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Title	The relationship between frailty and diabetes: An investigation of self-rated health, depression symptoms and quality of life in the Study of Health Aging and Retirement in Europe.
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Abstract

Aims: To assess the impact of diabetes and frailty on self-rated health, depressive symptoms and quality of life (QoL).

Methods: Data were pooled for participants aged ≥50 years from five waves of the Survey of Health, Ageing and Retirement in Europe. Measures included diabetes (self-reported), physical frailty (≥3/5 criteria), low self-rated health (SRH; "poor" or "fair"), depression (screened using the EURO-D ≥4) and low QoL (CASP-12 <35). Logistic regression was used to adjust for confounding.

Results: Participants with diabetes (n=11,661/97,691) were more likely to be older (68 vs. 64 years, p<0.001), male (50% vs. 45%, p<0.001) and frail (21% vs. 8%, p<0.001). Age, sex, diabetes and frailty were all independently associated with low SRH, depression and low QoL. Frailty had the highest adjusted odds ratios for low SRH (9.43; 95% CI:8.89–10.02), depression (6.39; 95% CI:6.07–6.71) and low QoL (9.65; 95% CI:9.17–10.16). For diabetes, the adjusted odds ratios were 2.82 (2.70–2.95), 1.49 (1.42–1.56) and 1.67 (1.60–1.74), respectively. Participants with both diabetes and frailty reported the worst self-rated health, the most depression symptoms and the lowest QoL.

Conclusions: Frailty was prevalent in older people with diabetes and independently associated with self-rated health, depressive symptoms and low QoL. Prompt identification and management of frailty should be a key consideration in diabetes care.

Keywords: Frailty; Diabetes; Quality of life; Depression

Introduction

Diabetes is a common and metabolically distinct condition in older adults, where poor management can result in serious complications and premature death.[1] Middle aged adults with type 2 diabetes have also presented several metabolic abnormalities compared with younger patients such as an alteration of glucose-induced insulin release, an increase in hepatic glucose production while fasting, and a marked resistance to insulin-mediated glucose disposal.[1] The Diabetes Atlas estimates the 2019 age-standardised prevalence of diabetes in Europe for those aged 20-79 years is 6.3% (4.9%–9.2%) and is expected to rise.[2] Diabetes is already highly prevalent in older adults, with the Global Burden of Disease study (2019) estimating that one in four males (25.3%; 23.4%–27.6%) and more than one in five females aged ≥70 years (22.5%; 20.6%–24.4%) living in Europe have diabetes.[3]

Findings from nearly half a million participants in the UK Biobank study illustrate that people with diabetes have a higher prevalence of frailty.[4] Frailty is often described as a clinical syndrome characterised by decreased reserve or vulnerability to stressors, and is a useful predictor of adverse outcomes including disability, hospitalisation, and mortality.[5,6] It is prevalent both in Europe[7] and worldwide[8]. The most common assessment method is the physical phenotype; which includes measures of weight loss, exhaustion, low physical inactivity, weak hand grip and slow walking speed, although these criteria are frequently modified.[9,10] Research to date illustrates that both frailty and diabetes are associated with numerous psychosocial impacts defined as depression and reduced quality of life (QoL).[11-14] However, few studies assess the combined impact of both conditions.

Both depressive symptoms and reduced QoL are considered key correlates of diabetes by the European Depression in Diabetes (EDID) Research Consortium, highlighting the need for increased awareness and monitoring.[14] In addition, the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study found that psychosocial problems significantly impact diabetes self-care.[15] A growing body of evidence suggests that physiological stress is linked with both the onset and progression of type 2 diabetes mellitus.[16] Thus, psychosocial factors are a key consideration in the management of diabetes and its prognostic trajectory. We speculated that the presence of both diabetes and frailty would have a greater impact on physical, psychological and social dimensions of health than either condition individually or the absence of both conditions. Using a large European dataset the cross-sectional associations of diabetes and frailty with self-rated health, depression symptoms and low QoL were assessed.

Subjects, Materials and Methods

This study is a secondary cross-sectional analysis pooling results from multiple waves of the Survey of Health, Ageing and Retirement in Europe (SHARE), a large longitudinal study including multiple countries. Responses to the regular questionnaires at waves 1, 2, 4, 5 and 6.[17-21] were included, taking each participant's initial interview. The third wave was excluded since a different questionnaire (known as SHARELIFE), assessing life history was used. The SHARE applied probabilistic country-specific sampling strategies to locate a representative sample of middle-aged and older community dwellers in each country. Further details on the sampling methods and procedures are provided elsewhere.[22] The countries included in the SHARE have changed over time most have follow-up assessments available.

Those aged ≥50 years and their partners (any age) if living in the same household were eligible for inclusion in the SHARE. Exclusion criteria were those unable to speak the language(s) of their country, as well as those who were unlocated, living abroad, hospitalised or incarcerated for the whole study period. Some countries included a small number of nursing home residents. In addition, this secondary analysis excluded participants aged <50 years or missing a precise age, as well as those missing three or more frailty criteria,[9] the self-rated health question, or any of the 24 items needed for the depression and QoL assessments. Included participants came from 21 countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Luxembourg, Netherlands, Poland, Portugal, Slovenia, Spain, Sweden, Switzerland).

Survey responses were collected by trained personnel using computer-assisted interviews. A small number of physical assessments including grip strength were performed. The SHARE applied regular questionnaires in waves 1, 2, 4, 5 and 6 which are comparable across countries participating in a wave. These questionnaires are also consistent between waves, although some questions have been added, removed or modified over time. Diabetes status was self-reported in the SHARE and was obtained from a positive response to either "Has a doctor ever told you that you have diabetes?" or "Do you currently take drugs at least once a week for diabetes?". Frailty was measured using a cut-off of $\geq$3 on a five-item frailty phenotype (including appetite/food intake, fatigue, low physical activity, weak hand grip and walking difficulties).[23,24] A description of these five items is provided in the Appendix, and they were considered a close approximation of the original frailty phenotype criteria (weight loss, exhaustion, low physical inactivity, weak hand grip and walking speed).[9,23]

Low self-rated health was assessed using the following five-category question: “Would you say your health is: poor, fair, good, very good or excellent?”. A cut-off of “poor” or “fair” was used for low self-rated health.[25] Depressive symptoms were assessed using the 12-item EURO-D scale and a cut-off of ≥4 positive symptoms was applied for a positive depression screening.[26,27] QoL was measured using the 12-item SHARE version of the control, autonomy, self-realisation and pleasure scale (CASP-12).[28] This scale contains three questions within each of its four sub-components (control, autonomy, self-realisation and pleasure), and each question is scored from 1-4 depending on its frequency occurrence (often, sometimes, rarely, never), resulting in a total score between 12 (worst) and 48 (best). For this study a cut-off of <35 was used to represent low QoL.[29] The EURO-D and CASP-12 items are listed in the Appendix.

Other descriptive variables assessed include body mass index, education, employment, alcohol consumption, smoking, polypharmacy (≥5 drug types), comorbidities, sensory disorders, cognitive impairment, limitations in activities, doctor visits, hospitalisations and institutionalisation. Cognitive impairment was measured based on a previous study summing problems with mathematics, orientation, verbal fluency and recall.[24] Basic activities daily living (BADL) limitations were measured using an adaption of the Katz et al. index and instrumental activities of daily living (IADL) limitations using an adaption of the scale by Lawton and Brody.[30] Full details on how all descriptive variables were measured are provided in the Appendix.

Statistical analyses were conducted using IBM Statistics SPSS version 26. Given the large sample size normality of data was assumed.[31] Hypothesis tests were carried out using independent sample t-tests for continuous variables and the 2-tailed Pearson Chi-Square test for categorical variables. Logistic regression was used to determine if diabetes and frailty were independently associated with worse self-rated health, depression and low QoL. Cronbach’s alpha was used to measure the internal consistency (reliability) of the 12 items included in the EURO-D and CASP-12 indices.

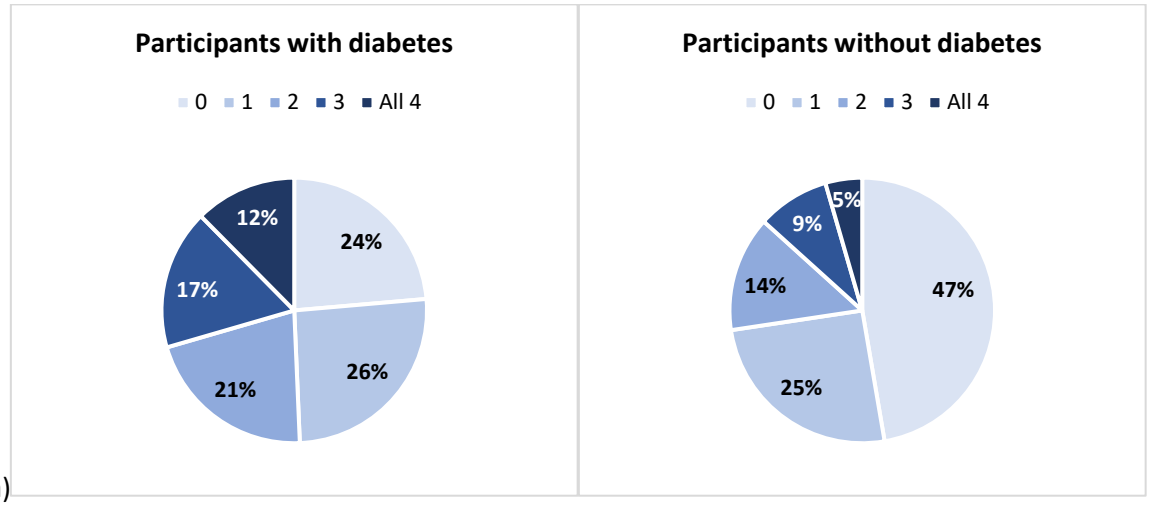
Results

Sample description

In total, 119,978 people participated in a regular questionnaire of the SHARE (waves 1-6). Considering those with complete data for the variables of interest (n=101,427, 85%), there were 97,691 aged ≥50 years eligible for inclusion in this secondary analysis. Of these, 12% (11,661/97,691) reported diabetes and 10% (9,607/97,691) were categorised as frail. Descriptive statistics and missing data for participants according to their diabetes and frailty status are presented in Appendix Tables S1-S4. With the exception of alcohol consumption and smoking status, those with diabetes, as well as those with frailty, had a significantly higher prevalence of risks, diseases and negative outcomes.

Participants with diabetes were more likely to be frail (21% vs. 8%; p<0.001), have low self-rated health (63% vs. 33%; p<0.001), depression (38% vs. 26%; p=0.070) and low QoL (48% vs. 31%, p<0.001). Frail participants were much more likely to have diabetes (25% vs. 11%; p<0.001), low self-rated health (85% vs. 31%; p<0.001), depression (74% vs. 22%; p<0.001) and low QoL (75% vs. 28%; p<0.001). The sum of these conditions by diabetes and frailty status are displayed in Figure 1 and full results for overlapping conditions with numbers are available in Appendix Table S4.

(a)



(b)

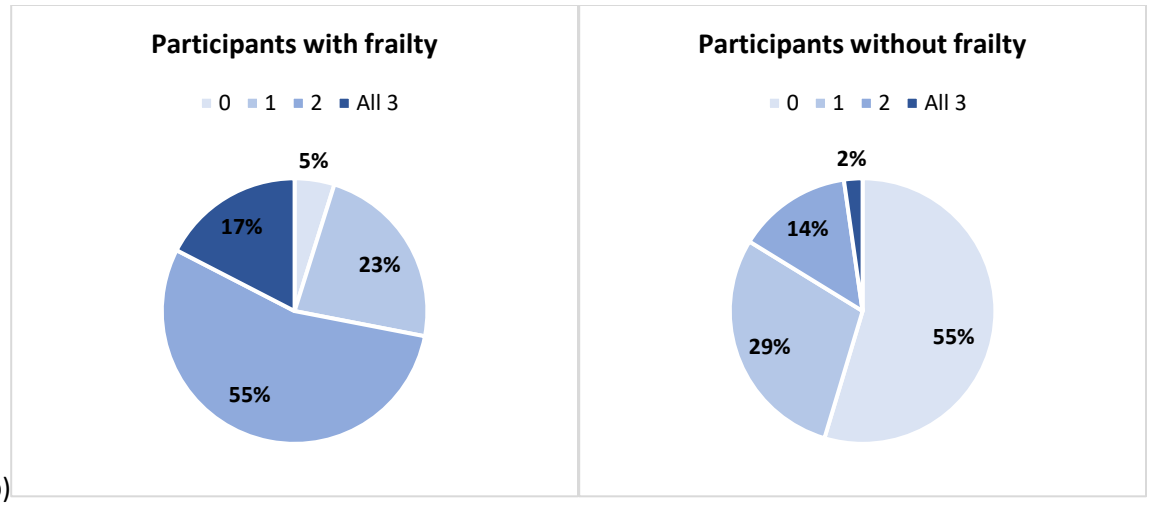


Figure 1: Pie charts illustrating (a) the proportion of participants (with and without diabetes) according to the sum of either frailty (≥3 frailty criteria), low self-rated health (poor/fair), depression (EURO-D ≥4) and low QoL (CASP-12 <35); and (b) the proportion of participants (with and without frailty) according to the sum of either low self-rated health, depression and low QoL.

Frailty in participants with diabetes

For those with diabetes, frail participants were more likely to be older (72.53 vs. 66.59, p<0.001) and female (64% vs. 46%, p<0.001) and were significantly more likely to have many of the risks, diseases, or negative outcomes included in Appendix Table S1 (all p<0.001). Frailty was also associated with low self-rated health (90% vs. 56%, p<0.001), higher mean number of depressive symptoms (5.54 vs. 2.50, p<0.001) and lower mean QoL scores (29.53 vs. 36.11, p<0.001). Using binary cut-offs, more individuals screened positive for depression (75% vs. 29%, p<0.001), and had low QoL (79% vs. 40%, p<0.001). Adjusting for age and sex, frailty was independently associated with low self-rated health [odds ratio (OR): 6.70 (95% CI: 5.81–7.74)], depression [OR 7.68 (6.89–8.56)] and low QoL [OR 5.26 (4.72–5.87)].

Frailty with diabetes compared to frailty without diabetes

Among frail participants, those with diabetes were similar in terms of age (p=0.314) and sex (p=0.144) but had higher mean frailty scores (3.45 vs. 3.39; p<0.001), characterised by a slightly higher frequency of walking problems (86% vs. 81%; p<0.001) and weak grip strength (65% vs. 63%; p=0.046). Other

statistically significant differences included higher mean body mass index (30 vs. 27 kg/m^2; p<0.001), more frequent cognitive impairment (41% vs. 36%; p=0.009), polypharmacy (41% vs. 17%; p<0.001) and limitations in everyday activities from health problems (93% vs. 88%; p<0.001). They also had a higher mean number of doctor visits (15 vs. 13; p<0.001) and were more likely to experience an overnight hospital stay in the last 12 months (37% vs. 30%, p<0.001). Results varied for individual diseases and there were no significant differences for the number nights in hospital (p=0.356) or nursing home admissions (p=0.604).

Frail adults with diabetes were also more likely to report low self-rated health (90% vs. 84%; p<0.001), as illustrated in Figure 2. While the prevalence of positive depression screens were similar (75% vs. 74%, p=0.149) they had a slightly higher mean number of depressive symptoms (5.54 vs. 5.32, p<0.001). As illustrated in Table 1, significant differences were found for poor concentration (51% vs. 45%, p<0.001), pessimism (45% vs. 41%, p<0.001) and suicidality (26% vs. 23%, p<0.001). They were also more likely to report low QoL (79% vs. 74%, p<0.001) and had a lower mean QoL score (29.53 vs. 30.39, p<0.001). Nine CASP-12 components including limitations in all four subsections were significantly lower (Table 2).

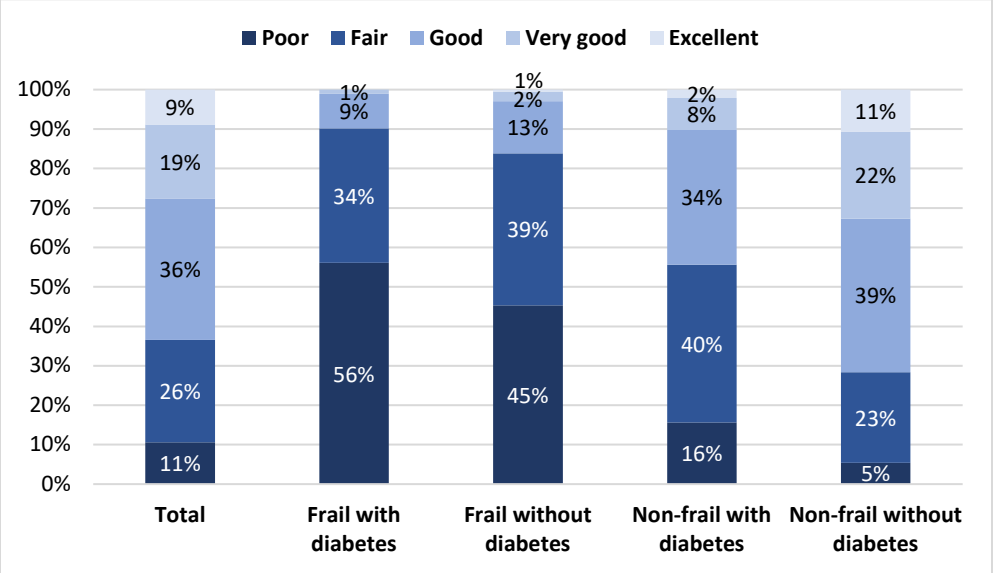


Figure 2: Differences in self-rated health according to diabetes and frailty status.

Table 1. The presence of the EURO-D items and four sub-scales (affective suffering, motivation, items shared with frailty assessment and the remaining three items) by diabetes and frailty status.

EURO-D items	Total	Frail with diabetes	Frail without diabetes	p-value difference	Non-frail with diabetes	Non-frail without diabetes	p-value difference
	n=97,691	n=2,398	n=7,209		n=9,263	n=78,821	
Affective suffering	52,906 (54.2%)	2,002 (83.5%)	5,899 (81.8%)	0.066	5,152 (55.6%)	39,853 (50.6%)	<0.001
Sadness/depressed	38,463 (39.4%)	1,636 (68.2%)	4,773 (66.2%)	0.070	3,682 (39.7%)	28,372 (36%)	<0.001
Pessimism	17,936 (18.4%)	1,082 (45.1%)	2,947 (40.9%)	<0.001	1,922 (20.7%)	11,985 (15.2%)	<0.001
Suicidality	7,071 (7.2%)	612 (25.5%)	1,679 (23.3%)	0.026	707 (7.6%)	4,073 (5.2%)	<0.001
Tearfulness	23,983 (24.5%)	1,139 (47.5%)	3,251 (45.1%)	0.041	2,224 (24%)	17,369 (22%)	<0.001
Motivation	29,674 (30.4%)	1,616 (67.4%)	4,604 (63.9%)	0.002	2,976 (32.1%)	20,478 (26%)	<0.001
Reduced Interest	9,102 (9.3%)	759 (31.7%)	2,123 (29.4%)	0.042	832 (9%)	5,388 (6.8%)	<0.001
Poor concentration	17,834 (18.3%)	1,213 (50.6%)	3,241 (45%)	<0.001	1,796 (19.4%)	11,584 (14.7%)	<0.001
Low enjoyment	13,112 (13.4%)	861 (35.9%)	2,431 (33.7%)	0.051	1,233 (13.3%)	8,587 (10.9%)	<0.001
Frailty items	36,357 (37.2%)	2,248 (93.7%)	6,740 (93.5%)	0.665	3,497 (37.8%)	23,872 (30.3%)	<0.001
Reduced appetite	8,228 (8.4%)	993 (41.4%)	3,069 (42.6%)	0.318	561 (6.1%)	3,605 (4.6%)	<0.001
Fatigue	33,850 (34.7%)	2,131 (88.9%)	6,418 (89%)	0.826	3,225 (34.8%)	22,076 (28%)	<0.001
Other items	49,288 (50.5%)	1,806 (75.3%)	5,376 (74.6%)	0.470	4,906 (53%)	37,200 (47.2%)	<0.001
Guilt	8,472 (8.7%)	316 (13.2%)	1,019 (14.1%)	0.240	736 (7.9%)	6,401 (8.1%)	0.559
Sleep problems	33,352 (34.1%)	1,474 (61.5%)	4,297 (59.6%)	0.107	3,420 (36.9%)	24,161 (30.7%)	<0.001
Irritability	27,929 (28.6%)	1,080 (45%)	3,108 (43.1%)	0.100	2,853 (30.8%)	20,888 (26.5%)	<0.001
EURO-D score	2.45 (2.30)	5.54 (2.60)	5.32 (2.56)	<0.001	2.50 (2.17)	2.09 (2.00)	<0.001
Depressed (score ≥4)	26,582 (27.2%)	1,805 (75.3%)	5,319 (73.8%)	0.149	2,639 (28.5%)	16,819 (21.3%)	<0.001

Overall, the 12 EURO-D items showed good internal consistency (Cronbach's alpha value 0.72).

Table 2. Mean and standard deviation (SD) for the total CASP-12 score, its four sub-components and all 12 individual items.

CASP	Total	Frail with diabetes	Frail without diabetes	p-value difference	Non-frail with diabetes	Non-frail without diabetes	p-value difference
	n=97,691	n=2,398	n=7,209		n=9,263	n=78,821	
Limitation in control	8.70 (2.36)	6.30 (2.31)	6.52 (2.35)	<0.001	8.37 (2.35)	9.01 (2.21)	<0.001
Age prevents from doing things	2.66 (1.04)	1.67 (0.93)	1.79 (0.97)	<0.001	2.46 (1.01)	2.79 (1.00)	<0.001
Out of control	2.88 (0.98)	2.12 (1.02)	2.17 (1.02)	0.031	2.81 (1.00)	2.98 (0.94)	<0.001
Feel left out of things	3.16 (0.95)	2.51 (1.13)	2.56 (1.12)	0.069	3.10 (0.99)	3.24 (0.89)	<0.001
Limitation in autonomy	8.79 (1.97)	7.78 (2.04)	7.96 (1.99)	<0.001	8.64 (1.97)	8.91 (1.94)	<0.001
Do the things you want to do	3.22 (0.91)	2.51 (1.00)	2.61 (0.97)	<0.001	3.15 (0.88)	3.31 (0.87)	<0.001
Family responsibilities prevent	3.07 (0.98)	3.10 (1.07)	3.09 (1.06)	0.665	3.13 (0.98)	3.06 (0.96)	<0.001
Shortage of money stops	2.49 (1.11)	2.17 (1.15)	2.25 (1.16)	0.002	2.36 (1.12)	2.54 (1.10)	<0.001
Limitation in self-realization	9.26 (2.28)	6.46 (2.28)	6.80 (2.36)	<0.001	8.89 (2.20)	9.61 (2.07)	<0.001
Feel full of energy	3.15 (0.86)	2.03 (0.87)	2.18 (0.90)	<0.001	3.03 (0.84)	3.29 (0.77)	<0.001
Full of opportunities	3.08 (0.89)	2.26 (0.94)	2.36 (0.96)	<0.001	2.96 (0.89)	3.18 (0.84)	<0.001
Future looks good	3.03 (0.91)	2.17 (0.95)	2.27 (0.95)	<0.001	2.90 (0.92)	3.14 (0.86)	<0.001
Limitation in pleasure	10.33 (1.84)	8.99 (2.17)	9.12 (2.19)	0.011	10.21 (1.84)	10.49 (1.73)	<0.001
Look forward to each day	3.39 (0.88)	2.98 (0.97)	3.00 (0.97)	0.551	3.37 (0.87)	3.44 (0.85)	<0.001
Life has meaning	3.55 (0.73)	2.97 (0.94)	3.04 (0.93)	0.002	3.51 (0.74)	3.62 (0.67)	<0.001
Look back on life with happiness	3.38 (0.77)	3.04 (0.90)	3.09 (0.87)	0.024	3.32 (0.79)	3.43 (0.74)	<0.001
CASP score	37.07 (6.38)	29.53 (6.22)	30.39 (6.33)	<0.001	36.11 (6.15)	38.03 (5.86)	<0.001
Low QoL (CASP <35)	31,978 (32.7%)	1,891 (78.9%)	5,312 (73.7%)	<0.001	3,659 (39.5%)	21,116 (26.8%)	<0.001

Overall, the 12 CASP-12 items showed excellent internal consistency (Cronbach's alpha 0.82).

Non-frail with diabetes compared to non-frail without diabetes

Among non-frail participants, those with diabetes were more likely to be older (66.59 vs. 63.17, p<0.001) and male (54% vs. 46%, p<0.001) and were significantly more likely to have many of the risks, diseases, or negative outcomes included in Table S1 (all p<0.05). They were also more likely to report low self-rated health (56% vs. 28%; p<0.001), depression (29% vs. 21%, p<0.001) and low QoL (40% vs. 27%, p<0.001). They had a higher mean number of depressive symptoms (2.50 vs. 2.09; p<0.001) and a lower mean CASP-12 score (36.11 vs. 38.03, p<0.001). With the exception of guilt (p=0.559), all individual depressive symptoms were significantly higher among those with diabetes (p<0.001) (Table 1), and all CASP-12 items were significantly lower (all p<0.001) (Table 2).

Multivariate analysis

The above findings were supported by logistic regression analysis, which illustrated that both diabetes and frailty were independently associated with self-rated health, depression and low QoL (Table 3). Adjusting for age, diabetes and sex, the odds ratios (95% CIs) for frailty were 9.43 (8.89–10.02) for low self-rated health, 9.65 (9.17–10.16) for depressive symptoms and 6.39 (6.07–6.71) for low QoL. Results for diabetes adjusted for age, sex and frailty were 2.82 (2.70–2.95), 1.49 (1.42–1.56) and 1.67 (1.60–1.74), respectively.

Table 3. Logistic regression models illustrating the associations (odds ratio and 95% CI) between low self-rated health, depression symptoms and low quality of life (QoL) using different models including diabetes, frailty, age, and sex (n=97,691).

Models	Variables	Low self-rated health[a]	Depression[b]	Low QoL[c]
Model 1	Diabetes	3.41 (3.27–3.55)	1.78 (1.71–1.85)	2.05 (1.97–2.13)
Model 2	Frailty	12.89 (12.16–13.67)	10.12 (9.64–10.62)	7.66 (7.29–8.04)
Model 3	Diabetes	3.03 (2.91–3.16)	1.40 (1.34–1.46)	1.72 (1.65–1.79)
	Frailty	12.01 (11.32–12.74)	9.72 (9.26–10.20)	7.22 (6.88–7.58)
Model 4	Diabetes	2.82 (2.70–2.95)	1.49 (1.42–1.56)	1.67 (1.60–1.74)
	Frailty	9.43 (8.89–10.02)	9.65 (9.17–10.16)	6.39 (6.07–6.71)
	Age	1.03 (1.03–1.04)	1.00 (1.00–1.00)[1]	1.01 (1.01–1.02)
	Sex (female)	1.16 (1.13–1.19)	2.10 (2.03–2.16)	1.16 (1.13–1.19)
Model 5	Diabetes	2.60 (2.48–2.72)	1.05 (1.00–1.10)[3]	1.27 (1.21–1.33)
	Frailty	4.54 (4.26–4.84)	4.70 (4.44–4.96)	2.56 (2.43–2.71)
	Low SR health	-	2.67 (2.58–2.77)	2.68 (2.60–2.77)
	Depression	2.66 (2.57–2.76)	-	3.73 (3.61–3.86)
	Low QoL	2.68 (2.59–2.76)	3.74 (3.61–3.87)	-
	Age	1.03 (1.03–1.04)	0.99 (0.98–0.99)	1.01 (1.01–1.01)
	Sex (female)	0.99 (0.96–1.02)[2]	2.15 (2.08–2.23)	0.94 (0.91–0.97)

Data were presented as odds ratio with 95% confidence interval. [a]Self-rated health as 'Fair' or 'Poor'. [b]CASP-12 score <35. [c]EURO-D score ≥4; [1]Value <1 and p-value= 0.006; [2]P-value = 0.443; [3]P-value = 0.048; All other p-values <0.001.

Discussion

This study highlights that both diabetes and frailty are independently associated with symptoms of depression and low QoL. Frailty was more common for those with diabetes and frail participants with diabetes had a higher number of frailty criteria and depressive symptoms than other frail participants. These results agree with a previous analysis of the SHARE[25] and the existing literature that people with diabetes have a higher prevalence of frailty[4], low self-rated health[32], depression[11] and low QoL[14]. There was also a sizable overlap between the conditions with 31% of people with diabetes reporting both low self-rated health and depression. This is consistent with a previous study that found that self-rated health had a stronger association with depressive symptoms than objective physical indicators of diabetes.[32] Correlations between self-rated health, functional health and physical inactivity offer a potential explanation for these observations.[32,33]

Both physical frailty and diabetes were independent indicators of low self-rated health, depression and low QoL with the combination of both conditions being particularly concerning. For example, of those with frailty and diabetes, 90% had low self-rated health and 75% screened positive for depression and 79% reported low QoL. Compared to those who were frail without diabetes, those with both frailty and diabetes had a greater number of frailty criteria, depressive symptoms and lower QoL scores. Two of the five frailty criteria were significantly higher: walking problems and weak grip strength. They also reported more activity limitations, cognitive decline, polypharmacy and hospitalisations, indicating reductions in cognitive, functional and physical wellbeing. However, it is worth noting that due to the large sample size, small differences reached statistical significance but may not be clinically significant (e.g. the comparison between mean QoL scores for frail adults with and without diabetes: 29.53 vs. 30.39).

A previous review suggested that the link between the endocrine system and frailty may be particularly important,[34] and this study supports this hypothesis. Well-known complications of diabetes include micro and macrovascular complications and impaired cognition, the burden of which was also observed in this cohort (Appendix Table S2). Rather than being a separate process, these complications likely contribute to the development of frailty, bringing frailty into the spectrum of diabetes complications. As such, frailty should be considered as a core component of diabetes care as highlighted in numerous recommendations.[35-37] It must also be noted that frailty in those with diabetes might modify treatment success[38]; and can be associated with a normalisation of blood glucose levels increasing the risk of iatrogenic hypoglycaemia.[39] This normalisation in frail older people can occur through a number of mechanisms including reduced food (and therefore glucose) intake, weight loss (a measure of frailty which

also leads to reduction in insulin resistance) and declining renal function (reduced clearance of insulin and anti-diabetes medication). As such, guidelines have been provided for the relaxation of treatment targets in those with different levels of frailty,[37] and in some cases a complete withdrawal of anti-hyperglycaemic agents may be deemed appropriate after clinical re-evaluation of the risks and benefits.[39] Further research is needed into the effects of frailty on diabetes management with one recent publication suggesting frailty modifies the relationship between blood pressure and mortality in older patients with type 2 diabetes mellitus.[40]

While few studies have focused on interventions specifically for frailty with diabetes, general frailty guidelines suggest tailored care including physical activity, nutritional intervention and cognitive training may help prevent or reverse the onset of frailty.[41] The recent MID-Frail trial[42] showed that an intervention in nutrition and diabetes education in conjunction with an exercise programme could produce significant one-year improvements in function according to the Short Physical Performance Battery and reduced hospital care costs, which equated to estimated savings of €428.02 per patient per year. However, no significant changes were observed for burden on caregivers, institutionalization, severity of hypoglycaemia episodes, rate of hospitalization, QoL (EQ-5D-5L), or mortality.

Strengths of this study include the large sample size and the robust methods of the SHARE. Both the EURO-D and CASP-12 also had reasonable levels of internal consistency. The main limitation was that diabetes and depression were not measured using objective clinical criteria which may result in self-reporting bias. Further, it was not possible to measure if the participants were receiving insulin therapy which would likely impact on self-rated health, depression and QoL. In addition, the SHARE does not include all European countries, and the sampling strategy varies by country. However, robust methods were applied and the overall response rates were satisfactory, for example the household response rate at wave 1 was approximately 62%.[22]. A further limitation is that the frailty phenotype criteria often overlap with symptoms of depression or diseases such as cancer or Parkinson's disease. The modified criteria used in this analysis included reduced appetite/food intake instead of unintentional weight loss, and measures of fatigue and low physical activity are included in both the original and modified criteria published elsewhere and are valid.[23,24] Nevertheless, all items of the EURO-D were significantly associated with frailty illustrating that this association would still be observed if the overlapping items were not considered. While psychological vulnerability is an important component of frailty,[43] further clinical assessment would be required to verify whether the positive frailty criteria can be explained by another disease or psychological disorder. While there was some overlap between the frailty phenotype and the

measure of depression (EURO-D), there were no items shared between the frailty phenotype and the QoL (CASP-12) criteria. Additional research could assess longitudinal correlations between frailty and diabetes as well as objective outcomes such as mortality.

Conclusions

This study found that frailty is prevalent and independently associated with negative psychosocial factors including depressive symptoms and lower QoL among people with diabetes. While both frailty and diabetes were independently associated with poorer psychosocial health, the combination of both conditions was worse than either individually. Hence, there is a need to identify frailty, particularly in those with diabetes, in order to prevent and mitigate against their combined negative impact on psychosocial wellbeing.

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