

## Exploring Cognitive Frailty

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# *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  $\geq 60$  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.

29

## 30 2. Introduction

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

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

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

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

84

## 85 **3. Materials and Methods**

### 86 **3.1 Study Participants**

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

109 All participants were recruited between December 2015 and April 2017. Research protocols  
110 were approved by the local ethical committees (i.e. of the Vrije Universiteit Brussel for the frail  
111 sample; ECHW\_031; and of the University of Antwerp / Antwerp University Hospital for the  
112 community and clinical samples: B300201525772). Written, informed consent was obtained from all  
113 participants prior to data collection.

114

### 115 **3.2 Measurements**

116 First, the following socio-demographic characteristics were assessed in all three samples: age,  
117 gender, education, and marital status. Second, frailty was measured with the 25-item CFAI-Plus  
118 [8,10] This self-report questionnaire measures cognitive (e.g. 'I have trouble remembering things that  
119 happened recently'), environmental (e.g. 'My house is in a bad condition/poorly kept'), physical (e.g.  
120 'I have been hampered by my state of health in less demanding activities like carrying shopping  
121 bags'), psychological (e.g. 'I feel unhappy and depressed'), and social (e.g. 'I know many people  
122 whom I can totally trust') frailty. There are two components to both psychological and social frailty,  
123 respectively mood disorders and emotional loneliness, and social loneliness and social support  
124 network. Cognitive, environmental and social frailty are rated on a five-point scale (0 = completely  
125 disagree; 4 = completely agree), as is emotional loneliness (a subdomain of psychological frailty).  
126 Physical frailty is rated on a three-point scale (0 = not at all; 1 = up to three months; 2 = more than  
127 three months) and mood disorders (a subdomain of psychological frailty) on a four-point scale (0 =

128 not at all; 3 = considerably more than usual) [8, 10]. Scores for each frailty domain range from 0 to  
129 25, and cut-offs for high frailty are as follows, cognitive: 10.94 [8]; environmental: 7.51; physical:  
130 18.81; psychological: 11.51; social: 16.01 [21]. Third, the MoCA, a brief cognitive screening tool  
131 designed to detect MCI or mild dementia [22], was used to assess overall cognitive functioning in all  
132 three samples. The MoCA examines multiple domains of cognitive functioning including short-term  
133 memory, executive functioning, attention, and temporal and spatial orientation. Total score ranges  
134 from 0 to 30 and higher scores indicate better cognition. To correct for educational effects  
135 participants with  $\leq 12$  years of education received one extra point [23]. Lastly, in the clinical sample,  
136 impairments in six domains of cognitive functioning (such as memory, orientation, and personal care)  
137 were rated using the CDR [11].

138

### 139 **3.3 Statistical Analyses**

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

166



167 **4. Results**

168 **4.1 Sample characteristics**

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

192

193

- Insert Table 1 here -

194

195 **4.2 Prevalence per Frailty Domain, and Co-occurrence with Cognitive Frailty**

196 Table 2 shows the prevalence of frailty in each domain by sample. The prevalence of cognitive frailty  
197 was 35.1%, 51.1% and 80.9% in the community, frail and clinical samples, respectively.  
198 Environmental, physical, and social frailty were most prevalent in the frail group (16.8%, 16.8%, and  
199 15.8%, respectively), and psychological frailty in the clinical group (25.5%). Environmental and  
200 psychological frailty were least prevalent in the community sample, whereas physical and social  
201 frailty were least prevalent in the clinical sample.

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

207

208

- Insert Table 2 here -

209

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 -

217

## 218 5. Discussion

219 This study aimed to explore the prevalence of cognitive frailty in groups with different levels of  
220 cognitive impairment, as well as the associations between frailty domains in 495 community-dwelling  
221 older people aged  $\geq 60$  with different levels of objective cognitive impairment. Regarding the  
222 prevalence, it is shown that cognitive frailty as an independent domain was most prevalent in the  
223 clinical sample (80.9%), followed by the frail sample (51.6%) and finally the community sample  
224 (35.1%). This is consistent with previous research indicating that objective cognitive impairment and  
225 subjective cognitive complaints often co-occur [28]. These prevalence figures are also consistent with  
226 previous research on community samples. For example, Fritsch et al. [29] reported that 27.1% of  
227 participants living at home reported subjective memory complaints, whilst Mewton et al. [30]  
228 reported a prevalence of 33.5% in a similar sample. Nonetheless, in a recent literature review, lower  
229 prevalence rates of cognitive frailty were reported, namely 1.0–12.1% in community-dwelling  
230 samples, which increased up to 39.7% in clinical settings [31]. However, they only included studies in  
231 which physical functioning was taken into account in the definition of cognitive frailty as well. The  
232 combination of (subjective) cognitive complaints and physical frailty can explain the lower  
233 prevalence. Indeed if we combine cognitive and physical frailty our results are more in line with the  
234 previously discussed prevalence rates (see table 2). Another explanation could lay in the different  
235 ways cognitive frailty is operationalized in the different studies. The prevalence rates are also for  
236 reversible and potentially reversible cognitive frailty. In this study only reversible cognitive frailty was  
237 used. It is possible that cognitive complaints are more common in community based samples, then  
238 actual cognitive impairment.

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

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

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

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

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

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

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

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

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

306 associated with cognitive frailty in the community sample. Therefore, it can be argued that cognitive  
307 frailty indeed can be seen as a distinct construct – which should be further investigated.  
308

### 309 **5.1 Strengths and Limitations**

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

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

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

335

### 336 **5.2 Implications for Future Research and Clinical Practice**

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

349 detection of frailty and follow-up of older people deemed at risk of adverse outcomes. Moreover, it  
350 seems worthwhile to investigate the predictive value of cognitive frailty as a distinct construct [8],  
351 compared to cognitive frailty as defined by Kelaiditi et al. [12]. Although there seems to be a  
352 common ground (i.e. all of the respondents who were cognitively frail according to Kelaiditi et al. [12]  
353 (21.3%, not tabulated) were also frail according to the CFAI-Plus [8]), there also seem to be  
354 differences (i.e. 80.9% of the clinical sample was cognitively frail according to the CFAI-Plus [8]).

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

363

### 364 **5.3 Conclusion**

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

373

374 **6. Appendix**375 **Table 1. Sociodemographic Characteristics and MoCA and CFAI scores by Sample**

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

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

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

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

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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.



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

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

389

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

394

## 395 **8. Statements**

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405

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407 Research protocols were approved by the local ethical committee of the Vrije Universiteit Brussel  
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411

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413 The authors have no conflicts of interest to declare.

414

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422

423

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

427 SE, GARZ & ED: Conception and Design of the Study, Interpretation of the Data, Revising the Article,  
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