2016: Entering the Era of 120 because of SPRINT?

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Senator Keating from Lima, NY

The VA Cooperative Study, 1967

Cohort	143 men
Mean age	51 years
Eligibility	Diastolic BP 115-129 mmHg
Design	Double blind; placebo control
Therapy	HCTZ, reserpine, hydralazine
Duration	1.5 years
BP change	-43/30 mmHg

HCTZ=hydrochlorothiazide
VA Cooperative Study Group. JAMA. 1967;202:1028-1034. www.hypertensiononline.org

Ser-Ap-Es

- Best Selling Drug of 1970
- 60% Control rate
- Reserpine 0.1 mg (SERpasil), Hydralazine 25 mg (APresoline), and HCTZ 15 mg (ESidrix) TID
- Combinations are good things.

Benefits of Lowering BP

	Average Percent Reduction
Stroke incidence	35–40%
Myocardial infarction	20–25%
Heart failure	50%

JNC 8 Committee Members

- Blood pressure goal <140/90 for young people
- Blood pressure goal <150/90 for folks over 60
- Don't ruin a good thing

JNC 8 Committee Members

- Diabetics over 18: 140/90
- Renal Insufficiency over 18: 140/90

Is <130/80 mmHg justifiable for Patients with Diabetes based on the evidence

NICE says

- <140/90 for all people including diabetes.
- All those initially diagnosed should have ABPM to rule out masked HTN, non-dippers as well as white coat HTN
- At least two measurements/hour are taken during the person's usual waking hours (for example, between 08:00 and 22:00).

NICE Clinical Guideline 127, August 2011.

2013 ESH/ESC Hypertension Guidelines: Goal Recommendations

- Goal SBP<140 mm Hg
  - Patients at low-moderate risk
  - Diabetics
  - CKD (diabetic or non-diabetic)
  - CHD and CVA
- Goal SBP 140-150 mm Hg
  - >80 year old
- Goal DBP Target always <90 mm Hg*

** Values <85 mm Hg may be considered in diabetics.*

European Heart Journal 2013 Jul;34:2159-2219

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Would you prevent their stroke?

Hypertension is NOT Benign

- 54% of strokes and 47% of ischemic heart disease worldwide is due to high blood pressure
- HTN is present in:
  - 69% of patients with 1st MI
  - 77% of patients with 1st stroke
  - 74% patients with chronic heart failure
  - 60% patients with peripheral arterial disease

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Systolic Blood **Pr**essure **In**tervention **T**rial

SPRINT

Study Aim

"A definitive clinical trial…"

Non-diabetic patients

< 120 mm Hg **VS.** **< 140 mm Hg**

Major Inclusion criteria

1. Age ≥ 50 years old
2. Systolic BP : 130 – 180 mm Hg (treated or untreated)
3. Additional cardiovascular disease (CVD) risk:
   - i. Clinical or subclinical CVD (excluding stroke)
   - ii. CKD defined as eGFR 20 to less than 60 ml/min/1.73m²
   - iii. Framingham Risk Score for 10-year CVD risk ≥ 15%
   - iv. Age ≥ 75 years

At least one

Open-label

102 clinical sites (USA & Puerto Rico)

Sponsored by NHLBI

Major Exclusion criteria

1. Stroke
2. Diabetes mellitus
3. Polycystic kidney disease
4. CHF (symptoms or EF < 35%)
5. Proteinuria >1g/d
6. CKD with eGFR < 20 mL/min/1.73m² (MDRD)
7. Compliance concerns

Ongoing clinical trials

Primary Outcome

CVD composite, first occurrence of:

- Myocardial infarction (MI)
- Acute coronary syndrome (non-MI ACS)
- Stroke
- Acute decompensated heart failure (HF)
- Cardiovascular disease death

Secondary Outcomes

- All-cause mortality
- Primary outcome + all-cause mortality
- Renal:
  - Main secondary outcome
    - Participants with baseline CKD: incidence of decline in eGFR ≥ 50% or ESRD
- Additional secondary outcomes:
  - Participants without baseline CKD: incidence of decline in eGFR ≥30%
  - Participants with or without CKD at baseline: Incidence of albuminuria

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Trial ended early

- Planned for 5 - 6 year follow-up
  - But significant difference in primary outcome was reached at 3.26 years.

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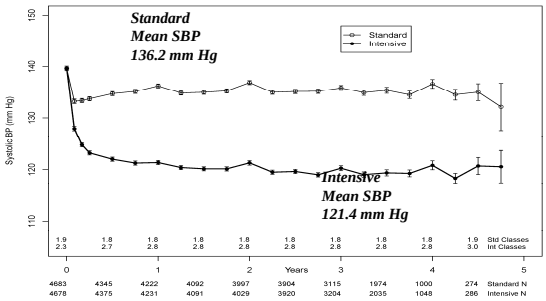
Systolic Blood Pressure Over Time BP Taken Properly!



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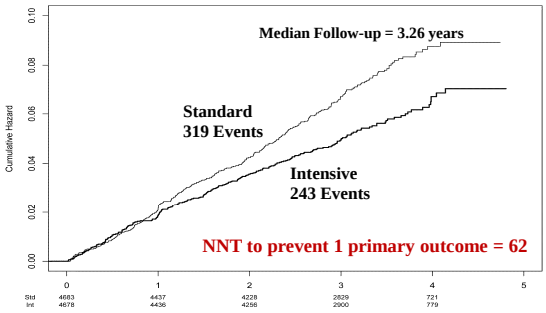
Primary Outcome

Hazard Ratio = 0.75 (95% CI; 0.64-0.89) P = <0.001



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Primary Outcome Subgroups

	Intensive	Standard		
	# of events	# of events	HR (95%, CI)	P-value
All MI	97	116	0.83 (0.64-1.09)	0.19
Non-MI ACS	40	40	1.00 (0.64-1.55)	0.99
Stroke	62	70	0.89 (0.63-1.25)	0.5
Heart Failure	62	100	0.62 (0.45- 0.84)	0.002
CVD death	37	65	0.57 (0.38-0.85)	0.005

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Serious Adverse Events

- Hypotension
- Syncope
- Bradycardia
- Electrolyte Abnormality
- Injurious Falls
- Acute Kidney Injury

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Serious Adverse Events

Event	Intensive	Standard	Hazard Ratio	P Value
Hypotension	110 (2.4%)	66 (1.4%)	1.67	0.001

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Serious Adverse Events

Event	Intensive	Standard	Hazard Ratio	P Value
Syncope	107 (2.3%)	80 (1.7%)	1.33	0.05

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Serious Adverse Events

Event	Intensive	Standard	Hazard Ratio	P Value
Bradycardia	87 (1.9%)	73 (1.6%)	1.19	0.28

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Serious Adverse Events

Event	Intensive	Standard	Hazard Ratio	P Value
Acute Kidney Injury	193 (4.1%)	117 (2.5%)	1.66	<0.001

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Serious Adverse Events

Event	Intensive	Standard	Hazard Ratio	P Value
Electrolyte Abnormality	144 (3.1%)	107 (2.3%)	1.35	0.02

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Serious Adverse Events

Event	Intensive	Standard	Hazard Ratio	P Value
Injurious Falls	105 (2.2%)	110 (2.3%)	0.95	0.71

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Limitations/Criticism

- Large portion of the hypertensive population excluded:
  - Diabetics, ESRD, Stroke
- Young hypertensive patients excluded
- Adverse events are increased and long term harm is not yet analyzed (i.e. AKI→CKD)
- Different outpatient exposure between treatment groups

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BENEFITS

	Absolute Risk Reduction	Relative Risk Reduction	NNT

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	Absolute Risk Reduction	Relative Risk Reduction	NNT
Primary Outcome (Combined CVD)	1.6%	25%	62

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Primary Outcome (Combined CVD)	1.6%	25%	62
Heart Failure	0.8%	38%	124

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BENEFITS

	Absolute Risk Reduction	Relative Risk Reduction	NNT
Primary Outcome (Combined CVD)	1.6%	25%	62
Heart Failure	0.8%	38%	124
CVD Death	0.6%	43%	167

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BENEFITS

	Absolute Risk Reduction	Relative Risk Reduction	NNT
Primary Outcome (Combined CVD)	1.6%	25%	62
Heart Failure	0.8%	38%	124
CVD Death	0.6%	43%	167
All Cause Mortality	1.2%	26%	85

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BENEFITS

	Absolute Risk Reduction	Relative Risk Reduction	NNT
Primary Outcome (Combined CVD)	1.6%	25%	62
Heart Failure	0.8%	38%	124
CVD Death	0.6%	43%	167
All Cause Mortality	1.2%	26%	85
Primary Outcome or Death	1.9%	21%	52

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These Benefits were Observed among **ALL** age groups including the **ELDERLY**

BUT NOT NURSING HOME!

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HARMS

	Absolute Risk Increase	Relative Risk Increase	NNH
All Adverse Events	1.3%	33%	80

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HARMS

	Absolute Risk Increase	Relative Risk Increase	NNH
All Adverse Events	1.3%	33%	80
Hypotension	1%	40%	106

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HARMS

	Absolute Risk Increase	Relative Risk Increase	NNH
All Adverse Events	1.3%	33%	80
Hypotension	1%	40%	106
Syncope	0.6%	25%	173

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HARMS

	Absolute Risk Increase	Relative Risk Increase	NNH
All Adverse Events	1.3%	33%	80
Hypotension	1%	40%	106
Syncope	0.6%	25%	173
Electrolyte Abnormalities	0.8%	26%	126

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HARMS

	Absolute Risk Increase	Relative Risk Increase	NNH
All Adverse Events	1.3%	33%	80
Hypotension	1%	40%	106
Syncope	0.6%	25%	173
Electrolyte Abnormalities	0.8%	35%	125
AKI	1.6%	39%	62

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