MAYO CLINIC

Evaluation and Management of Hypertension in Women

Vesna D. Garovic, M.D.

Moscow, Russia, December 2016

Women are not small men

"There is nothing as powerful as an idea whose time has come."

Victor Hugo, 1877

Objectives

- Update current recommendations on BP measurement and confirmation of HTN
- HTN in women throughout their reproductive age
- Review current recommendations regarding BP treatment goals
  - Discuss the Systolic Hypertension Intervention Trial (SPRINT)
- Sex-specific hypertension issues

Diagnosis of Hypertension
Office BP Measurement

- No caffeine, nicotine, exercise for 30 min
- Empty bladder
- Seated quietly for 5 minutes
- Feet on floor, back supported, arm supported at heart level
- Appropriate cuff size
- No talking during measurement

Office Blood Pressure Measurement

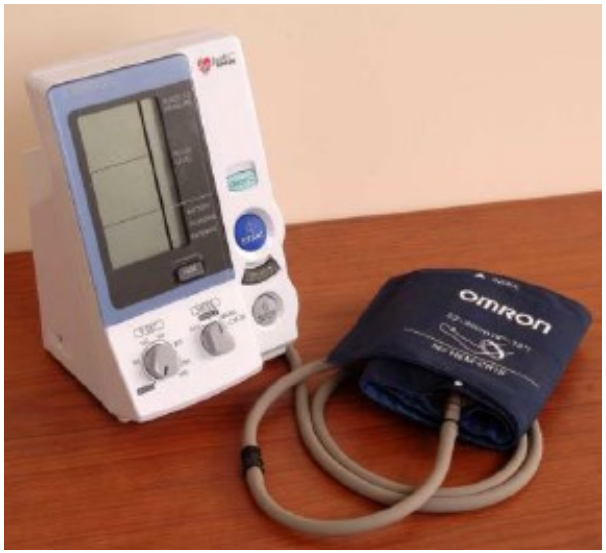
Automatic (oscillometric)

Measurement using electronic (oscillometric) upper arm devices is preferred to auscultatory devices

Obtain at least 3 readings and average the last 2.

Office Blood Pressure Measurement
Office Automated (Unattended)

Unattended automated procedure is ideal



Initial BP after 1 minute.

6 measurements are made at 1 minute intervals – device averages last 5 readings

HTN Treatment 2016
Confirmation of Diagnosis

- U.S. Preventive Services Task Force: High Blood Pressure in Adults: Screening – Statement
- ABPM (self-BP monitoring) better predictor than Office BP of fatal and non-fatal CVD
  - **ABPM is the reference standard for confirming the diagnosis of HTN**
  - **Good quality evidence suggests that confirmation using self- BP monitoring may also be acceptable**

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Ann Intern Med 2015

HTN Treatment 2016
Definition of HTN by Method of Measurement

Method	Equivalent BP (mm Hg)
Quality manual office BP	140/90
AOBP (attended)	
AOBP (unattended)	135/85
Home BP (3-7 days)	135/85
24 hour ABPM:	
Awake	135/85
Asleep	120/70
24-Hour	130/80

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Family Practice 2011;28:110, J Hypertens 2013;31:1731, Hypertension 2010;28:703

HTN Treatment 2016
Home Monitoring for HTN Follow-up

- Improves adherence/cost of treatment
- Identifies white-coat and masked effects
  - Appropriate training under medical supervision
  - AHA guidelines
  - Twice daily measurements (morning and evening – 2 readings averaged) for 3-7 days prior to each office visit

HTN Treatment 2016
Take Home Points

- **Automated methods** are preferred over the manual method for office BP measurement
- **24-hour ABPM** is the reference standard for confirming the diagnosis of HTN
- **Self-monitoring** is a suitable alternative for confirming HTN and SOC for follow-up care

Sex Differences in CV System

Anatomy: ↓ LV mass, LA, vessel size

CV function: ↓ 10% stroke volume, ↑ HR 3-5 bpm, ↑ EF; longer QTc; Hormone effects: on ECG, hematological indices; more prone to orthostatic hypotension, syncope

Physiology: ↓ sympathetic, ↑ parasympathetic activity; RAAS activity

Stress test: ↑ HR, CO, and SVR, increase in BP

NO SEX-SPECIFIC GUIDLEINES!!!

Sex-specific Risk Factors

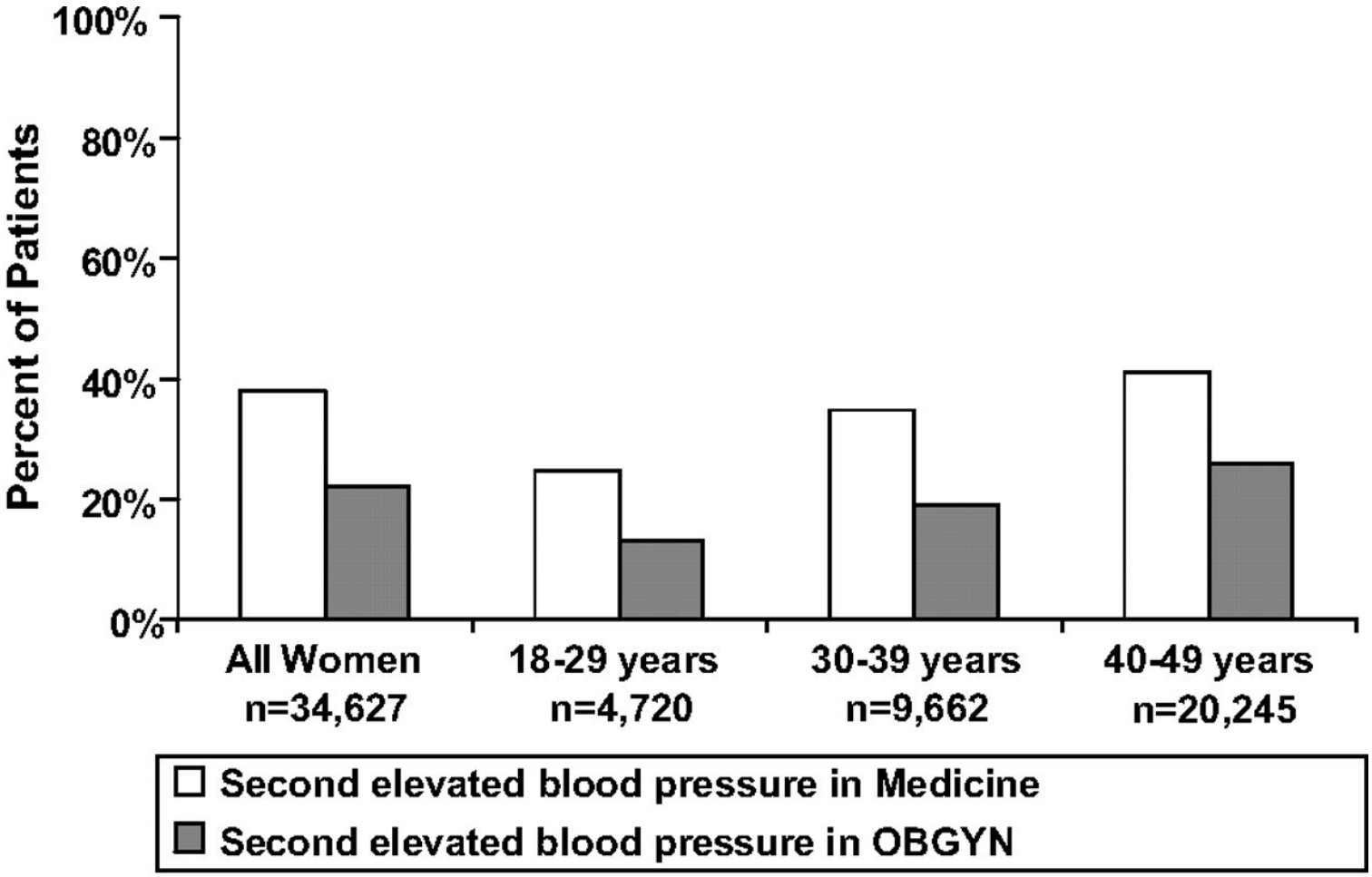
- Oral contraceptives
- Pregnancy
- Preeclampsia and gestational DM
- HRT

- Stronger, more prevalent in women, risk factors
  - Hypertension
  - DM
  - Atrial fibrillation
  - Migraine with aura

Oral Contraceptives and Hypertension

- OCs frequently cause a mild elevation in blood pressure within the normal range
- Overt hypertension can occur
- Early reports: preparations containing at least 50 mcg of estrogen and 1 to 4 mg of progestin, HTN incidence 5%
- Nurses' Health Study: RR of HTN compared with women who never used OC: 1.8 for current users and 1.2 for previous users
- Hypertensive OC users ↑increased risk of MI and stroke relative to nonusers

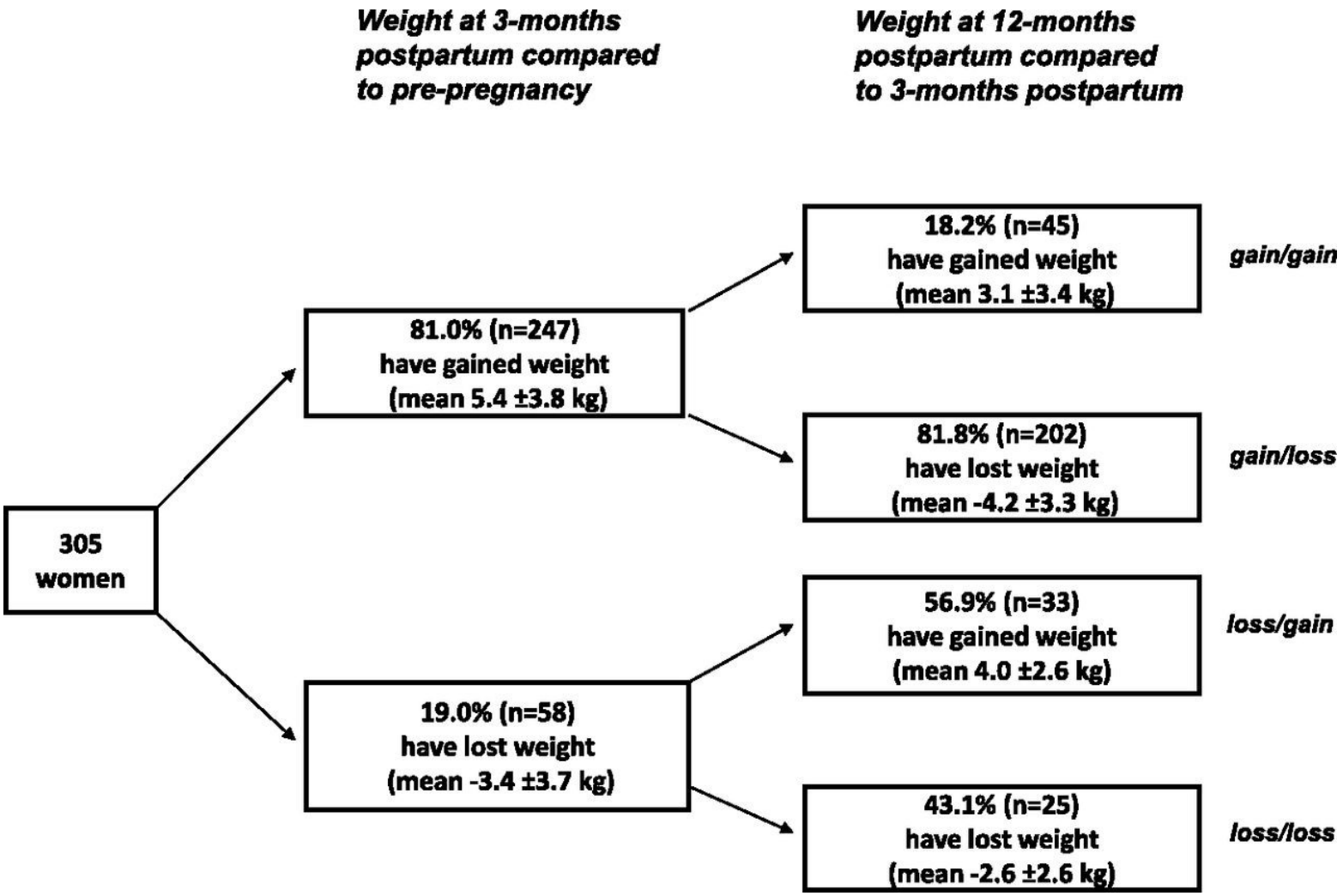
Hypertension recognized within 12 months of second consecutive elevated blood pressure, by patient age.



p<.001 for all comparisons

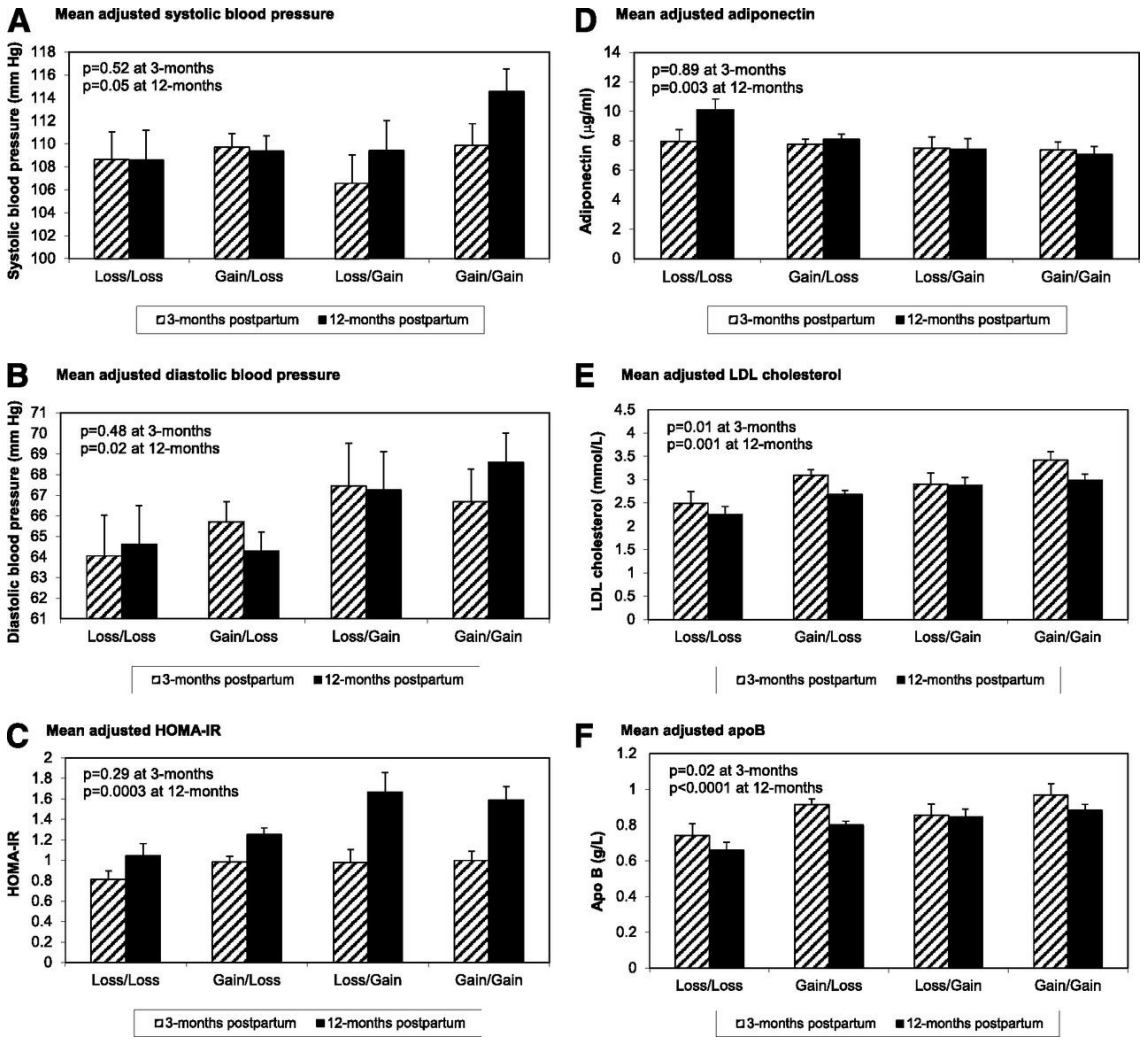
Julie Schmittdiel et al. Hypertension. 2011;57:717-722

Patterns of change in weight in women between prepregnancy and 3 months postpartum and between 3 and 12 months postpartum.



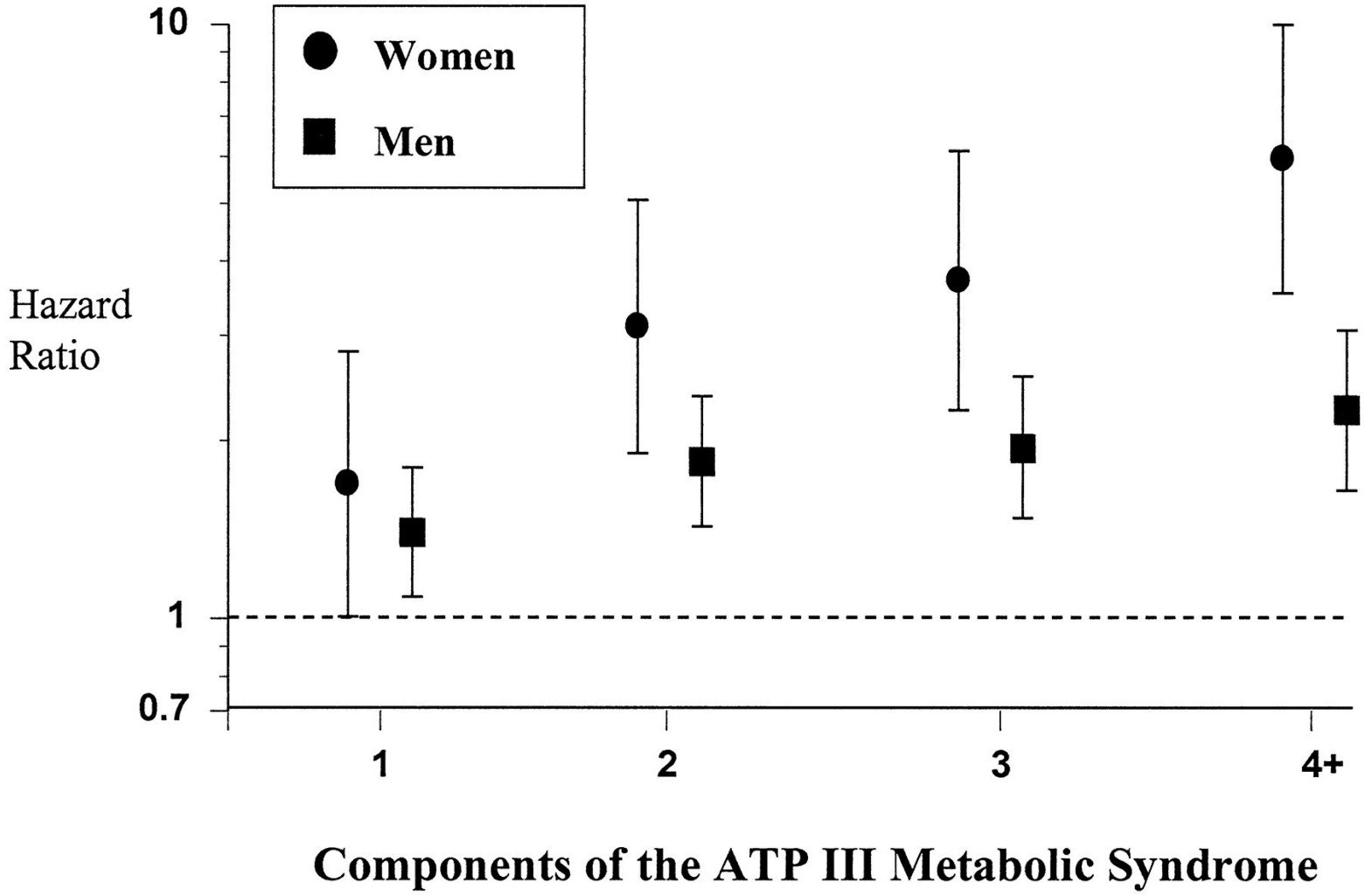
Simone Kew et al. Dia Care 2014;37:1998-2006

Mean adjusted levels in each group for the following cardiometabolic risk factors at 3 and 12 months postpartum: (A) systolic blood pressure, (B) diastolic blood pressure, (C) HOMA-IR, (D) adiponectin, (E) LDL cholesterol, and (F) apoB.



Simone Kew et al. Dia Care 2014;37:1998-2006

HRs of CHD associated with the presence of ≥ 1 components of the metabolic syndrome



Ann Marie McNeill et al. Dia Care 2005;28:385-390

Summary Recommendations
Women <50 years

- Closely monitor BP during and after pregnancy
- Yearly assessment of BP, lipids, FBG, and BMI

ACOG, Task force on HTN in pregnancy. Obstet Gynecol 2013

- Treatment according to current guidelines
- Life-style modifications

At present, suboptimal identification and treatment of CVD risks

Postmenopausal Hypertension

- After menopause, BP increases to levels > in men
- Lack of estrogen
  - ↓ endothelial nitric oxide production
  - ↑ angiotensin II receptor expression
  - ↑ salt-sensitivity

Sex Differences in HTN

- Compared to men, women are:
  - More aware of their diagnoses (85 vs. 80%)
  - More compliant (81 vs. 71%)
  - Better HTN control (55 vs 49%)

NCHS, 2015

  - More “white coat” HTN (43 vs 34%)

Sex-specific Responses to HTN Therapy

- ALLHAT: amlodipine vs. lisinopril, ↑ reduction in BP, ↓ stroke rate
- VALUE: amlodipine vs. valsartan, ↓ CVD morbidity and mortality
- Adverse effects
  - More hypokalemia/hyponatremia on diuretics
  - ACE-related cough
  - CCB-related peripheral edema

Treatment Goals

Condition	BP Goal (mm Hg)
HTN	<140/90
ISH	<140
Diabetes/CKD	<130/80
High-risk CAD	<130/80
Proteinuria (>1 gm/24 Hr)	<125/85
Systolic HF	<120/80

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Circulation 2007;115:2761-2788; National Kidney Foundation; JNC 7

Hypertension 2016
New Treatment Goals – JNC 8

- Age <60 years, DM, CKD
  - SBP <140 and DBP <90
- Age ≥60 years
  - SBP <150 and DBP <90

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JAMA 2014;311(5):507-520

Original Article

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group

N Engl J Med
Volume 373(22):2103-2116
November 26, 2015

A Randomized Trial of Intensive versus Standard Blood-Pressure Control - SPRINT

Main inclusion criteria:

- U.S. adults ≥ 50 years old
- SBP 130 – 180 mm Hg (treated or untreated)
- High CVD risk:
  - Clinical or subclinical CVD (previous MI, PCI, CABG, CEA, PAD, AAA, reduced ABI, CAC score ≥400, LVH)
  - CKD (eGFR 20 – 59 mL/min/1.73 m2
  - 10-year FRS ≥15%
  - Age ≥75 years

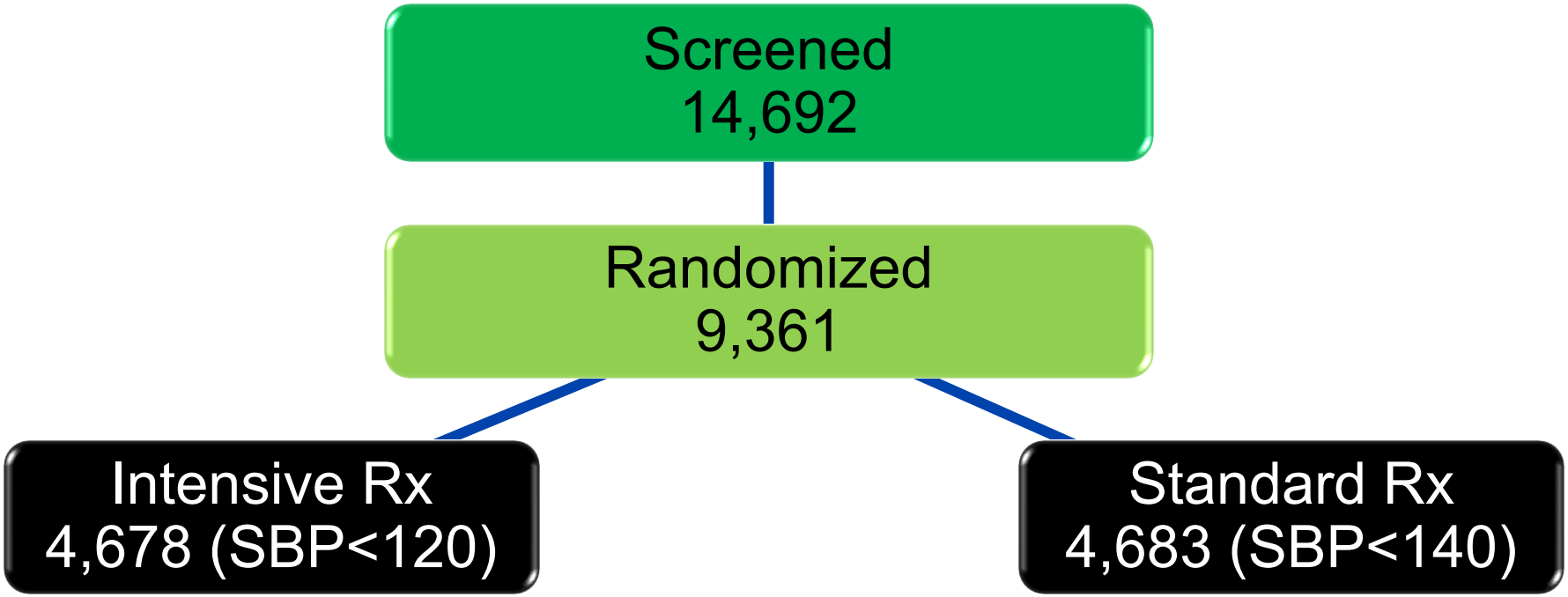
Main exclusion criteria:

- Diabetes (ACCORD) or prior stroke (SPS-3)

N Engl J Med 373(22):2103-2116
November 26, 2015

Systolic Blood Pressure Intervention Trial

102 SPRINT Clinical Centers



Primary composite outcome: MI, non-MI ACS, stroke, HF, death from CV cause

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

Systolic Blood Pressure Intervention Trial
Characteristics of the Study Sample

Criterion for ↑ CV risk	Intensive	Standard
Age ≥75 year	28.2%	28.2%
CKD	28.4%	28.1%
CVD	20.1%	20.0%
FRS ≥15%	61.4%	61.2%
Age: Overall	67.9 yr	67.9 yr
Race: Blacks	29.5%	30.4%
Female sex	36%	35.2%

Baseline BP 139.7/78.2 mm Hg on1.8 meds

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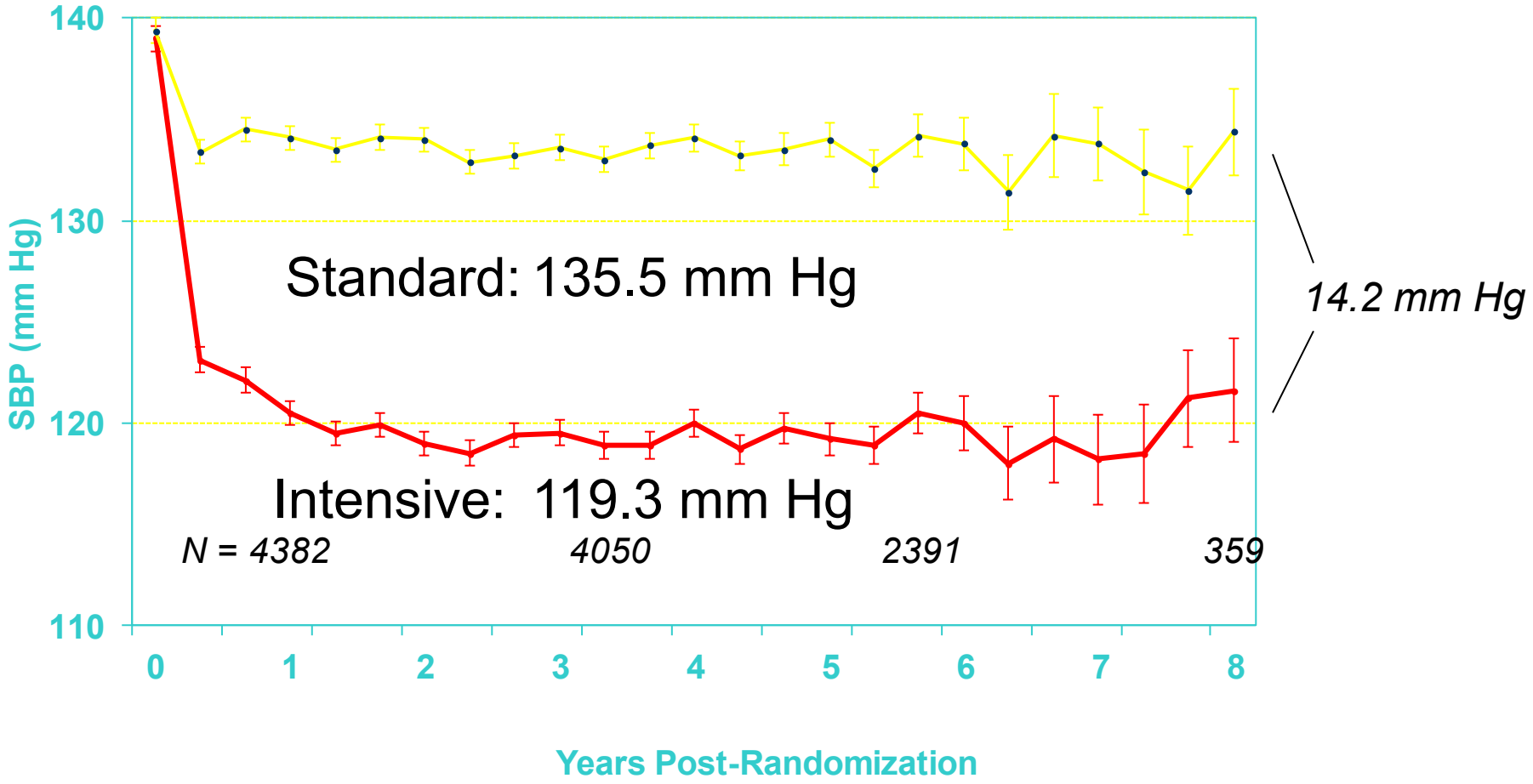
Wright JT et al. NEJM 2015;373:2103-16

Achieved Systolic Blood Pressure



Mean # Meds

Intensive:	*3.2*	*3.4*	*3.5*	*3.4*
Standard:	*1.9*	*2.1*	*2.2*	*2.3*

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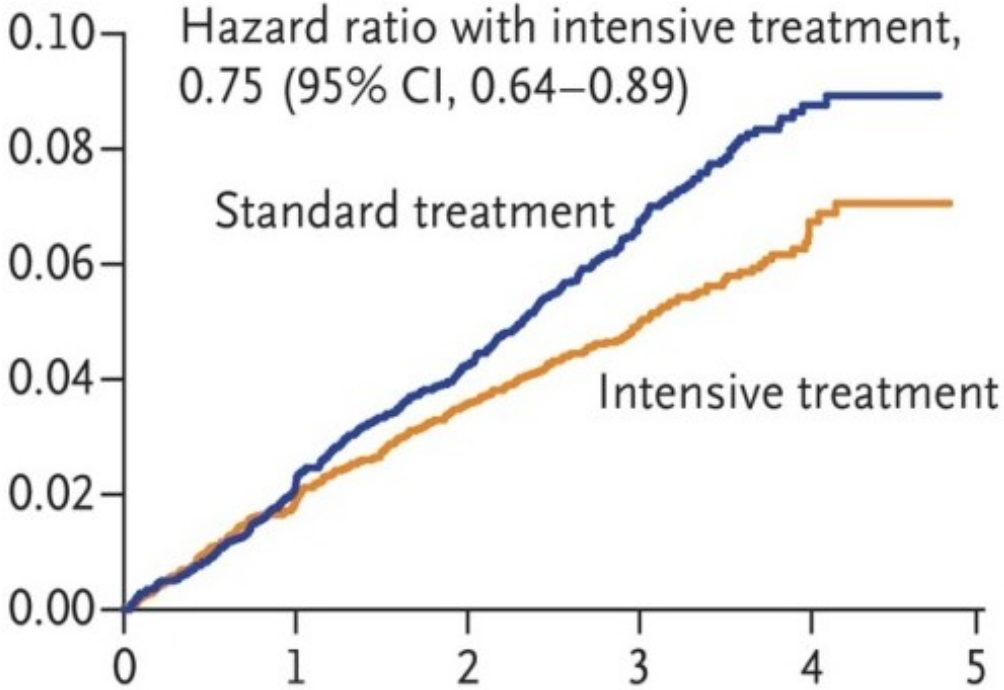
N Engl J Med. 2010;362:1575-85

SPRINT Primary Outcome
MI, ACS, stroke, HF, CV death

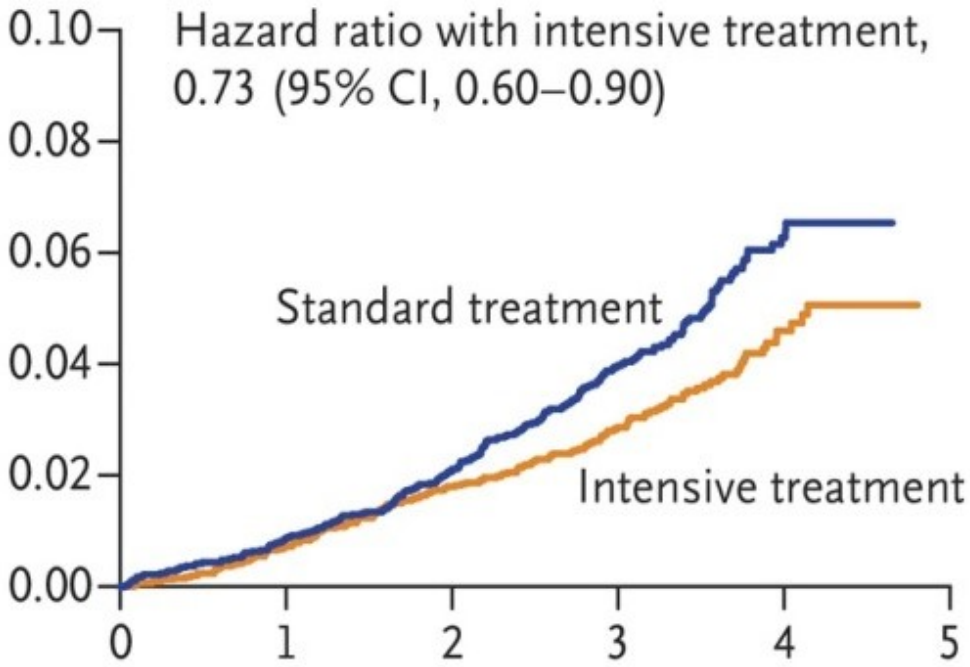
1.65%/yr vs 2.19% /yr



25%

The SPRINT Research Group. N Engl J Med 2015;373:2103-2116

SPRINT: All-cause Mortality
Cumulative Hazard



27%

The SPRINT Research Group. N Engl J Med 2015;373:2112

SPRINT
Components of the Primary Outcome

	Intensive Rx		Standard Rx		
	No of Events	Rate, %/year	No of Events	Rate, %/year	HR (95% CI)
MI	97	.65	116	.78	.83 (.64; 1.09)
Non-MI ACS	40	.27	40	.27	1.00 (.64; 1.55)
Stroke	62	.41	70	.47	.89 (.63; 1.25)
HF	**62**	**.41**	**100**	**.67**	**.62 (.45; .84)**
CVD death	**37**	**.25**	**65**	**.43**	**.57 (.38; .85)**

Systolic Blood Pressure Intervention Trial
SPRINT

- Serious AE:
  - Overall: 38.3% intensive vs 37.1% standard
  - Related: 4.7% intensive vs 2.1% standard
    - Syncope (3.5% vs 2.4%),
    - Hypotension (3.4% vs 2.0%)
    - AKI (4.4% vs 2.6%)
    - Electrolyte abnormalities:
      - Hyponatremia (3.8% vs 2.1%)
        Hypernatremia (0.1 vs 0)
      - Hypokalemia (2.4% vs 1.6%)

The SPRINT Research Group. N Engl J Med 2015;373:2103-2116

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD BP Study Group

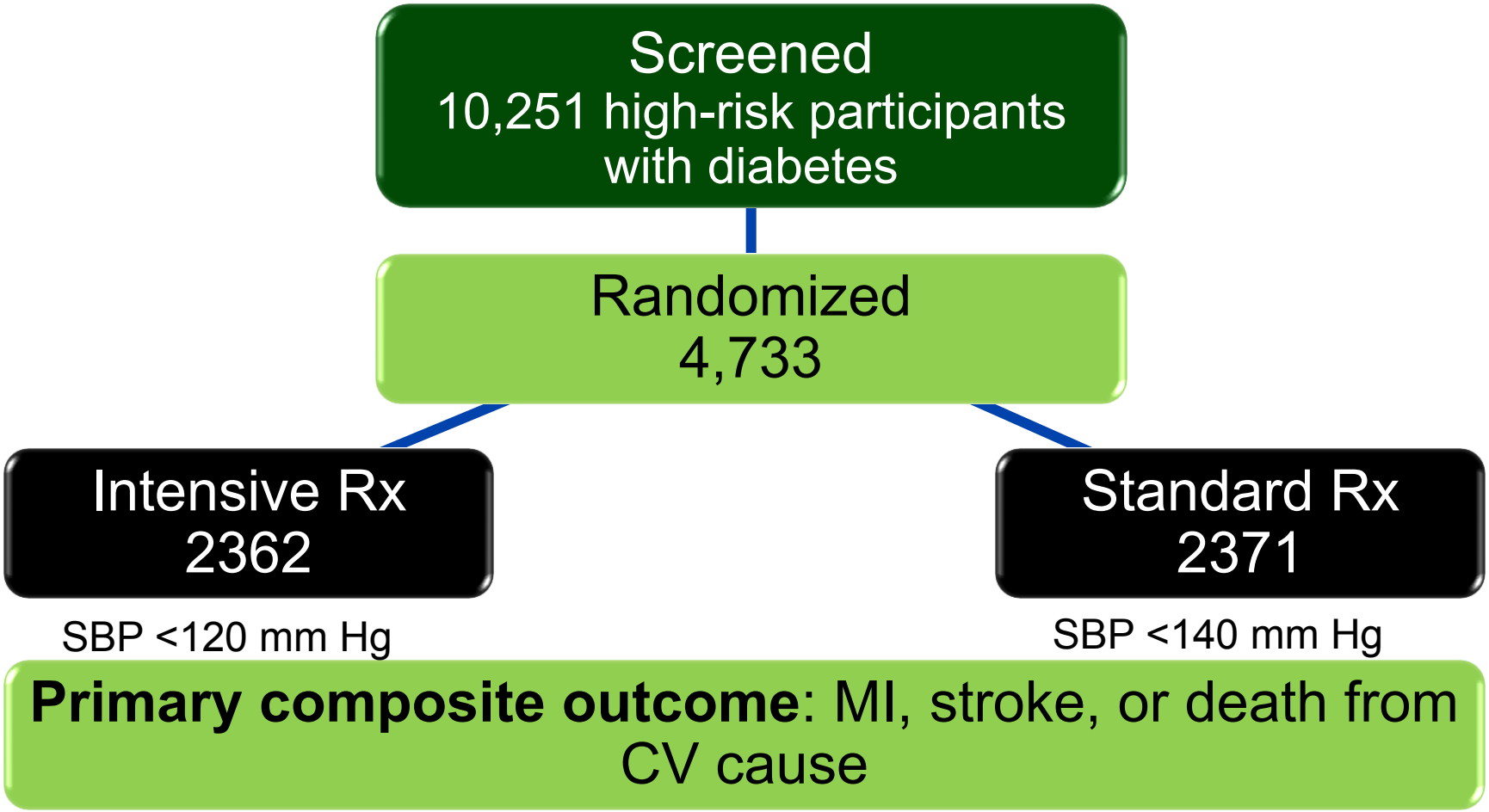
Main inclusion criteria:

- US and Canada
- ≥40 y/o with CVD or
- ≥55 y/o with substantial atherosclerosis, albuminuria, LVH or two CV risk factors (dyslipidemia, HTN, smoking, obesity)

Main exclusion criterion:

- Serum Cr ≥1.5 mg/dL

Action to Control CV Risk in Diabetes
77 ACCORD BP Clinical Centers



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N Engl J Med. 2010;362:1575-85

Primary and Secondary Outcomes

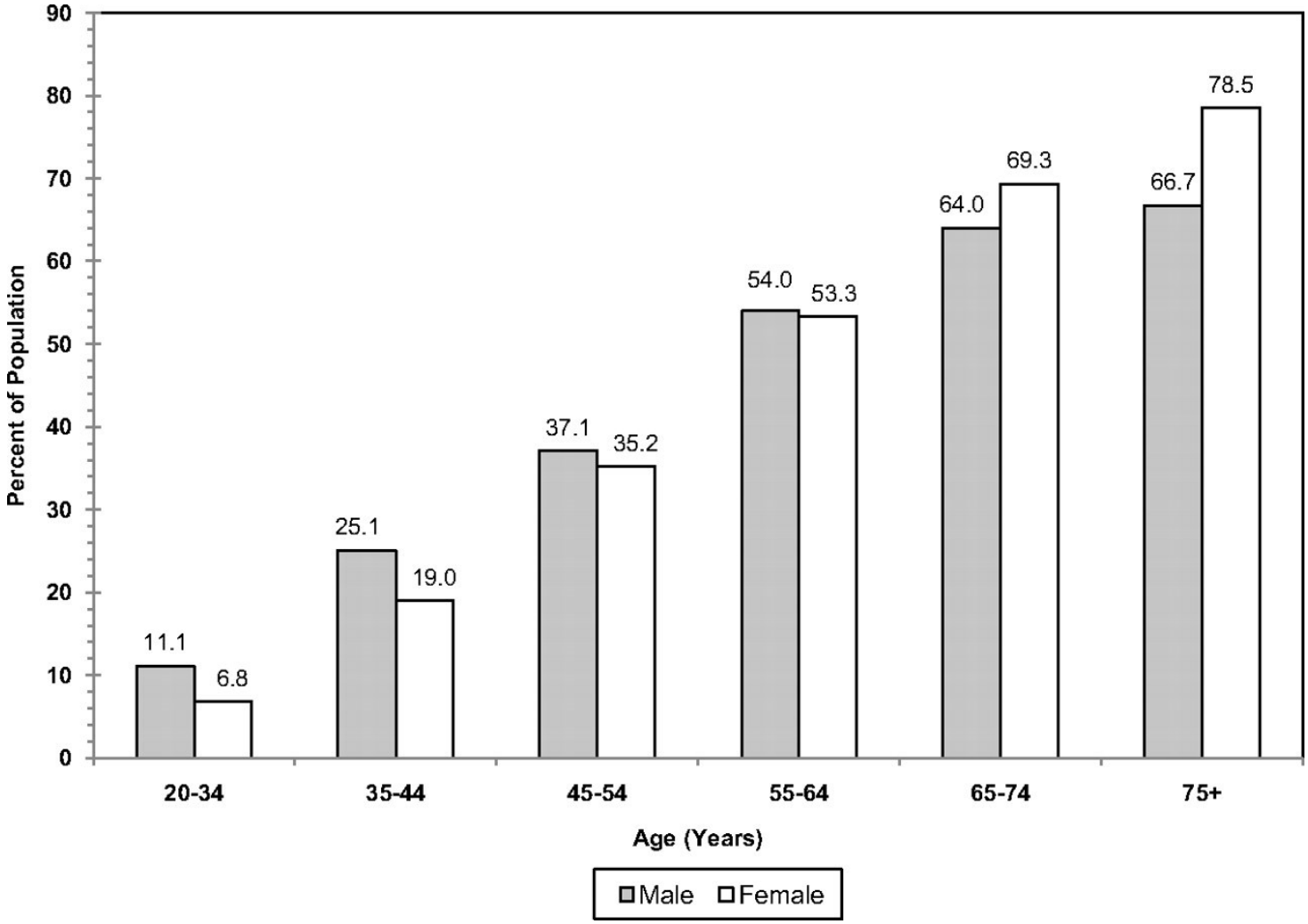
	Intensive Events (%/yr)	Standard Events (%/yr)	HR (95% CI)	*P*
Primary	208 (1.87)	237 (2.09)	0.89 (0.73-1.07)	0.20
Total Mortality	150 (1.28)	144 (1.19)	1.07 (0.85-1.35)	0.55
Cardiovascular Deaths	60 (0.52)	58 (0.49)	1.06 (0.74-1.52)	0.74
Nonfatal MI	126 (1.13)	146 (1.28)	0.87 (0.68-1.10)	0.25
Nonfatal Stroke	34 (0.30)	55 (0.47)	0.63 (0.41-0.97)	0.03
Total Stroke	36 (0.32)	62 (0.53)	**0.59 (0.39-0.89)**	**0.01**

N Engl J Med. 2010;362:1575-85

ACCORD vs SPRINT

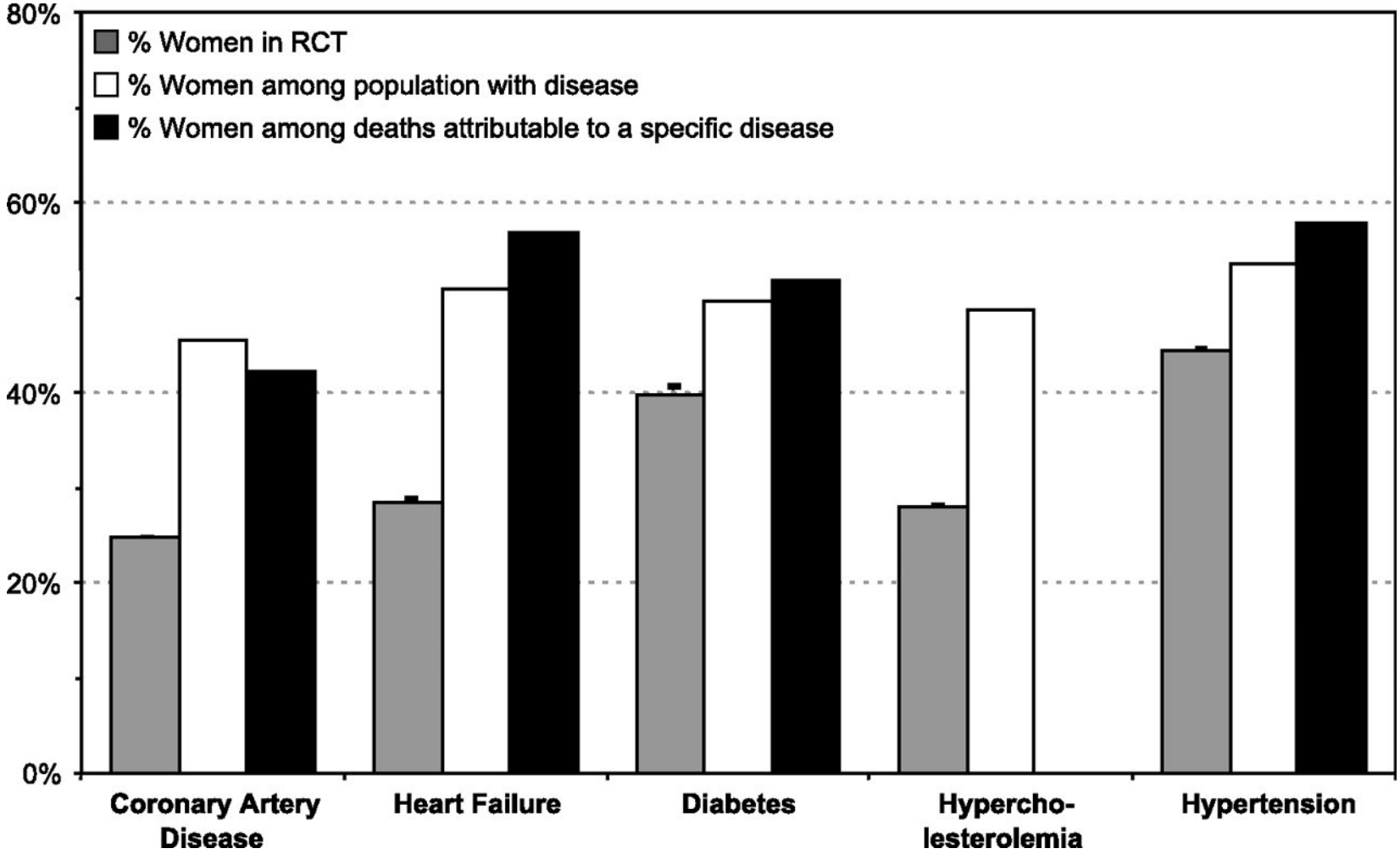
- Primary outcome included higher proportion of **events less sensitive** to BP reduction (did not include HF, a more BP sensitive event)
- Average **age younger** in ACCORD – 62 y/o vs 68 y/o in SPRINT
- ACCORD used **HCTZ**, SPRINT used **Chlorthalidone**
- Female sex 50% in ACCORD vs 35% in SPRINT

Prevalence of high blood pressure in adults ≥20 years of age by age and sex (National Health and Nutrition Examination Survey: 2005–2008).



Writing Group Members et al. Circulation. 2012;125:e2-e220

Proportion of women in RCTs compared with the proportion of women among the population with a given disease and proportion of women among deaths attributable to the disease.



Chiara Melloni et al. Circ Cardiovasc Qual Outcomes. 2010;3:135-142

SPRINT
Redefining Blood Pressure Targets

- Lower targets (<130 mm Hg?) for:
  - Adults ≥ 75 y/o (meet entry criteria, non-frail)
  - Adults ≥ 50 y/o with: (meet entry criteria)
    - Clinical or subclinical CVD
    - 10-yr FRS of ≥15%
    - CKD with eGFR 20-59 mL/min
  - Extend SPRINT to younger persons at high CV risk and to diabetics ???
- New guidelines likely will develop a risk-based method for selecting BP thresholds
- Sex-based, in women HTN
  - Under-recognized
  - Under-treated

HTN Treatment 2016
Management

- Set BP goal
- Begin Treatment
  - Lifestyle changes
  - Antihypertensive drug therapy

My Approach to Hypertension
-Juggling Guidelines with Emerging Evidence-

- Based on epidemiological data, BP 120/80 mm Hg optimal for women who tolerate that BP
- WHI: women with prehypertension, intermediate adverse outcomes between normotensive and hypertensive
- If intensifying, “start low and go slow”; shared decision making
- Future studies to address the applicability of SPRINT data
- Sex-specific risk factors

HTN Treatment 2016
Take Home Points

- The current BP goal of <140/90 mm Hg (150/90 in persons ≥ 60 y/o without DM or CKD) will likely be modified in updated guidelines from the AHA/ACC due out later this year.
  - BP goals will be based on a determination of individual risk, comorbidities, polypharmacy and employ shared-decision making
  - Sex-specific factors
    - Identifying and treating HTN in premenopausal women

Questions?

CV Event Rates in ACCORD BP and SPRINT

Event	Standard (% per yr)		Intensive (% per yr)		Hazard Ratio	
	ACCORD	SPRINT	ACCORD	SPRINT	ACCORD	SPRINT
All Deaths	1.19	1.40	1.28	1.03	1.07	0.73
Death from CV causes	0.49	0.43	0.52	0.25	1.06	0.57
Nonfatal MI	1.28	0.77	1.13	0.63	0.87	0.82
All Stroke	0.53	0.47	0.32	0.41	0.59	0.89
Nonfatal Stroke	0.47	0.45	0.30	0.39	0.63	0.88
All HF	0.78	0.67	0.73	0.41	0.94	0.62
ACCORD Primary Outcome*	2.09	1.52	1.87	1.15	0.88	0.75

*Results for application of the ACCORD composite in both SPRINT and ACCORD.

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Cushman et al. Hypertension 2016;67:263-265

A Randomized Trial of Intensive versus Standard Blood-Pressure Control - SPRINT

Main exclusion criteria:

- Diabetes
- Prior stroke
- PCKD
- HF (symptoms or EF<35%)
- Proteinuria >1g/d
- SBP >180 mm Hg
- CKD with eGFR <20 cc/min
- Nursing home patient or dementia

N Engl J Med 373(22):2103-2116
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Systolic Blood Pressure Intervention Trial
SPRINT

- Representative medications from all major classes provided at no cost to participants
- Recommended to use drugs with strongest evidence for CVD outcomes: thiazides (chlorthalidone), CCB (amlodipine), ACEI/ARB and for comorbidities (e.g., ACEI/ARB in CKD).
- Standardized BP measurements: Omron, average of 3 seated readings after 5 minute rest
- Monthly visits until goal achieved:
  - Standard group: medication reduction if SBP< 135 mm Hg (goal 135-139 mm Hg)
  - DBP goal <90 mm Hg