

Supplemental Online Content

Lyu C, Siu K, Xu I, Osman I, Zhong J. Social isolation changes and long-term outcomes among older adults. *JAMA Netw Open*. 2024;7(7):e2424519. doi:10.1001/jamanetworkopen.2024.24519

eFigure 1. Flow chart of the study design

eFigure 2. The standardized mean difference for covariates

eFigure 3. The cumulative incidence curves of CVD and stroke for social isolation change from baseline to second social isolation measure and the social isolation status

eFigure 4. Unadjusted hazard ratios of changes in isolation on distal outcomes stratified by the social isolation status

eFigure 5. Sensitivity analysis 1: adjusted hazard ratios of changes in binary isolation group on distal outcomes stratified by the social isolation status

eFigure 6. Sensitivity analysis 2: Adjusted hazard ratios of changes in isolation group on distal outcomes among individuals who did not die within 2 years post second SII measurement

eFigure 7. Sensitivity analysis 3: Adjusted hazard ratios of changes in isolation group on distal outcomes stratified by the social isolation status incorporating HRS sampling weights

eTable 1. ICD-10 Diagnosis codes from Medicare Chronic Conditions Warehouse

eTable 2. Social Isolation Index change from baseline to second social isolation measurement stratified by isolation status

eTable 3. Demographic and clinical characteristics of the HRS analysis cohort by social isolation group from baseline to second social isolation measure

eTable 4. The hazard ratios of full covariates on distal outcomes stratified by the social isolation status

This supplemental material has been provided by the authors to give readers additional information about their work.

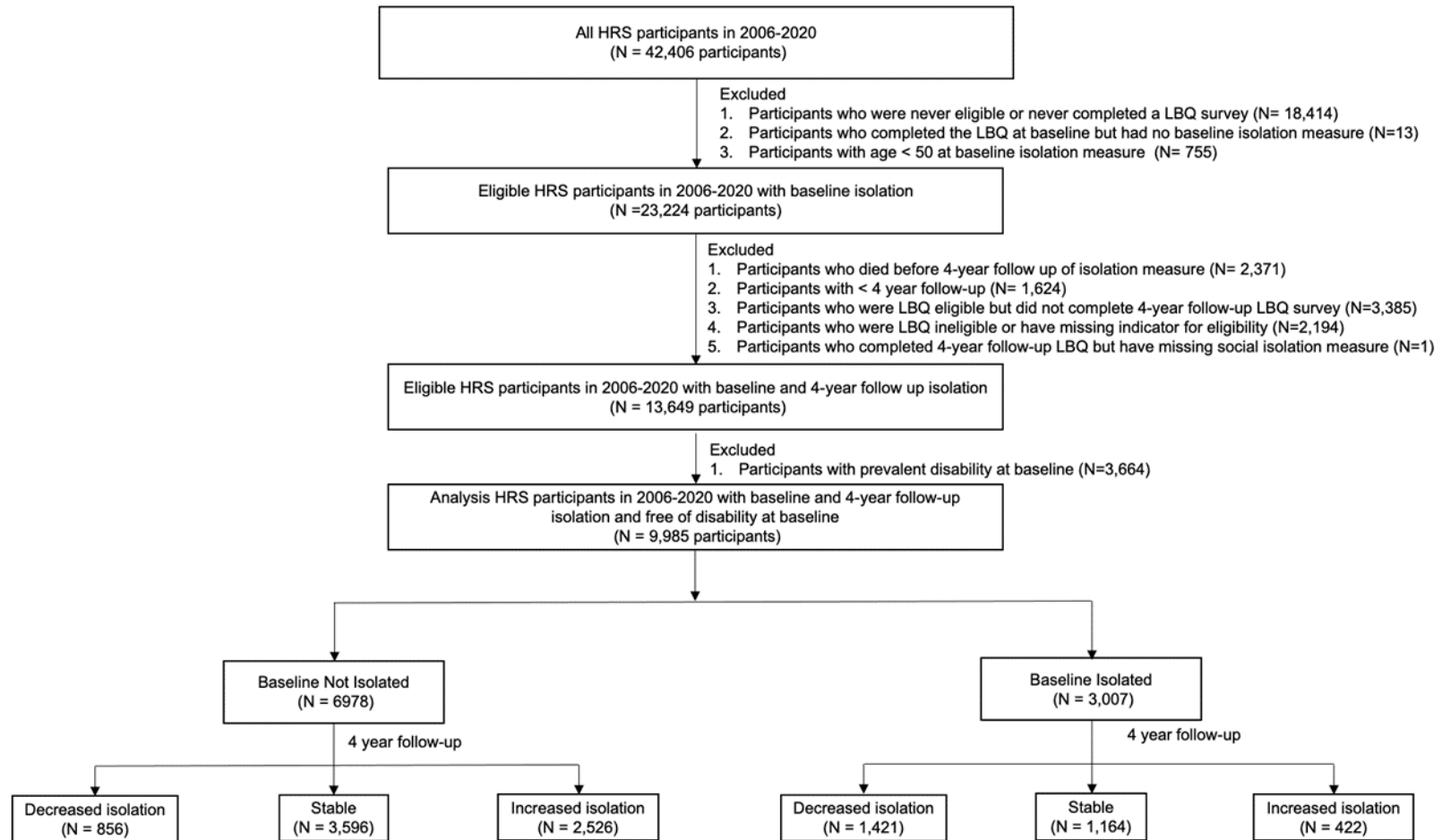
Online-Only Supplementary Material

Efigure 1: Flow chart of the study design.

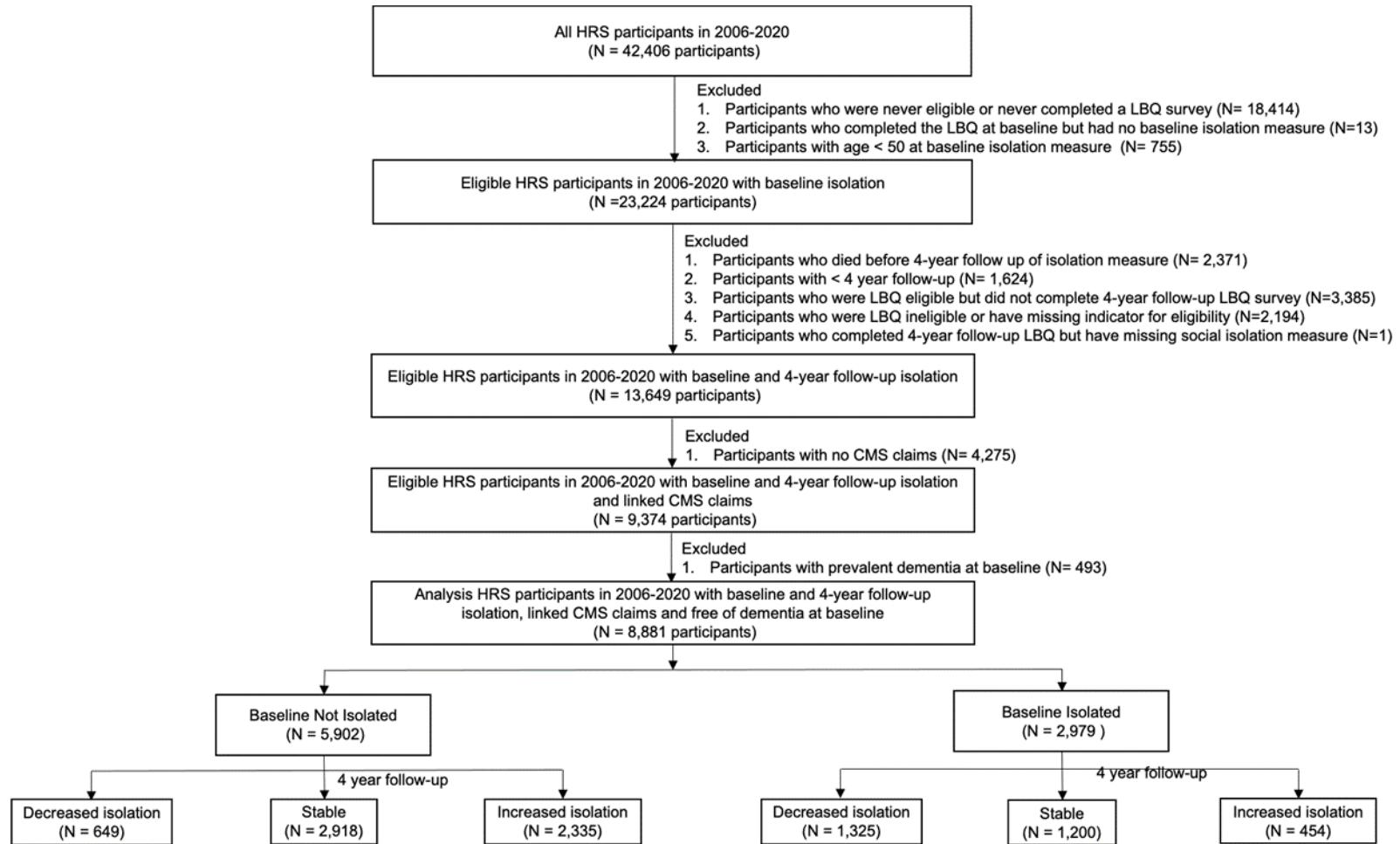
The flow charts are listed for A) disability (ADL>0), B) Dementia (AD or ADRD), C) CVD (acute myocardial infarction, atrial fibrillation, congestive heart failure, ischemic heart disease or stroke) and D) stroke. In addition to the exclusion criteria in

Figure 1, we further excluded the individuals with no linked Medicare claims or with the outcome missing or the outcome before first measurement of social isolation.

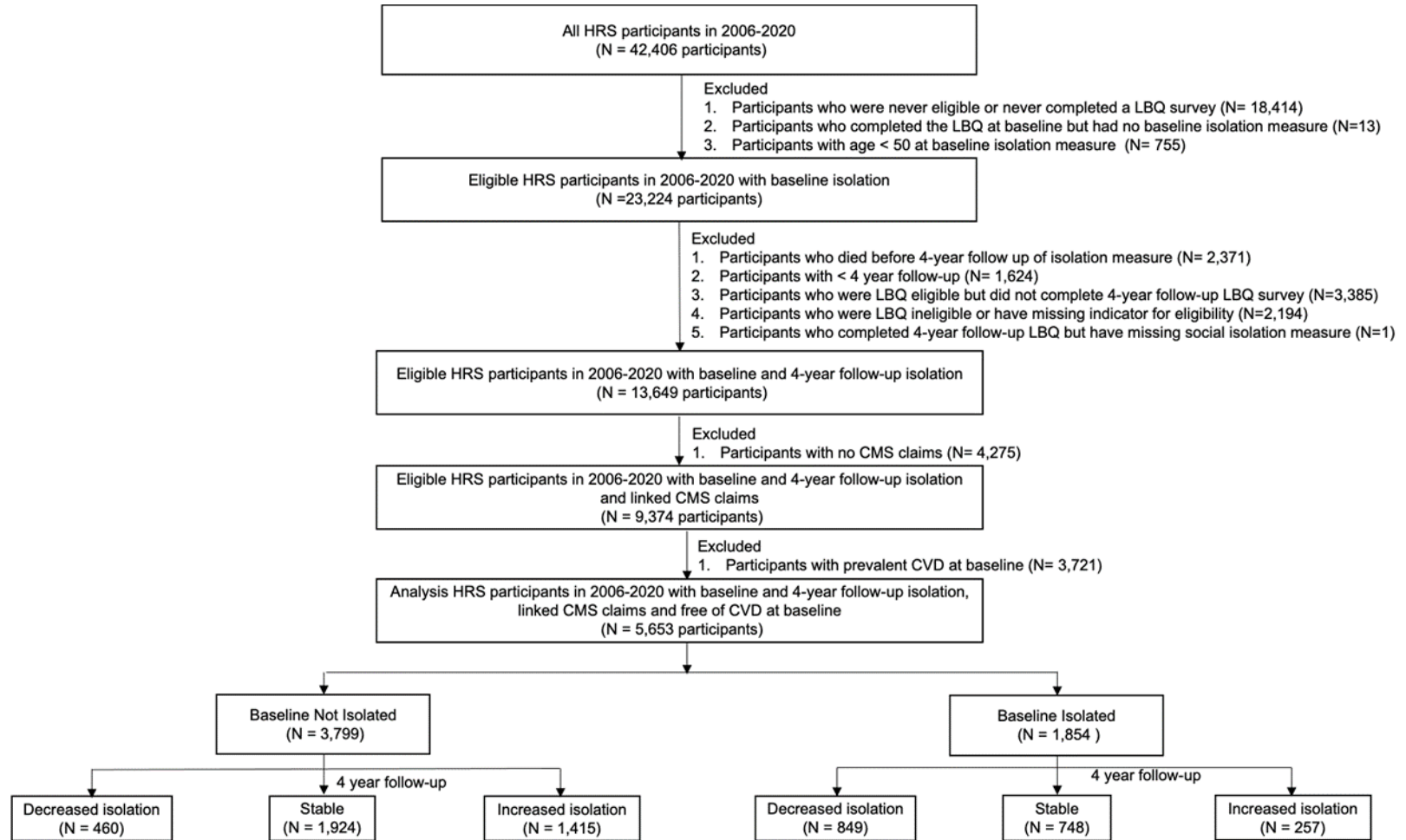
A)



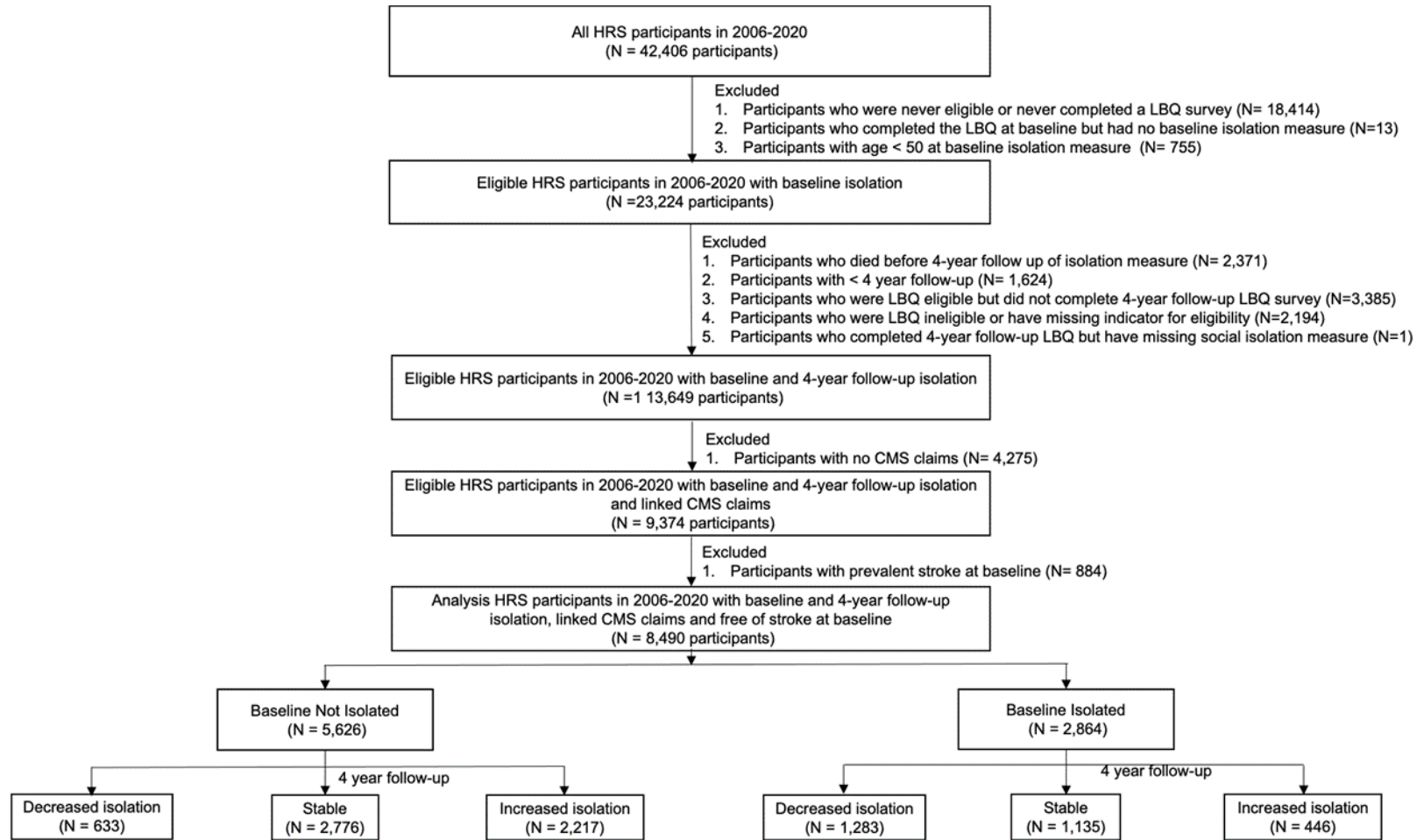
B)



C)

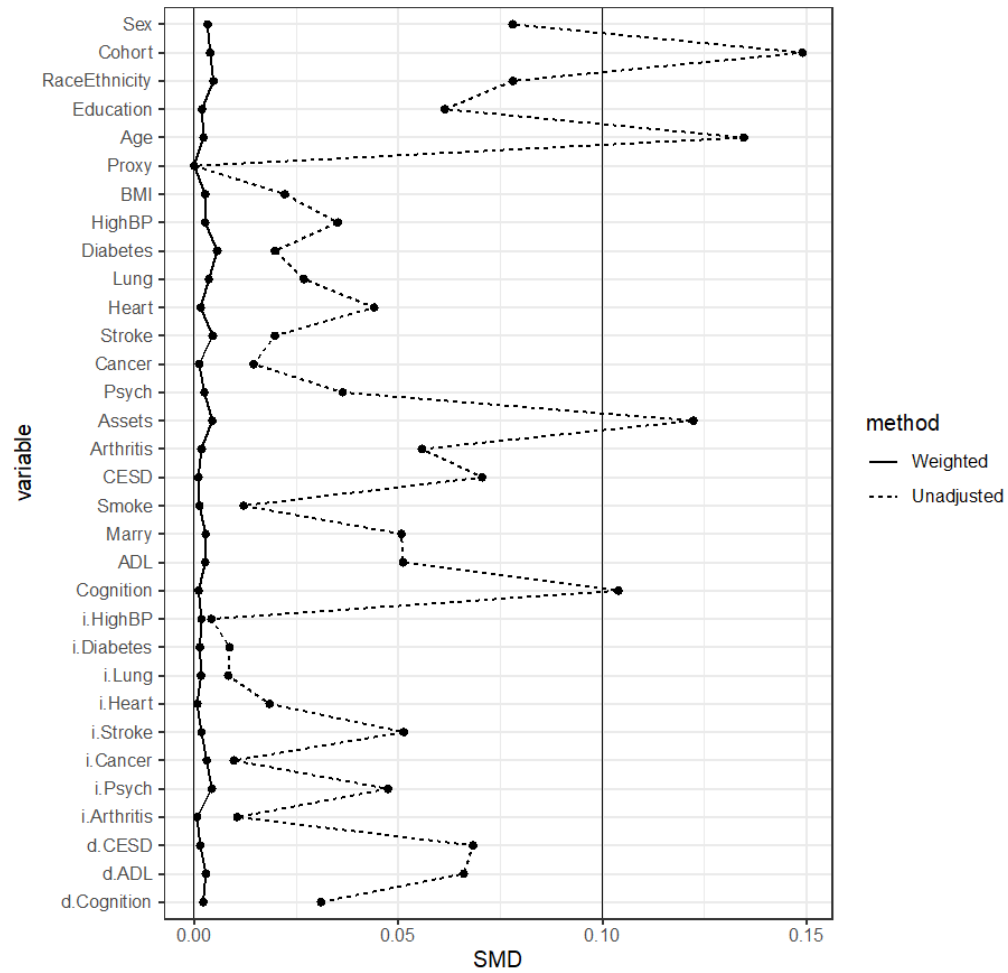


D)



Efigure 2: The standardized mean difference for covariates

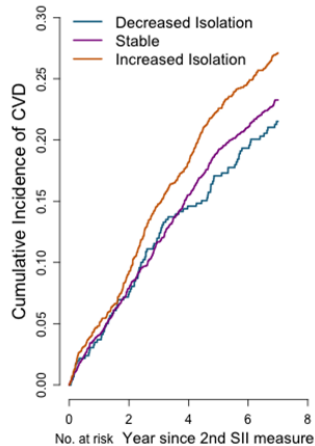
The standardized mean difference (SMD) was calculated for each covariate before and after inverse probability of treatment weighting. The solid line refers to weighted SMD and the dash line represents the unadjusted one.



Efigure 3: The cumulative incidence curves of CVD and stroke for social isolation change from baseline to second social isolation measure and the social isolation status.

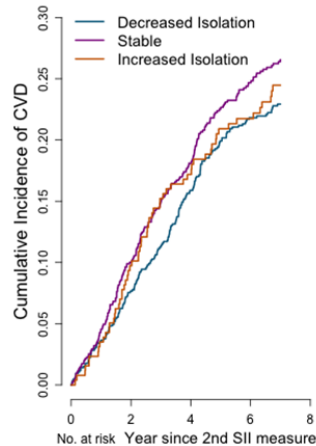
The outcomes include A-B) CVD; and C-D) stroke. The figures were stratified by the social isolation status: A, C) baseline non-isolation and B, D) baseline isolation. The x-axis of each figure is the year since second social isolation measure. The year since second social isolation measure is the 4 year later since the first measurement of social isolation. The curves are colored by the three isolation change groups from baseline to second social isolation measure (blue: decreased isolation, purple: stable and orange: increased isolation). The number of participants at risk at each time point were listed in the table below each figure.

A) Baseline Not Isolated CVD



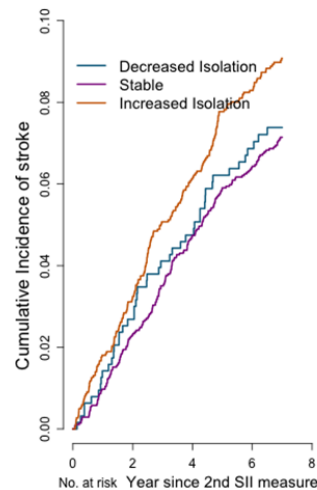
460	426	391	358	Decreased Isolation
1924	1772	1612	1443	Stable
1415	1284	1142	1004	Increased Isolation

B) Baseline Isolated CVD



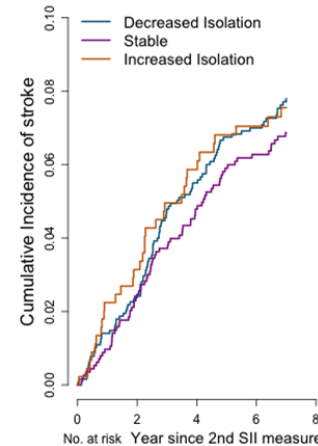
849	784	706	615	Decreased Isolation
748	673	600	524	Stable
257	232	210	186	Increased Isolation

C) Baseline Not Isolated Stroke



633	616	601	571	Decreased Isolation
2776	2712	2621	2481	Stable
2217	2145	2055	1934	Increased Isolation

D) Baseline Isolated Stroke

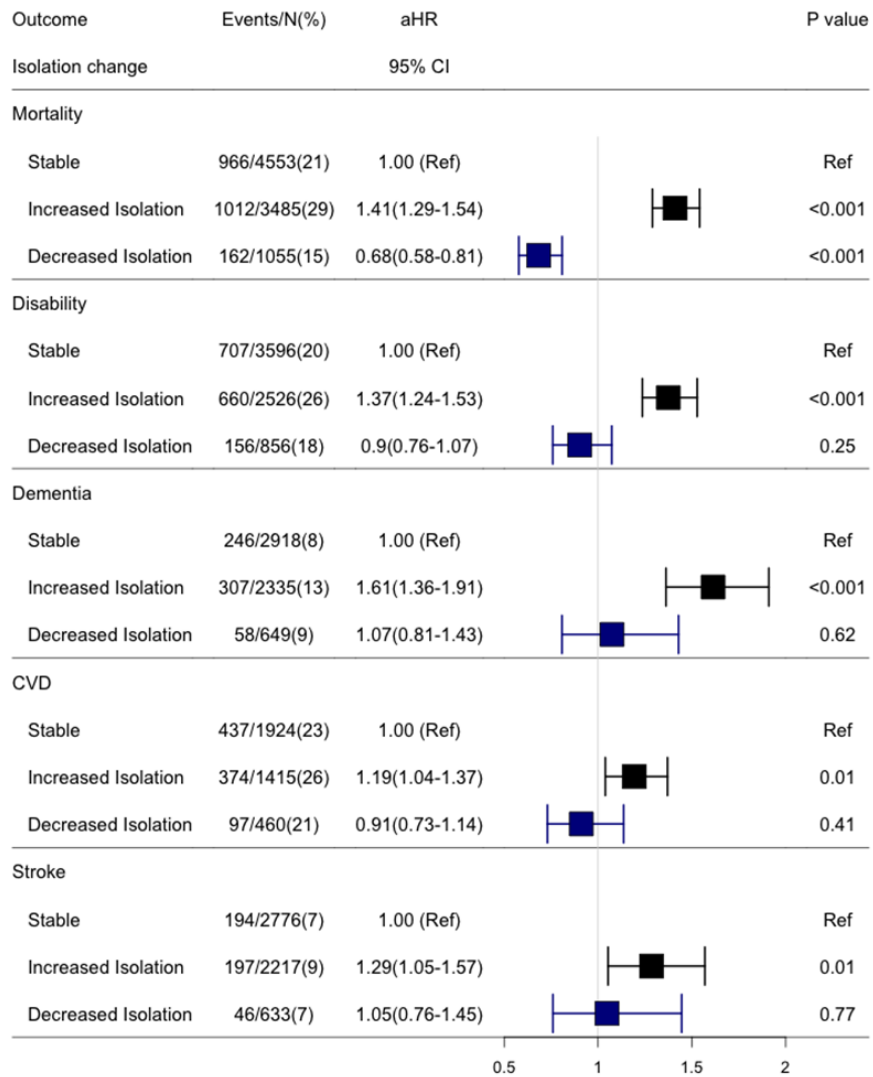


1283	1252	1196	1114	Decreased Isolation
1135	1107	1067	1006	Stable
446	432	414	389	Increased Isolation

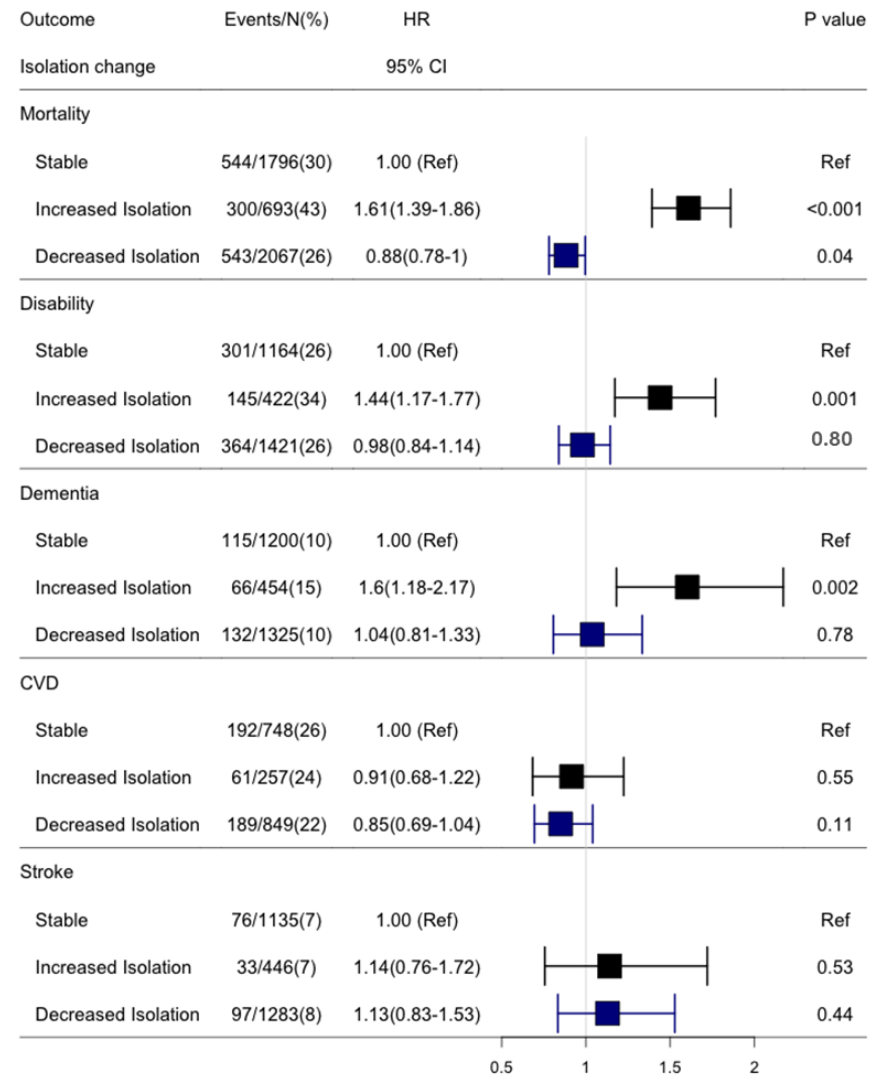
Efigure 4: Unadjusted hazard ratios of changes in isolation on distal outcomes stratified by the social isolation status

The hazard ratios (95% confident interval) between isolation change group are estimated for each outcome with stable social isolation as the reference group with no covariate adjustment nor IPTW use. The p-value column presents the p-values testing the corresponding HR of diabetes to the null hypothesis (HR=1).

A) Baseline Not Isolated



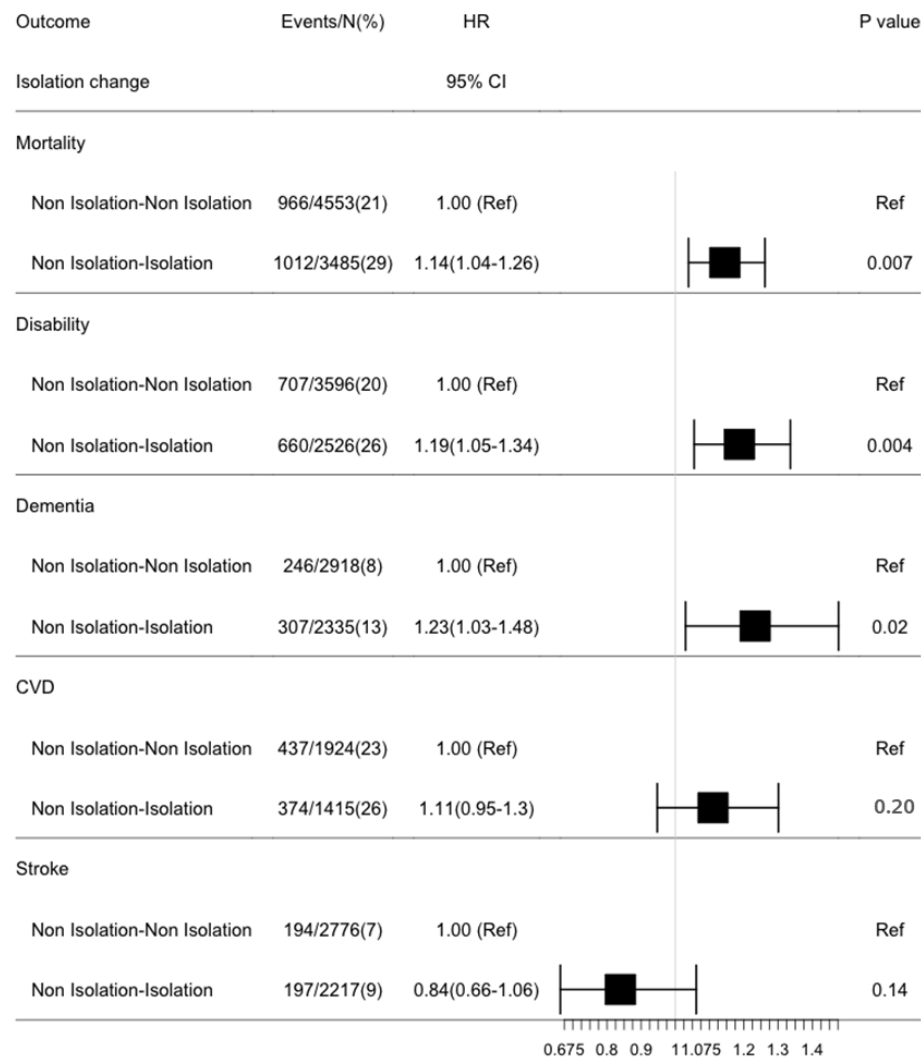
B) Baseline Isolated



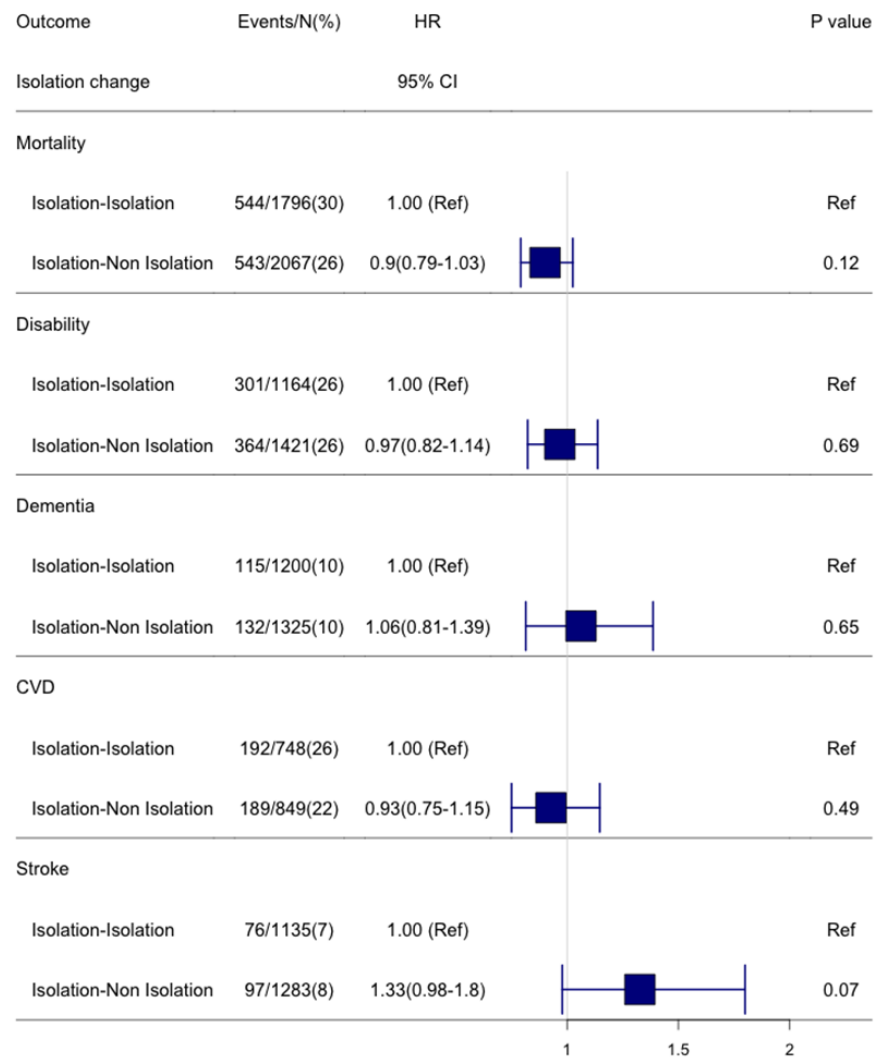
Efigure 5: Sensitivity analysis 1: adjusted hazard ratios of changes in binary isolation group on distal outcomes stratified by the social isolation status

The hazard ratios (95% confident interval) between binary isolation change group are estimated for each outcome with stable social isolation as the reference group with covariate adjustment and IPTW use. The p-value column presents the p-values testing the corresponding HR of diabetes to the null hypothesis (HR=1).

A) Baseline Not Isolated



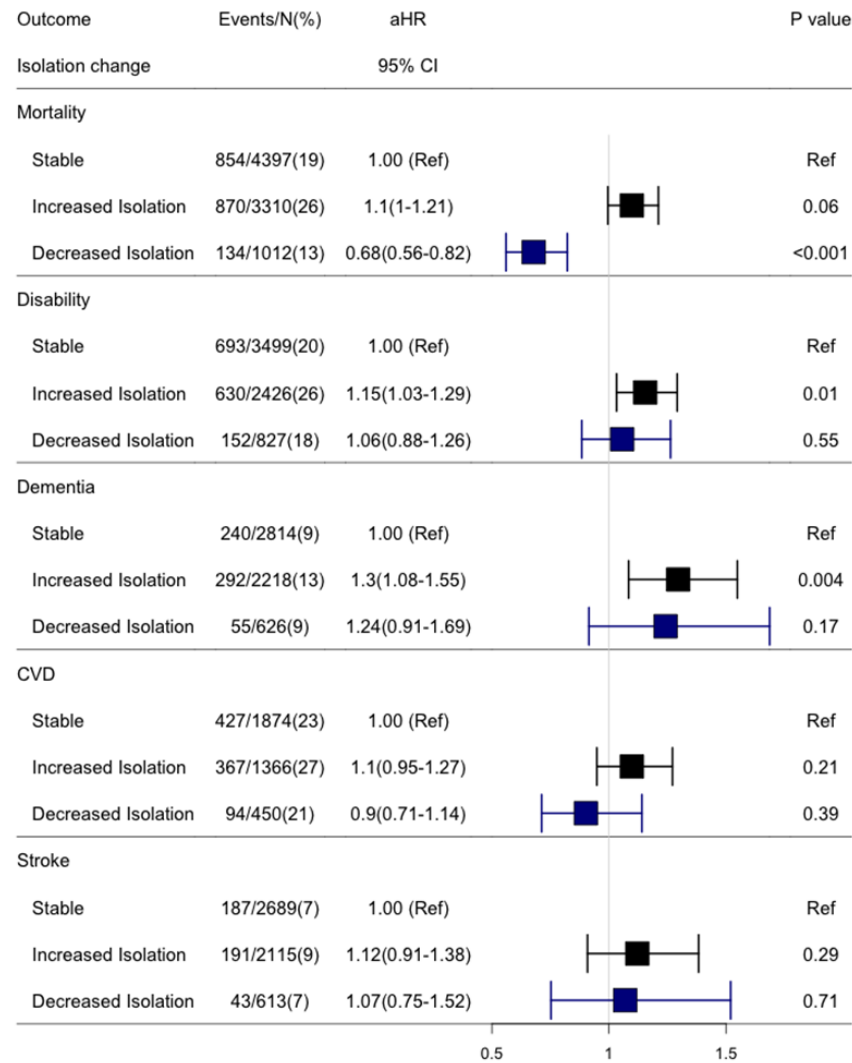
B) Baseline Isolated



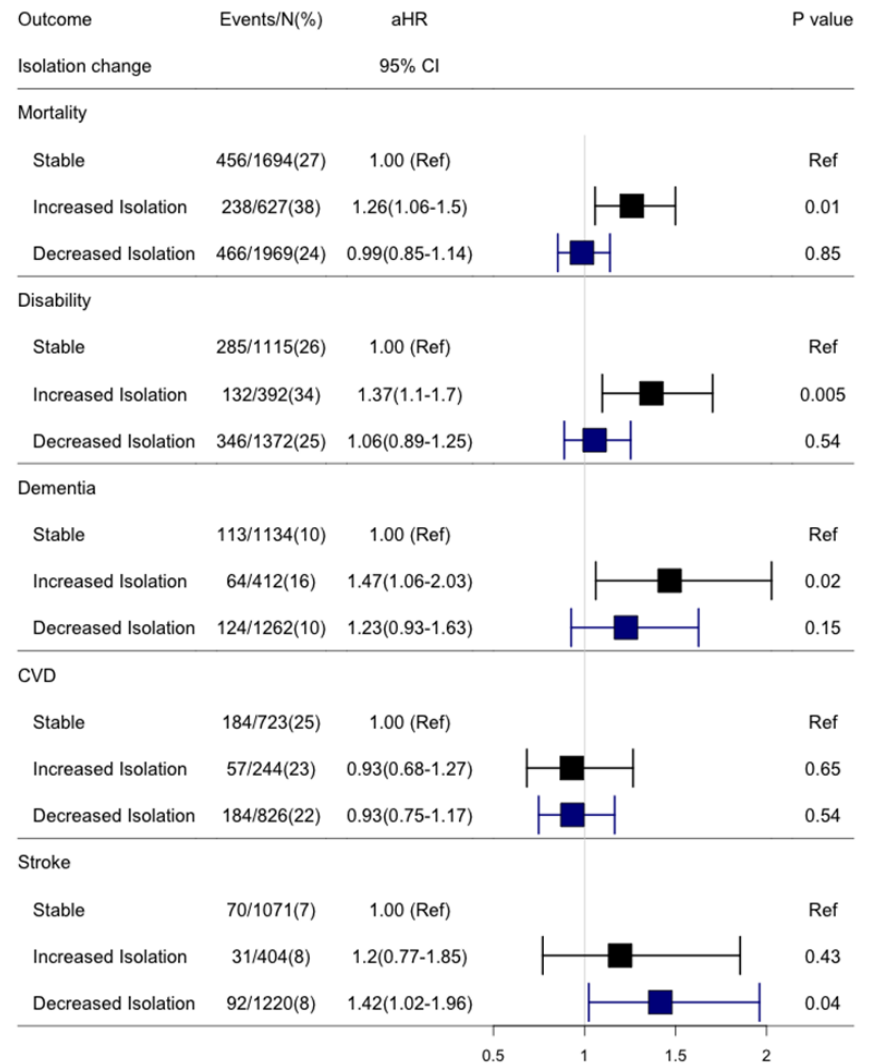
Efigure 6: Sensitivity analysis 2: Adjusted hazard ratios of changes in isolation group on distal outcomes among individuals who did not die within 2 years post second SII measurement

The hazard ratios (95% confident interval) between isolation change group are estimated for each outcome with stable social isolation as the reference group with covariate adjustment and IPTW use. The p-value column presents the p-values testing the corresponding HR of diabetes to the null hypothesis (HR=1).

A) Baseline Not Isolated



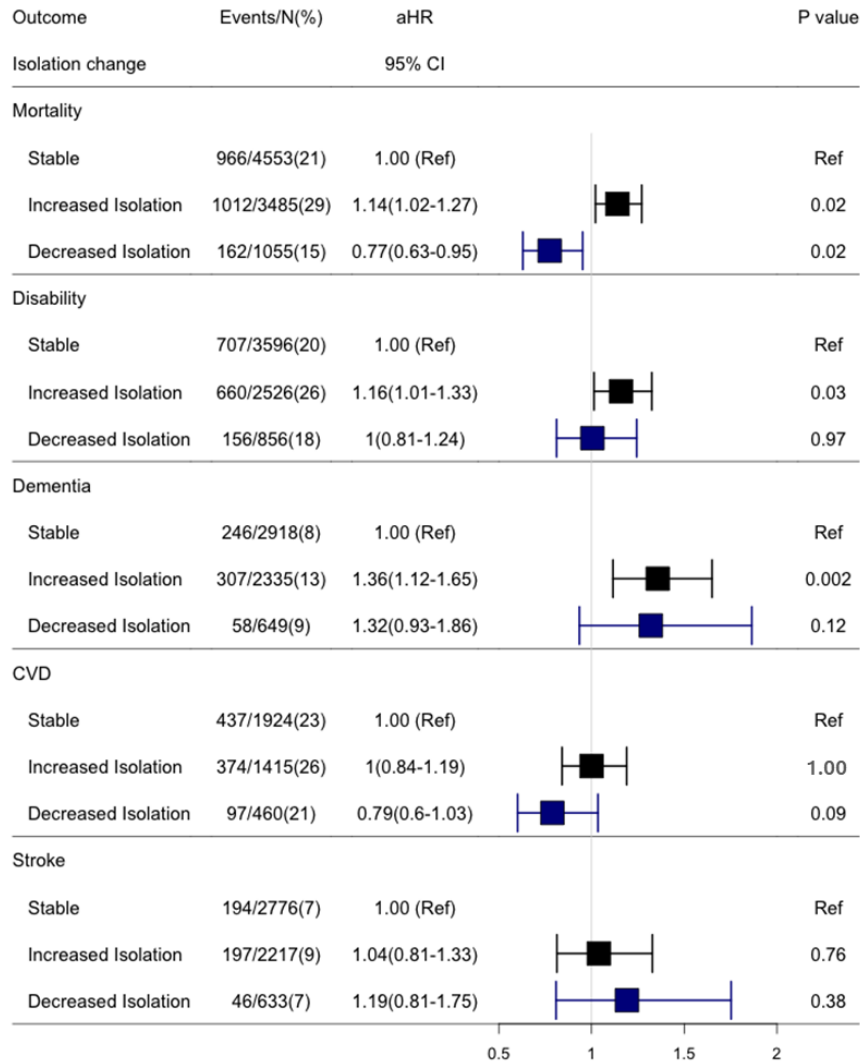
B) Baseline Isolated



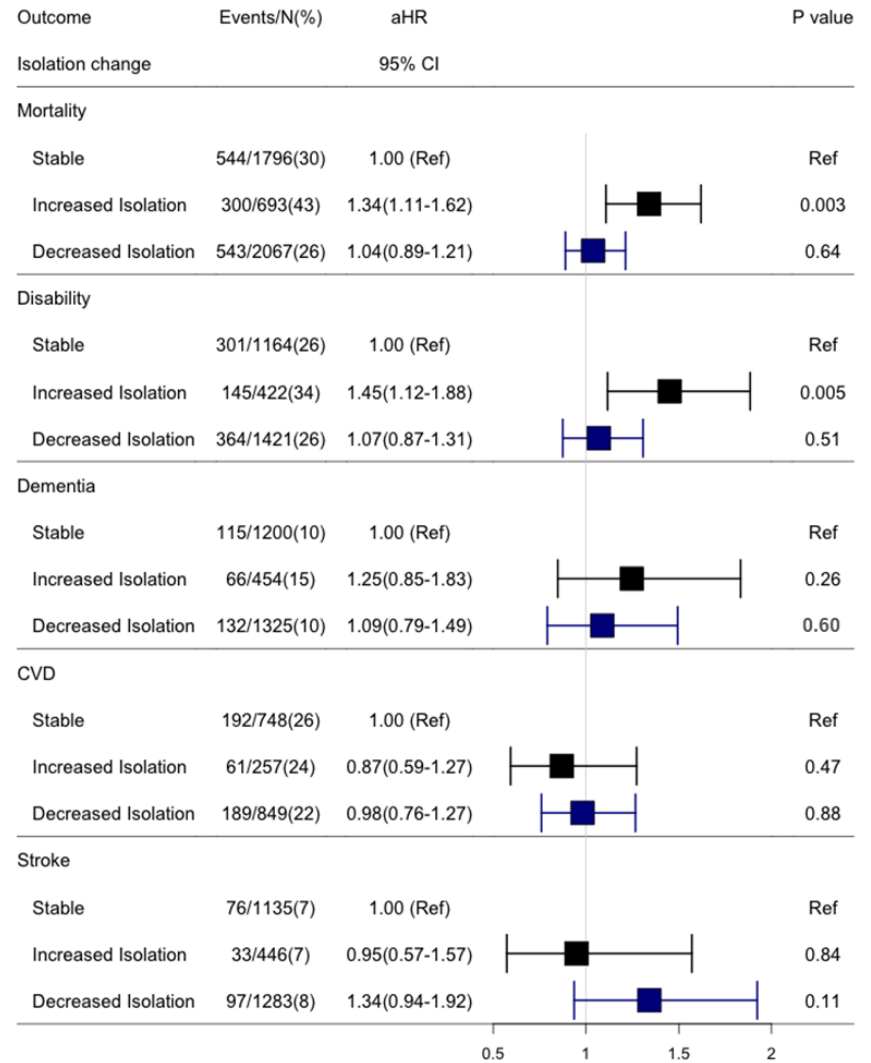
Efigure 7: Sensitivity analysis 3: Adjusted hazard ratios of changes in isolation group on distal outcomes stratified by the social isolation status incorporating HRS sampling weights

The hazard ratios (95% confident interval) between isolation change group are estimated for each outcome with stable social isolation as the reference group with covariate adjustment, IPTW use and HRS sampling weights. The p-value column presents the p-values testing the corresponding HR of diabetes to the null hypothesis (HR=1).

A) Baseline Not Isolated



B) Baseline Isolated



Etable 1: ICD-10 Diagnosis codes from Medicare Chronic Conditions Warehouse.

Outcome	ICD-10 Codes
Atrial fibrillation	I48.0, I48.1, I48.11, I48.19, I48.2, I48.20, I48.21, I48.3, I48.4, I48.91
Congestive heart failure	I09.81, I11.0, I13.0, I13.2, I42.0, I42.5, I42.6, I42.7, I42.8, I43, I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I50.89, I50.9, P29.0
Ischemic heart disease	I20.0, I20.1, I20.8, I24.0, I24.1, I24.8, I25.10, I25.110, I25.111, I25.118, I25.119, I25.3, I25.41, I25.42, I25.5, I25.6, I25.700, I25.701, I25.708, I25.710, I25.711, I25.718, I25.719, I25.720, I25.721, I25.728, I25.729, I25.730, I25.731, I25.738, I25.739, I25.750, I25.751, I25.758, I25.759, I25.760, I25.761, I25.768, I25.769, I25.790, I25.791, I25.798, I25.799, I25.810, I25.811, I25.812, I25.82, I25.83, I25.84, I25.89, I25.9
Acute myocardial infarction	I21.01, I21.02, I21.09, I21.11, I21.19, I21.21, I21.29, I21.3, I21.4, I21.9, I21.A1, I21.A9, I22.0, I22.1, I22.2, I22.8, I22.9
Stroke*	G45.0, G45.1, G45.2, G45.3, G45.8, G45.9, G46.0, G46.1, G46.2, G46.3, G46.4, G46.5, G46.6, G46.7, G46.8, G97.31, G97.32, I60.00, I60.01, I60.02, I60.10, I60.11, I60.12, I60.2, I60.20, I60.21, I60.22, I60.30, I60.31, I60.32, I60.4, I60.50, I60.51, I60.52, I60.6, I60.7, I60.8, I60.9, I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9, I62.00, I62.01, I62.02, I62.9, I63.00, I63.011, I63.012, I63.013, I63.019, I63.02, I63.031, I63.032, I63.033, I63.039, I63.09, I63.10, I63.111, I63.112, I63.113, I63.119, I63.12, I63.131, I63.132, I63.133, I63.139, I63.19, I63.20, I63.211, I63.212, I63.213, I63.219, I63.22, I63.231, I63.232, I63.233, I63.239, I63.29, I63.30, I63.311, I63.312, I63.313, I63.319, I63.321, I63.322, I63.323, I63.329, I63.331, I63.332, I63.333, I63.339, I63.341, I63.342, I63.343, I63.349, I63.39, I63.40, I63.411, I63.412, I63.413, I63.419, I63.421, I63.422, I63.423, I63.429, I63.431, I63.432, I63.433, I63.439, I63.441, I63.442, I63.443, I63.449, I63.49, I63.50, I63.511, I63.512, I63.513, I63.519, I63.521, I63.522, I63.523, I63.529, I63.531, I63.532, I63.533, I63.539, I63.541, I63.542, I63.543, I63.549,

	I63.59, I63.6, I63.8, I63.81, I63.89, I63.9, I67.841, I67.848, I67.89, I97.810, I97.811, I97.820, I97.821
Alzheimer's Disease	G30.0, G30.1, G30.8, G30.9
Alzheimer's Disease and Related Disorders or Senile Dementia	F01.50, F01.51, F02.80, F02.81, F03.90, F03.91, F04, F05, F06.1, F06.8, G13.8, G30.0, G30.1, G30.8, G30.9, G31.01, G31.09, G31.1, G31.2, G94, R41.81, R54

* If any of the qualifying claims have any of the following codes in any DX position then Stroke diagnosis was excluded: S06.340A, S06.341A, S06.350A, S06.351A, S06.360A, S06.361A, S06.370A, S06.371A, S06.380A, S06.381A, S06.5X0A, S06.5X1A, S06.6X0A, S06.6X1A, S06.810A, S06.811A, S06.820A, S06.821A, S06.890A, S06.891A, S06.9X0A, S06.9X1A, S06.A0XA, S06.A1XA, S06.342A, S06.343A, S06.344A, S06.345A, S06.346A, S06.347A, S06.348A, S06.349A, S06.352A, S06.353A, S06.354A, S06.355A, S06.356A, S06.357A, S06.358A, S06.359A, S06.362A, S06.363A, S06.364A, S06.365A, S06.366A, S06.367A, S06.368A, S06.369A, S06.372A, S06.373A, S06.374A, S06.375A, S06.376A, S06.377A, S06.378A, S06.379A, S06.382A, S06.383A, S06.384A, S06.385A, S06.386A, S06.387A, S06.388A, S06.389A, S06.5X2A, S06.5X3A, S06.5X4A, S06.5X5A, S06.5X6A, S06.5X7A, S06.5X8A, S06.5X9A, S06.6X2A, S06.6X3A, S06.6X4A, S06.6X5A, S06.6X6A, S06.6X7A, S06.6X8A, S06.6X9A, S06.812A, S06.813A, S06.814A, S06.815A, S06.816A, S06.817A, S06.818A, S06.819A, S06.822A, S06.823A, S06.824A, S06.825A, S06.826A, S06.827A, S06.828A, S06.829A, S06.892A, S06.893A, S06.894A, S06.895A, S06.896A, S06.897A, S06.898A, S06.899A, S06.9X2A, S06.9X3A, S06.9X4A, S06.9X5A, S06.9X6A, S06.9X7A, S06.9X8A, S06.9X9A

Etable 2: Social Isolation Index change from baseline to second social isolation measurement stratified by isolation status

	Baseline Non-isolation	Baseline Isolation
Decreased isolation, mean (SD)	-1.00 (0)	-1.37 (0.63)
Stable, mean (SD)	0 (0)	0 (0)
Increased isolation, mean (SD)	1.30 (0.62)	1.41 (0.60)

Etable 3: Demographic and clinical characteristics of the HRS analysis cohort by social isolation group from baseline to second social isolation measure.

A) Demographic characteristics of the HRS analysis cohort with **baseline not isolated** and by social isolation group from baseline to second social isolation measure

	Decreased Isolation, No. (%)	Stable, No. (%)	Increased Isolation, No. (%)	P value^a
Patients, No.	1055	4553	3485	
Sex				<0.001
Male	513 (48.6)	1906 (41.9)	1374 (39.4)	
Female	542 (51.4)	2647 (58.1)	2111 (60.6)	
Cohort^b				<0.001
AHEAD	16 (1.5)	135 (3.0)	174 (5.0)	
CODA	81 (7.7)	404 (8.9)	452 (13.0)	
HRS	344 (32.6)	1566 (34.4)	1221 (35.0)	
WB	185 (17.5)	771 (16.9)	497 (14.3)	
BB	429 (40.7)	1677 (36.8)	1141 (32.7)	
Race and ethnicity^c				<0.001
Hispanic	93 (8.8)	365 (8.0)	345 (9.9)	
Non-Hispanic Black	121 (11.5)	598 (13.1)	535 (15.4)	
Non-Hispanic White	811 (76.9)	3482 (76.5)	2517 (72.2)	
Other	30 (2.8)	108 (2.4)	88 (2.5)	
Educational Level, y				<0.001
<12	122 (11.6)	640 (14.1)	650 (18.7)	
12	329 (31.2)	1496 (32.9)	1185 (34.0)	

>12	604 (57.3)	2417 (53.1)	1650 (47.3)	
Baseline characteristics				
Age, mean (SD), y	63.54 (8.67)	64.65 (9.09)	66.30 (9.77)	<0.001
Proxy vs Self	1043 (98.9)	4499 (98.8)	3446 (98.9)	0.96
Baseline Year				0.21
2006	449 (42.6)	1839 (40.4)	1447 (41.5)	
2008	337 (31.9)	1586 (34.8)	1225 (35.2)	
2010	138 (13.1)	561 (12.3)	383 (11.0)	
2012	107 (10.1)	466 (10.2)	336 (9.6)	
2014	24 (2.3)	101 (2.2)	94 (2.7)	
BMI, mean (SD)^d	28.36 (5.55)	28.54 (5.75)	28.57 (5.70)	0.56
Hypertension	484 (45.9)	2327 (51.1)	1892 (54.3)	<0.001
Diabetes	156 (14.8)	755 (16.6)	637 (18.3)	0.02
Lung Disease	52 (4.9)	257 (5.6)	254 (7.3)	0.002
Heart Disease	181 (17.2)	785 (17.2)	707 (20.3)	0.001
Stroke	54 (5.1)	210 (4.6)	195 (5.6)	0.14
Cancer	120 (11.4)	554 (12.2)	466 (13.4)	0.15
Psychiatric problems	103 (9.8)	498 (10.9)	462 (13.3)	0.13
Arthritis	499 (47.3)	2397 (52.6)	1964 (56.4)	0.001
Total Assets, quantile				<0.001
1st	129 (12.2)	543 (11.9)	533 (15.3)	
2nd	159 (15.1)	779 (17.1)	737 (21.1)	
3rd	260 (24.6)	1181 (25.9)	959 (27.5)	
4th	507 (48.1)	2050 (45.0)	1256 (36.0)	
CES-D score, mean (SD)	0.91 (1.51)	1.01 (1.60)	1.28 (1.84)	<0.001
Current Smoker	101 (9.6)	508 (11.2)	437 (12.5)	0.02
Married vs not married	100 (9.5)	735 (16.1)	820 (23.5)	<0.001

ADL score, mean (SD)^e	0.15 (0.58)	0.16 (0.59)	0.24 (0.77)	<0.001
Cognition, mean (SD)	16.61 (3.74)	16.32 (3.80)	15.58 (3.98)	<0.001
Incidence Disease from Baseline to Second Social Isolation Measure				
Hypertension	86 (8.2)	357 (7.8)	274 (7.9)	0.94
Diabetes	73 (6.9)	259 (5.7)	188 (5.4)	0.17
Lung Disease	23 (2.2)	111 (2.4)	104 (3.0)	0.20
Heart Disease	63 (6.0)	282 (6.2)	243 (7.0)	0.29
Stroke	25 (2.4)	102 (2.2)	137 (3.9)	<0.001
Cancer	40 (3.8)	183 (4.0)	151 (4.3)	0.67
Psychiatric Problem	25 (2.4)	128 (2.8)	133 (3.8)	0.01
Arthritis	85 (8.1)	332 (7.3)	277 (7.9)	0.47
Change from Baseline to Second Social Isolation Measure, mean (SD)				
CES-D score	-0.02 (1.37)	0.02 (1.40)	0.09 (1.57)	0.03
ADL score^e	0.01 (0.55)	0.04 (0.57)	0.10 (0.72)	<0.001
Cognition	-0.36 (2.98)	-0.37 (2.91)	-0.54 (3.07)	0.03
Follow up years for each outcome, median (range)				
Mortality	8 (0.5-10)	8 (0.1-10)	8 (0.3-10)	
Disability	8 (0-10)	8 (0-10)	8 (0-10)	
Dementia	7 (0.1-7)	7 (0-7)	7 (0-7)	
CVD	7 (0.1-7)	7 (0-7)	7 (0-7)	
Stroke	7 (0.1-7)	7 (0.1-7)	7 (0.1-7)	

B) Demographic characteristics of the HRS analysis cohort with baseline isolated and by social isolation group from baseline to second social isolation measure

	Decreased Isolation, No. (%)	Stable, No. (%)	Increased Isolation, No. (%)	P value ^a
Patients, No.	2067	1796	693	
Sex				<0.001
Male	919 (44.5)	631 (35.1)	295 (42.6)	
Female	1148 (55.5)	1165 (64.9)	398 (57.4)	
Cohort^b				<0.001
AHEAD	82 (4.0)	101 (5.6)	67 (9.7)	
CODA	183 (8.9)	193 (10.7)	101 (14.6)	
HRS	679 (32.8)	612 (34.1)	215 (31.0)	
WB	289 (14.0)	236 (13.1)	81 (11.7)	
BB	834 (40.3)	654 (36.4)	229 (33.0)	
Race and ethnicity^c				0.07
Hispanic	256 (12.4)	194 (10.8)	79 (11.4)	
Non-Hispanic Black	405 (19.6)	305 (17.0)	110 (15.9)	
Non-Hispanic White	1342 (64.9)	1245 (69.3)	486 (70.1)	
Other	64 (3.1)	52 (2.9)	18 (2.6)	
Educational level				0.003
<12	477 (23.1)	452 (25.2)	203 (29.3)	
12	697 (33.7)	635 (35.4)	238 (34.3)	
>12	893 (43.2)	709 (39.5)	252 (36.4)	
Baseline characteristics				
Age, mean (SD)	64.80 (9.53)	65.85 (9.84)	67.88 (10.80)	<0.001
Proxy vs self	2043 (98.8)	1767 (98.4)	683 (98.6)	0.48

Baseline Year				0.27
2006	787 (38.1)	659 (36.7)	260 (37.5)	
2008	695 (33.6)	673 (37.5)	264 (38.1)	
2010	294 (14.2)	235 (13.1)	87 (12.6)	
2012	234 (11.3)	189 (10.5)	67 (9.7)	
2014	57 (2.8)	40 (2.2)	15 (2.2)	
BMI, mean (SD)^d	29.00 (6.08)	28.99 (6.63)	28.43 (6.51)	0.10
Hypertension	1139 (55.1)	1018 (56.7)	398 (57.4)	0.46
Diabetes	431 (20.9)	365 (20.3)	148 (21.4)	0.83
Lung disease	188 (9.1)	181 (10.1)	71 (10.2)	0.50
Heart disease	394 (19.1)	370 (20.6)	167 (24.1)	0.02
Stroke	132 (6.4)	129 (7.2)	67 (9.7)	0.02
Cancer	258 (12.5)	205 (11.4)	77 (11.1)	0.48
Psychiatric problems	363 (17.6)	327 (18.2)	148 (21.4)	0.08
Arthritis	1110 (53.7)	1056 (58.8)	385 (55.6)	0.006
Total assets, quantile				0.001
1st	584 (28.3)	549 (30.6)	242 (34.9)	
2nd	478 (23.1)	456 (25.4)	173 (25.0)	
3rd	473 (22.9)	396 (22.0)	142 (20.5)	
4th	532 (25.7)	395 (22.0)	136 (19.6)	
CES-D score, mean (SD)	1.71 (2.16)	1.85 (2.25)	2.18 (2.35)	<0.001
Current Smoker	336 (16.3)	343 (19.1)	145 (20.9)	0.008
Married vs not married	949 (45.9)	1182 (65.8)	449 (64.8)	<0.001
ADL score, mean (SD)^e	0.34 (0.94)	0.39 (1.00)	0.51 (1.13)	<0.001
Cognition, mean (SD)	15.08 (4.17)	15.27 (4.09)	14.14 (4.41)	<0.001
Incidence Disease from Baseline to Second Social Isolation Measure				
Hypertension	177 (8.6)	149 (8.3)	65 (9.4)	0.69
Diabetes	104 (5.0)	104 (5.8)	34 (4.9)	0.50

Lung disease	70 (3.4)	88 (4.9)	34 (4.9)	0.04
Heart disease	128 (6.2)	127 (7.1)	50 (7.2)	0.46
Stroke	61 (3.0)	51 (2.8)	30 (4.3)	0.13
Cancer	90 (4.4)	67 (3.7)	28 (4.0)	0.62
Psychiatric problem	67 (3.2)	59 (3.3)	45 (6.5)	<0.001
Arthritis	163 (7.9)	139 (7.7)	57 (8.2)	0.92
Change from Baseline to Second Social Isolation Measure, mean (SD)				
CESD score	-0.13 (1.74)	-0.10 (1.68)	-0.06 (1.97)	0.60
ADL score^e	0.07 (0.78)	0.10 (0.83)	0.26 (1.05)	<0.001
Cognition	-0.47 (3.14)	-0.58 (3.06)	-0.79 (3.21)	0.06
Follow up years for each outcome, median (range)				
Mortality	8 (0.5-10)	8 (0.4-10)	8 (0.3-10)	
Disability	8 (0-10)	8 (0-10)	8 (0-10)	
Dementia	7 (0-7)	7 (0.2-7)	7 (0-7)	
CVD	7 (0-7)	7 (0-7)	7 (0.1-7)	
Stroke	7 (0-7)	7 (0.1-7)	7 (0-7)	

a. P-values are from the two-sample t-test or Wilcoxon rank sum test for comparing continuous covariates and the chi-square test for comparing categorical covariates; p value <0.05 was considered as significant and marked in red color.

b. Other race includes American Indian, Alaskan Native, Asian, Native Hawaiian, and Pacific Islander, other race or unknown.

c. HRS included six birth cohorts: the Study of Assets and Health Dynamics Among the Oldest Old (AHEAD) cohort, born prior to 1924; the Children of the Depression (CODA) cohort, born 1924 to 1930; the original HRS cohort, born 1931 to 1941; the War Baby (WB) cohort, born 1942 to 1947; the Baby Boomer (BB) cohort, born 1948 to 1959.

d. BMI: body mass index

e. ADL: activities of daily living

f. Model-adjusted 27-point cognition score

Etable 4: The hazard ratios of full covariates on distal outcomes stratified by the social isolation status

A) The hazard ratios of full covariates on mortality stratified by the social isolation status

	Baseline Non-isolation		Baseline Isolation	
	aHR (95% CI)	P value	aHR (95% CI)	P value
Baseline isolation (ref: baseline non-isolation)	0.98 (0.84, 1.14)	0.75	1.03 (0.88, 1.19)	0.75
Increased isolation (ref: stable)	1.10 (1.01, 1.21)	0.04	1.29 (1.09, 1.51)	0.002
Decreased isolation (ref: stable)	0.73 (0.61, 0.87)	<0.001	0.98 (0.86, 1.12)	0.78
Sex = female (ref: male)	0.75 (0.70, 0.82)	<0.001	0.75 (0.70, 0.82)	<0.001
Cohort = CODA (ref: AHEAD)	1.14 (0.98, 1.34)	0.09	1.14 (0.98, 1.34)	0.09
Cohort = HRS (ref: AHEAD)	1.33 (1.06, 1.67)	0.01	1.33 (1.06, 1.67)	0.01
Cohort = WB (ref: AHEAD)	1.56 (1.12, 2.19)	0.01	1.56 (1.12, 2.19)	0.009
Cohort = BB (ref: AHEAD)	2.16 (1.43, 3.27)	<0.001	2.16 (1.43, 3.27)	<0.001
Race and ethnicity = Non-Hispanic Black (ref: Hispanic)	1.33 (1.10, 1.60)	0.004	1.33 (1.10, 1.60)	0.004
Race and ethnicity = Non-Hispanic White (ref: Hispanic)	1.64 (1.39, 1.94)	<0.001	1.64 (1.39, 1.94)	<0.001
Race and ethnicity = Other (ref: Hispanic)	1.14 (0.79, 1.63)	0.48	1.14 (0.79, 1.63)	0.48
Educational level = 12 (ref: < 12)	0.99 (0.90, 1.10)	0.89	0.99 (0.90, 1.10)	0.89
Educational level > 12 (ref: < 12)	1.00 (0.89, 1.11)	0.93	1.00 (0.89, 1.11)	0.93
Age at baseline	1.12 (1.11, 1.13)	<0.001	1.12 (1.11, 1.13)	<0.001
BMI at baseline	1.00 (1.00, 1.01)	0.35	1.00 (1.00, 1.011)	0.35
Hypertension at baseline	1.15 (1.06, 1.25)	0.001	1.15 (1.06, 1.25)	0.001
Diabetes at baseline	1.34 (1.22, 1.46)	<0.001	1.34 (1.22, 1.46)	<0.001
Lung disease at baseline	1.63 (1.44, 1.85)	<0.001	1.63 (1.44, 1.85)	<0.001
Heart disease at baseline	1.42 (1.30, 1.54)	<0.001	1.42 (1.30, 1.54)	<0.001
Stroke at baseline	1.34 (1.18, 1.53)	<0.001	1.34 (1.18, 1.53)	<0.001
Cancer at baseline	1.48 (1.35, 1.62)	<0.001	1.48 (1.35, 1.62)	<0.001
Psychiatric problems at baseline	0.96 (0.85, 1.09)	0.57	0.96 (0.85, 1.09)	0.57
Arthritis at baseline	0.97 (0.90, 1.06)	0.53	0.97 (0.90, 1.06)	0.53
CES-D score at baseline	1.06 (1.03, 1.08)	<0.001	1.06 (1.03, 1.08)	<0.001
Smoker at baseline	1.91 (1.71, 2.14)	<0.001	1.91 (1.71, 2.14)	<0.001
Married vs not married at baseline =not married (ref: married)	0.98 (0.89, 1.08)	0.66	0.98 (0.89, 1.08)	0.66
ADL at baseline	1.03 (0.98, 1.09)	0.22	1.03 (0.98, 1.09)	0.22
Total assets at baseline = 2 nd quantile (ref: 1 st quantile)	1.00 (0.89, 1.13)	0.97	1.00 (0.89, 1.13)	0.97

Total assets at baseline = 3 rd quantile (ref: 1 st quantile)	0.84 (0.74, 0.95)	0.006	0.84 (0.74, 0.95)	0.006
Total assets at baseline = 4 th quantile (ref: 1 st quantile)	0.80 (0.71, 0.91)	0.001	0.80 (0.71, 0.91)	0.001
Cognition at baseline	0.96 (0.95, 0.97)	<0.001	0.96 (0.95, 0.97)	<0.001
Social isolation at baseline	1.07 (0.99, 1.14)	0.08	1.07 (0.99, 1.14)	0.08
Incident hypertension from baseline to second social isolation measure	1.02 (0.88, 1.17)	0.82	1.02 (0.88, 1.17)	0.82
Incident diabetes from baseline to second social isolation measure	1.04 (0.88, 1.22)	0.64	1.04 (0.88, 1.22)	0.64
Incident lung disease from baseline to second social isolation measure	1.93 (1.66, 2.26)	<0.001	1.93 (1.66, 2.26)	<0.001
Incident heart disease from baseline to second social isolation measure	1.37 (1.20, 1.56)	<0.001	1.37 (1.20, 1.56)	<0.001
Incident stroke from baseline to second social isolation measure	1.53 (1.29, 1.81)	<0.001	1.53 (1.29, 1.81)	<0.001
Incident cancer from baseline to second social isolation measure	1.78 (1.50, 2.10)	<0.001	1.78 (1.50, 2.10)	<0.001
Incident psychiatric problems from baseline to second social isolation measure	1.06 (0.87, 1.29)	0.56	1.06 (0.87, 1.29)	0.56
Incident arthritis from baseline to second social isolation measure	0.94 (0.80, 1.09)	0.40	0.94 (0.80, 1.09)	0.40
CES-D score change from baseline to second social isolation measure	1.07 (1.04, 1.10)	<0.001	1.07 (1.04, 1.10)	<0.001
Baseline isolation: increased isolation	1.16 (0.97, 1.40)	0.11	0.86 (0.71, 1.03)	0.11
Baseline isolation: decreased isolation	1.35 (1.08, 1.67)	0.008	0.74 (0.60, 0.93)	0.008

B) The hazard ratios of full covariates on disability stratified by the social isolation status

	Baseline Non-isolation		Baseline Isolation	
	aHR (95% CI)	P value	aHR (95% CI)	P value
Baseline isolation (ref: baseline non-isolation)	1.02 (0.85, 1.23)	0.83	0.98 (0.81, 1.18)	0.83
Increased isolation (ref: stable)	1.15 (1.03, 1.28)	0.01	1.35 (1.09, 1.68)	0.006
Decreased isolation (ref: stable)	1.04 (0.88, 1.25)	0.63	1.05 (0.88, 1.24)	0.59
Sex=female (ref: male)	1.00 (0.91, 1.10)	0.94	1.00 (0.91, 1.10)	0.94
Cohort = CODA (ref: AHEAD)	0.92 (0.73, 1.16)	0.48	0.92 (0.73, 1.16)	0.48
Cohort = HRS (ref: AHEAD)	0.83 (0.62, 1.11)	0.21	0.83 (0.62, 1.11)	0.21
Cohort = WB (ref: AHEAD)	0.73 (0.49, 1.08)	0.12	0.73 (0.49, 1.08)	0.12
Cohort = BB (ref: AHEAD)	0.77 (0.48, 1.23)	0.27	0.77 (0.48, 1.23)	0.27
Race and ethnicity = Non-Hispanic Black (ref: Hispanic)	0.84 (0.70, 1.02)	0.08	0.84 (0.70, 1.02)	0.08
Race and ethnicity = Non-Hispanic White (ref: Hispanic)	0.84 (0.71, 0.99)	0.04	0.84 (0.71, 0.99)	0.04
Race and ethnicity = Other (ref: Hispanic)	0.78 (0.56, 1.10)	0.15	0.78 (0.56, 1.10)	0.15
Educational level = 12 (ref: < 12)	0.97 (0.85, 1.10)	0.64	0.97 (0.85, 1.10)	0.64
Educational level > 12 (ref: < 12)	1.02 (0.89, 1.16)	0.79	1.02 (0.89, 1.16)	0.79
Age at baseline	1.05 (1.03, 1.06)	<0.001	1.05 (1.03, 1.06)	<0.001
BMI at baseline	1.04 (1.03, 1.05)	<0.001	1.04 (1.03, 1.05)	<0.001
Hypertension at baseline	0.97 (0.88, 1.07)	0.59	0.97 (0.88, 1.07)	0.59
Diabetes at baseline	1.20 (1.07, 1.34)	0.002	1.20 (1.07, 1.34)	0.002
Lung disease at baseline	1.20 (1.01, 1.42)	0.04	1.20 (1.01, 1.42)	0.04
Heart disease at baseline	1.12 (1.00, 1.26)	0.04	1.12 (1.00, 1.26)	0.04
Stroke at baseline	1.16 (0.95, 1.42)	0.15	1.16 (0.95, 1.42)	0.15
Cancer at baseline	1.09 (0.97, 1.24)	0.16	1.09 (0.97, 1.4)	0.16
Psychiatric problems at baseline	1.09 (0.94, 1.26)	0.27	1.09 (0.94, 1.26)	0.27
Arthritis at baseline	1.57 (1.42, 1.73)	<0.001	1.57 (1.42, 1.73)	<0.001
CES-D score at baseline	1.23 (1.19, 1.27)	<0.001	1.23 (1.19, 1.27)	<0.001
Smoker at baseline	1.36 (1.19, 1.55)	<0.001	1.36 (1.19, 1.55)	<0.001
Married vs not married at baseline = not married (ref: married)	0.98 (0.88, 1.10)	0.74	0.98 (0.88, 1.10)	0.74
Total assets at baseline = 2 nd quantile (ref: 1 st quantile)	0.92 (0.80, 1.06)	0.26	0.92 (0.80, 1.06)	0.26
Total assets at baseline = 3 rd quantile (ref: 1 st quantile)	0.72 (0.62, 0.83)	<0.001	0.72 (0.62, 0.83)	<0.001
Total assets at baseline = 4 th quantile (ref: 1 st quantile)	0.72 (0.61, 0.83)	<0.001	0.72 (0.61, 0.83)	<0.001
Cognition at baseline	0.98 (0.97, 1.00)	0.01	0.98 (0.97, 1.00)	0.01

Social isolation at baseline	1.03 (0.94, 1.12)	0.53	1.03 (0.94, 1.12)	0.53
Incident hypertension from baseline to second social isolation measure	1.14 (0.98, 1.34)	0.10	1.14 (0.98, 1.34)	0.10
Incident diabetes from baseline to second social isolation measure	0.96 (0.78, 1.17)	0.67	0.96 (0.78, 1.17)	0.67
Incident lung disease from baseline to second social isolation measure	1.28 (1.01, 1.63)	0.05	1.28 (1.01, 1.63)	0.05
Incident heart disease from baseline to second social isolation measure	1.17 (0.99, 1.38)	0.07	1.17 (0.99, 1.38)	0.07
Incident stroke from baseline to second social isolation measure	1.45 (1.14, 1.83)	0.002	1.45 (1.14, 1.83)	0.002
Incident cancer from baseline to second social isolation measure	1.07 (0.86, 1.33)	0.52	1.07 (0.86, 1.33)	0.52
Incident psychiatric problems from baseline to second social isolation measure	1.32 (1.03, 1.68)	0.03	1.32 (1.03, 1.68)	0.03
Incident arthritis from baseline to second social isolation measure	1.70 (1.46, 1.99)	<0.001	1.70 (1.46, 1.99)	<0.001
CES-D score change from baseline to second social isolation measure	1.20 (1.16, 1.24)	<0.001	1.20 (1.16, 1.24)	<0.001
Baseline isolation: increased isolation	1.18 (0.924, 1.50)	0.19	0.85 (0.67, 1.08)	0.19
Baseline isolation: decreased isolation	1.00 (0.789, 1.28)	0.98	0.997 (0.78, 1.27)	0.98

C) The hazard ratios of full covariates on dementia stratified by the social isolation status

	Baseline Non-isolation		Baseline Isolation	
	aHR (95% CI)	P value	aHR (95% CI)	P value
Baseline isolation (ref: baseline non-isolation)	0.85 (0.63, 1.14)	0.28	1.18 (0.87, 1.59)	0.28
Increased isolation (ref: stable)	1.29 (1.08, 1.54)	0.004	1.40 (1.02, 1.93)	0.04
Decreased isolation (ref: stable)	1.27 (0.94, 1.71)	0.12	1.27 (0.96, 1.68)	0.09
Sex = female (ref: male)	1.27 (1.09, 1.48)	0.002	1.27 (1.09, 1.48)	0.002
Cohort = CODA (ref: AHEAD)	1.14 (0.86, 1.50)	0.37	1.14 (0.86, 1.50)	0.37
Cohort = HRS (ref: AHEAD)	1.08 (0.71, 1.64)	0.71	1.08 (0.71, 1.64)	0.71
Cohort = WB (ref: AHEAD)	0.47 (0.25, 0.88)	0.02	0.47 (0.25, 0.88)	0.02
Cohort = BB (ref: AHEAD)	0.55 (0.26, 1.16)	0.12	0.55 (0.26, 1.16)	0.12
Race and ethnicity = Non-Hispanic Black (ref: Hispanic)	1.73 (1.21, 2.47)	0.003	1.73 (1.21, 2.47)	0.003
Race and ethnicity = Non-Hispanic White (ref: Hispanic)	1.66 (1.20, 2.31)	0.002	1.66 (1.20, 2.31)	0.002
Race and ethnicity = Other (ref: Hispanic)	1.42 (0.76, 2.63)	0.27	1.42 (0.76, 2.63)	0.27
Educational level = 12 (ref: < 12)	1.20 (0.99, 1.46)	0.06	1.20 (0.99, 1.46)	0.06
Educational level > 12 (ref: < 12)	1.30 (1.05, 1.60)	0.02	1.30 (1.05, 1.60)	0.02
Age at baseline	1.07 (1.05, 1.10)	<0.001	1.07 (1.05, 1.10)	<0.001
BMI at baseline	0.98 (0.96, 0.99)	0.001	0.98 (0.96, 0.99)	0.001
Hypertension at baseline	1.01 (0.86, 1.18)	0.91	1.01 (0.86, 1.18)	0.91
Diabetes at baseline	1.34 (1.13, 1.59)	0.001	1.34 (1.13, 1.59)	0.001
Lung disease at baseline	0.88 (0.70, 1.12)	0.31	0.88 (0.70, 1.12)	0.31
Heart disease at baseline	1.00 (0.84, 1.17)	0.95	1.00 (0.84, 1.17)	0.95
Stroke at baseline	1.46 (1.16, 1.83)	0.001	1.46 (1.16, 1.83)	0.001
Cancer at baseline	0.90 (0.75, 1.08)	0.25	0.90 (0.75, 1.08)	0.25
Psychiatric problems at baseline	1.48 (1.20, 1.83)	<0.001	1.48 (1.20, 1.83)	<0.001
Arthritis at baseline	1.02 (0.87, 1.21)	0.78	1.02 (0.87, 1.21)	0.78
CES-D score at baseline	1.10 (1.05, 1.15)	<0.001	1.10 (1.05, 1.15)	<0.001
Smoker at baseline	1.36 (1.08, 1.71)	0.009	1.36 (1.08, 1.71)	0.009
Married vs not married at baseline = not married (ref: married)	0.84 (0.70, 1.00)	0.05	0.84 (0.70, 1.00)	0.05
ADL at baseline	1.09 (1.00, 1.18)	0.04	1.09 (1.00, 1.18)	0.04
Total assets at baseline = 2 nd quantile (ref: 1 st quantile)	1.05 (0.83, 1.34)	0.67	1.05 (0.83, 1.34)	0.67
Total assets at baseline = 3 rd Quantile (ref: 1 st quantile)	0.93 (0.73, 1.18)	0.54	0.93 (0.73, 1.18)	0.54
Total assets at baseline = 4 th Quantile (ref: 1 st quantile)	0.89 (0.69, 1.15)	0.39	0.89 (0.69, 1.15)	0.39

Cognition at baseline	0.92 (0.90, 0.94)	<0.001	0.92 (0.90, 0.94)	<0.001
Social isolation at baseline	1.02 (0.88, 1.17)	0.80	1.02 (0.88, 1.17)	0.80
Incident hypertension from baseline to second social isolation measure	1.04 (0.79, 1.37)	0.78	1.04 (0.79, 1.37)	0.78
Incident diabetes from baseline to second social isolation measure	1.11 (0.81, 1.52)	0.50	1.11 (0.81, 1.52)	0.50
Incident lung disease from baseline to second social isolation measure	0.59 (0.37, 0.92)	0.02	0.59 (0.37, 0.92)	0.02
Incident heart disease from baseline to second social isolation measure	1.08 (0.85, 1.38)	0.51	1.08 (0.85, 1.38)	0.51
Incident stroke from baseline to second social isolation measure	1.49 (1.09, 2.02)	0.01	1.49 (1.09, 2.02)	0.01
Incident cancer from baseline to second social isolation measure	1.08 (0.78, 1.49)	0.64	1.08 (0.78, 1.49)	0.64
Incident psychiatric problems from baseline to second social isolation measure	1.61 (1.12, 2.32)	0.01	1.61 (1.12, 2.32)	0.01
Incident arthritis from baseline to second social isolation measure	1.08 (0.80, 1.46)	0.61	1.08 (0.80, 1.46)	0.61
CES-D score change from baseline to second social isolation measure	1.084 (1.026, 1.144)	0.004	1.08 (1.03, 1.14)	0.004
Baseline isolation: increased isolation	1.084 (0.751, 1.567)	0.67	0.92 (0.64, 1.33)	0.67
Baseline isolation: decreased isolation	1.001 (0.672, 1.491)	1.00	1.00 (0.67, 1.49)	1.00