What Else Will We Learn from SPRINT?

David M. Reboussin, PhD

Wake Forest University School of Medicine

For the SPRINT Study Research Group

SPRINT
Systolic Blood Pressure Intervention Trial

Cognitive outcomes

- *One of SPRINT's specific aims was to address hypotheses related to dementia, cognitive decline, and brain changes on MRI.*
- *2800 participants received extended cognitive testing in addition to the screening tests performed on the entire cohort*
- *From a subset of clinics, a total of 640 participants were recruited to undergo brain MRI at baseline and after 4 years of follow-up*

SPRINT
Systolic Blood Pressure Intervention Trial

Cognitive outcomes

- *Main secondary outcome: Incident dementia (all-cause)*
- *Additional secondary outcomes:*
  - *Global and Domain-Specific rate of cognitive decline*
  - *Incident Mild Cognitive Impairment (MCI)*
  - *Brain MRI for*
    - *Microvascular disease burden*
    - *Total Brain Volume*

- *Cognitive testing was done at baseline, 2 years, and 4 years or closeout.*

SPRINT
Systolic Blood Pressure Intervention Trial

Cognitive outcomes

- *We expected a majority of the incident mild cognitive impairment and dementia to be ascertained at or beyond the Year 4 visit*
- *When the intervention was stopped, very few participants had completed the Year 4 visit and only about 1% of the follow-up MRI data had been obtained*
- *The Steering Committee and clinics remain blinded to the cognitive results until mid-2016*

SPRINT
Systolic Blood Pressure Intervention Trial

Subgroups

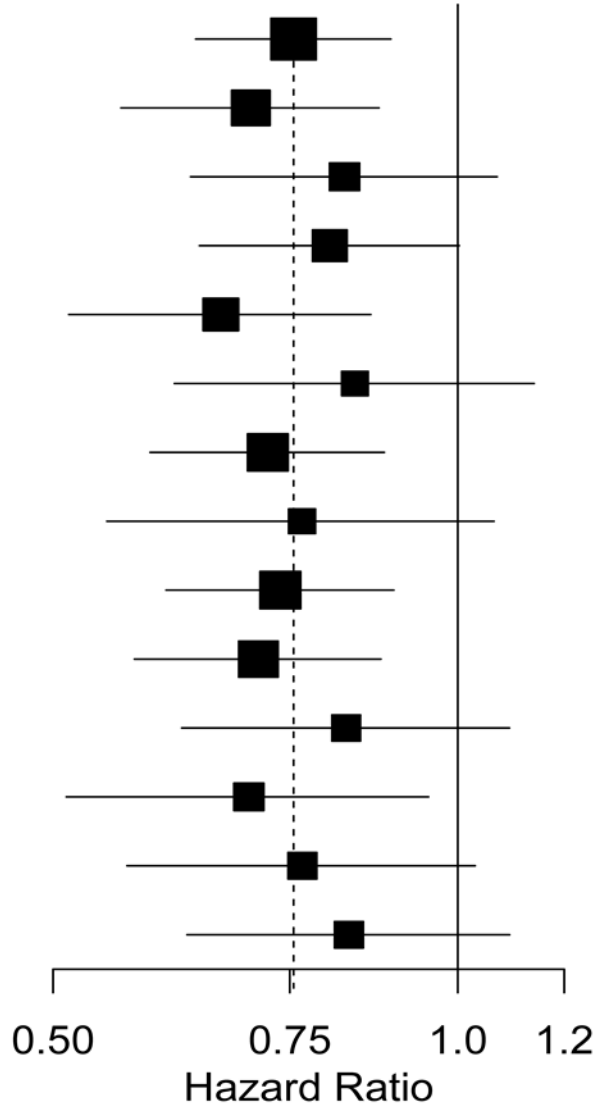
SPRINT
Systolic Blood Pressure Intervention Trial

Subgroups

- *None of the subgroups exhibit substantial heterogeneity with respect to the intervention effect.*
- *However, there is interest in exploratory analysis focused on some of our targeted subgroups, especially seniors and participants with CKD at baseline.*
- *Addressing special concern for how intensive lowering of SBP affects seniors is a high priority: a presentation at GSA later this month, which will also assess impact by frailty and gait speed, with rapid publication*

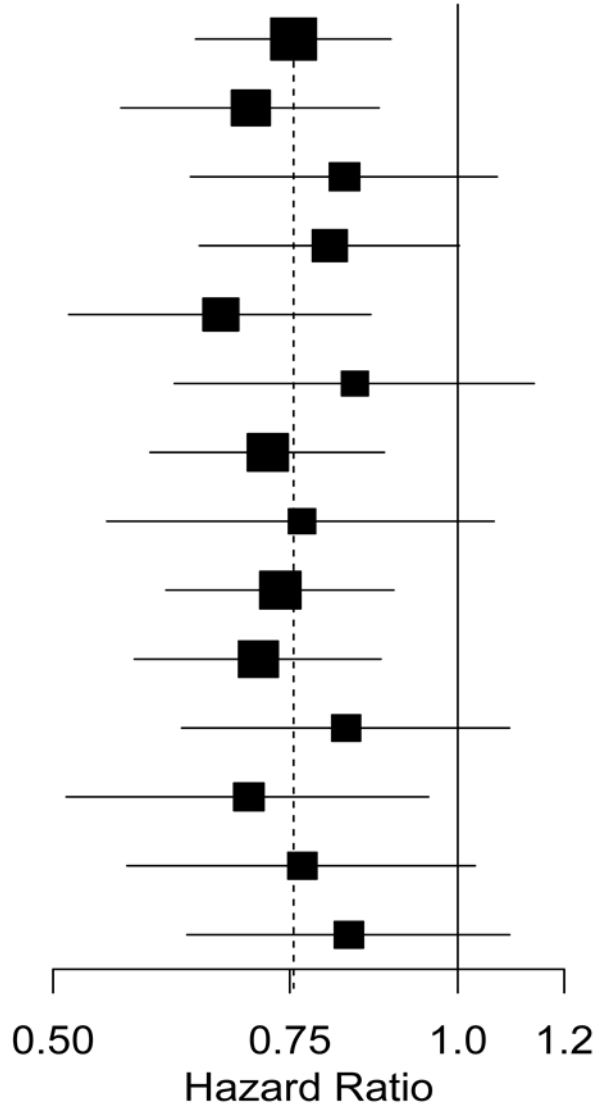
Subgroup	HR	P*
Overall	0.75 (0.64,0.89)	
No Prior CKD	0.70 (0.56,0.87)	0.36
Prior CKD	0.82 (0.63,1.07)	
Age < 75	0.80 (0.64,1.00)	0.32
Age ≥ 75	0.67 (0.51,0.86)	
Female	0.84 (0.62,1.14)	0.45
Male	0.72 (0.59,0.88)	
African−American	0.77 (0.55,1.06)	0.83
Non African−American	0.74 (0.61,0.90)	
No Prior CVD	0.71 (0.57,0.88)	0.39
Prior CVD	0.83 (0.62,1.09)	
SBP ≤ 132	0.70 (0.51,0.95)	0.77
132 < SBP < 145	0.77 (0.57,1.03)	
SBP ≥ 145	0.83 (0.63,1.09)	

*Unadjusted for multiplicity



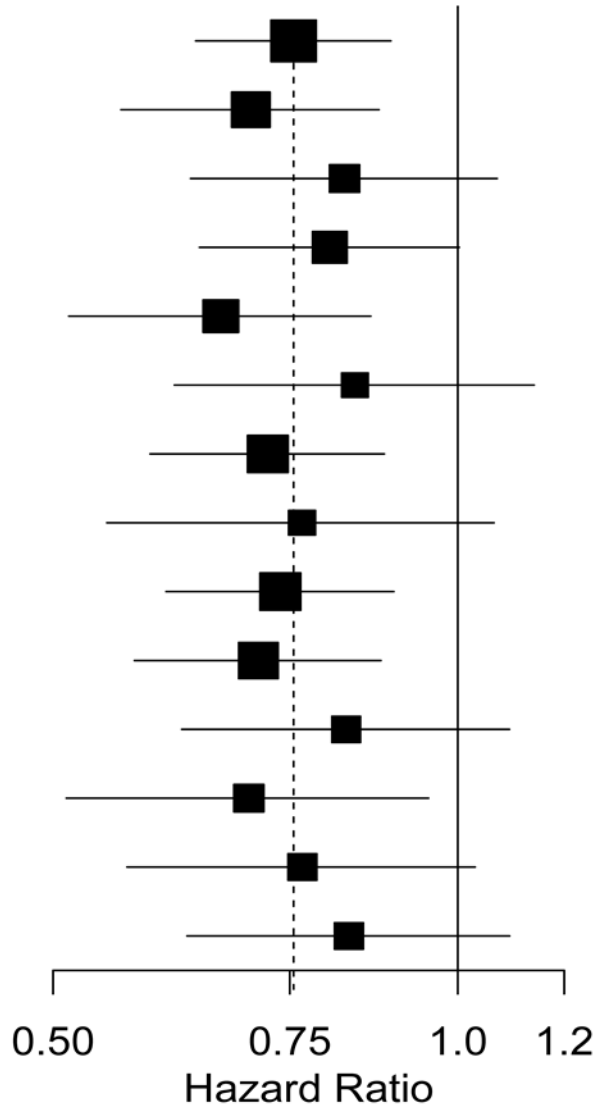
Subgroup	HR	P*
Overall	0.75 (0.64,0.89)	
No Prior CKD	0.70 (0.56,0.87)	0.36
Prior CKD	0.82 (0.63,1.07)	
Age < 75	0.80 (0.64,1.00)	0.32
Age ≥ 75	0.67 (0.51,0.86)	
Female	0.84 (0.62,1.14)	0.45
Male	0.72 (0.59,0.88)	
African−American	0.77 (0.55,1.06)	0.83
Non African−American	0.74 (0.61,0.90)	
No Prior CVD	0.71 (0.57,0.88)	0.39
Prior CVD	0.83 (0.62,1.09)	
SBP ≤ 132	0.70 (0.51,0.95)	0.77
132 < SBP < 145	0.77 (0.57,1.03)	
SBP ≥ 145	0.83 (0.63,1.09)	

*Unadjusted for multiplicity



Subgroup	HR	P*
Overall	0.75 (0.64,0.89)	
No Prior CKD	0.70 (0.56,0.87)	0.36
Prior CKD	0.82 (0.63,1.07)	
Age < 75	0.80 (0.64,1.00)	0.32
Age ≥ 75	0.67 (0.51,0.86)	
Female	0.84 (0.62,1.14)	0.45
Male	0.72 (0.59,0.88)	
African−American	0.77 (0.55,1.06)	0.83
Non African−American	0.74 (0.61,0.90)	
No Prior CVD	0.71 (0.57,0.88)	0.39
Prior CVD	0.83 (0.62,1.09)	
SBP ≤ 132	0.70 (0.51,0.95)	0.77
132 < SBP < 145	0.77 (0.57,1.03)	
SBP ≥ 145	0.83 (0.63,1.09)	

*Unadjusted for multiplicity



SPRINT
Systolic Blood Pressure Intervention Trial

Subgroups

- *Effects on participants with CKD at baseline is another high priority topic, along with effects on renal outcomes in participants with and without CKD at baseline*

- *Manuscripts on cardiovascular outcomes in the CKD subgroup and renal outcomes in the CKD and non-CKD subgroups are being developed*

SPRINT
Systolic Blood Pressure Intervention Trial

Other outcomes

- *Effects on specific cardiovascular outcomes: heart failure, stroke, MI*
- *Effects on safety outcomes*

Serious Adverse Events* (SAE) During Follow-up

	Number (%) of Participants		
	Intensive	Standard	HR (P Value)
All SAE reports	1793 (38.3)	1736 (37.1)	1.04 (0.25)
SAEs associated with Specific Conditions of Interest			
Hypotension	110 (2.4)	66 (1.4)	1.67 (0.001)
Syncope	107 (2.3)	80 (1.7)	1.33 (0.05)
Injurious fall	105 (2.2)	110 (2.3)	0.95 (0.71)
Bradycardia	87 (1.9)	73 (1.6)	1.19 (0.28)
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35 (0.020)
Acute kidney injury or acute renal failure	193 (4.1)	117 (2.5)	1.66 (<0.001)

*Fatal or life threatening event, resulting in significant or persistent disability, requiring or prolonging hospitalization, or judged important medical event.

SPRINT
Systolic Blood Pressure Intervention Trial

Serious Adverse Events* (SAE) During Follow-up

	Number (%) of Participants		
	Intensive	Standard	HR (P Value)
All SAE reports	1793 (38.3)	1736 (37.1)	1.04 (0.25)
SAEs associated with Specific Conditions of Interest			
Hypotension	110 (2.4)	66 (1.4)	1.67 (0.001)
Syncope	107 (2.3)	80 (1.7)	1.33 (0.05)
Injurious fall	105 (2.2)	110 (2.3)	0.95 (0.71)
Bradycardia	87 (1.9)	73 (1.6)	1.19 (0.28)
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35 (0.020)
Acute kidney injury or acute renal failure	193 (4.1)	117 (2.5)	1.66 (<0.001)

*Fatal or life threatening event, resulting in significant or persistent disability, requiring or prolonging hospitalization, or judged important medical event.

SPRINT
Systolic Blood Pressure Intervention Trial

SPRINT Primary Outcome and its Components

Event Rates and Hazard Ratios

	Intensive		Standard			
	No. of Events	Rate, %/year	No. of Events	Rate, %/year	HR (95% CI)	P value
Primary Outcome	243	1.65	319	2.19	0.75 (0.64, 0.89)	<0.001
All MI	97	0.65	116	0.78	0.83 (0.64, 1.09)	0.19
Non-MI ACS	40	0.27	40	0.27	1.00 (0.64, 1.55)	0.99
All Stroke	62	0.41	70	0.47	0.89 (0.63, 1.25)	0.50
All HF	62	0.41	100	0.67	0.62 (0.45, 0.84)	0.002
CVD Death	37	0.25	65	0.43	0.57 (0.38, 0.85)	0.005

SPRINT Primary Outcome and its Components

Event Rates and Hazard Ratios

	Intensive		Standard			
	No. of Events	Rate, %/year	No. of Events	Rate, %/year	HR (95% CI)	P value
Primary Outcome	243	1.65	319	2.19	0.75 (0.64, 0.89)	<0.001
All MI	97	0.65	116	0.78	0.83 (0.64, 1.09)	0.19
Non-MI ACS	40	0.27	40	0.27	1.00 (0.64, 1.55)	0.99
All Stroke	62	0.41	70	0.47	0.89 (0.63, 1.25)	0.50
All HF	62	0.41	100	0.67	0.62 (0.45, 0.84)	0.002
CVD Death	37	0.25	65	0.43	0.57 (0.38, 0.85)	0.005

SPRINT
Systolic Blood Pressure Intervention Trial

Extended follow-up

- *Discussions are in progress regarding follow-up of participants beyond mid-2016*
- *Continued surveillance for cognitive decline and dementia*
- *Additional measurements of renal function over a longer follow-up period*

SPRINT
Systolic Blood Pressure Intervention Trial

Thank You

Cognitive outcomes

- Dementia and cognitive function
  - Main secondary outcome: Incident dementia (all-cause)
  - Additional secondary outcomes:
    - Global and Domain-Specific rate of cognitive decline
    - Incident Mild Cognitive Impairment (MCI)
    - Brain MRI for
      - Microvascular disease burden
      - Total Brain Volume

- Cognitive testing was done at baseline, 2 years, and 4 years or closeout.

SPRINT
Systolic Blood Pressure Intervention Trial

Other outcomes