

**SUPPLEMENTARY MATERIAL**

**Supplementary Table S1.** Stratified associations of sarcopenia and social isolation with CVD mortality and cancer mortality in the UK Biobank

	CVD Mortality			Cancer Mortality		
	Cases/Person-years	HR (95% CI)	P value	Cases/Person-years	HR (95% CI)	P value
<b>Non-sarcopenia</b>						
Least isolation	1,844/2,134,406	1		5,406/2,134,406	1	
Moderate isolation	1,981/1,849,814	<b>1.19 (1.12–1.27)</b>	<b>&lt;0.001</b>	5,233/1,849,814	<b>1.10 (1.06–1.15)</b>	<b>&lt;0.001</b>
Most isolation	968/632,566	<b>1.52 (1.41–1.65)</b>	<b>&lt;0.001</b>	2,092/632,566	<b>1.24 (1.18–1.31)</b>	<b>&lt;0.001</b>
<b>Probable and Confirmed Sarcopenia</b>						
Least isolation	166/132,993	1		424/132,993	1	
Moderate isolation	212/124,907	<b>1.37 (1.12–1.69)</b>	<b>0.002</b>	444/124,907	1.11 (0.97–1.27)	0.120
Most isolation	114/45,269	<b>1.81 (1.42–2.32)</b>	<b>&lt;0.001</b>	206/45,269	<b>1.35 (1.14–1.60)</b>	<b>&lt;0.001</b>
<b>P-interaction</b>		0.34			0.21	

**Note.** Model adjusted for age, sex, ethnicity, Townsend deprivation index, education level, smoking status, alcohol intake, physically active, healthy diet score, body mass index and the number of baseline diseases. Multiplicative interaction was evaluated using *P* value for the product term between the social isolation level (least vs most) and sarcopenia status (non-sarcopenia vs sarcopenia). Abbreviations: CVD, cardiovascular disease; *CI*, confidence interval; *HR*, hazard ratio.

**Supplementary Table S2.** Associations of the items of social isolation with all-cause mortality

	CLHLS		UK Biobank	
	Cases/ Person-years	HR (95% CI)	Cases/ Person-years	HR (95% CI)
<b>Living alone</b>				
No	6,997/51,092	1	19,695/4,035,717	1
Yes	1,252/9,801	<b>0.84 (0.79–0.90)</b>	6,975/884,238	<b>1.33 (1.29–1.37)</b>
<b>Contact with friends/family</b>				
More	8,212/60,597	1	20,681/3,848,614	1
Less	37/296	0.81 (0.58–1.14)	5,989/1,071,341	<b>1.13 (1.09–1.16)</b>
<b>Leisure/Social activities</b>				
More	973/12,463	1	18,124/3,485,633	1
Fewer	7,276/48,430	<b>1.21 (1.13–1.30)</b>	8,546/1,434,322	<b>1.10 (1.07–1.13)</b>
<b>Marital status</b>				
Married	6,997/25,818	1	NA	NA
Lack of a spouse	6,334/35,075	<b>1.28 (1.21–1.37)</b>	NA	NA

**Note.** Model adjusted for age, sex, ethnicity (UK Biobank only), residence (CLHLS only), Townsend deprivation index (UK Biobank only), economic level (CLHLS only), education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, the number of baseline diseases, sarcopenia, and the remaining items of social isolation. Abbreviations: CLHLS, Chinese Longitudinal Healthy Longevity Survey; *CI*, confidence interval; *HR*, hazard ratio.

**Supplementary Table S3.** Joint associations of leisure/social activities and sarcopenia with all-cause mortality risk in the CLHLS

	<b>Cases/ Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>Sarcopenia and leisure/social activities Category</b>			
Non-sarcopenia & More leisure/social activities	543/9,231	<b>1</b>	-
Non-sarcopenia & Fewer leisure/social activities	1,644/23,020	1.06 (0.96–1.17)	0.258
Probable and Confirmed Sarcopenia & More leisure/social activities	430/3,233	<b>1.35</b> <b>(1.19–1.54)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & Fewer leisure/social activities	5,632/25,409	<b>1.81</b> <b>(1.65–2.00)</b>	<b>&lt;0.001</b>
<b>Additive Interaction (Probable and Confirmed Sarcopenia &amp; Fewer)</b>			
<i>RERI</i>	-	<b>0.40</b> <b>(0.25–0.56)</b>	-
<b>Multiplicative Interaction (Probable and Confirmed Sarcopenia &amp; Fewer)</b>			
	-	-	<b>0.0008</b>

**Note.** Model adjusted for age, sex, residence, economic level, education level, smoking status, alcohol intake, physically active, healthy diet score, body mass index and the number of baseline diseases. Abbreviations: *CI*, confidence interval; *HR*, hazard ratio; *RERI*, relative risk due to interaction.

**Supplementary Table S4.** Joint associations of marital status and sarcopenia with all-cause mortality risk in the CLHLS

	<b>Cases/ Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>Sarcopenia and marital status Category</b>			
Non-sarcopenia & Married	914/18,670	<b>1</b>	-
Non-sarcopenia & Lack of a spouse	1,273/13,581	<b>1.31 (1.20–1.43)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & Married	1,001/7,148	<b>1.81 (1.65–1.99)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & Lack of a spouse	5,061/21,495	<b>2.07 (1.90–2.26)</b>	<b>&lt;0.001</b>
<b>Additive Interaction (Probable and Confirmed Sarcopenia &amp; Lack of a spouse)</b>			
<i>RERI</i>	-	-0.05 (-0.21–0.12)	-
<b>Multiplicative Interaction (Probable and Confirmed Sarcopenia &amp; Lack of a spouse)</b>			
	-	-	<b>0.017</b>

**Note.** Model adjusted for age, sex, residence, economic level, education level, smoking status, alcohol intake, physically active, healthy diet score, body mass index and the number of baseline diseases. Abbreviations: *CI*, confidence interval; *HR*, hazard ratio; *RERI*, relative risk due to interaction.

**Supplementary Table S5.** Joint associations of living alone and sarcopenia with all-cause mortality risk in the UK Biobank

	<b>Cases/ Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>Sarcopenia and living alone Category</b>			
Non-sarcopenia & No	18,088/3,802,272	<b>1</b>	-
Non-sarcopenia & Yes	6,210/814,514	<b>1.32 (1.28–1.36)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & No	1,607/233,445	<b>1.14 (1.08–1.20)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & Yes	765/69,724	<b>1.59 (1.47–1.71)</b>	<b>&lt;0.001</b>
<b>Additive Interaction (Probable and Confirmed Sarcopenia &amp; Yes)</b>			
<i>RERI</i>	-	0.13 (-0.01–0.26)	-
<b>Multiplicative Interaction (Probable and Confirmed Sarcopenia &amp; Yes)</b>			
	-	-	0.255

**Note.** Model adjusted for age, sex, ethnicity, Townsend deprivation index, education level, smoking status, alcohol intake, physically active, healthy diet score, body mass index and the number of baseline diseases; Abbreviations: *CI*, confidence interval; *HR*, hazard ratio; *RERI*, relative risk due to interaction.

**Supplementary Table S6.** Joint associations of contact with friends/family and sarcopenia with all-cause mortality risk in the UK Biobank

	<b>Cases/ Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>Sarcopenia and contact with friends/family Category</b>			
Non-sarcopenia & More contact with friends/family	18,088/3,607,978	<b>1</b>	-
Non-sarcopenia & Less contact with friends/family	5,418/1,008,807	<b>1.11 (1.07–1.14)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & More contact with friends/family	1,801/240,635	<b>1.13 (1.08–1.19)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & Less contact with friends/family	571/62,534	<b>1.43 (1.32–1.56)</b>	<b>&lt;0.001</b>
<b>Additive Interaction (Probable and Confirmed Sarcopenia &amp; More)</b>			
<i>RERI</i>	-	<b>0.20 (0.07–0.33)</b>	-
<b>Multiplicative Interaction (Probable and Confirmed Sarcopenia &amp; Less)</b>			
	-	-	<b>0.007</b>

**Note.** Model adjusted for age, sex, ethnicity, Townsend deprivation index, education level, smoking status, alcohol intake, physically active, healthy diet score, body mass index and the number of baseline diseases; Abbreviations: *CI*, confidence interval; *HR*, hazard ratio; *RERI*, relative risk due to interaction.

**Supplementary Table S7.** Joint associations of leisure/social activities and sarcopenia with all-cause mortality risk in the UK Biobank

	<b>Cases/ Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>Sarcopenia and leisure/social activities Category</b>			
Non-sarcopenia & More leisure/social activities	16,503/3,270,319	<b>1</b>	-
Non-sarcopenia & Fewer leisure/social activities	7,795/1,346,467	<b>1.10 (1.08–1.14)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & More leisure/social activities	1,621/215,313	<b>1.17 (1.11–1.23)</b>	<b>&lt;0.001</b>
Probable and Confirmed Sarcopenia & Fewer leisure/social activities	751/87,856	<b>1.30 (1.20–1.39)</b>	<b>&lt;0.001</b>
<b>Additive Interaction (Probable and Confirmed Sarcopenia &amp; Fewer)</b>			
<i>RERI</i>	-	0.03 (-0.09–0.14)	-
<b>Multiplicative Interaction (Probable and Confirmed Sarcopenia &amp; Fewer)</b>			
	-	-	0.886

**Note.** Model adjusted for age, sex, ethnicity, Townsend deprivation index, education level, smoking status, alcohol intake, physically active, healthy diet score, body mass index and the number of baseline diseases; Abbreviations: *CI*, confidence interval; *HR*, hazard ratio; *RERI*, relative risk due to interaction.

**Supplementary Table S8.** Joint associations of sarcopenia and social isolation with all-cause mortality after excluding those who died within the first two years of enrollment

	<b>Cases/Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>CLHLS (n = 11,303)</b>			
<b>Non-sarcopenia</b>			
Least isolation	234/5,710	<b>1</b>	
Moderate isolation	641/14,817	0.93 (0.80–1.08)	0.932
Most isolation	812/11,173	<b>1.19 (1.02–1.38)</b>	<b>0.016</b>
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	89/1,038	<b>1.59 (1.25–2.04)</b>	<b>&lt;0.001</b>
Moderate isolation	742/7,140	<b>1.57 (1.35–1.83)</b>	<b>&lt;0.001</b>
Most isolation	2,577/17,806	<b>1.75 (1.50–2.03)</b>	<b>&lt;0.001</b>
<b>UK Biobank (n = 384,045)</b>			
<b>Non-sarcopenia</b>			
Least isolation	9,239/2,133,662	<b>1</b>	
Moderate isolation	9,387/1,848,999	<b>1.14 (1.11–1.18)</b>	<b>&lt;0.001</b>
Most isolation	4,076/632,154	<b>1.36 (1.31–1.41)</b>	<b>&lt;0.001</b>
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	798/132,913	<b>1.08 (1.01–1.16)</b>	<b>0.040</b>
Moderate isolation	960/124,838	<b>1.37 (1.28–1.47)</b>	<b>&lt;0.001</b>
Most isolation	468/45,237	<b>1.72 (1.56–1.89)</b>	<b>&lt;0.001</b>

**Note.** Model adjusted for age, sex, ethnicity (UK Biobank only), residence (CLHLS only), Townsend deprivation index (UK Biobank only), economic level (CLHLS only), education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, and the number of baseline diseases. Abbreviations: *CI*, confidence interval; CLHLS, Chinese Longitudinal Healthy Longevity Survey; *HR*, hazard ratio.

**Supplementary Table S9.** Joint associations of sarcopenia and social isolation with all-cause mortality after excluding those who had cancer or cardiovascular diseases at baseline

	<b>Cases/Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>CLHLS (n = 12,390)</b>			
<b>Non-sarcopenia</b>			
Least isolation	232/4,814	<b>1</b>	
Moderate isolation	709/13,244	0.96 (0.83–1.11)	0.960
Most isolation	1,017/10,425	<b>1.26 (1.09–1.45)</b>	<b>0.001</b>
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	78/756	<b>1.36 (1.05–1.77)</b>	<b>0.018</b>
Moderate isolation	906/6,048	<b>1.64 (1.41–1.90)</b>	<b>&lt;0.001</b>
Most isolation	4,235/17,328	<b>1.99 (1.72–2.30)</b>	<b>&lt;0.001</b>
<b>UK Biobank (n = 333,014)</b>			
<b>Non-sarcopenia</b>			
Least isolation	6,878/1,863,301	<b>1</b>	
Moderate isolation	6,897/1,610,895	<b>1.15 (1.11–1.18)</b>	<b>&lt;0.001</b>
Most isolation	3,071/550,225	<b>1.40 (1.34–1.46)</b>	<b>&lt;0.001</b>
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	560/109,900	1.08 (0.99–1.18)	0.076
Moderate isolation	686/103,552	<b>1.38 (1.28–1.49)</b>	<b>&lt;0.001</b>
Most isolation	347/37,363	<b>1.82 (1.64–2.03)</b>	<b>&lt;0.001</b>

**Note.** Model adjusted for age, sex, ethnicity (UK Biobank only), residence (CLHLS only), Townsend deprivation index (UK Biobank only), economic level (CLHLS only), education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, and the number of baseline diseases. Abbreviations: *CI*, confidence interval; CLHLS, Chinese Longitudinal Healthy Longevity Survey; *HR*, hazard ratio.

**Supplementary Table S10.** Joint associations of sarcopenia and social isolation with all-cause mortality after using multiple imputations for missing covariates

	<b>Cases/Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>CLHLS (n = 14,789)</b>			
<b>Non-sarcopenia</b>			
Least isolation	280/5,779	<b>1</b>	
Moderate isolation	819/15,075	0.97 (0.85–1.11)	0.671
Most isolation	1,098/11,563	<b>1.24 (1.09–1.42)</b>	<b>&lt;0.001</b>
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	117/1,095	<b>1.49 (1.20–1.85)</b>	<b>0.003</b>
Moderate isolation	1167/7,717	<b>1.73 (1.51–1.98)</b>	<b>&lt;0.001</b>
Most isolation	5,090/20,749	<b>2.02 (1.77–2.31)</b>	<b>&lt;0.001</b>
<b>UK Biobank (n = 475,538)</b>			
<b>Non-sarcopenia</b>			
Least isolation	12,303/2,587,751	<b>1</b>	
Moderate isolation	12,997/2,686,696	<b>1.16 (1.13–1.19)</b>	<b>&lt;0.001</b>
Most isolation	5,754/787,975	<b>1.38 (1.34–1.43)</b>	<b>&lt;0.001</b>
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	1,149/171,051	<b>1.11 (1.05–1.18)</b>	<b>0.005</b>
Moderate isolation	1,357/164,430	<b>1.34 (1.27–1.42)</b>	<b>&lt;0.001</b>
Most isolation	668/60,621	<b>1.66 (1.54–1.80)</b>	<b>&lt;0.001</b>

**Note.** Model adjusted for age, sex, ethnicity (UK Biobank only), residence (CLHLS only), Townsend deprivation index (UK Biobank only), economic level (CLHLS only), education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, and the number of baseline diseases. Abbreviations: *CI*, confidence interval; CLHLS, Chinese Longitudinal Healthy Longevity Survey; *HR*, hazard ratio.

**Supplementary Table S11.** Joint associations of sarcopenia and social isolation with all-cause mortality after further adjusting for loneliness and psychological scores in model in the two cohorts

	Cases/Person-years	HR (95% CI)	P value
<b>CLHLS (n = 12,695)</b>			
<b>Non-sarcopenia</b>			
Least isolation	276/5,677	1	
Moderate isolation	793/14,829	0.96 (0.84–1.10)	0.563
Most isolation	1,011/11,137	<b>1.19 (1.03–1.36)</b>	<b>0.016</b>
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	111/1,043	<b>1.47 (1.18–1.83)</b>	<b>&lt;0.001</b>
Moderate isolation	990/7,094	<b>1.59 (1.38–1.82)</b>	<b>&lt;0.001</b>
Most isolation	3,666/16,768	<b>1.85 (1.61–2.12)</b>	<b>&lt;0.001</b>
<b>UKB (n = 356,284)</b>			
<b>Non-sarcopenia</b>			
Least isolation	9,063/1,989,861	1	
Moderate isolation	9,181/1,705,069	<b>1.14 (1.11–1.17)</b>	<b>&lt;0.001</b>
Most isolation	3,949/576,183	<b>1.33 (1.28–1.38)</b>	<b>&lt;0.001</b>
<b>Sarcopenia</b>			
Least isolation	775/121,311	<b>1.08 (1.01–1.17)</b>	<b>0.028</b>
Moderate isolation	902/112,101	<b>1.34 (1.25–1.44)</b>	<b>&lt;0.001</b>
Most isolation	448/39,776	<b>1.70 (1.54–1.87)</b>	<b>&lt;0.001</b>

**Note.** Model adjusted for age, sex, ethnicity (UK Biobank only), residence (CLHLS only), Townsend deprivation index (UK Biobank only), economic level (CLHLS only), education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, the number of baseline diseases, loneliness, and psychological scores. In the UK Biobank, loneliness was assessed by two questions from questionnaires: “Do you often feel lonely?” (1 point for the response of “yes” and 0 point for “no”) and “How often are you able to confide in someone close to you?” (1 point for the response of “never or almost never” and 0 point for the response of “once every few months”, “once a month”, “once a week”, “2–4 times a week”, or “almost daily”). The loneliness score was determined by adding up the scores from two questions, resulting in a range of 0–2 points. Individuals were allocated into two groups according to the loneliness score: the no-loneliness group (0 or 1 point) and the loneliness group (2 points). Psychological score was measured with the two questions from the Patient Health Questionnaire-2, including the frequency of depressed mood and disinterest or absence of enthusiasm in the previous 2 weeks. For each item, if participants answered, “not at all,” “several days,” “more than half the days,” or “nearly every day,” they were coded as 0, 1, 2, and 3, respectively. The total psychological score ranged from 0 to 6 by adding the scores for the two items. In the CLHLS, Loneliness was measured using one single item, asking participants how often they felt lonely. Participants who responded “sometimes,” “often,” or “always” were classified as “lonely,” participants who responded “never” or “seldom” were classified as “not lonely. Psychological score was measured by five items: (1) Do you always look on the bright side of things? (2) Are you as happy as when you were young? (3) Do you often feel fearful or anxious? (4) Do you feel the older you get, the more useless you are? (5) I can make my own decisions concerning my personal affairs. The 5-point response scale to each item ranged from “never” to “always” (possible range from 0 to 25, with a higher score indicating a lower psychological well-being). Abbreviations: *CI*, confidence interval; CLHLS, Chinese Longitudinal Healthy Longevity Survey; *HR*, hazard ratio.

**Supplementary Table S12.** Joint associations of sarcopenia and social isolation with all-cause mortality after excluding those died after the COVID-19 pandemic in the UK Biobank ( $n = 379,291$ )

	Cases/Person-years	HR (95% CI)	P value
<b>Non-sarcopenia</b>			
Least isolation	7,340/2,104,789	1	
Moderate isolation	7,593/1,820,314	1.16 (1.12–1.20)	<0.001
Most isolation	3,333/619,877	1.37 (1.31–1.43)	<0.001
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	657/130,636	1.12 (1.03–1.21)	0.006
Moderate isolation	747/121,694	1.34 (1.24–1.45)	<0.001
Most isolation	381/43,939	1.72 (1.55–1.90)	<0.001

**Note.** Model adjusted for age, sex, ethnicity, Townsend deprivation index, education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, and the number of baseline diseases. Abbreviations: *CI*, confidence interval; *HR*, hazard ratio.

**Supplementary Table S13.** Joint associations of sarcopenia and social isolation with all-cause mortality after excluding those younger than 65 years old in the UK Biobank ( $n = 70,270$ )

	Cases/Person-years	HR (95% CI)	P value
<b>Non-sarcopenia</b>			
Least isolation	4,132/380,213	1	
Moderate isolation	3,960/302,146	1.15 (1.10–1.20)	<0.001
Most isolation	1,509/89,746	1.35 (1.27–1.43)	<0.001
<b>Probable and Confirmed Sarcopenia</b>			
Least isolation	458/43,050	1.03 (0.93–1.13)	0.585
Moderate isolation	518/37,265	1.35 (1.23–1.48)	<0.001
Most isolation	221/11,646	1.58 (1.38–1.81)	<0.001

**Note.** Model adjusted for age, sex, ethnicity, Townsend deprivation index, education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, and the number of baseline diseases. Abbreviations: *CI*, confidence interval; *HR*, hazard ratio.

**Supplementary Table S14.** Joint associations of sarcopenia and social isolation with all-cause mortality after selecting participants of the same age range in the two cohorts and adjusting the same covariates

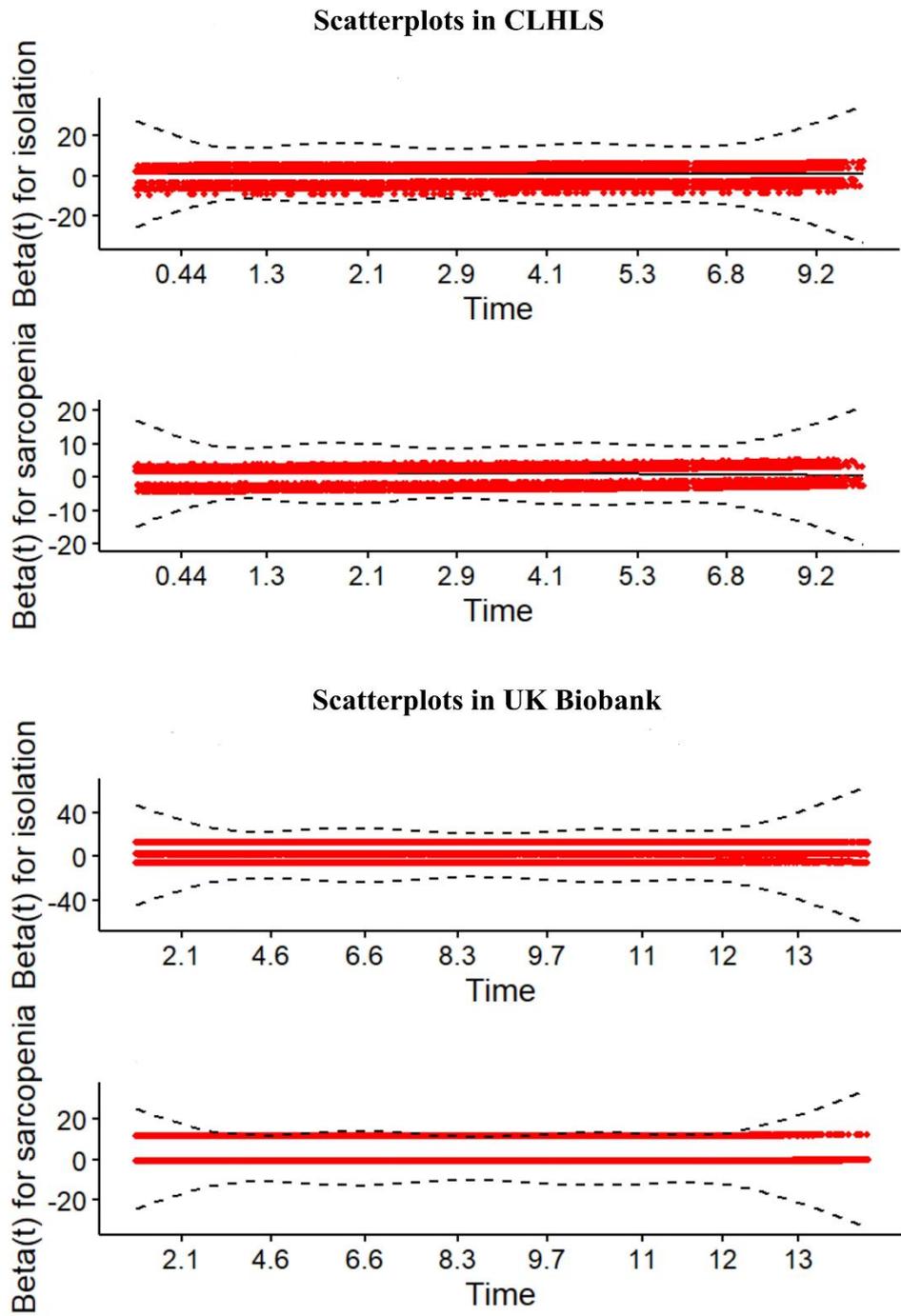
	Cases/Person-years	HR (95% CI)	P value
<b>CLHLS (n = 14,457)</b>			
<b>Non-sarcopenia</b>			
Least isolation	280/5,758	<b>1</b>	
Moderate isolation	817/15,018	1.03 (0.90–1.18)	0.667
Most isolation	1,090/11,475	<b>1.34 (1.17–1.54)</b>	<b>&lt;0.001</b>
<b>Sarcopenia</b>			
Least isolation	116/1,070	<b>1.55 (1.25–1.92)</b>	<b>&lt;0.001</b>
Moderate isolation	1,122/7,547	<b>1.83 (1.60–2.10)</b>	<b>&lt;0.001</b>
Most isolation	4,824/20,025	<b>2.20 (1.93–2.51)</b>	<b>&lt;0.001</b>
<b>UKB (n = 70,270)</b>			
<b>Non-sarcopenia</b>			
Least isolation	4,132/380,213	<b>1</b>	
Moderate isolation	3,960/302,146	<b>1.19 (1.14–1.24)</b>	<b>&lt;0.001</b>
Most isolation	1,509/89,746	<b>1.44 (1.36–1.53)</b>	<b>&lt;0.001</b>
<b>Sarcopenia</b>			
Least isolation	458/43,050	1.04 (0.94–1.14)	0.466
Moderate isolation	518/37,265	<b>1.39 (1.26–1.52)</b>	<b>&lt;0.001</b>
Most isolation	221/11,646	<b>1.73 (1.51–1.98)</b>	<b>&lt;0.001</b>

**Note.** Model adjusted for age, sex, smoking status, alcohol intake, body mass index, and the number of baseline diseases. Abbreviations: *CI*, confidence interval; *HR*, hazard ratio.

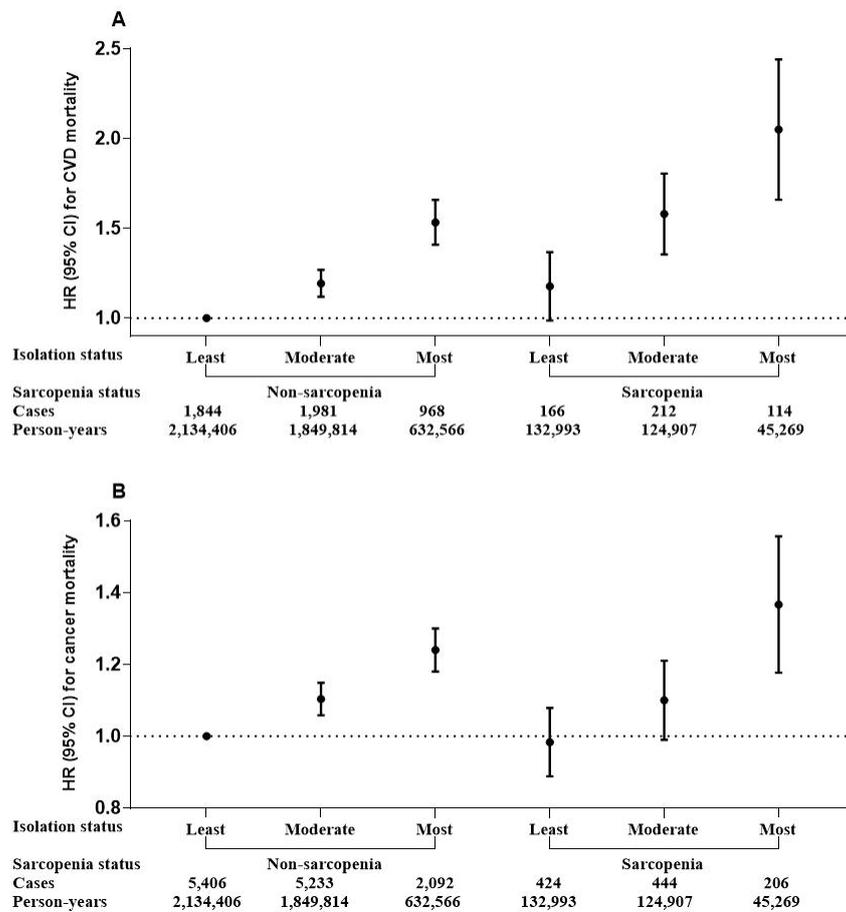
**Supplementary Table S15.** Joint associations of sarcopenia and social isolation with all-cause mortality after restricting follow-up duration to within 5 years in the two cohorts

	<b>Cases/Person-years</b>	<b>HR (95% CI)</b>	<b>P value</b>
<b>CLHLS (n = 14,457)</b>			
<b>Non-sarcopenia</b>			
Least isolation	155/3,816	<b>1</b>	
Moderate isolation	458/9,750	0.98 (0.81–1.17)	0.800
Most isolation	676/8,063	<b>1.23 (1.03–1.47)</b>	<b>0.025</b>
<b>Sarcopenia</b>			
Least isolation	81/830	<b>1.52 (1.16–2.00)</b>	<b>0.002</b>
Moderate isolation	815/5,914	<b>1.75 (1.46–2.08)</b>	<b>&lt;0.001</b>
Most isolation	4,027/17,076	<b>2.16 (1.82–2.57)</b>	<b>&lt;0.001</b>
<b>UKB (n = 385,910)</b>			
<b>Non-sarcopenia</b>			
Least isolation	2,133/826,870	<b>1</b>	
Moderate isolation	2,350/719,671	<b>1.20 (1.13–1.27)</b>	<b>&lt;0.001</b>
Most isolation	1,069/248,235	<b>1.43 (1.32–1.54)</b>	<b>&lt;0.001</b>
<b>Sarcopenia</b>			
Least isolation	181/52,636	1.07 (0.92–1.25)	0.368
Moderate isolation	233/49,758	<b>1.40 (1.23–1.61)</b>	<b>&lt;0.001</b>
Most isolation	115/18,289	<b>1.67 (1.38–2.01)</b>	<b>&lt;0.001</b>

**Note.** Model adjusted for age, sex, ethnicity (UK Biobank only), residence (CLHLS only), Townsend deprivation index (UK Biobank only), economic level (CLHLS only), education level, smoking status, alcohol intake, healthy diet score, physically active, body mass index, and the number of baseline diseases. Abbreviations: *CI*, confidence interval; CLHLS, Chinese Longitudinal Healthy Longevity Survey; *HR*, hazard ratio.



**Supplementary Figure S1.** The results of the proportional hazards assumption.



**Supplementary Figure S2.** Joint associations of sarcopenia and social isolation with CVD mortality (A) and cancer mortality (B) in the UK Biobank. Model adjusted for age, sex, ethnicity, Townsend deprivation index, education level, smoking status, alcohol intake, physically active, healthy diet score, body mass index and the number of baseline diseases. *RERI* (95% *CI*): 0.32 (-0.10–0.75) for CVD mortality and 0.25 (-0.17–0.81) for cancer mortality. Additive interaction was evaluated using *RERI* between the social isolation level (least vs most) and sarcopenia status (non-sarcopenia vs sarcopenia). Abbreviations: CVD, cardiovascular disease; *CI*, confidence interval; *HR*, hazard ratio; *RERI*, relative excess risk due to interaction.

## SUPPLEMENTARY METHODS

### Assessment of sarcopenia

In the CLHLS cohort, sarcopenia was defined according the Asian Working Group on Sarcopenia in Older People 2019 (AWGSOP2) criteria involving three dimensions<sup>[1]</sup>: muscle strength assessed by the question “Are you able to lift 5 kg of weight?” (low level for answering about “with problem” or “not able to”)<sup>[2]</sup>; low muscle mass assessed by ASM index ( $ASM/height^2$ )  $< 3.98 \text{ kg/m}^2$  for women and  $< 6.37 \text{ kg/m}^2$  for men based on the 20% lowest percentile of the study population<sup>[3]</sup>; physical performance assessed by the questions “Are you able to walk 1 km?” or “Are you able to crouch and stand three times?” (low level for answering about “with problem” or “not able to”)<sup>[2]</sup>. ASM was calculated through an equation applicable to Chinese population<sup>[3,4]</sup>:  $ASM \text{ (kg)} = 0.193 \times \text{weight (kg)} + 0.107 \times \text{height (m)} - 4.157 \times \text{sex} - 0.037 \times \text{age (years)} - 2.631$ , with sex taking value 2 if female and 1 if male.

In the UK Biobank cohort, grip strength was measured using a Jamar J00105 hydraulic hand dynamometer. Each hand was measured once and the average of the two values (kg) was used for subsequent analysis (Field ID: 46, 47). Appendicular skeletal muscle mass (ASM) was measured using bioimpedance analysis with a Tanita BC-418MA body composition analyzer, but participants including those with a pacemaker, those unable to stand, and those unwilling to remove their shoes were not available. So appendicular lean mass (ALM; Field ID: 23125, 23121, 23113, 23117) was adopted as ASM to estimate muscle mass and estimated using a previously validated equation<sup>[5]</sup>:  $ALM \text{ (kg)} = (0.958 \times [\text{Appendicular fat-free mass (kg)}]) - (0.166 \times G) - 0.308$ , with G representing value 0 if female and 1 if male. UK Biobank lacked the objective measurements of physical performance including gait speed or the Short Physical Performance Battery (SPPB) specified by the European Working Group on

Sarcopenia in Older People 2019 (EWGSOP2) criteria, so we replaced it with slow walking pace of < 3 miles/h (equivalent to < 1.3 m/s; Field ID: 924)<sup>[5,6]</sup>.

### **Assessment of social isolation**

In the CLHLS cohort, social isolation was scored based on the following four dimensions<sup>[7]</sup>: (1) whether they lived alone (1 point for living alone); (2) whether they had a spouse (1 point for unmarried, divorced, separated, and widowed population); (3) whether they had frequent contact with children or siblings ((including face-to-face or remote contact, 1 point for infrequent visits from children or siblings); (4) how often they participate in either of two social activities (including playing chess or cards and attending a religion group, 1 point for < 1 time/month).

In the UK Biobank cohort, social isolation was scored based on the following three questions<sup>[8]</sup>: (1) 'How often do you visit friends or family or have them visit you?' (1 point for answering about < 1 time/week; Field ID: 1031); (2) 'Which of the following leisure or social activities (sports club or gym, pub or social club, religious group, adult education class, other group activity) do you engage in once a week or more often?' (1 point for answering none of the above; Field ID: 6160); and (3) 'Including yourself, how many people are living together in your household?' (1 point for answering living alone; Field ID: 709).

### **Assessment of covariates**

In the CLHLS, covariates included age (years, continuous), sex (women, men), residence (city, rural), economic level (rich, fair/poor), education level (high, low), smoking status (never, former, and current), alcohol intake (never, former, and current), healthy diet score (continuous), physically active (yes, no), body mass index (BMI, underweight: <18.5, normal: 18.5–24, and overweight/obesity : ≥24 kg/m<sup>2</sup>), and the number of baseline diseases (0, 1, and ≥ 2). Education was categorized into two

groups (High: elementary school or above; Low: no formal schooling). Economic level was measured using one item “how do you rate your living standard compared to locals?” with five response options: very rich, rich, fair, poor, and very poor. The options of “very rich” and “rich” were combined, as were the options “fair”, “poor” and “very poor”. Two categories of economic level (rich, fair/poor) were then used in the final analyses. Physically active was measured using a question “Do you do exercise regularly at present, such as walking, jogging, playing ball, and qigong” and categorized as yes or no. The body mass index was calculated based on weight (kg) divided by the square of the height (m). Healthy diet score was calculated according to the frequency of intake of fruits, vegetables, fish, bean products, tea, garlic, egg, sugar, and salt-preserved vegetable<sup>[9]</sup>. For two out of the 9 variables, sugar and salt-preserved vegetables, the answer of ‘always or almost every day’, ‘sometimes or occasionally’ or ‘rarely or never’ at each participant’s first survey received a score of 0, 1, or 2, respectively; for the other 7 variables, the same three responses received scores of 2, 1, or 0, respectively. Scores for the 9 variables were then summed to obtain a scale ranging from 0 to 18, with higher scores indicating healthier dietary patterns. Baseline self-reported diseases included hypertension, diabetes, coronary heart disease, stroke, and cancer.

In the UK Biobank, covariates were collected at baseline, including age (years, continuous; Field ID: 21022), sex (women, men; Field ID: 31), ethnicity (white, others; Field ID: 21000), Townsend Deprivation Index (TDI; continuous; Field ID: 189), education level (high, low; Field ID: 6138), smoking status (never, former, and current; Field ID: 20116), alcohol intake (never, former, and current; Field ID: 20117), healthy diet score (continuous), physically active (yes, no; Field ID: 22036), body mass index (BMI, underweight: <18.5, normal: 18.5–25, and overweight/obesity: ≥25 kg/m<sup>2</sup>; Field ID: 21001) and the number of baseline diseases (0, 1, and ≥ 2). Physical activity information was evaluated by

whether a person met the 2017 UK physical activity guidelines of 150 minutes of walking or moderate activity per week or 75 minutes of vigorous activity. Dietary information is evaluated using a more recent dietary recommendation for cardiovascular health<sup>[10]</sup>, which considered adequate consumption of fruit ( $\geq 3$  servings/day; Field ID: 1289, 1299), vegetables ( $\geq 3$  servings/day; Field ID: 1309, 1319), whole grains ( $\geq 3$  servings/day; Field ID: 1438, 1448, 1458, 1468), fish ( $\geq 2$  servings/week; Field ID: 1329, 1339), dairy products ( $\geq 2$  servings/day; Field ID: 1408, 1418), and vegetable oils ( $\geq 2$  servings/day; Field ID: 1438, 2654) and reduced consumption of refined grains ( $\leq 2$  servings/day; Field ID: 1438, 1448, 1458, 1468), processed meats ( $\leq 1$  servings/week; Field ID: 1349), unprocessed meats ( $\leq 2$  servings/week; Field ID: 1359, 1369, 1379, 1389), and sugar sweetened beverages (no consumption; Field ID: 6144). If the intake target is reached, assign a value of 1; otherwise, assign a value of 0. Scores for the 10 variables were then summed to obtain a scale ranging from 0 to 10, with higher scores indicating healthier dietary patterns. Hypertension was defined based on self-reported diagnosis, or blood pressure measurements (systolic blood pressure [SBP]  $\geq 140$  mmHg or diastolic blood pressure [DBP]  $\geq 90$  mmHg), or doctor diagnosis or any self-reported use of antihypertensive medications (Field ID: 4079, 4080, 6150, 6177, 20002); diabetes was defined based on self-reported diagnosis, or biochemical measurements (glycated hemoglobin [HbA1c]  $\geq 6.5\%$  or casual plasma glucose  $\geq 11.1$  mmol/L) or any self-reported use of antihyperglycemic medications (Field ID: 20003, 6153, 6177, 20002, 2443, 30750); coronary heart disease (Field ID: 6150, 20002), stroke (Field ID: 6150, 20002), and cancer (Field ID: 2453, 20001) were defined based on self-reported diagnosis or doctor diagnosis.

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