

Loneliness, social isolation and incident chronic kidney disease among diabetes patients

Supplementary Materials

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Table S1. Definitions of prevalent diabetes.

	Source and definition
Diabetes at baseline: both possible (including type 1, type 2 and other types of diabetes) and probable (including type 1, type 2 and other types of diabetes) diabetes at baseline	Self-reported at baseline ¹ ; Medication for diabetes at baseline ¹ ; International Classification of Diseases, Ninth Revision (ICD-9): 250, 6480 (if incident time \leq Date of attending assessment centre); International Classification of Diseases, Tenth Revision (ICD10): E10, E11, E12, E13, E14, O24 (if incident time \leq Date of attending assessment centre).

1. Eastwood SV, Mathur R, Atkinson M, et al. Algorithms for the capture and adjudication of prevalent and incident diabetes in UK Biobank. *PLoS One*. 2016. 11(9): e0162388.

Table S2. Assessment of social isolation and loneliness in the UK Biobank

Indicators	UK Biobank field ID	Touchscreen questions	Responses	Score
Social isolation indicators	709	Including yourself, how many people are living together in your household?	Not living alone.	0
			Living alone	1
	1031	How often do you visit friends or family or have them visit you?	Almost daily	0
			2–4 times a week	
			About once a week	
About once a month				
6160	Which of the following (sports club or gym, pub or social club, religious group, adult education class, other group activity) do you attend once a week or more often?	Once every few months	1	
		Never or almost never		
		No friends/family outside household		
		None of the above		
Loneliness indicators	2020	Do you often feel lonely?	No	0
			Yes	1
	2110	How often are you able to confide in someone close to you?	Almost daily	0
			2–4 times a week	
			About once a week	
About once a month				
			Once every few months	1
			Never or almost never	

Table S3. Baseline characteristics of participants with diabetes by social isolation score.

Characteristics	Social isolation score			
	0	1	2	3
No. of participants	8631 (45.5)	7914 (41.7)	2193 (11.6)	234 (1.2)
Age, years	59.9 (7.0)	59.4 (7.1)	58.6 (7.2)	58.2 (6.9)
Female sex, n (%)	3053 (35.4)	3144 (39.7)	827 (37.7)	66 (28.2)
White ethnicity, n (%)	7560 (87.6)	6989 (88.3)	1920 (87.6)	204 (87.2)
Townsend deprivation index	-1.1 (3.1)	-0.3 (3.4)	0.7 (3.6)	2.2 (3.4)
Body mass index, kg/m ²	30.7 (5.5)	31.3 (5.9)	31.6 (6.0)	32.3 (6.8)
Diabetes duration, years	8.4 (10.4)	8.3 (10.2)	8.4 (10.6)	9.2 (10.9)
Current smoker, n (%)	676 (7.9)	892 (11.3)	391 (18.0)	55 (23.5)
Current drinker, n (%)	7536 (87.5)	6659 (84.3)	1752 (80.0)	173 (74.6)
Physical activity, n (%) ^a	4995 (57.9)	3750 (47.4)	931 (42.5)	74 (31.6)
Healthy diet score	2.7 (1.2)	2.6 (1.3)	2.5 (1.3)	2.4 (1.3)
Depression score	0.6 (1.4)	0.8 (1.4)	1.2 (1.6)	1.7 (2.0)
eGFR, mL/min/1.73 m ²	93.9 (13.6)	93.3 (13.6)	92.6 (14.3)	92.1 (14.0)
Antihypertensive medication, n (%)	5202 (61.3)	4717 (60.6)	1357 (63.1)	148 (64.4)
Cholesterol-lowering medication, n (%)	6465 (76.2)	5842 (75.0)	1620 (75.4)	176 (76.5)
Diabetes medication, n (%)	5970 (69.2)	5600 (70.8)	1601 (73.0)	178 (76.1)

Values are means (SD) for continuous variables and n (%) for categorical variables.

BMI=body mass index; eGFR= estimated glomerular filtration rate.

^a, physical activity was calculated as minutes of moderate or vigorous physical activity or an equivalent combination per week. According to the guideline, being physically active was defined as engaging in >150 minutes of moderate-intensity activity weekly, >75 minutes of vigorous-intensity activity or a comparable mix of the two.

Table S4. Multivariable-adjusted HRs (95% CIs) of individual social isolation factors for chronic kidney among baseline diabetes patients

Social isolation factors	Chronic kidney disease			
	No. of cases/total	Model 1 HR	Model 2 HR	Model 3 HR
Living alone				
0	831/14 597	1 (Reference)	1 (Reference)	1 (Reference)
1	289/4286	1.11 (0.97 to 1.28)	1.12 (0.98 to 1.29)	1.09 (0.93 to 1.27)
Frequency of social visits				
0	1007/16 799	1 (Reference)	1 (Reference)	1 (Reference)
1	106/2003	0.98 (0.80 to 1.20)	0.98 (0.80 to 1.20)	1.06 (0.85 to 1.32)
Weekly Leisure/social Activities				
0	679/12 148	1 (Reference)	1 (Reference)	1 (Reference)
1	443/6713	1.23 (1.10 to 1.40)	1.17 (1.03 to 1.32)	1.02 (0.89 to 1.18)

Model 1 was adjusted for sex, age, race, Townsend deprivation index.

Model 2: Model 1+ physical activity, healthy diet score, smoking, alcohol use, body mass index.

Model 3: Model 2+ estimated glomerular filtration rate, diabetes duration, the use of diabetes medication, cholesterol-lowering medication, antihypertensive medication, and depression score.

Table S5. Sensitivity analyses of the multivariable-adjusted HRs (95% CIs) of individual loneliness factors for chronic kidney among baseline diabetes patients.

Loneliness factors	Chronic Kidney Disease		
	No. of cases/total	Model 1	Model 1+Social isolation scale
Feeling lonely			
0	813/14 254	1 (Reference)	1 (Reference)
1	299/4361	1.22 (1.04 to 1.43)	1.21 (1.02 to 1.45)
Confiding in someone close			
0	783/13 636	1 (Reference)	1 (Reference)
1	301/4584	1.06 (0.91 to 1.24)	0.96 (0.81 to 1.40)

Model 1 was adjusted for sex, age, race, Townsend deprivation index, physical activity, healthy diet score, smoking, alcohol use, body mass index, estimated glomerular filtration rate, diabetes duration, the use of diabetes medication, cholesterol-lowering medication, antihypertensive medication and depression score. Feeling lonely and confiding in someone close were mutually adjusted in the sensitivity analyses.

Table S6. Stratified analyses for the association between loneliness scale and hazard of chronic kidney disease among baseline diabetes patients.

Subgroups	Loneliness scale			P-trend	P for interaction
	0 HR	1 HR	2 HR		
Age					0.761
<60 years old	1 (reference)	1.12 (0.80 to 1.57)	1.18 (0.74 to 1.91)	0.412	
≥60 years old	1 (reference)	1.04 (0.87 to 1.24)	1.18 (0.88 to 1.58)	0.313	
Sex					0.332
Women	1 (reference)	1.19 (0.91 to 1.55)	1.35 (0.90 to 2.01)	0.094	
Men	1 (reference)	1.00 (0.82 to 1.22)	1.17 (0.85 to 1.61)	0.483	
Race					0.244
Non-Whites	1 (reference)	1.36 (0.79 to 2.33)	1.76 (0.78 to 3.98)	0.134	
Whites	1 (reference)	1.03 (0.87 to 1.22)	1.19 (0.91 to 1.54)	0.265	
Townsend deprivation index					0.282
Low (Q1)	1 (reference)	1.07 (0.74 to 1.53)	0.55 (0.24 to 1.26)	0.437	
Intermediate (Q2–Q4)	1 (reference)	1.12 (0.91 to 1.37)	1.18 (0.85 to 1.64)	0.213	
High (Q5)	1 (reference)	0.97 (0.68 to 1.39)	1.78 (1.13 to 2.78)	0.061	
Regular physical activity					0.091
No	1 (reference)	0.92 (0.73 to 1.15)	1.12 (0.81 to 1.56)	0.884	
Yes	1 (reference)	1.25 (0.99 to 1.57)	1.32 (0.91 to 1.93)	0.042	
Diet score					0.562
< Median	1 (reference)	1.06 (0.84 to 1.34)	1.15 (0.81 to 1.65)	0.408	
≥ Median	1 (reference)	1.06 (0.85 to 1.32)	1.28 (0.91 to 1.81)	0.209	
Smoking status					0.522
Non-current	1 (reference)	1.03 (0.87 to 1.22)	1.17 (0.90 to 1.53)	0.290	
Current	1 (reference)	1.26 (0.74 to 2.13)	1.74 (0.86 to 3.52)	0.138	
Drinking status					0.703
Non-current	1 (reference)	1.04 (0.70 to 1.53)	0.90 (0.49 to 1.66)	0.867	
Current	1 (reference)	1.06 (0.89 to 1.27)	1.29 (0.99 to 1.70)	0.095	
Obesity					0.077
No	1 (reference)	1.16 (0.91 to 1.48)	1.56 (1.07 to 2.28)	0.026	
Yes	1 (reference)	0.99 (0.80 to 1.22)	1.03 (0.74 to 1.43)	0.954	
eGFR					0.826
<90 mL/min per 1.73 m ²	1 (reference)	1.07 (0.89 to 1.28)	1.21 (0.92 to 1.61)	0.187	
≥90 mL/min per 1.73 m ²	1 (reference)	1.01 (0.72 to 1.43)	1.16 (0.69 to 1.96)	0.654	
Diabetes Duration					0.314
<5 years	1 (reference)	0.93 (0.71 to 1.21)	1.02 (0.67 to 1.56)	0.825	
5-10 years	1 (reference)	1.10 (0.81 to 1.48)	1.27 (0.80 to 2.01)	0.302	
≥10 years	1 (reference)	1.22 (0.93 to 1.59)	1.38 (0.91 to 2.09)	0.085	
Diabetes medication					0.495
No	1 (reference)	1.15 (0.82 to 1.61)	1.55 (0.92 to 2.63)	0.113	
Yes	1 (reference)	1.05 (0.88 to 1.26)	1.17 (0.88 to 1.55)	0.275	
Cholesterol-lowering medication					0.061
No	1 (reference)	0.87 (0.58 to 1.31)	0.54 (0.24 to 1.21)	0.145	
Yes	1 (reference)	1.09 (0.92 to 1.30)	1.36 (1.04 to 1.76)	0.032	
Antihypertensive medication					0.593
No	1 (reference)	0.99 (0.71 to 1.37)	1.17 (0.70 to 1.96)	0.697	
Yes	1 (reference)	1.09 (0.90 to 1.30)	1.26 (0.95 to 1.67)	0.115	
Depressive score					0.824

<3	1 (reference)	1.03 (0.87 to 1.23)	1.23 (0.93 to 1.63)	0.212
≥3	1 (reference)	1.28 (0.75 to 2.18)	1.34 (0.73 to 2.45)	0.343

Model was adjusted for sex, age, race, Townsend deprivation index, physical activity, healthy diet score, smoking, alcohol use, body mass index, estimated glomerular filtration rate, diabetes duration, the use of diabetes medication, cholesterol-lowering medication, antihypertensive medication and depression score.

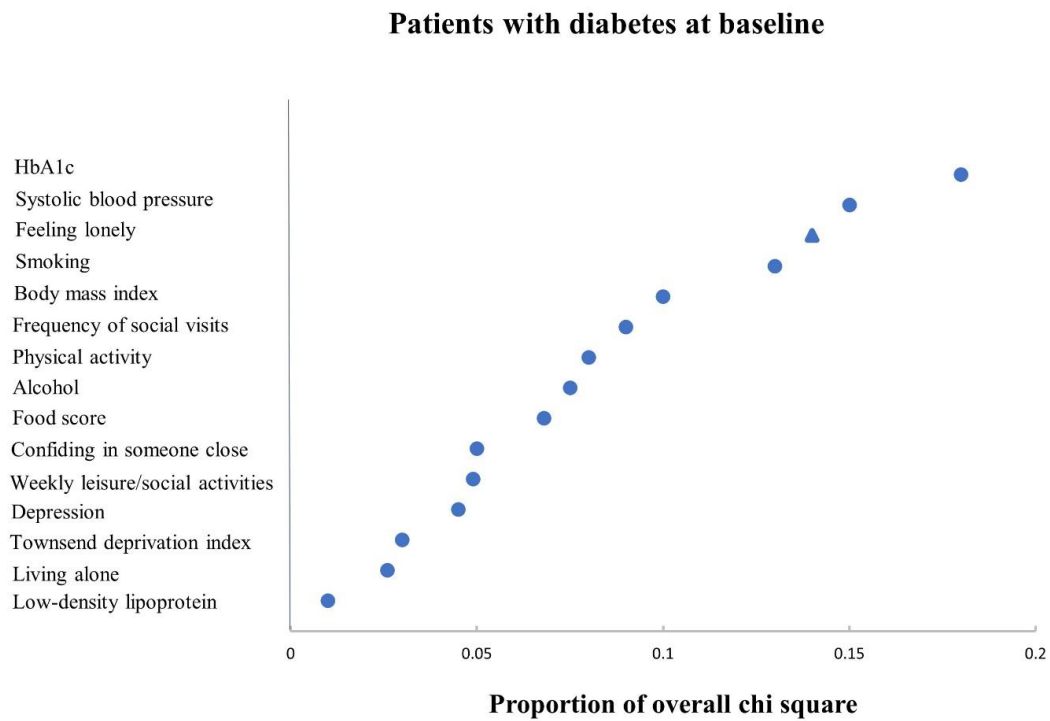


Figure S1. Relative importance of predictors for incident of chronic kidney disease, by estimation of explained log-likelihood explained by each predictor, in patients with diabetes at baseline.