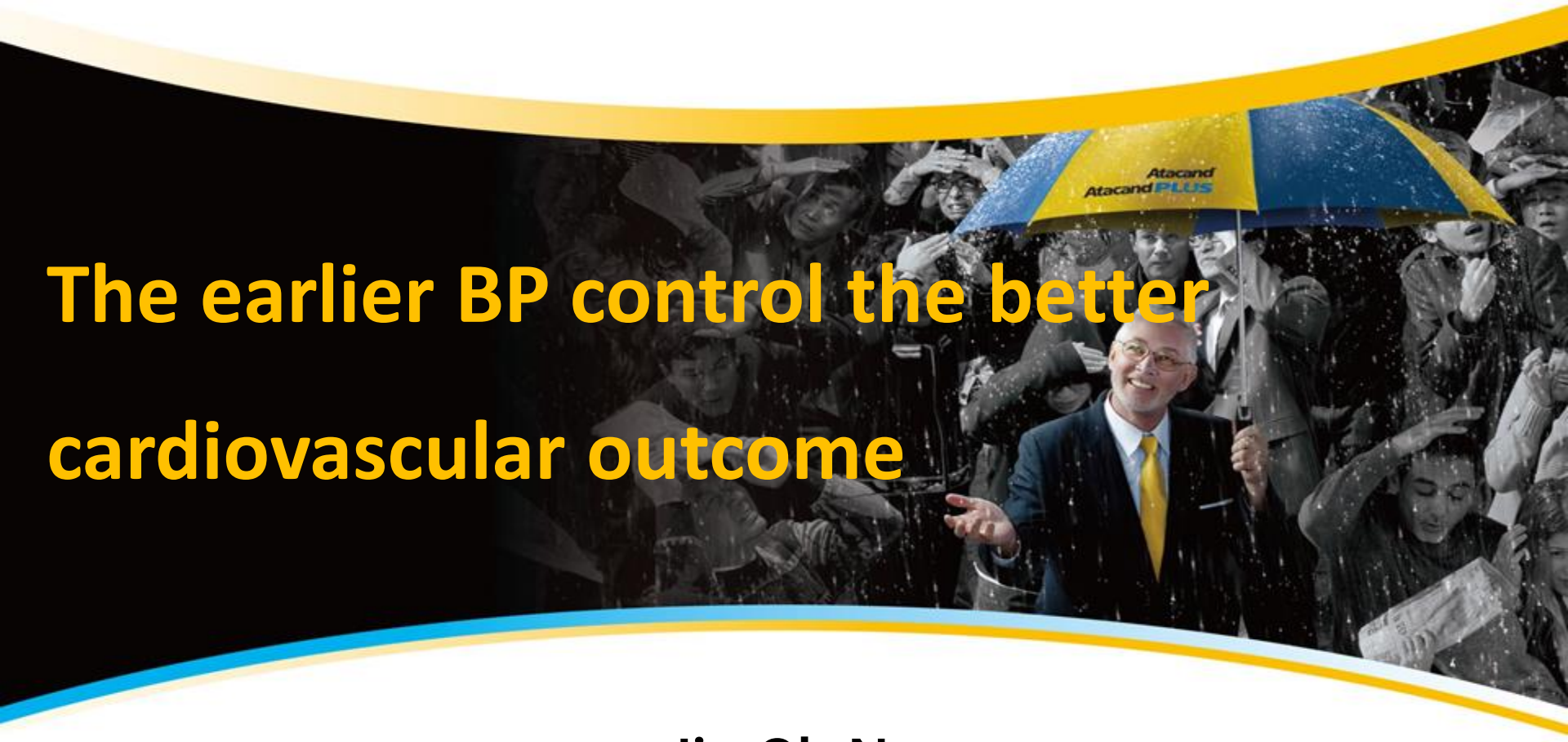
# The earlier BP control the better cardiovascular outcome




**Jin Oh Na**
**Cardiovascular center**
**Korea University Medical College**

AstraZeneca

녹십자
GREEN CROSS

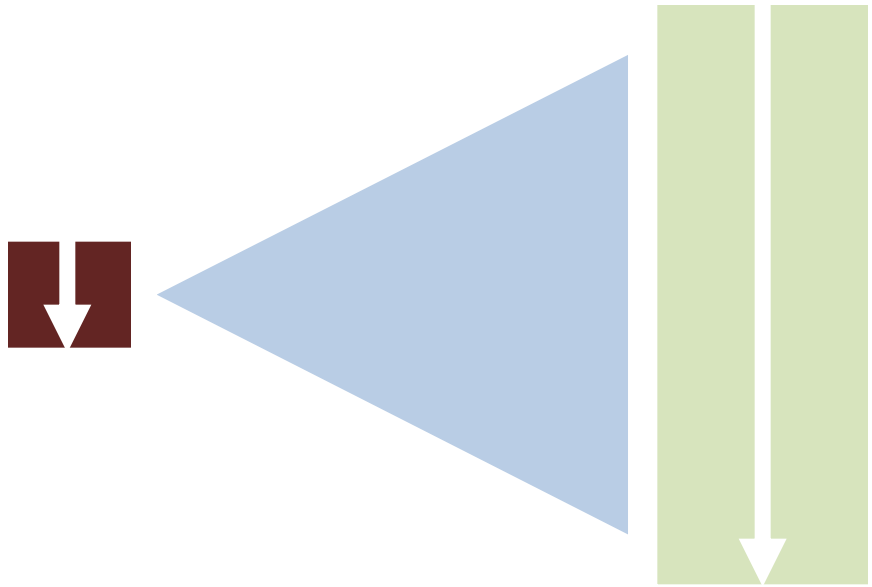
# Index

- Introduction
- HOPE-3 Trial
- Sprint Study
- Summary

# Each 2 mmHg decrease in SBP reduces CV risk by 7-10%

- Meta-analysis of 61 prospective, observational studies
- 1 million adults aged 40–69 y with BP > 115/75 mmHg
- 12.7 million person-years

**2 mmHg** decrease in mean SBP



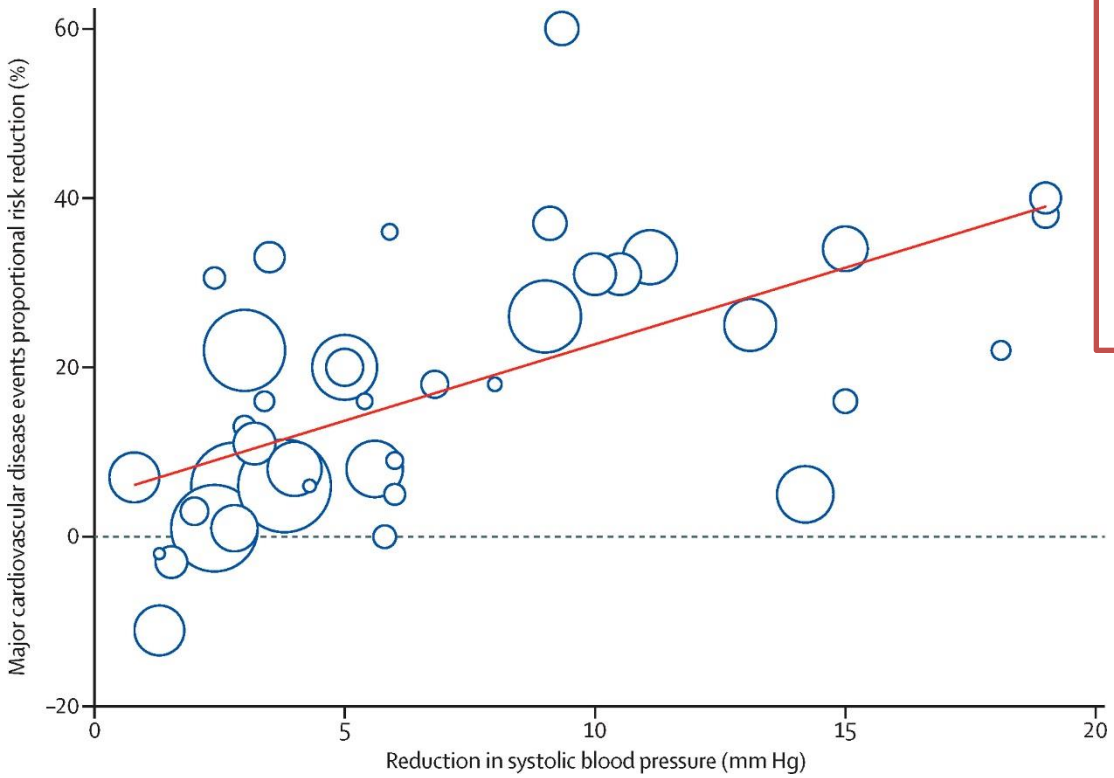
**7% reduction** in risk of IHD and other vascular disease mortality

**10% reduction** in risk of stroke mortality

Lewington S, et al. *Lancet.* 2010;360:1903-13.

# Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis

- 123 studies till 2015.7
- N = 613,815




**Every 10mmHg of SBP reduction;**

- ✓ **MACE** (RR 0·80, 95% CI 0·77–0·83),
- ✓ **CAD** (RR 0·83, 0·78–0·88),
- ✓ **Stroke** (RR 0·73, 0·68–0·77),
- ✓ **Heart failure** (RR 0·72, 0·67–0·78),
- ✓ **All-cause mortality** (RR 0·87, 0·84–0·91)

Strong support for lowering blood pressure to systolic blood pressures less than 130 mm Hg

Ettehad D, et al. *Lancet.* 2016;387:957-67.

# BP Control

## ’J-curved’ Theory

## Vs.

## ‘The Lower The Better’ Theory

# HOPE-3 Study
## (Heart Outcomes Prevention Evaluation)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

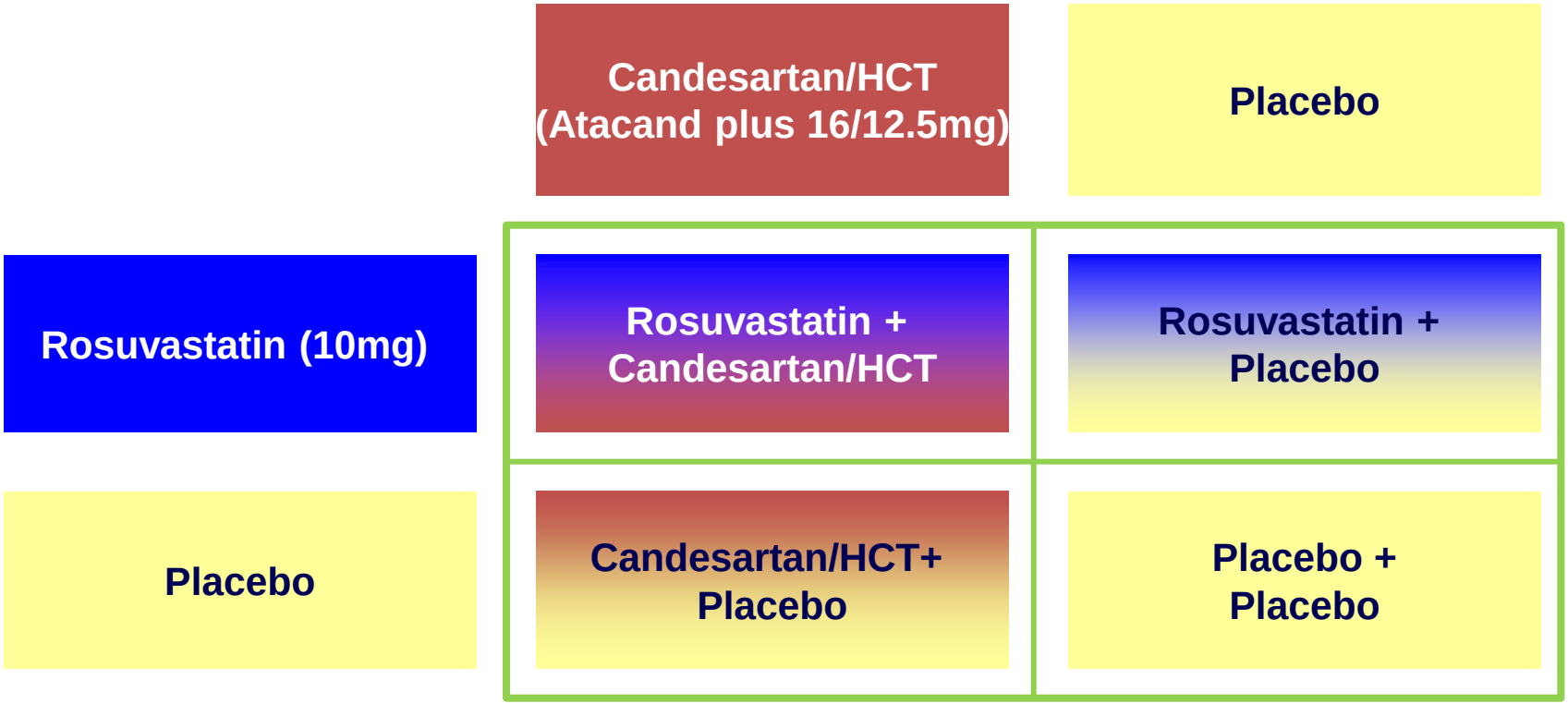
# Blood-Pressure Lowering in Intermediate-Risk Persons without Cardiovascular Disease

Eva M. Lonn, M.D., Jackie Bosch, Ph.D., Patricio López-Jaramillo, M.D., Ph.D., Jun Zhu, M.D., Lisheng Liu, M.D., Prem Pais, M.D., Rafael Diaz, M.D., Denis Xavier, M.D., Karen Sliwa, M.D., Ph.D., Antonio Dans, M.D., Alvaro Avezum, M.D., Ph.D., Leopoldo S. Piegas, M.D., Ph.D., Katalin Keltai, M.D., Ph.D., Matyas Keltai, M.D., Ph.D., Irina Chazova, M.D., Ph.D., Ron J.G. Peters, M.D., Ph.D., Claes Held, M.D., Ph.D., Khalid Yusoff, M.D., Basil S. Lewis, M.D., Petr Jansky, M.D., Alexander Parkhomenko, M.D., Ph.D., Kamlesh Khunti, M.D., Ph.D., William D. Toff, M.D., Christopher M. Reid, Ph.D., John Varigos, B.Sc., Lawrence A. Leiter, M.D., Dora I. Molina, M.D., Robert McKelvie, M.D., Ph.D., Janice Pogue, Ph.D.,* Joanne Wilkinson, B.A., Hyejung Jung, M.Sc., Gilles Dagenais, M.D., and Salim Yusuf, M.B., B.S., D.Phil., for the HOPE-3 Investigators†

This article was published on April 2, 2016, at NEJM.org.

# HOPE-3: 2 x 2 Factorial Design

N = 14,000 people at intermediate risk for CVD




Follow-up for an average of 6 years

# HOPE-3: BP, cholesterol, BP+cholesterol

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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Eva M. Lonn, M.D., Jackie Bosch, Ph.D., Patricio López-Jaramillo, M.D
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ABSTRACT

BACKGROUND

Antihypertensive therapy reduces the risk of cardiovascular events among persons and among those with a systolic blood pressure of 160 mm Hg but its role in persons at intermediate risk and with lower blood pressure

METHODS

In one comparison from a 2-by-2 factorial trial, we randomly assign participants at intermediate risk who did not have cardiovascular disease either candesartan at a dose of 16 mg per day plus hydrochlorothiazide of 12.5 mg per day or placebo. The first coprimary outcome was the co death from cardiovascular causes, nonfatal myocardial infarction, o stroke; the second coprimary outcome additionally included resuscitat arrest, heart failure, and revascularization. The median follow-up was

RESULTS

The mean blood pressure of the participants at baseline was 138.1/81.9 m decrease in blood pressure was 6.0/3.0 mm Hg greater in the active-treatm than in the placebo group. The first coprimary outcome occurred in 260 p (4.1%) in the active-treatment group and in 279 (4.4%) in the placebo gro ratio, 0.93; 95% confidence interval [CI], 0.79 to 1.10; P=0.40); the sec mary outcome occurred in 312 participants (4.9%) and 328 participants spectively (hazard ratio, 0.95; 95% CI, 0.81 to 1.11; P=0.51). In one of prespecified hypothesis-based subgroups, participants in the subgroup fo third of systolic blood pressure (>143.5 mm Hg) who were in the active group had significantly lower rates of the first and second coprimary outc those in the placebo group; effects were neutral in the middle and lo (P=0.02 and P=0.009, respectively, for trend in the two outcomes).

CONCLUSIONS

Therapy with candesartan at a dose of 16 mg per day plus hydrochloro a dose of 12.5 mg per day was not associated with a lower rate of maj vascular events than placebo among persons at intermediate risk who di cardiovascular disease. (Funded by the Canadian Institutes of Health Re AstraZeneca; ClinicalTrials.gov number, NCT00468923.)





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Cholesterol Lowering in Intermediate- Persons without Cardiovascular Dise

S. Yusuf, J. Bosch, G. Dagenais, J. Zhu, D. Xavier, L. Liu, P. Pais, P. López
L.A. Leiter, A. Dans, A. Avezum, L.S. Piegas, A. Parkhomenko, K. Keltai,
K. Sliwa, R.J.G. Peters, C. Held, I. Chazova, K. Yusoff, B.S. Lewis, P.
K. Khunti, W.D. Toff, C.M. Reid, J. Varigos, G. Sanchez-Vallejo, R. M
J. Pogue, * H. Jung, P. Gao, R. Diaz, and E. Lonn, for the HOPE-3 Inves

ABSTRACT

BACKGROUND

Previous trials have shown that the use of statins to lower cholesterol redu of cardiovascular events among persons without cardiovascular disease. T have involved persons with elevated lipid levels or inflammatory markers a mainly white persons. It is unclear whether the benefits of statins can be an intermediate-risk, ethnically diverse population without cardiovascul

METHODS

In one comparison from a 2-by-2 factorial trial, we randomly assigned participants in 21 countries who did not have cardiovascular disease and we mediate risk to receive rosuvastatin at a dose of 10 mg per day or placeb coprimary outcome was the composite of death from cardiovascular cause myocardial infarction, or nonfatal stroke, and the second coprimary out tionally included revascularization, heart failure, and resuscitated cardiac median follow-up was 5.6 years.

RESULTS

The overall mean low-density lipoprotein cholesterol level was 26.5% lo rosuvastatin group than in the placebo group. The first coprimary outcom in 235 participants (3.7%) in the rosuvastatin group and in 304 participa in the placebo group (hazard ratio, 0.76; 95% confidence interval [CI], 0. P=0.002). The results for the second coprimary outcome were consiste results for the first (occurring in 277 participants [4.4%] in the rosuvast and in 363 participants [5.7%] in the placebo group; hazard ratio, 0.75; 95 to 0.88; P<0.001). The results were also consistent in subgroups defined to cardiovascular risk at baseline, lipid level, C-reactive protein level, bloo and race or ethnic group. In the rosuvastatin group, there was no exces tes or cancers, but there was an excess of cataract surgery (in 3.8% of t pants, vs. 3.1% in the placebo group; P=0.02) and muscle symptoms ( the participants, vs. 4.7% in the placebo group; P=0.005).

CONCLUSIONS

Treatment with rosuvastatin at a dose of 10 mg per day resulted in a si lower risk of cardiovascular events than placebo in an intermediate-r cally diverse population without cardiovascular disease. (Funded by the Institutes of Health Research and AstraZeneca; HOPE-3 ClinicalTrials.g NCT00468923.)





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Blood-Pressure and Cholesterol Lowering in Persons without Cardiovascular Disease

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Patricio López-Jaramillo, M.D., Ph.D., Jun Zhu, M.D., Denis Xavier, M.D.,
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*Deceased.

†A complete list of the Heart Outco
Prevention Evaluation (HOPE)–3
investigators is provided in the Sup
mentary Appendix, available at N
org.

This article was published on Apr
2016, at NEJM.org.

DOI: 10.1056/NEJMoa1600177


ABSTRACT

BACKGROUND

Elevated blood pressure and elevated low-density lipoprotein (LDL) cholesterol increase the risk of cardiovascular disease. Lowering both should reduce the risk of cardiovascular events substantially.

METHODS

In a trial with 2-by-2 factorial design, we randomly assigned 12,705 participants at intermediate risk who did not have cardiovascular disease to rosuvastatin (10 mg per day) or placebo and to candesartan (16 mg per day) plus hydrochlorothiazide (12.5 mg per day) or placebo. In the analyses reported here, we compared the 3180 participants assigned to combined therapy (with rosuvastatin and the two antihypertensive agents) with the 3168 participants assigned to dual placebo. The first coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, and the second coprimary outcome additionally included heart failure, cardiac arrest, or revascularization. The median follow-up was 5.6 years.

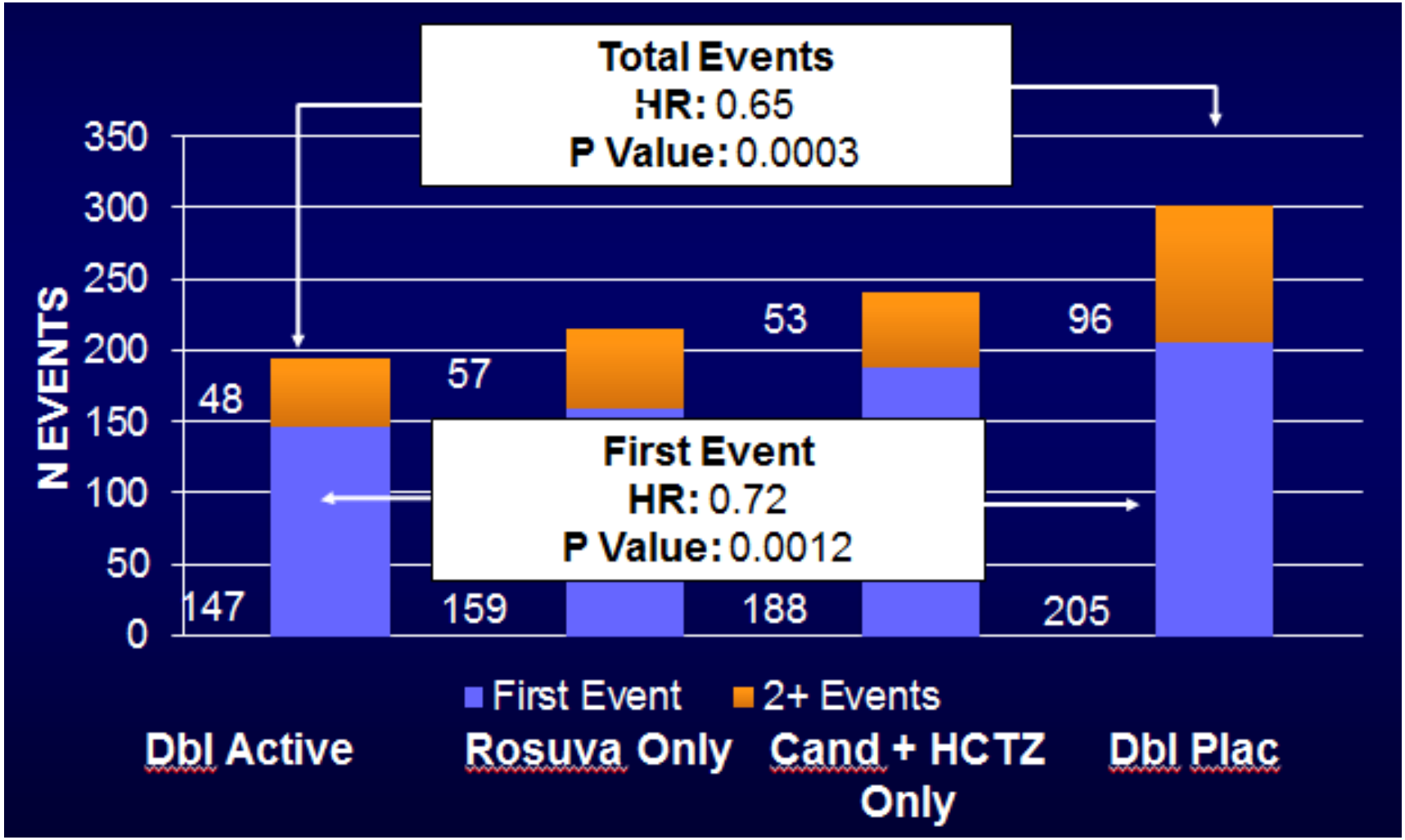
RESULTS

The decrease in the LDL cholesterol level was 33.7 mg per deciliter (0.87 mmol per liter) greater in the combined-therapy group than in the dual-placebo group, and the decrease in systolic blood pressure was 6.2 mm Hg greater with combined therapy than with dual placebo. The first coprimary outcome occurred in 113 participants (3.6%) in the combined-therapy group and in 157 (5.0%) in the dual-placebo group (hazard ratio, 0.71; 95% confidence interval [CI], 0.56 to 0.90; P=0.005). The second coprimary outcome occurred in 136 participants (4.3%) and 187 participants (5.9%), respectively (hazard ratio, 0.72; 95% CI, 0.57 to 0.89; P=0.003). Muscle weakness and dizziness were more common in the combined-therapy group than in the dual-placebo group, but the overall rate of discontinuation of the trial regimen was similar in the two groups.

CONCLUSIONS

The combination of rosuvastatin (10 mg per day), candesartan (16 mg per day), and hydrochlorothiazide (12.5 mg per day) was associated with a significantly lower rate of cardiovascular events than dual placebo among persons at intermediate risk who did not have cardiovascular disease. (Funded by the Canadian Institutes of Health Research and AstraZeneca; ClinicalTrials.gov number, NCT00468923.)

# HOPE-3 Study_1st & Recurrent CV Events



ORIGINAL ARTICLE

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ABSTRACT

**BACKGROUND**

Antihypertensive therapy reduces the risk of cardiovascular events among high-risk persons and among those with a systolic blood pressure of 160 mm Hg or higher, but its role in persons at intermediate risk and with lower blood pressure is unclear.

**METHODS**

In one comparison from a 2-by-2 factorial trial, we randomly assigned 12,705 participants at intermediate risk who did not have cardiovascular disease to receive either candesartan at a dose of 16 mg per day plus hydrochlorothiazide at a dose of 12.5 mg per day or placebo. The first coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke; the second coprimary outcome additionally included resuscitated cardiac arrest, heart failure, and revascularization. The median follow-up was 5.6 years.

- Intermediate-risk patients without CVD (annual risk of MACE = 1%)
- n = 12,705
- Primary outcome : MI, stroke, CVD death
- Mean f/up = 5.6 years
- Candesartan 16mg + HCZ 12.5mg
- Placebo

Lonn EM, et al. *NEJM.* 2016 Apr. 2.

# HOPE-3 Study Design (1)

- Multicenter, long-term, international, double-blind, randomized, placebo-controlled trial at 228 centers in 21 countries
- 2-by-2 factorial trial, randomly assigned 12,705 participants

- **Inclusion criteria**:
  -Age: ≥ 55 years old (Men) / ≥ 65 years old (Women)
  -Cardiovascular disease group excluded
  -Median 5.6 years f/up
  -Intermediate risk group (BP: 120~155mmHg)
  -Mean (±SD) systolic : 138.2±14.7 mm Hg
  **-Candesartan 16 mg/day & hydrochlorothiazide 12.5mg/day**
  vs Placebo

# HOPE-3 Study Design (2)

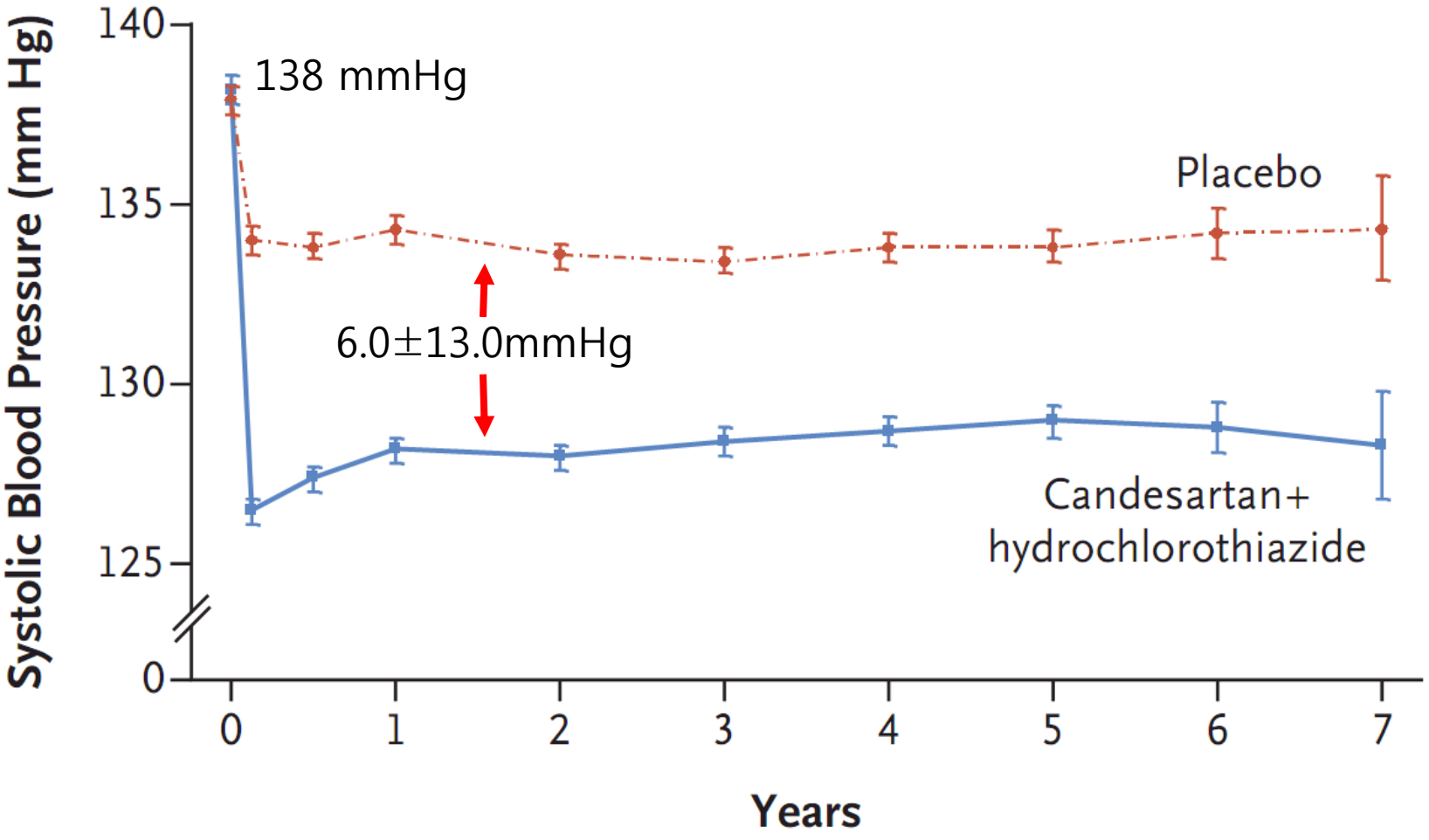
- **First coprimary outcome**:

  composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke;

- **Second coprimary outcome:**

  additionally included resuscitated cardiac arrest, heart failure, and revascularization

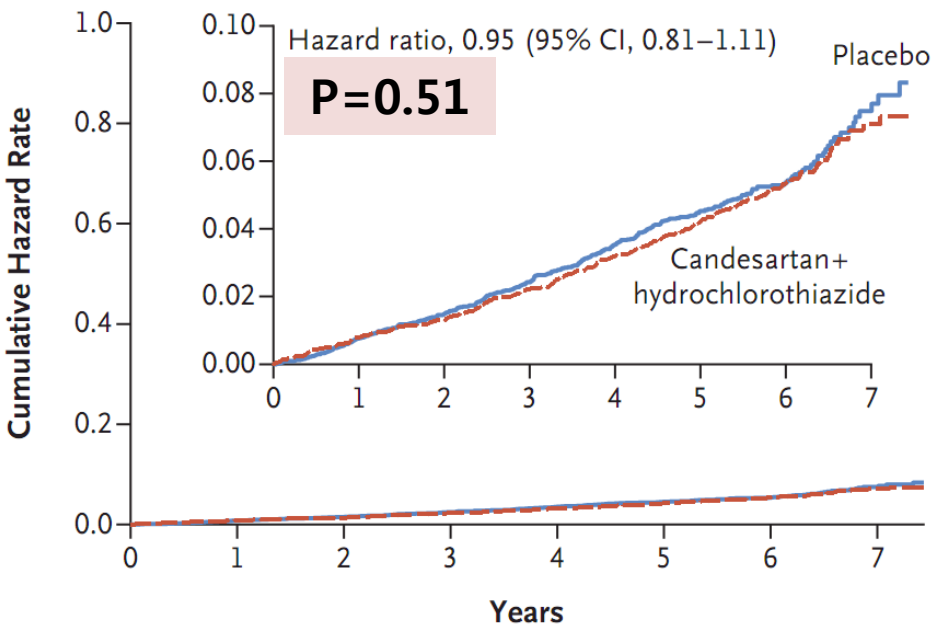
# HOPE-3 Study_Result
## Mean systolic BP



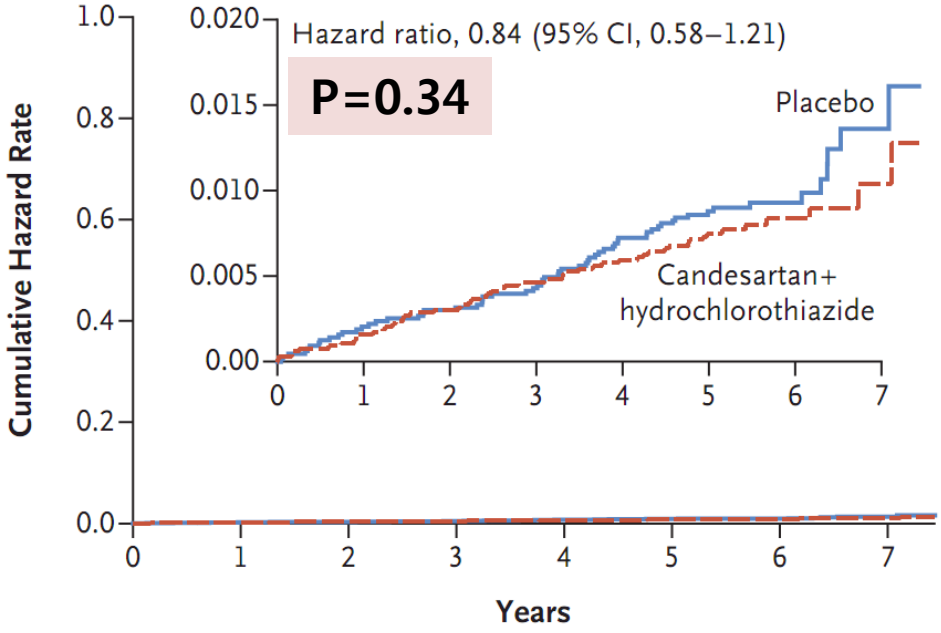

Lonn EM, et al. *NEJM.* 2016 Apr. 2.

# HOPE-3 Study_Result

< Death from CVD, MI, stroke, cardiac arrest, revascularization, HF>



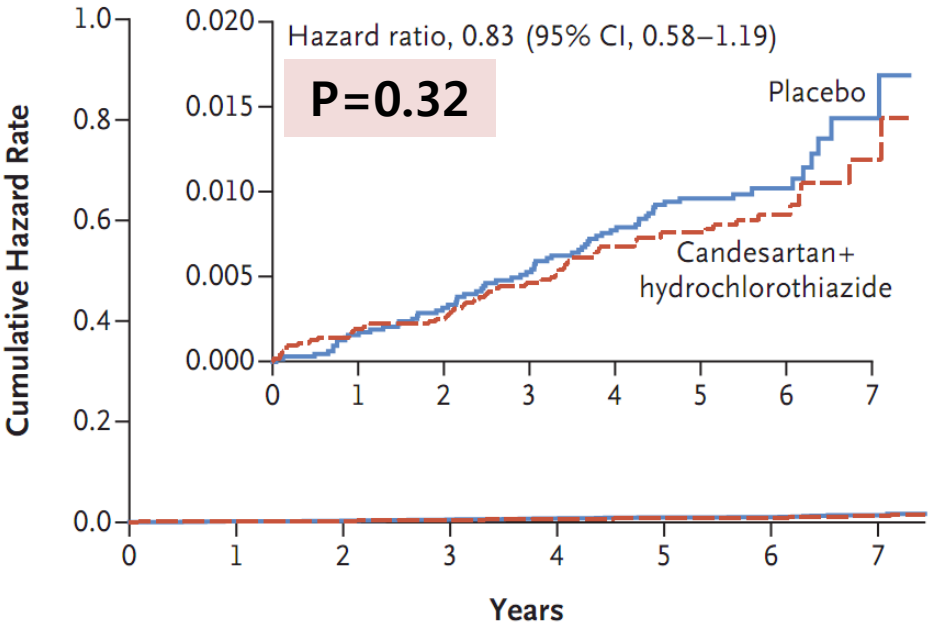

< MI >



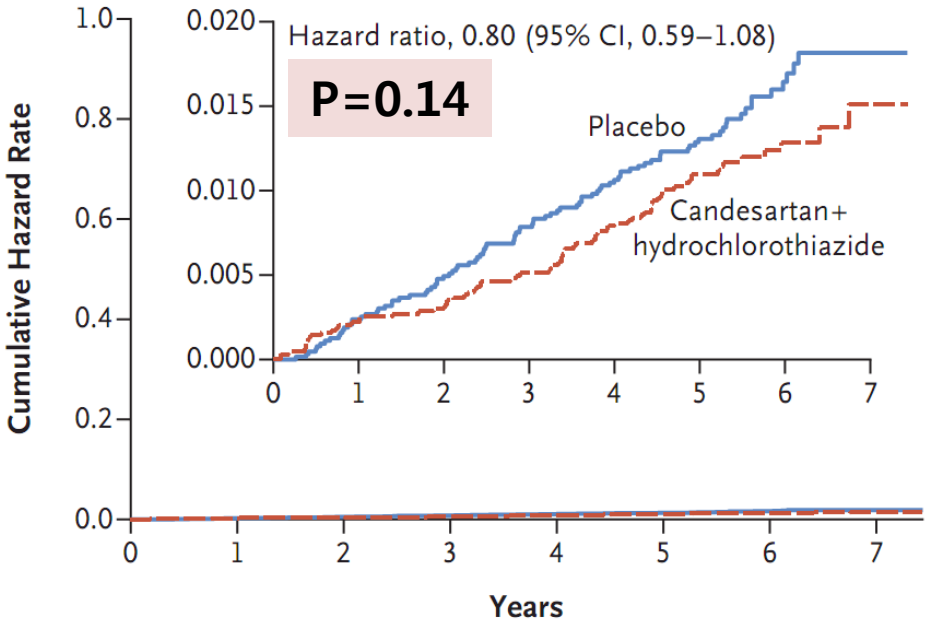

Lonn EM, et al. *NEJM.* 2016 Apr. 2.

# HOPE-3 Study_Result

## 〈 Coronary revascularization〉




## 〈 Stroke 〉

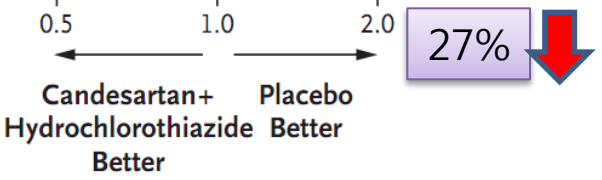



Lonn EM, et al. *NEJM.* 2016 Apr. 2.

# HOPE-3 Study_Result : by Thirds of SBP
# CV Death, MI, Stroke (Cardiac Arrest, Revascularization, Heart Failure)

**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) | |




- In one of the three subgroups of participants with uncomplicated mild hypertension, treatment significantly reduced the risk of CV events.

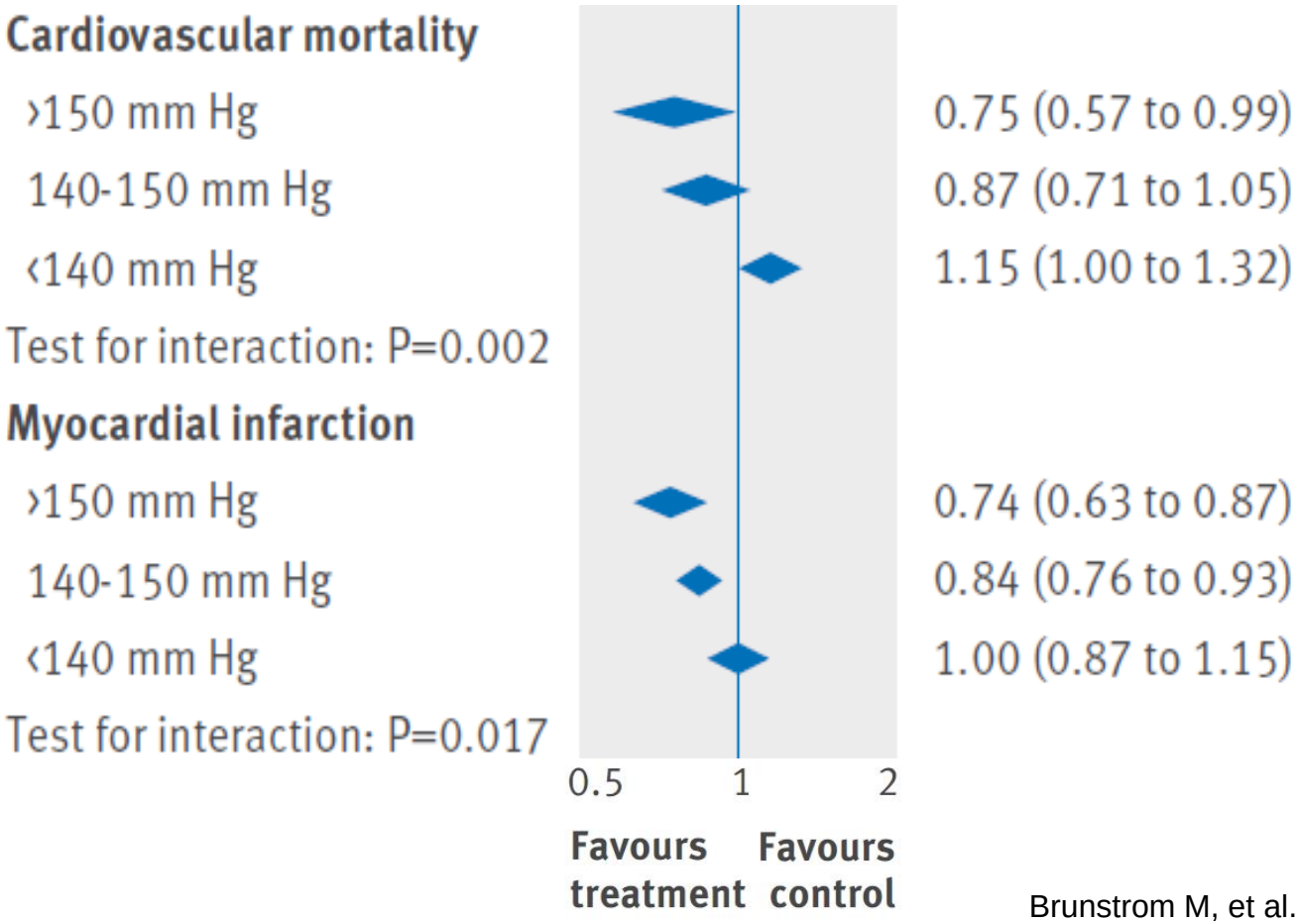
Lonn EM, et al. *NEJM.* 2016 Apr. 2.

# HOPE-3 Study Conclusion

- Therapy with candesartan at a dose of 16 mg per day plus hydrochlorothiazide at a dose of 12.5 mg per day was not associated with a lower rate of major cardiovascular events than placebo
- Subgroup for the upper third of **systolic blood pressure (>143.5 mm Hg) had significantly lower rates (27%) of the first and second coprimary outcomes than those in the placebo group;**
- Results were neutral in the middle third, and trended towards harm in the lowest third of SBP
- Treatment increased lightheadedness, but not syncope or renal dysfunction
- HOPE-3 Study supports **'J-curved' theory**
- Contradicting to SPRINT study of **'The Lower the Better' theory**

# Meta analysis of BP Lowering Trials in DM (49 trial, 73,738 participants with DM)

Results by Baseline Levels

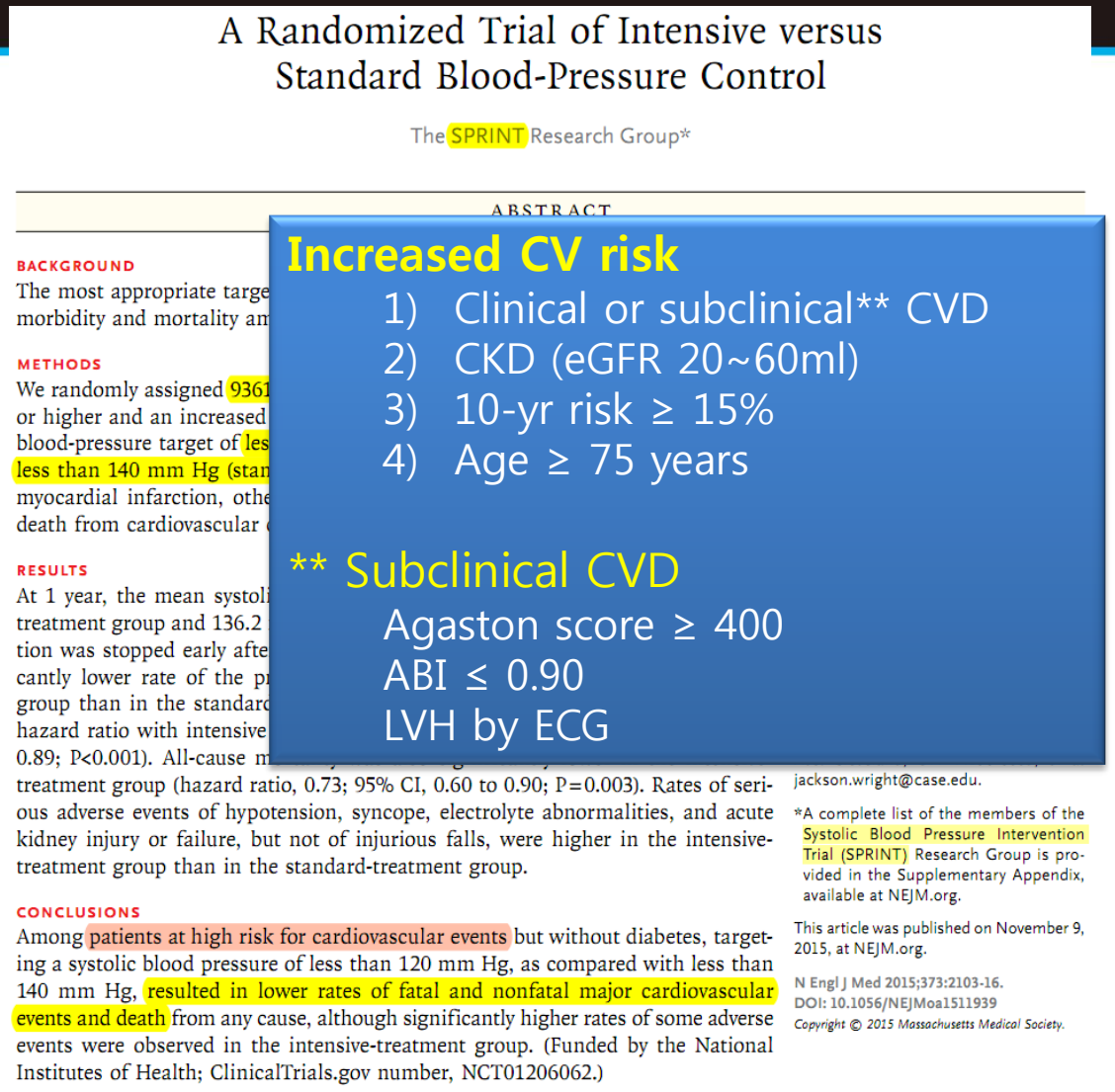



Brunstrom M, et al. *BMJ.* 2016;352:i717

# SPRINT Study

# SPRINT study

## (Systolic Blood Pressure Intervention Trial)



A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

ABSTRACT

BACKGROUND

The most appropriate targe
morbidity and mortality an

METHODS

We randomly assigned 9361
or higher and an increased
blood-pressure target of les
less than 140 mm Hg (stan
myocardial infarction, othe
death from cardiovascular

RESULTS

At 1 year, the mean systoli
treatment group and 136.2
tion was stopped early afte
cantly lower rate of the pr
group than in the standard
hazard ratio with intensive
0.89; P<0.001). All-cause m
treatment group (hazard ratio, 0.73; 95% CI, 0.60 to 0.90; P=0.003). Rates of serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure, but not of injurious falls, were higher in the intensive-treatment group than in the standard-treatment group.

CONCLUSIONS

Among patients at high risk for cardiovascular events but without diabetes, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause, although significantly higher rates of some adverse events were observed in the intensive-treatment group. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT01206062.)

jackson.wright@case.edu.

*A complete list of the members of the Systolic Blood Pressure Intervention Trial (SPRINT) Research Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 9, 2015, at NEJM.org.

N Engl J Med 2015;373:2103-16.
DOI: 10.1056/NEJMoa1511939
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**Increased CV risk**

1) Clinical or subclinical** CVD
2) CKD (eGFR 20~60ml)
3) 10-yr risk ≥ 15%
4) Age ≥ 75 years

** Subclinical CVD

Agaston score ≥ 400
ABI ≤ 0.90
LVH by ECG

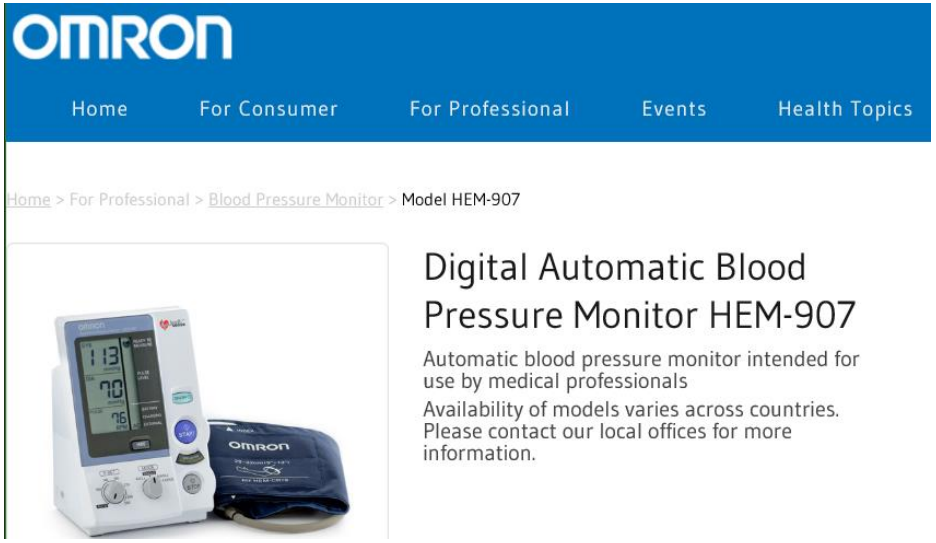
- Age ≥50, SBP 130-180mmHg
- Increased CV risk (except diabetes and CVA)
- n = 9,361
- Primary outcome : MI, stroke, CVD death, ACS s MI, acute dHF
- Mean f/up = 3.26 years

- Intensive therapy: SBP 〈 120mmHg
- Standard therapy: SBP 〈 140mmHg

Wright JT Jr, et al. *NEJM.* 2015;373:2103-16.

# Sprint Design

- A randomized, controlled, open label trial sponsored by the NIH and conducted at 102 US sites.
- Inclusion criteria. Age ≥ 50 years old, systolic BP: 130~180 mm Hg +
  - Clinical or subclinical CVD (other than stroke)
  - CKD, defined as eGFR (MDRD): 20 ~ 60 mL/min/1.73 $m^2$
  - Framingham risk score ≥ 15%
  - Age ≥ 75 or older.
- **<u>Major exclusion criteria</u>**
  - Diabetes
  - Stroke
  - Polycystic kidney disease,
  - CKD: eGFR < 20 mL/min/1.73 $m^2$
  - Proteinuria (excretion > 1 g/day)
- SBP target < 120 vs. < 140 mmHg

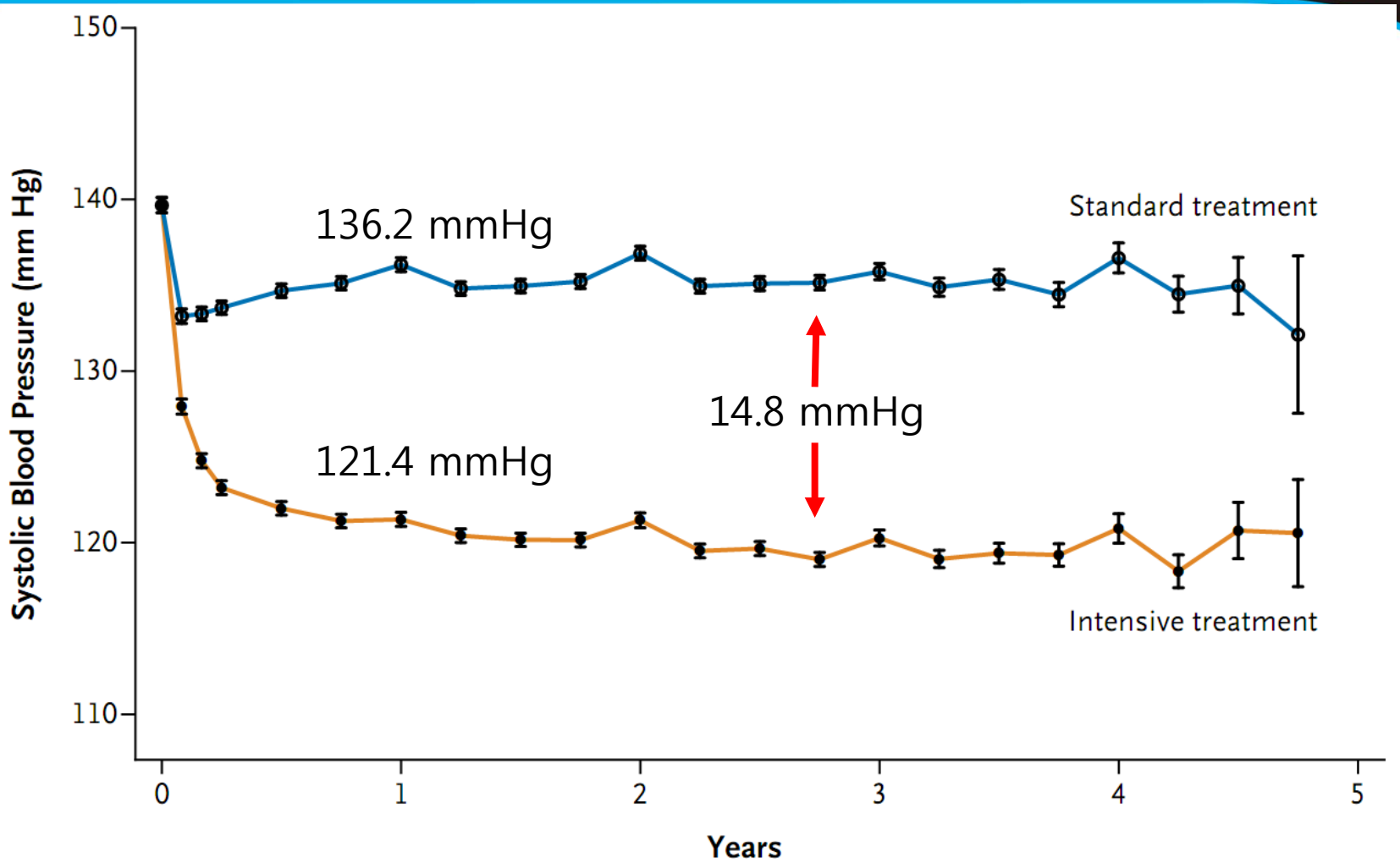


# Sprint Study Design / Without DM

- Primary composite outcome
  - MI, other acute coronary syndrome, stroke, HF or death from CV causes

- Mean age 67.9, 28% ≥75 y-o
- Mean Framingham risk score: 20%, 20% already had CV disease
- Mean baseline BP 139.7/78.2 mmHg
- Mean eGFR: 71 mL/min/1.73 $m^2$
- Mean total cholesterol 190 mg/dL, FBS 99 mg/dL, BMI 30 kg/m2

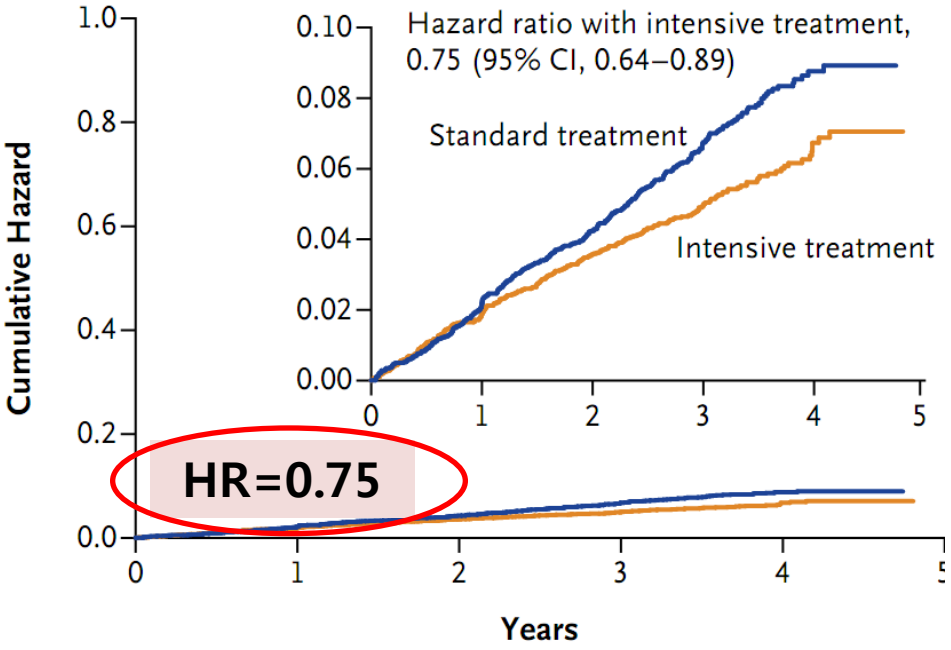
# Sprint Study – result of systolic BP



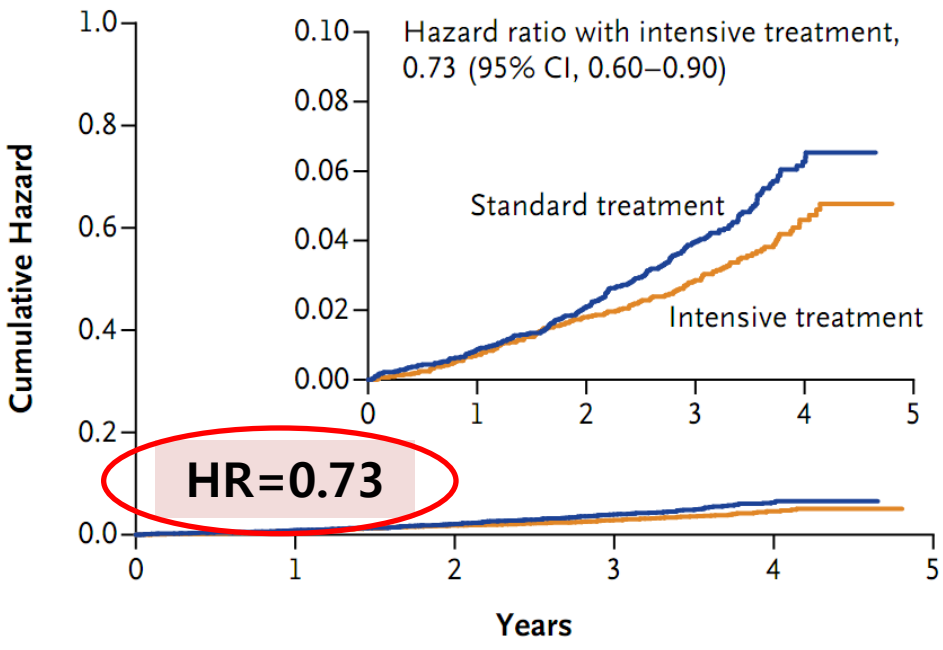

Wright JT Jr, et al. *NEJM.* 2015;373:2103-16.

# Sprint Study - results

## ⟨ Primary outcome ⟩




## ⟨ Death from any cause ⟩

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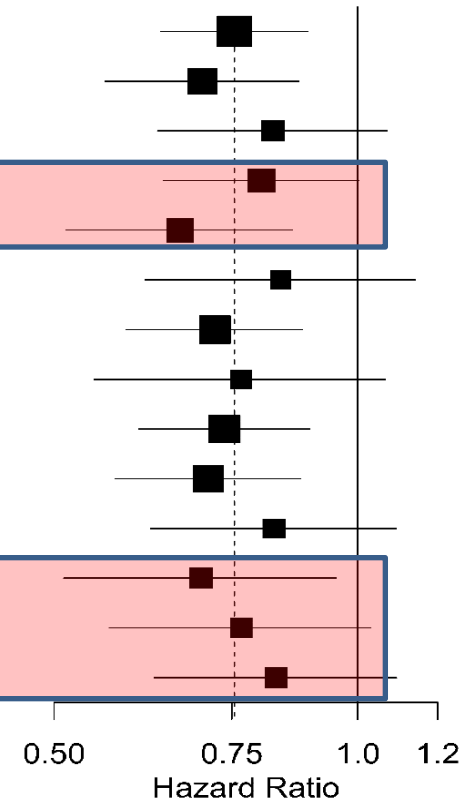
# Sprint Study - results

| 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
*Treatment by subgroup interaction

# Sprint Study - results

**Table 2. Primary and Secondary Outcomes and Renal Outcomes.***

| Outcome | Intensive Treatment | | Standard Treatment | | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|---|---|
| | *no. of patients (%)* | *% per year* | *no. of patients (%)* | *% per year* | | |
| **All participants** | **(N=4678)** | | **(N=4683)** | | | |
| Primary outcome† | 243 (5.2) | 1.65 | 319 (6.8) | 2.19 | 0.75 (0.64–0.89) | <0.001 |
| Secondary outcomes | | | | | | |
| Myocardial infarction | 97 (2.1) | 0.65 | 116 (2.5) | 0.78 | 0.83 (0.64–1.09) | 0.19 |
| Acute coronary syndrome | 40 (0.9) | 0.27 | 40 (0.9) | 0.27 | 1.00 (0.64–1.55) | 0.99 |
| Stroke | 62 (1.3) | 0.41 | 70 (1.5) | 0.47 | 0.89 (0.63–1.25) | 0.50 |
| Heart failure | 62 (1.3) | 0.41 | 100 (2.1) | 0.67 | 0.62 (0.45–0.84) | 0.002 |
| Death from cardiovascular causes | 37 (0.8) | 0.25 | 65 (1.4) | 0.43 | 0.57 (0.38–0.85) | 0.005 |
| Death from any cause | 155 (3.3) | 1.03 | 210 (4.5) | 1.40 | 0.73 (0.60–0.90) | 0.003 |
| Primary outcome or death | 332 (7.1) | 2.25 | 423 (9.0) | 2.90 | 0.78 (0.67–0.90) | <0.001 |

Wright JT Jr, et al. *NEJM.* 2015;373:2103-16.

# Sprint Trial Design / Medication

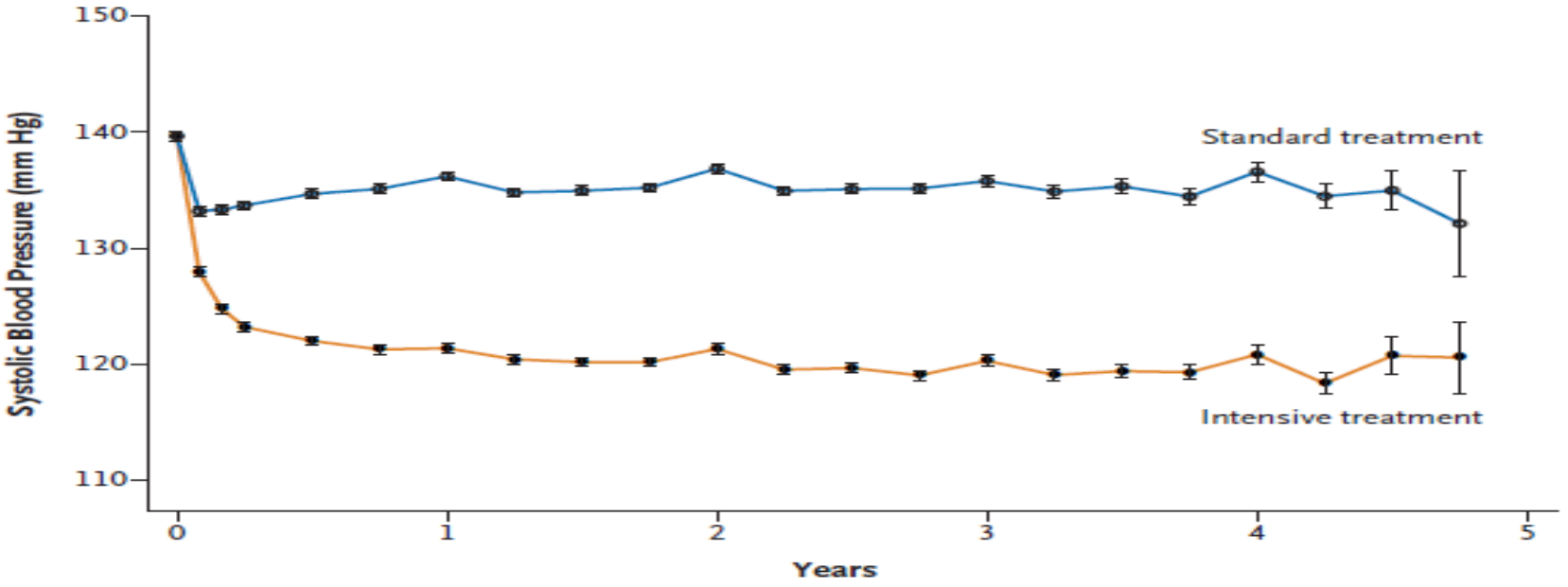
TABLE 1

## Antihypertensive medications used in SPRINT

| Medication class | Intensive therapy (%) | Standard therapy (%) |
|---|---|---|
| Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers | 76.7 | 55.2 |
| Thiazide-type diuretics | 54.9 | 33.3 |
| Dihydropyridine calcium channel blockers | 52.8 | 31.3 |
| Beta-blockers | 41.1 | 30.8 |
| Aldosterone antagonists | 8.7 | 4.0 |
| Other potassium-sparing diuretics | 3.1 | 2.5 |
| Nondihydropyridine calcium channel blockers | 4.7 | 4.3 |
| Direct vasodilators | 7.3 | 2.4 |

Information from SPRINT Research Group; Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015; 373:2103–2116.

# Number of antihypertensive medications




| 구분 | Mean BP | 0 yr | 1 yr | 2 yr | 3 yr | 4 yr | 5 yr |
|---|---|---|---|---|---|---|---|
| Standard | 136.2mmHg | 1.7 | 1.8 | 1.8 | 1.8 | 1.8 | 1.9 |
| Intensive | 121.4mmHg | 2.3 | 2.7 | 2.8 | 2.8 | 2.8 | 3.0 |

# SPRINT Study / Adverse Event

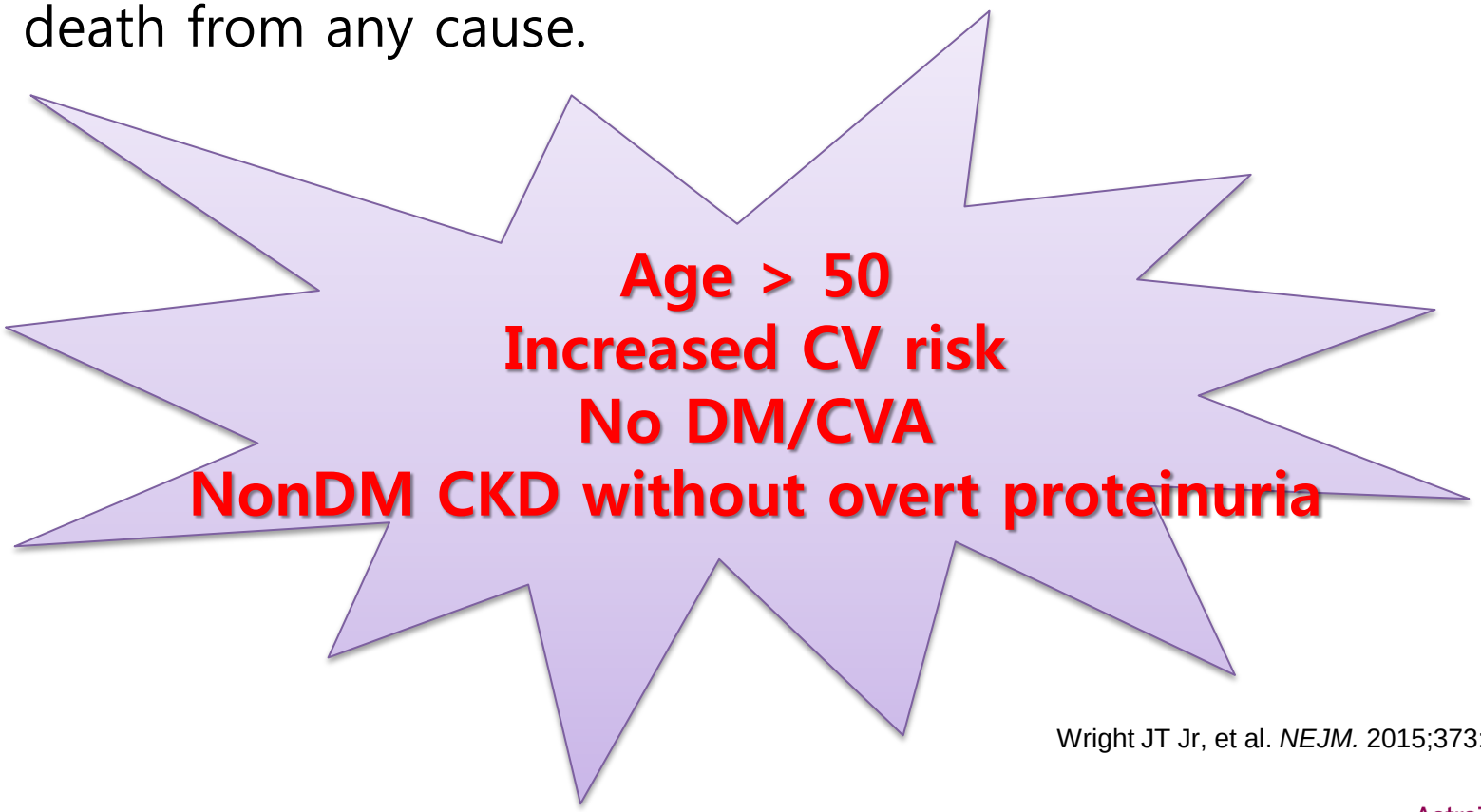
| Adverse events (ER+SAE) | % of patients | | |
|---|---|---|---|
| | Intensive therapy | Standard therapy | Hazard Ratio |
| **Hypotension** | 3.4 | 2.0 | **1.70** |
| **Syncope** | 3.5 | 2.4 | **1.44** |
| **Hyponatremia** | 3.8 | 2.1 | **1.76** |
| **Hypokalemia** | 2.4 | 1.6 | **1.5** |
| Injurious fall | 7.1 | 7.1 | 1.00 |
| **Orthostatic hypotension without dizziness** | 16.6 | 18.3 | **0.88** |
| Orthostatic hypotension with dizziness | 1.3 | 1.5 | 0.85 |
| **Acute kidney injury** | 4.4 | 2.6 | **1.71** |

# Sprint Study – 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
- Trial stopped early, due to benefit, after median follow-up of 3.26 years
- Incidence of primary outcome (composite of CVD events) 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.

# Sprint Study - Conclusion

- Among patients at high risk for CV events, intensive therapy resulted in **lower** rate of major CV events and death from any cause.

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# HOPE-3 vs. Sprint Study

## < HOPE-3 >

- Intermediate-risk patients without CVD (annual risk of MACE = 1%)
- n = 12,705
- Primary outcome : MI, stroke, CVD death
- Mean f/up = 5.6 years
- Candesartan 16mg + HCZ 12.5mg
- Placebo

## < SPRINT >

- Age ≥50, SBP 130-180mmHg
- Increased CV risk (except diabetes and CVA)
- n = 9,361
- Primary outcome : MI, stroke, CVD death, ACS s MI, acute dHF
- Mean f/up = 3.26 years
- Intensive therapy: SBP 〈 120mmHg
- Standard therapy: SBP 〈 140mmHg
- *Automated BP measurement*

# Summary

- According to HOPE-3 study, basal SBP is the key indicator, and Subgroup for the upper third of systolic blood pressure (>143.5 mm Hg) had significantly lower rates **(27%)** of the first and second coprimary outcomes
- Less aggressive BP control for **intermediate-risk patients** is reasonable according to HOPE-3 trial.
- Intensive BP control may be used in **selected**, **high-risk patients** treated in specialized settings using automated BP measurements.

- 'J-curve' theory vs. 'The lower the better' theory has been conflict.

# BP Control

**Standard Treatment**

**Vs.**

**Intensive Treatment**

# Thank you!