International Journal of Nursing Studies 92 (2019) 16–26

Contents lists available at ScienceDirect

International Journal of Nursing Studies

journal homepage: www.elsevier.com/ijns

Defining frailty for healthcare practice and research: A qualitative systematic review with thematic analysis

Duygu Sezgin[a,*], Mark O'Donovan[a], Nicola Cornally[b], Aaron Liew[a,c,1], Rónán O'Caoimh[a,b,1]

[a] Clinical Sciences Institute, National University of Ireland, Galway, Galway City, Ireland
[b] School of Nursing and Midwifery, University College Cork, Cork, Ireland
[c] Portiuncula University Hospital, Galway, Ireland

ARTICLE INFO

Article history:
Received 20 September 2018
Received in revised form 13 December 2018
Accepted 17 December 2018

Keywords:
Definition
Frailty
Meta-aggregation
Qualitative analysis
Systematic review

ABSTRACT

Objective: To identify and examine definitions of frailty using qualitative thematic analysis.
Design: A qualitative meta-aggregative systematic review.
Data sources: The database search was performed using ASSIA, CINAHL, Cochrane Library, Embase, PsycINFO, PubMed and Google Scholar databases. Studies providing definitions of frailty, published in English from 1st January 2000 to 25th July 2018 were included.
Review methods: Data were extracted by independent reviewers for qualitative thematic analysis.
Results: In total, 86 studies met inclusion criteria. Five major themes with specific sub-themes were identified following thematic analysis including: (1) types of definitions *(operational, conceptual, theoretical, older adults' perspective);* (2) characteristics of frailty *(a multi-domain and dimensional state, deficits/decline, weakness, a continuum-dynamic concept, clinically identifiable)*; (3) associated factors *(age, comorbidity, nutrition, sarcopenia, social networks and environment)*; (4) mechanism *(reduced adaptability, hormonal dysregulation);* and (5) changes in health status and adverse outcomes *(disability, increased risk of mortality, other healthcare related outcomes such as increased dependency or risk of falls).*
Conclusions: Several themes were found that defined frailty, focusing predominantly on operational definitions and frailty as a physical syndrome. A universally accepted standard definition, which includes all dimensions of frailty is currently warranted.

What is already known about the topic?

There is no standard definition of frailty in the literature.

1 Many assessment tools have been utilised to identify frailty, although research proposing definitions of frailty is scarce.

What this paper adds

1 This study highlights key characteristics and associated factors related to frailty, calling attention to the growing importance of a multidimensional approach to defining frailty.
2 Most studies use operational definitions that focus on frailty as a physical phenotype; few incorporated the perspective of older adults.
3 The conceptual map developed in this study through a qualitative analysis approach can aid nurses, physicians, and other allied health professionals to improve their understanding of different aspects of frailty.

1. Introduction

Frailty, a geriatric syndrome associated with functional decline (limitations and impairments in activities of daily living), is prevalent in the ageing population (Apostolo et al., 2018; Cardona-Morrell and Hillman, 2015; Espinoza et al., 2010; O'Caoimh et al., 2018a,b). Multiple factors including psychosocial and socioeconomic status, insufficient social supports, poor nutrition, inadequate physical activity, multi-morbidity and chronic diseases are associated with frailty, rendering older adults vulnerable to various adverse outcomes

* Corresponding author at: National University of Ireland Galway, College of Medicine, Nursing & Health Sciences, Ireland.
E-mail address: duygu.sezgin@nuigalway.ie (D. Sezgin).
[1] Co-senior author.

https://doi.org/10.1016/j.ijnurstu.2018.12.014
0020-7489/

and potentially increased mortality (Chen et al., 2016a; Espinoza et al., 2010; Fairhall et al., 2015; Kaiser et al., 2009; Le Cossec et al., 2016; Liu et al., 2015; Mohile et al., 2015; Morley et al., 2013; Vaes et al., 2017; Veronese et al., 2017). The prevalence rates in community-dwelling adults not only vary between studies with higher levels found in acute and long-term care settings compared to community samples, but they also vary by the approach used to classify frailty (Collard et al., 2012; Espinoza et al., 2010; O'Caoimh et al., 2018a; Santos-Eggimann et al., 2009). Furthermore, they vary among those with chronic diseases including dementia (Chen et al., 2016b).

Cardona-Morrell et al. (2017) reported that no standard systematic assessment of frailty is available or consistently applied in hospital, emergency department, general practice, and residential care settings. Although, the most common classification framework used is the Physical Phenotype developed by Fried et al. (2001), other measures are also widely used (Bieniek et al., 2016; Buta et al., 2016; Turusheva et al., 2016).

Currently, there is no internationally agreed consensus for the definition of frailty (Borges and Menezes, 2011; Rodriguez-Manas et al., 2013). Few systematic reviews exploring definitions of frailty have been published (Borges and Menezes, 2011; Junius-Walker et al., 2018) and none to our knowledge have conducted a qualitative systematic review of the underlying themes contributing to a comprehensive definition of frailty. Such a qualitative systematic review is warranted since several valid thematic components have been used to define frailty in the literature, rendering direct comparisons between studies using different definitions difficult. Qualitative reviews are important since they aid in generating summaries of current literature using a synthesis approach and their findings can produce valuable generalisations contributing to theory and practice (Hannes and Pearson, 2012; Sandelowski et al., 1997). This method was favoured over a concept analysis, which is traditionally grounded in theoretical literature, negating the inclusion of important and relevant empirical findings (Botes, 2002). Furthermore, this pragmatic approach is best suited to research questions that serve to directly inform policy and practice (Lockwood et al., 2015). Therefore, the aim is to conduct a qualitative (aggregative) systematic review of the current literature to identify and examine definitions of frailty, and how they are characterised and operationalised in published studies.

2. Methods

The study was conducted as a qualitative meta-aggregative review. This approach allowed for data to be pooled, compared and then summarised to understand the construct under review (frailty) (Dixon-Woods et al., 2006; Seers, 2015). In this aim, the steps of the meta-aggregation were followed: development of the research question, search of the literature for the evidence, critical appraisal of the included studies, aggregation of the findings, developing categories, and further synthesis (Hannes and Pearson, 2012). The research question "What is the definition of frailty in the current literature?" was generated and a further search for evidence was conducted through systematically reviewing the literature. Our protocol was registered on the PROSPERO database (CRD42018095110). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses and the Consolidated Criteria for Reporting Qualitative Research checklists were used for reporting process.

2.1. Eligibility criteria

Studies with any design (including editorials and opinion pieces from grey, empirical and theoretical literature) that incorporated a definition of frailty or discussed its characteristics, were considered for inclusion. These could be conducted in any setting (including primary care, secondary care, general practice or residential care settings), but peer-reviewed, in English, and published between 1st January 2000 and 25th July 2018 (inclusive),

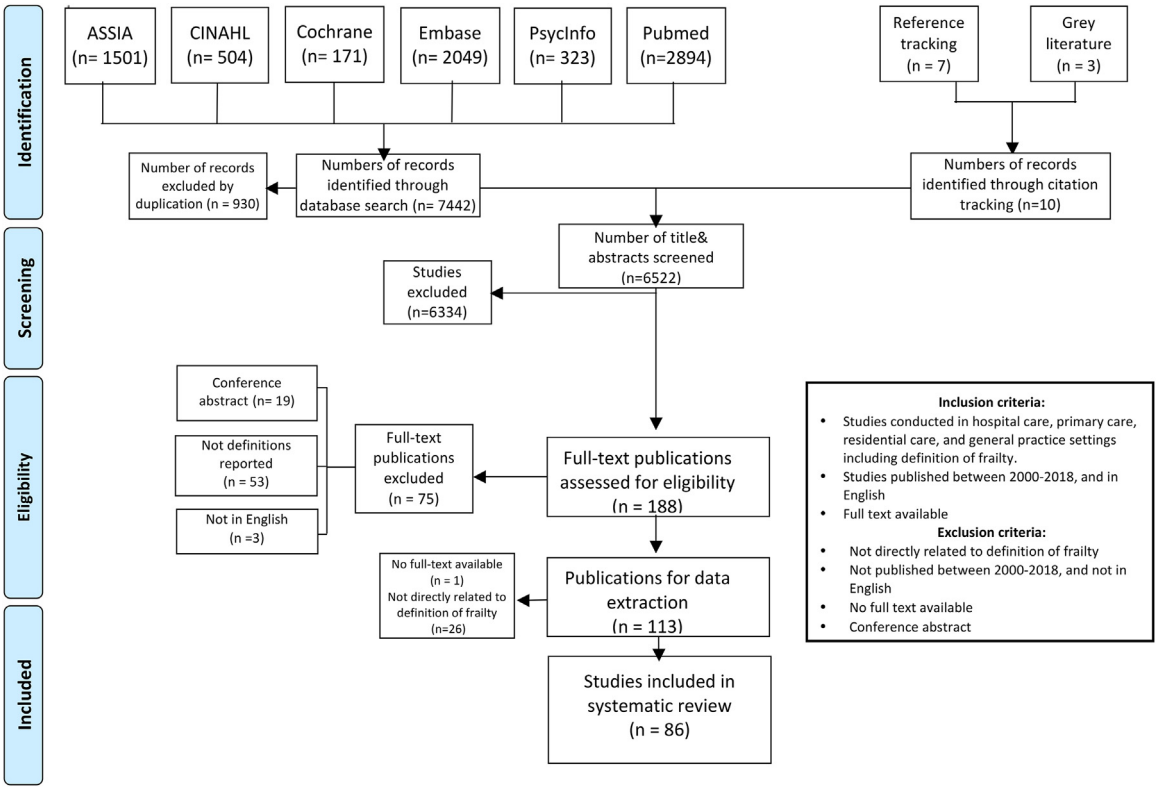

Fig. 1. Definition of frailty systematic review flow diagram.

with available full texts. Studies published as conference abstracts, without full text, that did not include a definition or describe characteristics of frailty, that were not peer reviewed, published before 1st January 2000, or in a language other than English, were excluded. In addition, this review excluded non-medical/nursing literature e.g. sociological definitions of frailty. As frailty is predominantly associated with age, this study only examined research related to older people, albeit no age cut-off was applied.

2.2. Information sources

The search was conducted using ASSIA, CINAHL, Cochrane library, Embase, PsycINFO, and PubMed databases. Reference tracking of included studies were performed to access further information and retrieve data from the primary sources. A hand searching of the literature was also conducted on Google scholar to gather information from grey literature.

2.3. Search strategy

A comprehensive search strategy was designed, and this included multiple search strings and numerous databases. Subsequently the literature was searched systematically to develop a refined list of quotations/narratives related to definition of frailty. The search was performed with the following terms: "Frail*" or "pre-frail*" or "pre frail*" and "definition*" or "defined as" or "Consensus statement".

2.4. Study selection

Titles and abstracts of studies were screened by a single reviewer (DS) considering inclusion and exclusion criteria and selected studies underwent full text evaluation. Full texts were assessed by two independent reviewers (DS and ROC). Disagreements were discussed and resolved by a third reviewer (AL).

2.5. Data collection process

A data extraction form was developed and used by reviewers for extraction (DS and MOD), and synthesis (DS and ROC). The following data were extracted from the included studies: article identification number, reviewer, article title, year, author(s) name, country of origin, type of publication, population/ participant characteristics, setting, assessment tools (if any), definition of frailty. Definitions and/or characteristics of frailty were extracted as first order constructs by taking direct quotes from studies and were pooled into the data extraction form (Butler et al., 2016). Quality appraisal was conducted using the Joanna Briggs Institute Checklist for Text and Opinion (See Supplementary Fig. 1).

2.6. Synthesis of the results and additional analyses

A thematic analysis was performed on the extracted data using NVivo software (NVivo Pro version 11.4) where the definitions, statements or quotations related to frailty were categorised under themes and coded accordingly. Codes were developed to reflect the meaning of frequently occurring statements within each category. Common emerging codes were grouped to form sub-themes, after which a final list of codes was merged to form specific major themes with their associated sub-themes.

3. Results

The results of the search strategy are summarised in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram (Moher et al., 2009) (Fig. 1). A total of 86 out of 6522 studies were included in the analysis; most were review articles including opinion pieces and editorials. Features of included studies including their design, country of origin, setting, and the frailty assessment instrument used (where applicable) are summarised in Supplementary Table 1. The Joanna Briggs Institute quality appraisal confirmed the inclusion of all 86 studies (Supplementary Table 2). Overall, data related to definitions of frailty were categorised according to five major themes with their associated sub-themes. The major themes were "types of definitions", "characteristics of frailty", "associated factors", "mechanism", and "adverse health status change/outcomes". A conceptual map of these five themes is depicted in Fig. 2. A word cloud presenting the most commonly repeated phrases identified in the included studies is shown in Fig. 3.

3.1. Theme 1. Types of definitions

Various definitions of frailty were reported in the included studies. These definitions can be grouped under several sub-themes. The most common sub-themes were "operational

Table 1
Number of studies categorised under themes and sub-themes.

Theme	Number of studies categorised under	Subtheme	Number of studies categorised under
Theme 1: Types of definitions	78*	Operational definition	56
		Conceptual definition	27
		Theoretical definition	25
		Definition of frailty from older adults' perspective	3
Theme 2: Characteristics of frailty	29*	Multi-domain and multi-dimensional state	16
		Deficits/decline	9
		Continuum- dynamic concept	9
		Weakness	4
		Clinically identifiable	3
Theme 3: Associated factors	21*	Age	6
		Comorbidity	6
		Nutritional deficits	8
		Sarcopenia	5
		Social networks and environment	3
Theme 4. Mechanism	14*	Reduced adaptability	11
		Hormonal dysregulation	4
Theme 5. Adverse health status change/outcomes	27*	Disability	13
		Increased risk of mortality	8
		Other healthcare-related outcomes	12

*Studies were categorised under sub-themes multiple times.

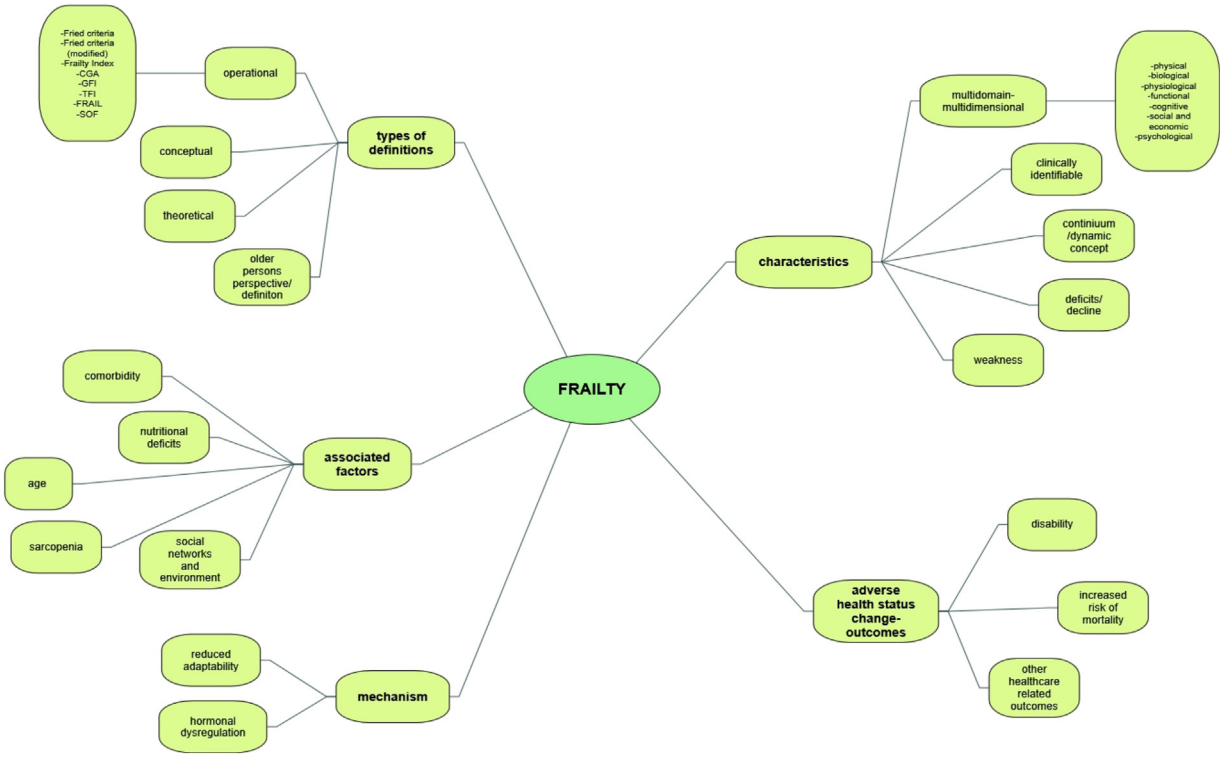

Fig. 2. Conceptual map of frailty reported in studies: Major themes with subthemes.

definitions" (n = 56) which included frailty assessments, and "conceptual definitions" (n = 27) (Table 1). Only a small number of studies reported definitions of frailty based on the perspective of older adults (n = 3). Similarly, we found only few papers using a consensus approach to define frailty (Dartigues and Amieva, 2014; Gobbens et al., 2010a; Kelaiditi et al., 2013; Rodriguez-Manas et al., 2013).

3.1.1. Operational definition

Frailty was primarily defined using operational definitions in the majority of the studies (Apóstolo et al., 2017; Canevelli and Cesari, 2015; Cesari et al., 2014a; Gobbens et al., 2010b). Gwyther et al. (2017) concluded that *". . . most did so in terms of an operational definition, i.e. one that is based on observable criteria and regularly used to identify or diagnose frailty"*. This definition utilises an array of assessment tools to identify frailty based on a set of physical criteria or a combination of several deficits in a multidimensional approach (Carvalho et al., 2017; Fried et al., 2001; Mohandas et al., 2011; Rockwood and Mitnitski, 2011). The most commonly mentioned operational definitions among all studies were the Frailty Phenotype by Fried et al. (2001) (n = 44) and the Frailty Index by Rockwood and Mitnitski (2011) (n = 26). Other common operational definitions included those provided by the Tilburg Frailty Indicator (Gobbens et al., 2010c), Groningen Frailty Indicator (Peters et al., 2012), Frail Scale (Morley et al., 2012), and by Comprehensive Geriatric Assessment (Wieland and Hirth, 2003).

3.1.2. Conceptual definition

Frailty was also defined according to a conceptual definition in many studies included in this systematic review (Abate et al., 2007; Bernabei et al., 2017; Boers and Cruz Jentoft, 2015; Evenhuis et al., 2013; Gobbens et al., 2010b, 2010d; Gordon et al., 2014; Grenier, 2007; Mohandas et al., 2011; Sunfrail Project, 2018; Wou and Conroy, 2013). The majority described a clinical syndrome with reduced physiological reserve leading to disability and other studies suggested that frailty is associated with an increased risk of vulnerability (Abate et al., 2007; Abellan van Kan et al., 2010; Ahmed et al., 2007; Bergman et al., 2007; Calvani et al., 2015; Gordon et al., 2014; Keevil and Romero-Ortuno, 2015). Abellan van Kan et al. (2008a) proposed that, *"Frailty is a clinical condition and should be considered as a predisability state"*. Some studies reported the term "vulnerability" as an outcome of frailty (Gordon et al., 2014), while others (Bissot et al., 2016; Cesari et al., 2014b; Donatelli and Somes, 2017) described frailty as a state of vulnerability. Specifically, Bergman et al. (2007) stated that, *"the core feature of frailty is increased vulnerability to stressors due to impairments"*.

Abellan van Kan et al. (2010) also referred to frailty as a multisystem syndrome, *"a clinical syndrome resulting from multi-system impairments separated from the normal aging process. As a syndrome, associated impairments such as sarcopenia, functional decline, neuroendocrine dysregulation, and immune impairments can occur in combination"*.

Similarly, Ahmed et al. in their narrative overview of frailty as an emerging syndrome stated that the current evidence suggests that frailty is a *"fairly common biological syndrome in the elderly, identified by decreased reserves in multiple organ systems. It is manifested as loss of skeletal muscle mass (sarcopenia), abnormal function in inflammatory and neuroendocrine systems, and poor energy regulation"*, providing evidence that it is a defined syndrome associated with ageing and loss of reserve (Ahmed et al., 2007). Frailty is described in some studies (n = 9) as a complex predominantly geriatric syndrome (Calvani et al., 2015; Dent et al., 2016; Fulop et al., 2015; Ruan et al., 2015), with multiple causes (Dent et al., 2016; Fulop et al., 2015; Keevil and Romero-Ortuno, 2015; Mohandas et al., 2011; Sargent and Brown, 2017), and characterised by reduced homeostatic reserves (Calvani et al., 2015; Fulop et al., 2015; Nash, 2013; Sargent and Brown, 2017; Storey and Thomas, 2004) and diminished strength (Keevil and Romero-Ortuno, 2015; Nash, 2013). Fulop et al. (2015) stated that frailty is: *"A complex geriatric syndrome, because of its multicausal nature, thus resulting from the cumulative erosion of reserves in*

Fig. 3. Frailty as a word cloud reported in studies.

multiple physiological systems and organs manifested by a homeostasis" where Dent et al. (2016) indicated *"Frailty may be considered to be a geriatric syndrome reflecting multi-system dysfunction and in which individuals are able to dynamically transition between severity states"*. According to Tocchi (2015), *frailty is described as "a tenuous state of health that is the result of the complex interplay of physiological, psychosocial, and environmental stressors that increases an older adult's susceptibility to adverse health outcomes.* Other similar studies suggest that there is an intricate connection between function and conceptual definitions of frailty as a syndrome (Bernabei et al., 2017; Gobbens et al., 2010b).

3.1.3. Theoretical definition

Abellan Van Kan et al. (2008b) proposed the importance of models to define frailty as *"Domains, diagnostic criteria, assessment tools and obviously the definition of frailty will change depending on the model of frailty adopted"* and concluded that there are two main models to identify frailty in the current literature; the Physical phenotype, and the Multi-domain phenotype. Cederholm et al. proposed that the physical phenotype of frailty; *"Encompasses states as exhaustion, weakness, and slowness, whereas sarcopenia, combining mass and function, is more strictly focused on muscles"* (Cederholm, 2015) while the multi-domain phenotype included nutritive, cognitive, and sensory domains (Cigolle et al., 2009; Gobbens et al., 2010a). Overall, a theoretical definition, which described frailty as a multi-dimensional construct is generally accepted (Cigolle et al., 2009; Gobbens et al., 2010a; Sargent and Brown, 2017; Sieber, 2017).

Different types of frailty were reported in the literature with frailty being categorised as either one, or a combination of, physical (Aubertin-Leheudre et al., 2015; Calvani et al., 2015; Cesari et al., 2014b; Cruz-Jentoft, 2013; Fougère et al., 2015; Fried et al., 2001; Gordon et al., 2014; Studenski et al., 2004), cognitive (Aubertin-Leheudre et al., 2015; Canevelli and Cesari, 2015; Dartigues and Amieva, 2014; Kelaiditi et al., 2013; Rodríguez-Mañas and Sinclair, 2014; Ruan et al., 2015; Sargent and Brown, 2017), nutritional (Bales and Ritchie, 2002; Bartali et al., 2006; Visvanathan, 2009), and social (Bunt et al., 2017; Makizako et al., 2015; Rodríguez-Mañas and Sinclair, 2014; Tsutsumimoto et al., 2017) domains.

3.1.4. Definition of frailty from older adults' perspective

Schoenborn et al. (2018) reported that older adults perceive frailty as having multiple physical symptoms which associate with older age. However, some of them perceive frailty as a state different from a medical syndrome; *"Frailty is a generalization and I don't think it has really any place in the medical conversation"* and refer to the condition in psychological terms, as a state of mind. As stated; *"I think frailty is a state of mind . . . thinking of yourself as frail then you gonna have some subsequent frail behavior."* (Schoenborn et al., 2018). Another study investigating older adults' perspective of frailty concluded that frailty was associated with physical appearance (the body, size, strength and power) and emotional experiences (helplessness and irresponsibility) (Grenier, 2007). Puts et al. (2009) stated that *"frailty is viewed as a state that is characterized by reduced health together with psychological and social limitations that leads to a situation in which a person is not able to do what he/she enjoys"*.

3.2. Theme 2. Characteristics of frailty

Frailty was described as a clinically identifiable geriatric syndrome with multiple dimensions, deficits and weakness, across a continuum (Abellan van Kan et al., 2008a; Calvani et al., 2015; Rodriguez-Manas et al., 2013; Siriwardhana et al., 2018; Walston et al., 2006).

3.2.1. Multi-domain and multi-dimensional state

Most studies indicated that frailty is both a multi-domain and multi-dimensional state (n = 16) including physical, biological, physiological, functional, cognitive, psychological, social and economic aspects (Abellan van Kan et al., 2010, 2008a; Bunt et al., 2017; Fried et al., 2004; Gallucci et al., 2009; Gobbens et al., 2010e; Gwyther et al., 2017; Maxwell and Wang, 2017; Rodriguez-

Manas et al., 2013; Vella Azzopardi et al., 2018). The multi-domain model of frailty is important because it does not assume that frailty is homogenous across populations.

The physical domain of frailty was reported by Maxwell and Wang (2017) as *"characterised by gradual loss of energy, strength, endurance, and motor control (e.g. grip strength, gait speed, balance"*. The biological dimension to frailty was emphasised by Mohandas et al. (2011) who described it as *"a process where inflammation, neuroendocrine deregulation, and sarcopenia contribute to a gradual decline in health"*. The recently completed Sunfrail Project (2018) defined frailty as a *"physiological syndrome characterised by reduction of functional reserves and resistance to 'stressors"*.

There may however be an overemphasis on physical aspects of frailty. Ernsth-Bravell and Mölstad (2010) reported that frailty has a functional domain; *"functional components, such as decreased function in balance, mobility and activity, are often included in the definition of frailty"*. Similarly, other domains such as cognition should be included; Kelaiditi et al. (2013) suggested that *"at present, the concept of frailty has focused principally on the physical domain. However, some recent work has started considering cognition in the definition of frailty"*.

Psychological, social and economic domains of frailty are also reported, associated with financial capacity, well-being, functional limitations, depression, and social capital (Manthorpe and Iliffe, 2015). Markle-Reid and Browne (2003) described frail older adults *"as those who are unable to fulfil social roles and perform activities of daily living"*.

3.2.2. Deficits/decline

A characteristic hallmark of frailty is deficit accumulation as mentioned in many studies (n = 9). Biological, functional, and psychological deficits including social limitations, and general decline were reported to be associated with frailty (Calvani et al., 2015; Gwyther et al., 2017; Kelaiditi et al., 2013; Lang et al., 2009; Maxwell and Wang, 2017; Rockwood and Mitnitski, 2011; Siriwardhana et al., 2018; Sunfrail Project, 2018). Frailty was reported as a state of accumulating deficits by Rockwood and Mitnitski (2011) where Nash (2013) reported frailty as *"a geriatric syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems"*.

3.2.3. Continuum- dynamic concept

Nine studies described frailty as a continuum and a dynamic concept between robustness and disability and death (Abellan van Kan et al., 2008a; Alexa et al., 2013; Dent et al., 2016; Gobbens et al., 2010b; Hogan et al., 2003; Maxwell and Wang, 2017; Mohandas et al., 2011; Sunfrail Project, 2018). Frailty was described by Abellan van Kan et al. (2008a) as *" . . . a part of a continuum situated between the normal physiological changes of aging and the final state of disability and death"*. Similarly, Alexa et al. (2013) stated that *"Frailty is a part of different "vicious loops" including sarcopenia, neuromuscular impairment, falls and fractures, immobilization, malnutrition, impaired protein synthesis"*. A dynamic state associated with gradual losses was referred (Sunfrail Project, 2018) with Maxwell and Wang (2017) stating that: *"frailty is characterised by gradual loss of energy, strength, endurance, and motor control"*. Frailty was reported by Waltson et al. as being associated with *"instability"* (Walston et al., 2006).

3.2.4. Weakness

Weakness was described as one of the main characteristics of frailty (n = 4) (Fried et al., 2001; Rodriguez-Manas et al., 2013; Theou and Rockwood, 2015) as Rockwood et al. (1996) stated: *"Medical practitioners have often used the term "frailty" to characterize the weakest and most vulnerable subset of older adults"*.

3.2.5. Clinically identifiable

Three studies specifically referred to frailty as a clinically identifiable condition (Gwyther et al., 2017; Rodriguez-Manas et al., 2013); with Siriwardhana et al. (2018) stating that frailty is: *"an important clinically identifiable state . . . "*.

3.3. Theme 3. Associated factors

Factors mostly associated with frailty were described in literature as "age" (n = 6), "comorbidity" (n = 6), "nutritional deficits" (n = 8), and "sarcopenia" (n = 5). Social networks and environment have also been described as antecedent or factors associated with frailty (Tocchi, 2015; Manthorpe and Iliffe, 2015; Markle-Reid and Browne, 2003).

3.3.1. Age

Age was reported in many studies as a main associated factor related to frailty (Malaguarnera et al., 2013; Markle-Reid and Browne, 2003; Nash, 2013; Puts et al., 2009; Topinková, 2008; Xue, 2011). However, Storey and Thomas (2004) argued that the relationship between age and frailty should be considered from a different perspective; *"Frailty is not the result of ageing ... It is more prevalent with increasing age, but some young people are frail and most older people are not"*.

3.3.2. Comorbidity

Comorbidity was reported as another factor associated with frailty (Alexa et al., 2013; Carvalho et al., 2017; Markle-Reid and Browne, 2003; Topinková, 2008) as described by Gielen et al. (2012) frailty is a *" . . . combination of functional deficits and comorbid disorders"*. Similarly, Storey and Thomas (2004) indicated that *"Frail elders tend to have multiple coexisting illnesses or conditions (comorbidities), because illnesses that occur late in life are persistent, less lethal, and thus accumulate . . . "*

3.3.3. Nutritional deficits

Evidence also suggests that frailty is associated with nutritional deficits. Many studies reported the effect of malnutrition and weight loss on the development of frailty (Alexa et al., 2013; Fried et al., 2001; Nash, 2013; Rockwood and Mitnitski, 2011; Topinková, 2008; Visvanathan, 2009). While classically associated with reduced body mass and sarcopenia, there is also a connection between obesity and frailty; *" . . . biological markers linked to frailty, such as C-reactive proteins, also have been associated with obesity"* (Mohandas et al., 2011).

Alexa et al. (2013) suggested that frailty is part of vicious circle including malnutrition and impaired protein synthesis as well as other factors. However, it was argued that interventions targeting nutrition could help reverse frailty; *"Evidence suggests that cognitive frailty can be reversible with nutritional . . . interventions, singly or in combination"* (Maxwell and Wang, 2017).

3.3.4. Sarcopenia

Some studies stated that there is a connection between physical aspects of frailty and sarcopenia

(Afilalo, 2016; Cesari et al., 2014b; Nash, 2013). It is stated by Cruz-Jentoft (2013) that *"Sarcopenia can be considered as being a key pathway between frailty and disability"*. However, the difference between frailty and sarcopenia was explained by Cederholm (2015); *"frailty is age related, whereas sarcopenia is also related to disease, starvation, and disuse"* and Afilalo (2016) stated that *"Sarcopenia, on the other hand, is a more age-related, slowly progressive decline in muscle mass and strength, moderately affecting daily living activities. Frailty can be reversible, but this is not true for sarcopenia, which is a normal physiological change."*

3.3.5. Social networks and environment

Social engagement and environmental factors are reported to be associated with frailty (Tocchi, 2015; Manthorpe and Iliffe, 2015; Markle-Reid and Browne, 2003). Frail older adults were described as having diminished ability to perform social and practical activities of daily living (Markle-Reid and Browne, 2003) and being vulnerable to sudden changes in their environment (Manthorpe and Iliffe, 2015).

3.4. Theme 4. Mechanism

The mechanism of frailty was mostly explained by reduced adaptability (n = 11) and hormonal dysregulation (n = 4).

3.4.1. Reduced adaptability

Frailty was frequently described as an increased vulnerability to stressors (Cigolle et al., 2009; Fried et al., 2004; Makizako et al., 2015; Maxwell and Wang, 2017; Nash, 2013; Sunfrail Project, 2018; Walston et al., 2006; Wou and Conroy, 2013). Loss of reserve was also reported as a dimension of frailty (Storey and Thomas, 2004). Manthorpe and Iliffe (2015) explained the mechanism associated with this as a *" . . . distinctive state related to the ageing process, as multiple body systems gradually lose their in-built reserves. This means the person vulnerable to sudden changes in health triggered by seemingly small events such as minor infection or a change in meditation"*. Similarly, Cigolle et al. (2009) stated that frailty is associated with *" . . . decreased reserve and resistance to stressors . . . "*. Alexa et al. (2013) described this mechanism as *"high vulnerability and reduced ability to remain homeostasis"*.

3.4.2. Hormonal dysregulation

The role of hormonal dysregulation was also highlighted in several papers (Bortz, 2002; Mohandas et al., 2011; Nash, 2013; Sieber, 2017). Sieber (2017) reported that *"present concepts favour a multiple hormonal dysregulation leading to frailty."* Bortz (2002) described the relation between frailty and hormonal dysregulation as *"Sarcopenia, neuroendocrine dysregulation, and immune dysfunction are the "physiologic triad" felt to underpin the syndrome"*.

3.5. Theme 5. Adverse health status change/outcomes

Frailty was often conceptualised by authors as associated with adverse health outcomes (De Lepeleire et al., 2009; Gobbens et al., 2010e; Makizako et al., 2015; Maxwell and Wang, 2017; McMillan and Hubbard, 2012; Sunfrail Project, 2018; Topinková, 2008), mostly commonly disability (n = 13), increased risk of mortality (n = 8), and other outcomes such as dependency and falls (n = 12).

3.5.1. Disability

Many studies reported disability as an adverse outcome associated with frailty (Alexa et al., 2013; Cesari et al., 2014b; Malaguarnera et al., 2013; Mohandas et al., 2011; Morley, 2016; O'Caoimh et al., 2018b; Puts et al., 2009; Sargent and Brown, 2017; Sunfrail Project, 2018; Theou and Rockwood, 2015). Frailty was described as a period between naturally occurring changes of ageing and disability (Abellan van Kan et al., 2008a). The relationship between disability and frailty was discussed in many studies with most concluding that while related they are two different syndromes/conditions. Dent et al. (2016) reported that *"Multiple reasons exist as to why it is so difficult to define frailty, including . . . the inherent difficulty in distinguishing frailty from both ageing and disability"*. Heuberger (2011) explained the difference as frailty being a *"predecessor to disability . . . there was an event or stressor that catapulted the frail older adult into frank disability . . . "*. Keevil and Romero-Ortuno (2015) also mentioned this distinction but highlighted that they can be found together, reporting that *"There is also wide agreement that frailty is distinct from disability and co-morbidity, although all may co-exist"*.

3.5.2. Increased risk of mortality

Many definitions of frailty identified increased risk of mortality as being associated with frailty (Gwyther et al., 2017; Keevil and Romero-Ortuno, 2015; Makizako et al., 2015; McMillan and Hubbard, 2012; Siriwardhana et al., 2018; Sunfrail Project, 2018). For example, Hogan et al. (2003) described frailty as *" . . . the midpoint between independence and pre-death"*. Similarly, Rockwood and Mitnitski (2011) stated that frail people are *"at an increased risk of adverse health outcomes (including death)"*.

3.5.3. Other healthcare-related outcomes

Many studies highlighted that frailty results in an increased risk for hospital and institutional (long-term nursing) care as it requires specialised geriatric interventions and increases dependency levels (Gwyther et al., 2017; Makizako et al., 2015; Malaguarnera et al., 2013; Markle-Reid and Browne, 2003; Siriwardhana et al., 2018; Sunfrail Project, 2018). Manthorpe and Iliffe (2015) described dependency as an outcome in frail adults affirming that a *"heightened risk of adverse health outcomes-can increase reliance (sometimes termed dependency) on others"*. Lally and Crome (2007) concluded *"subsequent exposure to further minor environmental stresses may be sufficient in a frail person to lead to dependency"*. Increased risk of falls was also reported as a negative outcome of frailty (Gwyther et al., 2017; Siriwardhana et al., 2018), and this features in the definition proposed by the Sunfrail Project (2018) *"decreased physiological reserve contributing to an increased risk of falls . . . "*.

4. Discussion

To our knowledge, this systematic review provides the first qualitative meta-aggregative systematic review with thematic analysis of frailty, an increasingly important and highly prevalent age-associated syndrome, which despite an increasing number of research publications and numerous validated screening and assessment instruments still lacks a gold standard consensus definition (de Vries et al., 2011). This systematic review revealed that there is a great deal of heterogeneity among the many studies' definitions and terminology relating to the construct of frailty available in the current literature. We noted that not all studies proposed their own definition of frailty, but rather used definitions or elements derived from other studies. While this suggests that a consensus approach to categorising frailty is beginning to emerge, no clear pattern was evident, and we concur that as yet no internationally agreed gold standard definition exists (Borges & Menezes., 2011; Rodriguez-Manas et al., 2013). Most empirical studies focused predominantly on physical aspects of frailty and many referred to operational definitions regarding its assessment. Both empirical studies and non-empirical findings including editorials and opinion pieces referred to a multidimensional construct, and others described cognitive, social, and nutritional frailty (Aubertin-Leheudre et al., 2015; Bales and Ritchie, 2002; Bartali et al., 2006; Bunt et al., 2017; Canevelli and Cesari, 2015; Dartigues and Amieva, 2014; Kelaiditi et al., 2013; Makizako et al., 2015; Rodríguez-Mañas and Sinclair, 2014; Ruan et al., 2015; Sargent and Brown, 2017; Tsutsumimoto et al., 2017; Visvanathan, 2009). Although there is no consensus definition, our systematic review attempted to derive a comprehensive definition for frailty, encompassing its complex nature. Specifically, we categorised the main domains of frailty and developed a conceptual map to depict the current perspectives of various definitions of frailty.

Definitions or terminology describing frailty were reported in the literature in many different contexts and settings, which may have influenced how they were defined and used. Many definitions considered frailty as a concept; framing frailty as a physical syndrome, and a state of vulnerability and limitations (Bergman et al., 2007; Nash, 2013; Rockwood and Mitnitski, 2011). Most studies described methods to identify frailty rather than clarifying the main components of the syndrome, and many descriptions of frailty were unidimensional with studies not considering the psychosocial aspects. These were predominantly those focusing on physical frailty. In contrast, some studies addressed frailty as a multidimensional and multifactorial construct (Dent et al., 2016; Fulop et al., 2015) often using the deficit accumulation model exemplified by the Frailty Index. Specific focus on the psychological, social, economic and other domains of frailty is warranted for future studies.

Few studies reported frailty definitions or constructs that incorporated the perspectives of healthcare professionals, experts in frailty, or older adults including those with frailty. Likewise, few consensus studies were available (Morley et al., 2013; Rodriguez-Manas et al., 2013). The literature investigating general clinicians' and allied health professionals' perceptions of frailty show that there is a knowledge gap and a lack of understanding of the nature of frailty, especially the malleability and potential for reversibility of the syndrome (D'Avanzo et al., 2017; Gwyther et al., 2018). While some policy makers and healthcare providers conceive that frailty is not amenable to intervention (Gwyther et al., 2018), others believe it can be prevented by screening and applying proactive interventions at the pre-frail stage (D'Avanzo et al., 2017). This is of great importance since health care professionals including nurses providing care to older adults are responsible for delivering holistic care to this cohort and a better understanding of their view of frailty would help better categorise frailty from a practical perspective (Nicholson et al., 2017). These need to consider not only the physical or biological aspects of frailty, but also psychological, social, economic and other dimensions and their impact on patient care. This study highlighted key characteristics and associated factors related to frailty including multi-domain constructs, deficits, weakness, and a clinically identifiable continuum in relation to older age, comorbidities, sarcopenia, and nutrition, highlighting the growing importance of the multidimensional approach to defining frailty. The conceptual map, which was developed following the thematic analysis could be used to aid nurses and other health professionals in considering all aspects of frailty, the whole picture, when managing the care of older adults and their families. This could also help support nurse and healthcare professional education on frailty, something which has been highlighted as important but still under-developed (Windhaber et al., 2018).

Although the data were obtained through a systematic review of the existing literature and a robust thematic analysis process, a few limitations were encountered. This systematic review was limited to studies in English only, potentially missing some relevant non-English papers. Furthermore, our systematic review was limited to only those studies published after 2000, predominantly after the publication of the seminal paper describing the frailty phenotype by Fried et al. (Fried et al., 2001). Subsequently, we performed an extensive review of the reference lists from relevant studies to avoid missing other potentially important papers published prior to 2000. Another limitation is that a critical appraisal of the quality of the included studies may not be meaningful. Although a quality assessment was conducted using the Joanna Briggs Institute checklist for text and opinion papers, the heterogeneity of the papers included limited the utility of this. However, it was not the intention of the paper to review all aspects of frailty in detail. Instead, we aimed to identify existing definitions by type. Additional themes identified from these were included to explore the definitions and enrich the discussion. We believe the validity and nature of the empirical evidence is more important and this review should not be considered a comprehensive overview of all the themes identified. An evaluation of the evidence behind these statements was not the primary objective. In addition, another limitation is that data were obtained only from the medical/nursing but not the sociological literature. However, the views of health care practitioners' and older adults' on factors contributing to a definition of frailty in the medical and nursing literature were considered; albeit few were found suggesting that this is an inherent limitation of current frailty discussions and definitions.

5. Conclusions

This study re-affirmed that there is as yet no agreed definition of frailty in the medical literature (Borges and Menezes, 2011), though several key features were found across studies. The two most commonly used frailty classification approaches, acknowledged to measure different constructs – the Fried Frailty Phenotype and the deficit accumulation theory as measured using a Frailty Index (Cesari et al., 2014), still predominate the discourse, though most studies we found in this systematic review considered frailty as a physical syndrome and focused on its assessment. We derived a conceptual map through a qualitative analysis approach to improve understanding of the different aspects of frailty, highlighting that frailty is more complex than a mere unidimensional measure of physical vulnerability. Instead it is a multi-domain, multi-dimensional construct predisposing to adverse health outcomes. We suggest that a unifying consensus definition for frailty could be reached by the integration of evidence from the literature together with the opinions of international multidisciplinary experts, practicing healthcare professionals and older people themselves. It is urgently needed and should be a focus for ongoing and future research, particularly as it is over five years since the last published Delphi consensus studies (Morley et al., 2013; Rodriguez-Manas et al., 2013). This will not only facilitate the delivery of tailored treatment strategies, but also help in the development of preventative strategies (Puts et al., 2017; Sacha et al., 2017).

Author contributions

DS, ROC, NC, AL, MOD- Made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data.

DS, ROC, NC, AL, MOD- Involved in drafting the manuscript or revising it critically for important intellectual content;

DS, ROC, NC, AL, MOD- Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content;

DS, ROC, NC, AL, MOD- Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding statement

This research received no specific grant from any funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

None.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijnurstu.2018.12.014.

References

Abate, M., Di Iorio, A., Di Renzo, D., Paganelli, R., Saggini, R., Abate, G., 2007. Frailty in the elderly: the physical dimension. Europa Medicophysica 43 (3), 407–415.
Abellan van Kan, G., Rolland, Y.M., Morley, J.E., Vellas, B., 2008a. Frailty: toward a clinical definition. J. Am. Med. Dir. Assoc. 9 (2), 71–72. doi:http://dx.doi.org/10.1016/j.jamda.2007.11.005.
Abellan van Kan, G., Rolland, Y., Houles, M., Gillette-Guyonnet, S., Soto, M., Vellas, B., 2010. The assessment of frailty in older adults. Clin. Geriatr. Med. 26 (2), 275–286. doi:http://dx.doi.org/10.1016/j.cger.2010.02.002.
Abellan Van Kan, G., Rolland, Y., Bergman, H., Morley, J.E., Kritchevsky, S.B., Vellas, B., 2008b. The I.A.N.A. Task force on frailty assessment of older people in clinical practice. J. Nutr. Health Aging 12 (1), 29–37. doi:http://dx.doi.org/10.1007/BF02982161.
Afilalo, J., 2016. Conceptual models of frailty: the sarcopenia phenotype. Can. J. Cardiol. 32 (9), 1051–1055. doi:http://dx.doi.org/10.1016/j.cjca.2016.05.017.
Ahmed, N., Mandel, R., Fain, M.J., 2007. Frailty: an emerging geriatric syndrome. Am. J. Med. 120 (9), 748–753. doi:http://dx.doi.org/10.1016/j.amjmed.2006.10.018.
Alexa, I.D., Ilie, A.C., Moroşanu, A., Voica, A., 2013. Approaching Frailty as the New Geriatric Syndrome, Vol. 117. , pp. 680–685.
Apóstolo, J., Cooke, R., Bobrowicz-Campos, E., Santana, S., Marcucci, M., Cano, A., Holland, C., 2017. Predicting risk and outcomes for frail older adults: an umbrella review of frailty screening tools. JBI Database System. Rev. Implement. Rep. 15 (4), 1154–1208. doi:http://dx.doi.org/10.11124/JBISRIR-2016-003018.
Apostolo, J., Cooke, R., Bobrowicz-Campos, E., Santana, S., Marcucci, M., Cano, A., Holland, C., 2018. Effectiveness of interventions to prevent pre-frailty and frailty progression in older adults: a systematic review. JBI Database System. Rev. Implement. Rep. 16 (1), 140–232. doi:http://dx.doi.org/10.11124/JBISRIR-2017-003382.
Aubertin-Leheudre, M., Woods, A.J., Anton, S., Cohen, R., Pahor, M., 2015. Frailty clinical phenotype: a physical and cognitive point of view. Nestlé Nutr. Inst. Workshop Ser. 83, 55–63. doi:http://dx.doi.org/10.1159/000382061.
Bales, C.W., Ritchie, C.S., 2002. Sarcopenia, weight loss, and nutritional frailty in the elderly. Annu. Rev. Nutr. 22, 309–323. doi:http://dx.doi.org/10.1146/annurev.nutr.22.010402.102715.
Bartali, B., Frongillo, E.A., Bandinelli, S., Lauretani, F., Semba, R.D., Fried, L.P., Ferrucci, L., 2006. Low nutrient intake is an essential component of frailty in older persons. J. Gerontol. A Biol. Sci. Med. Sci. 61 (6), 589–593.
Bergman, H., Ferrucci, L., Guralnik, J., Hogan, D.B., Hummel, S., Karunananthan, S., Wolfson, C., 2007. Frailty: an emerging research and clinical paradigm - issues and controversies. J. Gerontol. – Ser. A Biol. Sci. Med. Sci. 62 (7), 731–737.
Bernabei, R., Benjak, T., Kern, A., Junius-Walker, U., Macijauskiene, J., Onder, G., Caballero-Mora, M.Á., 2017. Knowing Frailty at Individual Level: a Systematic Review. (Vol. 724099/ADVANTAGE, pp. 1-30). European Union.
Bieniek, J., Wilczynski, K., Szewieczek, J., 2016. Fried frailty phenotype assessment components as applied to geriatric inpatients. Clin. Interv. Aging 11, 453–459. doi:http://dx.doi.org/10.2147/cia.S101369.
Bissot, M., Henin, P.Y., Aunac, S., Colinet, B., Barvais, L., Simonet, O., De Kock, M., 2016. Preoperative frailty assessment: a review. Acta Anaesthesiol. Belg. 67 (4), 157–173.
Boers, M., Cruz Jentoft, A.J., 2015. A new concept of health can improve the definition of frailty. Calcif. Tissue Int. 97 (5), 429–431. doi:http://dx.doi.org/10.1007/s00223-015-0038-x.
Borges, L.L., Menezes, R.L., 2011. Definitions and markers of frailty: a systematic review of literature. Rev. Clin. Gerontol. 21 (1), 67–77. doi:http://dx.doi.org/10.1017/S0959259810000304.
Bortz, I.W.M., 2002. A conceptual framework of frailty: a review. J. Gerontol. – Ser. A Biol. Sci. Med. Sci. 57 (5), M283–M288.
Botes, A., 2002. Concept analysis: some limitations and possible solutions. Curationis 25 (3), 23–27. doi:http://dx.doi.org/10.4102/curationis.v25i3.779.
Bunt, S., Steverink, N., Olthof, J., Schans, C., Hobbelen, J., 2017. Social frailty in older adults: a scoping review. Eur. J. Ageing 14 (3), 323–334. doi:http://dx.doi.org/10.1007/s10433-017-0414-7.
Buta, B.J., Walston, J.D., Godino, J.G., Park, M., Kalyani, R.R., Xue, Q.L., Varadhan, R., 2016. Frailty assessment instruments: systematic characterization of the uses and contexts of highly-cited instruments. Ageing Res. Rev. 26, 53–61. doi:http://dx.doi.org/10.1016/j.arr.2015.12.003.
Butler, A., Hall, H., Copnell, B., 2016. A guide to writing a qualitative systematic review protocol to enhance evidence-based practice in nursing and health care. Worldviews Evid. Nurs. 13 (3), 241–249. doi:http://dx.doi.org/10.1111/wvn.12134.
Calvani, R., Marini, F., Cesari, M., Tosato, M., Anker, S.D., Von Haehling, S., et al., 2015. Biomarkers for physical frailty and sarcopenia: State of the science and future developments. J. Cachexia Sarcopenia Muscle 6 (4), 278–286. doi:http://dx.doi.org/10.1002/jcsm.12051.
Canevelli, M., Cesari, M., 2015. Cognitive frailty: what is still missing? J. Nutr. Health Aging 19 (3), 273–275. doi:http://dx.doi.org/10.1007/s12603-015-0464-5.
Cardona-Morrell, M., Hillman, K., 2015. Development of a tool for defining and identifying the dying patient in hospital: criteria for Screening and triaging to Appropriate alternative care (CriSTAL). BMJ Support. Palliat. Care 5 (1), 78–90. doi:http://dx.doi.org/10.1136/bmjspcare-2014-000770.
Cardona-Morrell, M., Lewis, E., Suman, S., Haywood, C., Williams, M., Brousseau, A. A., et al., 2017. Recognising older frail patients near the end of life: what next? Eur. J. Intern. Med. 45, 84–90. doi:http://dx.doi.org/10.1016/j.ejim.2017.09.026.
Carvalho, I.Ad., Beard, J., Thiyagarajan, J.A., Sumi, Y., 2017. WHO Clinical Consortium on Healthy Ageing. Topic Focus: Frailty and Intrinsic Capacity Report of Consortium Meeting. (Vol. WHO/FWC/ALC/17.2, pp. 1-36). World Health Organisation, Geneva, Switzerland.
Cederholm, T., 2015. Overlaps between frailty and Sarcopenia definitions. Nestlé Nutr. Inst. Workshop Ser. 83, 65–69. doi:http://dx.doi.org/10.1159/000382063.
Cesari, M., Gambassi, G., Abellan van Kan, G., Vellas, B., 2014a. The frailty phenotype and the frailty index: different instruments for different purposes. Age Ageing 43 (1), 10–12. doi:http://dx.doi.org/10.1093/ageing/aft160.
Cesari, M., Landi, F., Vellas, B., Bernabei, R., Marzetti, E., 2014b. Sarcopenia and physical frailty: two sides of the same coin. Front. Aging Neurosci. 6.
Chen, L.Y., Chen, X.J., Yan, J., Chen, L.K., 2016a. Frailty is associated with long-term adverse outcome among hospitalized older patients: a prospective cohort study in China. Eur. Geriatr. Med. 7, S117.
Chen, S., Honda, T., Narazaki, K., Chen, T., Nofuji, Y., Kumagai, S., 2016b. Global cognitive performance and frailty in non-demented community-dwelling older adults: findings from the Sasaguri Genkimon Study. Geriatr. Gerontol. Int. 16 (6), 729–736. doi:http://dx.doi.org/10.1111/ggi.12546.
Cigolle, C.T., Ofstedal, M.B., Tian, Z., Blaum, C.S., 2009. Comparing models of frailty: the health and retirement study. J. Am. Geriatr. Soc. 57 (5), 830–839. doi:http://dx.doi.org/10.1111/j.1532-5415.2009.02225.x.
Collard, R.M., Boter, H., Schoevers, R.A., Voshaar, R.C.O., 2012. Prevalence of frailty in community-dwelling older persons: a systematic review. J. Am. Geriatr. Soc. 60 (8), 1487–1492. doi:http://dx.doi.org/10.1111/j.1532-5415.2012.04054.x.
Cruz-Jentoft, A., 2013. Sarcopenia: a clinical review. Rev. Clin. Gerontol. 23 (4), 267–274. doi:http://dx.doi.org/10.1017/S0959259813000154.
D'Avanzo, B., Shaw, R., Riva, S., Apostolo, J., Bobrowicz-Campos, E., Kurpas, D., Holland, C., 2017. Stakeholders' views and experiences of care and interventions for addressing frailty and pre-frailty: a meta-synthesis of qualitative evidence. PLoS One 13 (1) e0191763 doi:http://dx.doi.org/10.1371/journal.pone.0191763.
Dartigues, J.F., Amieva, H., 2014. Cognitive frailty: rational and definition from an (I.a.N.a./i.a.g.g.) international consensus group. J. Nutr. Health Aging 18 (1), 95. doi:http://dx.doi.org/10.1007/s12603-013-0437-5.
De Lepeleire, J., Iliffe, S., Mann, E., Degryse, J.M., 2009. Frailty: an emerging concept for general practice. Br. J. Gen. Pract. 59 (562), e177–182. doi:http://dx.doi.org/10.3399/bjgp09X420653.
de Vries, N.M., Staal, J.B., van Ravensberg, C.D., Hobbelen, J.S., Olde Rikkert, M.G., Nijhuis-van der Sanden, M.W., 2011. Outcome instruments to measure frailty: a systematic review. Ageing Res. Rev. 10 (1), 104–114. doi:http://dx.doi.org/10.1016/j.arr.2010.09.001.
Dent, E., Kowal, P., Hoogendijk, E.O., 2016. Frailty measurement in research and clinical practice: a review. Eur. J. Intern. Med. 31, 3–10. doi:http://dx.doi.org/10.1016/j.ejim.2016.03.007.
Dixon-Woods, M., Cavers, D., Agarwal, S., Annandale, E., Arthur, A., Harvey, J., Sutton, A.J., 2006. Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. BMC Med. Res. Methodol. 6, 35. doi:http://dx.doi.org/10.1186/1471-2288-6-35.
Donatelli, N.S., Somes, J., 2017. What is Frailty? J. Emerg. Nurs. 43 (3), 272–274. doi:http://dx.doi.org/10.1016/j.jen.2017.03.003.
Ernsth-Bravell, M., Mölstad, S., 2010. Easy-to-use definition of frailty for guiding care decisions in elderly individuals: Probability or utopia? Aging health 6 (6), 697–699. doi:http://dx.doi.org/10.2217/ahe.10.68.
Espinoza, S.E., Jung, I., Hazuda, H., 2010. Lower frailty incidence in older Mexican Americans than in older european Americans: the San Antonio longitudinal study of aging. J. Am. Geriatr. Soc. 58 (11), 2142–2148. doi:http://dx.doi.org/10.1111/j.1532-5415.2010.03153.x.
Evenhuis, H., Schoufour, J., Echteld, M., 2013. Frailty and intellectual disability: a different operationalization? Dev. Disabil. Res. Rev. 18 (1), 17–21. doi:http://dx.doi.org/10.1002/ddrr.1124.
Fairhall, N., Kurrle, S.E., Sherrington, C., Lord, S.R., Lockwood, K., John, B., Cameron, I. D., 2015. Effectiveness of a multifactorial intervention on preventing development of frailty in pre-frail older people: study protocol for a randomised controlled trial. BMJ Open 5 (2) e007091 doi:http://dx.doi.org/10.1136/bmjopen-2014-007091.
Fougère, B., Vellas, B., Van Kan, G.A., Cesari, M., 2015. Identification of biological markers for better characterization of older subjects with physical frailty and sarcopenia. Transl. Neurosci. 6 (1), 103–110. doi:http://dx.doi.org/10.1515/tnsci-2015-0009.
Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., McBurnie, M.A., 2001. Frailty in older adults: evidence for a phenotype. J. Gerontol. A Biol. Sci. Med. Sci. 56 (3), M146–M156.
Fried, L.P., Ferrucci, L., Darer, J., Williamson, J.D., Anderson, G., 2004. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J. Gerontol. – Ser. A Biol. Sci. Med. Sci. 59 (3), 255–263.

Fulop, T., McElhaney, J., Pawelec, G., Cohen, A.A., Morais, J., Dupuis, G., Larbi, A., 2015. Frailty, inflammation and immunosenescence. Interdiscip. Top. Gerontol. Geriatr. 41, 26–40.
Gallucci, M., Ongaro, F., Amici, G.P., Regini, C., 2009. Frailty, disability and survival in the elderly over the age of seventy: evidence from "the Treviso Longeva (TRELONG) Study". Arch. Gerontol. Geriatr. 48 (3), 281–283. doi:http://dx.doi.org/10.1016/j.archger.2008.02.005.
Gielen, E., Verschueren, S., O'Neill, T.W., Pye, S.R., O'Connell, M.D.L., Lee, D.M., Boonen, S., 2012. Musculoskeletal frailty: a geriatric syndrome at the core of fracture occurrence in older age. Calcif. Tissue Int. 91 (3), 161–177. doi:http://dx.doi.org/10.1007/s00223-012-9622-5.
Gobbens, R.J.J., Luijkx, K.G., Wijnen-Sponselee, M.T., Schols, J.M.G.A., 2010a. Towards an integral conceptual model of frailty. J. Nutr. Health Aging 14 (3), 175–181. doi:http://dx.doi.org/10.1007/s12603-010-0045-6.
Gobbens, R.J., Luijkx, K.G., Wijnen-Sponselee, M.T., Schols, J.M., 2010b. Toward a conceptual definition of frail community dwelling older people. Nurs. Outlook 58 (2), 76–86. doi:http://dx.doi.org/10.1016/j.outlook.2009.09.005.
Gobbens, R.J., van Assen, M.A., Luijkx, K.G., Wijnen-Sponselee, M.T., Schols, J.M., 2010c. The tilburg frailty Indicator: psychometric properties. J. Am. Med. Dir. Assoc. 11 (5), 344–355. doi:http://dx.doi.org/10.1016/j.jamda.2009.11.003.
Gobbens, R.J., Luijkx, K.G., Wijnen-Sponselee, M.T., Schols, J.M., 2010d. In search of an integral conceptual definition of frailty: opinions of experts. J. Am. Med. Dir. Assoc. 11 (5), 338–343. doi:http://dx.doi.org/10.1016/j.jamda.2009.09.015.
Gobbens, R.J., van Assen, M.A.L.M., Luijkx, K.G., Wijnen-Sponselee, M.T., Schols, J.M.G.A., 2010e. Determinants of frailty. J. Am. Med. Dir. Assoc. 11 (5), 356–364. doi:http://dx.doi.org/10.1016/j.jamda.2009.11.008.
Gordon, A.L., Masud, T., Gladman, J.R., 2014. Now that we have a definition for physical frailty, what shape should frailty medicine take? Age Ageing 43 (1), 8–9. doi:http://dx.doi.org/10.1093/ageing/aft161.
Grenier, A., 2007. Constructions of frailty in the English language, care practice and the lived experience. Ageing Soc. 27 (3), 425–445. doi:http://dx.doi.org/10.1017/S0144686X06005782.
Gwyther, H., Cooke, R., Shaw, R., Marcucci, M., Cano, A., Holland, C., 2017. Perceptions and experiences of frailty interventions: quantitative and qualitative results from a survey of partners within the European Innovation Partnership on Active and Healthy Ageing (EIP-AHA). Ageing Soc. 1–25. doi:http://dx.doi.org/10.1017/s0144686x17000265.
Gwyther, H., Shaw, R., Dauden, E.A.J., D'Avanzo, B., Kurpas, D., Bujnowska-Fedak, M., Holland, C., 2018. Understanding frailty: a qualitative study of European healthcare policy-makers' approaches to frailty screening and management. BMJ Open 8 (1) e018653 doi:http://dx.doi.org/10.1136/bmjopen-2017-018653.
Hannes, K., Pearson, A., 2012. Obstacles to the Implementation of Evidence-Based Practice in Belgium: A Worked Example of Meta-Aggregation *Synthesizing Qualitative Research* (pp. 21-39). .
Heuberger, R.A., 2011. The frailty syndrome: a comprehensive review. J. Nutr. Gerontol. Geriatr. 30 (4), 315–368. doi:http://dx.doi.org/10.1080/21551197.2011.623931.
Hogan, D.B., MacKnight, C., Bergman, H., 2003. Models, definitions, and criteria of frailty. Aging Clin. Exp. Res. 15 (3 Suppl), 1–29.
Junius-Walker, U., Onder, G., Soleymani, D., Wiese, B., Albaina, O., Bernabei, R., group, A.J.W., 2018. The essence of frailty: a systematic review and qualitative synthesis on frailty concepts and definitions. Eur. J. Intern. Med. doi:http://dx.doi.org/10.1016/j.ejim.2018.04.023.
Kaiser, M.J., Bandinelli, S., Lunenfeld, B., 2009. The nutritional pattern of frailty - Proceedings from the 5th Italian Congress of Endocrinology of Aging, Parma, italy, 27-28 March 2009. Aging Male 12 (4), 87–94. doi:http://dx.doi.org/10.3109/13685530903296706.
Keevil, V.L., Romero-Ortuno, R., 2015. Ageing well: a review of sarcopenia and frailty. Proc. Nutr. Soc. 74 (4), 337–347. doi:http://dx.doi.org/10.1017/S0029665115002037.
Kelaiditi, E., Cesari, M., Canevelli, M., Abellan Van Kan, G., Ousset, P.J., Gillette-Guyonnet, S., Vellas, B., 2013. Cognitive frailty: rational and definition from an (I.A.N.A./I.A.G.G.) International Consensus Group. J. Nutr. Health Aging 17 (9), 726–734. doi:http://dx.doi.org/10.1007/s12603-013-0367-2.
Lally, F., Crome, P., 2007. Understanding frailty. Postgrad. Med. J. 83 (975), 16–20. doi:http://dx.doi.org/10.1136/pgmj.2006.048587.
Lang, P.O., Michel, J.P., Zekry, D., 2009. Frailty syndrome: a transitional state in a dynamic process. Gerontology 55 (5), 539–549. doi:http://dx.doi.org/10.1159/000211949.
Le Cossec, C., Perrine, A.L., Beltzer, N., Fuhrman, C., Carcaillon-Bentata, L., 2016. Pre-frailty, frailty, and multimorbidity: prevalences and associated characteristics from two French national surveys. J. Nutr. Health Aging 20 (8), 860–869. doi:http://dx.doi.org/10.1007/s12603-016-0802-2.
Liu, L.K., Lee, W.J., Chen, L.Y., Hwang, A.C., Lin, M.H., Peng, L.N., Chen, L.K., 2015. Association between frailty, osteoporosis, falls and hip fractures among community-dwelling people aged 50 years and older in Taiwan: results from I-Lan longitudinal aging study. PLoS One 10 (9) e0136968 doi:http://dx.doi.org/10.1371/journal.pone.0136968.
Lockwood, C., Munn, Z., Porritt, K., 2015. Qualitative research synthesis: methodological guidance for systematic reviewers utilizing meta-aggregation. Int. J. Evid. Healthc. 13 (3), 179–187.
Makizako, H., Shimada, H., Tsutsumimoto, K., Lee, S., Doi, T., Nakakubo, S., Suzuki, T., 2015. Social frailty in community-dwelling older adults as a risk factor for disability. J. Am. Med. Dir. Assoc. 16 (11) doi:http://dx.doi.org/10.1016/j.jamda.2015.08.023 1003.e1007-1003.e1011.
Malaguarnera, M., Vacante, M., Frazzetto, P.M., Motta, M., 2013. What is the frailty in elderly? Value and significance of the multidimensional assessments. Arch. Gerontol. Geriatr. 56 (1), 23–26. doi:http://dx.doi.org/10.1016/j.archger.2011.09.017.
Manthorpe, J., Iliffe, S., 2015. Frailty - from bedside to buzzword? J. Integr. Care 23 (3), 120–128.
Markle-Reid, M., Browne, G., 2003. Conceptualizations of frailty in relation to older adults. J. Adv. Nurs. 44 (1), 58–68. doi:http://dx.doi.org/10.1046/j.1365-2648.2003.02767.x.
Maxwell, C.A., Wang, J., 2017. Understanding frailty: a nurse's guide. Nurs. Clin. North Am. 52 (3), 349–361. doi:http://dx.doi.org/10.1016/j.cnur.2017.04.003.
McMillan, G.J., Hubbard, R.E., 2012. Frailty in older inpatients: what physicians need to know. QJM 105 (11), 1059–1065. doi:http://dx.doi.org/10.1093/qjmed/hcs125.
Mohandas, A., Reifsnyder, J., Jacobs, M., Fox, T., 2011. Current and future directions in frailty research. Popul. Health Manag. 14 (6), 277–283. doi:http://dx.doi.org/10.1089/pop.2010.0066.
Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., Group, P., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 339, b2535. doi:http://dx.doi.org/10.1136/bmj.b2535.
Mohile, S.G., Velarde, C., Hurria, A., Magnuson, A., Lowenstein, L., Pandya, C., Dale, W., 2015. Geriatric assessment-guided care processes for older adults: a Delphi consensus of geriatric oncology experts. J. Compr. Canc. Netw. 13 (9), 1120–1130. doi:http://dx.doi.org/10.6004/jnccn.2015.0137.
Morley, J.E., 2016. Frailty and sarcopenia in elderly. Wien. Klin. Wochenschr. 128, 439–445. doi:http://dx.doi.org/10.1007/s00508-016-1087-5.
Morley, J.E., Malmstrom, T.K., Miller, D.K., 2012. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J. Nutr. Health Aging 16 (7), 601–608.
Morley, J.E., Vellas, B., van Kan, G.A., Anker, S.D., Bauer, J.M., Bernabei, R., Walston, J., 2013. Frailty consensus: a call to action. J. Am. Med. Dir. Assoc. 14 (6), 392–397. doi:http://dx.doi.org/10.1016/j.jamda.2013.03.022.
Nash, D.T., 2013. Frailty: the forthcoming medical crisis. Consultant 53 (9), 654–655.
Nicholson, C., Morrow, E.M., Hicks, A., Fitzpatrick, J., 2017. Supportive care for older people with frailty in hospital: an integrative review. Int. J. Nurs. Stud. 66, 60–71. doi:http://dx.doi.org/10.1016/j.ijnurstu.2016.11.015.
O'Caoimh, R., Galluzzo, L., Rodriguez-Laso, A., Van der Heyden, J., Ranhoff, A.H., Lamprini-Koula, M., 2018a. Prevalence of frailty at population level in European ADVANTAGE Joint Action Member States: a systematic review and meta-analysis. Ann. Ist. Super. Sanita 54 (3) doi:http://dx.doi.org/10.4415/ANN_18_03_14.
O'Caoimh, R., William Molloy, D., Fitzgerald, C., Velsen, V.L., Cabrita, M., Nassabi, M. H., Vollenbroek-Hutten, M., 2018b. ICT-supported interventions targeting pre-frailty: healthcare recommendations from the personalised ICT supported service for independent living and active ageing (PERSSILAA) study. In: Röcker, C. (Ed.), Information and Communication Technologies for Ageing Well and E-Health. Springer International Publishing AG Vol. CCIS 869, pp. 1–24).
Peters, L.L., Boter, H., Buskens, E., Slaets, J.P., 2012. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. J. Am. Med. Dir. Assoc. 13 (6), 546–551. doi:http://dx.doi.org/10.1016/j.jamda.2012.04.007.
Puts, M.T.E., Shekary, N., Widdershoven, G., Heldens, J., Deeg, D.J.H., 2009. The meaning of frailty according to Dutch older frail and non-frail persons. J. Aging Stud. 23 (4), 258–266. doi:http://dx.doi.org/10.1016/j.jaging.2008.03.002.
Puts, M.T.E., Toubasi, S., Andrew, M.K., Ashe, M.C., Ploeg, J., Atkinson, E., McGilton, K., 2017. Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a scoping review of the literature and international policies. Age Ageing 46 (3), 383–392. doi:http://dx.doi.org/10.1093/ageing/afw247.
Rockwood, K., Mitnitski, A., 2011. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. Clin. Geriatr. Med. 27 (1), 17–26. doi:http://dx.doi.org/10.1016/j.cger.2010.08.008.
Rockwood, K., Stolee, P., McDowell, I., 1996. Factors associated with institutionalization of older people in Canada: testing a multifactorial definition of frailty. J. Am. Geriatr. Soc. 44 (5), 578–582.
Rodriguez-Manas, L., Feart, C., Mann, G., Vina, J., Chatterji, S., Chodzko-Zajko, W., Vega, E., 2013. Searching for an operational definition of frailty: a Delphi method based consensus statement: the frailty operative definition-consensus conference project. J. Gerontol. A Biol. Sci. Med. Sci. 68 (1), 62–67. doi:http://dx.doi.org/10.1093/gerona/gls119.
Rodríguez-Mañas, L., Sinclair, A.J., 2014. Frailty: The quest for new domains, clinical definitions and subtypes. Is this justified on new evidence emerging? J. Nutr. Health Aging 18 (1), 92–94. doi:http://dx.doi.org/10.1007/s12603-013-0433-9.
Ruan, Q., Yu, Z., Chen, M., Bao, Z., Li, J., He, W., 2015. Cognitive frailty, a novel target for the prevention of elderly dependency. Ageing Res. Rev. 20, 1–10. doi:http://dx.doi.org/10.1016/j.arr.2014.12.004.
Sacha, J., Sacha, M., Sobon, J., Borysiuk, Z., Feusette, P., 2017. Is it time to begin a public campaign concerning frailty and pre-frailty? A review article. Front. Physiol. 8, 484. doi:http://dx.doi.org/10.3389/fphys.2017.00484.
Sandelowski, M., Docherty, S., Emden, C., 1997. Focus on qualitative methods qualitative metasynthesis: issues and techniques. Res. Nurs. Health 20, 365–371. doi:http://dx.doi.org/10.1002/(sici)1098-240x(199708)20:460;365::aid-nur962;3.0.co;2-e.
Santos-Eggimann, B., Cuenoud, P., Spagnoli, J., Junod, J., 2009. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. J. Gerontol. A Biol. Sci. Med. Sci. 64 (6), 675–681. doi:http://dx.doi.org/10.1093/gerona/glp012.
Sargent, L., Brown, R., 2017. Assessing the current state of cognitive frailty: measurement properties. J. Nutr. Health Aging 21 (2), 152–160. doi:http://dx.doi.org/10.1007/s12603-016-0735-9.

Schoenborn, N.L., Van Pilsum Rasmussen, S.E., Xue, Q.L., Walston, J.D., McAdams-Demarco, M.A., Segev, D.L., Boyd, C.M., 2018. Older adults' perceptions and informational needs regarding frailty. BMC Geriatr. 18 (1), 46. doi:http://dx.doi.org/10.1186/s12877-018-0741-3.

Seers, K., 2015. Qualitative systematic reviews: their importance for our understanding of research relevant to pain. Br. J. Pain 9 (1), 36–40. doi:http://dx.doi.org/10.1177/2049463714549777.

Sieber, C.C., 2017. Frailty – from concept to clinical practice. Exp. Gerontol. 87, 160–167. doi:http://dx.doi.org/10.1016/j.exger.2016.05.004.

Siriwardhana, D.D., Hardoon, S., Rait, G., Weerasinghe, M.C., Walters, K.R., 2018. Prevalence of frailty and prefrailty among community-dwelling older adults in low-income and middle-income countries: a systematic review and meta-analysis. BMJ Open 8 (3) e018195 doi:http://dx.doi.org/10.1136/bmjopen-2017-018195.

Storey, E., Thomas, R.L., 2004. Understanding and ameliorating frailty in the elderly. Top. Geriatr. Rehabil. 20 (1), 4–13.

Studenski, S., Hayes, R.P., Leibowitz, R.Q., Bode, R., Lavery, L., Walston, J., et al., 2004. Clinical global impression of change in physical frailty: development of a measure based on clinical judgement. J. Am. Geriatr. Soc. 52 (9), 1560–1566. doi:http://dx.doi.org/10.1111/j.1532-5415.2004.52423.x.

Sunfrail Project, 2018. What Is Frailty? Retrieved 11/6/2018 2018, from. . http://www.sunfrail.eu/what-is-frailty/.

Theou, O., Rockwood, K., 2015. Comparison and clinical applications of the frailty phenotype and frailty index approaches. Interdiscip. Top. Gerontol. Geriatr. 41, 74–84. doi:http://dx.doi.org/10.1159/000381166.

Tocchi, C., 2015. Frailty in older adults: an evolutionary concept analysis. Res. Theory Nurs. Pract. 29 (1), 66–84.

Topinková, E., 2008. Aging, disability and frailty. Ann. Nutr. Metab. 52 (SUPPL. 1), 6–11. doi:http://dx.doi.org/10.1159/000115340.

Tsutsumimoto, K., Doi, T., Makizako, H., Hotta, R., Nakakubo, S., Makino, K., Shimada, H., 2017. Association of social frailty with both cognitive and physical deficits among older people. J. Am. Med. Dir. Assoc. 18 (7), 603–607. doi:http://dx.doi.org/10.1016/j.jamda.2017.02.004.

Turusheva, A., Frolova, E., Korystina, E., Zelenukha, D., Tadjibaev, P., Gurina, N., Degryse, J.M., 2016. Do commonly used frailty models predict mortality, loss of autonomy and mental decline in older adults in northwestern Russia? A prospective cohort study. BMC Geriatr. 16, 98. doi:http://dx.doi.org/10.1186/s12877-016-0276-4.

Vaes, B., Depoortere, D., Van Pottelbergh, G., Mathei, C., Neto, J., Degryse, J., 2017. Association between traditional cardiovascular risk factors and mortality in the oldest old: untangling the role of frailty. BMC Geriatr. 17 (1), 234. doi:http://dx.doi.org/10.1186/s12877-017-0626-x.

Vella Azzopardi, R., Beyer, I., Vermeiren, S., Petrovic, M., Van Den Noortgate, N., Bautmans, I., Gorus, E., 2018. Increasing use of cognitive measures in the operational definition of frailty—a systematic review. Ageing Res. Rev. 43, 10–16. doi:http://dx.doi.org/10.1016/j.arr.2018.01.003.

Veronese, N., Cereda, E., Stubbs, B., Solmi, M., Luchini, C., Manzato, E., Correll, C.U., 2017. Risk of cardiovascular disease morbidity and mortality in frail and pre-frail older adults: results from a meta-analysis and exploratory meta-regression analysis. Ageing Res. Rev. 35, 63–73. doi:http://dx.doi.org/10.1016/j.arr.2017.01.003.

Visvanathan, R., 2009. Nutritional frailty: unrecognised it threatens independence. Int. J. Evid. Healthc. 7 (4), 231–232. doi:http://dx.doi.org/10.1111/j.1744-1609.2009.00147.x.

Walston, J., Hadley, E.C., Ferrucci, L., Guralnik, J.M., Newman, A.B., Studenski, S.A., et al., 2006. 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. Am. Geriatr. Soc. 54 (6), 991–1001. doi:http://dx.doi.org/10.1111/j.1532-5415.2006.00745.x.

Wieland, D., Hirth, V., 2003. Comprehensive geriatric assessment. Cancer Control 10 (6), 454–462. doi:http://dx.doi.org/10.1177/107327480301000603.

Windhaber, T., Koula, M.L., Ntzani, E., Velivasi, A., Rizos, E., Doumas, M.T., Roller-Wirnsberger, R.E., 2018. Educational strategies to train health care professionals across the education continuum on the process of frailty prevention and frailty management: a systematic review. Aging Clin. Exp. Res. 1–7. doi:http://dx.doi.org/10.1007/s40520-018-0918-9.

Wou, F., Conroy, S., 2013. The frailty syndrome. Medicine (United Kingdom) 41 (1), 13–15. doi:http://dx.doi.org/10.1016/j.mpmed.2012.10.004.

Xue, Q.L., 2011. The frailty syndrome: definition and natural history. Clin. Geriatr. Med. 27 (1), 1–15. doi:http://dx.doi.org/10.1016/j.cger.2010.08.009.