Exploring cognitive frailty : prevalence and associations with other frailty domains in older people with different degrees of cognitive impairment

Exploring cognitive frailty: prevalence and associations with various frailty domains in older people with and without cognitive impairment

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Short title

Cognitive frailty and the association with other frailty domains

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Keywords

Cognitive Frailty; Cognitive Decline; Multidimensional Frailty; Mild Cognitive Impairment; Community-Dwelling

1. Abstract

Background: Cognitive frailty has long been defined as the co-occurrence of mild cognitive deficits and physical frailty. However, recently, a new approach to cognitive frailty has been proposed: cognitive frailty as a distinct construct. Nonetheless, the relationship between this relatively new construct of cognitive frailty and other frailty domains is unclear.

Objectives: The aims of this study were to explore the prevalence of cognitive frailty in groups with different levels of cognitive impairment, as well as to explore the associations between frailty domains, and if this varies with level of objective cognitive impairment.

Method: Cross-sectional data from three research projects among community-dwelling people aged ≥60 years, with increasing levels of objective cognitive impairment, were used: (1) a randomly selected sample (n=353); (2) a sample at increased risk of frailty (n=95); and (3) a sample of memory clinic patients who scored 0.5 on the Clinical Dementia Rating scale – according to the 'original' definition of cognitive frailty (n=47). Multidimensional frailty was assessed with the Comprehensive Frailty Assessment Instrument – Plus, and general cognitive functioning with the Montreal Cognitive Assessment. Descriptive statistics and linear regression were used to determine the prevalence of cognitive frailty and to explore the relationship between cognitive frailty and the other types of frailty in each sample.

Results: The prevalence of cognitive frailty increased along with the level of objective cognitive impairment in the three samples (range: 35.1–80.9%), while its co-occurrence with (one of) the other types of frailty was most frequent in the frail and community samples. Regarding its relationship with the other domains, cognitive frailty was positively associated with psychological frailty's subdomain mood disorder symptoms in all three samples ($p \leq .01$), while there was no significant association with environmental frailty and social loneliness. The associations between cognitive frailty and the other types of frailty differed between the samples.

Conclusion: Psychological and cognitive frailty are strongly associated, irrespective of the objective level of cognitive impairment. In addition, it is shown that cognitive frailty can occur independently from the other frailty domains, including physical frailty, and therefore it can be seen as a distinct concept.

2. Introduction

With the global growth of the proportion of elderly people [1], and recognition of the importance of aging in place [2-4], frailty has become an increasingly important concept. Instead of focusing purely on physical aspects [5], there is a growing tendency to view frailty from a multidimensional perspective. In these multidimensional approaches, psychological and social factors [6-7], cognitive functioning [6,8-9], and environmental factors are taken into account as well [10].

In recent years, especially increasing attention has been paid to cognitive frailty – resulting in several conceptualizations, along with different ways to measure it. Initially, merely memory problems were taken into account, i.e. in the Groningen Frailty Indicator [9] and Tilburg Frailty Indicator [6]. In 2013, an international consensus group defined cognitive frailty as the presence of physical frailty and a score of 0.5 on the Clinical Dementia Rating scale (CDR; [11]), without the presence of dementia [12]. It was conceptualized as a condition that increases the risk of cognitive impairment [12-14], but is not a clinical condition itself [12]. This definition was further refined in 2015 by Panza and colleagues [Panza, 2015]. They suggested classifying cognitive frailty into a reversible and a potentially reversible form. The reversible form is comparable to Subjective Cognitive Impairment and can be seen as precursor of potentially reversible cognitive frailty. The potentially reversible form is related to mild cognitive impairment (MCI), which means there has to be objective cognitive impairment. The new concept of reversible cognitive frailty has shown to be a short- and long-term predictor of all-cause mortality and overall dementia in a Italian longitudinal study with 2150 older participants [Solfrizzi et al. 2017]. In 2018 a new measure of cognitive frailty was developed by De Roeck et al. [8] based on the reversible form of Panza et al. [Panza, 2015], in which several components of cognitive functioning, such as learning abilities and attention, are taken into account. The main distinction between this measure and the definition as proposed by Kelaiditi et al. [12] and Panza et al. [Panza, 2015] is that cognitive frailty was defined as a distinct concept and thus that it can occur without the presence of physical frailty. It seems worthwhile to verify the definition by De Roeck et al. [8], because on a conceptual level, cognitive frailty indeed differs from the other types of frailty as it measures additional aspects (e.g. difficulty learning new things).

In addition to a lack of research on cognitive frailty as a distinct construct and its prevalence, little is known about its relationship with other types of frailty. Most previous research has examined the relationship between objective cognitive impairment, as measured by instruments, rather than cognitive frailty (i.e. subjective complaints), and one or more other types of frailty. For example, Gobbens et al. [6] found that cognitive impairment, as assessed with the Mini Mental State Examination, was correlated with physical and social frailty, but not with psychological frailty. The most frequently studied relationship is that between objective cognitive impairment and physical frailty [13, 15-17], which have consistently been found to be positively associated. The combination of cognitive and physical dysfunction has been linked to adverse outcomes, such as increased risk of progression to dementia [18] or other neurocognitive disorders [19]. There have been no studies examining the relationship between environmental frailty and cognitive impairment and no studies investigating how stable these potential associations are across levels of cognitive frailty. However, associations between cognitive frailty and the other domains may vary between groups (e.g. the general community-dwelling older population versus memory clinic patients). Gaining insight into the associations between the domains in different populations, would make it possible to make interventions more individually tailored (i.e. by knowing on which frailty domains the focus should be in each population).

To conclude, it seems worthwhile to gain further insight into the conceptualization of cognitive frailty as a distinct concept [8], as it differs from the other domains on a conceptual level. In addition, while previous research indicates that it is important to assess cognitive frailty in relation to the other domains, there is a dearth of research in this area, which makes it more difficult to design effective interventions. Multidisciplinary, tailored interventions can only be developed and implemented when (1) the underlying conceptualization of concepts such as cognitive frailty are clear; (2) the relationships between the different types of frailty are understood; and (3) information about individuals' pattern of frailty is available. The aims of this study were, therefore, to explore the prevalence of cognitive frailty in groups with different levels of cognitive impairment, as well as to explore the associations between frailty domains.

3. Materials and Methods

3.1 Study Participants

Cross-sectional data from three different research projects were used. The general inclusion criteria were as follows: community-dwelling people aged 60 years and over, living in Flanders or Brussels. The first sample was a random sample of 353 individuals; people with a diagnosis of dementia, MCI, severe psychiatric disorders or analphabetism were excluded. These participants were recruited and tested by final year undergraduate psychology students from the Vrije Universiteit Brussel (Brussels, Belgium). The second sample compromised 121 older people with a high probability of being frail who were recruited on behalf of the Detection, Support and Care of Older People: Prevention and Empowerment (D-SCOPE) project with help from different Flemish care organizations and through snowball-sampling. More details about the selection of this sample can be found in Dury et al. (2018) [Dury 2018] People with a diagnosis of dementia or severe psychiatric disorder were excluded. During the selection process risk profiles for frailty, described in detail in a manuscript from Dury et al. (2017) [20] were taken into account in order to oversample frail older people. Data were collected by six trained PhD students. The third sample consisted of 47 memory clinic patients with a reported CDR score of 0.5, who had visited the Memory Clinic of the Hospital Network Antwerp. The exclusion criteria were a history of neurological diseases or comorbid neurological disorder, and severe psychiatric illness. Data were collected by one trained PhD student (psychologist). Hereafter the three samples will be referred to as the 'community', 'potentially frail' and 'clinical' samples, respectively. People were excluded from all samples if there were missing values in the CFAI–Plus or Montreal Cognitive assessment (MoCA; for more details see heading Measurements) (community sample n=2; frail sample n=26; clinical sample: n=0). All three studies are part of a bigger research project. This bigger research project is called D-SCOPE. Therefore, the same neuropsychologists trained the different administrators in the same way for the different studies.

All participants were recruited between December 2015 and April 2017. Research protocols were approved by the local ethical committees (i.e. of the Vrije Universiteit Brussel for the frail sample; ECHW_031; and of the University of Antwerp / Antwerp University Hospital for the community and clinical samples: B300201525772). Written, informed consent was obtained from all participants prior to data collection.

3.2 Measurements

First, the following socio-demographic characteristics were assessed in all three samples: age, gender, education, and marital status. Second, frailty was measured with the 25-item CFAI-Plus [8,10] This self-report questionnaire measures cognitive (e.g. 'I have trouble remembering things that happened recently´), environmental (e.g. 'My house is in a bad condition/poorly kept'), physical (e.g. 'I have been hampered by my state of health in less demanding activities like carrying shopping bags'), psychological (e.g. 'I feel unhappy and depressed'), and social (e.g. 'I know many people whom I can totally trust') frailty. There are two components to both psychological and social frailty, respectively mood disorders and emotional loneliness, and social loneliness and social support network. Cognitive, environmental and social frailty are rated on a five-point scale (0 = completely disagree; 4 = completely agree), as is emotional loneliness (a subdomain of psychological frailty). Physical frailty is rated on a three-point scale (0 = not at all; 1 = up to three months; 2 = more than three months) and mood disorders (a subdomain of psychological frailty) on a four-point scale (0 =

not at all; 3 = considerably more than usual) [8, 10]. Scores for each frailty domain range from 0 to 25, and cut-offs for high frailty are as follows, cognitive: 10.94 [8]; environmental: 7.51; physical: 18.81; psychological: 11.51; social: 16.01 [21]. Third, the MoCA, a brief cognitive screening tool designed to detect MCI or mild dementia [22], was used to assess overall cognitive functioning in all three samples. The MoCA examines multiple domains of cognitive functioning including short-term memory, executive functioning, attention, and temporal and spatial orientation. Total score ranges from 0 to 30 and higher scores indicate better cognition. To correct for educational effects participants with ≤12 years of education received one extra point [23]. Lastly, in the clinical sample, impairments in six domains of cognitive functioning (such as memory, orientation, and personal care) were rated using the CDR [11].

3.3 Statistical Analyses

First, descriptive statistics for each sample were calculated and the included and excluded group for the frail sample were compared with independent sample t-test. Due to the small sample size of de excluded group in the community sample, no analysis were performed. Second, skewness and kurtosis of each variable were checked in each sample to determine whether the distribution violated the assumption of normality [24]. Because the clinical sample was small-sized, the cut-off for non-normality was set at $z > 1.96$ for both skewness and kurtosis [25]. For the medium-sized frail sample, the cut-off for non-normality was set at $z > 3.29$, and absolute values of skewness and kurtosis were assessed for the community sample ($n>300$) [25]. Third, differences between the three samples were assessed using one-way ANOVAs in the case of normally distributed variables (age; MoCA; cognitive frailty; and social frailty's subdomain potential support network), Kruskal-Wallis tests in the case of non-normally distributed variables (environmental and physical frailty; psychological frailty (including both subdomains); and social frailty (including the subdomain emotional loneliness), and chi-squared tests for categorical variables (gender). Any overall differences were analyzed pairwise using independent sample *t*-tests (normally distributed variables) or Mann-Whitney *U* tests (non-normally distributed variables). In addition, co-occurrence of cognitive frailty was assessed using crosstabs and chi-squared tests. Finally, multiple linear regression models were used to examine the relationship between cognitive frailty and the other frailty domains. These analyses were conducted separate in each sample, after checking collinearity using the VIF and tolerance statistics [26]. Because previous research had shown that cognition has different relationships with social loneliness (social frailty subdomain) and emotional loneliness (psychological frailty subdomain) [27], the subdomains were taken into account, rather than the overall domains. To conclude, age and environmental and physical frailty, and the subdomains of psychological and social frailty were predictors, while cognitive frailty was the dependent variable. Age was taken into account as it was associated with cognitive frailty (data not presented). Statistical significance was set at $p \leq 0.05$ and analyses were performed using SPSS 24 (IBM Corp., Armonk, NY, USA).

4. Results

4.1 Sample characteristics

Initially 523 participants were enrolled for this study (community sample *n*=355; frail sample *n*=121; clinical sample *n*=47). After applying the exclusion criteria a total of 495 participants were included in the analysis (community sample *n*=353; frail sample *n*=95; clinical sample *n*=47). In the frailty group there was significant difference in age and physical frailty between the excluded (age M=82 years SD=8.4 years, physical frailty M=20.5, SD=7.6) and included sample (age M=78 years SD=8.6years, physical frailty M=10.8, SD=8.7) (Age *p*=.035; physical frailty *p*<.001). For all other parameters (MoCA score, psychological, social, environmental and cognitive frailty) there were no significant differences between the in- and excluded participants from the frail sample (*p*<.050). Table 1 shows socio-demographic characteristics, mean MoCA and frailty scores by sample. There were significant differences between the three samples with respect to MoCA score and cognitive, environmental, physical, and psychological frailty, including its subdomain mood disorder symptoms. In addition, there was a trend for a difference in the level of social frailty between the three groups, and a significant difference for its subdomain social loneliness. Post hoc tests (not tabulated) revealed differences between the community and frail samples with respect to mean MoCA score (*p*<.001) and cognitive (*p*=.006), environmental (*p*<.001), and psychological (*p*=.002) frailty (p<.001), as well as the psychological frailty subdomains of mood disorders (*p*<.001) and emotional loneliness (*p*=.031). The community and clinical samples differed with respect to mean age (*p* = .034), mean MoCA score (*p*<.001), cognitive frailty (*p*<.001), environmental frailty (*p*<.001), and psychological frailty (*p* = .002), including both subdomains (mood disorders (*p*<.001) and emotional loneliness (*p* = .034)). Lastly, the frail and clinical samples differed with respect to mean age (*p* = .043), mean MoCA score (*p*=.009), cognitive (*p*<.001) and environmental frailty (*p*<.001), and psychological frailty (*p* = .002), including both subdomains (mood disorders (*p*<.001) and emotional loneliness (*p* = .031)) (post hoc comparisons are not tabulated).

- Insert Table 1 here -

4.2 Prevalence per Frailty Domain, and Co-occurrence with Cognitive Frailty

Table 2 shows the prevalence of frailty in each domain by sample. The prevalence of cognitive frailty was 35.1%, 51.1% and 80.9% in the community, frail and clinical samples, respectively. Environmental, physical, and social frailty were most prevalent in the frail group (16.8%, 16.8%, and 15.8%, respectively), and psychological frailty in the clinical group (25.5%). Environmental and psychological frailty were least prevalent in the community sample, whereas physical and social frailty were least prevalent in the clinical sample.

Regarding the co-occurrence, 50–100% of the respondents who were frail on an environmental, physical or psychological level also reported cognitive frailty. Regarding social frailty, 100% of the respondents in the frail and clinical sample who were socially frail also reported cognitive frailty. In the community sample, only 24.4% of the people who were socially frail reported co-occurring cognitive frailty.

- Insert Table 2 here -

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210 ### 4.3 Relationship between Cognitive Frailty and the Other Domains

211 Table 3 shows the findings from the multiple linear regression analyses. In the community sample,
212 cognitive frailty was positively associated with age, physical frailty, mood disorder symptoms and
213 emotional loneliness, and negatively associated with potential support network. In both the frail and
214 clinical sample, only mood disorders were related to cognitive frailty.

215

216 - Insert Table 3 here –

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5. Discussion

This study aimed to explore the prevalence of cognitive frailty in groups with different levels of cognitive impairment, as well as the associations between frailty domains in 495 community-dwelling older people aged ≥60 with different levels of objective cognitive impairment. Regarding the prevalence, it is shown that cognitive frailty as an independent domain was most prevalent in the clinical sample (80.9%), followed by the frail sample (51.6%) and finally the community sample (35.1%). This is consistent with previous research indicating that objective cognitive impairment and subjective cognitive complaints often co-occur [28]. These prevalence figures are also consistent with previous research on community samples. For example, Fritsch et al. [29] reported that 27.1% of participants living at home reported subjective memory complaints, whilst Mewton et al. [30] reported a prevalence of 33.5% in a similar sample. Nonetheless, in a recent literature review, lower prevalence rates of cognitive frailty were reported, namely 1.0–12.1% in community-dwelling samples, which increased up to 39.7% in clinical settings [31]. However, they only included studies in which physical functioning was taken into account in the definition of cognitive frailty as well. The combination of (subjective) cognitive complaints and physical frailty can explain the lower prevalence. Indeed if we combine cognitive and physical frailty our results are more in line with the previously discussed prevalence rates (see table 2). Another explanation could lay in the different ways cognitive frailty is operationalized in the different studies. The prevalence rates are also for reversible and potentially reversible cognitive frailty. In this study only reversible cognitive frailty was used. It is possible that cognitive complaints are more common in community based samples, then actual cognitive impairment.

Regarding the relationship with the other frailty domains, it was observed that the co-occurrence of cognitive frailty with (one of) the other types of frailty was most frequent in the frail and community samples. When assessing the specific associations between cognitive frailty and the other types of frailty in each group, three patterns were observed consistently. First, social loneliness (e.g. not having enough people to rely on, an aspect of social frailty) was not related to cognitive frailty in any of the samples. This might seem unexpected, as Holmén et al. [27] found that social loneliness was negatively related to cognitive impairment. Nonetheless, because the people in our clinical sample were aware of their impairment and it was at an early stage, it seems likely that they were receiving social support from people around them.

Second, environmental frailty was not associated with cognitive frailty in all three samples. Nonetheless, while only 50% of the community-dwelling sample who was environmentally frail also reported cognitive frailty, this increased to 68.8% in the frail, and even 100% in the clinical sample. Therefore, it seems plausible that due to the low sample size of the clinical group, there was not sufficient statistical power to identify a significant association. It is known that adaptations are sometimes needed to enable aging in place in people with cognitive impairment [32]. Therefore, we hypothesized that respondents in the clinical group had a relatively high awareness of their illness, and consequently might have been aware that they would need to make adjustments to their home if their cognitive impairment was to worsen.

Third, the mood disorders variable (psychological frailty subdomain), which captures minor depressive symptoms (e.g. feeling unhappy and depressed) [10], was positively associated with cognitive frailty in all three samples. Although it is well-known that depression is associated with objective cognitive deficits [33], there is less evidence on its relationship with subjective cognitive complaints. Nonetheless, Zlatar et al. [34] found that subjective cognitive complaints were associated

with depression, even after adjusting for objective cognitive impairment. It is also possible that the combination of subjective cognitive complaints and depressive symptoms might be a precursor of dementia [34]. Our findings and those of Seo et al. [35] seem related, as mood disorders and cognitive frailty were associated in all samples, but co-occurred more frequently at higher levels of cognitive impairment (93.3% of those in the clinical sample who had mood disorders also reported cognitive frailty). It therefore is important to assess the cognitive frailty level of people who report mood disorders, and to assess mood disorders in people who report cognitive frailty.

Differences between samples were also observed. First, emotional loneliness (e.g. missing having people around), which is a component of psychological frailty, was strongly associated with cognitive frailty in the community sample, but not in the frail or clinical samples. Previous research by Holmén et al. [27] found that emotional loneliness decreased with cognitive functioning, which might explain why we only detected an association between emotional loneliness and cognitive frailty in participants with relatively high levels objective cognitive functioning. Therefore, our findings indicate that the same relationship might hold for cognitive frailty (i.e. emotional loneliness decreases in people with lower levels of cognitive frailty), although we were not able to determine causal relationships.

Analysis of the potential social support network component of social frailty suggested that it was negatively associated with higher cognitive frailty, but only in the community sample. Previous studies have found that people who lack social ties are at increased risk of objective cognitive decline relative to their counterparts with more extensive social networks, as social networks are important for mental stimulation and maintenance or enhancement of cognitive reserve [36]. On this basis we might have expected to find the same negative association in all three samples, but it should be remembered that we measured subjective cognitive functioning (cognitive frailty) rather than objective cognitive impairment and there is a difference between one's potential social support network and one's actual social network.

Furthermore, physical frailty was only associated with cognitive frailty in the community sample. Numerous studies have examined the association between physical frailty and objective cognitive impairment. An overview by Canevelli et al. [13] concluded that cognitive impairment and physical frailty were strongly linked, but the vast majority of studies on which this review was based have assessed community-dwelling older people, i.e. a sample analogous to our community sample, the only sample in which we observed an association between physical and cognitive frailty. In addition, physical frailty increases with age [20], and our clinical sample had the lowest mean age of the three samples, which might explain why physical frailty was not (yet) that prevalent and was not associated with cognitive frailty.

Lastly, age was strongly associated with cognitive frailty, but only in the community sample, yet on the basis of previous research [37] we had expected to find this association in all three groups. Possible explanation are that participants in the frail sample were selected on the basis of a broad range of risk variables, not just age [20], and the participants in the clinical sample were relatively young, as mentioned before.

Regarding the conceptualization of cognitive frailty as a distinct construct, only ten of the older people in the clinical sample (21.3%) would be regarded cognitively frail based on the definition by Kelaiditi et al. [12] – i.e. being physical frail and scoring 0.5 on the CDR. Nonetheless, these ten people were all part of the respondents from the clinical group who were regarded cognitively frail according to the CFAI–Plus [8] (80.9%; findings not tabulated). In addition, physical frailty was only

associated with cognitive frailty in the community sample. Therefore, it can be argued that cognitive frailty indeed can be seen as a distinct construct – which should be further investigated.

5.1 Strengths and Limitations

This study has several strengths. First, we analyzed three different samples with varying levels of objective cognitive impairment, including a random sample of people living in their own homes. We thus were able to explore whether the relationship between cognitive frailty and other types of frailty varied with level of cognitive functioning. Second, we assessed several aspects of frailty, whereas most previous studies have only looked at one or two frailty domains (usually physical and social frailty).

Some limitations of the study should also be acknowledged. First, full neuropsychological assessments of the community and frail sample were not available. Our aim, however, was to get an overall indication of level of cognitive functioning in each sample and the MoCA is appropriate for this purpose. Second, there was a relatively high proportion of potential participants whom were excluded from the frail sample due to missing data, and it is likely, especially because there older and more physically frail, that the most frail participants were excluded from the frail sample. Third we cannot state with certainty that none of the participants in the community and frail samples had MCI or dementia. If without our knowing people with cognitive decline are included in this samples cognitive frailty prevalence estimates in these two samples could be biased. Fourth all frailty domains are measured with the CFAI-plus, we therefore have to be careful to generalize the results as these are probably partly restricted to our assessment method. Fifth we used the initial samples from each individual study and assumed to find a different level of actual cognitive performance in each sample. With our study design there is overlap in cognitive performance between the samples. Therefore we are not sure that the found differences were caused/associated to cognitive status or also other aspects not included. Another option was pooling all the data and redefine groups based on their actual cognitive performance. However we believe that it was important to keep the initial samples. As each sample represents a different group of people to focus on for interventions.

Lastly, the community sample was by far the largest (*n*=353; frail *n*=95, clinical *n*=47), so the analyses of this sample had greater statistical power.

5.2 Implications for Future Research and Clinical Practice

In today's aging society, with the number of frail older people increasing, there is a need for longitudinal research on the time course of relationships between the different frailty domains. Our results suggest that both researchers and clinicians should pay special attention to the relationship between cognitive and psychological frailty. Longitudinal research projects could study whether the presence of both cognitive and psychological frailty, and specific mood disorders, can indeed be used as a marker for risk of dementia, as suggested by Seo et al., [35]. When this is the case, this sample might particularly benefit from early, multimodal prevention strategies integrating interventions focusing on cognitive and psychological functioning. In addition, longitudinal research is needed to evaluate the temporal course of interactions between the various frailty domains, for example to determine whether the pattern of associations between frailty domains is different in the general population of older people living in the community from what it is in more vulnerable populations such as our frail and clinical sample. This knowledge could be used to develop clinical guidelines for

detection of frailty and follow-up of older people deemed at risk of adverse outcomes. Moreover, it seems worthwhile to investigate the predictive value of cognitive frailty as a distinct construct [8], compared to cognitive frailty as defined by Kelaiditi et al. [12]. Although there seems to be a common ground (i.e. all of the respondents who were cognitively frail according to Kelaiditi et al. [12] (21.3%, not tabulated) were also frail according to the CFAI–Plus [8]), there also seem to be differences (i.e. 80.9% of the clinical sample was cognitively frail according to the CFAI–Plus [8]).

From a clinical perspective it appears that it would be sensible to assess a broad spectrum of frailty domains in the general population of older people living at home, but to focus on mood disorders and cognitive frailty in people in a clinical setting. Therefore the CFAI-plus is very useful as a first screening instrument. The CFAI-plus measures five frailty domains and makes it easy to compare the frailty domains with each other. Moreover the same amount of attention is paid to each frailty domain. In this way clinicians can easily see on which domains they have to focus their attention. In line with this idea it is useful to see each frailty domain as a separate concept. In this way none of the domains is overlooked.

5.3 Conclusion

In older people living at home cognitive frailty increases with level of cognitive impairment and is often accompanied by one or more other types of frailty, especially physical and social frailty. It is important to include cognitive frailty in multidimensional clinical assessments of frailty. Robust associations were found between cognitive and psychological frailty, in particular the mood disorders subdomain. Physical and social frailty, and more specifically the (lack of a) potential social support network, seem to be particularly associated with cognitive frailty in the general population of older people living at home. Moreover, cognitive frailty can be seen as an independent domain, as it can occur separately from physical frailty.

6. Appendix

Table 1. Sociodemographic Characteristics and MoCA and CFAI scores by Sample

	Community (*n*=353)	Frail (n=95)	Clinical (n=47)	*p*-value
Sociodemographic characteristics				
Age (mean, *SD*))	77.7 (8.3)	78.2 (8.3)	75.3 (6.8)	.129
Gender ((%)				
Female	55.0%	57.9%	53.4%	.736
Cognition (mean, *SD*)				
MoCA	25.1 (3.2)	21.6 (4.6)	19.5 (4.3)	**≤.001**
Frailty (mean, *SD*)				
CFAI-Plus				
Cognitive	6.8 (5.4)	8.5 (5.31)	15.7 (7.3)	**≤.001**
Environmental	2.6 (3.5)	4.6 (4.14)	3.5 (4.7)	**≤.001**
Physical	9.1 (8.4)	10.8 (8.77)	4.9 (7.7)	**≤.001**
Psychological	4.4 (4.5)	6.6 (5.75)	6.8 (6.9)	**.003**
Mood disorders	1.7 (2.2)	2.7 (2.7)	3.9 (4.0)	**≤.001**
Emotional loneliness	2.8 (2.9)	3.9 (3.8)	2.8 (3.5)	.093
Social	9.8 (4.9)	10.1 (5.04)	8.1 (4.2)	.053
Social loneliness	3.2 (3.3)	3.2 (3.0)	2.0 (2.4)	.029
Potential support network	6.6 (3.0)	6.9 (3.0)	6.1 (2.3)	.346

Note: MoCA: high scores indicate good cognitive functioning (range: 0-30). CFAI-Plus: high scores indicate high frailty (domain ranges: 0-25, subdomain ranges (psychological and social frailty): 0-12.5). Differences between the three samples were assessed using one-way ANOVAs in the case of normally distributed variables and Kruskal-Wallis tests in the case of non-normally distributed variables; Pairwise comparisons are reported in the text.

Table 2. Prevalence of Cognitive Frailty and Other Types of Frailty by Sample

	Community (*n*=353)	**Frail (*n*=95)**	**Clinical (*n*=47)**
Frailty			
Cognitive	35.1% (*n*=124)	51.6% (*n*=49)	80.9% (*n*=38)
Environmental	9.6% (*n*=34)	16.8% (*n*=16)	14.9% (*n*=7)
Co-occurrence	***n*=17 *****	***n*=11 ***	*n*=7
Physical	12.7% (*n*=45)	16.8% (*n*=16)	8.5% (*n*=4)
Co-occurrence	***n*=25 *****	***n*=14 ***	*n*=3
Psychological	7.1% (*n*=25)	22.1% (*n*=21)	25.5% (*n*=12)
Co-occurrence	***n*=14 *****	***n*=17 ****	*n*=11
Social	12.7% (*n*=45)	15.8% (*n*=15)	6.4% (*n*=3)
Co-occurrence	***n*=11**	***n*=15 ***	*n*=3

Note: Prevalence figures represent the proportion of participants with above-threshold scores (see Methods section for thresholds). Co-occurrence relates to cognitive frailty. * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$ and was measured using crosstabs and chi-squared tests.

Table 3. Relationship between age and the various types of frailty by sample

	Community (*n*=353)			Frail (*n*=95)			Clinical (*n*=47)		
	B	SE	β	B	SE	β	B	SE	β
Age	.205	.032	**.315*** **	.043	.058	.067	-.095	.142	-.088
Environmental	.056	.074	.037	.152	.126	.118	.368	.247	.235
Physical	.097	.032	**.151** **	.069	.062	.114	.080	.131	.084
Psychological									
Mood disorders	.353	.136	**.143** **	.919	.216	**.466*** **	.999	.355	**.543** **
Emotional loneliness	.351	.105	**.187*** **	.131	.163	.094	-.277	.461	-.131
Social									
Potential support network	-.222	.084	**-.123** **	-.241	.180	-.136	-.251	.500	-.081
Social loneliness	.039	.078	.024	-.059	.180	-.034	-.261	.602	-.084

Note: Multiple linear regression models were used. The independent variables were as follows: age, environmental frailty, physical frailty, mood disorders and emotional loneliness (psychological frailty subdomains), social loneliness and potential social support (social frailty subdomains); the dependent variable was cognitive frailty. * $p \leq .05$,** $p \leq .01$, *** $p \leq .001$

8. Statements

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8.2. Statement of Ethics

Research protocols were approved by the local ethical committee of the Vrije Universiteit Brussel (ECHW_031), and the ethical committee of the University of Antwerp and Antwerp University Hospital (B300201525772). Written, informed consent was obtained from all participants prior to data collection.

8.3. Disclosure Statement

The authors have no conflicts of interest to declare.

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8.5. Author Contributions

EEDR & AvdV: Conception and Design of the Study, Data Collection, Analysis and Interpretation of the Data, Drafting the Article, and Final Approval of this Version to be submitted.

SE, GARZ & ED: Conception and Design of the Study, Interpretation of the Data, Revising the Article, and Final Approval of this Version to be submitted.

D-SCOPE: Conception and Design of the Study

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