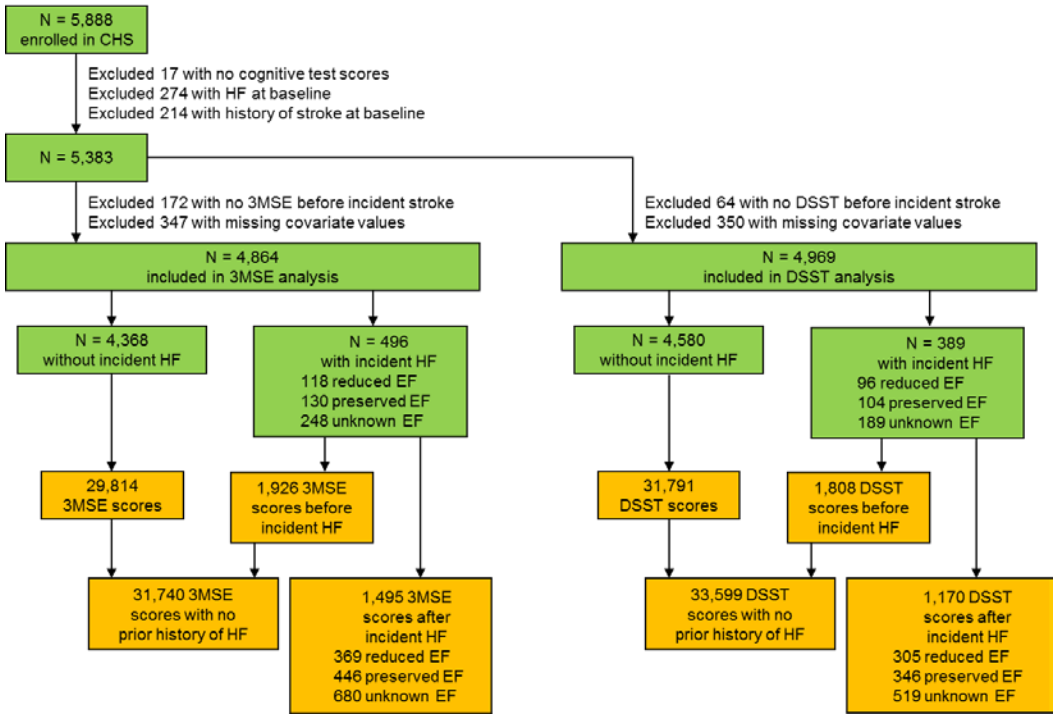
SUPPLEMENTAL MATERIAL

Supplemental Figure 1. Flowchart of participants and cognitive test scores for analysis



Summary of cognitive test scores not obtained or not analyzed due to censoring or missed exams during follow-up:

	3MSE analysis (n = 4,864 participants included)			DSST analysis (n = 4,969 participants included)		
	Overall	**No prior history of HF**	**After incident HF**	**Overall**	**No prior history of HF**	**After incident HF**
Number of potential scores if there were no censoring	36,759 (100%)	34,854 (100%)	1,905 (100%)	41,348 (100%)	39,400 (100%)	1,948 (100%)
Scores obtained and analyzed	34,854 (90.4%)	31,740 (91.1%)	1,495 (78.5%)	34,769 (84.1%)	33,599 (85.3%)	1,170 (60.1%)
Scores not obtained						
Censoring: death	4 (0.0%)	4 (0.0%)	0 (0.0%)	4 (0.0%)	4 (0.0%)	0 (0.0%)
Censoring: dropout	965 (2.6%)	825 (2.4%)	140 (7.3%)	4,389 (10.6%)	3,823 (9.7%)	566 (29.1%)
Intermittently missed exam	1,682 (4.6%)	1,555 (4.5%)	127 (6.7%)	1,403 (3.4%)	1,306 (3.3%)	97 (5.0%)
Scores obtained; not analyzed						
Censoring: incident stroke	873 (2.4%)	730 (2.1%)	143 (7.5%)	783 (1.9%)	668 (1.7%)	115 (5.9%)

Abbreviations: 3MSE = Modified Mini-Mental State Examination; CHS = Cardiovascular Health Study; DSST = Digit Symbol Substitution Test; EF = ejection fraction; HF = heart failure.

Participants with only one cognitive assessment: Of 4,864 participants included in the 3MSE analysis, 215 (4%) contributed only one 3MSE score to the analysis. Of 4,969 participants included in the DSST analysis, 293 (6%) contributed only one DSST score to the analysis.

Missing covariate values: In the 3MSE analysis, of 347 participants excluded due to missing covariate values, 183 (53%) were missing chronic obstructive pulmonary disease, another 74 (21%) were missing diabetes, and the remaining 90 (26%) were missing other covariates. In the DSST analysis, of 350 participants excluded due to missing covariate values, 188 (54%) were missing chronic obstructive pulmonary disease, another 77 (22%) were missing diabetes, and the remaining 85 (24%) were missing other covariates.

3MSE scores estimated from telephone-based cognitive assessments: In the 3MSE analysis, 1,163 3MSE scores with no prior history of HF and 163 3MSE scores after incident HF were estimated from telephone-based measures of global cognitive performance.[1]

Supplemental Table 1. Characteristics at study enrollment and incident conditions by incident heart failure (HF) status for participants included in analysis of Digit Symbol Substitution Test (DSST)*

Characteristic†	Participants diagnosed with incident HF during follow-up (N = 389)	Participants not diagnosed with incident HF during follow-up (N = 4,580)
Age, y, mean (SD)	74.6 (5.8)	72.9 (5.3)
Birth year, mean (SD)	1915 (5.9)	1917 (5.4)
Male, %	52.7	40.8
Black race, %	9.5	14.0
Years of education through 12th grade, mean (SD)	10.9 (2.0)	11.0 (1.9)
Any education beyond 12th grade, %	43.2	43.9
Former smoking, %	44.7	41.6
Current smoking, %	11.6	11.9
Any current alcohol use, %	44.5	52.2
Drinks/week, mean (SD)	4.6 (7.2)	5.1 (8.6)
Beta-blocker use, %	18.0	12.2
Angiotensin converting enzyme inhibitor use, %	6.4	6.1
Systolic blood pressure, mm Hg, mean (SD)	140.3 (22.1)	135.6 (21.4)
Body mass index, kg/m^2, mean (SD)	27.5 (4.8)	26.5 (4.6)
Chronic kidney disease, %	44.0	37.1
Chronic obstructive pulmonary disease, %	16.5	12.2
Anemia, %	7.5	7.4
Diabetes		
At enrollment, %	22.9	13.8
Incident, %	8.0	4.1
Hypertension		
At enrollment, %	64.3	56.4
Incident, %	22.6	20.8
Coronary heart disease		
At enrollment, %	32.4	15.5
Incident, %	31.9	6.7
Atrial fibrillation		
At enrollment, %	5.1	1.7
Incident, %	37.5	6.3

* The 4,969 participants included in this table (389 + 4,580) had at least one Digit Symbol Substitution Test (DSST) score and were included in regression models for DSST.

† All percentages in the table are column percentages. Mean drinks per week was calculated among participants who reported any current alcohol use. For diabetes, hypertension, coronary heart disease, and atrial fibrillation, percentages of participants with the condition present at enrollment and of those with the incident condition occurring during follow-up were mutually exclusive and therefore sum to the total percentage of participants with the condition either present at enrollment or occurring during follow-up (mean of 6.5 years). Incident diabetes, hypertension, coronary heart disease, or atrial fibrillation may have occurred before or after incident HF diagnosis.

Supplemental Table 2. Coefficients and standard errors from regression models

	3MSE analysis		DSST analysis	
	Estimate	**Standard error**	**Estimate**	**Standard error**
Intercept	74.712	0.660	14.964	0.959
Age, per year*	-0.550	0.026	-0.529	0.019
Age-squared	-0.055	0.003	-0.037	0.002
Incident HF, yes vs no	-0.861	0.366	-1.227	0.422
Time since incident HF diagnosis, per year	-0.500	0.157	-0.293	0.167
Age × incident HF	-0.034	0.065	0.004	0.075
Age-squared × incident HF	-0.002	0.006	0.009	0.007
Age × time since incident HF diagnosis	-0.012	0.036	0.018	0.039
Age-squared × time since incident HF diagnosis	-0.004	0.003	-0.004	0.003
Birth year, per year*	0.065	0.032	0.431	0.035
Male vs female	-1.010	0.197	-3.423	0.301
Black race vs white race	-4.812	0.273	-8.856	0.432
Years of education through 12^{th} grade, per year	1.433	0.058	2.164	0.086
Any education beyond 12^{th} grade, yes vs no	1.960	0.205	3.907	0.318
Former smoking, yes vs never smoking	-0.053	0.204	-0.166	0.314
Current smoking, yes vs never smoking	-1.268	0.286	-3.838	0.458
Any current alcohol use, yes vs no	0.717	0.205	2.206	0.316
Drinks/d, per drink*	0.135	0.099	0.015	0.159
Beta-blocker use, yes vs no	0.640	0.274	0.082	0.423
Angiotensin converting enzyme inhibitor use, yes vs no	0.102	0.387	-1.127	0.592
Systolic blood pressure, per mm Hg*	-0.016	0.005	-0.030	0.007
Body mass index, per kg/m^2*	-0.003	0.020	-0.063	0.032
Chronic kidney disease, yes vs no	0.066	0.203	0.115	0.305
Chronic obstructive pulmonary disease, yes vs no	-0.300	0.275	-1.230	0.422
Anemia, yes vs no	-0.674	0.383	-2.542	0.558
Diabetes, yes vs no†	-0.305	0.215	-1.348	0.267
Hypertension, yes vs no†	0.233	0.156	0.186	0.164
Coronary heart disease, yes vs no†	-0.359	0.188	-0.522	0.223
Atrial fibrillation, yes vs no†	-0.200	0.249	-0.829	0.260

Abbreviations: 3MSE = Modified Mini-Mental State Examination; DSST = Digit Symbol Substitution Test; HF = heart failure.

* Age was centered at 77 years. Birth year was centered at 1917. Systolic blood pressure was centered at 135 mm Hg. Body mass index was centered at 26.68 kg/m^2. Drinks per day was drinks per week divided by 7.

† Diabetes, hypertension, coronary heart disease, and atrial fibrillation were time-varying variables, updated at the occurrence of incident diagnosis. All other variables were measured at enrollment.

Supplemental Table 3. Characteristics of four previously published studies with follow-up longer than one year, comparing longitudinal cognitive changes in adults with heart failure versus without heart failure

Study	Participants	Timing of cognitive assessments	Heart failure identification	Handling of prevalent and incident heart failure	Exclusion of participants based on attrition during follow-up	Results: HF significantly associated with faster cognitive decline	Results: HF not significantly associated with rate of cognitive decline
Hjelm, et al: Octogenarian Twin Study (OCTO-twin) within Swedish Twin Registry[2]	Ages ≥ 80 N = 702 95 prevalent HF 96 incident HF 511 no HF	5 assessments spanning 8 years	Medical record review	Prevalent and incident HF grouped together; all cognitive test scores from incident HF cases, including those obtained before HF diagnosis, used to model cognitive trajectories in HF group	No participants excluded based on attrition; all available cognitive test scores used from participants who died or had missing cognitive assessments	Short-term memory: • Digit span Episodic memory: • Prose recall	Processing speed: • Digit symbol substitution • Picture matching Visuospatial ability: • Block design Semantic memory: • Information task • Verbal meaning Episodic memory: • Picture memory • Memory-in-reality
Alwerdt, et al: Advanced Cognitive Training for Independent and Vital Elderly Study (ACTIVE)[3]	Ages ≥ 65 N = 692 35 prevalent HF 37 incident HF 620 no HF	6 assessments spanning 5 years	Participant self-report of being diagnosed with HF by doctor or nurse	Prevalent and incident HF cases analyzed as separate groups; all cognitive test scores from incident HF cases, including those obtained before HF diagnosis, used to model cognitive trajectories in incident HF group	No participants excluded based on attrition; all available cognitive test scores used from participants who died or had missing cognitive assessments	Reasoning: • Word series	Processing speed: • Complex reaction time • Useful field of view • Digit symbol substitution Memory: • Verbal learning • Behavioral memory stories • Auditory verbal learning Reasoning: • Letter sets • Letter series
Almeida, et al: Heart-Mind Study[4]	Ages ≥ 45 N = 158 77 prevalent HF 81 no HF	3 assessments spanning 2 years	Standardized protocol; only participants with LVEF < 0.4 included in HF group	Prevalent HF cases analyzed; no ascertainment of incident HF	No participants excluded based on attrition; all available cognitive test scores used from participants who died or had missing cognitive assessments	Global cognitive ability: • CAMCOG	Processing speed: • Digit copying • Digit coding Memory: • Immediate recall • Short-delayed recall • Long-delayed recall
Verhaegen, et al: Berlin Aging Study (BASE)[5]	Ages ≥ 70 N = 196 101 prevalent HF 49 incident HF 46 no HF	2 assessments spanning 4 years	Standardized protocol	Prevalent and incident HF cases analyzed as separate groups; baseline cognitive test scores obtained before HF diagnosis used to model cognitive change scores in incident HF group	Approximately 300 participants excluded who contributed baseline cognitive data but died or were lost to follow-up prior to second measurement occasion	None	Global cognitive ability: Composite of • Perceptual speed • Episodic memory • Fluency • Knowledge

Abbreviations: CAMCOG = Cambridge Cognitive Examination of the Elderly; HF = heart failure; LVEF = left ventricular ejection fraction.

SUPPLEMENTAL REFERENCES

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5. Verhaegen P, Borchelt M, Smith J. Relation between cardiovascular and metabolic disease and cognition in very old age: cross-sectional and longitudinal findings from the berlin aging study. *Health Psychol*. 2003;22:559-569. doi: 10.1037/0278-6133.22.6.559.