

Supplementary material

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Supplementary Table 1. Baseline characteristics of the study population by depression in survival/death-discordant twin pairs (n=7,092 twins)

Characteristics	Depression		<i>P</i> value
	No (n=6890)	Yes (n=200)	
Age (years)	61.99 ± 8.25	59.77 ± 7.53	<0.001
Sex			0.030
Female	3556 (51.74)	119 (59.50)	
Male	3326 (48.26)	81 (40.50)	
Education level			
<8 years	2816 (40.86)	66 (33.00)	0.077
8–10 years	2880 (40.63)	90 (45.00)	
≥11 years	1276 (18.51)	44 (22.00)	
Marital status			
Single	1996 (28.96)	116 (58.00)	<0.001
Married/cohabiting	4896 (71.04)	84 (42.00)	
Smoking status			<0.001
Never	3305 (47.95)	51 (25.50)	
Former/current smoking	3587 (52.05)	149 (74.50)	
Alcohol consumption			<0.001
No/mild drinking	6339 (91.98)	147 (71.00)	
Heavy drinking	553 (8.02)	58 (29.00)	
Physical exercise			0.112
Inactive	1791 (25.99)	62 (31.00)	
Active	5101 (74.01)	138 (69.00)	
Zygoty			0.056
Monozygotic	1214 (17.61)	28 (14.00)	
Dizygotic	4860 (70.52)	138 (69.00)	
Undetermined zygoty	818 (11.87)	34 (17.00)	
Body mass index (kg/m ²)	25.31 ± 3.61	25.59 ± 4.07	0.276
<20	329 (4.77)	14 (7.00)	0.051
20–24.9	3131 (45.43)	73 (36.50)	
25–29.9	2771 (40.21)	88 (44.00)	
≥30	661 (9.59)	25 (12.50)	
Type 2 diabetes	472 (6.85)	20 (10.00)	0.084
Hypertension	357 (5.18)	21 (10.50)	0.001
Cardiovascular disease	819 (11.88)	42 (21.00)	<0.001
Cancer	748 (10.85)	22 (11.00)	0.948

Data were presented as means ± standard deviations or number (%).

Supplementary table 2. Odds ratios (ORs, 95% confidence intervals) for the association of depression at different ages with all-cause mortality by gender: results from generalized estimating equation models

Depression at different ages	No. of subjects	All-cause mortality		
		Cases	Basic-adjusted OR ^a	Multi-adjusted OR ^b
Female				
Depression-free	23272	6185	Reference	Reference
Depression	768	308	2.44 (2.00–2.97)	1.71 (1.44–2.14)
Early-life depression	369	76	2.43 (1.78–3.31)	1.67 (1.22–2.29)
Midlife depression	310	151	2.24 (1.69–2.97)	1.60 (1.21–2.11)
Late-life depression	89	81	4.17 (2.07–8.38)	3.77 (1.78–7.97)
Male				
Depression-free	20468	6097	Reference	Reference
Depression	411	171	2.32 (1.79–3.01)	1.58 (1.21–2.06)
Early-life depression	205	61	2.53 (1.76–3.65)	1.73 (1.21–2.48)
Midlife depression	177	82	1.94 (1.32–2.85)	1.32 (0.89–1.96)
Late-life depression	29	28	9.16 (1.30–65.56)	/
Depression × gender	/	/	1.18 (0.78–1.49)	1.11 (0.80–1.54)

^a Adjusted for age, sex, and education level

^b Further adjusted for smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer

P for multiplicative interaction between depression and gender on all-cause mortality was 0.53.

Supplementary table 3. Odds ratios (ORs, 95% confidence intervals) for the association of joint exposure of depression and gender with all-cause mortality: results from generalized estimating equation models

Joint exposure		No. of subjects	All-cause mortality		
Depression	Gender		Cases	Basic-adjusted OR ^a	Multi-adjusted OR ^b
No	Female	23272	6185	Reference	Reference
No	Male	20468	6097	2.44 (2.00–2.97)	1.49 (1.40–1.58)
Yes	Female	308	308	2.44 (2.00–2.97)	1.77 (1.46–2.16)
Yes	Male	411	171	2.43 (1.78–3.31)	2.38 (1.83–3.09)

^a Adjusted for age and education level

^b Further adjusted for smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer

Measures of additive interaction for all-cause mortality:

The relative excess risk due to interaction: 0.12, 95% CI: -0.56–0.79

The attributable proportion: 0.05, 95% CI: -0.23–0.32

Synergy index: 1.09, 95% CI: 0.66–1.81.

Supplementary Table 4. Mediating effects of dementia on the association of depression with all-cause mortality (n=35,032): results from generalized structural equation modeling

Mediator: Dementia	Basic-adjusted β (95% CI) ^a	<i>P</i>	Multi-adjusted β (95% CI) ^b	<i>P</i>
Direct effect of depression	0.84 (0.64–1.04)	<0.001	0.49 (0.29–0.69)	<0.001
Mediating effects	0.72 (0.39–1.05)	<0.001	0.73 (0.39–1.06)	<0.001
Percent mediation	46.19% (33.23%–59.14%)	<0.001	59.83% (44.92%–74.75%)	<0.001

^a Adjusted for age, sex, and education level

^b Further adjusted for smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer

Supplementary table 5. Odds ratios (ORs, 95% confidence intervals) for the association of depression at different ages with non-suicide and suicide mortality: results from generalized estimating equation models

Depression at different ages	Non-suicide mortality			Suicide mortality		
	Cases	Basic-adjusted OR ^a	Multi-adjusted OR ^b	Cases	Basic-adjusted OR ^a	Multi-adjusted OR ^b
Depression-free	12198	Reference	Reference	84	Reference	Reference
Depression	467	2.31 (1.97–2.71)	1.65 (1.40–1.93)	12	6.47 (3.53–11.85)	4.40 (2.29–8.44)
Early-life depression	130	2.69 (2.14–3.38)	1.63 (1.29–2.07)	7	7.17 (3.34–15.40)	4.64 (2.08–10.39)
Midlife depression	228	2.24 (1.79–2.79)	1.47 (1.16–1.85)	5	6.57 (2.61–16.52)	4.76 (1.82–12.49)
Late-life depression	109	4.65 (2.41–9.00)	4.07 (2.00–8.29)	0	/	/

^a Adjusted for age, sex, and education level

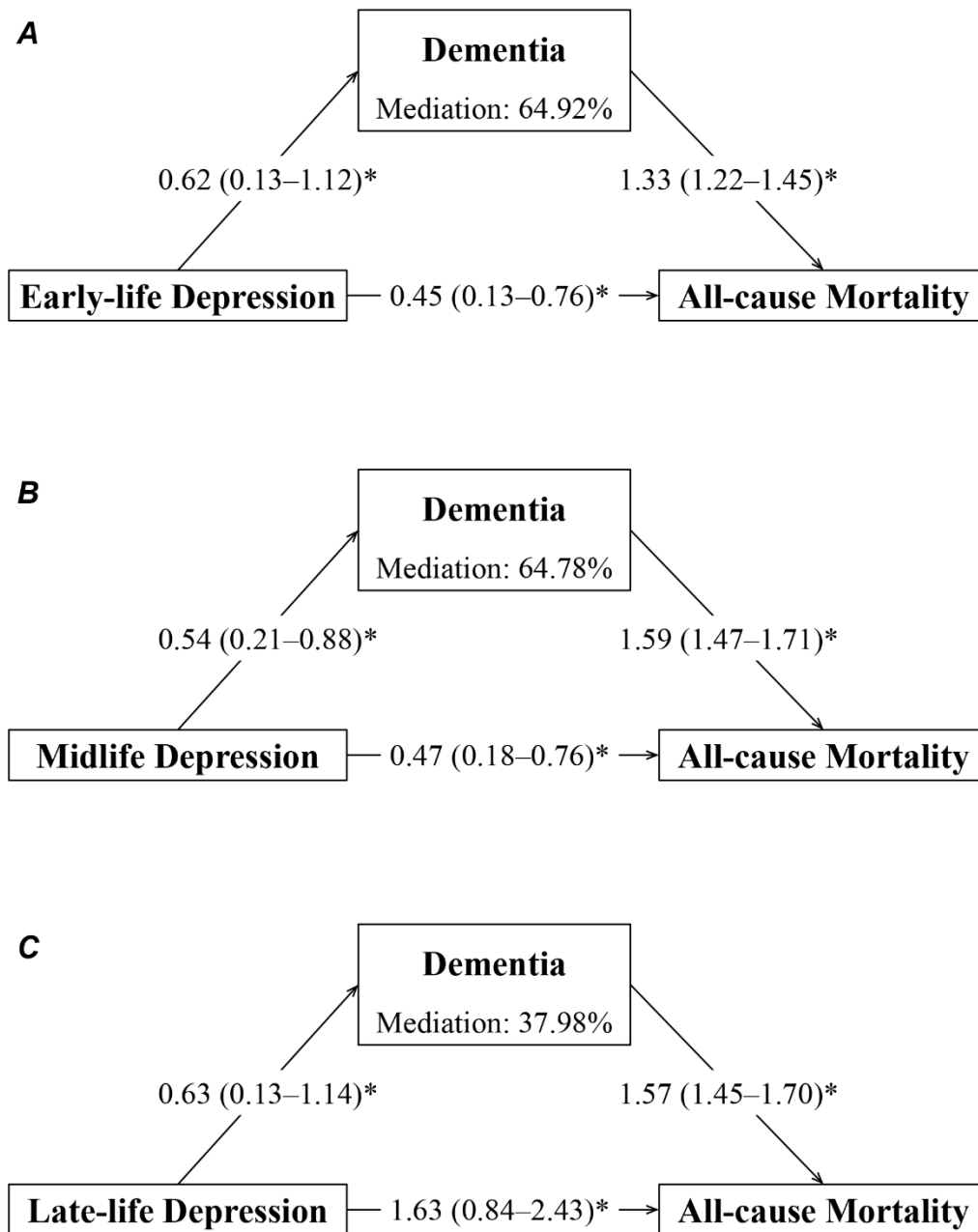
^b Further adjusted for smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer

Supplementary table 6. Odds ratios (ORs, 95% confidence intervals) for the association of depression at different ages with all-cause mortality by excluding participants with missing data in covariates (n=37,364): results from generalized estimating equation models

Depression at different ages	No. of subjects	All-cause mortality		
		Cases	Basic-adjusted OR ^a	Multi-adjusted OR ^b
Depression-free	36432	6313	Reference	Reference
Depression	932	274	2.26 (1.92–2.66)	1.62 (1.37–1.91)
Early-life depression	539	120	2.06 (1.63–2.59)	1.46 (1.15–1.84)
Midlife depression	368	137	2.38 (1.88–3.02)	1.71 (1.34–2.18)
Late-life depression	25	17	4.40 (1.93–9.99)	3.64 (1.37–9.67)

^a Adjusted for age, sex, and education level

^b Further adjusted for smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer

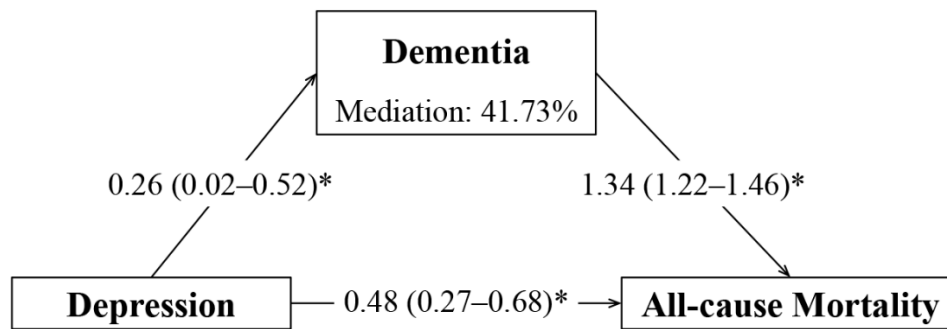


Supplementary Figure 1. Mediating effects of dementia on the association of (A) early-life, (B) midlife, and (C) late-life depression with all-cause mortality

Models were adjusted for age, sex, education level, smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer.

Numbers next to arrows indicate beta-coefficients (95% confidence intervals).

* $P < 0.05$

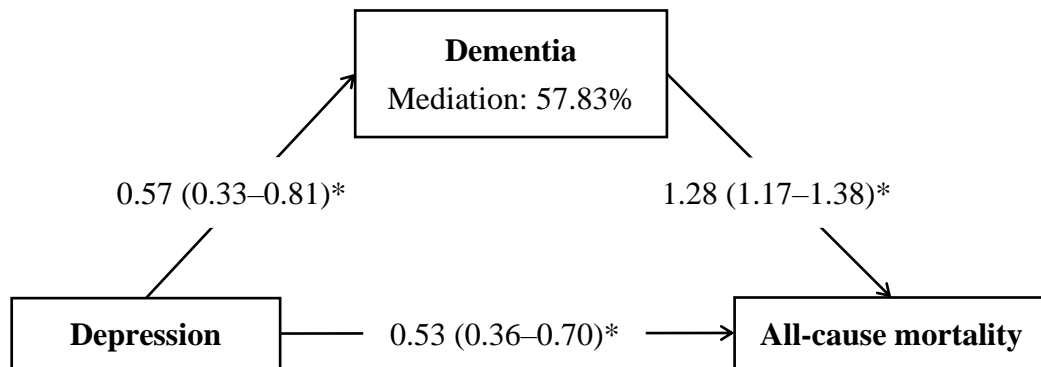


Supplementary Figure 2. Mediating effects of dementia at least 10 years after depression on the association of depression with all-cause mortality

Models were adjusted for age, sex, education level, smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer.

Numbers next to arrows indicate beta-coefficients (95% confidence intervals).

* $P < 0.05$



Supplementary Figure 3. Mediating effects of dementia on the association of depression with all-cause mortality by only excluding participants who had dementia before depression

Models were adjusted for age, sex, education level, smoking status, alcohol consumption, marital status, physical exercise, body mass index, type 2 diabetes, hypertension, cardiovascular disease, and cancer.

Numbers next to arrows indicate beta-coefficients (95% confidence intervals).

* $P < 0.001$