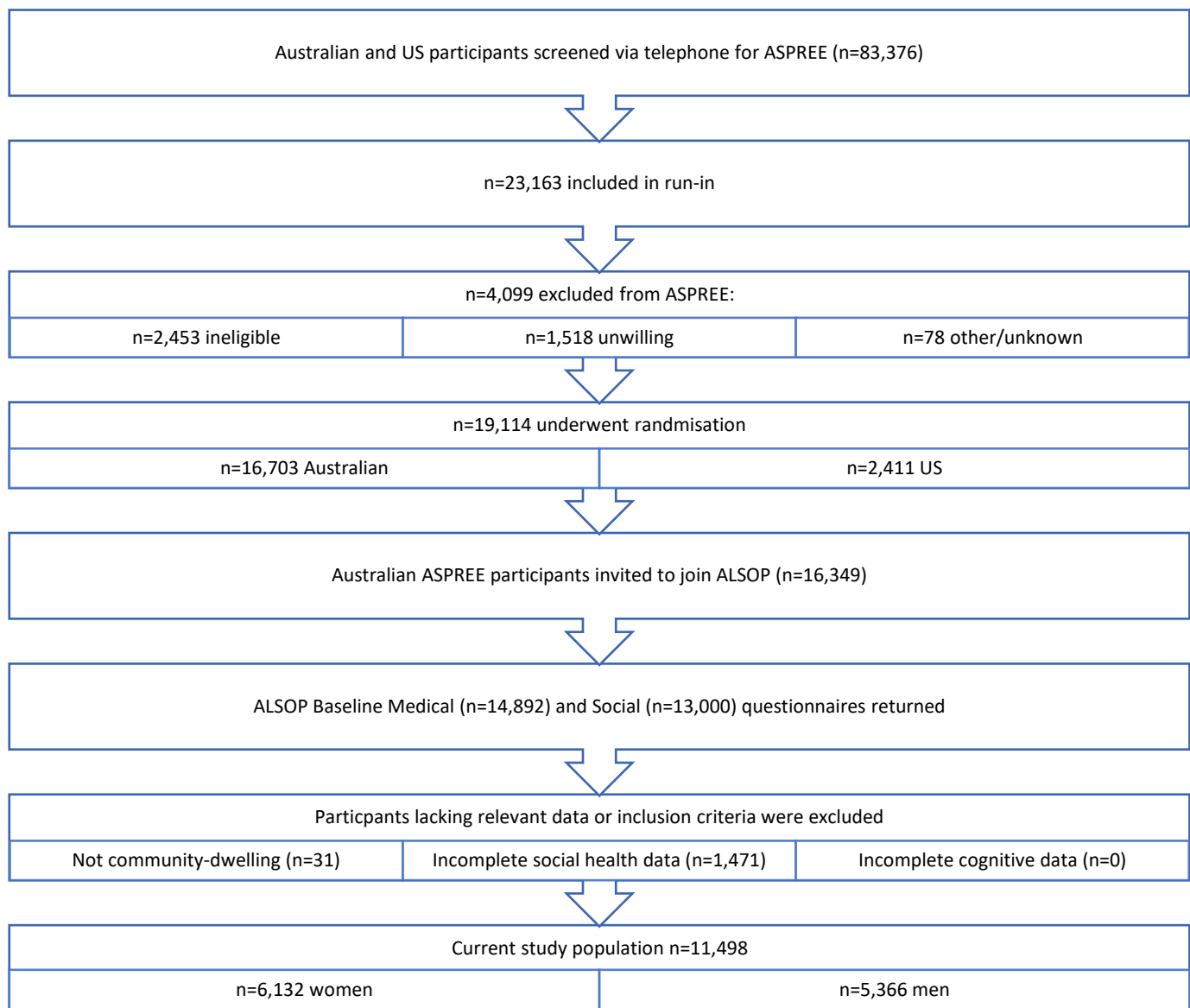


## Appendices

### Appendix A: ASPREE and ALSOP Study Characteristics

**Table A1: ASPREE Inclusion and Exclusion Criteria**

Inclusion Criteria	Exclusion Criteria <sup>65</sup>
<ul style="list-style-type: none"><li>• Men and women 70 years and over living in Australia or the U.S.</li><li>• Or aged 65 years and over for U.S. African American and Hispanic/Latino men and women</li><li>• Willing and able to provide informed consent</li><li>• Accepting of study requirements</li></ul>	<ul style="list-style-type: none"><li>• History of diagnosed cardiovascular event</li><li>• Clinical diagnosis of atrial fibrillation</li><li>• Serious intercurrent illness likely to cause death in <math>\leq 5</math> years</li><li>• Current or recurrent condition with high risk of major bleeding</li><li>• Anaemia</li><li>• Contraindication/allergy to aspirin</li><li>• Current participation in a clinical trial</li><li>• Current continuous use of aspirin for secondary prevention OR any other anti-platelet drug or anticoagulant</li><li>• Systolic blood pressure <math>\geq 180</math> mmHg and/or a diastolic blood pressure <math>\geq 105</math> mmHg</li><li>• A diagnosis of dementia or a Modified Mini-Mental State Examination (3MS) score <math>\leq 77</math></li><li>• Severe difficulty/inability to perform any one of the 6 Katz Activities of Daily Living</li><li>• Pill-taking compliance <math>&lt; 80\%</math> during the placebo run-in phase</li></ul>



**Figure A1: ASPREE, ALSOP and the current study's participant screening and inclusion**

*Ineligible participants were those who did not meet the inclusion/exclusion criteria. All Australian ASPREE participants were invited to join the ALSOP sub-study with 89% success rate. This figure depicts the responses to the ALSOP Baseline Medical and Social questionnaires and flowchart of inclusion in the current study.<sup>24</sup>*

## Appendix B: Defining Social Health

**Table B1: Determinants of Social Health**

Component Measured	Derivation	Question(s)	Cut off
<b>Social Isolation</b>	LSNS	<ul style="list-style-type: none"> <li>How many friends/relatives do you see or hear from at least once a month?</li> </ul>	≤4 per month
		<ul style="list-style-type: none"> <li>How often do you go to a club/local organisation/neighbourhood/other small group, church/temple/place of worship/take part in related activities, or attend an educational class?</li> </ul>	<1 per month
<b>Low Social Support</b>	LSNS	<ul style="list-style-type: none"> <li>How many friends/relatives do you feel at ease with that you can talk about private matters?</li> <li>How many friends/relatives do you feel close to such that you could call on them for help?</li> </ul>	<4 people
<b>Loneliness</b>	CES-D	<ul style="list-style-type: none"> <li>During the past week I felt lonely.</li> </ul>	3-7 days

*LSNS=Lubben Social Network Scale; CES-D=Center for Epidemiological Studies – Depression*

**Table B2: Defining Social Health**

	Derivation	Total n (%)	Women n (%)	Men n (%)
<b>Total</b>			<b>6,132 (53.3%)</b>	<b>5,366 (47.7%)</b>
<b>Social Isolation</b>				
<b>How often do you go to a club, local organisation, neighbourhood or other small group?</b>	<b>SNS-621</b>			
Never		1,880 (16.4%)	878 (14.3%)	1,002 (18.7%)
Rarely (<1 per month)		1,491 (13%)	689 (11.2%)	802 (15%)
Sometimes (1 – 3 per month)		2,553 (22.2%)	1,457 (23.8%)	1,096 (20.4%)
Often (>1 per week)		5,083 (44.2%)	2,870 (46.8%)	2,213 (41.2%)
Always (most days)		491 (4.3%)	238 (3.9%)	253 (4.7%)
<b>How often do you attend an educational class?</b>	<b>SNS-621</b>			
Never		7,690 (66.9%)	3,796 (61.9%)	3,894 (72.6%)
Rarely (<1 per month)		2,280 (19.8%)	1,286 (21%)	994 (18.5%)
Sometimes (1 – 3 per month)		696 (6%)	447 (7.3%)	249 (4.6%)
Often (>1 per week)		900 (7%)	581 (9.5%)	219 (4.1%)
Always (most days)		32 (0.3%)	22 (0.4%)	10 (0.2%)
<b>How often do you go to a church, temple or other place of worship, or take part in related activities?</b>	<b>SNS-621</b>			
Never		6,162 (53.6%)	2,988 (48.7%)	3,174 (59.2%)
Rarely (<1 per month)		1,813 (15.8%)	955 (15.6%)	858 (16%)
Sometimes (1 – 3 per month)		696 (6.1%)	409 (6.7%)	287 (5.4%)
Often (>1 per week)		2,484 (21.6%)	1,546 (25.2%)	938 (17.5%)
Always (most days)		343 (3%)	234 (3.8%)	109 (2%)
<b>How many friends do you see or hear from at least once a month?</b>	<b>SNS-621</b>			
None		214 (1.9%)	78 (1.3%)	136 (2.5%)
1		234 (2%)	100 (1.6%)	134 (2.5%)
2		777 (6.8%)	380 (6.2%)	397 (7.4%)

3-4		2,873 (25%)	1,538 (25.1%)	1,355 (24.9%)
5-8		3,360 (29.2%)	1,930 (31.5%)	1,430 (26.7%)
9+		4,040 (35.1%)	2,106 (34.3%)	1,934 (36%)
<b>How many relatives do you see or hear from at least once a month?</b>	<b>SNS-621</b>			
None		162 (1.41%)	87 (1.4%)	75 (1.4%)
1		405 (3.5%)	207 (3.4%)	198 (3.7%)
2		892 (7.8%)	490 (8%)	402 (7.5%)
3-4		3,279 (28.5%)	1,717 (28%)	1,562 (29.1%)
5-8		3,820 (33.2%)	2,093 (34.1%)	1,727 (32.2%)
9+		2,940 (25.6%)	1,538 (25.1%)	1,402 (26.1%)
<b>Social Support</b>				
<b>How many friends do you feel you can talk with about private matters?</b>	<b>SNS-621</b>			
None		951 (8.3%)	348 (5.7%)	603 (11.2%)
1		867 (7.5%)	461 (7.5%)	406 (7.6%)
2		2,484 (21.6%)	1,362 (22.2%)	1,122 (20.9%)
3-4		4,414 (38.4%)	2,518 (41.1%)	1,896 (35.3%)
5-8		1,874 (16.3%)	1,053 (17.2%)	821 (15.3%)
9+		908 (7.9%)	390 (6.4%)	518 (9.7%)
<b>How many relatives do you feel you can talk with about private matters?</b>	<b>SNS-621</b>			
None		383 (3.3%)	163 (2.7%)	220 (4.1%)
1		826 (7.2%)	429 (7%)	397 (7.4%)
2		1,811 (15.8%)	1,058 (17.3%)	753 (14%)
3-4		4,590 (39.9%)	2,494 (40.7%)	2,096 (39.1%)
5-8		2,571 (22.4%)	1,352 (21.6%)	1,246 (23.2%)
9+		1,317 (11.5%)	663 (10.8%)	654 (12.2%)
<b>How many friends do you feel you could call upon for help?</b>	<b>SNS-621</b>			
None		588 (5.1%)	282 (4.6%)	306 (5.7%)
1		743 (6.5%)	400 (6.5%)	343 (6.4%)
2		2,191 (19.1%)	1,252 (20.4%)	939 (17.5%)
3-4		4,575 (39.8%)	2,483 (40.5%)	2,092 (39%)

5-8		2,250 (19.6%)	1,221 (19.9%)	1,029 (19.2%)
9+		1,151 (10%)	494 (8.1%)	657 (12.2%)
<b>How many relatives do you feel you could call upon for help?</b>	<b>SNS-621</b>			
None		288 (2.5%)	165 (2.7%)	123 (2.3%)
1		594 (5.2%)	352 (5.7%)	242 (4.5%)
2		1,624 (14.1%)	896 (14.6%)	728 (13.6%)
3-4		4,391 (38.2%)	2,310 (37.7%)	2,081 (38.8%)
5-8		3,041 (26.5%)	1,595 (26%)	1,446 (27%)
9+		1,560 (13.6%)	814 (13.3%)	746 (13.9%)
<hr/>				
<b>Loneliness</b>				
<b>During the past week I felt lonely.</b>	<b>CES-D</b>			
Rarely or none of the time (<1 day)		9,932 (86.4%)	5,140 (83.8%)	4,792 (89.3%)
Some or a little of the time (1-2 days)		1,007 (8.8%)	657 (10.7%)	350 (6.5%)
Occasionally or a moderate amount of time (3-4 days)		428 (3.7%)	259 (4.2%)	169 (3.2%)
All of the time (5-7 days)		131 (1.1%)	76 (1.2%)	55 (1%)

*SNS-621=Social Network Scale; CES-D=Centre for Epidemiological Studies – Depression Scale*

Appendix C: Baseline Demographic, Social Health and Cognitive Health Data

**Table C1: Baseline Demographic Data for Women and Men**

	Women n (%)	Men n (%)	P value
<b>Total</b>	6,132 (53.3%)	5,366 (46.7%)	
<b>Age (years)</b>			
Mean ± SD	75.1 ± 4.2	75 ± 4.2	
70-74	3,641 (59.4%)	3,307 (61.6%)	0.04
75-79	1,629 (26.6%)	1,326 (24.7%)	
80+	862 (14.1%)	733 (13.7%)	
<b>Country Born</b>			
Australia	4,784 (78%)	3,934 (73.3%)	<0.001
Not Australia	1,348 (22%)	1,432 (26.7%)	
<b>Education (years)</b>			
≤12	3,755 (61.2%)	2,951 (55%)	<0.001
>12	2,377 (38.8%)	2,415 (45%)	
<b>Paid or Volunteer Work</b>			
No	1,369 (22.3%)	1,438 (26.8%)	<0.001
Paid/Volunteer Work <sup>a</sup>	4,763 (77.7%)	3,927 (73.2%)	
<b>Partner Status</b>			
Unpartnered	2,842 (46.3%)	999 (18.6%)	<0.001
Partnered <sup>b</sup>	3,290 (53.7%)	4,367 (81.4%)	
<b>Living Situation</b>			
At home with family/friends	3,636 (59.3%)	4,339 (80.9%)	<0.001
At home alone	2,496 (40.7%)	1,027 (19.1%)	
<b>BMI (kg/m<sup>2</sup>)</b>			
Mean ± SD	28 ± 5.1	27.9 ± 3.8	0.04
<b>Depressive Symptoms (CES-D Score)</b>			
Mean ± SD	3.3 ± 3.3	2.8 ± 3	
<8	5,516 (90%)	4,959 (92.4%)	<0.001
≥8	616 (10%)	407 (7.6%)	
<b>Smoking History</b>			
Current/Former	2,042 (33.3%)	3,050 (56.8%)	<0.001
Never	4,091 (66.7%)	2,316 (43.2%)	

SD=Standard Deviation; BMI=Body Mass Index; CES-D=Centre for Epidemiological Studies – Depression Scale

<sup>a</sup> Paid/Volunteer work includes caring and babysitting

<sup>b</sup> Partner status includes married, de facto, and living with partner

**Table C2: Baseline Social Health in Women and Men**

	Women	Men	P value
	n (%)	n (%)	
<b>Total</b>	<b>6,132 (53.3%)</b>	<b>5,366 (46.7%)</b>	
<b>Social Isolation</b>			
Not socially isolated	6,049 (98.6%)	5,224 (97.4%)	<0.001
Socially isolated	83 (1.4%)	142 (2.6%)	
<b>Social Support</b>			
Socially supported	6,026 (98.3%)	5,242 (97.7%)	0.03
Low social support	106 (1.7%)	124 (2.3%)	
<b>Loneliness</b>			
Not lonely	5,797 (94.5%)	5,142 (95.8%)	<0.001
Lonely	335 (5.5%)	224 (4.2%)	
<b>Composite Social Health</b>			
Positive	5,655 (92.2%)	4,930 (91.9%)	
Discordant <sup>a</sup>	142 (2.3%)	212 (4%)	<0.001
Lonely	335 (5.5%)	224 (4.2%)	

<sup>a</sup>Discordant Social Health=socially isolated and/or low social support, but not lonely

**Table C3: Baseline Distribution of Cognitive Scores Stratified by Gender**

	Women		Men		P value
	n (%)	Mean ± SD	n (%)	Mean ± SD	
<b>Total</b>	<b>6,132 (53.3%)</b>		<b>5,366 (46.7%)</b>		
<b>3MS Overall Score</b>	6,132 (53.3%)	94.5 ± 4.0	5,366 (46.7%)	93.1 ± 4.5	<0.001
<b>COWAT Overall Score</b>	6,125 (53.3%)	13 ± 4.6	5,359 (46.7%)	11.8 ± 4.6	<0.001
<b>SDMT Overall Score</b>	6,112 (53.3%)	39.1 ± 9.7	5,349 (47.7%)	36.4 ± 9.7	<0.001
<b>HVLT-R Delayed Recall Score</b>	6,098 (53.3%)	8.4 ± 2.6	5,343 (47.7%)	7.4 ± 2.8	<0.001

SD=Standard Deviation; 3MS=Modified Mini-Mental State Examination; COWAT=Controlled Oral Word Association Test; SDMT=Symbol-Digit Modalities Test; HVLT-R=Hopkin's Verbal Learning Test – Revised



Appendix D: Age-Adjusted Analyses of Associations of Social Health

**Table D1: Age-Adjusted Analyses of Baseline Social Health and Baseline Cognitive Function in Women and Men**

	3MS					COWAT					SDMT					HVLTR-Delayed Recall				
	Mean ± SD	β	95% CI		P value	Mean ± SD	β	95% CI		P value	Mean ± SD	β	95% CI		P value	Mean ± SD	β	95% CI		P value
<b>Women</b>	<b>94.5 ± 4</b>					<b>12.9 ± 4.6</b>					<b>39.1 ± 9.7</b>					<b>8.4 ± 2.6</b>				
Socially Isolated (vs. not)	93.2 ± 4.5	-1.35	-2.21	-0.49	<0.001	11.6 ± 4.5	-1.41	-2.41	-0.42	0.01	36.7 ± 10.5	-2.51	-4.51	-0.50	0.01	7.6 ± 2.9	-0.86	-1.42	-0.30	<0.001
Low Social Support (vs. not)	93 ± 4.7	-1.59	-2.36	-0.83	<0.001	11.8 ± 4.5	-1.18	-2.07	-0.30	0.01	36.3 ± 10.8	-2.80	-4.58	-1.03	<0.001	7.5 ± 2.8	-0.91	-1.42	-0.41	<0.001
Lonely (vs. not)	94 ± 4.1	-0.47	-0.90	-0.03	0.04	12.5 ± 4.8	-0.44	-0.94	0.07	0.09	37 ± 9.9	-1.72	-2.74	-0.70	<0.001	8.3 ± 2.6	-0.07	-0.36	0.21	0.62
<b>Mutually Adjusted</b>																				
Socially Isolated (vs. not)		-0.88	-1.78	0.02	0.06		-1.11	-2.15	-0.06	0.04		-1.67	-3.77	0.42	0.12		-0.61	-1.19	-0.02	0.04
Low Social Support (vs. not)		-1.34	-2.13	-0.54	<0.001		-0.87	-1.79	0.06	0.07		-2.26	-4.12	-0.40	0.02		-0.75	-1.27	-0.22	0.01
Lonely (vs. not)		-0.43	-0.87	0.01	0.05		-0.41	-0.91	0.10	0.11		-1.66	-2.68	-0.64	<0.001		-0.05	-0.33	0.23	0.73
<b>Composite Social Health</b>																				
Positive	94.6 ± 4		Reference			13 ± 4.6		Reference			39.3 ± 9.6		Reference			8.4 ± 2.6		Reference		
Discordant <sup>a</sup>	93 ± 4.5	-1.63	-2.29	-0.97	<0.001	12 ± 4.7	-0.99	-1.75	-0.22	0.01	36.7 ± 10.4	-2.72	-4.25	-1.18	<0.001	7.6 ± 2.8	-0.93	-1.36	-0.49	<0.001
Lonely	94 ± 4.1	-0.51	-0.94	-0.07	0.02	12.5 ± 4.8	-0.46	-0.97	0.05	0.07	37 ± 9.9	-1.79	-2.81	-0.77	<0.001	8.3 ± 2.6	-0.09	-0.38	0.19	0.52
<b>Men</b>	<b>93.1 ± 4.5</b>					<b>11.8 ± 4.6</b>					<b>36.4 ± 9.7</b>					<b>7.4 ± 2.8</b>				
Socially Isolated (vs. not)	92.9 ± 4.6	-0.24	-0.99	0.50	0.52	11.7 ± 4.6	-0.01	-0.77	0.75	0.97	33.8 ± 8.8	-2.71	-4.26	-1.16	<0.001	7.2 ± 3	-0.16	-0.62	0.31	0.51
Low Social Support (vs. not)	93 ± 4.5	0.01	-0.78	0.81	0.98	11.2 ± 4.5	-0.53	-1.35	0.28	0.20	36 ± 8.9	-0.03	-1.71	1.65	0.97	6.9 ± 2.8	-0.42	-0.91	0.07	0.10
Lonely (vs. not)	92.4 ± 4.4	-0.50	-1.10	0.10	0.10	11.3 ± 4.1	-0.44	-1.06	0.17	0.16	34.3 ± 9	-1.33	-2.58	-0.07	0.04	6.9 ± 2.9	-0.30	-0.67	0.07	0.11
<b>Mutually Adjusted</b>																				
Socially Isolated (vs. not)		-0.24	-1.00	0.53	0.55		0.14	-0.65	0.93	0.73		-2.81	-4.42	-1.21	<0.001		-0.05	-0.52	0.43	0.85

Low Social Support (vs. not)	0.09	-0.73	0.91	0.83	-0.56	-1.40	0.28	0.19	0.76	-0.97	2.50	0.39	-0.40	-0.91	0.11	0.13				
Lonely (vs. not)	-0.49	-1.09	0.10	0.11	-0.44	-1.05	0.17	0.16	-1.23	-2.48	0.02	0.05	-0.29	-0.66	0.08	0.13				
<b>Composite Social Health</b>																				
Positive	93.1 ± 4.5	<i>Reference</i>			11.8 ± 4.6	<i>Reference</i>			36.6 ± 9.7	<i>Reference</i>			7.4 ± 2.8	<i>Reference</i>						
Discordant <sup>a</sup>	93.0 ± 4.6	-0.06	-0.67	0.56	0.86	11.2 ± 4.4	-0.59	-1.22	0.04	0.07	34.7 ± 9	-1.64	-2.93	-0.35	0.01	7.2 ± 2.9	-0.20	-0.58	0.18	0.30
Lonely	92.4 ± 4.4	-0.50	-1.10	0.09	0.10	11.3 ± 4.1	-0.47	-1.08	0.14	0.13	34.3 ± 9	-1.40	-2.65	-0.14	0.03	6.9 ± 2.9	-0.31	-0.68	0.06	0.11

*SD=Standard Deviation; β=Coefficient; CI=Confidence Interval; 3MS=Modified Mini-Mental State Examination; COWAT=Controlled Oral Word Association Test;*

*SDMT=Symbol-Digit Modalities Test; HVLT-R=Hopkin's Verbal Learning Test – Revised*

*<sup>a</sup>Discordant Social Health=socially isolated and/or low social support, but not lonely*

**Table D2: Age-Adjusted Analyses of Longitudinal Associations Between Social Health and Cognitive Decline**

	No Cognitive Decline n (%)	Cognitive Decline n (%)	HR	95% CI		P value
<b>Women</b>	<b>5,230 (85.3%)</b>	<b>824 (13.4%)</b>				
Socially Isolated (vs. not)	64 (81%)	15 (19%)	1.35	0.81	2.26	0.25
Low Social Support (vs. not)	82 (80.4%)	20 (19.6%)	1.44	0.92	2.25	0.11
Lonely (vs. not)	282 (85.2%)	49 (14.8%)	1.05	0.78	1.40	0.76
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			1.23	0.72	2.10	0.46
Low Social Support (vs. not)			1.37	0.86	2.18	0.19
Lonely (vs. not)			1.03	0.77	1.38	0.83
<b>Composite Social Health</b>						
Positive	4,836 (86.6%)	750 (13.4%)		<i>Reference</i>		
Discordant	112 (81.8%)	25 (18.3%)	1.34	0.90	2.00	0.15
Lonely	282 (85.2%)	49 (14.8%)	1.05	0.79	1.41	0.72
<b>Men</b>	<b>4,531 (84.4%)</b>	<b>780 (14.5%)</b>				
Socially Isolated (vs. not)	122 (86.5%)	19 (13.5%)	0.94	0.60	1.49	0.80
Low Social Support (vs. not)	103 (83.7%)	20 (16.3%)	1.23	0.79	1.92	0.36
Lonely (vs. not)	181 (81.5%)	41 (18.5%)	1.17	0.85	1.60	0.34
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			0.89	0.56	1.43	0.64
Low Social Support (vs. not)			1.26	0.80	1.99	0.32
Lonely (vs. not)			1.16	0.85	1.60	0.34
<b>Composite Social Health</b>						
Positive	4,169 (85.5%)	709 (14.5%)		<i>Reference</i>		
Discordant <sup>a</sup>	181 (85.8%)	30 (14.2%)	1.00	0.69	1.44	1.00
Lonely	181 (81.5%)	41 (18.5%)	1.17	0.85	1.60	0.34

Derived from a population of 11,498 followed for mean  $4.5 \pm 1.2$  SD years. Cognitive decline had 40,249 person years of observation (mean  $3.5 \pm 1.5$  SD years; median 3.1, IQR 5.0-2.9 years; range 0.6 – 7.1 years).

HR=Hazard Ratio; CI=Confidence Interval

<sup>a</sup>Discordant Social Health=socially isolated and/or low social support, but not lonely

**Table D3: Age-Adjusted Analyses of Longitudinal Associations Between Social Health and Dementia**

	No Dementia n (%)	Dementia n (%)	HR	95% CI		P value
<b>Dementia Trigger</b>	<b>11,092 (96.5%)</b>	<b>406 (3.5%)</b>				
Socially Isolated (vs. not)	216 (96%)	9 (4%)	1.14	0.59	2.20	0.70
Low Social Support (vs. not)	215 (93.5%)	15 (6.5%)	1.85	1.11	3.10	0.02
Lonely (vs. not)	536 (95.9%)	23 (4.1%)	1.05	0.69	1.61	0.81
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			0.92	0.46	1.84	0.81
Low Social Support (vs. not)			1.89	1.10	3.25	0.02
Lonely (vs. not)			1.04	0.68	1.59	0.85
<b>Composite Social Health</b>						
Positive	10,223 (96.6%)	362 (3.4%)		reference		
Discordant <sup>a</sup>	333 (94.1%)	21 (5.9%)	1.71	1.10	2.66	0.02
Lonely	536 (95.9%)	23 (4.1%)	1.08	0.71	1.64	0.73
<b>Dementia Case</b>	<b>11,269 (98%)</b>	<b>229 (2%)</b>				
Socially Isolated (vs. not)	219 (97.3%)	6 (2.7%)	1.37	0.61	3.08	0.45
Low Social Support (vs. not)	221 (96.1%)	9 (3.9%)	1.97	1.01	3.84	0.05
Lonely (vs. not)	549 (98.2%)	10 (1.8%)	0.78	0.41	1.48	0.45
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			1.11	0.47	2.62	0.82
Low Social Support (vs. not)			1.94	0.95	3.93	0.07
Lonely (vs. not)			0.77	0.41	1.45	0.42
<b>Composite Social Health</b>						
Positive	10,378 (98%)	207 (2%)		reference		
Discordant <sup>a</sup>	342 (96.6%)	12 (3.4%)	1.72	0.96	3.08	0.07
Lonely	549 (98.2%)	10 (1.8%)	0.80	0.42	1.51	0.49

Derived from a population of 11,498 followed for mean  $4.5 \pm 1.2$  SD years. Dementia trigger had 51,151 person years of observation (mean  $4.4 \pm 1.3$  SD years; median 4.5, IQR 5.5-3.5 years; range 0.2 – 7.3 years). Dementia cases had 51,400 person years of observation (mean  $4.5 \pm 1.2$  SD years; median 4.5, IQR 5.5-3.5 years; range 0.2 – 7.3 years).

HR=Hazard Ratio; CI=Confidence Interval

<sup>a</sup>Discordant Social Health=socially isolated and/or low social support, but not lonely

Appendix E: Multivariable Adjusted Analyses of Associations of Social Health without CES-D

Table E1: Fully Adjusted Multivariable Analyses without CES-D of Baseline Social Health and Baseline Cognitive Function in Women and Men

	3MS					COWAT					SDMT					HVLTR-Delayed Recall				
	Mean ± SD	β	95% CI		P value	Mean ± SD	β	95% CI		P value	Mean ± SD	β	95% CI		P value	Mean ± SD	β	95% CI		P value
<b>Women</b>	<b>94.5 ± 4</b>					<b>12.9 ± 4.6</b>					<b>39.1 ± 9.7</b>					<b>8.4 ± 2.6</b>				
Socially Isolated (vs. not)	93.2 ± 4.5	-1.15	-1.99	-0.30	0.01	11.6 ± 4.5	-1.22	-2.19	-0.25	0.01	36.7 ± 10.5	-2.41	-4.38	-0.43	0.02	7.6 ± 2.9	-0.81	-1.36	-0.25	<0.001
Low Social Support (vs. not)	93.0 ± 4.7	-1.39	-2.14	-0.64	<0.001	11.8 ± 4.5	-1.00	-1.86	-0.14	0.02	36.3 ± 10.8	-2.72	-4.48	-0.97	<0.001	7.5 ± 2.8	-0.86	-1.36	-0.37	<0.001
Lonely (vs. not)	94.0 ± 4.1	-0.38	-0.81	0.06	0.09	12.5 ± 4.8	-0.30	-0.79	0.20	0.25	37 ± 9.9	-1.62	-2.63	-0.60	<0.001	8.3 ± 2.6	-0.06	-0.34	0.23	0.70
<b>Mutually Adjusted</b>																				
Socially Isolated (vs. not)		-0.74	-1.63	0.14	0.10		-0.97	-1.98	0.05	0.06		-1.61	-3.68	0.46	0.13		-0.57	-1.15	0.01	0.06
Low Social Support (vs. not)		-1.17	-1.96	-0.39	<0.001		-0.73	-1.63	0.18	0.11		-2.21	-4.05	-0.38	0.02		-0.71	-1.23	-0.18	0.01
Lonely (vs. not)		-0.35	-0.78	0.08	0.12		-0.27	-0.77	0.23	0.28		-1.56	-2.57	-0.54	<0.001		-0.04	-0.32	0.25	0.80
<b>Composite Social Health</b>																				
Positive	94.6 ± 4		<i>Reference</i>			13 ± 4.6		<i>Reference</i>			39.3 ± 9.6		<i>Reference</i>			8.4 ± 2.6		<i>Reference</i>		
Discordant <sup>a</sup>	93.0 ± 4.5	-1.46	-2.11	-0.81	<0.001	12 ± 4.7	-0.84	-1.58	-0.09	0.03	36.7 ± 10.4	-2.67	-4.19	-1.15	<0.001	7.6 ± 2.8	-0.89	-1.32	-0.46	<0.001
Lonely	94.0 ± 4.1	-0.42	-0.85	0.02	0.06	12.5 ± 4.8	-0.32	-0.82	0.18	0.21	37 ± 9.9	-1.69	-2.70	-0.67	<0.001	8.3 ± 2.6	-0.08	-0.36	0.21	0.59
<b>Men</b>	<b>93.1 ± 4.5</b>					<b>11.8 ± 4.6</b>					<b>36.4 ± 9.7</b>					<b>7.4 ± 2.8</b>				
Socially Isolated (vs. not)	92.9 ± 4.6	0.09	-0.64	0.81	0.81	11.7 ± 4.6	0.24	-0.50	0.99	0.52	33.8 ± 8.8	-1.90	-3.39	-0.42	0.01	7.2 ± 3	0.00	-0.46	0.46	1.00
Low Social Support (vs. not)	93.0 ± 4.5	0.28	-0.49	1.05	0.48	11.2 ± 4.5	-0.34	-1.13	0.46	0.41	36 ± 8.9	0.44	-1.16	2.04	0.59	6.9 ± 2.8	-0.30	-0.79	0.19	0.23
Lonely (vs. not)	92.4 ± 4.4	-0.32	-0.91	0.26	0.28	11.3 ± 4.1	-0.28	-0.88	0.32	0.36	34.3 ± 9	-0.90	-2.09	0.30	0.14	6.9 ± 2.9	-0.23	-0.60	0.14	0.22
<b>Mutually Adjusted</b>																				
Socially Isolated (vs. not)		0.04	-0.71	0.79	0.91		0.36	-0.41	1.13	0.37		-2.09	-3.62	-0.55	0.01		0.09	-0.39	0.56	0.72

Low Social Support (vs. not)	0.28 -0.52 1.07 0.49	-0.42 -1.24 0.40 0.32	1.02 -0.63 2.67 0.23	-0.32 -0.82 0.18 0.22
Lonely (vs. not)	-0.33 -0.91 0.25 0.27	-0.29 -0.89 0.31 0.35	-0.84 -2.04 0.36 0.17	-0.23 -0.60 0.14 0.22
<b>Composite Social Health</b>				
Positive	93.1 ± 4.5 <i>Reference</i>	11.8 ± 4.6 <i>Reference</i>	36.6 ± 9.7 <i>Reference</i>	7.4 ± 2.8 <i>Reference</i>
Discordant <sup>a</sup>	93.0 ± 4.6 0.20 -0.39 0.80 0.50	11.2 ± 4.4 -0.40 -1.01 0.22 0.21	34.7 ± 9 -1.06 -2.29 0.17 0.09	7.2 ± 2.9 -0.08 -0.46 0.30 0.68
Lonely	92.4 ± 4.4 -0.32 -0.90 0.27 0.29	11.3 ± 4.1 -0.30 -0.90 0.30 0.33	34.3 ± 9 -0.95 -2.14 0.25 0.12	6.9 ± 2.9 -0.24 -0.60 0.13 0.21

*SD=Standard Deviation; β=Coefficient; CI=Confidence Interval; 3MS=Modified Mini-Mental State Examination; COWAT=Controlled Oral Word Association Test; SDMT=Symbol-Digit Modalities Test; HVLt-R=Hopkin's Verbal Learning Test – Revised*

*Adjusted for age (continuous), gender, level of education (≤12 or >12 years), place of birth (Australia or not Australia), and BMI (continuous).*

<sup>a</sup>*Discordant Social Health=socially isolated and/or low social support, but not lonely*

**Table E2: Fully adjusted Multivariable Analyses without CES-D of Longitudinal Associations Between Social Health and Cognitive Decline**

	No Cognitive Decline n (%)	Cognitive Decline n (%)	HR	95% CI		P value
<b>Women</b>	<b>5,230 (85.3%)</b>	<b>824 (13.4%)</b>				
Socially Isolated (vs. not)	64 (81%)	15 (19%)	1.31	0.78	2.19	0.31
Low Social Support (vs. not)	82 (80.4%)	20 (19.6%)	1.41	0.91	2.20	0.13
Lonely (vs. not)	282 (85.2%)	49 (14.8%)	1.05	0.78	1.40	0.75
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			1.19	0.69	2.04	0.53
Low Social Support (vs. not)			1.35	0.85	2.15	0.21
Lonely (vs. not)			1.03	0.77	1.38	0.82
<b>Composite Social Health</b>						
Positive	4,836 (86.6%)	750 (13.4%)		<i>Reference</i>		
Discordant	112 (81.8%)	25 (18.3%)	1.31	0.88	1.96	0.19
Lonely	282 (85.2%)	49 (14.8%)	1.06	0.79	1.41	0.71
<b>Men</b>	<b>4,531 (84.4%)</b>	<b>780 (14.5%)</b>				
Socially Isolated (vs. not)	122 (86.5%)	19 (13.5%)	0.93	0.59	1.47	0.76
Low Social Support (vs. not)	103 (83.7%)	20 (16.3%)	1.23	0.79	1.92	0.36
Lonely (vs. not)	181 (81.5%)	41 (18.5%)	1.14	0.83	1.57	0.40
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			0.88	0.55	1.41	0.60
Low Social Support (vs. not)			1.26	0.80	2.00	0.32
Lonely (vs. not)			1.14	0.83	1.57	0.41
<b>Composite Social Health</b>						
Positive	4,169 (85.5%)	709 (14.5%)		<i>Reference</i>		
Discordant <sup>a</sup>	181 (85.8%)	30 (14.2%)	1.00	0.69	1.44	1.00
Lonely	181 (81.5%)	41 (18.5%)	1.14	0.83	1.57	0.40

Derived from a population of 11,498 followed for mean 4.5 ± 1.2 SD years. Cognitive decline had 40,249 person years of observation (mean 3.5 ± 1.5 SD years; median 3.1, IQR 5.0-2.9 years; range 0.6 – 7.1 years).

Adjusted for age (continuous), gender, level of education (≤12 or >12 years), place of birth (Australia or not Australia), BMI (continuous).

HR=Hazard Ratio; CI=Confidence Interval

<sup>a</sup>Discordant Social Health=socially isolated and/or low social support, but not lonely

**Table E3: Fully adjusted Multivariable Analyses without CES-D of Longitudinal Associations Between Social Health and Dementia**

	No Dementia n (%)	Dementia n (%)	HR	95% CI		P value
<b>Dementia Trigger</b>	<b>11,092 (96.5%)</b>	<b>406 (3.5%)</b>				
Socially Isolated (vs. not)	216 (96%)	9 (4%)	0.97	0.48	1.96	0.93
Low Social Support (vs. not)	215 (93.5%)	15 (6.5%)	1.78	1.06	2.99	0.03
Lonely (vs. not)	536 (95.9%)	23 (4.1%)	1.06	0.69	1.61	0.79
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			0.78	0.38	1.63	0.52
Low Social Support (vs. not)			1.88	1.10	3.23	0.02
Lonely (vs. not)			1.05	0.69	1.60	0.83
<b>Composite Social Health</b>						
Positive	10,223 (96.6%)	362 (3.4%)		<i>Reference</i>		
Discordant <sup>a</sup>	333 (94.1%)	21 (5.9%)	1.57	1.00	2.46	0.05
Lonely	536 (95.9%)	23 (4.1%)	1.08	0.71	1.65	0.73
<b>Dementia Case</b>	<b>11,269 (98%)</b>	<b>229 (2%)</b>				
Socially Isolated (vs. not)	219 (97.3%)	6 (2.7%)	1.37	0.61	3.09	0.45
Low Social Support (vs. not)	221 (96.1%)	9 (3.9%)	1.91	0.98	3.73	0.06
Lonely (vs. not)	549 (98.2%)	10 (1.8%)	0.79	0.42	1.49	0.46
<b>Mutually Adjusted</b>						
Socially Isolated (vs. not)			1.12	0.47	2.65	0.80
Low Social Support (vs. not)			1.88	0.92	3.81	0.08
Lonely (vs. not)			0.77	0.41	1.46	0.43
<b>Composite Social Health</b>						
Positive	10,378 (98%)	207 (2%)		<i>Reference</i>		
Discordant <sup>a</sup>	342 (96.6%)	12 (3.4%)	1.69	0.94	3.04	0.08
Lonely	549 (98.2%)	10 (1.8%)	0.81	0.43	1.52	0.51

Derived from a population of 11,498 followed for mean  $4.5 \pm 1.2$  SD years. Dementia trigger had 51,151 person years of observation (mean  $4.4 \pm 1.3$  SD years; median 4.5, IQR 5.5-3.5 years; range 0.2 – 7.3 years). Dementia cases had 51,400 person years of observation (mean  $4.5 \pm 1.2$  SD years; median 4.5, IQR 5.5-3.5 years; range 0.2 – 7.3 years).

Adjusted for age (continuous), gender, level of education ( $\leq 12$  or  $>12$  years), place of birth (Australia or not Australia), BMI (continuous).

HR=Hazard Ratio; CI=Confidence Interval

<sup>a</sup>Discordant Social Health=socially isolated and/or low social support, but not lonely



## Appendix F: Potential Dose-Response Relationship Assessment Between Social Health and Cognitive Decline/Dementia

**Table F1: Potential Dose-Response Relationship Assessment Between Social Health and Cognitive Decline**

	HR	95% CI		P Values
<b>Social Isolation Quartiles: Women</b>				
Positive (Low Social Isolation)		<i>Reference</i>		
2	0.94	0.77	1.16	0.57
3	1.08	0.89	1.32	0.42
Negative (High Social Isolation)	1.07	0.88	1.31	0.49
<b>Social Isolation Quartiles: Men</b>				
Positive (Low Social Isolation)		<i>Reference</i>		
2	0.92	0.75	1.14	0.47
3	1.08	0.88	1.32	0.48
Negative (High Social Isolation)	1.30	1.06	1.59	0.01
<b>Low Social Support Quartiles: Women</b>				
Positive (High Social Support)		<i>Reference</i>		
2	0.92	0.75	1.12	0.38
3	0.93	0.76	1.14	0.47
Negative (Low Social Support)	0.90	0.74	1.08	0.26
<b>Low Social Support Quartiles: Men</b>				
Positive (High Social Support)		<i>Reference</i>		
2	1.01	0.82	1.24	0.94
3	1.09	0.88	1.36	0.43
Negative (Low Social Support)	1.12	0.92	1.37	0.25
<b>Loneliness Categories: Women</b>				
Positive (Low Loneliness)		<i>Reference</i>		
Medium	1.12	0.90	1.39	0.30
Negative (High Loneliness)	0.99	0.73	1.34	0.94
<b>Loneliness Categories: Men</b>				
Positive (Low Loneliness)		<i>Reference</i>		
Medium	0.99	0.74	1.32	0.95
Negative (High Loneliness)	0.90	0.64	1.28	0.57

Derived from a population of 11,498 followed for mean  $4.5 \pm 1.2$  SD years. Cognitive decline had 40,249 person years of observation (mean  $3.5 \pm 1.5$  SD years; median 3.1, IQR 5.0-2.9 years; range 0.6 – 7.1 years).

Adjusted for age (continuous), gender, level of education ( $\leq 12$  or  $>12$  years), place of birth (Australia or not Australia), BMI (continuous) and CES-D score ( $<8$  or  $\geq 8$ ).

HR=Hazard Ratio; CI=Confidence Interval

**Table F2: Potential Dose-Response Relationship Assessment Between Social Health and Dementia**

<b>DEMENTIA TRIGGER</b>	<b>HR</b>	<b>95% CI</b>		<b>P Values</b>
<b>Social Isolation Quartiles: Women</b>				
Positive (Low Social Isolation)		<i>Reference</i>		
2	0.84	0.55	1.31	0.45
3	0.81	0.52	1.26	0.35
Negative (High Social Isolation)	1.37	0.93	2.02	0.11
<b>Social Isolation Quartiles: Men</b>				
Positive (Low Social Isolation)		<i>Reference</i>		
2	0.80	0.54	1.20	0.28
3	1.11	0.77	1.61	0.56
Negative (High Social Isolation)	0.93	0.63	1.37	0.71
<b>Low Social Support Quartiles: Women</b>				
Positive (High Social Support)		<i>Reference</i>		
2	1.15	0.76	1.73	0.51
3	0.64	0.39	1.04	0.07
Negative (Low Social Support)	1.08	0.73	1.60	0.70
<b>Low Social Support Quartiles: Men</b>				
Positive (High Social Support)		<i>Reference</i>		
2	1.00	0.68	1.48	1.00
3	1.23	0.83	1.82	0.31
Negative (Low Social Support)	0.92	0.62	1.36	0.67
<b>Loneliness Categories</b>				
Positive (Low Loneliness)		<i>Reference</i>		
Medium	1.45	1.08	1.96	0.01
Negative (High Loneliness)	1.01	0.64	1.58	0.98
<b>DEMENTIA CASE</b>				
<b>Social Isolation Quartiles: Women</b>				
Positive (Low Social Isolation)		<i>Reference</i>		
2	1.16	0.63	2.11	0.63
3	1.09	0.59	2.00	0.79
Negative (High Social Isolation)	1.57	0.89	2.75	0.12
<b>Social Isolation Quartiles: Men</b>				
Positive (Low Social Isolation)		<i>Reference</i>		
2	0.96	0.57	1.60	0.87
3	1.10	0.67	1.81	0.70
Negative (High Social Isolation)	1.01	0.61	1.68	0.98
<b>Low Social Support Quartiles: Women</b>				
Positive (High Social Support)		<i>Reference</i>		
2	1.02	0.57	1.82	0.96
3	0.72	0.38	1.37	0.32
Negative (Low Social Support)	1.20	0.71	2.04	0.49
<b>Low Social Support Quartiles: Men</b>				
Positive (High Social Support)		<i>Reference</i>		
2	1.12	0.67	1.86	0.67
3	1.30	0.77	2.19	0.33
Negative (Low Social Support)	0.98	0.58	1.64	0.93

### Loneliness Categories

Loneliness Categories		Reference		
Positive (Low Loneliness)				
Medium	0.91	0.58	1.45	0.71
Negative (High Loneliness)	0.72	0.37	1.40	0.33

*Derived from a population of 11,498 followed for mean 4.5 ± 1.2 SD years. Dementia trigger had 51,151 person years of observation (mean 4.4 ± 1.3 SD years; median 4.5, IQR 5.5-3.5 years; range 0.2 – 7.3 years). Dementia cases had 51,400 person years of observation (mean 4.5 ± 1.2 SD years; median 4.5, IQR 5.5-3.5 years; range 0.2 – 7.3 years).*

*Adjusted for age (continuous), gender, level of education (≤12 or >12 years), place of birth (Australia or not Australia), BMI (continuous) and CES-D score (<8 or ≥8).*

*HR=Hazard Ratio; CI=Confidence Interval*