

Hope-3

# The Heart Outcomes Prevention Evaluation (HOPE) – 3 Trial: Cognitive & Functional Outcomes



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For the HOPE-3 Investigators

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## Rationale

- Cognitive impairment & dementia affect 5-7% of those over 60 years
- Elevated BP associated with cognitive impairment
- Statins linked to short term memory loss in observational studies, but not RCTs
- The HOPE-3 study evaluated BP lowering & rosuvastatin use in 12,705 intermediate CV risk:
  - Statin reduced CV events by 25% in all
  - BP lowering reduced CV events by 24% only in those with hypertension
- We evaluated the effect of these interventions on cognitive & functional decline

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# Cognitive Questionnaire Completion (Primary Outcome)



*Participants 70 years+ invited to complete questionnaires*

12,705 Randomized

3,086  $\geq$  70 years

2,361 Completed baseline questionnaire

219 Died

2,142 Alive at study end

1,626 Completed baseline & study end questionnaire (76%)

# Pre-Stated Outcomes: Cognitive & Functional

- **Primary Outcome:** Decline in processing speed (Digit Symbol Substitution Test [DSST])
- **Secondary Outcomes**
  - Decline in executive function (modified Montreal Cognitive Assessment [mMoCA])
  - Increase in psychomotor speed (Trail Making Test Part B [TMT-B])
- **Other Outcomes**
  - Change in function (functional questions [EQ 5D])
  - Study end: Standard Assessment of Global Activities in the Elderly [SAGE])

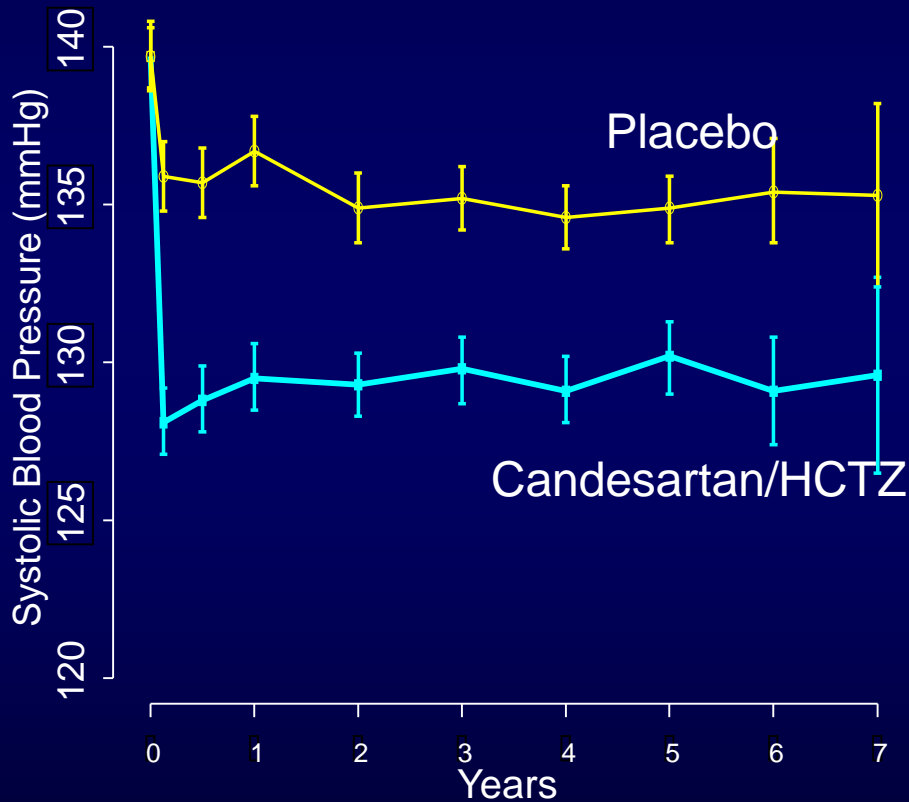
# Baseline Characteristics



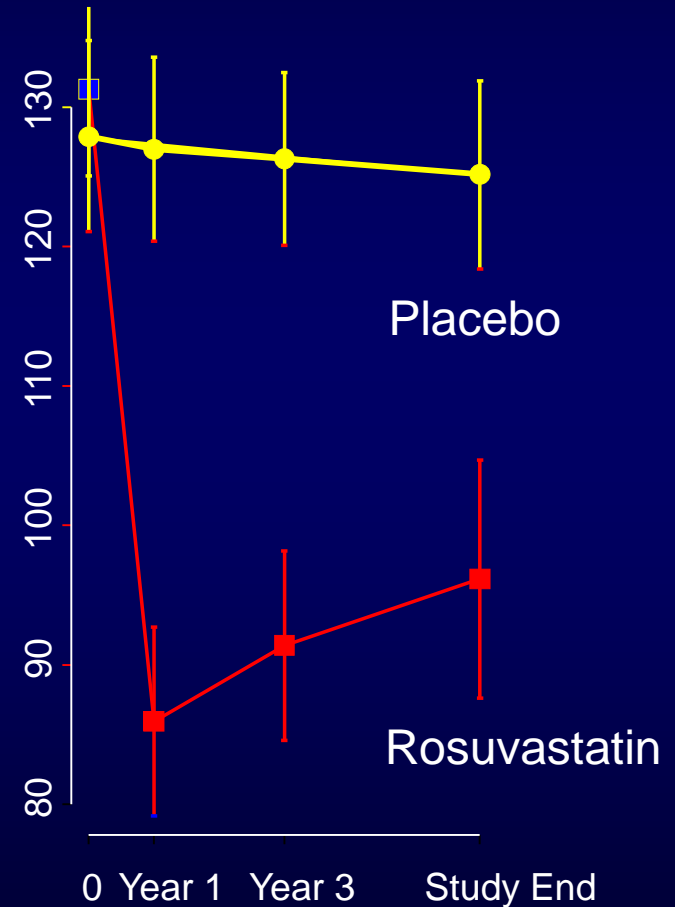
	Baseline + Study End	Baseline Only
Age (yrs, SD)	74 ( $\pm 3.5$ )	75 ( $\pm 4.1$ )
Female	59%	59%
Hypertension	45%	45%
Blood Pressure (mmHg)	140/79	139/79
LDL-Cholesterol (mg/dL)	127	128
Diabetes	6%	6%
Education >12 years	24%	13%
Ethnicity		
White Caucasian	24%	18%
Latin American	36%	54%
Chinese	24%	10%
Other Asian	13%	10%

# SBP and LDL Changes by Treatment Group

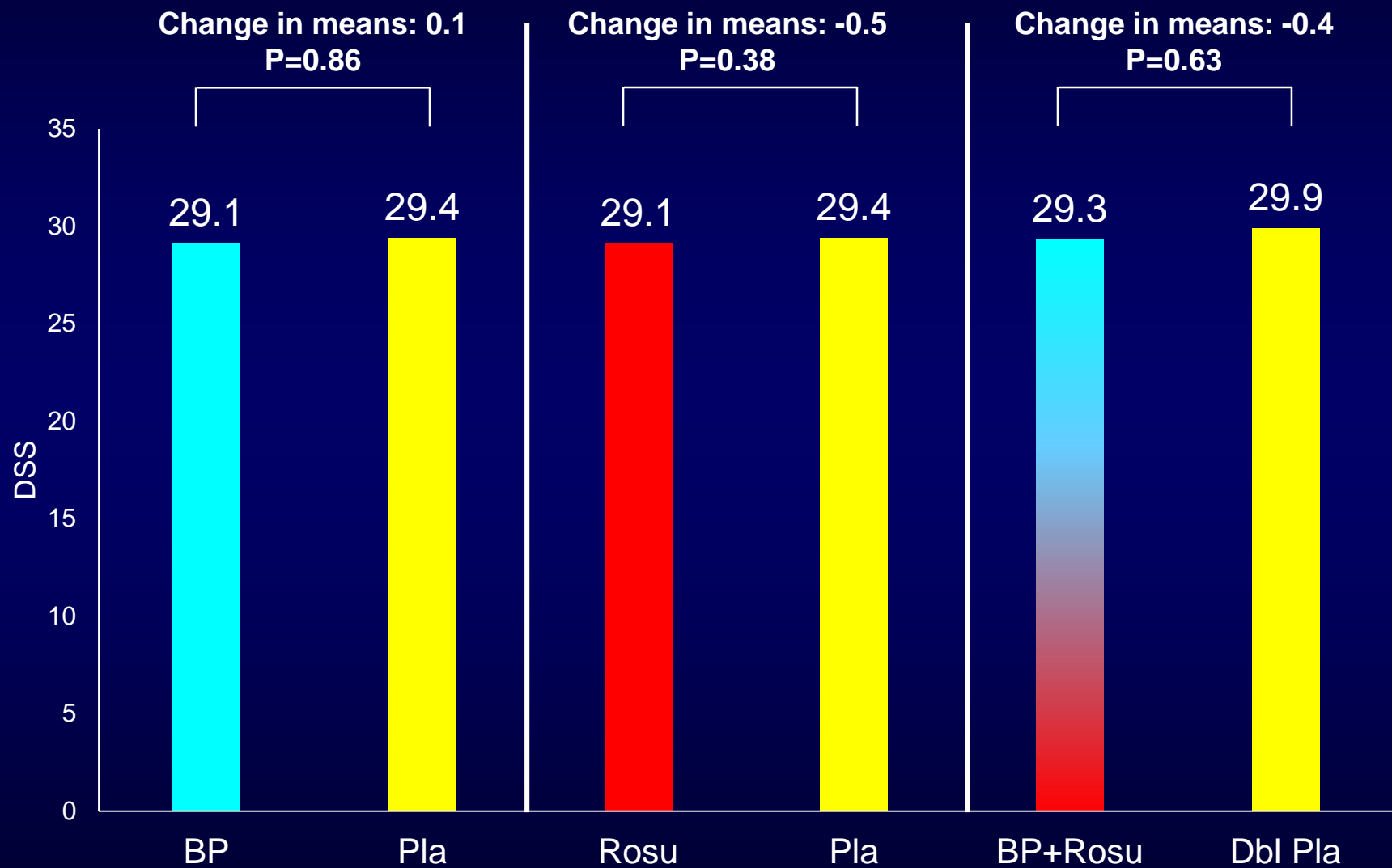
mean  $\Delta$  BP= 6/2.9 mmHg



mean  $\Delta$  24.9 mg/dl



# Study End DSST Score

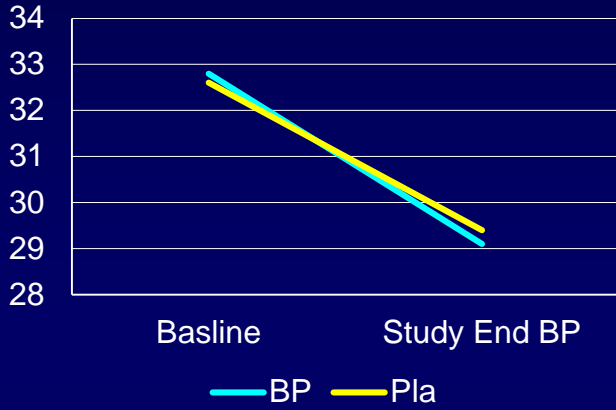


Sensitivity analysis demonstrated similar results

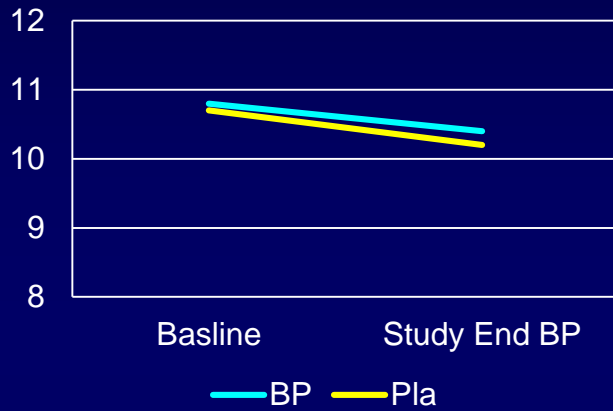
# Change in Cognitive Outcome by Treatment Group

## BP Lowering

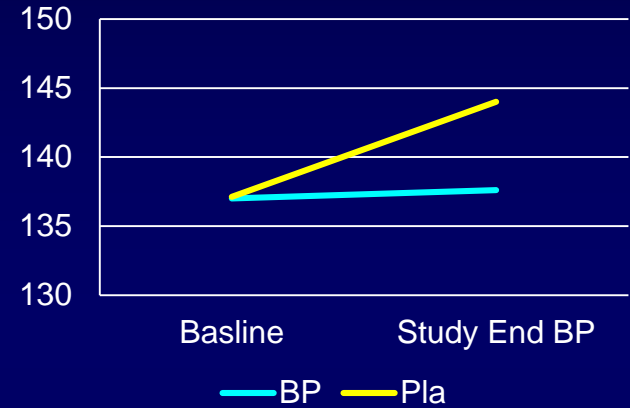
### DSST



### mMoCA

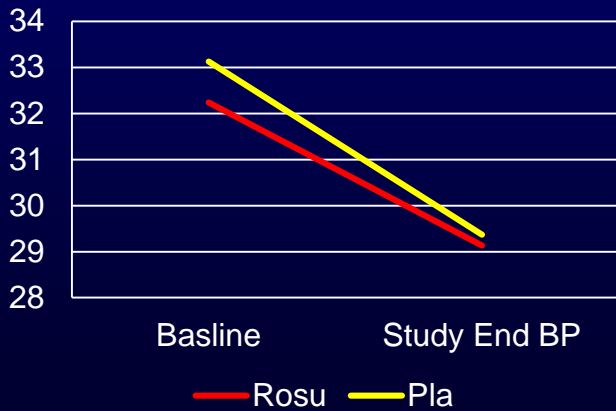


### TMT-B

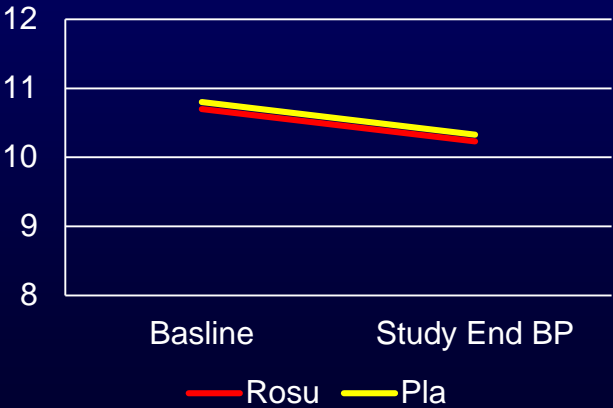


## Cholesterol Lowering

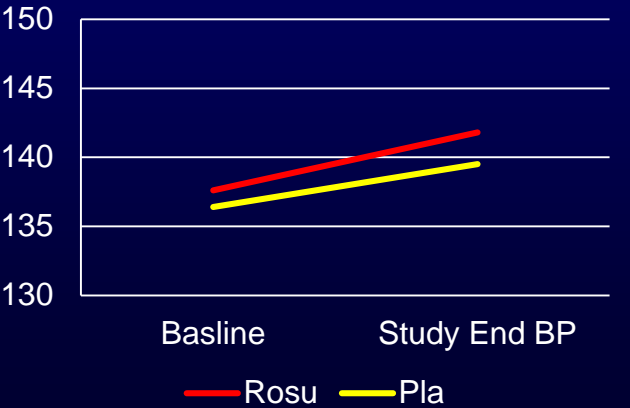
### DSST



### mMoCA



### TMT-B





# BP Lowering in Key Subgroups

## Overall

## Age-years

$\leq 72$  (Mean=71.0)

72-75 (Mean=73.3)

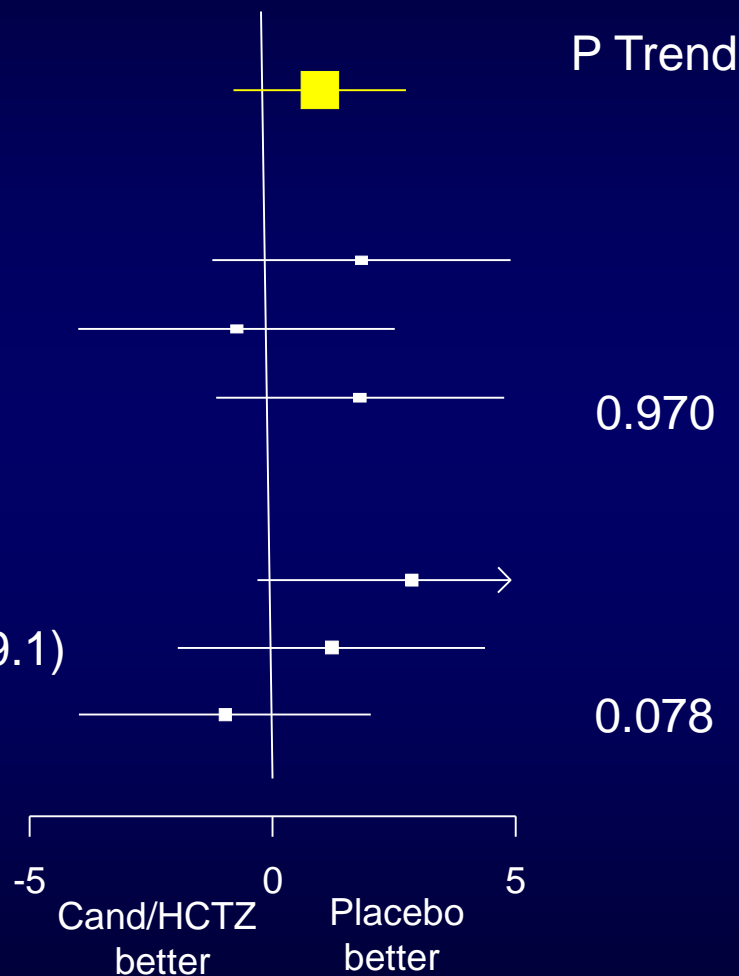
$> 75$  (Mean=78.1)

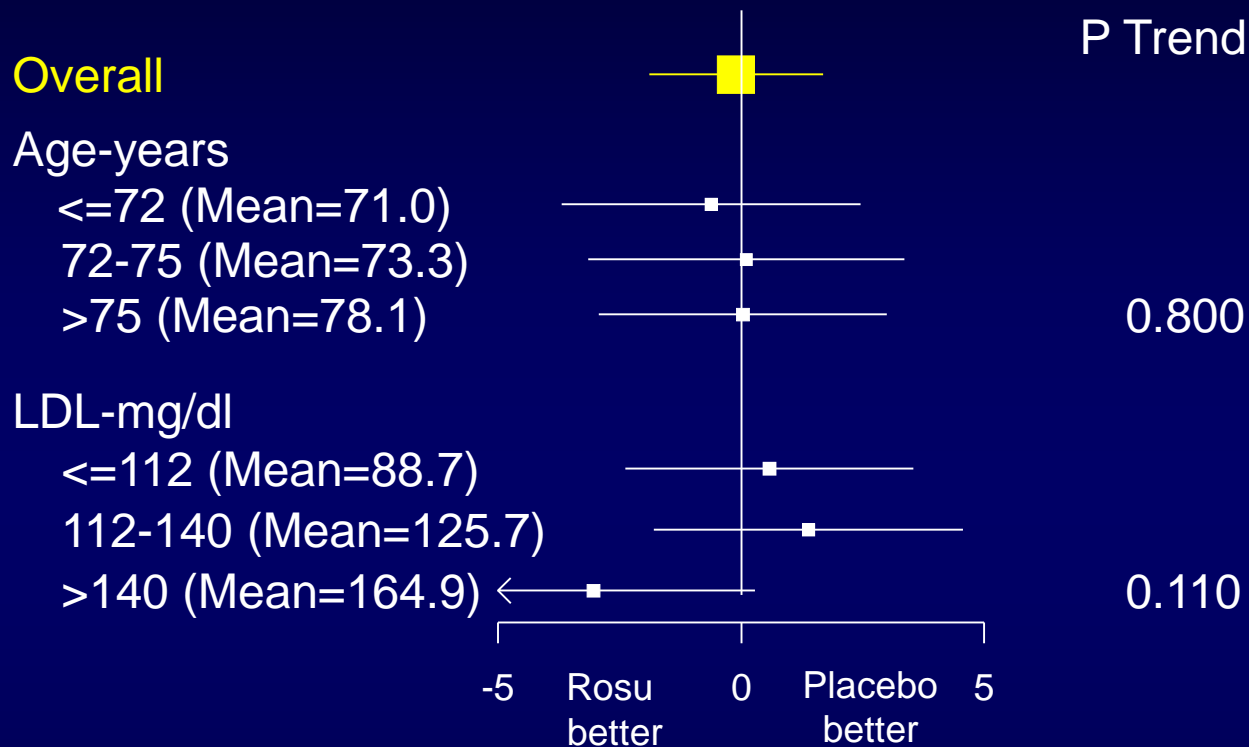
## SBP-mmHg

$\leq 133.0$  (Mean=123.8)

133.0-145.0 (Mean=139.1)

$> 145.0$  (Mean=156.3)





## Mean Δ DSST for Combination Treatment: High SBP and High HDL

	Double Active	Double Placebo	p
High SBP/High LDL	-4.7 (22.6)	-11.8 (16.5)	0.04

# Treatment Effect by Length of Intervention

## BP Lowering

	Active Mean (SD)	Placebo Mean (SD)	Difference Mean (95% CI)	P (Trend)
5 yrs	-5.9 (19.8)	-3.2 (18.0)	-2.7 (-6.4,0.98)	
5-5.5 yrs	-9.7 (19.0)	-6.7 (17.8)	-3.0 (-6.6,0.63)	
5.5-6.2 yrs	-3.4 (19.3)	-3.6 (21.1)	0.17 (-3.8,4.1)	
>6.2yrs	-4.4 (14.4)	-6.3 (15.7)	1.9 (-1.1,4.8)	0.036

**No significant difference in effects of rosuvastatin by duration of treatment**

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# Functional Outcomes by Treatment Group



	BP	Pla	P	Ros	Pla	P
New functional impairment (EQ-5D)	22%	22%	0.96	21%	23%	0.46
<b>Overall function at study end (SAGE)</b>						
Any functional impairment	59%	56%	0.19	57%	59%	0.89

# Conclusions

- HOPE-3 participants experienced cognitive and function decline over 5.6 years
- BP lowering and rosuvastatin use did not significantly prevent cognitive or functional decline
- Rosuvastatin had no adverse effect on cognitive function
- Subgroup analyses:
  - Trend for benefit in those with highest baseline BP and LDL
  - Longer duration of blood pressure lowering associated with less cognitive decline
  - Both findings require further confirmation

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\* Deceased

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