

Multidimensional Frailty and Pain in Community Dwelling Elderly

Tiago Coelho, OTR, PhD,^{*,†} Constância Paúl, PhD,[†] Robbert J. J. Gobbens, RN, PhD,^{‡,§}
and Lia Fernandes, MD, PhD[¶]

Department of Occupational Therapy, School of Allied Health Technologies, Polytechnic Institute of Porto, Vila Nova de Gaia, Portugal; [†]Department of Behaviour Sciences, UNIFAI/ICBAS, University of Porto, Porto, Portugal; [‡]Faculty of Health, Sports and Social Work, Inholland University of Applied Sciences, Amsterdam, The Netherlands; [§]Zonnehuisgroep Amstelland, Amstelveen, The Netherlands; [¶]Department of Clinical Neurosciences and Mental Health, Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal

Abstract

Objective

To examine the relationship between frailty and pain, particularly to analyze whether pain predicts physical, psychological and social frailty, after controlling for the effects of life-course determinants and comorbidity.

Design

Cross-sectional.

Methods

A nonprobabilistic sample of 252 community dwelling elderly was recruited. Frailty and determinants of frailty were assessed with the Tilburg Frailty Indicator and pain was measured with the Pain Impact Questionnaire. Hierarchical and logistic regression analyses were conducted.

Results

In this study, 52.4% of the participants were aged 80 years and over, and 75.8% were women. Pain and frailty were higher in women, and physical frailty was higher in those aged ≥ 80 years. After controlling for the effects of the determinants and comorbidity, pain predicted 5.8% of the variance of frailty, 5.9% of the variance of physical frailty, and 4.0% of the variance of psychological frailty, while the prediction of social frailty was nonsignificant. Overall, a greater pain impact score was associated with the presence of frailty (odds ratio 1.06; 95% CI 1.03–1.10; $P < 0.001$).

Conclusion

Frailty was independently predicted by pain, emphasizing the importance of its treatment, potentially contributing to the prevention of vulnerability, dependency, and mortality. Nonetheless, longitudinal studies are required to better understand the possible association between pain and frailty.

Introduction

Frailty is the term used in geriatrics to describe a clinical syndrome in which the individual is in a state of increased vulnerability to stressors, which entails a high risk of adverse outcomes, such as functional deterioration, hospitalization, institutionalization, and death 1-5. Although it is generally recognized that the prevalence of frailty increases with age, particularly affecting persons older than 80 years, the precise prevalence rates depend of the definition of frailty 4, 6. In fact, there are different approaches regarding the specific components of frailty 7-10. The presence of exclusively physical manifestations (weight loss, low physical activity, exhaustion, slowed performance, and weakness) that constitute the Frailty Phenotype 11, and the accumulation of various deficits (e.g., disabilities, symptoms, signs, diseases) that create a Frailty Index 2, are the most popular approaches. Currently, some definitions of frailty tend to include psychological and social components in addition to physical components, and exclude disability as part of frailty 1, 7, 8, 12, 13.

Frailty can occur as the result of the interplay between a significantly diminished physiological capacity, life-course determinants and medical conditions 5, 14, 15. These conditions, particularly chronic illnesses such as cancer and osteoarticular diseases, are likewise documented as an evident source of pain in the elderly 16, 17. In fact, pain is also highly prevalent in older populations, and its interference with everyday life increases significantly with age 18-20. Furthermore, if untreated, pain may have a severe impact on the physical, psychological and social domains of functioning 17, 21-24. Therefore, it seems reasonable to hypothesize that pain and frailty may be linked, and particularly that pain, in older individuals who most likely already suffer from chronic illness, can increase their vulnerability and lead to frailty situations.

To our knowledge, Blyth et al. 25 published the first study focused on specifically examining the relationship between frailty and pain, and found that those already frail (with ≥ 3 components of the Frailty Phenotype) were more likely to report pain. As then, several studies have corroborated the hypothesis of frailty being positively associated with pain 26-29. Although the direction of the association has not yet been established, the hypothesis of pain diminishing the physiological reserves needed to maintain homeostasis when faced with biological, psychological or social stressors, and precipitating frailty, proposed by Shega et al. 29 based on the concept of pain homeostenosis 30, seems to be well supported.

Considering the conceptualized relationship between pain and frailty, and that in previous research frailty has only been measured according to more traditional approaches to the concept (as a physical syndrome/Frailty Phenotype or as a result of the accumulation of deficits/Frailty Index), undervaluing the importance of psychosocial components, the present study aims to examine whether pain predicts multidimensional frailty (physical, psychological, and social) in a sample of community dwelling elderly individuals.

Methods

Study Design and Sample

A cross-sectional exploratory study was designed using a nonprobabilistic sample of 252 elderly persons from Porto, which is an urban area of Portugal. Participants volunteered after information regarding the study was disclosed in 16 local community institutions (social, recreation and day care centers, as well as senior universities).

Volunteers had to be community dwellers aged 65 years and over. Individuals who were unable to speak Portuguese, or with severe cognitive impairment (i.e., scored < 10 in Mini Mental State Examination [31](#), [32](#), according to guidelines of the National Institute for Health and Care Excellence [33](#)), were excluded. Consequently, five volunteers were excluded because of severe cognitive deficits (Figure [1](#)).

Participants were interviewed in the institutions through which they were contacted. Data collection was carried out from May to September 2013 by trained researchers. The study was approved by the institutional review board and all participants gave their written informed consent.

Measures

Frailty and determinants of frailty were assessed with the Tilburg Frailty Indicator (TFI) [34](#). The TFI is an operationalization of the Integral Conceptual Model of Frailty [12](#), [35-37](#), which defines it as a dynamic predisability state resulting from losses in physical, psychological and/or social domains. Besides clearly differentiating frailty from disability, this holistic definition is more in line with the conceptualization of health as physical, psychological and social well-being [35](#). Furthermore, previous studies have shown that this definition, operationalized by TFI, makes it a valid instrument to predict disability, health care utilization and quality of life [37-39](#). This tool consists of a brief self-report screening questionnaire divided in two subscales. The first subscale (10 items) assesses the determinants of frailty proposed in the model: sociodemographic characteristics (age, gender, marital status, ethnicity, level of education, income); life events in the last year (death of a loved one, serious illness, serious illness in a loved one, divorce or end of an important relationship, traffic accident, crime); assessment of how healthy the respondent's lifestyle is; satisfaction with their

home living environment; and the presence of two or more chronic diseases. The second subscale (15 items) measures physical frailty (physical health, unexplained weight loss, difficulty in walking, difficulty in maintaining balance, hearing problems, vision problems, lack of strength in hands, and physical tiredness), psychological frailty (cognition, depression and anxiety symptoms and coping), and social frailty (living alone, social relations and social support). All items are rated dichotomously (0-1), and scores for each frailty domain and a total frailty score are produced. Higher scores refer to higher frailty. In the present study, the Portuguese version of TFI 40 was used (internal consistency = 0.78) and individuals who scored ≥ 6 were considered frail.

Pain was measured with the Pain Impact Questionnaire (PIQ-6) 41. PIQ-6 is a brief (six-item) self-report questionnaire with a standard 4-week recall period. It was developed using conventional and item response theory methods, based on a bank of 65 pain items selected from 16 widely used generic and disease-specific measures. This tool comprises one item scored in a 6-point scale (regarding the presence/severity of pain) and five items scored in a 5-point scale (three questions about the impact of pain on functional status, and two questions regarding the impact of pain on emotional well-being). The total score ranges from 40 to 78 points, resulting from the sum of the weighted responses (each response choice is converted accordingly to a specific weight, calculated in the original validation study 41). Higher PIQ-6 scores indicate greater pain impact. The Portuguese version of PIQ-6 42 was used (internal consistency = 0.92).

Statistical Analysis

Descriptive statistical analysis was performed using proportions and measures of central tendency and dispersion, according to the variables' nature. Independent sample *t*-tests were performed to compare frailty and pain according to gender and age, to ascertain whether frailty was higher in women and in the group of oldest old individuals as described in the literature 4. Hierarchical regression analysis were conducted to ascertain whether pain (independent variable) predicted frailty in general and each frailty domain (dependent variables), after controlling for the effect of determinants of frailty (covariates) in frailty variance. Age, gender, marital status, ethnicity, level of education, income, life events, lifestyle, living environment, and comorbidity were included in the first step of the regression, and pain in the second, for each frailty score. As in previous studies 37, 43, life event "serious illness in the last year" was excluded from the analysis because it overlaps with comorbidity. Likewise, marital status was not considered for the prediction of total frailty and social frailty because it is closely linked with the TFI item "living alone". Secondly, a logistic regression analysis was conducted to ascertain whether pain is independently associated with the presence of frailty (TFI score ≥ 6), adjusting for relevant covariates. Two-tailed tests were

used throughout all analysis and a P value < 0.05 was considered statistically significant. All statistical analysis were conducted using IBM SPSS Statistics 22.0 (SPSS, Inc., Chicago, IL, USA).

Results

In the present study, 52.4% of the participants were aged 80 years and over (mean = 79.2 ± 7.3), and 75.8% were women. Most of the individuals were Portuguese (99.6%), widowed (55.6%), and had ≤ 4 years of education (78.2%) and low (≤ 500 euros) household income (40.9%). Serious illness of a loved one, serious illness and death of a loved one were the most often reported life events (28.2%, 22.2%, and 21.8%, respectively). In the sample, 54.4% described their lifestyle as healthy, 79.0% were satisfied with their living environment, and 53.2% reported the presence of two or more chronic illnesses. The mean pain impact score was $53.8 (\pm 10.7)$. The mean frailty total score was $6.0 (\pm 3.4)$, and $2.9 (\pm 2.2)$, $1.7 (\pm 1.1)$, and $1.4 (\pm 1.0)$ for physical, psychological, and social frailty, respectively. Furthermore, 54.8% of the participants were identified as frail. See Table 1 for further details regarding the characteristics of the participants.

Table 1. Characteristics of the participants ($n=252$) in regard to socio-demographic variables, frailty and pain

Characteristics	$n(\%)$
Sociodemographic characteristics	
Age (years), mean \pm SD	79.2 \pm 7.3
65–79	120 (47.6)
≥ 80	132 (52.4)
Sex (women)	191 (75.8)
Nationality (Portuguese)	251 (99.6)
Marital status	
Married/living with partner	49 (19.4)
Unmarried	24 (9.5)
Separated/divorced	39 (15.5)

Characteristics	n(%)
Widow/widower	140 (55.6)
Education (years), mean±SD	4.4±3.6
0	36 (14.3)
1-4	161 (63.9)
≥5	55 (21.9)
Monthly household income (euros)	
≤500	103 (40.9)
≥501	149 (59.1)
Life events	
Death of a loved one	55 (21.8)
Serious illness	56 (22.2)
Serious illness in a loved one	71 (28.2)
End of important relationship	8 (3.2)
Traffic accident	1 (0.4)
Crime	14 (5.6)
Lifestyle self-assessment	
Healthy	137 (54.4)
Not healthy, not unhealthy	92 (36.5)
Unhealthy	23 (9.1)
Satisfaction with home living environment	199 (79.0)
Self-reported comorbidity	134 (53.2)
Frailty	138 (54.8)
TFI total score (0-15), mean±SD	6.0±3.4
TFI physical domain score (0-8), mean±SD	2.9±2.2

Characteristics	n(%)
TFI psychological domain score (0-4), mean±SD	1.7±1.1
TFI social domain score (0-3), mean±SD	1.4±1.0
Pain	
PIQ-6 score (40-78), mean±SD	53.8±10.7

There were statistically significant differences between participants aged 65–79 years and

There were statistically significant differences between participants aged 65–79 years and those aged ≥80 years in physical frailty scores, although not in psychological, social and total frailty, and in pain. Conversely, there were significant differences between men and women in regard to total frailty, physical frailty, psychological frailty, social frailty, and pain. Frailty and pain impact was higher in women. See Table 2 for additional details regarding *t*-test results.

Table 2 Results of t-tests and descriptive statistics of frailty and pain scores by age group and gender

Measure	Age group				95%CI for Mean Difference	t	df
	65–79 years		≥80 years				
	M	SD	M	SD			
Frailty	5.6	3.6	6.4	3.3	21.7, 0.0	21.94	250
Physical frailty	2.5	2.3	3.2	2.2	21.3, -0.2	22.55*	250
Psychological frailty	1.6	1.1	1.8	1.1	20.4, 0.1	21.07	250
Social frailty	1.4	1.0	1.4	1.0	20.2, 0.3	0.16	250
Pain impact	53.1	11.0	54.4	10.5	24.0, 1.3	21.01	250
Measure	Gender				95%CI for Mean Difference	t	df
	Men		Women				
	M	SD	M	SD			
Frailty	4.8	3.2	6.4	3.4	22.6, -0.7	23.30 [†]	250
Physical frailty	2.3	2.1	3.1	2.2	21.4, -0.1	22.34*	250
Psychological frailty	1.4	1.1	1.8	1.1	20.8, -0.2	23.01 [†]	250
Social frailty	1.1	1.0	1.5	1.0	20.7, -0.1	22.76 [†]	250
Pain impact	48.1	9.1	55.6	10.6	210.4, -4.5	24.95 [‡]	250

**p* < 0.05.

[†]*p* < 0.01.

[‡]*p* < 0.001.

Regarding the regression analysis, variables that revealed low frequencies (<5%) were excluded: ethnicity (due to the low percentage of non-Portuguese individuals) and life events “divorce or end of important relationship” and “traffic accident”. A dummy variable “cohabit” (“1” for married/living with partner and “0” for unmarried, separated/divorced and widow/widower) was created as an alternative to marital status. Gender was rated “1” for women and “0” for men. Lifestyle was rated “1” for “healthy”, “2” for “not healthy, not unhealthy”, and “3” for “Unhealthy” in the hierarchical regression analysis, whereas in the logistic regression it was rated “0” for “healthy” and “1” for “not healthy, not unhealthy/unhealthy”.

The results of the hierarchical regression analysis (Table 3) indicated that after controlling for the effects of determinants of frailty, pain predicted 5.8% of the variance of frailty, 5.9% of the variance of physical frailty, and 4.0% of the variance of psychological frailty, while the prediction of social frailty was nonsignificant. Regression coefficients indicate that an increase in pain impact would imply an increase in frailty scores.

Table 3 Hierarchical regression of life-course determinants and comorbidity (step 1), and pain (step 2), predicting total frailty, physical frailty, psychological frailty, and social frailty

Step	DR ²	Frailty			
		DF	df	b	95%CI
Step 1: determinants*	0.460	18.59 [#]	(11, 240)	–	–
Step 2: pain	0.058	28.92 [#]	(1, 239)	0.09	0.06; 0.13
Physical frailty					
Step 1: determinants [†]	0.398	13.15 [#]	(12, 239)	–	–
Step 2: pain	0.059	25.77 [#]	(1, 238)	0.06	0.04; 0.09
Psychological frailty					
Step 1: determinants [†]	0.253	6.76 [#]	(12, 239)	–	–
Step 2: pain	0.040	13.32 [#]	(1, 238)	0.02	0.01; 0.04
Social frailty					
Step 1: determinants*	0.287	8.78 [#]	(11, 240)	–	–
Step 2: pain	0.005	1.59	(1, 239)	0.01	0.00; 0.02

*Age, gender, education, income, life events (death of a loved one, serious illness in a loved one and crime), lifestyle, living environment and comorbidity

[†]Age, gender, cohabitation, education, income, life events (death of a loved one, serious illness in a loved one and crime), life-style, living environment and comorbidity

[‡]P < 0.05.

[§]P < 0.01.

[#]P < 0.001.

Conversely, through the logistic regression analysis (Table 4) it was also possible to ascertain that the pain impact score was independently associated with frailty (odds ratio 1.06; 95% CI 1.03–1.10; $P < 0.001$).

Table 4 Logistic regression for the presence of frailty (TFI score ≥ 6) according to life-course determinants, comorbidity and pain

Factors	Odds Ratio	95%CI	P value
Age	1.04	0.99; 1.09	0.12
Gender (female male)	1.53	0.71; 3.30	0.28
Education	0.98	0.88; 1.08	0.65
Income	0.89	0.71; 1.10	0.28
Life events (yes vs. no)			
Death of a loved one	3.54	1.52; 8.22	<0.01
Serious illness in a loved one	0.75	0.36; 1.55	0.43
Crime	1.91	0.46; 7.91	0.37
Lifestyle (unhealthy vs. others)	2.06	1.09; 3.88	<0.05
Discontent with home living environment (yes vs. no)	4.90	1.97; 12.2	<0.001
Comorbidity (yes vs. no)	2.84	1.50; 5.39	<0.01
Pain	1.06	1.03; 1.10	<0.001

Discussion

More severe pain that interfered with daily life and well-being was independently associated with higher frailty, particularly with physical and psychological frailty. Although the present exploratory study cannot explain the causal direction of this association, these findings provide important evidence to support the hypothesis that pain can precipitate and/or worsen frailty in elderly populations.

The present study strengthens the current body of evidence regarding the possible relationship between frailty and pain, for two major reasons: first, a well-validated six-item tool, the PIQ-6 [41](#), was used to measure the severity of pain and its impact within a 4-week recall period, while in previous studies a single question was used to assess either the severity of pain (e.g., “How much bodily pain have you had during the past 4 weeks?” [26](#), [29](#)), or its interference with function (e.g., “During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?” [25](#)). The second reason underlined is that in previous studies frailty was assessed as a whole (with individuals being categorized as frail, prefrail and not frail), and considered exclusively as a physical condition [25](#), [27](#), [28](#) or as an accumulation of deficits mainly related to function and comorbidity [26](#), [29](#), in this study it was shown that pain has a different association with the overall scores of distinct domains of frailty: physical, psychological, and social.

Particularly, the present study showed that pain could predict physical frailty. This can be explained by the well-documented impact of pain on physical function. In fact, pain has been connected with mobility limitations, fatigue, and decreased nutritional intake [24](#), [44-46](#), which are components of physical frailty, or directly linked to them. Evidence also shows that pain can lead to sleep disturbances [17](#), [23](#), [24](#), [46](#), which in turn have been associated with higher physical frailty [47](#), [48](#).

This study also demonstrated that pain could be independently associated with psychological frailty. This was expected considering the robust evidence supporting the complex bidirectional relationship between psychological factors and pain [22](#), [49](#), [50](#). Previous research provides evidence of fewer complaints of pain in elderly individuals with good coping strategies and without depression [22](#). Conversely, some authors highlight that persistent pain can precipitate anxiety and depressive symptoms, as well as cognitive dysfunction [17](#), [18](#), [22](#), [51](#).

Finally, the present study found no association between pain and social frailty. Although some authors state that persistent pain can have a negative effect on socialization [22](#), the social impact of pain, while certainly related to its physical and psychological consequences, seems therefore less evident. In fact, a previous study shows that there are no significant differences in the social networks of elderly whether or not they are in pain [46](#). However, it is important to emphasize that the absence of an association between pain and this domain of frailty might be directly linked to the components of social frailty included in TFI (living alone, missing having people around, and not receiving enough social support). Indeed, this set of items might not have led to the detection of the lack of engagement in social activities, which can result from the presence of pain [52](#).

Consistent with other studies [6](#), [53-55](#), women were frailer and reported more pain than men. These sex-related differences seem to result from the interaction between biological, psychological, and social factors [53](#), [55-57](#). Also as expected [5](#), [6](#), particularly considering the physical toll of aging, the oldest old (≥ 80 years) had more physical frailty. Conversely, although there is some evidence about the impact of pain increasing with age [19](#), [20](#), PIQ-6 scores were not significantly different between age groups. It is not completely clear how age might affect an individual's experience of pain [22](#), [55](#), with several studies [23](#), [54](#), [58](#) showing that the prevalence of pain is similar across age groups.

The evidence provided by this study highlights the potential importance of the effective treatment of pain to prevent, attenuate or reverse frailty in the elderly. The management of pain is undoubtedly critical for successful aging and for the prevention of adverse health outcomes in later life, such as depression and disability [22](#), [59](#), [60](#). There is a vast array of pharmacological and nonpharmacological strategies that contribute to the relief of pain, particularly when individually tailored after a comprehensive assessment of the patient [22](#), [61](#). The most common strategy used is the prescription of analgesic drugs (nonopioids, opioids, and adjuvant drugs) [22](#). There is some evidence of the usefulness of other medications in pain management, such as vitamin D

supplement [17](#), [21](#), which is also considered to have a positive effect on physical frailty [4](#). Conversely, effective nonpharmacological approaches are reckoned to be adequate, including physical and occupational therapy, cognitive behavioral therapy and patient and caregiver education programs [21](#), [22](#), [29](#).

It is possible to argue that pain predicts only a small part of frailty, and that other factors should be targeted to diminish vulnerability in a more cost-effective manner. Nonetheless, several elements should be considered when approaching this topic. Primarily, in the present study, the prediction of frailty with pain is examined after controlling for the effect of a large group of well-established determinants of frailty, which could explain why pain only predicted 5.8% of the variance of frailty. Furthermore, the regression coefficient indicates that an increase of one point in the PIQ-6 score is associated with an increase of 0.09 in the total frailty score. Considering that the score of the PIQ-6 ranges from 40 to 78, maximum pain impact would mean that total frailty score would increase 3.4 points. As the maximum TFI score is 15, this increment should be considered as relevant. Finally, the prevention of frailty should be approached from a multidimensional perspective [4](#), [7](#), [62](#). Consequently, several modifiable predictors (e.g., lifestyle, home living environment, and pain) of frailty should be targeted to achieve better results.

The main strengths of the present study are the robust statistical procedures performed, and the bolstering of the current evidence supporting the possible association between pain and frailty, especially by analyzing its relationship to each domain of frailty and measuring it precisely. Nonetheless, some limitations should be noted. First, the non-probabilistic sampling method could limit the generalization of the findings. Second, the cross-sectional design does not allow the examination of the causality between frailty and pain. Third, considering that the same researcher assessed both frailty and pain, the possibility of bias could be increased. However, taking into account that both frailty and pain were measured through self-report instruments, the effect of bias is reduced. Fourth, pain was not categorized as persistent or acute, since it was measured over a 4-week recall period (persistent pain is only present when the painful sensation lasts for at least 3 months [21](#)). Considering the potentially cumulative impact of persistent pain over time, the association with frailty could have been different. Nonetheless, previous research has shown that the PIQ-6 score is significantly increased in populations with chronic pain [41](#). Therefore, in our study, higher PIQ-6 scores may indicate that the pain is persistent. Finally, considering the PIQ-6 score range, one could argue that the sample's overall pain impact score was low. The mean PIQ-6 score (53.8 ± 10.7) in the present study is quite similar to what has been previously observed in elderly individuals from a population-based sample [41](#). It is also lower than the pain impact documented in a clinical sample of individuals with chronic pain [41](#), [42](#). Although the results of this study are in agreement with what would be expected from a nonclinical sample, the low impact of pain might have contributed to a feeble association with frailty.

Future research including longitudinal studies will be needed to determine the causality between frailty and pain. The influence of the duration of the painful experience on frailty and each domain, its social impact as well as its association with the physical and psychological consequences of persistent pain, should also be examined. Additionally, studies should focus on analyzing the effectiveness of different pain treatments in preventing or reversing frailty.

In conclusion, this research provides significant evidence to support the potential importance of the assessment and management of pain to prevent frailty in the elderly.

References

- 1 Abellan van Kan, G, Rolland, Y, Bergman, H, et al. The I.A.N.A Task Force on frailty assessment of older people in clinical practice. *J Nutr Health Aging* 2008; 12(1): 29– 37.
- 2 Rockwood, K, Mitnitski, A. Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci* 2007; 62(7): 722– 7.
- 3 Fried, LP, Ferrucci, L, Darer, J, Williamson, JD, Anderson, G. Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004; 59(3): 255– 63.
- 4 Morley, JE, Vellas, B, Kan, GA, et al. Frailty consensus: A call to action. *J Am Med Dir Assoc* 2013; 14(6): 392– 7.
- 5 Fried, LP, Walston, J, Ferrucci, L. Frailty. In: JB Halter, JG Ouslander, ME Tinetti, S Studenski, KP High, S Asthana, eds. *Hazzard's Geriatric Medicine And Gerontology*, 6th edition. New York: McGraw-Hill; 2009: 631– 46.
- 6 Collard, RM, Boter, H, Schoevers, RA, Oude Voshaar, RC. Prevalence of frailty in community-dwelling older persons: A systematic review. *J Am Geriatr Soc* 2012; 60(8): 1487– 92.
- 7 Markle-Reid, M, Browne, G. Conceptualizations of frailty in relation to older adults. *J Adv Nurs* 2003; 44(1): 58– 68.
- 8 Sternberg, SA, Wershof Schwartz, A, Karunanathan, S, Bergman, H, Mark Clarfield, A. The identification of frailty: A systematic literature review. *J Am Geriatr Soc* 2011; 59(11): 2129– 38.
- 9 Bergman, H, Ferrucci, L, Guralnik, J, et al. Frailty: An emerging research and clinical paradigm— Issues and controversies. *J Gerontol A Biol Sci Med Sci* 2007; 62(7): 731– 7.
- 10 Hogan, DB, MacKnight, C, Bergman, H. Models, definitions, and criteria of frailty. *Aging Clin Exp Res* 2003; 15(3 Suppl): 1– 29.
- 11 Fried, LP, Tangen, CM, Walston, J, et al. Frailty in older adults: Evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; 56(3): M146– 56.
- 12 Gobbens, RJ, Luijckx, KG, Wijnen-Sponselee, MT, Schols, JM. Toward a conceptual definition of frail community dwelling older people. *Nurs Outlook* 2010; 58(2): 76– 86.

- 13 Levers, MJ, Estabrooks, CA, Ross Kerr, JC. Factors contributing to frailty: Literature review. *J Adv Nurs* 2006; 56(3): 282– 91.
- 14 Zaslavsky, O, Cochrane, BB, Thompson, HJ, et al. Frailty: A review of the first decade of research. *Biol Res Nurs* 2013; 15(4): 422– 32.
- 15 Avila-Funes, JA, Helmer, C, Amieva, H, et al. Frailty among community-dwelling elderly people in France: The three-city study. *J Gerontol A Biol Sci Med Sci.* 2008; 63(10): 1089– 96.
- 16 Becquemont, L, Benattar-Zibi, L, Bertin, P, et al. National observatory on the therapeutic management in ambulatory care patients aged 65 and over, with type 2 diabetes, chronic pain or atrial fibrillation. *Therapie* 2013; 68(4): 265– 83.
- 17 Davis, MP, Srivastava, M. Demographics, assessment and management of pain in the elderly. *Drugs Aging* 2003; 20(1): 23– 57.
- 18 Bruckenthal, P, Reid, MC, Reisner, L. Special issues in the management of chronic pain in older adults. *Pain Med* 2009; 10(Suppl 2): S67– 78.
- 19 Thomas, E, Peat, G, Harris, L, Wilkie, R, Croft, PR. The prevalence of pain and pain interference in a general population of older adults: Cross-sectional findings from the North Staffordshire Osteoarthritis Project (NorStOP). *Pain* 2004; 110(1–2): 361– 8.
- 20 Thomas, E, Mottram, S, Peat, G, Wilkie, R, Croft, P. The effect of age on the onset of pain interference in a general population of older adults: Prospective findings from the North Staffordshire Osteoarthritis Project (NorStOP). *Pain* 2007; 129(1–2): 21– 7.
- 21 American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older P. Pharmacological management of persistent pain in older persons. *J Am Geriatr Soc* 2009; 57(8): 1331– 46.
- 22 A. G. S. Panel on Persistent Pain in Older Persons. The management of persistent pain in older persons. *J Am Geriatr Soc* 2002; 50(6 Suppl): S205– 24.
- 23 Scudds, RJ, Ostbye, T. Pain and pain-related interference with function in older Canadians: The Canadian study of health and aging. *Disabil Rehabil* 2001; 23(15): 654– 64.
- 24 Rudy, TE, Weiner, DK, Lieber, SJ, Slaboda, J, Boston, JR. The impact of chronic low back pain on older adults: A comparative study of patients and controls. *Pain* 2007; 131(3): 293– 301.
- 25 Blyth, FM, Rochat, S, Cumming, RG, et al. Pain, frailty and comorbidity on older men: The CHAMP study. *Pain* 2008; 140(1): 224– 30.
- 26 Shega, JW, Andrew, M, Kotwal, A, et al. Relationship between persistent pain and 5-year mortality: A population-based prospective cohort study. *J Am Geriatr Soc* 2013; 61(12): 2135– 41.
- 27 Koponen, MPH, Bell, JS, Karttunen, NM, et al. Analgesic use and frailty among community-dwelling older people a population-based study. *Drug Aging* 2013; 30(2): 129– 36.
- 28 Chen, CY, Wu, SC, Chen, LJ, Lue, BH. The prevalence of subjective frailty and factors associated with frailty in Taiwan. *Arch Gerontol Geriatr* 2010; 50(Suppl 1): S43– 7.
- 29 Shega, JW, Dale, W, Andrew, M, et al. Persistent pain and frailty: A case for homeostenosis. *J Am Geriatr Soc* 2012; 60(1): 113– 7.

- 30 Karp, JF, Shega, JW, Morone, NE, Weiner, DK. Advances in understanding the mechanisms and management of persistent pain in older adults. *Br J Anaesth* 2008; 101(1): 111– 20.
- 31 Folstein, MF, Folstein, SE, McHugh, PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; 12(3): 189– 98.
- 32 Guerreiro, M, Silva, AP, Botelho, M, et al. Adaptação à população portuguesa do Mini Mental State Examination (MMSE). *Revista Portuguesa de Neurologia* 1994; 1(9): 9– 10.
- 33 NICE. Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease. 2011. Available at: <http://www.nice.org.uk/guidance/ta217>.
- 34 Gobbens, RJ, Assen, MA, Luijckx, KG, Wijnen-Sponselee, MT, Schols, JM. The Tilburg Frailty Indicator: Psychometric properties. *J Am Med Dir Assoc* 2010; 11(5): 344– 55.
- 35 Gobbens, RJ, Luijckx, KG, Wijnen-Sponselee, MT, Schols, JM. In search of an integral conceptual definition of frailty: Opinions of experts. *J Am Med Dir Assoc* 2010; 11(5): 338– 43.
- 36 Gobbens, RJ, Luijckx, KG, Wijnen-Sponselee, MT, Schols, JM. Towards an integral conceptual model of frailty. *J Nutr Health Aging* 2010; 14(3): 175– 81.
- 37 Gobbens, RJ, Assen, MA, Luijckx, KG, Schols, JM. Testing an integral conceptual model of frailty. *J Adv Nurs* 2012; 68(9): 2047– 60.
- 38 Gobbens, RJ, Assen, MA, Luijckx, KG, Schols, JM. The predictive validity of the Tilburg Frailty Indicator: Disability, health care utilization, and quality of life in a population at risk. *Gerontologist* 2012; 52(5): 619– 31.
- 39 Gobbens, RJ, Luijckx, KG, Assen, MA. Explaining quality of life of older people in the Netherlands using a multidimensional assessment of frailty. *Qual Life Res* 2012; 22(8): 2051– 61.
- 40 Coelho, T, Santos, R, Paúl, C, Gobbens, RJJ, Fernandes, L. Portuguese version of the Tilburg Frailty Indicator: Transcultural adaptation and psychometric validation. *Geriatr Gerontol Int* 2014.
- 41 Becker, J, Schwartz, C, Saris-Baglama, RN, Kosinski, M, Bjorner, JB. Using item response theory (IRT) for developing and evaluating the pain impact questionnaire (PIQ-6?). *Pain Med* 2007; 8(s3 Computer and): S129– S44.
- 42 Cavalheiro, LM, Gil, JA, Goncalves, RS, et al. Measuring the pain impact in adults with a chronic pain condition: Adaptation and validation of the Pain Impact Questionnaire (PIQ-6) to the Portuguese culture. *Pain Med* 2011; 12(10): 1538– 43.
- 43 Gobbens, RJ, Assen, MA, Luijckx, KG, Wijnen-Sponselee, MT, Schols, JM. Determinants of frailty. *J Am Med Dir Assoc* 2010; 11(5): 356– 64.
- 44 Hairi, NN, Cumming, RG, Blyth, FM, Naganathan, V. Chronic pain, impact of pain and pain severity with physical disability in older people—Is there a gender difference? *Maturitas* 2013; 74(1): 68– 73.
- 45 Pereira, LS, Sherrington, C, Ferreira, ML, et al. Self-reported chronic pain is associated with physical performance in older people leaving aged care rehabilitation. *Clin Interv Aging* 2014; 9: 259– 65.

- 46 Jakobsson, U, Kleivsgård, R, Westergren, A, Hallberg, IR. Old people in pain: A comparative study. *J Pain Symptom Manage* 2003; 26(1): 625– 36.
- 47 Ensrud, KE, Blackwell, TL, Redline, S, et al. Sleep disturbances and frailty status in older community-dwelling men. *J Am Geriatr Soc* 2009; 57(11): 2085– 93.
- 48 Ensrud, KE, Blackwell, TL, Ancoli-Israel, S, et al. Sleep disturbances and risk of frailty and mortality in older men. *Sleep Med* 2012; 13(10): 1217– 25.
- 49 Weiner, DK, Hanlon, JT. Pain in nursing home residents: Management strategies. *Drugs Aging* 2001; 18(1): 13– 29.
- 50 Hecke, O, Torrance, N, Smith, BH. Chronic pain epidemiology and its clinical relevance. *Br J Anaesth* 2013; 111(1): 13– 8.
- 51 Landro, NI, Fors, EA, Vapenstad, LL, et al. The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological functioning? *Pain* 2013; 154(7): 972– 7.
- 52 Bookwala, J, Harralson, TL, Parmelee, PA. Effects of pain on functioning and well-being in older adults with osteoarthritis of the knee. *Psychol Aging* 2003; 18(4): 844– 50.
- 53 Song, X, Mitnitski, A, Rockwood, K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. *J Am Geriatr Soc* 2010; 58(4): 681– 7.
- 54 Fillingim, RB, King, CD, Ribeiro-Dasilva, MC, Rahim-Williams, B, Riley, JL. Sex, gender, and pain: A review of recent clinical and experimental findings. *J Pain* 2009; 10(5): 447– 85.
- 55 Patel, KV, Guralnik, JM, Dansie, EJ, Turk, DC. Prevalence and impact of pain among older adults in the United States: Findings from the 2011 National Health and Aging Trends Study. *Pain* 2013; 154(12): 2649– 57.
- 56 Bartley, EJ, Fillingim, RB. Sex differences in pain: A brief review of clinical and experimental findings. *Br J Anaesth* 2013; 111(1): 52– 8.
- 57 Puts, MT, Lips, P, Deeg, DJ. Sex differences in the risk of frailty for mortality independent of disability and chronic diseases. *J Am Geriatr Soc* 2005; 53(1): 40– 7.
- 58 Covinsky, KE, Lindquist, K, Dunlop, DD, Yelin, E. Pain, functional limitations, and aging. *J Am Geriatr Soc* 2009; 57(9): 1556– 61.
- 59 Pruchno, RA, Wilson-Genderson, M, Cartwright, F. A two-factor model of successful aging. *J Gerontol B Psychol Sci Soc Sci* 2010; 65(6): 671– 9.
- 60 Abdulla, A, Adams, N, Bone, M, et al. Guidance on the management of pain in older people. *Age Ageing* 2013; 42(Suppl 1): i1– 57.
- 61 Rastogi, R, Meek, BD. Management of chronic pain in elderly, frail patients: Finding a suitable, personalized method of control. *Clin Interv Aging* 2013; 8: 37– 46.
- 62 Espinoza, S, Walston, JD. Frailty in older adults: Insights and interventions. *Cleve Clin J Med* 2005; 72(12): 1105– 12.