Supplementary Material

Loneliness, Not Social Support, Is Associated with Cognitive Decline and Dementia Across Two Longitudinal Population-Based Cohorts

Supplementary Table 1. Comparison of baseline characteristics between the included and excluded participants from the Rotterdam Study and the Swedish National study on Aging and Care in Kungsholmen.

	Rotterdam Study			SNAC-K		
	Included	**Excluded**	**p**	**Included**	**Excluded**	**p**
Loneliness, yes	722 (15%)	345 (27%)	<0.001	612 (23.31%)	237 (38.92%)	<0.01
Perceived social support, optimal	3314 (69%)	714 (56%)	<0.001	1483 (55.77%)	48 (24.62%)	<0.01
Marital status						
Married	3326 (69%)	607 (48%)		1265 (47.63%)	179 (25.87%)	
Single	233 (5%)	57 (5%)	<0.001	1391 (52.37%)	513 (74.13%)	<0.01
Widowed or divorced	1228 (26%)	465 (37%)				
No. children						
0 children	468 (10%)	147 (12%)		679 (26.46%)	229 (37.49%)	
1-2 children	2227 (47%)	522 (41%)	0.02	1380 (53.78%)	294 (48.12%)	<0.05
≥3 children	1442 (30%)	362 (29%)		507 (19.76%)	88 (14.40%)	

Supplementary Table 2. Correlation matrices of social support factors per study.

a. Rotterdam Study, correlation matrix of social health determinants

Social health determinant	1	2	3	4
1. Perceived social support	-			
2. Number of children	0.15	-		
3. Loneliness	-0.12	-0.02	-	
4. Marital status	0.04	0.12	-0.33	-

Spearman's rank correlation values. Bold correlations are significant at p<0.01.

b. SNAC-K, correlation matrix of social health determinants factors

Social health determinant	1	2	3	4
1. Perceived social support	-			
2. Number of children	0.06	-		
3. Loneliness	-0.11	-0.10	-	
4. Marital status	0.06	0.20	-0.30	-

Spearman's rank correlation values. Bold correlations are significant at p<0.01.

Supplementary Table 3. Associations of loneliness and social support with cognitive decline with Rotterdam Study (without inversing the MMSE score). Allows direct comparison to SNAC-K findings and is comparative to Table 3, however MMSE score is not inversed before log-transformation and standardization. Findings are comparable to inversed MMSE (but in opposite direction).

MMSE			
Determinants		Rotterdam Study	
	N; n[a]	Beta (95% CI)	p
Loneliness, yes	4,509; 9,194	-0.01 (-0.03; 0.00)	0.21
Perceived social support, optimal	4,510; 9,193	-0.01 (-0.01; 0.00)	0.18
Marital status	4,514; 9,201		
Married		0 [Reference]	-
Single		-0.01 (-0.03; 0.01)	0.36
Widowed or divorced		0.00 (-0.01; 0.01)	0.53
No. children	2,404; 4,959		
0 children		0.00 (-0.02; 0.01)	0.60
1-2 children		0 [Reference]	-
≥3 children		-0.01 (-0.02; 0.00)	0.24

*Please note that positive coefficients indicate better MMSE scores c.q. cognitive improvement for Rotterdam Study estimates.

Supplementary Table 4. Associations of loneliness and social support with cognitive decline and dementia risk, only adjusted for age, sex, and education.

a. Cognitive Decline
MMSE

Determinants	Rotterdam Study*			SNAC-K		
	N; assessments[a]	Beta (95% CI)	p	N; assessments[a]	Beta (95% CI)	p
Loneliness, yes	4,509; 9,194	0.02 (0.00; 0.03)	0.05	2,087; 8,208	-0.37 (-0.67; -0.07)	0.02
Perceived social support, optimal	4,510; 9,193	-0.01 (-0.02; 0.00)	0.20	1,800; 7,132	-0.01 (-0.27; 0.25)	0.94
Marital status	4,514; 9,201			2,110; 8,300		
Married		0 [Reference]	-		0 [Reference]	-
Single		0.02 (-0.00; 0.04)	0.10		0.13 (-0.22, 0.48)	0.47
Widowed/ divorced		-0.00 (-0.01; 0.01)	0.74		-0.22 (-0.51; 0.06)	0.12
Number of children	2,404; 4,959			2,030; 7,984		
No children		0.01 (-0.02; 0.04)	0.56		0.21 (-0.10; 0.51)	0.65
One or two children		0 [Reference]	-		0 [Reference]	-
≥ Three children		0.00 (-0.01; 0.02)	0.83		0.09 (-0.23; 0.43)	0.89
g-factor						
Determinants	**Rotterdam Study**			**SNAC-K**		
	N; assessments[a]	Beta (95% CI)	p	N; assessments[a]	Beta (95% CI)	p
Loneliness, yes	4,313; 8,572	0.01 (-0.00; 0.01)	0.10	1,982; 7,284	0.05 (0.09; 0.00)	0.03
Perceived social support, optimal	4,314; 8,571	-0.00 (-0.01; 0.00)	0.31	1,905; 6,700	0.01 (-0.03; 0.05)	0.68
Marital status	4,319; 8,581			2,002; 7,352		
Married		0 [Reference]	-		0 [Reference]	-
Single		0.00 (-0.01; 0.01)	0.66		0.00 (-0.05, 0.05)	0.88
Widowed/divorced		-0.00 (-0.01; 0.01)	0.90		-0.05 (-0.09, -0.01)	0.01
Number of children	3,827; 7,579			1,926; 7,068		
No children		-0.01 (-0.02; 0.00)	0.18		0.02 (-0.02; 0.06)	0.38
One or two children		0 [Reference]	-		0 [Reference]	-
≥Three children		-0.00 (-0.01; 0.00)	0.17		0.01 (-0.03; 0.06)	0.60

Estimates for the determinant*time interaction term are provided, obtained with linear mixed models. This term is interpretable as the decline of cognitive functioning over time. We specified fixed effects as time from baseline, determinant, determinant*time, time*age, age, sex, and level of education (model 1). We specified only a random intercept.

As outcomes were standardized, estimates indicate how categories of the determinants change the outcome in standard deviations per year.

*Please note that due to inversing the MMSE score, positive coefficients indicate not better but worse MMSE scores c.q. cognitive decline for Rotterdam Study estimates.

a N is number of unique participants, assessments could be made repeatedly up to three times for the same person

MMSE, Mini-Mental State Examination; CI, Confidence Interval; SNAC-K, Swedish National study on Aging and Care in Kungsholmen

b. Incident Dementia

Determinants	Incident dementia					
	Rotterdam Study			SNAC-K		
	Events/person-years	HR (95% CI)	p	Events/person-years	HR (95% CI)	p
Loneliness, yes	504/44,709	1.36 (1.10; 1.69)	0.01	292/12,399	2.11 (1.12; 3.98)	0.02
Perceived Social Support, optimal	503/44,700	0.89 (0.81; 0.97)	0.20	208/10,868	1.12 (0.56; 2.21)	0.75
Marital status	504/44,753			296/12,527		
Married		1 [Reference]	-		1 [Reference]	-
Single		0.72 (0.46; 1.12)	0.15		0.70 (0.23; 2.09)	0.52
Widowed/divorced		0.98 (0.88; 1.10)	0.87		1.05 (0.56; 1.57)	0.88
Number of children	504/39,529			289/12,048		
No children		0.83 (0.62; 1.11)	0.23		0.48 (0.21; 1.11)	0.09
One or two children		1 [Reference]	-		1 [Reference]	-
≥Three children		1.17 (0.97; 1.41)	0.10		1.34 (0.69; 2.61)	0.39

Hazard ratio estimates were obtained with Cox regression models using the full follow-up, and were adjusted for age, sex, and education (model 1).

CI; Confidence Interval, HR; Hazard ratio, SNAC-K, Swedish National study on Aging and Care in Kungsholmen

Supplementary Table 5. Indirect effects of mediation analysis: Social health (X) through depressive symptoms (M - Mediator) to cognitive decline or dementia (Y).
For total effects please refer to Tables 3 and 4. NS indicates that these small effect sizes are extremely likely to be "Not Statistically Significant", as calculating the p-value for the hand calculation of c – c' method is complicated [64].

Indirect effects on decline in Mini-Mental State Examination (MMSE)				
Determinants	Rotterdam Study		SNAC-K	
	Beta	p	Beta	p
Loneliness	0.004	NS	0.053	0.31
Perceived social support	<0.001	NS	-0.011	0.86
Marital status	<0.001	NS	-0.013	0.78
No. children	<-0.001	NS	-0.008	0.79
Indirect effects on decline in g-factor				
Determinants	Rotterdam Study		SNAC-K	
	Beta	p	Beta	p
Loneliness, yes	0.001	NS	-0.006	0.42
Perceived social support	<0.001	NS	<0.001	0.86
Marital status	<0.001	NS	0.001	0.75
No. children	<0.001	NS	<0.001	0.85
Indirect effects on incident dementia				
Determinants	Rotterdam Study		SNAC-K	
	HR	p	HR	p
Loneliness, yes	0.03	NS	0.042	0.64
Perceived social support	0.02	NS	0.046	0.90
Marital status	0.01	NS	<0.001	0.83
No. children	0.010	NS	<0.001	0.96