osteoporotic Fractures Index were useful in clinical and population settings, while Frailty Index based on CGA, Edmonton Frailty Scale and Clinical Frailty Scale were useful only in clinical settings (13). In general, of the 38 assessment tools, only the Frailty Index-CGA and Tilburg Frailty Indicator showed significant evidence of reliability and validity (18). There is still no consensus regarding which tool should be used for screening and diagnosing frailty (12). Fried criteria and Frailty Index of Accumulated

Deficits appear to be the most robust assessment tools to be used by clinicians and researchers today, and should consequently prove to be the most useful ones either for screening and diagnosing frailty (Fried criteria) or as an assessment and follow-up tool (Frailty index derived from CGA) (13).

#### 3.1.4 Interventions in Frailty

Supplementation of vitamin D might have positive effects on muscle strength and physical frailty in adults over 65 years old and vitamin D deficient individuals (20, 21). Regular physical activity effectively decreases the number of frailty criteria and the prevalence of frailty in community-dwelling sedentary older people (22). Exercise has a positive impact on some physical outcomes and on functional ability in frail older people (19). Multicomponent training interventions performed three times per week for 30-45 minutes per session over a period of more than 5 months seem to be superior to other exercise programs (19). A home modification and progressive competency-based exercise programme can reduce the level of frailty in older people (25).

In a community-dwelling pre-frail or frail older people, nutrition, cognitive training, physical activity and combination treatment in duration of 6 months improve frailty score and frailty status (23). Combined training of a shorter duration is effective, but the results are less sustainable (28).

CGA consisting of evaluation and management of frail older people can be an effective way to decrease frailty status (29, 30). When performed in geriatric wards, comprehensive geriatric assessment increases a patient's likelihood of being alive, at home and experiencing improved cognition (32).

Home-based physiotherapy seems to decrease frailty, but preventive home visits are not very effective (31, 33).

## 4 DISCUSSION

We identified four main areas essential for clinical management of frailty: definition of frailty, epidemiology of frailty, tools for screening and diagnosing frailty and successful interventions for decreasing frailty.

Frailty is not a disease with a disturbing set of symptoms and signs that would prompt an individual to seek the attention of medical personnel. A potentially frail individual should therefore primarily be approached in a proactive manner.

Studies show a unanimous consent that frailty carries the risk of poor outcomes. Defining frailty remains elusive, but the concept emerging from the efforts to do so encompasses the influence of irreversible or

non-preventable (age, ethnicity, etc.) and reversible or preventable (morbidity, income, lifestyle, etc.) determinants that cause a decline in physiologic reserve, resulting in poor homeostatic reserve that can be critically challenged with minor intrinsic or extrinsic stressors resulting in morbidity, decreased functional ability or disability, or death.

As a proactive approach is sensible, individuals should be screened and assessed for frailty when present. It is neither practical nor feasible to evaluate the entire population but targeting those with determinants associated with frailty and older population makes sense with support in epidemiological data.

There are many tools to screen for and diagnose or assess frailty in an individual person. As screening for frailty is performed more feasibly when focusing on physical frailty, it could be the first step in clinical management. Subsequent assessment should include CGA to identify all potential contributors and plan the interventions and follow-up. The CGA derived Frailty index is better suited for evaluating the effect of interventions than were the tools for assessing physical frailty (i.e., Fried criteria).

From a clinical point of view, the evidence that physical interventions, provided that they are sufficiently intensive and performed over a sufficient time span, are successful in the treatment of frailty is highly regarded. To the best of our knowledge, only the data from one RCT show both the effect of cognitive training as well as the explicit effect of nutrition intervention (protein, energy, vitamin and mineral supplementation) on frailty (24). Although it is recommended to supplement vitamin D in older people in order to alleviate the consequences of frailty, there are only conditional data to support treatment of frailty with vitamin D. In this regard, we consider vitamin D as more of a marker than a risk factor or contributor for frailty. CGA appears to have a central role in the management of frailty. There are robust data of its effectiveness when performed in specialized wards for hospitalized frail older people, who are the most vulnerable frail population. Interventions are much more effective when implemented in those populations that at the greatest risk, and in this regard, geriatric wards should be highly encouraged to perform CGA.

The value of our review lies in a comprehensive evaluation of all the elements necessary to provide care to a frail person. We believe the presented work is very informative, not only for busy clinicians unfamiliar with concept of frailty, but also for service planners, providers and payers, since frailty prevention, postponement or treatment involves many stakeholders and/or requires a multidisciplinary approach.

There are some limitations to our review. Because there is no generally accepted definition of frailty, we very likely missed many studies that could otherwise be included in this review. We did not find a substantial body of new research on this topic, therefore, the majority of interventions have already been more or less firmly and explicitly recommended in the report from the consensus conference with the participation of experts from six major international, European and US societies published in 2013 (17).

We are aware of the development of drugs to treat sarcopenia and we look forward to studies that will evaluate those drugs in the context of frailty prevention and treatment (34).

To the best of our knowledge, several questions remain unanswered, such as whether different age groups require different approaches to the issue of frailty, whether management and treatment of multimorbidity can have an effect on frailty, and whether public health measures can be effective in preventing and treating frailty.

## 5 CONCLUSION

The aim of this research was to define interventions in a successful clinical management of frail people. For the purposes of this research, a systematic literature review method was used. The method proved to be appropriate and the aim was achieved. Our research can serve as a base for a comprehensive model of clinical management of frailty.

Results of this review show that prevalence of frailty ranges from 5% to more than 45%, depending on the definition and age group. Although not ideal, Fried criteria and Frailty Index of Accumulated Deficits can be recommended for clinical work and research purposes. They can be used consequently, as Fried criteria are more feasible for screening, whereas Frailty Index, derived from comprehensive geriatric assessment, is better suited for management and follow-up. Comprehensive geriatric assessment is a multidimensional, multidisciplinary diagnostic instrument addressing medical, psychosocial, functional and social capabilities and limitations of older persons, which aims to generate a plan of treatment and follow-up and is, therefore, a core activity in geriatric medicine (6). Multicomponent physical training of appropriate duration and frequency, and multidimensional interventions combining vitamin D, nutrition, cognitive training and physical activity, particularly when based on comprehensive geriatric assessment, are effective to reduce frailty.

The main drawback of the current literature review is the fact that it does not include a meta-analysis of included results.



## CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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## ETHICAL APPROVAL

Not applicable.

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