Can we still SPRINT after HOPE-3?

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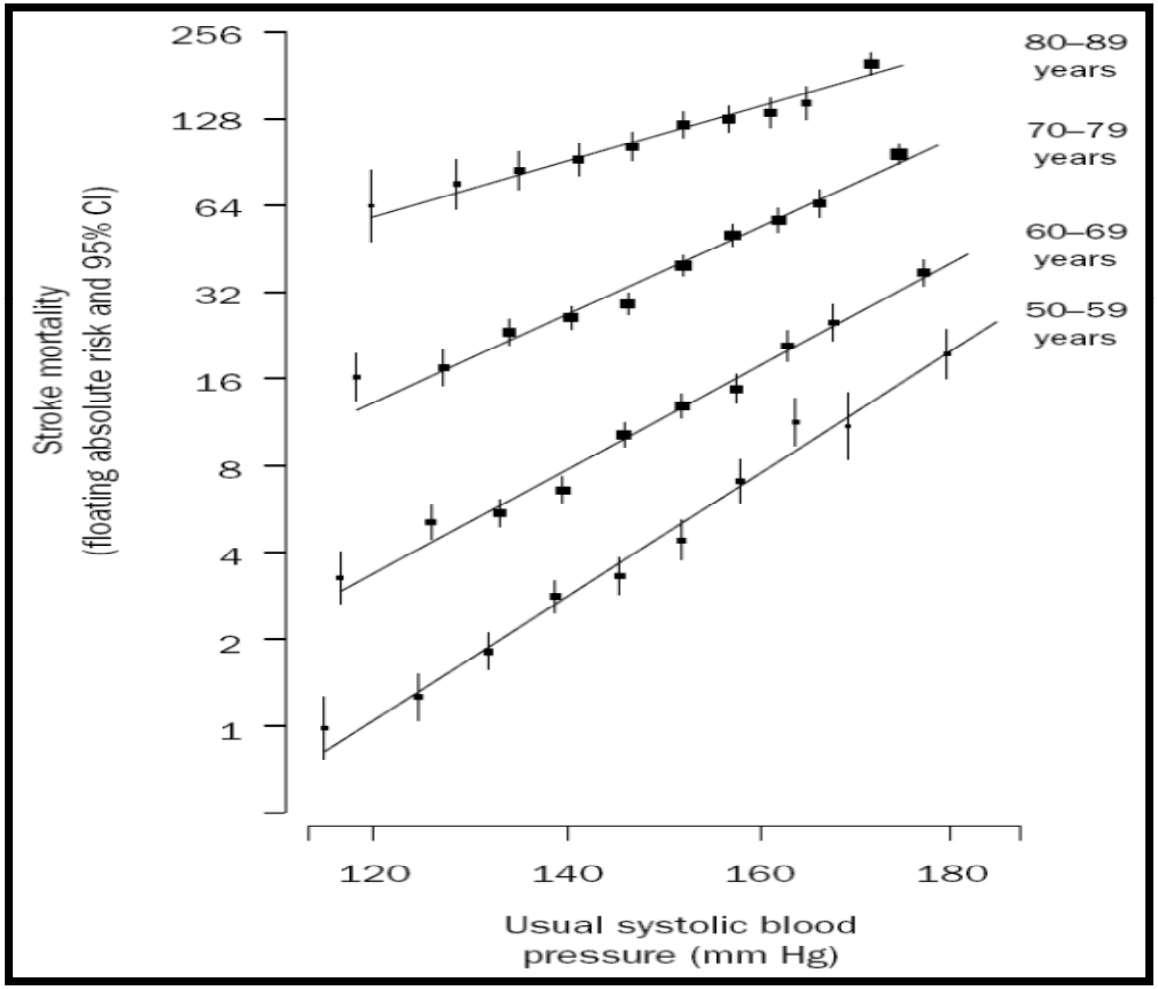
- **Relationships with commercial interests:**
  - **Grants/Research Support:** CIHR, AbbVie, Bayer
  - **Speakers Bureau/Honoraria:** Servier, Pfizer, Valeant
  - **Consulting Fees:** AbbVie (SONAR Canadian Lead)
  - **Other:** None

Objectives

- Describe the impact of BP lowering
- Describe the SPRINT study design
  - Describe the benefits and risks of lowering systolic blood pressure to less than 120 mmHg
  - Introduce the new CHEP SPRINT recommendation and discuss its impact on practice
- Describe HOPE3

The Burden of Hypertension
Blood Pressure and Risk of Stroke Mortality



Lancet 2002;360: 1903-13

Benefits of Treating Hypertension

- Younger than 60 (reducing BP 10/5-6 mmHg)
  - reduces the risk of stroke by **42%**
  - reduces the risk of coronary event by **14%**
- Older than 60 (reducing BP 15/6 mmHg)
  - reduces overall mortality by **15%**
  - reduces cardiovascular mortality by **36%**
  - reduces incidence of stroke by **35%**
  - reduces coronary artery disease by **18%**

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group

SPRINT
Systolic Blood Pressure Intervention Trial

Background

- Observational studies identify strong association between BP and risk of CVD, with no evidence of threshold for the relationship
- Clinical trials demonstrate antihypertensive drug therapy reduces risk of CVD
- However, optimal target for SBP lowering is uncertain

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Systolic Blood Pressure Intervention Trial

SPRINT Design

Examine effect of more intensive high blood pressure treatment than is currently recommended

↓

Randomized controlled trial
Target systolic blood pressure
N = 9,361

Intensive treatment	Standard treatment
Target SBP <120 mm Hg	Target SBP <140 mm Hg
N = 4,678	N = 4,683

ITT analysis

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Systolic Blood Pressure Intervention Trial

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Major inclusion criteria

- ≥50 years old
- Systolic blood pressure: 130-180 mm Hg (treated or untreated)
- Additional cardiovascular disease risk:
  - Clinical or subclinical CVD (excluding stroke)
  - Chronic kidney disease, defined as eGFR 20-<60 ml/min/1.73m^2
  - Framingham Risk Score for 10-year CVD risk ≥ 15%
  - Age ≥ 75 years

At least one

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CVD Indication

Clinical CVD (other than stroke)

a) Previous myocardial infarction (MI), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), carotid endarterectomy (CE), carotid stenting

b) Peripheral artery disease (PAD) with revascularization

c) Acute coronary syndrome with or without resting ECG change, ECG changes on a graded exercise test (GXT), or positive cardiac imaging study

d) At least a 50% diameter stenosis of a coronary, carotid, or lower extremity artery

e) Abdominal aortic aneurysm (AAA) ≥5 cm with or without repair

Subclinical CVD

a) Coronary artery calcium score ≥ 400 Agatston units within the past 2 years.

b) Ankle brachial index (ABI) ≤0.90 within the past 2 years.

c) Left ventricular hypertrophy (LVH) by ECG (based on computer reading), echocardiogram report, or other cardiac imaging procedure report within the past 2 years.

Major exclusion criteria

- Stroke
- Diabetes mellitus
- Polycystic kidney disease
- Congestive heart failure (symptoms or EF <35%)
- Proteinuria >1g/d
- CKD with eGFR <20 ml/min/1.73m^2 (MDRD)
- Adherence concerns

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Demographic & baseline characteristics

	Total (N = 9,361)	Intensive (N = 4,678)	Standard (N = 4,683)	Targeted
Mean (SD) age, years	67.9 (9.4)	67.9 (9.4)	67.9 (9.5)	
% ≥ 75 years	28.2%	28.2%	28.2%	**35%**
Female, %	35.6%	36.0%	35.2%	**50%**
White, %	57.5%	57.7%	57.7%	**60%**
African-American, %	29.9%	29.5%	30.4%	
Hispanic, %	10.5%	10.8%	10.3%	
Prior CVD, %	20.1%	20.1%	20.0%	
Mean 10y Framingham CVD risk, %	20.1%	20.1%	20.1%	
Taking antihypertensive meds, %	90.6%	90.8%	90.4%	
Mean (SD) number of antihypertensive meds	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)	
CKD	28%	28%	28%	**46%**
Mean (SD) BL BP, mm Hg Systolic	139.7 (15.6)	139.7 (15.8)	139.7 (15.4)	
Diastolic	78.1 (11.9)	78.1 (11.9)	78.0 (12.0)	

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Selected baseline laboratory characteristics

	Total (N = 9,361)	Intensive (N = 4,678)	Standard (N = 4,683)
Mean (SD) eGFR, mL./min/1,73m^2	71.7 (20.6)	71.8 (20.7)	71.7 (20.5)
% with eGFR<60 mL./min/1,73m^2	28.3	28.4	28.1
Mean (SD) urine albumin/creatinine, mg/g	42.6 (166.3)	44.1 (178.7)	41.1(152.9)
Mean (SD) total cholesterol, mg/dL	190.1 (41.2)	190.2 (41.4)	190.0 (40.9)
Mean (SD) fasting plasma glucose, mg/dL	98.8 (13.5)	98.8 (13.7)	98.8 (13.4)

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Primary outcome & primary hypothesis

- Primary outcome:
  - CVD composite: 1st occurrence of:
    - Myocardial infarction (MI)
    - Acute coronary syndrome (non-MI ACS)
    - Stroke
    - Acute decompensated heart failure (HF)
    - Cardiovascular disease death
- Primary hypothesis*:
  - CVD composite event rate lower in the intensive compared to standard treatment

* Estimated power of 88.7% to detect a 20% difference
- Based on recruitment of 9,250 participants, 4-6 years of follow-up and loss to follow-up of 2%/year

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Additional outcomes

- All-cause mortality
- Primary outcome + all-cause mortality
- Renal
  - Main secondary outcome:
    - Participants with CKD at baseline: incidence of decline in eGFR ≥50% or ESRD
  - Additional secondary outcomes:
    - Participants without CKD at baseline: incidence of decline in eGFR ≥30% (to <60 mL/min/1.73m^2)
    - Participants with or without CKD at baseline: incidence of albuminuria (doubling of urinary albumin/creatinine (<10 to >10 mg/g))

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BP Intervention

- BP monitored monthly for 3 months and every 3 months thereafter
  - (additional visits could be scheduled)
- Antihypertensive medication titration decisions based on mean BP (3 readings each visit),
  - using a structured stepped-care approach
- Agents from all major antihypertensive drug classes available free of charge
- Periodic assessment for orthostatic hypotension and related symptoms

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Treatment formulary

Class	Drug	Available strength	Usual dose range/day	Usual daily frequency
Diuretics	Chlorthalidone	25 mg	12-25 mg	1
	Furosemide	20, 40, 80 mg	20-80 mg	2
	Spironolactone	25 mg	25-50 mg	1
	Triamterene/HCTZ	75/50 mg	37.5/25mg – 75/50mg	1
	Amiloride*	5 mg	5 – 10 mg	1-2
	Amiloride/HCTZ	5/50 mg	5/50 mg	1
	Hydrochlorothiazide (HCTZ)	12.5, 25 mg	12.5-50 mg	1
ACEi	Lisinopril	5, 10, 20, 40 mg	5-40 mg	1
ACEi/diuretic	Lisinopril/HCTZ	20/12.5, 20/25 mg	10-40/12.5-50 mg	1
ARB, ARB/diuretic	Valsartan*	80, 160, 320 mg	80-320 mg	1-2
	Losartan	25, 50, 100 mg	25-100 mg	1-2
	Azilsartan	40, 80 mg	40-80 mg	1
	Azilsartan/ chlorthalidone	40/12.5, 40/25 mg	40/12.5-40/25 mg	1

HIGHLIGHTED text represents recommended first line therapies in Intensive Treatment Algorithm

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Treatment formulary

Class	Drug	Available strength	Usual dose range/day	Usual daily frequency
CCB	Diltiazem	120, 180, 240, 300 mg	120-540 mg	1
	Amlodipine	2.5, 5, 10 mg	2.5-10 mg	1
Beta-blockers	Metoprolol tartate	25, 50, 100 mg	50-200 mg	1-2
	Metoprolol ER	25, 50, 100, 200 mg	50-200 mg	1
	Atenolol	25, 50, 100 mg	50-200 mg	1
Beta blocker/ diuretic	Atenolol/ chlorthalidone	50/25 mg	50/25 mg	1
Vasodilators	Hydralazine	25, 50, 100 mg	50-200 mg	2
	Minoxidil	2.5, 10 mg	2.5,-80 mg	1-2
Alpha 2 agonists	Guanfacine	1, 2 mg	0.5-2 mg	1
	Clonidine patch	0.1, 0.2, 0.3 mg	0.1-0.3 mg	1 weekly
Alpha blocker	Doxazosin	1, 2, 4, 8 mg	1-16 mg	1
K+ supplements	KCl tablets	20 mEq	20-80 mEq	1-2

HIGHLIGHTED text represents recommended first line therapies in Intensive Treatment Algorithm

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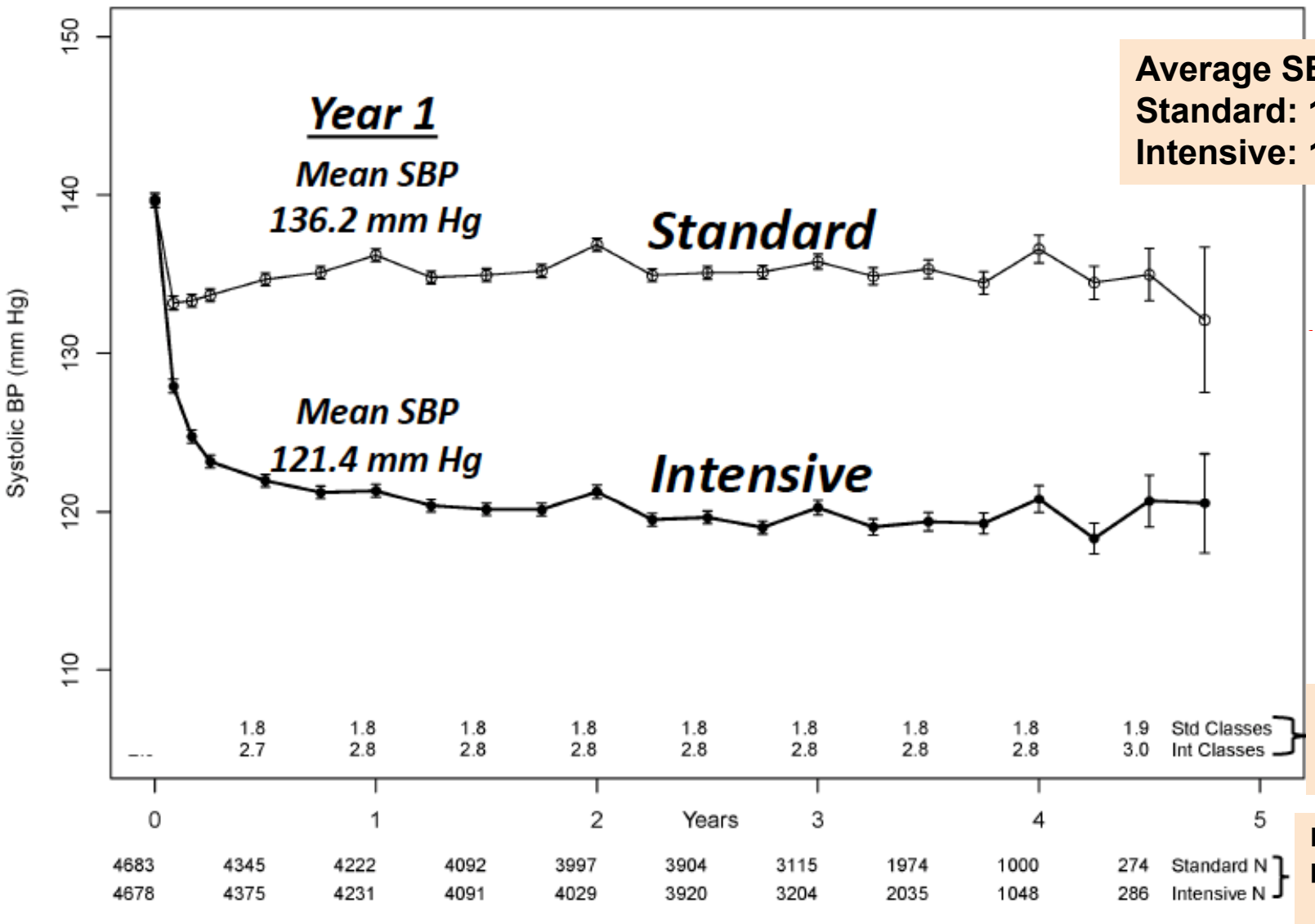
Systolic BP during follow up



Average SBP:
Standard: 134.6 mm Hg
Intensive: 121.5 mm Hg

Average no. of anti-hypertensive meds

No. of participants

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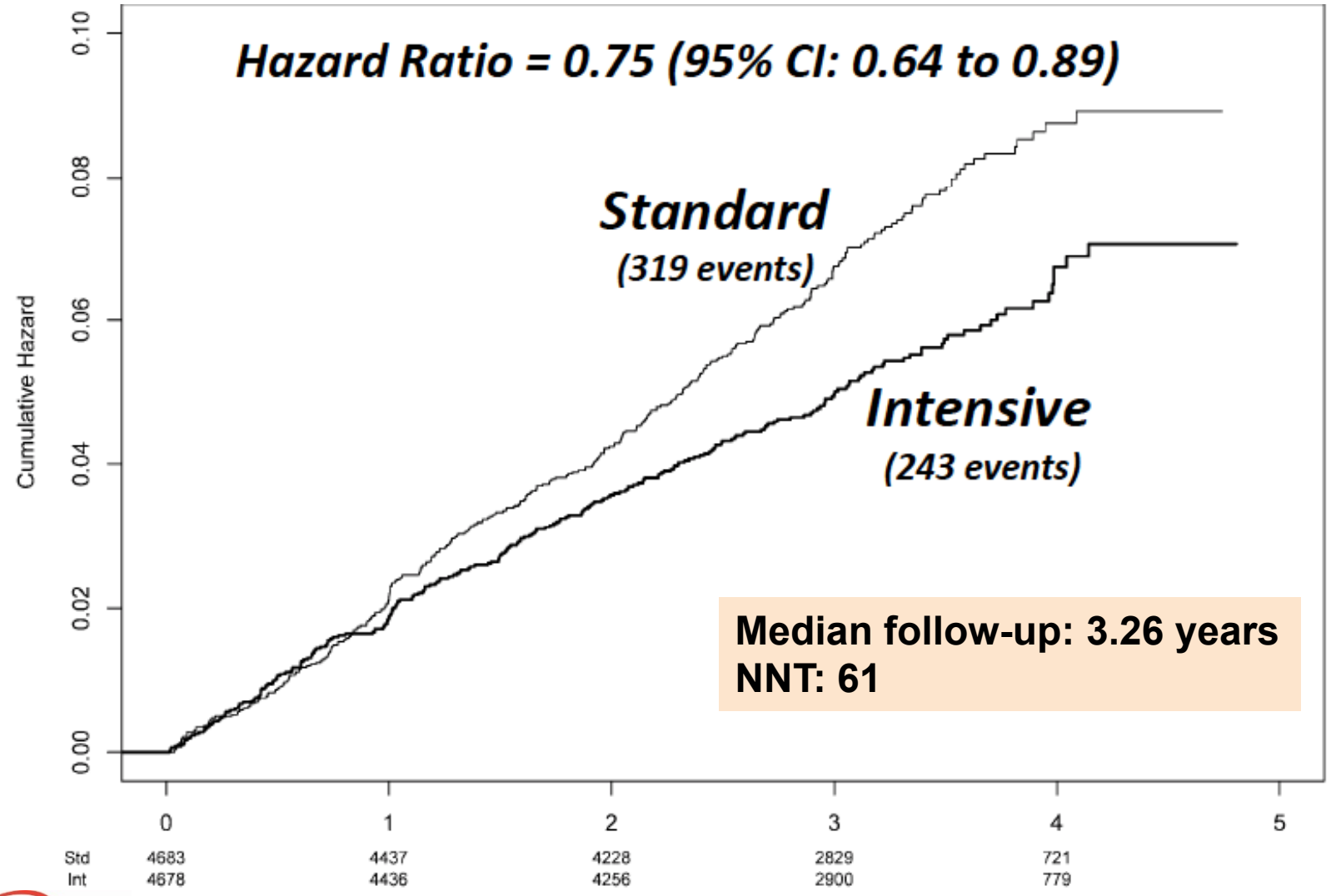
Primary outcome – cumulative hazard



Median follow-up: 3.26 years
NNT: 61

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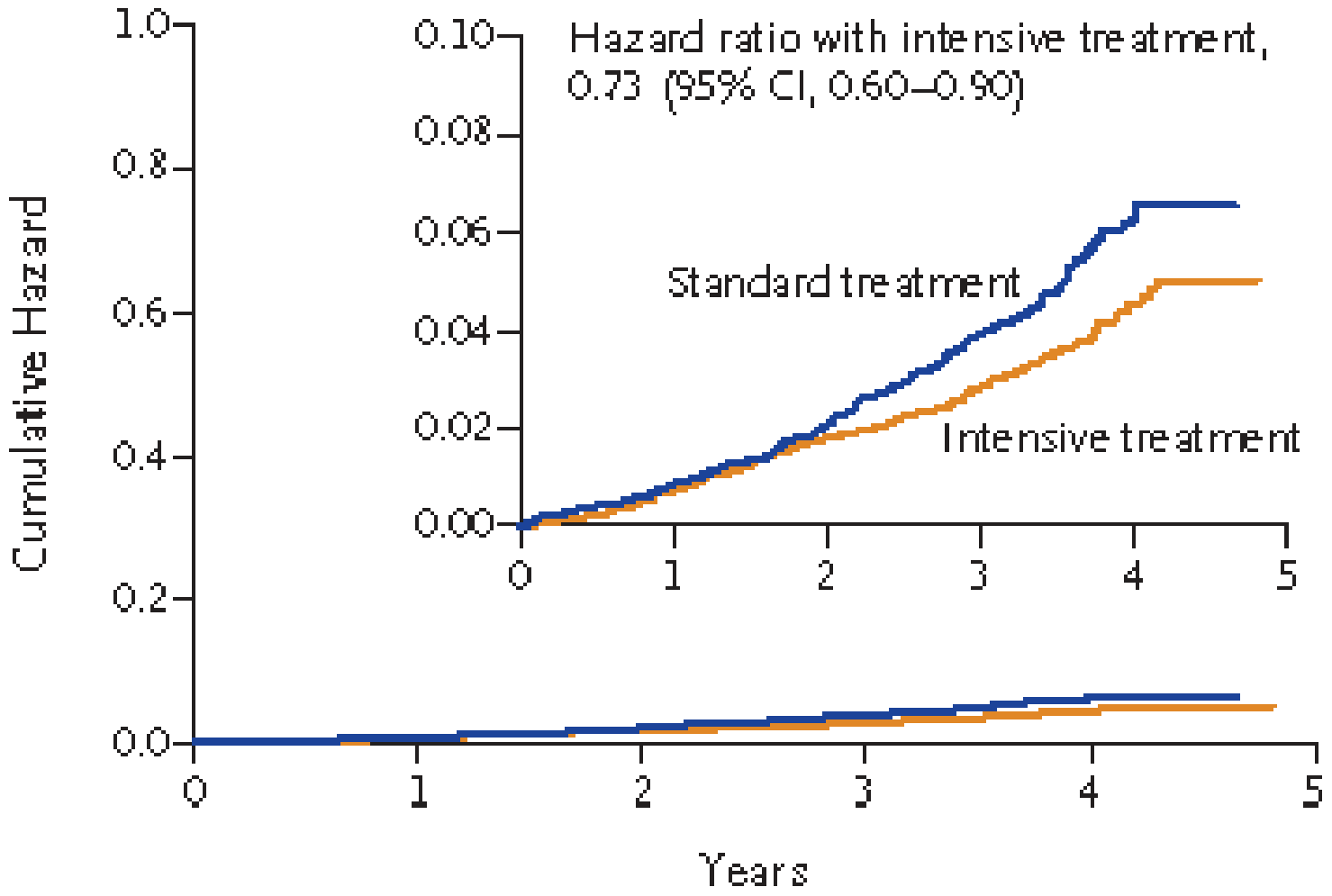
B Death from Any Cause



No. at Risk					
Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

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Primary outcome & components

	Intensive		Standard			
	No. of events	Rate, %/y	No. of events	Rate, %/y	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

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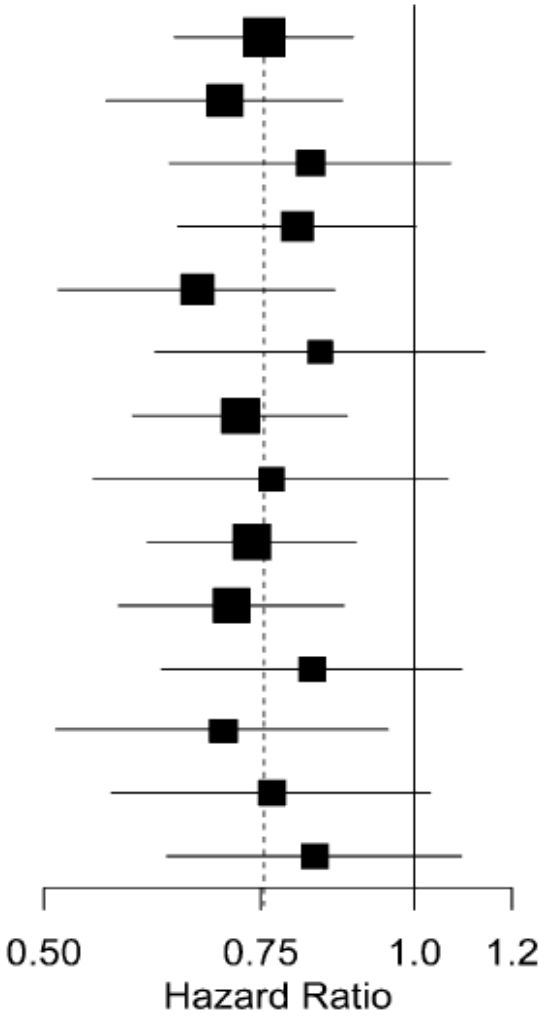
SPRINT Discussant Reboussin, Nov 9th, 2015

Primary outcomes in the 6 pre-specified subgroups of interest

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)	

*Treatment by subgroup interaction
*Unadjusted for multiplicity



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Renal disease outcomes

	Intensive		Standard		HR (95%CI)	P Value
	Events	%/y	Events	%/y		
Participants with CKD at baseline	N=1330		N=1316			
Primary CKD outcome						
Composite renal outcome	14	0,33	15	0,36	0,89 (0,42-1,87)	0,76
≥50% reduction in estimated GFR	10	0,23	11	0,26	0,87 (0,36-2,07)	0,75
Long term dialysis	6	0,14	10	0,24	0,57 (0,19-1,54)	0,27
Kidney transplantation	0	-	0	-	-	-
Secondary CKD outcome						
Incident albuminuria	49	3,02	59	3,90	0,72 (0,48-1,07)	0,11
Participants without CKD at baseline	(N=3332)		(N=3345)			
≥30% reduction in eGFR*	127	1,21	37	0,35	3,49 (2,44-5,10)	<0,001
Incident albuminuria**	110	2,00	135	2,41	0,81 (0,63-1,04)	0,10

*confirmed on a second occasion ≥90 days apart ** doubling of urinary albumin/creatinine from <10 to >10 mg/g

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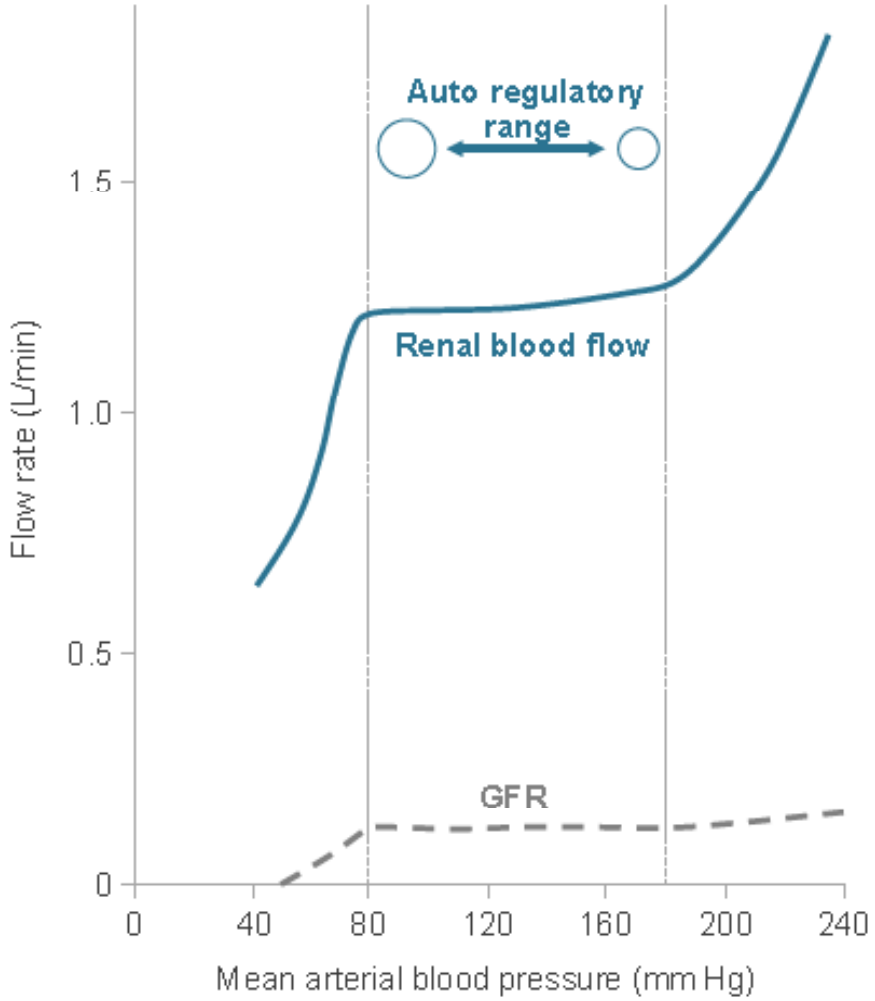
Autoregulation of Renal Blood Flow and GFR

- Autoregulation is an intrinsic form of homeostasis that stabilizes kidney function despite changes in systemic blood pressure
- The exact physiologic basis that stabilizes blood flow is complex



Autoregulatory effect demonstrated in animal studies.

Munger KA, Kost CK, Brenner BM, Maddox DA. The renal circulations and glomerular ultrafiltration. In: Taal MW, Brenner BM, eds. *Brenner & Rector's The Kidney*. 9th ed. Philadelphia, PA: Elsevier/Saunders; 2012:94-137.

Tanner GA. Renal physiology and body fluids. In: Rhoades R, Tanner GA, eds. *Medical Physiology*. 2nd ed. New York, NY: Lippincott Williams & Wilkins; 2003:377-448.

Serious adverse events* (SAE)

	Number (%) of participants		
All SAE reports	Intensive	Standard	HR (P value)
	1,793 (38.3)	1,736 (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.

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Additional monitored clinical measures at follow-up

	Number (%) of participants		
	Intensive	Standard	HR (P value)
Laboratory measures*			
Sodium <130 mmol/L	180 (3.9)	100 (2.2)	1.76 (<0.001)
Potassium <3.0 mmol/L	114 (2.5)	74 (1.6)	1.50 (0.006)
Potassium >5.5 mmol/L	176 (3.8)	171 (3.7)	1.00 (0.97)
Signs and symptoms			
Orthostatic hypotension**	777 (16.6)	857 (18.3)	0.88 (0.013)
Orthostatic hypotension with dizziness	62 (1.3)	71 (1.5)	0.85 (0.35)

* Detected on routine or PRN labs; routine labs drawn quarterly for first year, then q 6 months

** Drop in SBP ≥20 mm Hg or DBP ≥10 mm Hg 1 min after standing (measured at 1,6, and 12 months and yearly thereafter)

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Systolic Blood Pressure Intervention Trial

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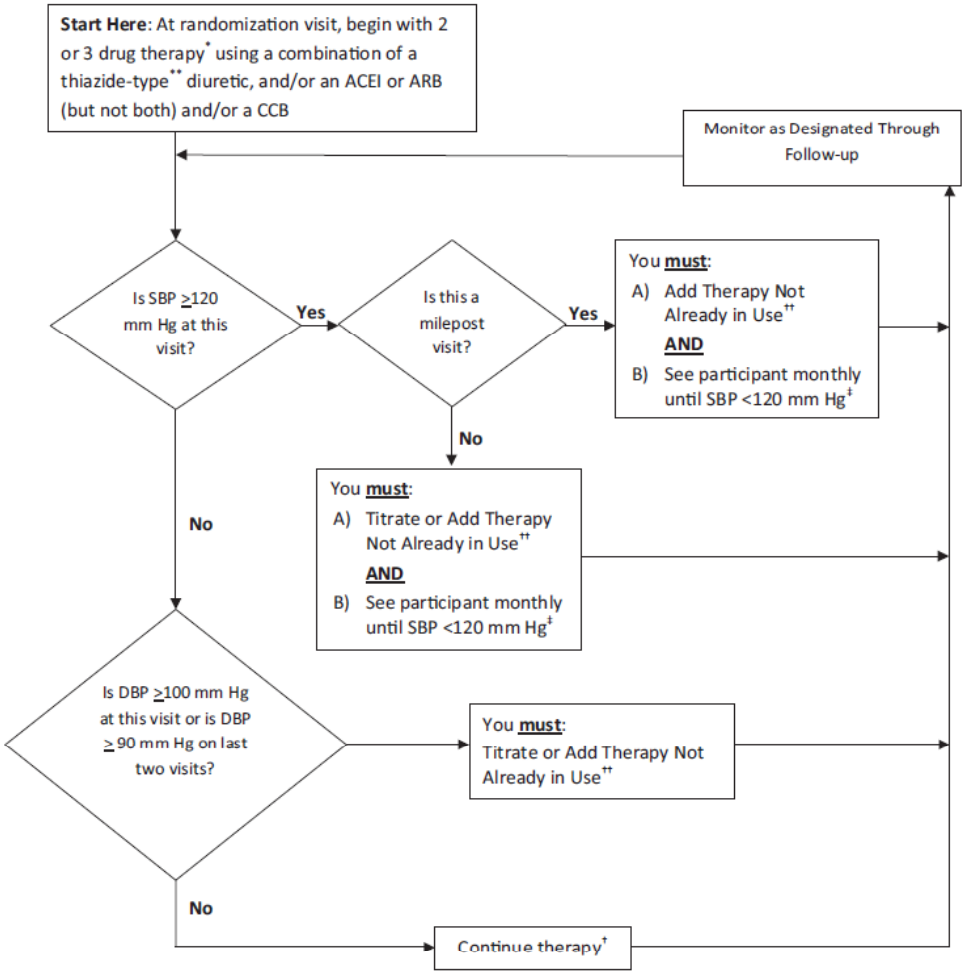
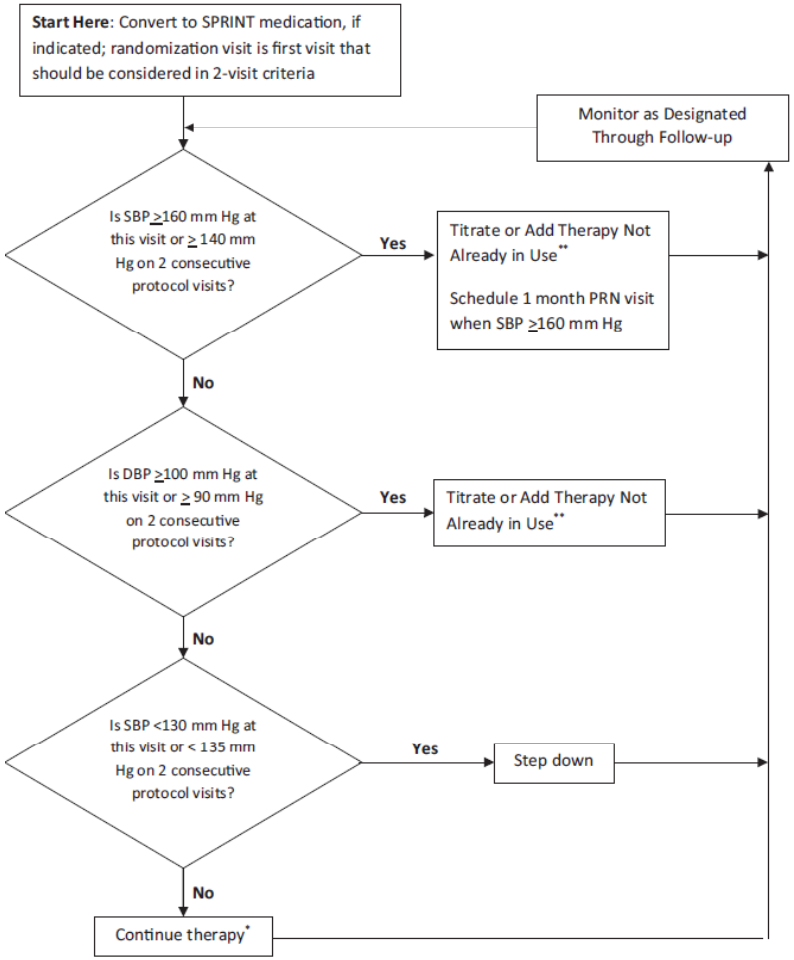
Intensive Treatment algorithm



- At randomization, begin with 2 or 3 drug therapy
- Use combination of thiazide-type diuretic, ACEi/ARB, CCB
- Include β –blocker or other agents as appropriate for compelling indications
- May begin with a single agent for participants 75 years old or older with SBP < 140 on 0-1 meds at study entry. A second medication should be added at the 1 Month visit if participant is asymptomatic and SBP > 130.
- May use loop diuretic for participants with advanced CKD

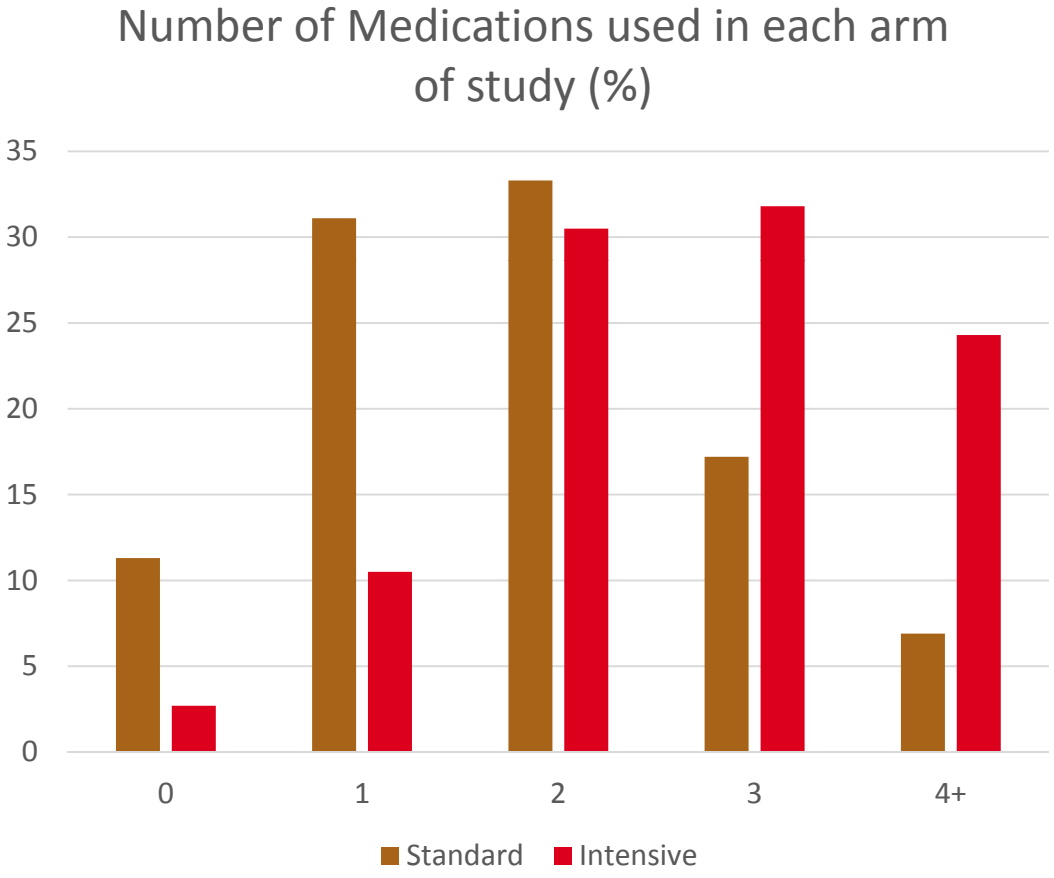
Standard Treatment algorithm



- At randomization, convert to SPRINT type medication
- Include β –blocker or other agents as appropriate for compelling indications

- Notice therapeutic inertia built into algorithm
- Notice Step down

Use of Antihypertensive Medication



	Intensive (N=4678)	*Standard (N=4683)*
Number of agents		
Average	**2.7 (1.2)**	**1.8 (1.1)**
0	**125 (2.7)**	**530 (11.3)**
1	**493 (10.5)**	**1455 (31.1)**
2	**1429 (30.5)**	**1559 (33.3)**
3	**1486 (31.8)**	**807 (17.2)**
4+	**1137 (24.3)**	**323 (6.9)**

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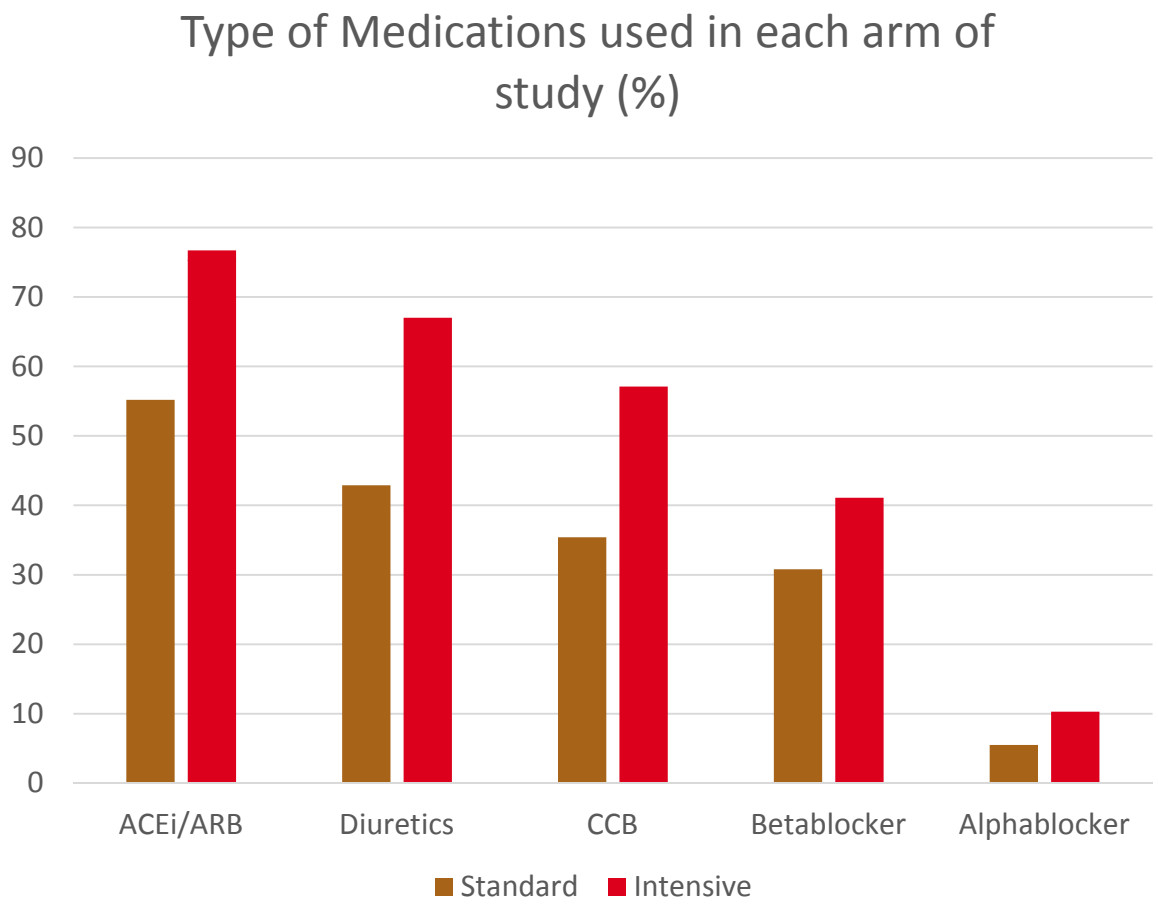
Systolic Blood Pressure Intervention Trial

SPRINT Medications
Classes Used



Intensive use of classes:

1. Diuretic (67%)
2. CCB (57.1%)
3. BB (41.1%)
4. ARB (39.7%)
5. ACEI (37.0%)

} 76.7%

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Systolic Blood Pressure Intervention Trial

Outcomes in select groups

Outcome of interest	Rate intensive	Rate standard	ARR	RRR	NNT for trial duration	NNT for 1 year
Primary	5.2	6.8	1.6	24	61	185
CV mortality	0.8	1.4	0.6	43	167	525
Mortality	3.3	4.5	1.2	27	83	260
Mortality in >75	5.54	8.04	2.5	31	40	126

Adverse Events in select groups

AE of interest	Rate intensive	Rate standard	ARI	RRI	NNH for trial duration	NNH for 1 year
Any SAE	38.3	37.1	1.2	3.2	84	263
AKI/ARF	4.1	2.5	1.6	64	63	197
>30% loss of eGFR	3.8	1.1	2.7	245	37	117
SAE in Age>75	48.6	48.4	0.2	0.4	500	1575

Which aspect of the treatment algorithm matters?

- Selection of patients?
- The achieved blood pressure?
- The algorithm of forced uptitration?
- Early control?
- The choice of medications used?
- Mandated use of 2 medications at randomization?
- The close follow up to minimize mortality from the SAEs?

SPRINT study group summary

- SPRINT examined effects of more intensive antihypertensive therapy than currently recommended
- Participants were US adults ≥50 years with hypertension and additional risk for CVD
- Rapid and sustained difference in SBP achieved between the two treatment arms
- Trial stopped early, due to benefit, after median follow-up of 3.26 years
- Incidence of composite of CVD events were 25% lower in Intensive compared to Standard Group and all-cause mortality reduced by 27%.
- Treatment effect similar in all six pre-specified groups of interest.

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Systolic Blood Pressure Intervention Trial

The SPRINT Research Group, NEJM, Nov 9th, 2015

Usual Office BP Threshold Values for Initiation of Pharmacological Treatment

Population	SBP	DBP
High Risk (SPRINT population)	≥130	NA
Diabetes	≥130	≥80
Moderate-to-high risk (TOD or CV risk factors)*	≥140	≥90
Low risk (no TOD or CV risk factors)	≥160	≥100

TOD = target organ damage ***AOBP threshold > 135/85**

Recommended Office BP Treatment Targets

Treatment consists of health behaviour ± pharmacological management

Population	SBP	DBP
High Risk (SPRINT)	<120	NA
Diabetes	< 130	< 80
All others (including CKD)*	< 140	< 90

* Target BP with AOBP < 135/85

New thresholds/targets for the high risk patient post-SPRINT: *who does this apply to??*

- Clinical or sub-clinical cardiovascular disease

  OR

- Chronic kidney disease (non-diabetic nephropathy, proteinuria <1 g/d, *estimated glomerular filtration rate 20-59 mL/min/1.73m^2)

  OR

- †Estimated 10-year global cardiovascular risk ≥15%

  OR

- Age ≥ 75 years

Patients with one or more clinical indications should consent to intensive management.

* Four variable MDRD equation

† Framingham Risk Score, D'Agastino, Circulation 2008

New thresholds/targets for the high risk patient post-SPRINT: *who does this NOT apply to??*

Limited or No Evidence:

- Heart failure (EF <35%) or recent MI (within last 3 months)
- Indication for, but not currently receiving a beta-blocker
- Frail or institutionalized elderly

Inconclusive Evidence:

- Diabetes mellitus
- Prior stroke
- eGFR < 20 ml/min/1.73m2

Contraindications:

- Patient unwilling or unable to adhere to multiple medications
- Standing SBP <110 mmHg
- Inability to measure SBP accurately
- Known secondary cause(s) of hypertension

New Guideline post-SPRINT

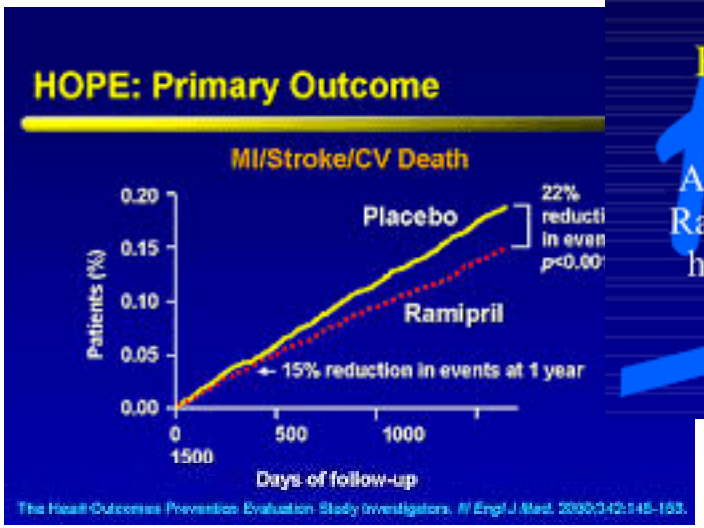
New 2016

For high-risk patients, aged ≥ 50 years, with systolic BP levels >/=130 mm Hg, intensive management to target a systolic BP </=120 mm Hg should be considered.

Intensive management should be guided by automated office BP measurements.

Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups.

Heart Outcomes Protection Evaluation



Hope

Heart Outcomes Prevention Evaluation Study

A large, simple, randomized trial of Ramipril and vitamin E in patients at high risk for cardiovascular events

Hope-Too

Hope-3

Population Health Research Institute

HEALTH THROUGH KNOWLEDGE

Heart Outcomes Prevention Evaluation - 3

- HT is the leading global CV risk factor
- 1 billion are hypertensive worldwide
- Graded increased risk for BP above 115 (according to WHO)
- Does lowering BP at any level above 115 mmHg improve outcomes?
- What about intermediate risk patients (10 year Framingham risk of < 10%)
- More events in the intermediate group than the high risk group

Eva Lonn, NEJM 2016

HOPE - 3

- 12,705 Median follow-up 5.6 years
- Men 55+ or women 65+ with one of:
  - Elevated waist/hip
  - Low HDL
  - Smoking
  - Dysglycemia
  - FHx of CVD
  - CKD stage 3
- Women age 60+ with 2 of these

Lonn E, NEJM 2016, HOPE 3 BP Lowering

HOPE - 3 BP

- Double blinded RCT
- Placebo controlled
- 228 centres in 21 countries
- 2 x 2 factorial design
- Fixed dose of Candesartan/HCTZ (16/12.5) or placebo
- Rosuvastatin 10 vs placebo

BP Measurement in HOPE - 3 BP

- Use the Omron automatic blood pressure monitor.
- Ask the participant to remove tight-fitting clothing from his/her arm.
- The participant must be sitting for >5 minutes.
- Put the participant's arm through the cuff loop making sure the bottom edge of the

cuff is approximately one-half inch (1.25cm) above the elbow and that the arrow on

the cuff is above the brachial artery.

- The entire cuff should be evenly tight around the participant's arm. Ask the

participant to remain still until the measurement is complete.

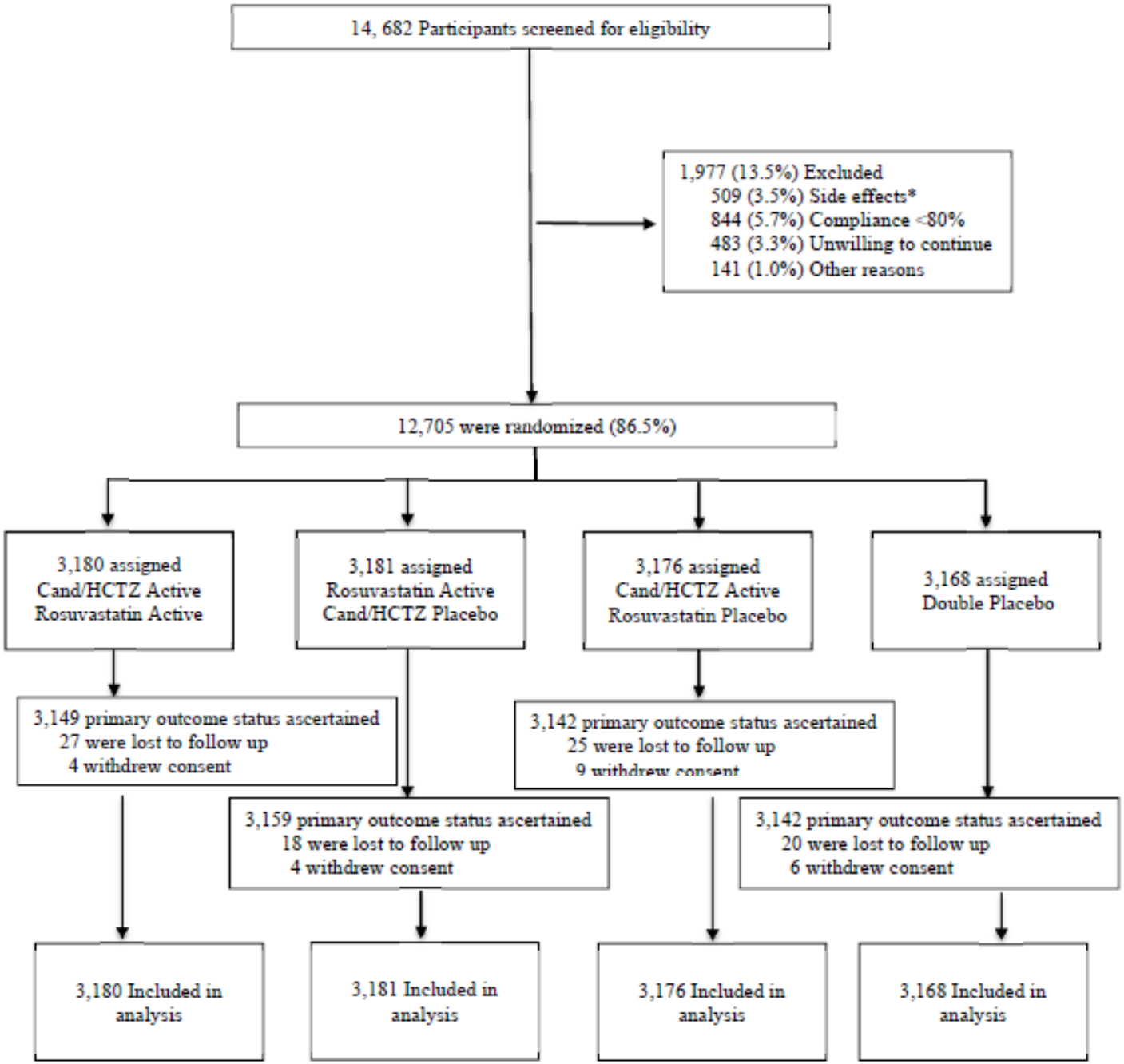
- Press the ON/OFF button. After the heart symbol (♥) appears on the digital panel,

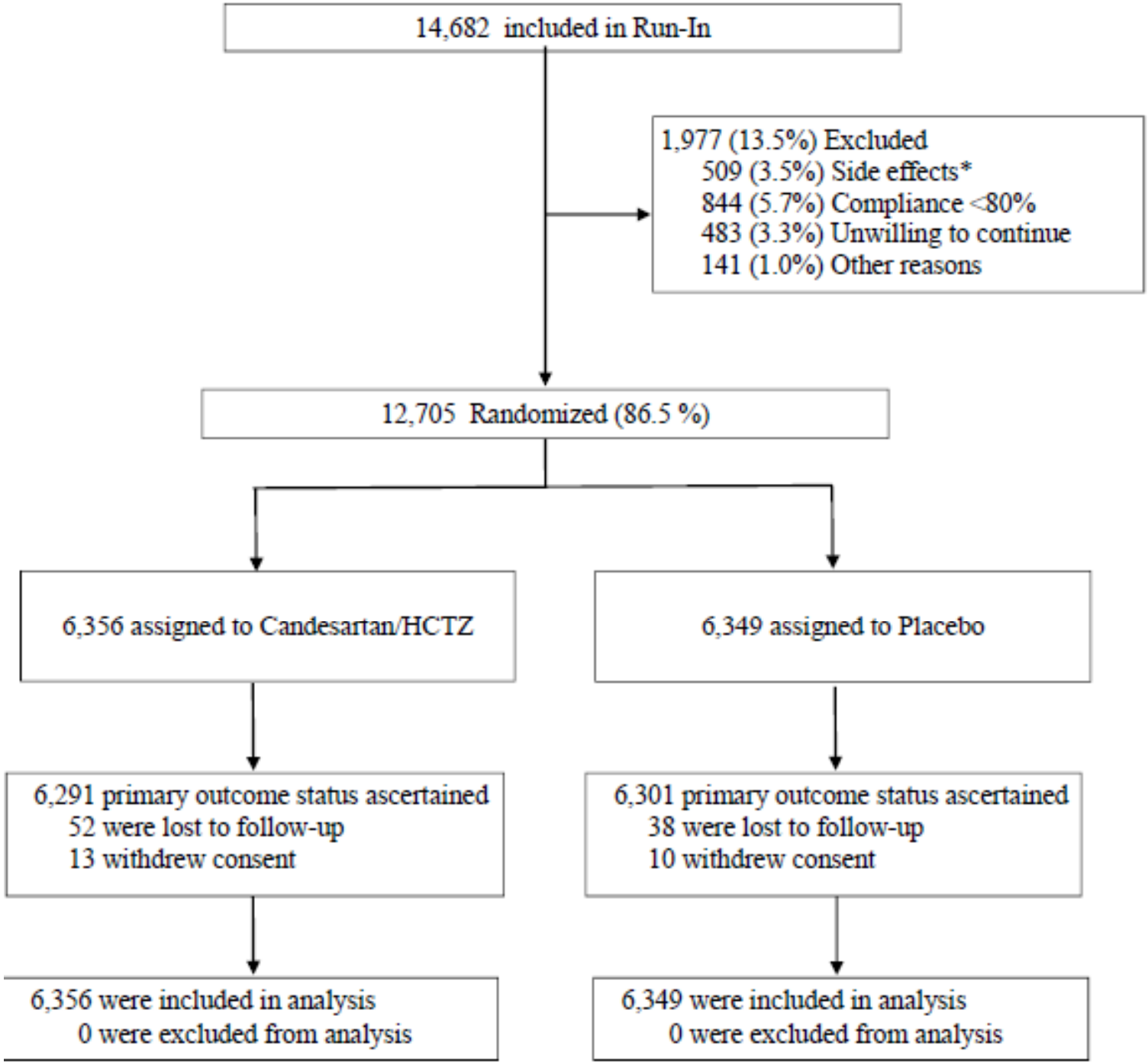
press the START button.

- After the measurement is complete, the monitor will display the systolic and

diastolic blood pressures and pulse. The cuff will automatically deflate.

- Take 2 readings on the right arm at least 1-minute apart.
- Record all readings.


14, 682 Participants screened for eligibility
1,977 (13.5%) Excluded
509 (3.5%) Side effects*
844 (5.7%) Compliance <80%
483 (3.3%) Unwilling to continue
141 (1.0%) Other reasons
12,705 were randomized (86.5%)
3,180 assigned
Cand/HCTZ Active
Rosuvastatin Active
3,181 assigned
Rosuvastatin Active
Cand/HCTZ Placebo
3,176 assigned
Cand/HCTZ Active
Rosuvastatin Placebo
3,168 assigned
Double Placebo
3,149 primary outcome status ascertained
27 were lost to follow up
4 withdrew consent
3,142 primary outcome status ascertained
25 were lost to follow up
9 withdrew consent
3,159 primary outcome status ascertained
18 were lost to follow up
4 withdrew consent
3,142 primary outcome status ascertained
20 were lost to follow up
6 withdrew consent
3,180 Included in analysis
3,181 Included in analysis
3,176 Included in analysis
3,168 Included in analysis


14,682 included in Run-In
1,977 (13.5%) Excluded
509 (3.5%) Side effects*
844 (5.7%) Compliance <80%
483 (3.3%) Unwilling to continue
141 (1.0%) Other reasons
12,705 Randomized (86.5 %)
6,356 assigned to Candesartan/HCTZ
6,349 assigned to Placebo
6,291 primary outcome status ascertained
52 were lost to follow-up
13 withdrew consent
6,301 primary outcome status ascertained
38 were lost to follow-up
10 withdrew consent
6,356 were included in analysis
0 were excluded from analysis
6,349 were included in analysis
0 were excluded from analysis

HOPE - 3

Rosuvastatin	Candesartan/HCTZ		Rosuvastatin Margins
	Active	Placebo	
Active	Rosuvastatin Active/ Candesartan/HCTZ Active n=3,180	Rosuvastatin Active/ Candesartan/HCTZ Placebo n=3,181	**Rosuvastatin Active n=6,361**
Placebo	Rosuvastatin Placebo/ Candesartan/HCTZ Active n=3,176	Rosuvastatin Placebo/ Candesartan/HCTZ Placebo n=3,168	**Rosuvastatin Placebo n=6,344**
Candesartan/HCTZ Margins	**Candesartan/HCTZ Active n=6,356**	**Candesartan/HCTZ Placebo n=6,349**	

HOPE - 3 BPM

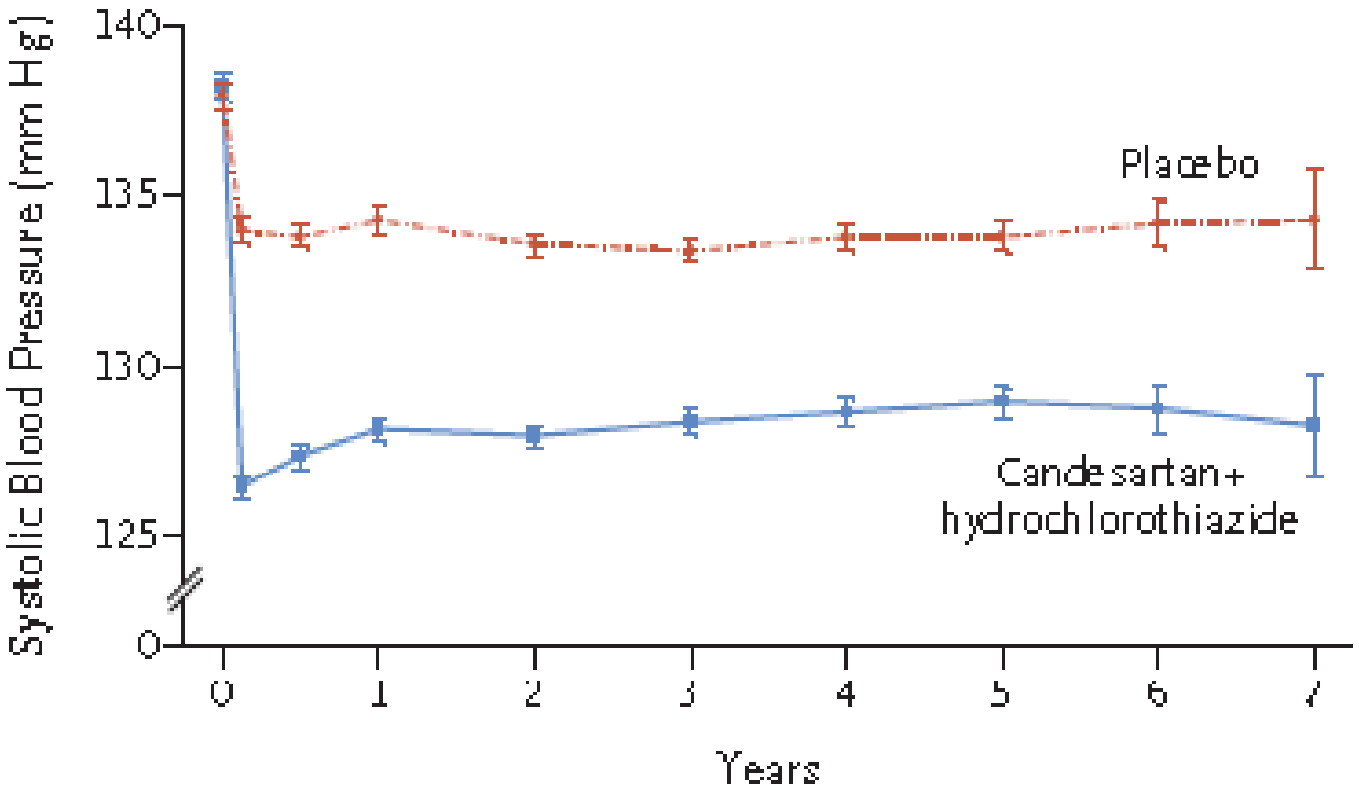
- Measured each visit then annually after 1st year
- 5 minutes rest
- 2 measures averaged.
- Standardized protocol using OMRON HEM-711DLXCAN

BP Change in HOPE - 3 BP

	Active	Placebo
SBP BL	138.2 +- 14.7	137.9 +- 14.8
Change from BL	10.0 +- 13.1	4.0 +- 12.9
DBP BL	82 +- 9.4	81.8 +- 9.3
Change from BL	5.7 +- 8.2	2.7 +- 7.9

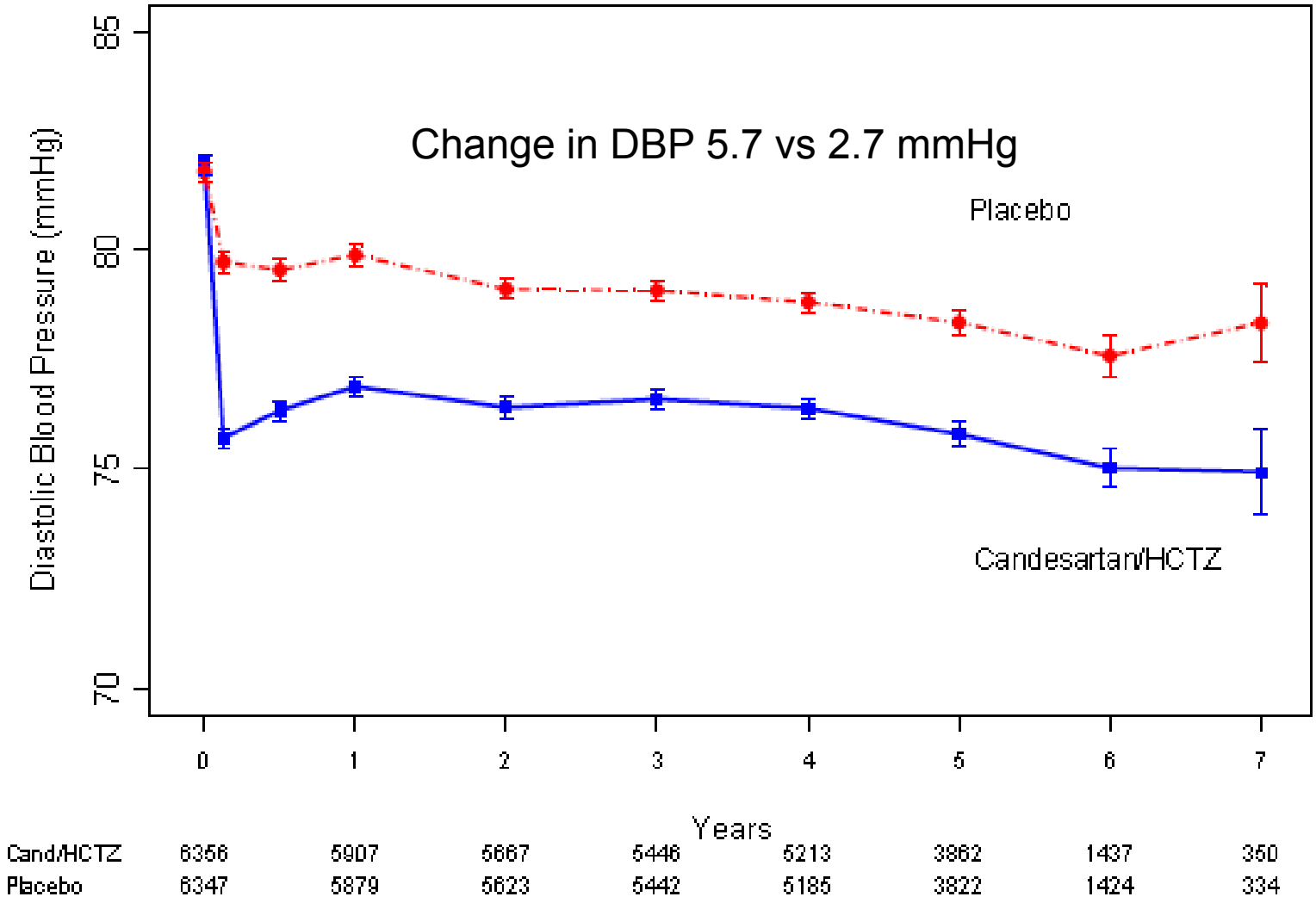
- 1/3 at baseline had a history of hypertension and 22% were on antihypertensives at baseline.
- Annual event rates were 0.8% vs 2.1% in ACCORD and 2.2% in SPRINT.

SBP Over Time



No. at Risk								
Candesartan+hydrochlorothiazide	6356	5907	5667	5446	5213	3862	1437	350
Placebo	6347	5879	5623	5442	5186	3822	1424	334

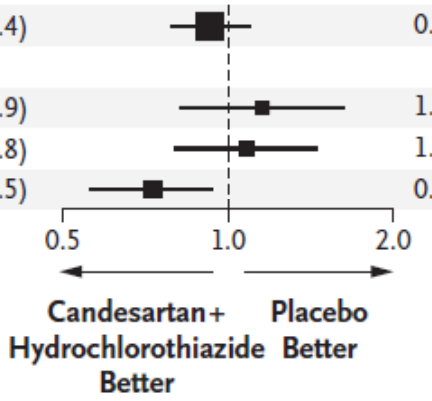
DBP


Change in DBP 5.7 vs 2.7 mmHg
Placebo
Candesartan/HCTZ
Diastolic Blood Pressure (mmHg)
85
80
75
70
0
1
2
3
4
5
6
7
Years
Cand/HCTZ 6356 5907 5667 5446 5213 3862 1437 350
Placebo 6347 5879 5623 5442 5185 3822 1424 334

HOPE - 3: CV Death, Nonfatal MI and Stroke by Tertiles of BL BP

A First Coprimary Outcome

Subgroup	Mean Systolic Blood Pressure	Difference in Blood Pressure	Candesartan+ Hydrochlorothiazide	Placebo	Hazard Ratio (95% CI)	P Value for Trend
	mm Hg		*no. of events/total no. of participants (%)*			
Overall	138.1	6.0/3.0	260/6356 (4.1)	279/6349 (4.4)	0.93 (0.79–1.10)	—
Systolic blood pressure						0.02
≤131.5 mm Hg	122.2	6.1/3.1	70/2080 (3.4)	62/2122 (2.9)	1.16 (0.82–1.63)	
131.6–143.5 mm Hg	137.6	5.6/2.7	87/2120 (4.1)	81/2141 (3.8)	1.08 (0.80–1.46)	
>143.5 mm Hg	154.1	5.8/3.0	103/2156 (4.8)	136/2084 (6.5)	0.73 (0.56–0.94)	



Lonn E, NEJM 2016, HOPE 3 BP Lowering

SPRINT and HOPE – 3
BP Conclusions

- Lower blood pressure is better – in Hypertensives
- Target a BP of 120 or less in SPRINT patients
- Diabetes still < 130/80
- Everyone else < 140/90
  - What about stroke???
- Prehypertension:
  - Non-pharmacologic therapy

Thank You

C-CHANGE PEARLS

Clinical Practice Guidelines Workshop

C•CHANGE

Informing through evidence, transforming through engagement™

Friday, September 16, 2016

Glasgow Hills Resort and Golf, New Glasgow, PEI

Focus: Management of patients with multi-morbidities; heart failure and hypertension; hypertension and diabetes

Approved for 4.5 Mainpro-M1 credits

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