

Supplementary Materials

Supplementary Figure 1. Interpersonal Support Evaluation List Short Form (ISEL-SF)

No.	Questions	Responses			
		Definitely	Probably	Probably	Definitely
		true	true	false	false
Appraisal support		Scores			
1.	There really is no one who can give me an objective view of how I'm handling my problems.	0	1	2	3
2.	When I need suggestions on how to deal with a personal problem, I know someone I can turn to.	3	2	1	0
3.	There is really no one I can trust to give me good financial advice.	0	1	2	3
4.	There is at least one person I know whose advice I really trust.	3	2	1	0
Self-esteem					
5.	Most of my friends are more interesting than I am.	0	1	2	3
6.	Most of my friends are more successful at making changes in their lives than I am.	0	1	2	3
7.	I am more satisfied with my life than most people are with theirs.	3	2	1	0
8.	I have a hard time keeping pace with my friends.	0	1	2	3
Belonging support					
9.	When I feel lonely, there are several people I can talk to.	3	2	1	0
10.	I often meet or talk with family or friends.	3	2	1	0
11.	I feel like I am not always included by my circle of friends.	0	1	2	3
12.	I don't often get invited to do things with others.	0	1	2	3
Tangible support					

13.	If I were sick and needed someone (friend, family member, or acquaintance) to take me to the doctor, I would have trouble finding someone.	0	1	2	3
14.	If I were sick, I could easily find someone to help me with my daily chores.	3	2	1	0
15.	If I had to go out of town for a few weeks, it would be difficult to find someone who would look after my house or apartment (the plants, pets, garden, etc.).	0	1	2	3
16.	It would be difficult to find someone who would lend me their car for a few hours.	0	1	2	3

NOTE: Form filled out by participant during ARIC Visit 2 with pen and paper. Order shown above lists statement by each subscale and is not reflective of the order of the questionnaire given at Visit 2. Participants instructed not to leave any questions blank unless instructed to skip to another question.

Supplementary Figure 2. The Lubben Social Network Scale (LSNS)

No.	Questions	Scores					
		0	1	2	3	4	5
		Responses					
1.	How many relatives do you see or hear from at least once a month?	0	1	2	3-4	5-8	≥9
2.	How many relatives do you feel close to? That is, how many of them do you feel at ease with, can talk to about private matters, or can call on for help?						
3.	Do you have any close friends? That is, do you have any friends with whom you feel at ease with, can talk to about private matters, or can call on for help? If so, how many?						
4.	How many of these friends do you see or hear from at least once a month?						
5.	Tell me about the relative with whom you have the most contact: How often do you see or hear from that person?	Less than monthly	Monthly	A few times a month	Weekly	A few times a week	Daily
6.	Tell me about the friend with whom you have the most contact. How often do you see or hear from that person?						
7.	When you have an important decision to make, how frequently do you have someone you can talk to about it?	Never	Seldom	Some-times	Often	Very often	Always
8.	When other people you know have an important decision to make, how frequently do they talk to you about it?						
9a.	Does anybody rely on you to something for them each day?	-	-	-	-	-	Yes

	E.g.: shopping, making dinner, doing repairs, cleaning house providing childcare, etc.?						
9b.	How frequently do you help anybody with things like shopping, filling out forms, doing repairs, providing childcare, etc.?	Never	Seldom	Some-times	Often	Very often	-
10.	Do you live alone or with other people?	Live alone	Live with other unrelated individuals (one point)		Live with other relative or friends (four points)		Live with spouse

NOTE: Form filled out by participant during ARIC Visit 2 with pen and paper. Order shown above is grouped by scoring and not reflective of the order of the questionnaire given at Visit 2. Participants instructed not to leave any questions blank unless instructed to skip to another question.

Supplementary Table 1. Characteristics of Participants in the Total ARIC Sample at Visit 2 and Present Study ARIC-PET Sample

Characteristics	Total ARIC Sample at Visit 2	Analytic ARIC-PET Sample at Visit 2
N	14,348	310
Age, y, mean (SD)	57.0 (5.7)	55.1 (5.1)
Race, N (%)		
Black	3,361 (24.5)	125 (40.3)
White	10,382 (75.5)	185 (59.7)
Sex, N (%)		
Female	7,579 (55.2)	175 (56.5)
Male	6,164 (44.9)	135 (43.6)
Field Center, N (%)		
Forsyth	3,625 (26.4)	69 (22.3)
Jackson	2,945 (21.4)	119 (38.4)
Minneapolis	3,712 (27.0)	---
Washington	3,461 (25.2)	122 (39.4)
APOE ε4 Status, N (%)		
Non-Carrier	9,114 (69.1)	212 (69.5)
Carrier	4,080 (30.9)	93 (30.5)
Education Level, N (%)		
Less than high school	2,910 (21.2)	46 (14.8)
High school or equivalent	5,714 (41.6)	135 (43.6)
More than high school	5,099 (37.2)	129 (41.6)
Psychosocial Health		
High	7,798 (56.7)	188 (60.7)
Intermediate	3,881 (28.2)	86 (27.7)
Low	2,064 (15.0)	36 (11.6)
Not Married, N (%)	2,857 (20.8)	56 (18.1)
Physically Inactive (0 min/wk), N (%)	4,897 (35.7)	120 (38.7)
Depressive/Fatigue Symptoms, N (%)	4,770 (35.2)	91 (29.4)
Hypertension, N (%)	4,903 (35.8)	91 (29.4)
Diabetes, N (%)	2,036 (14.9)	32 (10.3)
Body Mass Index (≥ 30 kg/m²), N (%)	3,979 (29.0)	89 (28.7)
Total Cholesterol (≥200 mg/dl), N (%)	7,838 (57.0)	146 (47.1)
Current smoker, N (%)	3,071 (22.4)	49 (15.8)
Current drinker, N (%)	7,807 (56.8)	164 (52.9)
Developed dementia by visit 7, N (%)	2,667 (19.4)	48 (15.5)
Died prior to visit 7, N (%)	6,552 (47.7)	23 (7.4)

NOTE: 32 Asian participants and 10 Indian participants that were part of ARIC at visit 2 were not included in ARIC-PET per exclusion criteria. No PET scans conducted at Minneapolis ARIC Field Center. Missing data at visit 2 for the total sample included *APOE* ε4 genotype (n = 549), education level (n = 20), marital status (n = 13), physical activity (n = 14), depressive/fatigue symptoms (n = 203), hypertension (n = 44), diabetes (n = 58), smoking status (n = 7), and drinking status (n = 5)
Abbreviations: *APOE* = apolipoprotein E

Supplementary Table 2. Adjusted Hazard Ratios for Association of Mid-Life Social Relationships and Elevated Florbetapir Global SUVR with Dementia Risk, Stratified by Sex (n = 305)

Variable	Female (n = 173)			Male (n = 132)		
	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Strong Social Relationships	0.39 (0.07 – 2.21)	0.56 (0.09 – 3.33)	0.55 (0.09 - 3.40)	0.34 (0.10 – 1.14)	0.42 (0.11 - 1.53)	0.66 (0.34 – 2.91)
Average Social Relationships	0.23 (0.03 – 1.50)	0.14 (0.02 - 1.05)	0.15 (0.02 - 1.15)	0.43 (0.12 - 1.48)	0.59 (0.16 - 2.18)	0.67 (0.17 – 2.58)
Poor Social Relationships	Reference	Reference	Reference	Reference	Reference	Reference
Elevated Florbetapir Global SUVR > 1.2	3.32 (1.00 –11.00)*	4.05 (1.14 –14.43)*	3.37 (0.91 – 12.40)	4.50 (1.77-11.48)**	5.57 (1.91-16.22)**	4.46 (1.49 –13.36)**
Age (per 1 year)	1.13 (1.03-1.25)*	1.14 (1.02 – 1.27)*	1.14 (1.02-1.28)*	1.17 (1.06 -1.30)**	1.21 (1.07 – 1.37)**	1.21 (1.07 – 1.37)**
Race (Black)	2.79 (1.05 - 7.36)*	4.05 (1.21– 13.53)*	3.90 (1.13 -13.41)*	1.35 (0.55 –3.30)	1.06 (0.39 – 2.90)	0.99 (0.34 -2.91)
APOE ε4 Carrier	2.90 (1.13-7.48)*	2.76 (0.90 – 8.48)	2.77 (0.94-8.19)	1.92 (0.85 –4.35)	2.45 (0.94 – 6.37)	2.11 (0.75 – 5.94)
Education						
Less than high school	3.57 (1.19-10.73)*	4.48 (1.24 -16.11)*	4.49 (1.24-16.27)*	1.64 (0.52 –5.13)	0.89 (0.22 – 3.53)	1.35 (0.31 – 5.80)
High school or equivalent	0.60 (0.19 – 1.90)	0.74 (0.20 – 2.70)	0.71 (0.20 - 2.56)	0.83 (0.31 – 2.20)	0.99 (0.29 – 3.46)	1.45 (0.40 – 5.32)
More than high school	Reference	Reference	Reference	Reference	Reference	Reference
Not Married	0.67 (0.13 –3.34)	1.04 (0.31-3.55)	1.27 (0.35-4.64)	0.67 (0.13-3.34)	0.98 (0.16 – 5.89)	1.21 (0.19 – 7.52)
Depressive/Fatigue Symptoms	-----	1.29 (0.41-4.11)	1.31 (0.40-4.34)	-----	1.64 (0.43 – 6.29)	1.78 (0.47 – 6.72)
Hypertension	-----	0.80 (0.24-2.75)	0.86 (0.25-2.91)	-----	1.88 (0.68 – 5.20)	2.17 (0.75 – 6.27)
Diabetes	-----	6.00 (1.39-25.88)*	4.55 (1.00- 20.70)*	-----	1.45 (0.43 – 4.85)	0.84 (0.21 – 3.34)
Body Mass Index (≥ 30 kg/m2)	-----	1.65 (0.58-4.71)	1.90 (0.63-5.69)	-----	2.17 (0.72 – 6.55)	2.48 (0.81 – 7.61)
Total Cholesterol (≥ 200 mg/dl)	-----	0.51 (0.16 – 1.66)	0.56 (0.17-1.86)	-----	0.45 (0.17 – 1.18)	0.47 (0.19 – 1.20)
Current smoker	-----	1.21 (0.30 – 4.87)	1.42 (0.14-2.00)	-----	1.17 (0.24 – 5.74)	1.21 (0.25 – 5.89)
Current drinker	-----	0.40 (0.11-1.43)	0.53 (0.14-5.69)	-----	0.67 (0.24 – 6.55)	0.87 (0.29 – 2.59)
Physical Inactivity	-----	0.88 (0.58 – 4.71)	0.86 (0.28-2.62)	-----	0.74 (0.25 - 2.22)	0.81 (0.27 – 2.42)
Having MCI at Visit 5	-----	-----	2.02 (0.65-6.24)	-----	-----	3.14 (1.12 –8.82)*

NOTE: Model 1 adjusted for age, race, *APOE* ϵ 4, education, and marital status. Model 2 adjusted for model 1 covariates in addition to depressive/fatigue symptoms, vascular risk factors, and physical inactivity. Model 3 adjusted for model 2 covariates in addition to having MCI at visit 5.
* $P \leq .05$; ** $P \leq .01$. Abbreviations: *APOE* = apolipoprotein E; CI= confidence interval; HR = hazard ratio; MCI = mild cognitive impairment; SUVR = standardized uptake value ratio

Supplementary Table 3. Adjusted Hazard Ratios for Association of Mid-Life Social Relationships and Elevated Florbetapir Global SUVR with Dementia Risk, Stratified by Cognitive Status at Visit 5 (n = 305)

Variable	Normal Cognition (n = 224)		MCI (n = 81)	
	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Strong Social Relationships	0.35 (0.06 – 1.93)	0.32 (0.05 – 2.10)	0.51 (0.15 – 1.74)	0.34 (0.07 – 1.52)
Average Social Relationships	0.31 (0.05 – 1.97)	0.29 (0.04 – 2.00)	0.27 (0.08 – 0.95)*	0.15 (0.04 – 0.66)*
Poor Social Relationships	Reference	Reference	Reference	Reference
Elevated Florbetapir Global SUVR > 1.2	3.10 (1.09 – 8.78)*	3.21 (1.01– 10.15)*	3.20 (1.01 – 10.12)*	6.92 (1.45 – 33.09)*
Age (per 1 year)	1.15 (1.05 – 1.27)**	1.16 (1.04– 1.29)**	1.14 (1.03 - 1.26)**	1.29 (1.11 – 1.51)**
Race (Black)	2.13 (0.79 – 5.76)	2.15 (0.77 – 5.99)	1.42 (0.59 – 3.44)	1.11 (0.32 – 3.80)
Sex (Female)	0.65 (0.26 – 1.62)	0.69 (0.25 – 1.90)	0.29 (0.09 – 0.90)*	0.28 (0.08 – 0.98)*
<i>APOE</i> ε4 Carrier	3.36 (1.35 – 8.39)**	3.40 (1.15 – 10.03)*	1.36 (0.59 – 3.18)	2.59 (0.78 – 8.61)
Education				
Less than high school	1.82 (0.60 – 5.49)	1.75 (0.49 – 6.29)	5.93 (1.75- 20.04)**	10.32 (1.89-56.27)**
High school or equivalent	0.37 (0.11 – 1.19)	0.46 (0.13 – 1.59)	2.40 (0.80 – 7.17)	2.03 (0.58 – 7.09)
More than high school	Reference	Reference	Reference	Reference
Not Married	1.58 (0.52 – 4.78)	1.73 (0.53 – 5.58)	1.49 (0.44 – 5.05)	1.07 (0.20 – 5.64)
Depressive/Fatigue Symptoms	-----	1.15 (0.36 - 3.66)	-----	0.95 (0.27 – 3.25)
Hypertension	-----	1.07 (0.37 – 3.03)	-----	2.51 (0.62 – 10.14)
Diabetes	-----	1.18 (0.24 – 5.66)	-----	1.16 (0.28 – 4.91)
Body Mass Index (≥ 30 kg/m²)	-----	1.21 (0.37 – 4.00)	-----	3.50 (1.14 – 10.77)*
Total Cholesterol (≥ 200 mg/dl)	-----	0.53 (0.18 – 1.52)	-----	0.26 (0.08 – 0.79)*
Current smoker	-----	0.86 (0.25 – 2.96)	-----	11.16 (1.25 – 99.38)*
Current drinker	-----	2.03 (0.64 – 6.42)	-----	0.12 (0.03 – 0.54)**
Physical Inactivity	-----	0.78 (0.26 – 2.34)	-----	1.05 (0.39 – 2.79)

NOTE: Model 1 adjusted for age, race, sex, *APOE* ε4, education, and marital status. Model 2 adjusted for model 1 covariates addition to depressive/fatigue symptoms, vascular risk factors, and physical inactivity.

* $P \leq .05$; ** $P \leq .01$. Abbreviations: *APOE* = apolipoprotein E; CI= confidence interval; HR = hazard ratio; MCI = mild cognitive impairment; SUVR = standardized uptake value ratio

Supplementary Table 4. Adjusted Hazard Ratios for Association of Mid-Life Social Relationships and Elevated Florbetapir Global SUVR with Dementia Risk, Excluding Participants with Prevalent Stroke at Visit 5 (n = 292)

Variable	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Strong Social Relationships	0.28 (0.10 – 0.76)*	0.29 (0.11 – 0.81)*	0.41 (0.15 – 1.14)
Average Social Relationships	0.26 (0.09 – 0.73)*	0.24 (0.08 – 0.69)**	0.26 (0.09 – 0.75)*
Poor Social Relationships	Reference	Reference	Reference
Elevated Florbetapir Global SUVR > 1.2	4.64 (2.15- 10.02)**	4.69 (2.10 – 10.47)**	3.58 (1.56 – 8.26)**
Age (per 1 year)	1.16 (1.08- 1.25)**	1.16 (1.07 – 1.24)**	1.17 (1.08 – 1.27)**
Race (Black)	1.55 (0.81 – 2.96)	1.72 (0.87 – 3.41)	1.69 (0.84 – 3.39)
Sex (Female)	0.56 (0.29 – 1.07)	0.60 (0.28 – 1.27)	0.57 (0.26 – 1.23)
APOE ε4 Carrier	2.71 (1.46 – 5.02)**	2.51 (1.33 – 4.73)**	2.58 (1.37 – 4.88)**
Education			
Less than high school	2.50 (1.14 – 5.51)*	2.66 (1.10 – 6.44)*	3.28 (1.32 – 8.14)**
High school or equivalent	0.77 (0.36 – 1.65)	0.88 (0.38 – 2.03)	1.05 (0.45 – 2.44)
More than high school	Reference	Reference	Reference
Not Married	1.15 (0.50 – 2.66)	0.82 (0.32 – 2.11)	1.02 (0.39 – 2.68)
Depressive/Fatigue Symptoms	----	0.92 (0.42 – 2.00)	1.00 (0.45 – 2.25)
Hypertension	----	1.09 (0.56 – 2.13)	1.31 (0.66 – 2.60)
Diabetes	----	2.53 (1.08 – 5.95)*	1.83 (0.74 – 4.53)
Body Mass Index (≥ 30 kg/m²)	----	1.66 (0.83 – 3.32)	1.85 (0.92 – 3.73)
Total Cholesterol (≥200 mg/dl)	----	0.58 (0.30 – 1.12)	0.61 (0.33 – 1.16)
Current smoker	----	1.06 (0.39 – 2.87)	1.29 (0.47 – 3.55)
Current drinker	----	0.57 (0.29 – 1.12)	0.75 (0.36 – 1.53)
Physical Inactivity	----	0.81 (0.41 – 1.59)	0.84 (0.43 – 1.64)
Having MCI at Visit 5	----	----	2.79 (1.35 – 5.75)**

NOTE: 13 participants excluded; 12 had prevalent stroke at visit 5 and 1 had missing stroke data at visit 5.

Model 1 adjusted for age, race, sex, *APOE* $\epsilon 4$, education, and marital status. Model 2 adjusted for model 1 covariates in addition to depressive/fatigue symptoms, vascular risk factors, and physical inactivity. Model 3 adjusted for model 2 covariates in addition to having MCI at visit 5.

* $P \leq .05$; ** $P \leq .01$

Abbreviations: *APOE* = apolipoprotein E; CI= confidence interval; HR = hazard ratio; MCI = mild cognitive impairment; SUVR = standardized uptake value ratio

Supplementary Table 5. Adjusted Hazard Ratios for Association of Mid-Life Social Relationships and Scaled Continuous Florbetapir Global SUVR with Dementia Risk (n = 305)

Variable	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Strong Social Relationships	0.40 (0.16 – 1.05)	0.47 (0.17 – 1.27)	0.57 (0.21 – 1.55)
Average Social Relationships	0.32 (0.12 – 0.88)*	0.34 (0.12 – 0.98)*	0.33 (0.12 – 0.94)*
Poor Social Relationships	Reference	Reference	Reference
Scaled Continuous Florbetapir Global SUVR	1.26 (1.15 - 1.37)**	1.28 (1.16 – 1.42)**	1.23 (1.11 – 1.37)**
Age (per 1 year)	1.12 (1.04 - 1.20)**	1.14 (1.06 – 1.22)**	1.14 (1.06 – 1.23)**
Race (Black)	2.12 (1.12 – 4.01)*	2.13 (1.07 – 4.24)*	2.20 (1.10 – 4.38)*
Sex (Female)	0.68 (0.36 – 1.30)	0.63 (0.30 – 1.30)	0.59 (0.28 – 1.24)
APOE ε4 Carrier	1.81 (0.98 – 3.37)	1.81 (0.97 – 3.39)	1.82 (0.97 – 3.41)
Education			
Less than high school	2.73 (1.23 – 6.02)*	2.09 (0.87 – 5.06)	2.78 (1.12 – 6.93)*
High school or equivalent	0.94 (0.46 – 1.96)	0.92 (0.42 – 2.01)	1.06 (0.48 – 2.35)
More than high school	Reference	Reference	Reference
Not Married	1.10 (0.49 – 2.49)	1.08 (0.45 – 2.60)	1.15 (0.47 – 2.81)
Depressive/Fatigue Symptoms	----	1.15 (0.53 – 2.51)	1.17 (0.53 – 2.59)
Hypertension	----	1.05 (0.55 – 1.99)	1.21 (0.62 – 2.35)
Diabetes	----	1.75 (0.71 – 4.29)	1.47 (0.58 – 3.71)
Body Mass Index (≥ 30 kg/m²)	----	1.89 (0.95 – 3.75)	1.95 (0.98 – 3.86)
Total Cholesterol (≥200 mg/dl)	----	0.44 (0.23 – 0.86)*	0.47 (0.24 – 0.90)*
Current smoker	----	1.12 (0.44 – 2.86)	1.38 (0.53 – 3.59)
Current drinker	----	0.60 (0.31 – 1.19)	0.73 (0.36 – 1.46)
Physical Inactivity	----	0.91 (0.47 – 1.75)	0.87 (0.45 – 1.66)
Having MCI at Visit 5	----	----	2.24 (1.06 – 4.72)*

NOTE: For scaling, SUVR was multiplied by 10. Model 1 adjusted for age, race, sex, *APOE* ϵ 4, education, and marital status. Model 2 adjusted for model 1 covariates addition to depressive/fatigue symptoms, vascular risk factors, and physical inactivity. Model 3 adjusted for model 2 covariates in addition to having MCI at visit 5.
* $P \leq .05$; ** $P \leq .01$

Abbreviations: *APOE* = apolipoprotein E; CI= confidence interval; HR = hazard ratio; MCI = mild cognitive impairment; SUVR = standardized uptake value ratio

Supplementary Table 6. Adjusted Hazard Ratios for Association of Continuous Mid-Life Psychosocial Measures and Elevated Florbetapir Global SUVR with Dementia Risk (n = 305)

	Social Support (ISEL-SF)			Social Isolation (LSNS)		
	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
ISEL-SF (Score 0 – 48)	0.99 (0.94 – 1.03)	1.00 (0.95 – 1.06)	1.01 (0.96 – 1.06)	----	----	----
LSNS (Score 0 – 50)	----	----	----	0.96 (0.92 – 1.01)	0.95 (0.90 – 1.01)	0.96 (0.90 – 1.01)
Elevated Florbetapir Global SUVR > 1.2	3.59 (1.75 – 7.36)**	3.54 (1.70 – 7.36)**	2.89 (1.35 – 6.19)**	3.68 (1.78 – 7.61)**	3.89 (1.84 – 8.21)**	3.22 (1.49 – 6.96)**
Age (per 1 year)	1.13 (1.06 – 1.20)**	1.13 (1.06 – 1.21)**	1.14 (1.07 – 1.23)**	1.13 (1.06 – 1.20)**	1.13 (1.06 – 1.21)**	1.14 (1.07 – 1.23)**
Race (Black)	1.55 (0.83 – 2.88)	1.81 (0.93 – 3.51)	1.72 (0.88 – 3.37)	1.53 (0.82 – 2.85)	1.78 (0.92 – 3.41)	1.65 (0.85 – 3.20)
Sex (Female)	0.53 (0.29 – 0.97)*	0.52 (0.26 – 1.05)	0.54 (0.27 – 1.08)*	0.55 (0.30 – 0.99)*	0.59 (0.30 – 1.16)	0.61 (0.31 – 1.21)
APOE ε4 Carrier	1.99 (1.10 – 3.59)*	1.85 (1.00 – 3.43)*	1.93 (1.04 – 3.59)*	2.12 (1.17 – 3.85)*	1.96 (1.06 – 3.63)*	2.01 (1.08 – 3.74)*
Education						
Less than high school	2.46 (1.16 – 5.19)*	2.58 (1.11 – 6.04)*	2.97 (1.27 – 6.95)*	2.38 (1.14 – 4.97)*	2.36 (1.04 – 5.35)*	2.67 (1.17 – 6.10)*
High school or equivalent	0.85 (0.41 – 1.74)	0.96 (0.44 – 2.11)	1.02 (0.47 – 2.24)	0.79 (0.38 – 1.62)	0.80 (0.36 – 1.78)	0.86 (0.39 – 1.90)
More than high school	Reference	Reference	Reference	Reference	Reference	Reference
Not Married	1.27 (0.59 – 2.77)	0.95 (0.39 – 2.29)	1.08 (0.44 – 2.67)	1.14 (0.51 – 2.52)	0.80 (0.33 – 1.94)	0.92 (0.37 – 2.29)
Depressive/Fatigue Symptoms	----	0.99 (0.43 – 2.30)	1.05 (0.45 – 2.42)	----	0.92 (0.43 – 1.94)	0.92 (0.43 – 1.95)
Hypertension	----	1.04 (0.55 – 1.99)	1.22 (0.63 – 2.37)	----	0.96 (0.50 – 1.85)	1.13 (0.58 – 2.22)
Diabetes	----	2.44 (1.10 – 5.41)*	1.67 (0.71 – 3.91)	----	2.43 (1.11 – 5.28)*	1.65 (0.71 – 3.83)
Body Mass Index (≥ 30 kg/m²)	----	1.82 (0.92 – 3.60)	1.93 (0.98 – 3.80)	----	1.71 (0.87 – 3.37)	1.87 (0.95 – 3.67)
Total Cholesterol (≥200 mg/dl)	----	0.52 (0.28 – 0.97)*	0.52 (0.28 – 0.96)*	----	0.46 (0.24 – 0.88)*	0.47 (0.25 – 0.89)*
Current smoker	----	1.21 (0.48 – 3.09)	1.42 (0.55 – 3.65)	----	1.15 (0.45 – 2.94)	1.33 (0.52 – 3.42)
Current drinker	----	0.53 (0.27 – 1.02)	0.65 (0.33 – 1.30)	----	0.50 (0.26 – 0.97)*	0.61 (0.31 – 1.23)
Physical Inactivity	----	0.73 (0.38 – 1.41)	0.75 (0.39 – 1.44)	----	0.74 (0.38 – 1.43)	0.77 (0.40 – 1.50)
Having MCI at Visit 5	----	----	2.47 (1.23 – 4.93)*	----	----	2.34 (1.17 – 4.68)*

NOTE: Models displaying HR (95% CI) for association between social support, elevated SUVR, and dementia risk shown on left and models displaying HR (95% CI) for association between social isolation, elevated SUVR, and dementia risk shown on right. Higher ISEL-SF scores indicate greater social support whereas higher LSNS scores indicate lower risk of isolation. Model 1 adjusted for age, race, sex, APOE ε4, education, and marital status. Model 2 adjusted for model 1 covariates in addition to depressive/fatigue symptoms, vascular risk factors, and physical inactivity. Model 3 adjusted for model 2 covariates in addition to having MCI at visit 5.

* $P \leq 0.05$; ** $P \leq 0.01$

Abbreviations: APOE = apolipoprotein E; CI = confidence interval; HR = hazard ratio; ISEL-SF = Interpersonal Support Evaluation List – Short Form; LSNS = Lubben Social Network Scale; MCI = mild cognitive impairment; SUVR = standardized uptake value ratio

Supplementary Table 7. Adjusted Hazard Ratios for Association of Mid-Life Social Support and Elevated Florbetapir Global SUVR with Dementia Risk (n = 305)

	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
High Social Support	1.12 (0.56 – 2.24)	1.75 (0.75 – 4.07)	1.81 (0.79 – 4.18)
Intermediate Social Support	0.38 (0.16 – 0.89)*	0.38 (0.15 - 0.97)*	0.48 (0.18 – 1.24)
Low Social Support	Reference	Reference	Reference
Elevated Florbetapir Global SUVR > 1.2	3.02 (1.47 – 6.22)**	3.26 (1.56- 6.84)**	2.76 (1.27 – 5.97)**
Age (per 1 year)	1.13 (1.06 – 1.21)**	1.14 (1.06 – 1.22)**	1.14 (1.06 – 1.23)**
Race (Black)	1.40 (0.76 – 2.60)	1.48 (0.75 – 2.93)	1.44 (0.72 – 2.87)
Sex (Female)	0.52 (0.28 – 0.97)*	0.46 (0.22 – 0.93)*	0.47 (0.23 – 0.96)*
APOE ε4 Carrier	2.12 (1.17 – 3.84)*	2.32 (1.22 – 4.40)**	2.32 (1.22 – 4.39)**
Education			
Less than high school	2.95 (1.39 – 6.26)**	2.96 (1.27 – 6.90)*	3.27 (1.40 – 7.65)**
High school or equivalent	0.99 (0.48 – 2.06)	1.05 (0.48 – 2.32)	1.12 (0.51 – 2.47)
More than high school	Reference	Reference	Reference
Not Married	1.25 (0.58 – 2.73)	0.85 (0.34 – 2.09)	0.97 (0.39 – 2.44)
Depressive/Fatigue Symptoms	----	1.29 (0.56 – 2.94)	1.26 (0.56 – 2.87)
Hypertension	----	1.43 (0.72 – 2.85)	1.49 (0.75 – 2.99)
Diabetes	----	2.30 (1.00 – 5.29)*	1.75 (0.73 - 4.25)
Body Mass Index (≥ 30 kg/m²)	----	1.68 (0.85 – 3.33)	1.76 (0.89 – 3.47)
Total Cholesterol (≥200 mg/dl)	----	0.54 (0.29 – 1.02)	0.53 (0.28 – 1.00)*
Current smoker	----	1.15 (0.45 – 2.90)	1.34 (0.52 – 3.45)
Current drinker	----	0.44 (0.22 – 0.85)*	0.53 (0.26 – 1.07)
Physical Inactivity	----	0.71 (0.36 – 1.41)	0.73 (0.37 – 1.43)
Having MCI at Visit 5	----	----	2.01 (0.98 – 4.11)

NOTE: Model 1 adjusted for age, race, sex, *APOE* ε4, education, and marital status. Model 2 adjusted for model 1 covariates in addition to depressive/fatigue symptoms, vascular risk factors, and physical inactivity. Model 3 adjusted for model 2 covariates in addition to having MCI at visit 5.

* $P \leq 0.05$; ** $P \leq 0.01$

Abbreviations: APOE = apolipoprotein E; CI = confidence interval; HR = hazard ratio; MCI = mild cognitive impairment; SUVR = standardized uptake value ratio

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Supplementary Table 8. Adjusted Hazard Ratios for Association of Mid-Life Social Isolation and Elevated Florbetapir Global SUVR with Dementia Risk (n = 305)

	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)
Low Risk	0.17 (0.05 – 0.66)**	0.13 (0.03 - 0.53)**	0.14 (0.03 – 0.55)**
Moderate Risk	0.36 (0.08– 1.64)	0.27 (0.05 – 1.29)	0.24 (0.05 – 1.17)
High Risk	0.05 (0 – 0.56)*	0.07 (0.01 – 0.81)*	0.08 (0.01 – 0.93)*
Isolated	Reference	Reference	Reference
Elevated Florbetapir Global SUVR > 1.2	3.71 (1.76 – 7.82)**	4.17 (1.91 – 9.10)**	3.44 (1.54 – 7.71)**
Age (per 1 year)	1.13 (1.06 – 1.21)**	1.13 (1.06 – 1.21)**	1.15 (1.07 – 1.24)**
Race (Black)	1.61 (0.86 – 3.01)	1.74 (0.90 – 3.40)	1.63 (0.83 – 3.20)
Sex (Female)	0.52 (0.28 – 0.97)*	0.59 (0.30 – 1.18)	0.64 (0.32 – 1.28)
APOE ε4 Carrier	2.11 (1.17 – 3.80)*	1.89 (1.02 – 3.48)*	1.93 (1.05 – 3.57)*
Education			
Less than high school	3.08 (1.45 – 6.55)**	2.78 (1.21 – 6.41)*	3.00 (1.30 – 6.91)**
High school or equivalent	0.76 (0.36 – 1.59)	0.74 (0.33 – 1.66)	0.77 (0.35 – 1.73)
More than high school	Reference	Reference	Reference
Not Married	1.28 (0.59 – 2.79)	0.93 (0.39 – 2.20)	1.05 (0.44 – 2.54)
Depressive/Fatigue Symptoms	----	1.00 (0.47 – 2.10)	1.01 (0.48 – 2.14)
Hypertension	----	1.03 (0.52 – 2.02)	1.24 (0.62 – 2.50)
Diabetes	----	2.66 (1.21 – 5.82)*	1.78 (0.76 – 4.18)
Body Mass Index (≥ 30 kg/m²)	----	1.71 (0.87 – 3.38)	1.87 (0.94 – 3.70)
Total Cholesterol (≥200 mg/dl)	----	0.54 (0.29 – 1.01)	0.54 (0.29 – 1.01)
Current smoker	----	1.12 (0.43 – 2.86)	1.37 (0.52 – 3.56)
Current drinker	----	0.55 (0.28 – 1.07)	0.66 (0.33 – 1.33)
Physical Inactivity	----	0.81 (0.41 – 1.60)	0.83 (0.42 – 1.64)
Having MCI at Visit 5	----	----	2.35 (1.15 – 4.81)*

NOTE: Model 1 adjusted for age, race, sex, *APOE* ε4, education, and marital status. Model 2 adjusted for model 1 covariates in addition to depressive/fatigue symptoms, vascular risk factors, and physical inactivity. Model 3 adjusted for model 2 covariates in addition to having MCI at visit 5.

* $P \leq 0.05$; ** $P \leq 0.01$

Abbreviations: APOE = apolipoprotein E; CI = confidence interval; HR = hazard ratio; MCI = mild cognitive impairment; SUVR = standardized uptake value ratio