

## DATA SUPPLEMENT

### Early but Not Late Onset Hypertension is Related to Midlife Cognitive Function

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Short title: Early-Onset Hypertension and Cognition

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**Table S1.** Comparison of characteristics between study sample and excluded participants at baseline (Year 0).

Characteristic	N(included/ excluded)	Included participants	Excluded participants	p-value
Age, years (SD)	2946/2167	25.0 (3.6)	24.6 (3.7)	<0.001
Women, (%)	2946/2167	1689 (57.3)	1097 (50.6)	<0.001
Black race, n (%)	2946/2165	1373 (46.6)	1269 (58.6)	<0.001
Body mass index, kg/m <sup>2</sup>	2937/2159	20.6 (4.0)	21.0 (4.4)	<0.01
Current smoker, n (%)	2930/2147	740 (25.3)	804 (37.5)	<0.001
Total cholesterol, mmol/l	2922/2142	4.6 (0.9)	4.6 (0.9)	0.07
HDL-cholesterol, mmol/l	2922/2142	1.4 (0.3)	1.4 (0.4)	<0.001
Systolic blood pressure, mmHg	2946/2167	110 (10)	111 (11)	<0.001
Diastolic blood pressure, mmHg	2946/2167	68.2 (9.0)	68.5 (10.2)	0.26
Antihypertensive medication use, n (%)	2944/2163	53 (1.8)	62 (2.9)	<0.05
Diabetes, n (%)	2946/2167	9 (0.3)	21 (1.0)	<0.01
Alcohol intake, ml/day (median, IQR)	2935/2157	4.8 (0-14.5)	4.8 (0-15.1)	<0.001
Education, years	2946/2164	13.9 (1.8)	13.2 (1.8)	<0.001
Sedentary time, h/day	N/A	N/A	N/A	

SD, standard deviation; IQR, interquartile range, BMI, body mass index; HDL, high density lipoprotein. Sedentary behavior time was not assessed at baseline.

**Table S2.** Mean unadjusted brain MRI measures at Year 30 exam according to hypertension onset age.

	All	HTN Onset Age			No HTN	p-value
		<35 y	35–44 y	≥45 y		
N	599	18	41	78	462	-
Total brain volume, cm <sup>3</sup>	1162 (123)	1061 (108)	1130 (121)	1141 (118)	1172 (123)	<0.001
White matter volume, cm <sup>3</sup>	529 (65)	485 (63)	518 (60)	521 (64)	533 (64)	0.005
Grey matter volume, cm <sup>3</sup>	633 (64)	576 (54)	612 (66)	620 (60)	639 (64)	<0.001
AWM volume, cm <sup>3</sup> (median, IQR)	0.55 (0.25–1.17)	0.46 (0.29–1.62)	0.93 (0.32–2.17)	0.69 (0.29–1.45)	0.52 (0.23–1.12)	0.25
WMFA	0.30 (0.02)	0.30 (0.02)	0.30 (0.02)	0.30 (0.02)	0.31 (0.02)	0.05

Values are reported as mean (SD) unless otherwise stated. HTN, hypertension; y, years; AWM, abnormal white matter; IQR, interquartile range; WMFA, white matter fractional anisotropy.

**Table S3.** Association between hypertension onset age and cognitive performance at Year 30 by sex.

Age of HTN onset	N	Cognitive function tests				
		RAVLT	DSST	Stroop test	Composite cognitive score	MoCA
<b>Men</b>						
	1257					
<35 years	53	-0.18±0.14	-0.25±0.12‡	-0.22±0.15	-0.22±0.09‡	-0.22±0.13
35–44 years	115	0.00±0.11	0.06±0.10	-0.10±0.12	-0.01±0.07	-0.08±0.10
≥45 years	186	-0.05±0.10	-0.15±0.08	-0.22±0.10‡	-0.14±0.07‡	-0.02±0.09
No HTN	903	Ref.	Ref.	Ref.	Ref.	Ref.
<b>Women</b>						
	1689					
<35 years	59	-0.03±0.13	-0.26±0.13‡	-0.24±0.13	-0.18±0.09§	-0.33±0.12†
35–44 years	162	-0.12±0.09	-0.10±0.09	-0.07±0.10	-0.09±0.07	-0.08±0.09
≥45 years	240	-0.02±0.08	-0.01±0.08	-0.01±0.08	-0.01±0.06	0.08±0.08
No HTN	1228	Ref.	Ref.	Ref.	Ref.	Ref.

Data presented as beta ( $\beta$ ) with standard error. All models are adjusted for age, race, education, diabetes, body mass index, smoking, alcohol intake, sedentary time, use of antihypertensive medication, and systolic blood pressure. \* $P < 0.001$ , † $P < 0.01$ , ‡ $P < 0.05$ , § $P = 0.05$ . HTN, hypertension; DSST, Digit Symbol Substitution test; RAVLT, Rey Auditory Verbal Learning test; MoCA, Montreal Cognitive Assessment.

**Table S4.** Association between hypertension onset age and cognitive performance at Year 30 according by race.

Age of HTN onset	N	Cognitive function tests				
		RAVLT	DSST	Stroop test	Composite cognitive score	MoCA
<b>Black race</b>						
<35 years	87	-0.14±0.11	-0.21±0.11	-0.11±0.14	-0.16±0.09	-0.24±0.12‡
35–44 years	203	-0.13±0.09	-0.01±0.09	-0.06±0.11	-0.07±0.07	-0.03±0.09
≥45 years	261	-0.09±0.08	-0.07±0.08	-0.08±0.10	-0.08±0.06	0.07±0.09
No HTN	822	Ref.	Ref.	Ref.	Ref.	Ref.
<b>White race</b>						
<35 years	25	-0.13±0.18	-0.24±0.17	-0.47±0.15†	-0.28±0.12‡	-0.30±0.15‡
35–44 years	74	-0.02±0.12	-0.10±0.11	-0.11±0.10	-0.08±0.08	-0.15±0.10
≥45 years	165	0.07±0.10	-0.06±0.09	-0.12±0.08	-0.04±0.06	0.01±0.08
No HTN	1309	Ref.	Ref.	Ref.	Ref.	Ref.

Data presented as beta ( $\beta$ ) with standard error. All models are adjusted for age, race, education, diabetes, body mass index, smoking, alcohol intake, sedentary time, use of antihypertensive medication, and systolic blood pressure. \* $P < 0.001$ , † $P < 0.01$ , ‡ $P < 0.05$ . HTN, hypertension; DSST, Digit Symbol Substitution test; RAVLT, Rey Auditory Verbal Learning test; MoCA, Montreal Cognitive Assessment.

**Table S5.** Association between hypertension onset age and cognitive performance at Year 30 using an alternative age of hypertension onset definition.

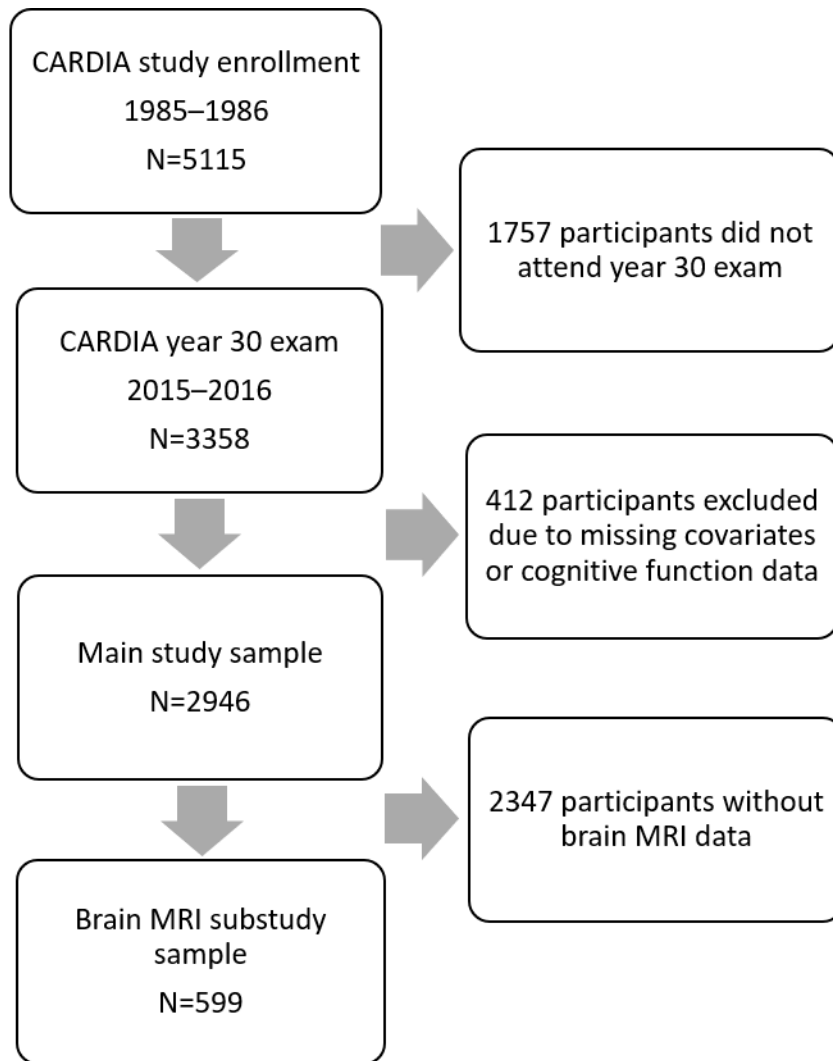
Age of HTN onset	N	Cognitive function tests				
		RAVLT	DSST	Stroop test	Composite cognitive score	MoCA
<b>Unadjusted model</b>						
<35 years	64	-0.54±0.12*	-0.74±0.12*	-0.33±0.12†	-0.54±0.09*	-0.63±0.12*
35–44 years	74	-0.57±0.12*	-0.55±0.11*	-0.54±0.11*	-0.56±0.09*	-0.54±0.11*
≥45 years	95	-0.32±0.10†	-0.49±0.10*	-0.49±0.10*	-0.43±0.08*	-0.42±0.10*
No HTN	2713	Ref.	Ref.	Ref.	Ref.	Ref.
<b>Minimally adjusted model</b>						
<35 years	64	-0.17±0.11	-0.36±0.11*	-0.11±0.11	-0.21±0.08†	-0.24±0.10‡
35–44 years	74	-0.24±0.10‡	-0.21±0.10‡	-0.31±0.11†	-0.25±0.07*	-0.14±0.09
≥45 years	95	0.00±0.09	-0.15±0.09	-0.24±0.09†	0.13±0.06‡	-0.02±0.08
No HTN	2713	Ref.	Ref.	Ref.	Ref.	Ref.
<b>Fully adjusted model</b>						
<35 years	64	-0.07±0.11	-0.25±0.11‡	-0.04±0.12	-0.12±0.08	-0.15±0.10
35–44 years	74	-0.15±0.10	-0.11±0.10	-0.23±0.11‡	-0.17±0.07‡	-0.04±0.10
≥45 years	95	0.08±0.09	-0.07±0.09	-0.14±0.10	-0.04±0.06	0.08±0.09
No HTN	2713	Ref.	Ref.	Ref.	Ref.	Ref.

Hypertension onset age defined here only as BP≥140/90 on two consecutive visits without considering antihypertensive medication use. Data presented as beta ( $\beta$ ) with standard error. Minimally adjusted model is adjusted for age, race, and education. Fully adjusted model age, race, education, diabetes, body mass index, smoking, alcohol intake, sedentary time, use of antihypertensive medication, and systolic blood pressure. \*P<0.001, †P<0.01, ‡P<0.05. HTN, hypertension; DSST, Digit Symbol Substitution test; RAVLT, Rey Auditory Verbal Learning test; MoCA, Montreal Cognitive Assessment.

**Table S6.** Association ( $\beta \pm SE$ ) of hypertension onset age with structural brain changes at Year 30.

Age of hypertension onset	Total brain volume	White matter volume	Grey matter volume	AWM volume	WMFA
N	599	599	599	599	599
Unadjusted model					
<35 years	-0.90±0.24*	-0.76±0.24†	-0.97±0.23*	0.06±0.24	-0.23±0.23
35–44 years	-0.34±0.16‡	-0.24±0.16	-0.41±0.16‡	0.29±0.16	-0.27±0.16
≥45 years	-0.25±0.12‡	-0.19±0.12	-0.30±0.12‡	0.14±0.12	-0.26±0.12‡
No hypertension	Ref.	Ref.	Ref.	Ref.	Ref.
Minimally adjusted model					
<35 years	-0.08±0.07	0.04±0.08	-0.19±0.11	-0.02±0.25	0.05±0.23
35–44 years	-0.02±0.05	0.04±0.05	-0.08±0.08	0.20±0.17	-0.15±0.16
≥45 years	-0.06±0.04	-0.03±0.04	-0.07±0.06	0.08±0.13	-0.18±0.12
No hypertension	Ref.	Ref.	Ref.	Ref.	Ref.
Fully adjusted model					
<35 years	-0.08±0.08	0.09±0.09	-0.24±0.13	-0.21±0.27	0.22±0.26
35–44 years	-0.02±0.06	0.07±0.07	-0.10±0.09	0.04±0.20	0.01±0.19
≥45 years	-0.04±0.05	0.01±0.06	-0.09±0.08	-0.14±0.17	0.03±0.16
No hypertension	Ref.	Ref.	Ref.	Ref.	Ref.

Values are for 1-SD difference estimate (beta) with standard error. Minimally adjusted model is adjusted for intracranial volume, age, sex, race, and education. Fully adjusted model is adjusted for intracranial volume, age, sex, race, education, diabetes, body mass index, smoking, alcohol intake, sedentary time, use of antihypertensive medication, and systolic blood pressure. \* $P < 0.001$ , † $P < 0.01$ , ‡ $P < 0.05$ . AWM, abnormal white matter; WMFA, white matter fractional anisotropy.



**Figure S1.** Study flow chart illustrating the flow of the CARDIA study participants through follow-up and the excluded participants.