

Hypertension: An Update HOPE 3

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"alifting the whole people"

Defining Hypertension

"The operational definition of hypertension is the level at which the benefits... of action exceed those of inaction."

-Rose G., 1980

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 26, 2016 VOL. 374 NO. 21

Blood-Pressure Lowering in Intermediate-Risk Persons
without Cardiovascular Disease

HOPE 3 Investigators. *New Engl J Med* 2016;374:2009-20.

Objectives

1. Present an overview of the HOPE 3 trial (hypertension arm)
2. Analyze the results and considerations for practice.

Background

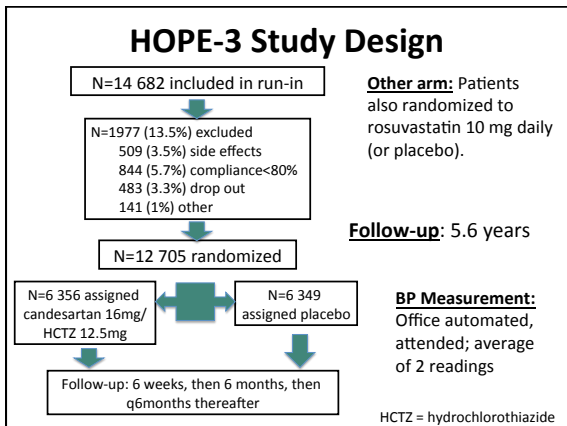
- For those at *intermediate risk of CVD* (defined as ~ 1% per year) who **do not have vascular disease, does the treatment of BP and lipids confer benefit?**
- R, C, DB, 2x2 factorial design, conducted in 21 countries
- Primary Outcomes: 2 co-primary outcomes:
 1. Death from CV cause, non-fatal MI or stroke
 2. #1 + resuscitated cardiac arrest, heart failure or revascularization
- Secondary Outcomes:
 1. Primary outcome #2 + angina with evidence of ischemia
 2. Fatal or non-fatal stroke

CVD = cardiovascular disease, MI = myocardial infarction

Inclusion Criteria

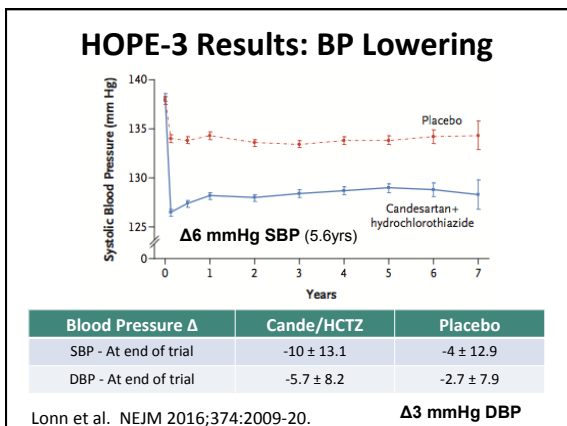
1. Age \geq 55 years (for men) and \geq 65 years (for women)
 2. At least one CV risk factor:
 - a. Waist/hip ratio \geq 0.85 in women, \geq 0.90 in men
 - b. Current or recent (within 5 yrs) tobacco use
 - c. Low HDL-C (<1.0 mmol/L in men and <1.3 in women)
 - d. Dysglycemia (IFG, IGT or DM treated with diet only)
 - e. Early renal dysfunction (microalbuminuria or eGFR<60 mL/min, or Scr>124 μ mol/L)
 - f. Family history of premature CAD in 1st degree relative
- No strict BP entry level, but most had SBP<160.

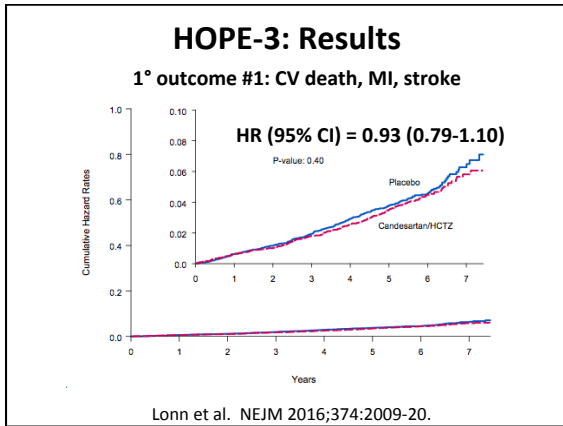
Lonn et al. NEJM 2016;374:2009-20.



Baseline Characteristics of HOPE-3 (n=12 705)

Characteristic	Mean or Percent
Age	66 years
Sex (female)	46%
BP	138/82
Cardiovascular risk factor – no. (%)	
Elevated waist:hip ratio	5511 (87%)
Hypertension	2398 (38%)
Low HDL-C	2297 (36%)
Tobacco use	1782 (28%)
Family history of premature CAD	1668 (26%)
Impaired fasting glucose or IGT	799 (13%)
Any antihypertensive	22%



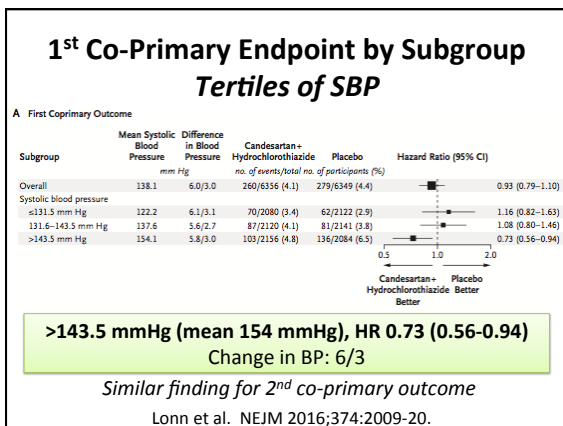


Results: Clinical Outcomes

Outcome	Cande + HCTZ N=6356 No. (%)	Placebo N=6349 No. (%)	HR, 95%CI	P-value
Co-Primary outcome 1*	260 (4.1)	279 (4.4)	0.93 (0.79-1.10)	0.40
Co-Primary outcome 2**	312 (4.9)	328 (5.2)	0.95 (0.81-1.11)	0.51
Secondary outcomes				
Co-P outcome 2 + angina	335 (5.3)	364 (5.7)	0.92 (0.79-1.06)	0.26
Stroke (fatal/non-fatal)	75 (1.2)	94 (1.5)	0.80 (0.59-1.08)	0.14

*Co-Primary Outcome #1: CV death, myocardial infarction, stroke
**Co-Primary Outcome #2: #1 + resuscitated cardiac arrest, heart failure, or revascularization

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Results as NNT
(for upper tertile BP subgroup)
(over 5.6 years)

Outcome	RRR	ARR	NNT
1st Co-Primary (CV death, MI, stroke)	26%	1.7	59
2nd Co-Primary (1st + HF/cardiac arrest/revacs)	24%	1.8	56
2nd outcome 1: 2 nd co-primary + angina	28%	2.3	44
2nd outcome 2: Stroke	40%	1.0	100

Lonn et al. NEJM 2016;374:2009-20.

HOPE-3: Safety

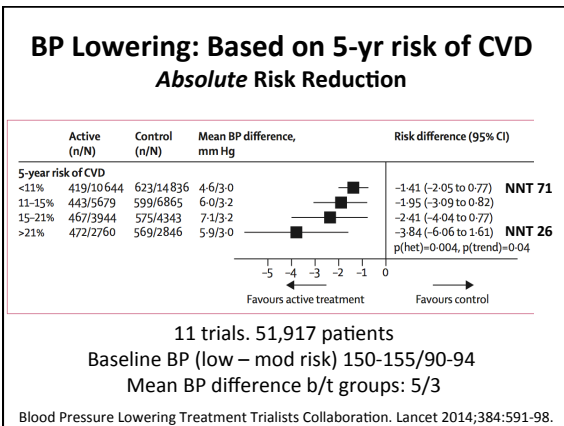
Item	Candesartan /HCTZ	Placebo	P-value
Permanent discontinuation of study drug	24.4%	25.2%	P=0.33
Incidence of symptomatic hypotension, dizziness or light-headedness	3.4%	2%	P<0.001
Syncope	No difference, 0.1% each arm		
Renal dysfunction or electrolyte abnormalities	No difference, 0.4% each arm		

No difference in rate of cancer, hospitalization for any cause and/or rates of serious, unexpected ADRs.

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Results in Context:

What do other studies tell us about BP lowering in low-moderate risk patients?



Discussion/Interpretation

- In HOPE 3, BP lowering in those at intermediate risk for primary prevention does not reduce CV events.
 - Lower CV risk and BP (138/82, “high normal”) compared to previous primary prevention trials
 - No benefit to be derived? Need to treat longer to realize benefit? Degree of BP lowering (compared to placebo) large enough? “Best” drugs used to lower BP?
- Baseline BP seems to matter
 - SBP<144 mmHg: no impact on primary endpoint at 5.6 years
 - SBP>144 mmHg: sub analysis indicates reduction in Major Adverse Cardiac Events (MACE), p=0.02

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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

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Recommended Office BP Treatment Targets

Treatment consists of health behaviour ± pharmacological management

Population	SBP	DBP
High Risk	≤120	NA
Diabetes	< 130	< 80
All others*	< 140	< 90

* Target BP with AOBP < 135/85

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2016
