Supplementary Online Content

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

eMethods

Neuropsychological measures used to estimate cognitive change
Neuropsychological measures are listed below according to their cognitive domain. Using a latent variable approach described in the section below,[1] all ten measures were used to generate a global cognitive Z-score. This global cognitive score was used to estimate 5-year cognitive change between Visits 5 and 6.

Memory: Logical Memory (immediate and delayed recall) from the Wechsler Memory Scale-III; Incidental Learning from the Wechsler Memory Scale-III; and the Delayed Word Recall Test.

Processing speed and executive function: Digit Span Backward from the Wechsler Adult Intelligence Scale-Revised (WAIS-R); Digit Symbol Substitution from the from the Wechsler Adult Intelligence Scale-Revised (WAIS-R); and the Trail Making Test (parts A and B).

Language: Boston Naming Test; Animal Fluency; and Letter Fluency.

Classification of medication use patterns
Participants were categorized into one of four of the following groups based on patterns of antihypertensive medication use at Visits 4 and 5: (1) no use; (2) stable use; (3) decreasing use; and (4) increasing use. At each visit, participants were asked to bring in all medication so that medications codes could be documented by trained study staff. All medications indicated for hypertension, including diuretics, calcium channel blockers, ACE inhibitors, Angiotensin II receptor antagonist, adrenergic receptor antagonists, aldosterone receptor antagonists, and alpha-2 adrenergic receptor agonists were identified. The total number of antihypertensive medications used at Visits 4 and 5 was determined for each participant. These totals were used to classify participants into one of the four categories (no use/stable use/decreasing use/increasing use).

Summary of methods for multiple imputation by chained equations (MICE)
In the present study, we used multiple imputation by chained equations (MICE) to impute Visit 6 global cognitive scores for participants who did not attend Visit 6. Multiple imputation is a method used to replace missing data with plausible values based on observed non-missing data. These imputation methods have been used for analyses of Atherosclerosis Risk in Communities (ARIC) data previously.[2] MICE, in particular, implements a series of imputation models to sequentially determine the missing values of each missing variable using a series of univariate imputation models. These models predict each missing variable using non-missing data and data that has been imputed during previous imputation iteration steps.

Of the 5,135 participants included in the present study, 1,915 of these participants either did not attend Visit 6 or attended Visit 6 and did not receive a comprehensive cognitive assessment. For these participants, Visit 6 global cognitive scores were imputed based on our exposure of interest (i.e., 24-year blood pressure pattern); demographic variables including age, center-race, education, family income level, and *APOE* ε4 status; physiological variables and cardiovascular risk factors, including BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status; medical comorbidity, including hypertension, diabetes, and prevalent coronary heart disease; health information collected through annual follow-up interviews, including a self-reported poor heath indicator, and number of hospitalizations; and cognitive measurements from three sources: in-person cognitive function evaluation (i.e. factor score at Visits 5), a cognitive function surveillance score derived from the Six-Item Screener (SIS) and Ascertain Dementia-8 (AD-8) questionnaires prior to Visit 6, and an indicator of suspected dementia prior to Visit 6. We also incorporated interaction terms of surveillance scores (SIS and AD-8) with 24-year blood pressure pattern, Visit 5 global cognitive score, and education level in order to capture the interactive effects of several key predictors of Visit 6 cognition. We excluded participants who died within one year after Visit 5. We used a series of 25 imputations to derive the current results. We have shown previously that stable imputation estimates can be ascertained after as few as 7 imputations.[2]

Derivation of the cognitive factor scores
Factor scores representing general cognitive performance were estimated in the ARIC study from a latent variable model that leveraged all available data across all visits. This approach was chosen because it facilitates use of all available data when measuring change over time.

The latent variable model for general cognitive performance consisted of a unidimensional confirmatory factor analysis of all tests in the ARIC NCS battery. It was estimated using Mplus version 7.3 using maximum likelihood with robust standard error estimation under the expectation-maximization algorithm. Cognitive tests were discretized using an equal-percentile discretization algorithm so that the estimation model is consistent with a two-parameter logistic item response theory model.[3] Factor scores, representing general cognitive performance for each person at each study visit, were estimated using the regression-based method and scaled to have a mean of 50 and standard deviation of 10 at ARIC visit 5.

Latent variable analysis more effectively addresses error in measurement of cognition assessed by the ARIC NCS battery than taking averages of tests, thus demonstrating less bias at the expense of a little more variability around estimates. The scores do this in 2 ways. First, by differential weighting of items: test scores in factor analysis give greater weight to tests that are empirically more correlated with other tests in the battery. Second, factor analysis allows for raw test scores to occupy different locations along the latent trait, thereby accommodating differences in difficulty of tests. Details are available in Gross et al., (2015).[1]

Summary of methods of inverse probability weighting

Elevated blood pressure and hypertension have been associated with mortality, morbidity, and disability in a manner which makes study attrition more common among participants with these characteristics, as is illustrated in eTable 3. In order to examine how differential attrition may have influenced the study results, the current study repeated the primary analyses using inverse probability weighting (IPW), a method that has been described in detail previously.[4,5] IPW is a weighting procedure which accounts for differential attrition by assigning larger weights to participants included in the analysis who have demographic, physiological, and clinical characteristics that are more strongly associated with study dropout. To obtain estimates which "adjust" for possible selection bias related to study dropout before Visit 5, IPW weights were calculated from predicted probabilities derived using logistic regression to model the probability of dropout due to study withdrawal between Visits 1 and 5 using participant demographic, physiological, and clinical data collected at ARIC Visit 1 (the ARIC study baseline) as covariate information. Specifically, the following covariates were included in the IPW model: age, center-race, APOE ε4 status, sex, education level, total cholesterol, total triglycerides, total HDL cholesterol, body mass index (BMI), and the presence of hypertension, diabetes, coronary heart disease, cancer, chronic obstructive pulmonary disease (COPD), and current and past cigarette smoking and alcohol use. After IPW weights were calculated by deriving the inverse of each participant's predicted probability of study dropout, these weights were applied in the Cox proportional hazard regression analysis of incident dementia in the full sample (the primary analysis) as part of a post-hoc sensitivity analysis. Results from this analysis of the relationship between 24-year blood pressure patterns and dementia risk, which incorporate IPW weights to adjust for study dropout, are presented in **eTable 8**.

Summary of methods for propensity score matching

Participants in each of the distinct 24-year blood pressure groups differ from participants in the mid- and late-life normotension (referent) group with regard to several demographic, physiological, and clinical characteristics (Table 1). As such, a number of these variables may serve as confounders in analyses which examine the relationship between 24-year blood pressure patterns and incident dementia. Therefore, bias related to confounding must be carefully considered. As an alternative method to control for confounding, we used propensity score matching.[6] This technique, which uses a matched case-control approach to reduce the imbalance between demographic, physiological, and clinical factors, was used to evaluate the robustness of the results derived from our primary analyses, which instead used traditional regression methods. Propensity score matching procedures are described below. Results of these analyses are presented in **eTables 9**.

We used propensity score matching to balance a subset of participants from distinct blood pressure groups on demographic, physiological, and clinical characteristics. We calculated four sets of propensity scores for four distinct group comparisons using logistic regression models with the following outcomes: 1) reference group versus midlife normotension/late-life hypertension; 2) reference group versus mid- and late-life hypertension; 3) reference group versus midlife normotension/late-life hypotension; and 4) reference group versus midlife hypertension/late-life hypotension. These propensity scores represent a participant's propensity for having a specific 24-year blood pressure pattern versus having a pattern of mid- and late-life normotension (the reference) based on known demographic, physiological, and clinical characteristics. Regression models used to derive propensity scores included the set of covariates included in the study's primary analyses: baseline age, sex, race, center, education, and

APOE ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5.

Next, we matched participants included in the four comparisons described above based on the calculated propensity scores using a 1:1 nearest-neighbor matching procedure (without replacement). We used a caliper of 0.06 (width approximately 0.2 of the standard deviation of the logit of the propensity scores), as this caliper has been shown to substantially reduce initial bias.[7] Using the propensity matched sample, we examined dementia risk associated with each longitudinal blood pressure pattern, comparing each group to the reference group using Cox proportional hazard models. We presented results from unadjusted models and models adjusted for demographic factors, physiological variables, cardiovascular risk factors, and comorbid disease (**eTable 9**).

eTable 1. Algorithm for classification of incident dementia

		Dementia assignment criteria	Cumulative dementia cases, No. (%)
Attended Visits 5 and 6		Dementia diagnosed at Visit 6 clinic examination based cognitive domain scores, FAQ, and CDR sum of boxes.	177 (3.7)
	Or		
		Dementia indicated using algorithmic diagnosis based on cognitive domain scores, FAQ, and CDR sum of boxes.	
Attended Visit 5, did not attend Visit 6		Impaired AD8 (score ≥ 2)	370 (7.7)
	Or		
		Any two impaired SIS (score ≤ 3, prorated)	
		One or more impaired SIS where only a single SIS is available due to participant death or withdrawing from study	382 (8.0)
		Dementia reported among hospital discharge codes	516 (10.8)
	Or		
		Dementia reported on death certificate	

AD8=Ascertain Dementia 8-item Informant Questionnaire; CDR=Clinical Dementia Rating; FAQ=Functional Activities Questionnaire; SIS= Six-Item Screener

eTable 2. Visit 5 participant characteristics stratified by 24-year measured hypertension definition blood pressure patterns [a]

	24-year longitudinal blood pressure patterns					
Characteristic, n (%) or mean (SD)	Mid- and late-life normotension	Midlife normotension, late-life hypertension	Mid- and late-life hypertension	Midlife normotension, late-life hypotension	Midlife hypertension, late-life hypotension	Midlife hypertension, late-life normotension
N	2,116	938	202	1,186	130	180
Demographic Variables						
Age, mean (SD)	74.2 (4.7)	75.7 (4.9)	76.1 (5.4)	76.2 (5.1)	79.8 (5.3)	74.8 (4.7)
Women, No. (%)	1,198 (56.6)	606 (64.6)	135 (66.8)	702 (59.2)	72 (55.4)	104 (57.8)
Men, No. (%)	918 (43.4)	332 (35.4)	67 (33.2)	484 (40.8)	58 (44.6)	76 (42.2)
Black, No. (%)	435 (20.6)	222 (23.7)	96 (47.5)	120 (10.1)	27 (20.8)	76 (42.2)
White, No. (%)	1,681 (79.4)	716 (76.3)	106 (52.5)	1,066 (89.9)	103 (79.2)	104 (57.8)
Center, No. (%)						
Minneapolis, Minnesota	679 (32.1)	297 (31.7)	46 (22.8)	427 (36.0)	45 (34.6)	51 (28.0)
Washington County, Maryland	517 (24.4)	217 (23.1)	37 (18.3)	441 (37.2)	46 (35.4)	31 (17.2)
Forsyth Count, North Carolina	510 (24.1)	219 (23.4)	28 (13.9)	205 (17.3)	13 (10.0)	27 (15.0)
Jackson, Mississippi	410 (19.4)	205 (21.9)	91 (45.1)	113 (9.5)	26 (20.0)	71 (39.4)
Education, No. (%)						
Less than high school	220 (10.4)	132 (14.1)	44 (21.8)	131 (11.1)	19 (14.6)	32 (17.8)
High school/GED/vocational	875 (41.4)	402 (42.9)	84 (41.6)	524 (44.2)	63 (48.5)	67 (37.2)
College/graduate/ professional	1,021 (48.3)	404 (43.1)	74 (36.6)	531 (44.8)	48 (36.9)	81 (45.0)
Apolipoprotein E ε4 alleles, No. (%) [b]						
0 (lowest AD risk)	1,510 (73.4)	655 (71.6)	125 (64.8)	827 (72.0)	90 (70.3)	123 (71.5)
1 (moderate AD risk)	505 (24.6)	239 (26.1)	61 (31.6)	299 (26.0)	36 (28.1)	46 (26.7)
2 (highest AD risk)	41 (2.0)	21 (2.3)	7 (3.6)	23 (2.0)	2 (1.6)	3 (1.7)
Physiological & Lab Variables, mean (SD)						
Body mass index, kg/m^2	29.0 (5.4)	28.7 (5.5)	30.2 (6.3)	27.8 (5.7)	28.5 (5.3)	30.6 (5.7)
Systolic blood pressure, mm Hg	124.8 (9.4)	152.2 (11.4)	156.3 (15.1)	117.5 (14.7)	125.2 (16.5)	126.9 (8.2)
Diastolic blood pressure, mm Hg	68.5 (6.1)	75.6 (9.0)	77.0 (10.3)	54.0 (4.6)	53.0 (5.4)	69.3 (6.6)
Total cholesterol, mg/dl	184.1 (41.7)	188.6 (42.0)	187.1 (36.2)	175.1 (40.0)	168.8 (39.5)	173.7 (36.7)
HDL-c, mg/dl	52.2 (13.5)	53.5 (15.0)	54.1 (13.9)	52.3 (13.8)	49.4 (12.5)	50.2 (12.5)
LDL-c, mg/dl	106.5 (34.9)	109.7 (34.8)	106.7 (30.4)	98.8 (32.5)	93.6 (32.5)	99.5 (31.8)
Cardiovascular Disease, No. (%)						
Diabetes mellitus	513 (24.2)	256 (27.3)	65 (32.2)	356 (30.0)	54 (41.5)	65 (36.1)

Coronary heart disease	205 (9.7)	109 (11.6)	26 (12.9)	233 (19.7)	38 (29.2)	25 (13.9)
Heart failure	62 (2.9)	39 (4.2)	15 (7.4)	78 (6.6)	11 (8.5)	10 (5.6)
Medication						
Antihypertensive, No. (%)	1,268 (59.9)	633 (67.5)	188 (93.1)	788 (66.4)	123 (94.6)	172 (95.6)
No. of antihypertensive medication, mean (SD)	1.1 (1.2)	1.2 (1.2)	2.0 (1.4)	1.4 (1.3)	2.4 (1.5)	2.2 (1.3)
Cholesterol lowering, No. (%)	1,150 (54.6)	467 (50.0)	114 (56.7)	716 (60.6)	96 (73.9)	112 (62.2)
Cigarette Smoking Status, No. (%) [c]						
Current	113 (5.3)	56 (6.0)	12 (5.9)	90 (7.5)	8 (6.2)	12 (6.7)
Former	1,121 (53.0)	457 (48.7)	94 (46.5)	606 (51.1)	63 (48.5)	92 (51.1)
Never	882 (41.7)	425 (45.3)	96 (47.5)	490 (41.3)	59 (45.4)	76 (42.2)
Alcohol Consumption, No. (%) [d]						
Current	1,147 (54.2)	443 (47.2)	80 (39.6)	596 (50.3)	55 (42.3)	81 (45.0)
Former	543 (25.7)	272 (29.0)	56 (27.7)	363 (30.6)	53 (40.8)	60 (33.3)
Never	426 (20.1)	223 (23.8)	66 (32.7)	227 (19.1)	22 (16.9)	39 (21.7)
Visit 6 Attendance Status, No. (%)						
Attended	1,525 (72.1)	635 (67.7)	123 (60.9)	790 (66.6)	73 (56.2)	128 (70.9)
Alive but did not attend	533 (25.2)	265 (28.3)	66 (32.7)	327 (27.6)	48 (36.9)	42 (23.6)
Death before Visit 6	58 (2.7)	38 (4.1)	13 (6.4)	69 (5.8)	9 (6.9)	10 (5.6)

Values are displayed as means (SD) for continuous variables, and column percentages for categorical variables unless otherwise specified. Participants with missing systolic or diastolic blood pressure at Visit 5 (n=9) were not included in measured hypertension definition analyses.
AD=Alzheimer's disease.
[a] The number with missing data are 24 for LDL-c, 139 for Apolipoprotein E genotype 6 for antihypertension medication use, and 19 for cholesterol lowering medication use.
[b] A greater number of Apolipoprotein E ε4 alleles is associated with a higher risk of late-onset Alzheimer's disease
[c] *Current* cigarette use was defined as a participant report of current cigarette use. *Former* cigarette use was defined as any report of current cigarette at a previous study visit, or a report of past cigarette use. Participants who reported no previous cigarette use were classified as *never.*
[d] *Current* alcohol use was defined as any alcohol consumption within the last 6 months. *Former* alcohol use was defined as any previous alcohol consumption, if no alcohol consumption was reported within the last 6 months. Participants who reported no previous consumption of alcohol were classified as *never*.

eTable 3. Visit 1 participant characteristics stratified according to study inclusion, dropout, and death

Characteristic, n (%) or mean (SD)	Attended Visit 5 and included in study N=4,761	Attended Visit 5 and not included in study [a] N=1,777	Dropped out and alive at Visit 5 N=3,375	Dead before end of Visit 5 N=5,879
Demographic variables				
Age, mean (SD) [b,c,d]	51.6 (4.9)	53.5 (5.6)	53.6 (5.6)	56.8 (5.5)
Women, No. *(%)* [c,d]	2,821 (59.3)	1,024 (57.6)	2,150 (63.7)	2,715 (46.2)
Men, No. (%) [c,d]	1,940 (40.8)	753 (42.4)	1,225 (36.3)	3,164 (53.8)
Black, No. *(%)* [b,c,d]	979 (20.6)	564 (31.7)	869 (25.8)	1,854 (31.5)
White, No. (%) [b,c,d]	3,782 (79.4)	1,195 (67.3)	2,489 (73.8)	4,012 (68.2)
Center, *No. (%)* [b,c,d]				
Minneapolis, Minnesota	1,545 (32.5)	370 (20.8)	830 (24.6)	1,264 (51.5)
Washington County, Maryland	1,292 (27.1)	482 (27.1)	726 (21.5)	1,520 (25.9)
Forsyth Count, North Carolina	1,005 (21.1)	428 (24.1)	1,123 (33.3)	1,479 (25.2)
Jackson, Mississippi	919 (19.3)	497 (28.0)	830 (24.6)	1,616 (27.5)
Education, *No. (%)* [b,c,d]				
Less than high school	580 (12.2)	410 (23.2)	785 (23.3)	1,992 (34.0)
High school/GED/vocational	2,021 (42.5)	692 (39.2)	1,466 (43.5)	2,233 (38.1)
College/graduate/ professional	2,160 (45.4)	664 (37.6)	1,119 (33.2)	1,643 (28.0)
Apolipoprotein E ε4 alleles, *No. (%)* [d]				
0 (lowest AD risk)	3,337 (72.2)	1,144 (67.1)	2,281 (70.2)	3,775 (66.7)
1 (moderate AD risk)	1,187 (25.7)	512 (30.1)	893 (27.5)	1,697 (30.0)
2 (highest AD risk)	97 (2.1)	48 (2.8)	75 (2.3)	188 (3.3)
Mean cognitive Z-score, mean (SD) [e]				
Composite cognitive score [b,c,d]	0.3 (0.9)	0.0 (1.0)	0.0 (0.9)	-0.3 (1.0)
Delayed Word Recall Test [b,c,d]	0.2 (0.9)	0.0 (1.0)	0.1 (1.0)	-0.3 (1.0)
Digit Symbol Substitution Test [b,c,d]	0.3 (0.9)	-0.1 (1.0)	0.0 (0.9)	-0.3 (0.9)
Word Fluency Test [b,c,d]	0.2 (1.0)	0.0 (1.0)	0.0 (1.0)	-0.2 (1.0)
Physiological and lab variables, mean (SD)				
Body mass index, kg/m^2 [b,c,d]	27.0 (4.8)	27.8 (5.3)	27.7 (5.3)	28.3 (5.8)
Systolic blood pressure, mm Hg [b,c,d]	115.8 (15.2)	119.9 (17.9)	120.3 (17.5)	126.9 (21.2)
Diastolic blood pressure, mm Hg [b,c,d]	72.6 (10.1)	74.2 (11.1)	73.4 (10.7)	74.8 (12.5)
Total cholesterol, mg/dl [c,d]	209.8 (39.5)	215.8 (42.0)	217.0 (42.1)	217.7 (43.7)
HDL-c, mg/dl [b,d]	53.5 (17.0)	52.4 (17.0)	53.0 (17.0)	49.0 (17.0)
LDL-c, mg/dl [b,c,d]	132.9 (37.6)	138.3 (39.2)	139.1 (39.8)	140.5 (40.2)
Chronic medical conditions, *No. (%)*				
Hypertension [b,c,d]	1,081 (22.8)	563 (31.9)	1,084 (32.2)	2,776 (47.5)
Diabetes mellitus [b,c,d]	169 (3.6)	131 (7.5)	209 (6.3)	1,052 (18.1)
Coronary heart disease [b,c,d]	68 (1.4)	56 (3.4)	81 (2.4)	561 (9.8)
Heart failure [b,c,d]	104 (2.2)	64 (3.8)	124 (3.7)	460 (8.0)
Medication, *No. (%)*				
Antihypertensive [b,c,d]	787 (16.6)	398 (22.5)	796 (23.7)	2,022 (34.7)
Cholesterol lowering [c,d]	94 (2.0)	45 (2.6)	105 (3.1)	208 (3.6)
Cigarette smoking status, *No. (%)* [b,c,d]				
Current	800 (16.8)	370 (20.9)	781 (23.1)	2,181 (37.1)
Former	1,579 (33.2)	587 (33.2)	1,036 (30.7)	1,872 (31.8)

Never	2,380 (50.0)	814 (46.0)	1,558 (46.2)	1,826 (31.1)
Alcohol consumption, *No. (%)* [b,c,d]				
Current	2,947 (62.0)	962 (54.6)	959 (28.4)	1,422 (24.2)
Former	673 (14.2)	306 (17.4)	580 (17.2)	1,434 (24.4)
Never	1,131 (23.8)	494 (28.0)	959 (28.4)	3,023 (51.4)

Values are displayed as means (SD) for continuous variables and frequency (column percentages) for categorical variables unless otherwise specified.

[a] 1,350 participants were excluded and 427 were lost to follow-up.

[b] P-value <0.05 for group difference between participants included in the study and participants who attended Visit 5 but were excluded from the study

[c] P-value <0.05 for group difference between participants included in the study and participants who dropped out of the cohort before Visit 5, but were alive at the start of Visit 5

[d] P-value <0.05 for group difference between participants included in the study and participants who died before Visit 5

[e] All cognitive measures were administered at ARIC Visit 2 (1990-1992; n=14,040)

eTable 4. Visit 5 participant characteristics stratified according to study inclusion

Characteristic, n (%) or mean (SD)	Attended Visit 5 and included in study N=4,761	Attended Visit 5 and not included in study [a] N=1,777
Demographic variables		
Age, mean (SD)[b]	75.2 (5.0)	77.3 (5.7)
Women, No. (%)	2,821 (59.3)	1,024 (57.6)
Men, No. (%)	1,940 (40.8)	753 (42.4)
Black, No. (%) [b]	979 (20.6)	564 (31.7)
White, No. (%) [b]	3,782 (79.4)	1,195 (67.3)
Center, *No. (%)* [b]		
Minneapolis, Minnesota	1,545 (32.5)	370 (20.8)
Washington County, Maryland	1,292 (27.1)	482 (27.1)
Forsyth Count, North Carolina	1,005 (21.1)	428 (24.1)
Jackson, Mississippi	919 (19.3)	497 (28.0)
Education, *No. (%)* [b]		
Less than high school	580 (12.2)	410 (23.2)
High school/GED/vocational	2,021 (42.5)	692 (39.2)
College/graduate/ professional	2,160 (45.3)	664 (37.6)
Apolipoprotein E ε4 alleles, *No. (%)* [b]		
0 (lowest Alzheimer's disease risk)	3,337 (72.2)	1,144 (67.1)
1 (moderate Alzheimer's disease risk)	1,187 (25.7)	512 (30.1)
2 (highest Alzheimer's disease risk)	97 (2.1)	48 (2.8)
Physiological and lab variables, mean (SD)		
Body mass index, kg/m^2	28.8 (5.6)	28.7 (6.3)
Systolic blood pressure, mm Hg [b]	129.9 (17.8)	133.0 (20.7)
Diastolic blood pressure, mm Hg [b]	66.3 (10.6)	66.4 (11.5)
Total cholesterol, mg/dl	182.1 (41.2)	179.4 (44.2)
HDL-c, mg/dl [b]	52.4 (13.9)	51.4 (14.4)
LDL-c, mg/dl	104.6 (34.2)	103.1 (36.4)
Cognitive Diagnosis, *No. (%)* [b]		
Normal	3,739 (78.8)	1,024 (58.8)
Mild cognitive impairment (MCI)	1,006 (21.2)	368 (21.1)
Dementia	--	344 (19.7)
Chronic medical conditions, *No. (%)*		
Hypertension [b]	3,523 (74.0)	1,302 (77.3)
Diabetes mellitus [b]	1,315 (27.6)	639 (37.4)
Coronary heart disease [b]	636 (13.4)	345 (20.7)
Heart failure [b]	215 (4.5)	183 (10.3)
Medication, *No. (%)*		
Antihypertensive	3,181 (66.8)	1,236 (70.0)
Cholesterol lowering	2,659 (56.1)	978 (55.7)
Cigarette smoking status, *No. (%)* [b]		
Current	291 (6.1)	72 (7.5)
Former	2,440 (51.3)	524 (54.7)
Never	2,030 (42.6)	362 (60.0)
Alcohol consumption, *No. (%)* [b]		
Current	2,406 (50.5)	574 (42.6)
Former	1,352 (28.4)	464 (34.5)
Never	1,003 (21.1)	309 (22.9)

Values are displayed as means (SD) for continuous variables and frequency (column percentages) for categorical variables unless otherwise specified.

[a] 1,350 participants were excluded and 427 were lost to follow-up.

[b] P-value <0.05 for group difference

eTable 5. The association of mid- to late-life standard hypertension definition blood pressure patterns with cognitive outcomes using a 25% systolic or diastolic blood pressure decline to define hypotension

24-year blood pressure patterns	Incident dementia (full sample) N=4,701 [a]	Incident dementia (attended Visit 6) N=3,248	Visit 6 mild cognitive impairment N=2,569	Cognitive change N=4,396
	HR (95% CI) n/N (%)	HR (95% CI) n/N (%)	OR (95% CI) n/N (%)	ß (95% CI) [b] N
Mid- and late-life normotension	1 [Reference] 76/1,137 (7%)	1 [Reference] 29/836 (3%)	1 [Reference] 99/694 (14%)	0 [Reference] 1,105
Midlife normotension, late-life hypertension	1.19 (0.91, 1.57) 182/1,880 (10%)	1.17 (0.74, 1.85) 62/1,331 (5%)	1.27 (0.96, 1.68) 193/1,061 (18%)	-0.01 (-0.05, 0.03) 1,785
Mid- and late-life hypertension	1.59 (1.18, 2.13) 166/1,144 (15%)	1.43 (0.86, 2.37) 52/738 (7%)	1.30 (0.93, 1.83) 102/558 (18%)	-0.02 (-0.07, 0.02) 1,015
Midlife normotension, 25% drop in SBP or DBP from Visit 4 to 5	1.34 (0.87, 2.08) 30/278 (11%)	2.34 (1.22, 4.46) 16/180 (9%)	0.99 (0.58, 1.69) 21/133 (15%)	0.00 (-0.06, 0.07) 267
Midlife hypertension, 25% drop in SBP or DBP from Visit 4 to 5	1.74 (1.18, 2.56) 48/262 (18%)	2.15 (1.12, 4.14) 16/163 (10%)	1.02 (0.58, 1.79) 19/120 (16%)	-0.03 (-0.10, 0.05) 224

Cox proportional hazard, logistic regression, and GEE regression (with a Gaussian distribution to model the continuous outcome of cognitive performance) models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5.

CI=confidence interval; DBP=diastolic blood pressure; HR=hazard ratio; n=number of dementia or MCI cases; N=total number of participants; OR=odds ratio; SBP=systolic blood pressure

[a] Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=27). Participants with missing Visit 4 or Visit 5 systolic and/or diastolic blood pressure were excluded from these analyses (n=33).

[b] Unstandardized estimates of additional 5-year cognitive change (Z-score) associated with blood pressure pattern.

eTable 6. The association of mid- to late-life standard hypertension definition blood pressure patterns with cognitive outcomes using a 25% systolic blood pressure decline to define hypotension

24-year blood pressure patterns	Incident dementia (full sample) n=4,695 [a]	Incident dementia (attended Visit 6) N=3,247	Visit 6 mild cognitive impairment N=2,568	Cognitive change N=4,392
	HR (95% CI) n/N (%)	HR (95% CI) n/N (%)	OR (95% CI) n/N (%)	ß (95% CI) [b] N
Mid- and late-life normotension	1 [Reference] 86/1,191 (7%)	1 [Reference] 34/871 (4%)	1 [Reference] 104/717 (20%)	0 [Reference] 1,158
Midlife normotension, late-life hypertension	1.11 (0.86, 1.45) 197/2,070 (10%)	1.07 (0.70, 1.65) 71/1,456 (5%)	1.22 (0.93, 1.60) 207/1,158 (18%)	-0.01 (-0.05, 0.03) 1,966
Mid- and late-life hypertension	1.53 (1.16, 2.02) 203/1,330 (15%)	1.33 (0.83, 2.14) 64/849 (8%)	1.21 (0.87, 1.68) 112/638 (18%)	-0.02 (-0.07, 0.02) 1,172
Midlife normotension, 25% drop in SBP from Visit 4 to 5	1.79 (0.70, 4.54) 5/34 (15%)	2.03 (0.45, 9.15) 2/20 (10%)	0.69 (0.15, 3.21) 2/16 (13%)	0.00 (-0.18, 0.17) 33
Midlife hypertension, 25% drop in SBP from Visit 4 to 5	1.29 (0.64, 2.59) 9/70 (13%)	1.57 (0.54, 4.55) 4/51 (8%)	1.55 (0.68, 3.50) 9/39 (23%)	-0.01 (-0.14, 0.11) 63

Cox proportional hazard, logistic regression, and GEE regression (with a Gaussian distribution to model the continuous outcome of cognitive performance) models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5.

CI=confidence interval; HR=hazard ratio; n=number of dementia or MCI cases; N=total number of participants; OR=odds ratio; SBP=systolic blood pressure

[a] Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=33). Participants with missing Visit 4 or Visit 5 systolic and/or diastolic blood pressure were excluded from these analyses (n=33).

[b] Unstandardized estimates of additional 5-year cognitive change (Z-score) associated with blood pressure pattern.

eTable 7. The association of mid- to late-life standard hypertension definition blood pressure patterns with cognitive outcomes using a 25% diastolic blood pressure decline to define hypotension

24-year blood pressure patterns	Incident dementia (full sample) N=4,699 [a]	Incident dementia (attended Visit 6) N=3,246	Visit 6 mild cognitive impairment N=2,567	Cognitive change N=4,396
	HR (95% CI) n/N (%)	HR (95% CI) n/N (%)	OR (95% CI) n/N (%)	ß (95% CI) [b] N
Mid- and late-life normotension	1 [Reference] 76/1,138 (7%)	1 [Reference] 29/836 (3%)	1 [Reference] 99/694 (14%)	0 [Reference] 1,106
Midlife normotension, late-life hypertension	1.20 (0.91, 1.58) 183/1,886 (10%)	1.17 (0.74, 1.85) 62/1,335 (5%)	1.27 (0.97, 1.68) 194/1,064 (18%)	-0.01 (-0.05, 0.02) 1,791
Mid- and late-life hypertension	1.59 (1.19, 2.14) 168/1,159 (15%)	1.44 (0.87, 2.39) 53/747 (7%)	1.30 (0.92, 1.83) 103/565 (18%)	-0.02 (-0.07, 0.02) 1,027
Midlife normotension, 25% drop in DBP from Visit 4 to 5	1.31 (0.84, 2.04) 29/271 (11%)	2.39 (1.25, 4.56) 16/176 (9%)	0.96 (0.56, 1.65) 20/133 (15%)	0.01 (-0.06, 0.08) 260
Midlife hypertension, 25% drop in DBP from Visit 4 to 5	1.76 (1.19 2.61) 46/245 (14%)	2.16 (1.11, 4.22) 15/152 (10%)	1.05 (0.59, 1.88) 18/111 (16%)	-0.02 (-0.10, 0.06) 212

Cox proportional hazard, logistic regression, and GEE regression (with a Gaussian distribution to model the continuous outcome of cognitive performance) models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5.

CI = confidence interval; HR=hazard ratio; n=number of dementia or MCI cases; N=total number of participants; OR=odds ratio

[a] Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=29). Participants with missing Visit 4 or Visit 5 systolic and/or diastolic blood pressure were excluded from these analyses (n=33).

[b] Unstandardized estimates of additional 5-year cognitive change (Z-score) associated with blood pressure pattern

eTable 8. The association of mid- to late-life standard hypertension definition blood pressure patterns with dementia after incorporating inverse probability weighting

24-year blood pressure patterns [a]	Incident dementia (full sample) N=4,508
	HR (95% CI) n/N (%)
Mid- and late-life normotension	1 [Reference] 51/800 (6%)
Midlife normotension, late-life hypertension	1.23 (0.88, 1.72) 146/1,489 (10%)
Mid- and late-life hypertension	1.51 (1.05, 2.16) 126/964 (13%)
Midlife normotension, late-life hypotension	1.22 (0.85, 1.75) 91/883 (10%)
Midlife hypertension, late-life hypotension	1.58 (1.05, 2.39) 74/372 (20%)

Cox proportional hazard models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. Attrition weights were derived using logistic regression to model the probability of dropout due to withdrawal between Visits 1 and 5. The following covariates were used in the logistic regression model: age, center-race, *APOE* ε4 status, sex, education level, total cholesterol, total triglycerides, total HDL cholesterol, body mass index (BMI), and the presence of hypertension, diabetes, coronary heart disease, cancer, chronic obstructive pulmonary disease (COPD), and current and past cigarette smoking and alcohol use. Participants with missing Visit 1 covariate information were excluded (n=230). Inverse probability weights were applied to the Cox proportional hazard models to derive these results. Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=23).
CI = confidence interval; HR=hazard ratio; n=number of dementia cases; N=total number of participants.

eTable 9. The association of mid- to late-life standard hypertension definition blood pressure patterns with dementia using a propensity score-matched sample

Comparison groups	Reference group (mid- and late-life normotension) n/N (%)	Comparison group n/N (%)	Incident dementia (full sample) HR (95% CI) unadjusted model	Incident dementia (full sample) HR (95% CI) fully adjusted model [a]
Midlife normotension, late-life hypertension	52/755 (7%)	49/755 (6%)	0.93 (0.63, 1.38) N=1,510	1.16 (0.76, 1.75) N=1,510
Mid- and late-life hypertension	35/470 (7%)	47/470 (10%)	1.28 (0.82, 1.98) N=940	1.80 (1.12, 2.88) N=940
Midlife normotension, late-life hypotension	44/568 (8%)	34/568 (6%)	0.74 (0.47, 1.16) N=1,136	0.76 (0.47, 1.20) N=1,136
Midlife hypertension, late-life hypotension	22/210 (11%)	41/210 (20%)	1.95 (1.16, 3.28) N=420	2.42 (1.35, 4.34) N=420

A subset of participants from each 24-year blood pressure group were matched to a subset of participants from the reference group based on calculated propensity scores using a 1:1 nearest-neighbor matching procedure (without replacement). See the eMethods above for a detailed description of propensity score matching methods. Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=23).
CI = confidence interval; HR=hazard ratio; n=number of dementia cases; N=total number of participants
[a] Cox proportional hazard regression models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5.

eTable 10. The association of mid- to late-life standard hypertension definition blood pressure patterns with dementia and cognitive change among participants cognitively normal at baseline (Visit 5)

24-year blood pressure patterns	Incident dementia (full sample) N=3,738	Incident dementia (attended Visit 6) N=2,692	Cognitive change N=3,573
	HR (95% CI) n/N (%)	HR (95% CI) n/N (%)	ß (95% CI) [a] N
Mid- and late-life normotension	1 [Reference] 32/701 (5%)	1 [Reference] 15/528 (3%)	0 [Reference] 680
Midlife normotension, late-life hypertension	0.93 (0.60, 1.43) 67/1,239 (5%)	0.75 (0.38, 1.44) 26/907 (3%)	-0.01 (-0.06, 0.03) 1,192
Mid- and late-life hypertension	1.15 (0.73, 1.82) 65/785 (8%)	0.80 (0.39, 1.64) 25/559 (4%)	-0.01 (-0.06, 0.04) 725
Midlife normotension, late-life hypotension	0.79 (0.48, 1.29) 37/729 (5%)	0.56 (0.25, 1.23) 13/536 (2%)	0.00 (-0.05, 0.05) 714
Midlife hypertension, late-life hypotension	1.64 (0.98, 2.75) 39/284 (14%)	1.07 (0.43, 2.64) 10/162 (6%)	-0.05 (-0.13, 0.03) 262

Cox proportional hazard and GEE regression (with a Gaussian distribution to model the continuous outcome of cognitive performance) models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=23).

CI = confidence interval; HR=hazard ratio; n=number of dementia cases; N=total number of participants

[a] Unstandardized estimates of additional 5-year cognitive change (Z-score) associated with blood pressure pattern.

eTable 11. The association of mid- to late-life standard hypertension definition blood pressure patterns with dementia after combining 24-year blood pressure groups with similar mid- and late-life blood pressure patterns

Combined midlife 24-year blood pressure patterns	Incident dementia (full sample) N=4,761
	HR (95% CI) n/N (%)
Combined midlife normotension group [a]	1 [Reference] 293/3,319 (9%)
Combined midlife hypertension group [b]	1.41 (1.17, 1.71) 223/1,442 (15%)
Combined late-life 24-year blood pressure patterns	**Incident dementia (full sample) N=4,761**
	HR (95% CI) n/N (%)
Combined late-life normotension group [c]	1 [Reference] 61/856 (7%)
Combined late-life hypertension group [d]	1.11 (0.83, 1.48) 287/2,589 (11%)
Combined late-life hypotension group [e]	1.11 (0.82, 1.52) 168/1,316 (13%)

Cox proportional hazard models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5.

CI = confidence interval; HR=hazard ratio; n=number of dementia cases; N=total number of participants

[a] The *combined midlife normotension group* includes all participants with midlife normotension as categorized using standard hypertension criteria.

[b] The *combined midlife hypertension group* includes all participants with midlife hypertension as categorized using standard hypertension criteria.

[c] The *combined late-life normotension group* includes all participants with late-life normotension as categorized using standard hypertension criteria.

[d] The *combined late-life hypertension group* includes all participants with late-life hypertension as categorized using standard hypertension criteria.

[e] The *combined late-life hypotension group* includes all participants with late-life hypotension as categorized using standard hypertension criteria.

eTable 12. The age-stratified association of mid- to late-life standard hypertension definition blood pressure patterns with dementia

24-year blood pressure patterns	Incident dementia (full sample) Visit 5 Age < 74 N=2,053	Incident dementia (full sample) Visit 5 Age ≥ 74 N=2,685	Interaction
	HR (95% CI) n/N (%)	HR (95% CI) n/N (%)	*P*
Mid- and late-life normotension	1 [Reference] 14/459 (3%)	1 [Reference] 39/374 (10%)	--
Midlife normotension, late-life hypertension	1.41 (0.74, 2.68) 36/715 (5%)	1.09 (0.75, 1.58) 113/844 (13%)	0.29
Mid- and late-life hypertension	1.48 (0.74, 2.95) 31/446 (7%)	1.45 (0.99, 2.14) 107/584 (18%)	0.46
Midlife normotension, late-life hypotension	0.98 (0.43, 2.23) 12/339 (4%)	1.09 (0.74, 1.62) 79/588 (13%)	0.91
Midlife hypertension, late-life hypotension	2.73 (1.20, 6.20) 14/94 (15%)	1.43 (0.93, 2.20) 63/295 (21%)	0.02

Cox proportional hazard models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. A dichotomous interaction term was used to assess the age interaction (age <74/≥74).
Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=23).
CI=confidence interval; HR=hazard ratio; n=number of dementia cases; N=total number of participants

eTable 13. The race-stratified association of mid- to late-life standard hypertension definition blood pressure patterns with dementia

24-year blood pressure patterns	Incident dementia (full sample) Black N=968	Incident dementia (full sample) White N=3,770	Interaction
	HR (95% CI) n/N (%)	HR (95% CI) n/N (%)	*P*
Mid- and late-life normotension	1 [Reference] 11/93 (12%)	1 [Reference] 42/740 (6%)	--
Midlife normotension, late-life hypertension	0.91 (0.45, 1.82) 42/299 (14%)	1.27 (0.88, 1.82) 107/1,260 (8%)	0.10
Mid- and late-life hypertension	1.17 (0.59, 2.30) 67/429 (16%)	1.55 (1.05, 2.30) 71/601 (12%)	0.13
Midlife normotension, late-life hypotension	1.40 (0.59, 3.30) 13/68 (19%)	1.08 (0.73, 1.60) 78/859 (9%)	0.77
Midlife hypertension, late-life hypotension	1.05 (0.45, 2.48) 15/79 (19%)	1.77 (1.16, 2.71) 62/310 (20%)	0.02

Cox proportional hazard models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=23).
CI=confidence interval; HR=hazard ratio; n=number of dementia cases; N=total number of participants

eTable 14. The association of mid- to late-life standard hypertension definition blood pressure patterns with cognitive change after the inclusion of participants with low baseline cognitive scores

24-year blood pressure patterns	Cognitive change N=4,721
	ß (95% CI) [a] N
Mid- and late-life normotension	0 [Reference] 829
Midlife normotension, late-life hypertension	0.00 (-0.06, 0.03) 1,554
Mid- and late-life hypertension	0.00 (-0.04, 0.05) 1,026
Midlife normotension, late-life hypotension	-0.01 (-0.05, 0.04) 924
Midlife hypertension, late-life hypotension	-0.03 (-0.10, 0.05) 388

GEE regression (with a Gaussian distribution to model the continuous outcome of cognitive performance) models were adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and Visit 5 BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. A low baseline cognitive score was defined as having one or more cognitive domain score in the bottom 5th percentile at the baseline cognitive assessment (Visit 5). Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=23).
CI = confidence interval; N=total number of participants;
[a] Unstandardized estimates of additional 5-year cognitive change (Z-score) associated with blood pressure pattern.

eTable 15. Cox proportional hazard regression models of dementia risk associated with individual covariates

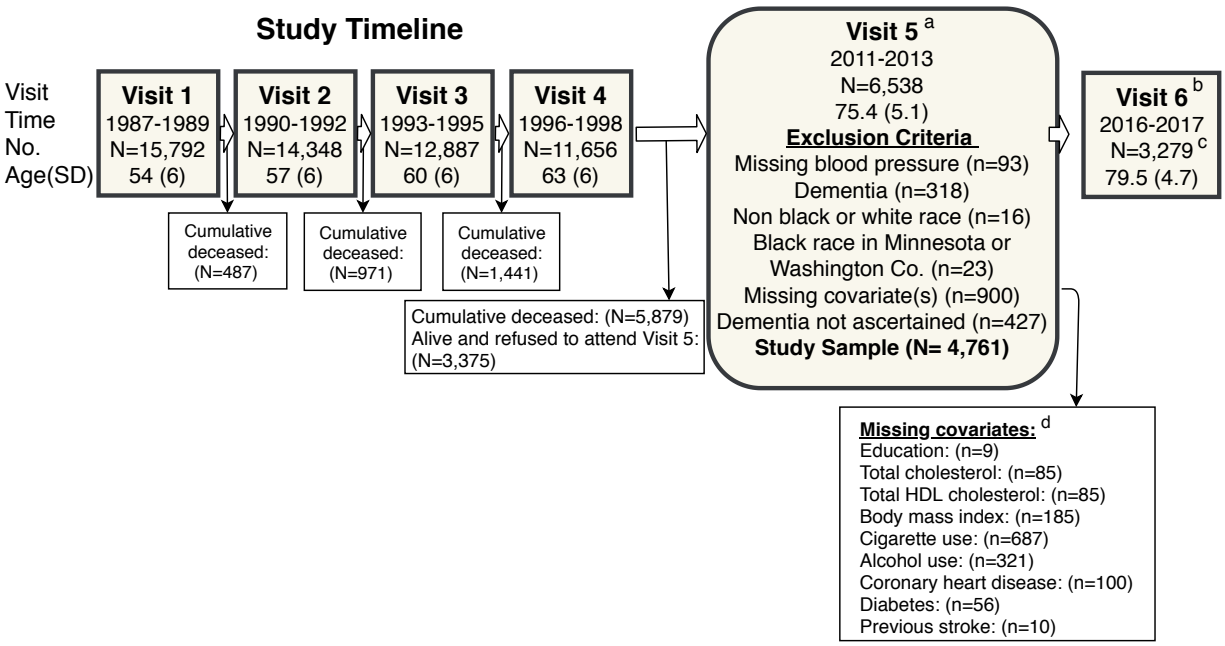
Variable	Hazard Ratio (95% CI)	
	Incident dementia (full sample) N=4,738	Incident dementia (attended Visit 6) N=3,264
Female	0.72 (0.59, 0.88)	0.60 (0.43, 0.85)
Black	1.38 (1.07, 1.79)	1.34 (0.85, 2.11)
Visit 5 Age		
65-70	1 [Reference]	1 [Reference]
71-75	1.76 (1.20, 2.57)	1.89 (1.06, 3.36)
76-80	3.36 (2.31, 4.87)	3.29 (1.85, 5.87)
81-85	6.54 (4.48, 9.54)	5.14 (2.80, 9.44)
86-90	10.40 (6.68, 16.20)	5.52 (2.12, 14.37)
Education		
Less than high school	1 [Reference]	1 [Reference]
High school/GED/vocational	0.80 (0.63, 1.02)	0.72 (0.48, 1.09)
College/graduate/ professional	0.53 (0.41, 0.69)	0.42 (0.27, 0.65)
Apolipoprotein E ε4 alleles		
0	1 [Reference]	1 [Reference]
≥1	1.53 (1.27, 1.84)	1.57 (1.15, 2.14)
Visit 5 BMI		
Underweight	2.93 (1.69, 5.06)	--
Normal	1 [Reference]	1 [Reference]
Overweight	0.78 (0.62, 0.98)	0.79 (0.54, 1.17)
Obese	0.68 (0.53, 0.88)	0.76 (0.50, 1.16)
Visit 5 total cholesterol, mg/dl		
<200	1 [Reference]	1 [Reference]
200 to 239	0.99 (0.78, 1.26)	0.92 (0.61, 1.37)
≥240	1.57 (1.14, 2.16)	1.58 (0.92, 2.69)
HDL-c, mg/dl		
<40	1 [Reference]	1 [Reference]
40-59	1.14 (0.89, 1.46)	1.56 (0.98, 2.48)
≥60	1.19 (0.87, 1.63)	1.73 (0.98, 3.05)
Visit 5 Medical Comorbidity		
Diabetes mellitus	1.24 (1.01, 1.51)	1.00 (0.70, 1.44)
Coronary heart disease	1.06 (0.83, 1.37)	1.01 (0.65, 1.56)
Heart failure	1.41 (1.00, 1.99)	1.12 (0.56, 2.25)
Stroke	1.79 (1.25, 2.56)	1.38 (0.71, 2.70)
Cigarette Smoking Status		
Current	1.27 (0.85, 1.90)	1.11 (0.54, 2.29)
Former	1.00 (0.82, 1.22)	0.94 (0.67, 1.32)
Never	1 [Reference]	1 [Reference]
Alcohol Consumption		
Current	0.63 (0.48, 0.81)	0.52 (0.34, 0.80)
Former	1.01 (0.80, 1.28)	0.83 (0.55, 1.23)
Never	1 [Reference]	1 [Reference]

All models are unadjusted.
HR = hazard ratio

eTable 16. Visit 4 to 5 antihypertensive medication use according to mid- to late-life standard hypertension definition blood pressure patterns

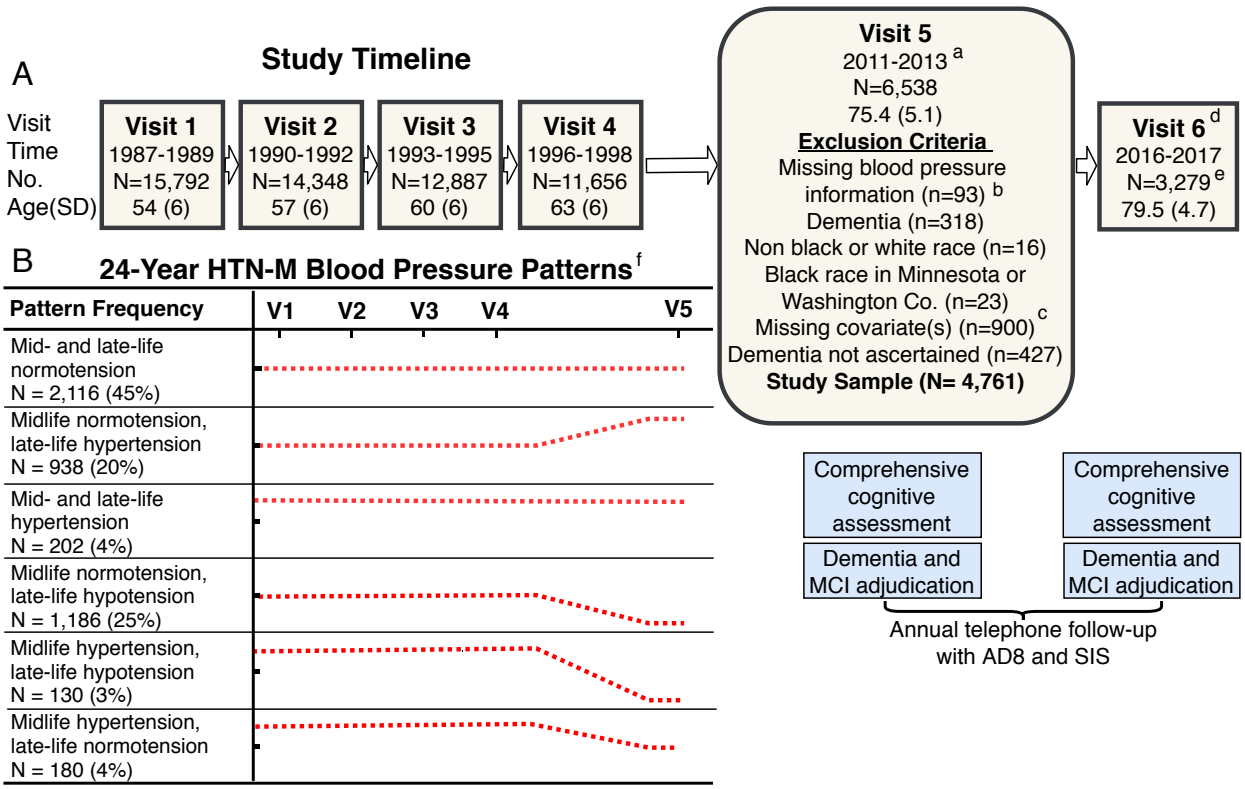
24-year blood pressure patterns	No medication N=1,503	Stable medication N=410	Decreasing medication N=241	Increasing medication N=2,584
Mid- and late-life normotension, N=833	650 (78.0%)	17 (2.0%)	11 (1.3%)	155 (18.6%)
Midlife normotension, late-life hypertension, N=1,559	455 (29.2%)	68 (4.4%)	43 (2.8%)	993 (63.7%)
Mid- and late-life hypertension, N=1,030	43 (4.2%)	221 (21.5%)	116 (11.3%)	650 (63.1%)
Midlife normotension, late-life hypotension, N=927	345 (37.2%)	39 (4.2%)	27 (2.9%)	516 (55.7%)
Midlife hypertension, late-life hypotension, N=389	10 (2.6%)	65 (16.7%)	44 (11.3%)	270 (69.4%)

Values are displayed as frequencies and (row percentages). Participants with midlife hypertension/late-life normotension were not included in the standard hypertension definition analyses because of small sample size (n=23).



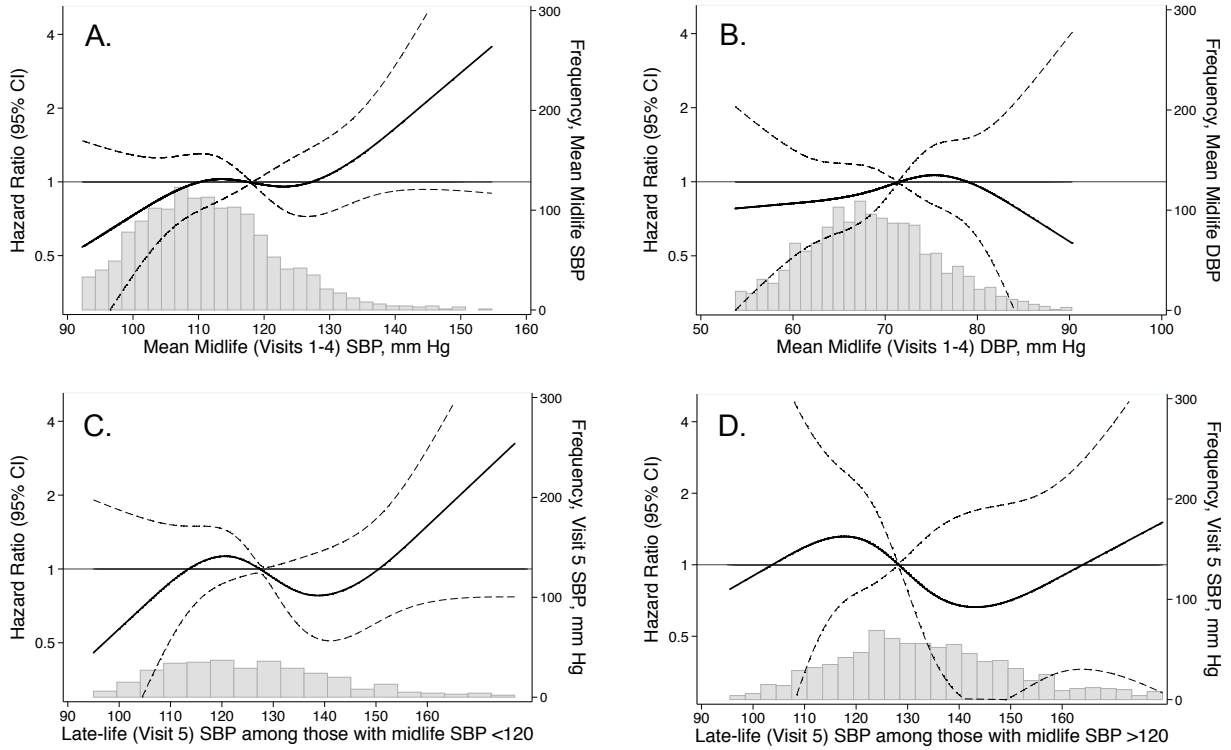
eFigure 1. Study flowchart with detailed study attrition and exclusion information

[a] Of the participants who attended Visit 4, 3,304 participants and 2,247 participants died before Visit 5 and did not attend Visit 5, respectively. There were 433 participants who did not attend Visit 4, but attended Visit 5.
[b] Of the participants in the analytic sample who attended Visit 5, 198 participants and 1,284 participants died before Visit 6 and did not attend Visit 6, respectively.
[c]This number was derived from the subset of participants included in the analytic sample. In total, 4,003 participants attended Visit 6.
[d] A subset of participants were missing information for more than one covariate; these values are not mutually exclusive.



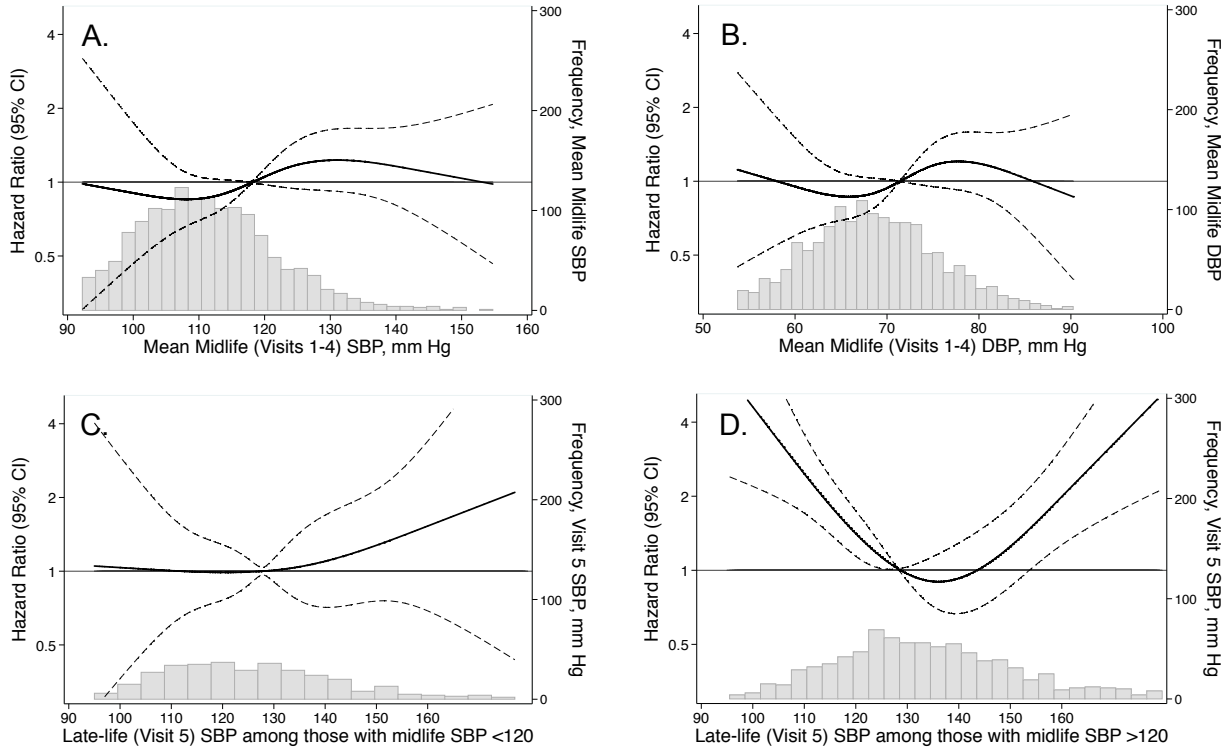
eFigure 2. Study flowchart and longitudinal measured hypertension definition blood pressure patterns

(A) Study design and primary exclusion criteria. (B) Blood pressure pattern groups based on blood pressure levels at Visits 1 to 5. Dotted lines represent the approximate 24-year blood pressure pattern. Hypertension was defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg. Hypotension was defined as systolic blood pressure <90 or diastolic blood pressure <60, irrespective of current antihypertensive medication use or hypertension diagnosis.
AD8 = Ascertain Dementia 8-Item Questionnaire; BP = blood pressure; MCI = mild cognitive impairment; SIS = Six Item Screener; V=Visit
[a] Of the participants who attended Visit 4, 3,304 participants and 2,247 participants died before Visit 5 and did not attend Visit 5, respectively. There were 433 participants who did not attend Visit 4, but attended Visit 5.
[b] Participants missing blood pressure or antihypertensive medication use information necessary to determine Visit 5 hypertension status using the standard hypertension criteria were excluded.
[c] Participants were excluded for missing education (n=9), total cholesterol (n=85), total HDL cholesterol (n=85), BMI (n=185), smoking status (n=687), drinking status (n=321), coronary heart disease (n=100), diabetes (n=56), and previous stroke (n=10). A subset of participants were missing information for more than one covariate; these values are not mutually exclusive.
[d] Of the participants in the analytic sample who attended Visit 5, 198 participants and 1,284 participants died before Visit 6 and did not attend Visit 6, respectively.
[e] This number was derived from the subset of participants included in the analytic sample. In total, 4,003 participants attended Visit 6.
[f] Blood pressure patterns were defined using the measured blood pressure definition. Midlife hypertension was defined as meeting hypertension criteria for two consecutive visits between Visits 1 and 4; persons not meeting this criterion were classified as midlife normotensive. Late-life normotension, hypertension, and hypotension were defined at Visit 5. Participants with missing systolic or diastolic blood pressure at Visit 5 (n=9) were not included in the measured hypertension definition analysis.



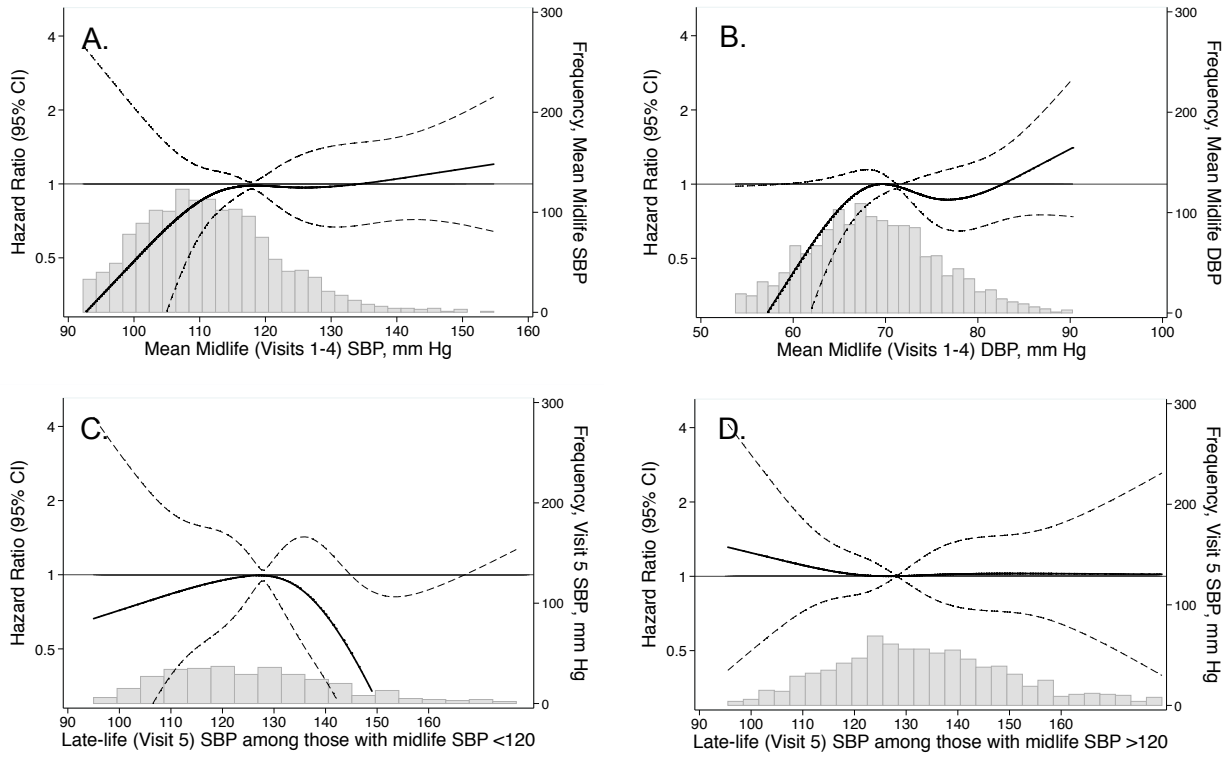
eFigure 3. Adjusted hazard ratios (95% CI) for the association of midlife and late-life blood pressure with incident dementia among participants who did not use antihypertensive medication during midlife or late-life

(A) The association of mean midlife systolic blood pressure (measured at Visits 1-4) with dementia risk (n=1,471). (B) The association of mean midlife diastolic blood pressure (measured at Visits 1-4) with dementia risk (n=1,477). (C) The association of late-life systolic blood pressure with dementia risk among individuals with a mean midlife systolic blood pressure <120 mm Hg (n=1,224). (D) The association of late-life systolic blood pressure with dementia risk among individuals with a mean midlife systolic blood pressure ≥120 mm Hg (n= 257). Hazard ratios (solid line) and 95% confidence intervals (dashed lines) are derived from Cox proportional hazard regression models adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. Models used to examine late-life blood pressure were also adjusted for mean midlife systolic blood pressure. Systolic blood pressure values were centered at the sample median and modeled using a restricted cubic spline with knots at the 5th, 35th, 65th, and 95th percentiles. Histograms of time-averaged systolic blood pressure are displayed as solid bars. Participants with extreme blood pressure values (in the bottom 1st and top 99th percentile) were excluded from these analyses. DBP = diastolic blood pressure; SBP = systolic blood pressure



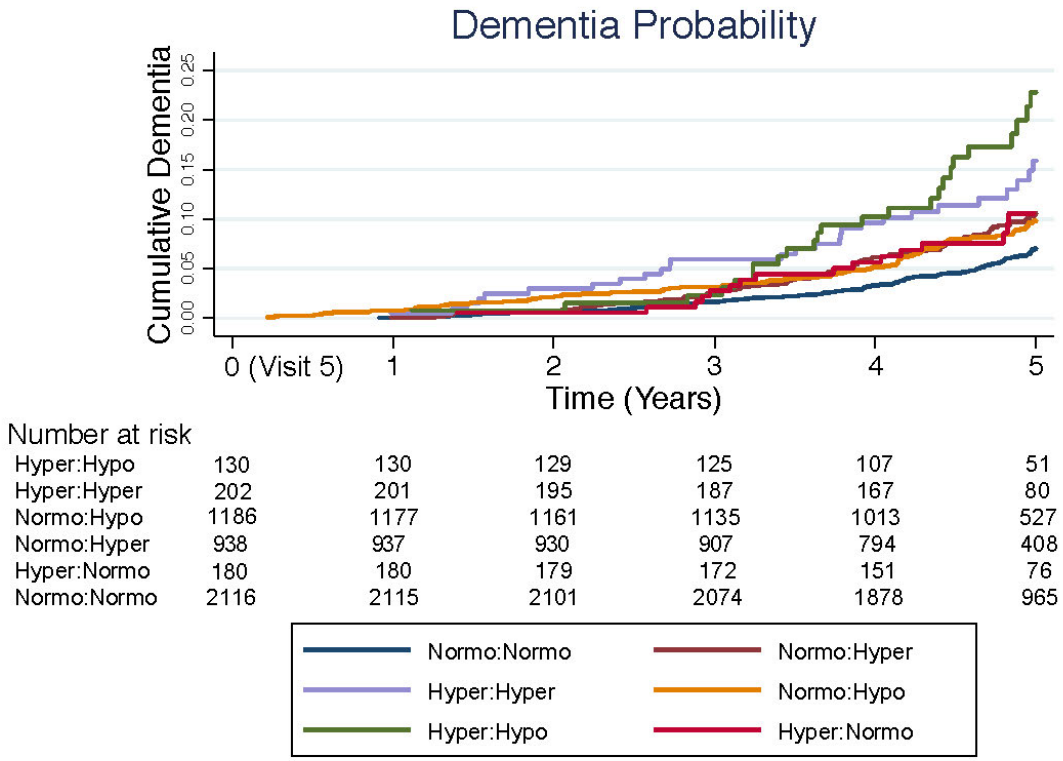
eFigure 4. Adjusted hazard ratios (95% CI) for the association of midlife and late-life blood pressure with incident dementia among participants who only used antihypertensive medication during late-life

(A) The association of mean midlife systolic blood pressure (measured at Visits 1-4) with dementia risk (n=1,837). (B) The association of mean midlife diastolic blood pressure (measured at Visits 1-4) with dementia risk (n=1,869). (C) The association of late-life systolic blood pressure with dementia risk among individuals with a mean midlife systolic blood pressure <120 mm Hg (n=958). (D) The association of late-life systolic blood pressure with dementia risk among individuals with a mean midlife systolic blood pressure ≥120 mm Hg (n= 895). Hazard ratios (solid line) and 95% confidence intervals (dashed lines) are derived from Cox proportional hazard regression models adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. Models used to examine late-life blood pressure were also adjusted for mean midlife systolic blood pressure. Systolic blood pressure values were centered at the sample median and modeled using a restricted cubic spline with knots at the 5th, 35th, 65th, and 95th percentiles. Histograms of time-averaged systolic blood pressure are displayed as solid bars. Participants with extreme blood pressure values (in the bottom 1st and top 99th percentile) were excluded from these analyses. DBP = diastolic blood pressure; SBP = systolic blood pressure



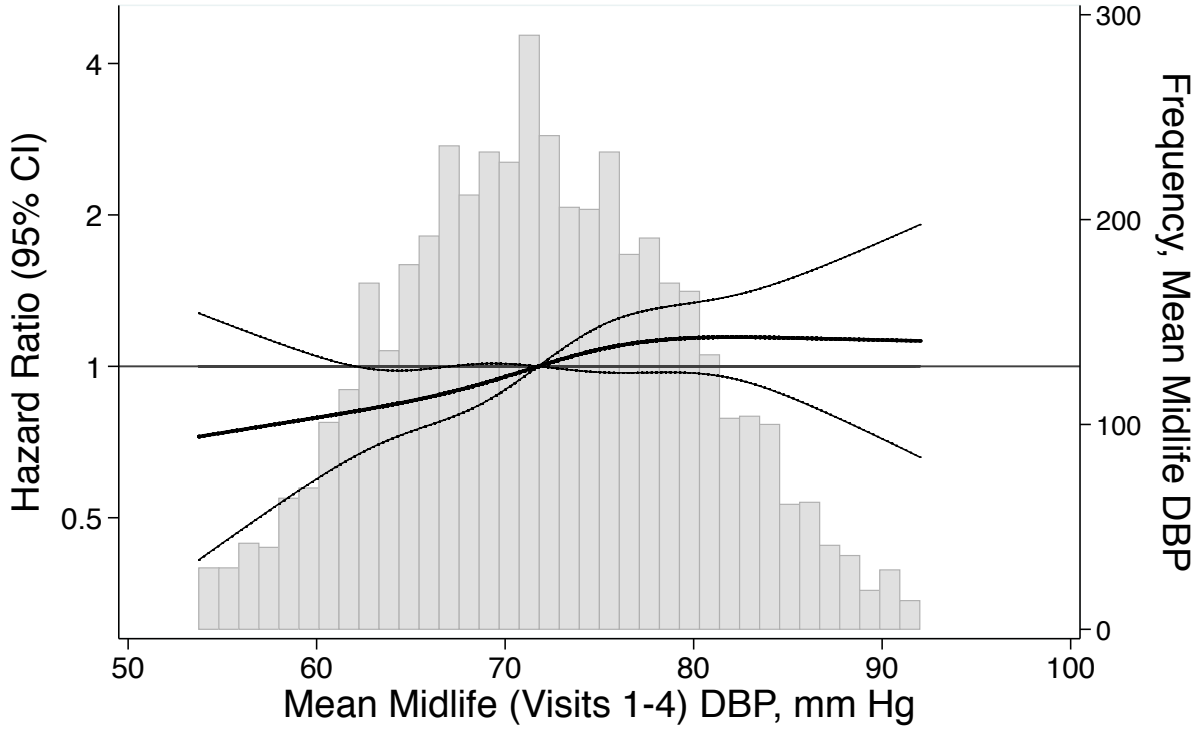
eFigure 5. Adjusted hazard ratios (95% CI) for the association of midlife and late-life blood pressure with incident dementia among participants who used antihypertensive medication during midlife and late-life

(A) The association of mean midlife systolic blood pressure (measured at Visits 1-4) with dementia risk (n=1,178). (B) The association of mean midlife diastolic blood pressure (measured at Visits 1-4) with dementia risk (n=1,178). (C) The association of late-life systolic blood pressure with dementia risk among individuals with a mean midlife systolic blood pressure <120 mm Hg (n=331). (D) The association of late-life systolic blood pressure with dementia risk among individuals with a mean midlife systolic blood pressure ≥120 mm Hg (n= 844). Hazard ratios (solid line) and 95% confidence intervals (dashed lines) are derived from Cox proportional hazard regression models adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5. Models used to examine late-life blood pressure were also adjusted for mean midlife systolic blood pressure. Systolic blood pressure values were centered at the sample median and modeled using a restricted cubic spline with knots at the 5th, 35th, 65th, and 95th percentiles. Histograms of time-averaged systolic blood pressure are displayed as solid bars. Participants with extreme blood pressure values (in the bottom 1st and top 99th percentile) were excluded from these analyses. DBP = diastolic blood pressure; SBP = systolic blood pressure



eFigure 6. Kaplan-Meier curves for time to dementia onset for measured hypertension definition blood pressure groups

Kaplan-Meier curves for time to dementia onset in the full analytic sample (N=4,752) based on 24-year middle- to late-life blood pressure patterns as defined using measured hypertension definition criteria. Participants with missing systolic or diastolic blood pressure at Visit 5 (n=9) were not included in the measured hypertension definition analysis.
Hyper:Hyper = mid- and late-life hypertension; Hyper:Hypo = midlife hypertension, late-life hypotension; Hyper:Normo = midlife hypertension, late-life normotension; Normo:Hyper = midlife normotension, late-life hypertension; Normo:Hypo = midlife normotension, late-life hypotension; Normo:Normo = mid-and late-life normotension.



eFigure 7. Adjusted hazard ratios (95% CI) for the association of mean midlife diastolic blood pressure with incident dementia

Hazard ratios (solid line) and 95% confidence intervals (dashed lines) are derived from a Cox proportional hazard regression model adjusted for baseline age, sex, race-center, education, and *APOE* ε4 status, and BMI, total cholesterol, HDL-c, cigarette smoking and alcohol use status, and prevalent diabetes, coronary heart disease, heart failure, and previous stroke defined at Visit 5 (n=4,663). Mean midlife blood pressure was defined based on blood pressure measurements obtained at Visits 1-4. Mean midlife blood pressure values were centered at the median and modeled using a restricted cubic spline, with knots at the 5th, 35th, 65th, and 95th percentiles. Histograms of mean midlife blood pressure are displayed as solid bars.
DBP = diastolic blood pressure

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