Selected age-associated changes in the cardiovascular system

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Selected age-associated changes in the cardiovascular system

Difficult to separate aging and disease
Changes in vasculature greater than changes in heart
Common, costly, with unsettled clinical issues

Overview
What I will not cover
Atrial fibrillation
Hypertension

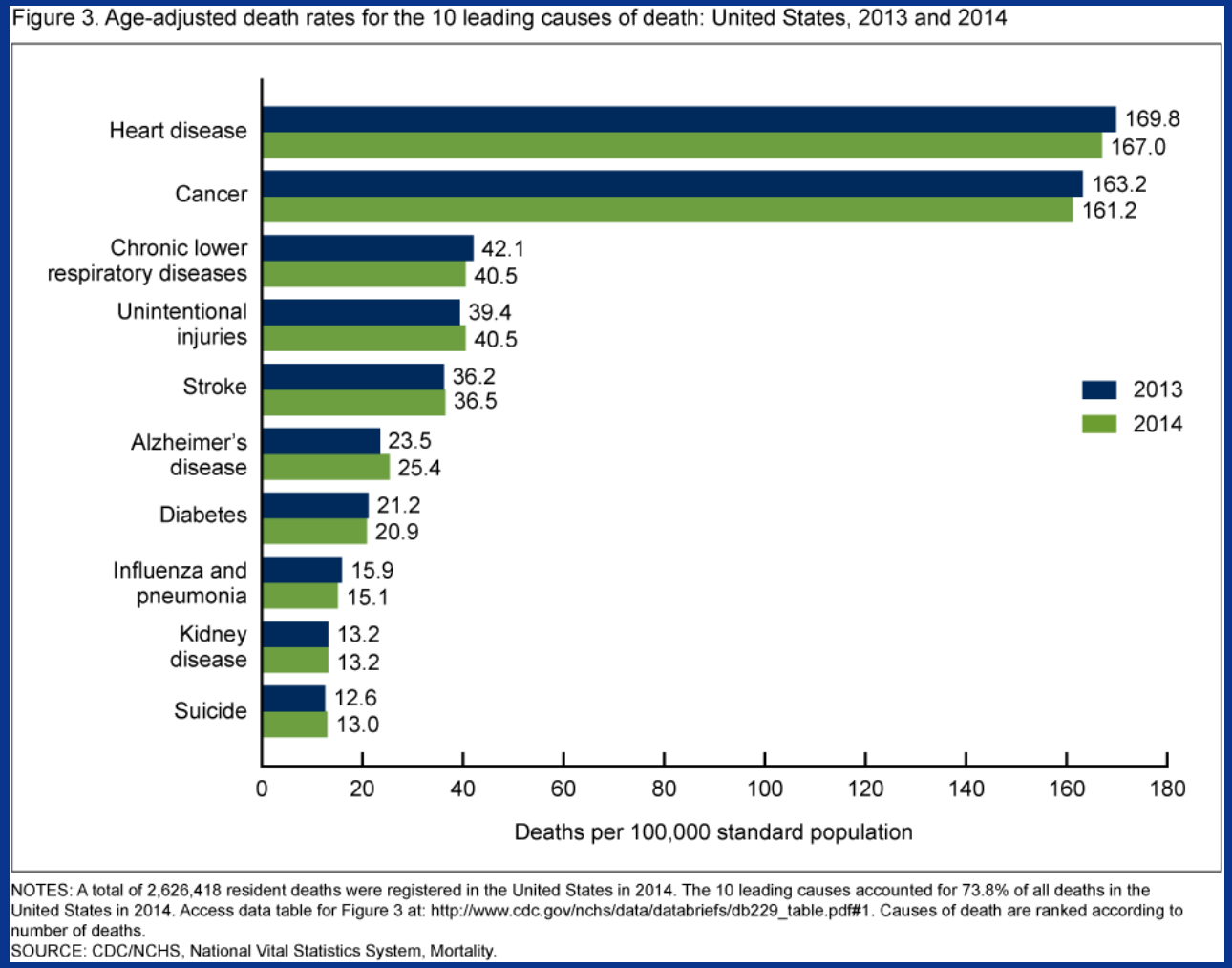
Importance of cardiovascular disease in old age

Mortality

Morbidity

Costs

Comorbidity



Beneficiaries ≥65 y of Age (N = 2,426,865) (Mean Number of Conditions 5.8; Median 6)		
	N	%
Hypertension	2,015,235	83.0
Ischemic heart disease	1,549,125	63.8
Hyperlipidemia	1,507,395	62.1
HF	1,247,748	51.4
Anemia	1,027,135	42.3
Arthritis	965,472	39.8
Diabetes mellitus	885,443	36.5
CKD	784,631	32.3
COPD	561,826	23.2
Cataracts	546,421	22.5

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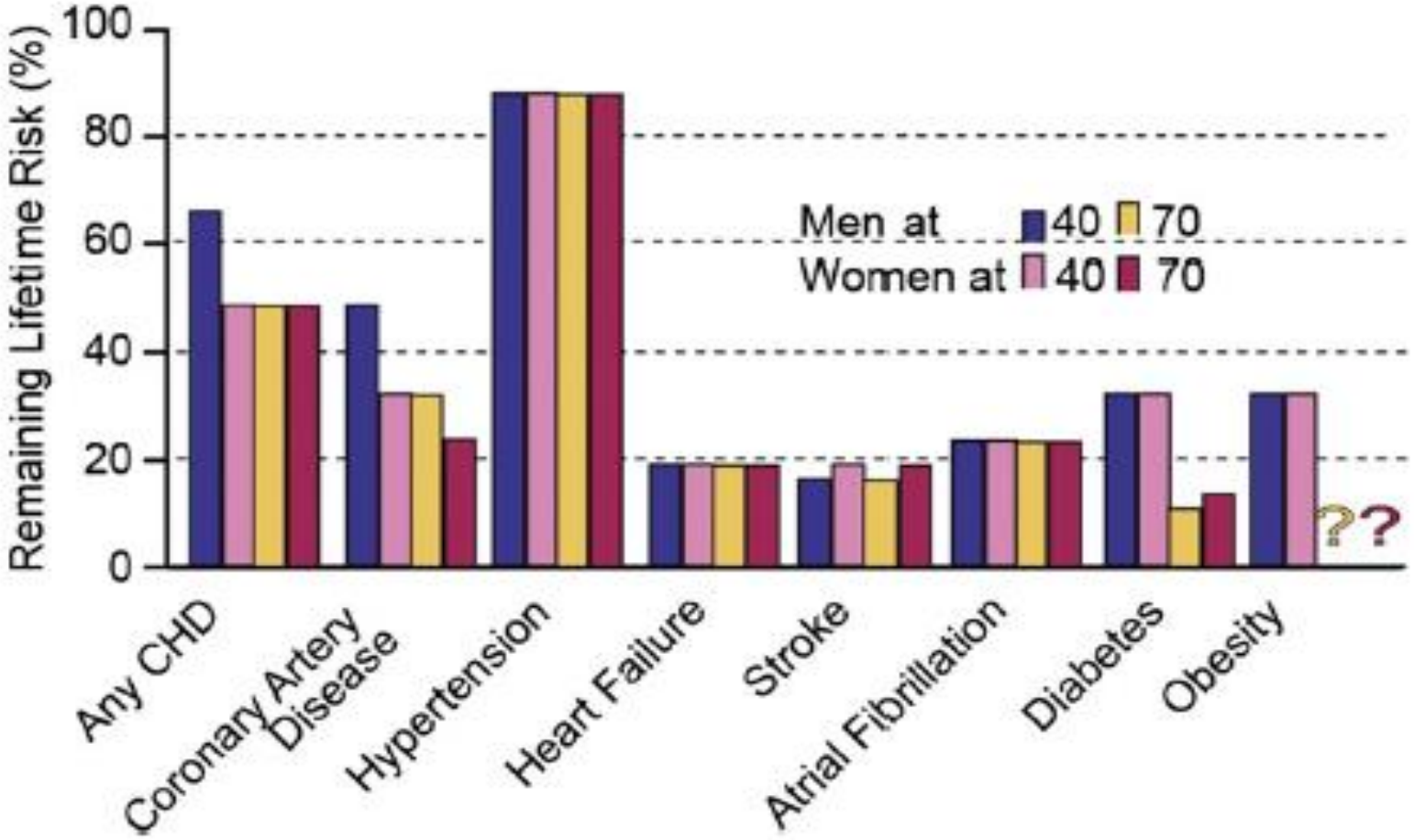
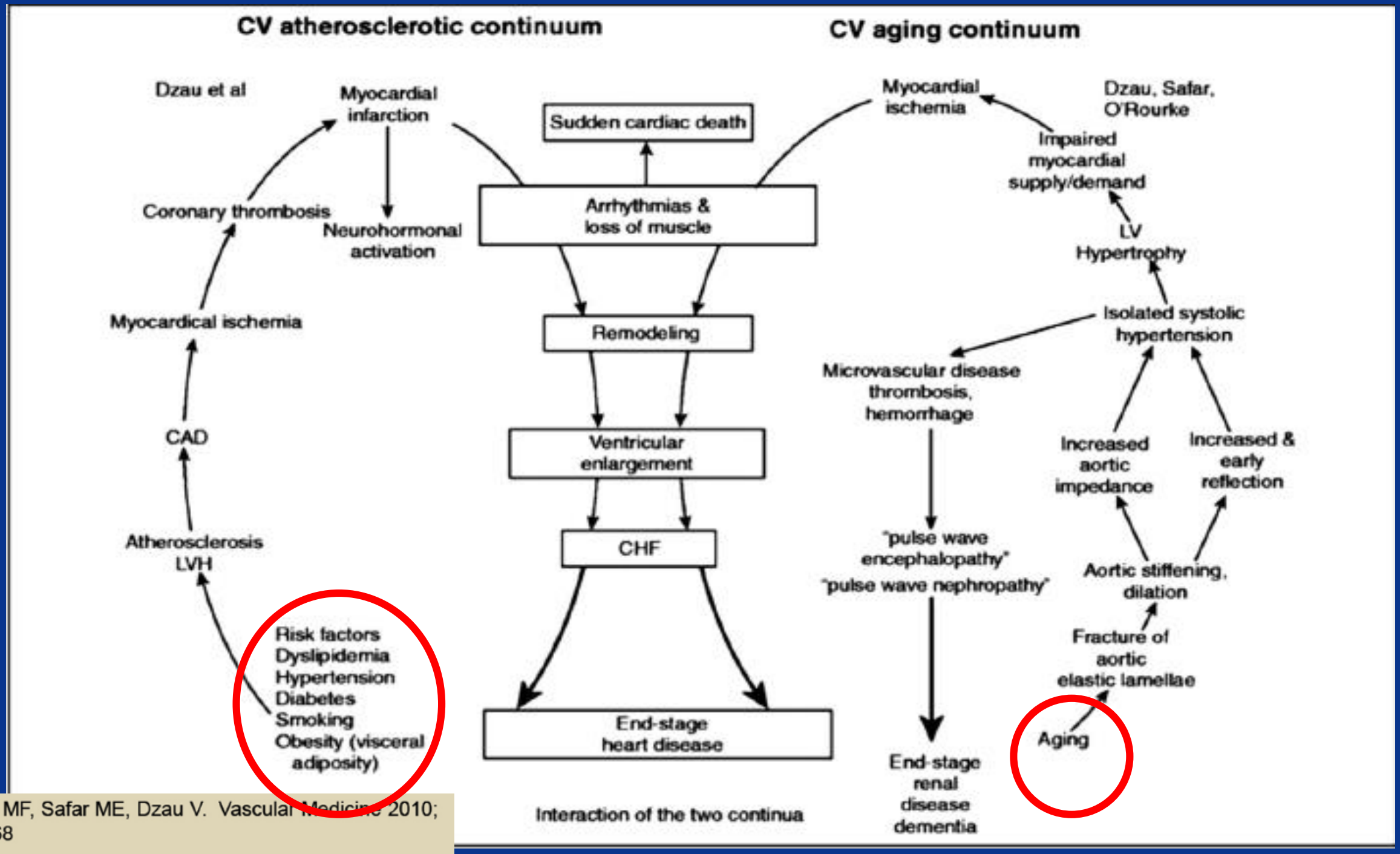


Fig. 1. The remaining lifetime risk for CVD and other diseases among men and women is staggering: The odds of having a chronic CV disease are 50%, for hypertension 85%, and for chronic heart failure 20%. At age 70, the lifetime risk of CVD in individuals free of disease is virtually the same as that at age 40, and is indicative of the extremely high likelihood for incurring CVD during one's lifetime.

Adapted from *E.G. Lakatta / Journal of Molecular and Cellular Cardiology 83 (2015) 1–13*



O'Rourke MF, Safar ME, Dzau V. Vascular Medicine 2010; 15:461-468

….The greatest difficulty in studying the effects of aging on cardiovascular structure and function lies in separating the effects of aging itself from…disease processes and life-style changes….

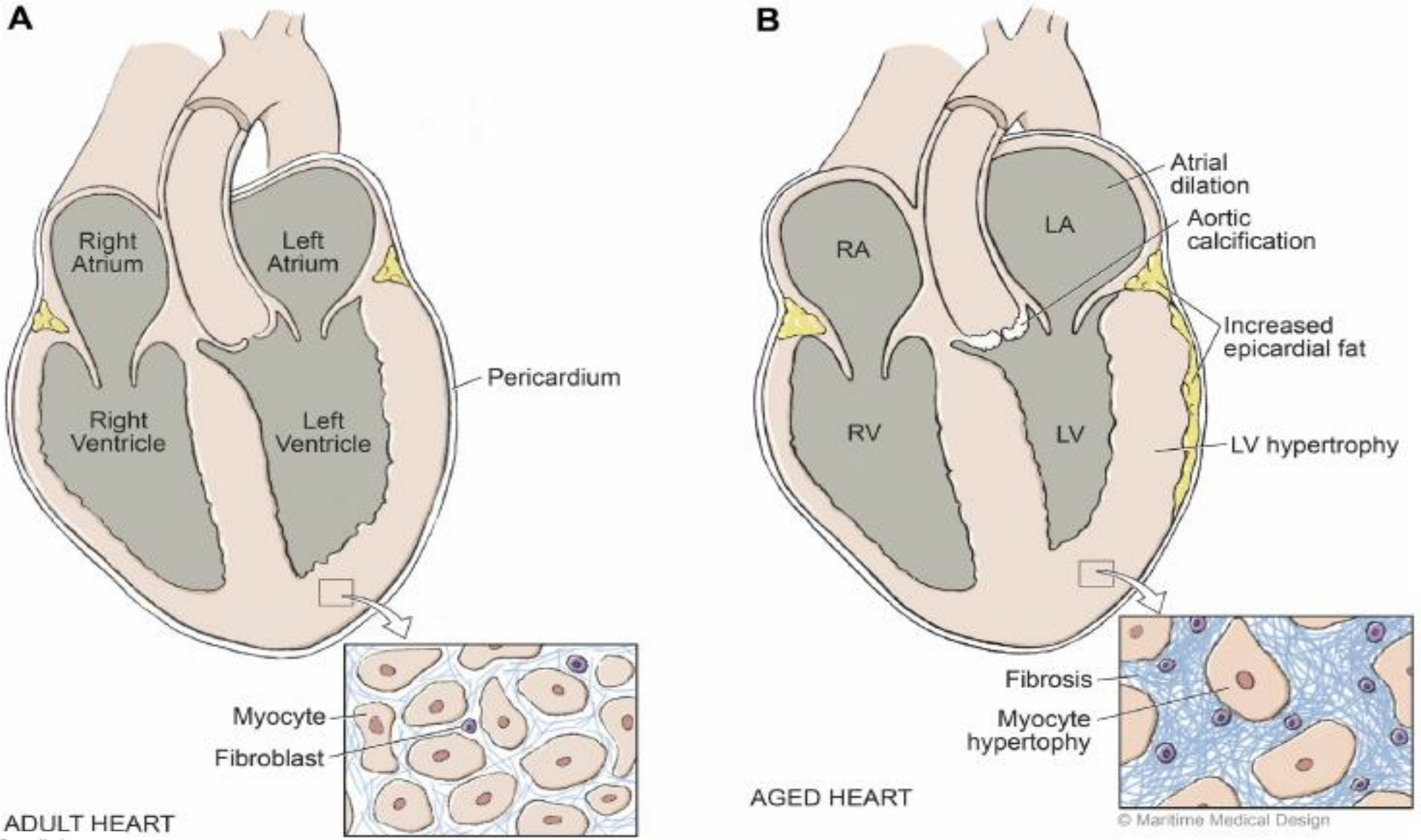
Modest left ventricular (LV) hypertrophy – 30% between 25 and 80

Systolic left ventricular function is unaffected by aging
Under normal function without stress, no functional issues

LV stiffening leads to slower filling and leaves older person more reliant on atrial contraction for blood pressure filling

Left atrium thickens and dilates increasing risk of afib

Am J Cardiol. 1986 Feb 12;57(5):33C-44C.



Canadian Journal of Cardiology
Volume 32 2016

….The greatest difficulty in studying the effects of aging on cardiovascular structure and function lies in separating the effects of aging itself from…disease processes and life-style changes….

Age-related decline in maximal exercise heart rate

Aerobic exercise capacity (total work or maximal oxygen consumption declines with age-physical activity decreases markedly

Am J Cardiol. 1986 Feb 12;57(5):33C-44C.

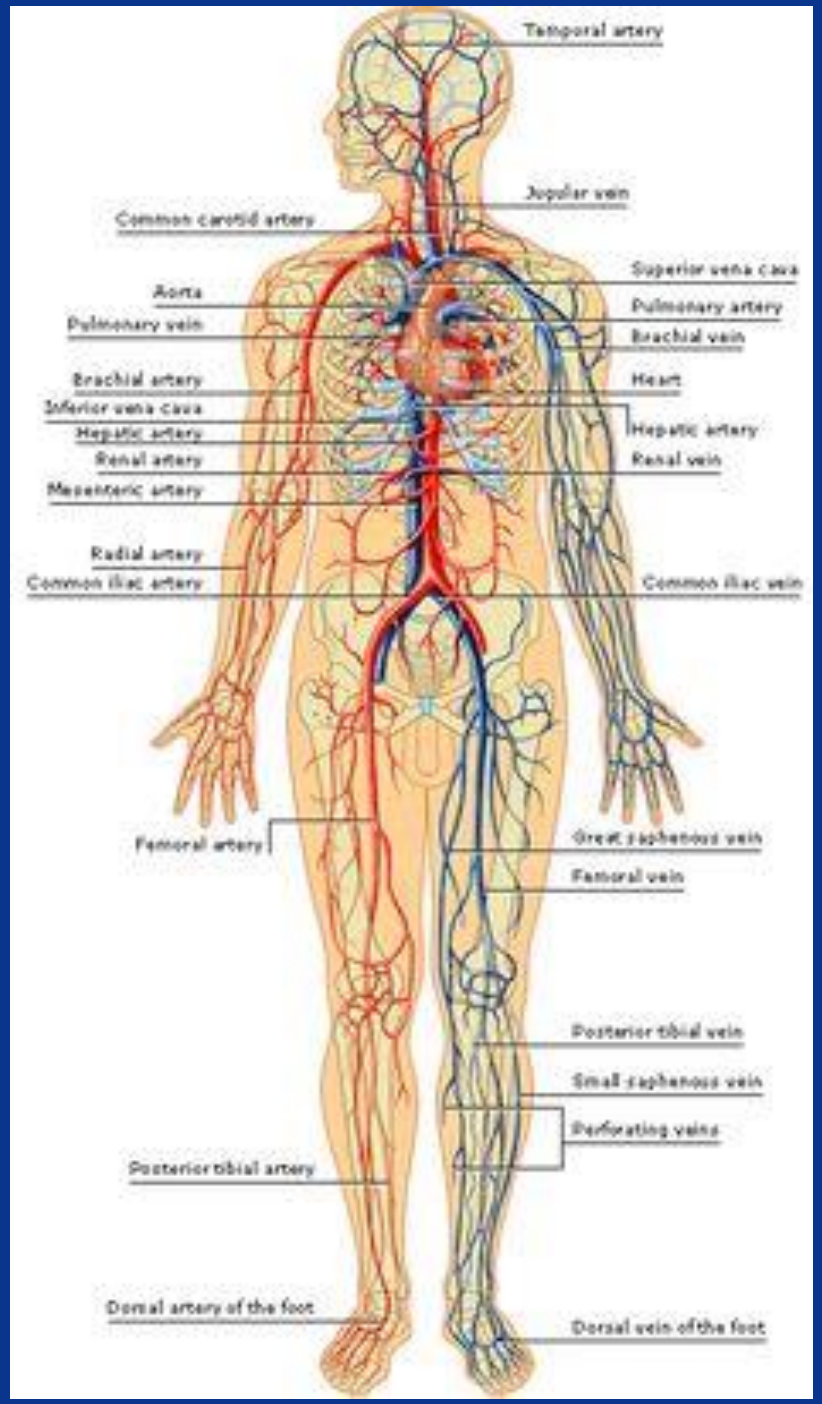
Table 1
Changes in cardiorespiratory reserve in healthy, community-dwelling persons during peak cycle exercise between the ages of 20 and 80 years.
From Ref. [44].

Peak oxygen consumption	(50%)	↓
Peak $(A-V)O_2$	(25%)	↓
Cardiac index	(25%)	↓
Heart rate	(25%)	↓
Stroke volume	No change	
End diastolic volume	(30%)	↑
Peripheral vascular reserve	(30%)	↑
End diastolic volume	(275%)	↑
LV contractility	(60%)	↓
LV ejection fraction	(15%)	↓
Plasma catecholamines		↑
Cardiac and vascular response to beta-adrenergic stimulation		↓

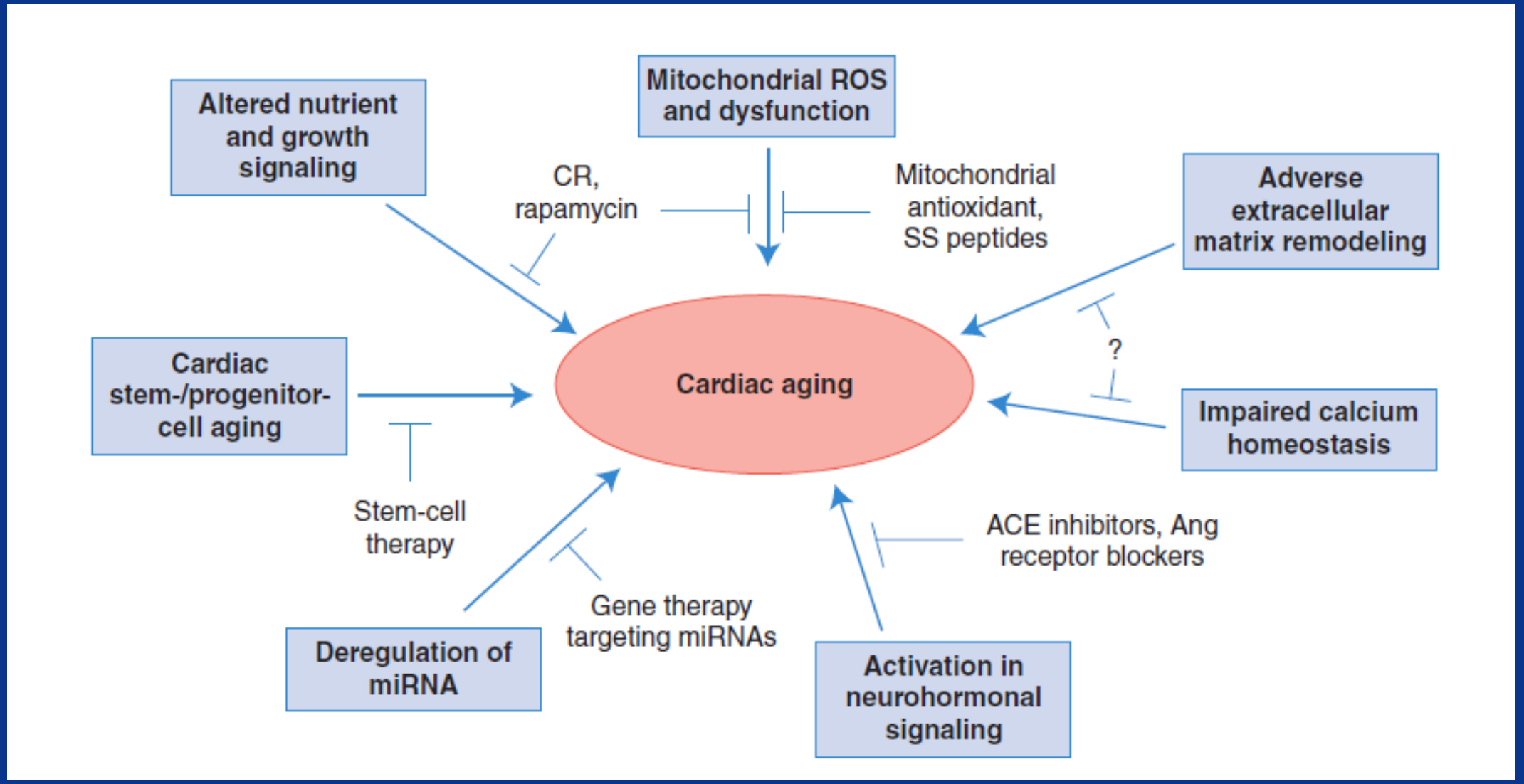
….The greatest difficulty in studying the effects of aging on cardiovascular structure and function lies in separating the effects of aging itself from…disease processes and life-style changes….

Age-related stiffening of arterial tree
Increased systolic blood pressure
Greater load on the heart
With age-stiffening, thickening, fibrosis, and calcification of arteries--hypertension

Am J Cardiol. 1986 Feb 12;57(5):33C-44C.


Temporal artery
Jugular vein
Common carotid artery
Superior vena cava
Aorta
Pulmonary artery
Pulmonary vein
Brachial vein
Brachial artery
Heart
Inferior vena cava
Hepatic artery
Hepatic artery
Renal vein
Renal artery
Mesenteric artery
Radial artery
Common iliac artery
Common iliac vein
Femoral artery
Great saphenous vein
Femoral vein
Posterior tibial vein
Small saphenous vein
Perforating veins
Posterior tibial artery
Dorsal artery of the foot
Dorsal vein of the foot

Mechanisms Contributing to Cardiac Aging



Cold Spring Harb Perspect Med 2015;5:a025148

Consequences

↓ Stroke volume, cardiac output

↓ Ability to increase heart rate in response to stress

↑ Aortic volume and systolic blood pressure

No change in resting heart rate

↑ Risk of extra systoles

Electrocardiogram changes

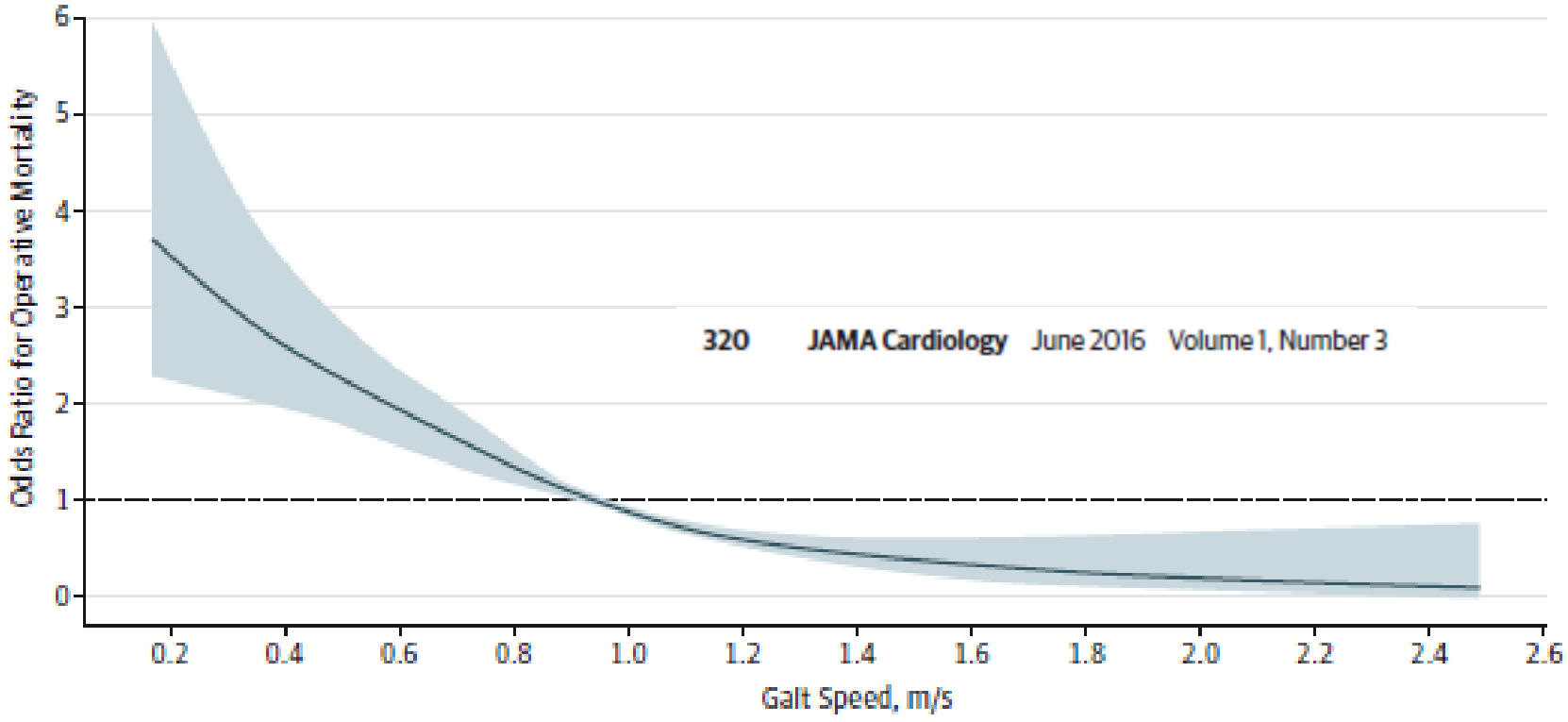
Orthostatic

Hypotensions

↑ FALLS

Accumulation of other age-related problems……..

Figure 2. Unadjusted Association Between Gait Speed and Operative Mortality

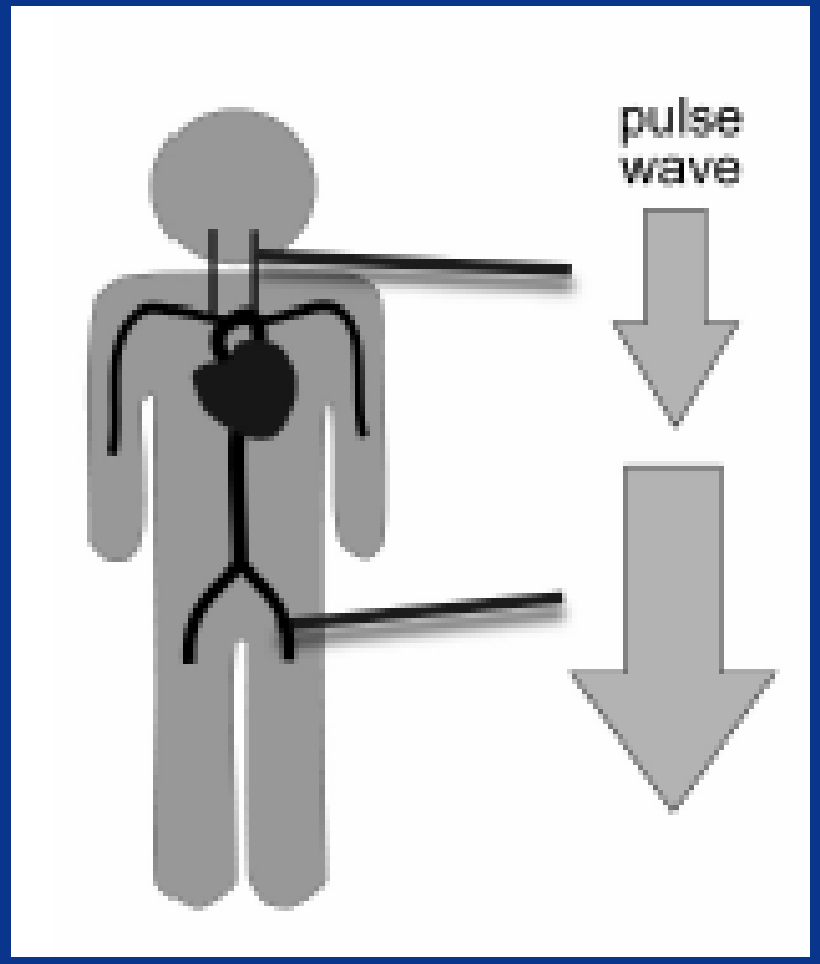


Decreasing gait speed was associated with increasing odds of operative mortality. The blue area indicates the 95% CI. The dashed line indicates the reference odds ratio of 1.0.

Selected age-associated changes in the cardiovascular system

Overview
What I will not cover

Pulse wave velocity



Transmission of systolic pressure to the end organ secondary to aortic stiffening

Advances in Physiology Education • doi:10.1152/advan.00088.2014 • http://advan.physiology.org

Selected age-associated changes in the cardiovascular system

Overview
What I will not cover

- Pulse wave velocity
- Congestive heart failure with preserved ejection fraction

Table 1 Heart failure patterns typical of very old adults versus those typical of middle-aged adults. Based on ref [45]

Characteristic	Older adults	Middle-aged adults
Prevalence	6–18 %	<1 %
Gender	Predominantly women	Predominantly men
Etiology	Hypertension	Coronary heart disease
Left ventricular systolic function	Normal	Impaired
Left ventricular diastolic function	Impaired	Normal or mildly impaired
Comorbidities	Multiple	Few

Curr Heart Fail Rep (2013) 10:387–400

Selected age-associated changes in the cardiovascular system

Overview

What I will not cover

- Pulse wave velocity
- Congestive heart failure with preserved ejection fraction
- Kidney disease in relation to vascular changes
- Role of exercise and diet in ameliorating if not reversing some of these changes
- Atherosclerosis
- Inflammation

Selected age-associated changes in the cardiovascular system

Difficult to separate aging and disease
Changes in vasculature greater than changes in heart
Common, costly, with unsettled clinical issues

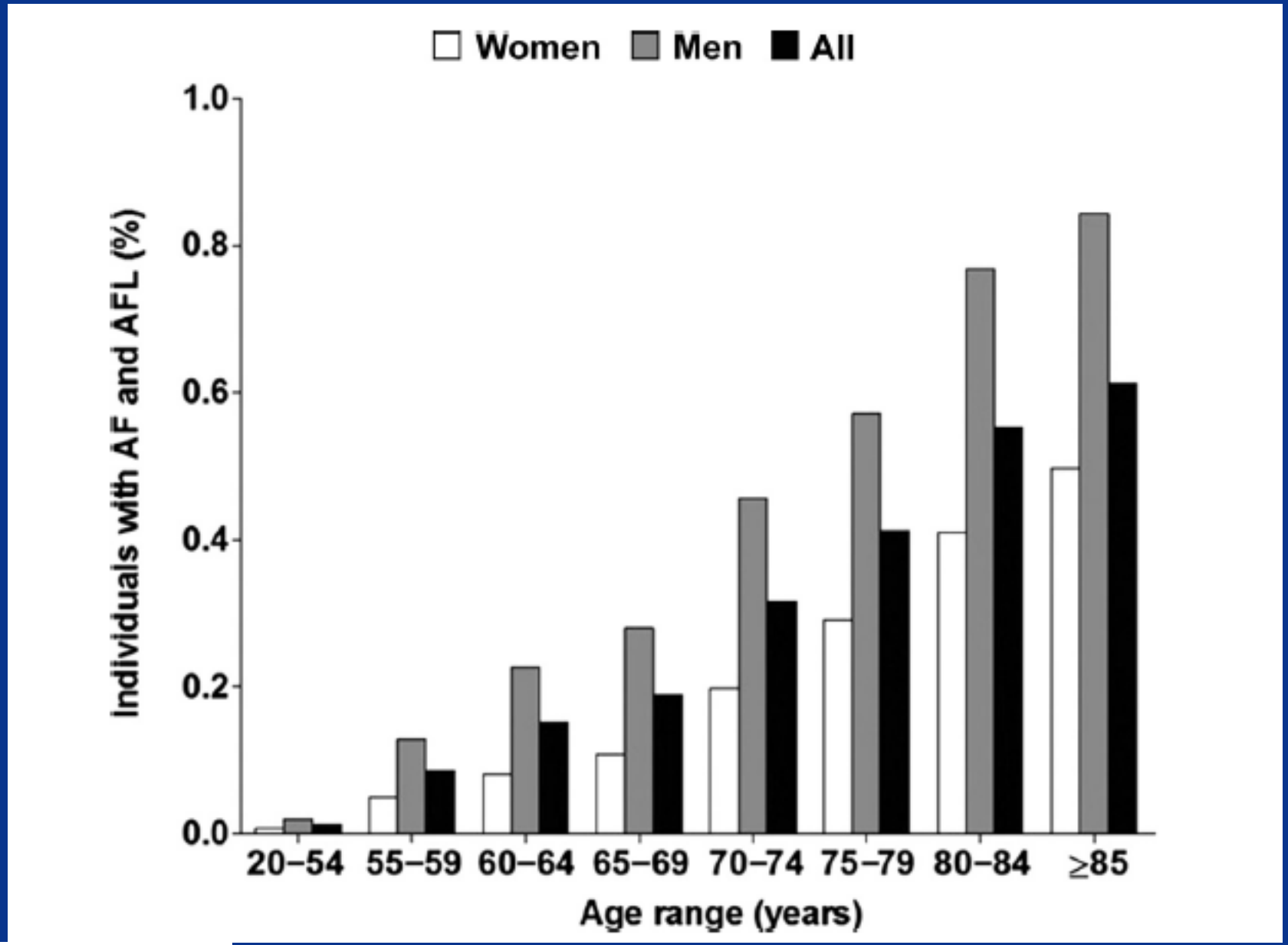
Overview
What I will not cover
Atrial fibrillation
Hypertension

What is atrial fibrillation?

Atrial fibrillation is an irregular heart rhythm caused by a disturbance in the electrical system of the heart so that the atria and ventricles no longer beat in a coordinated way.

Most of the symptoms relate to how fast the heart is beating.

However, increased risk of stroke is a complication.



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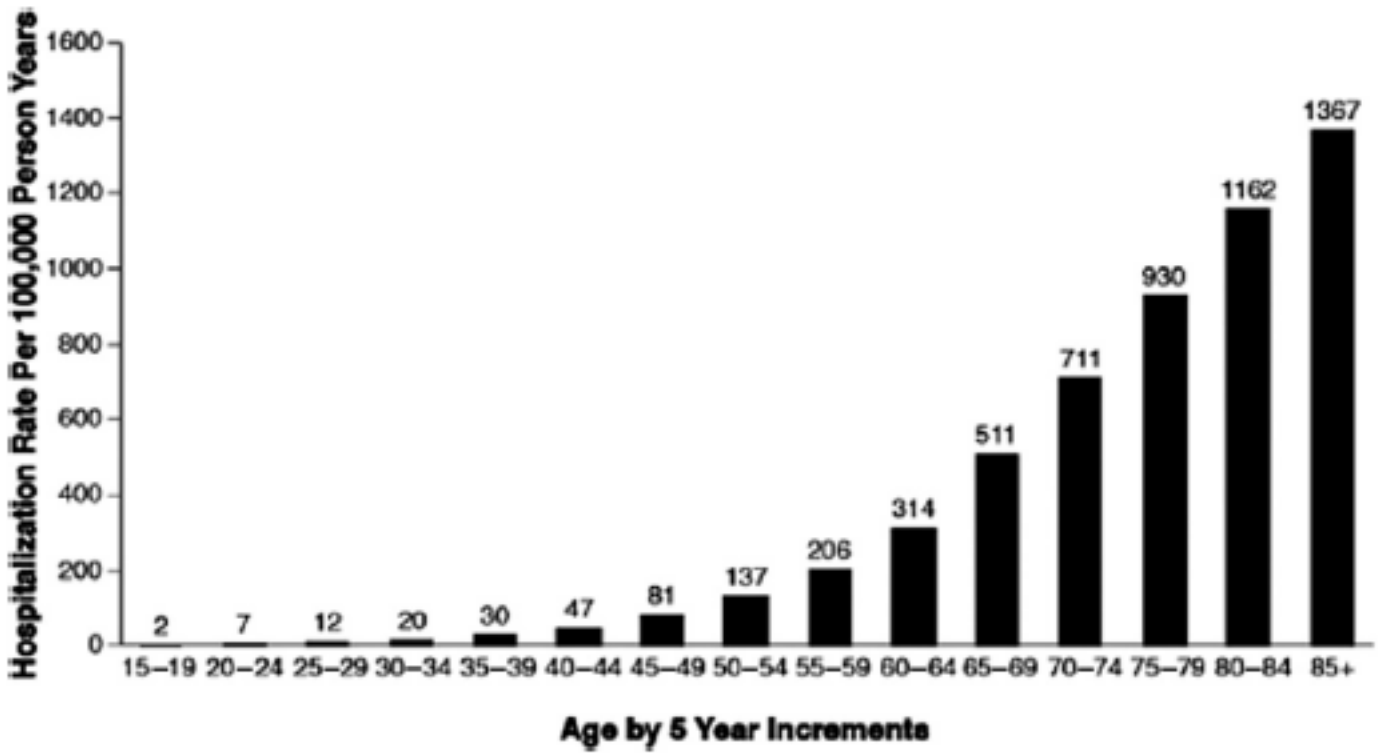

Fig. 5. Atrial fibrillation hospitalization rates per 100,000 person-years by age group. Data from 129,846 hospitalizations at 1051 hospitals (2009–2010) in the Nationwide Inpatient Sample. Results based on calculating the proportion of the US population in each age group hospitalized with atrial fibrillation. US population based on US census data for each age group. (*From* Naderi S, Wang Y, Miller AL, et al. The impact of age on the epidemiology of atrial fibrillation hospitalizations. Am J Med 2014;127:158.e3; with permission.)

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Risk Factors for Atrial Fibrillation[5]
Increasing age
Hypertension
Diabetes mellitus
Heart failure
Valvular heart disease
Myocardial infarction
Obesity
Obstructive sleep apnea
Cardiothoracic surgery
Smoking
Exercise
Alcohol use
Hyperthyroidism
Increased pulse pressure
European ancestry
Family history
Genetic variants

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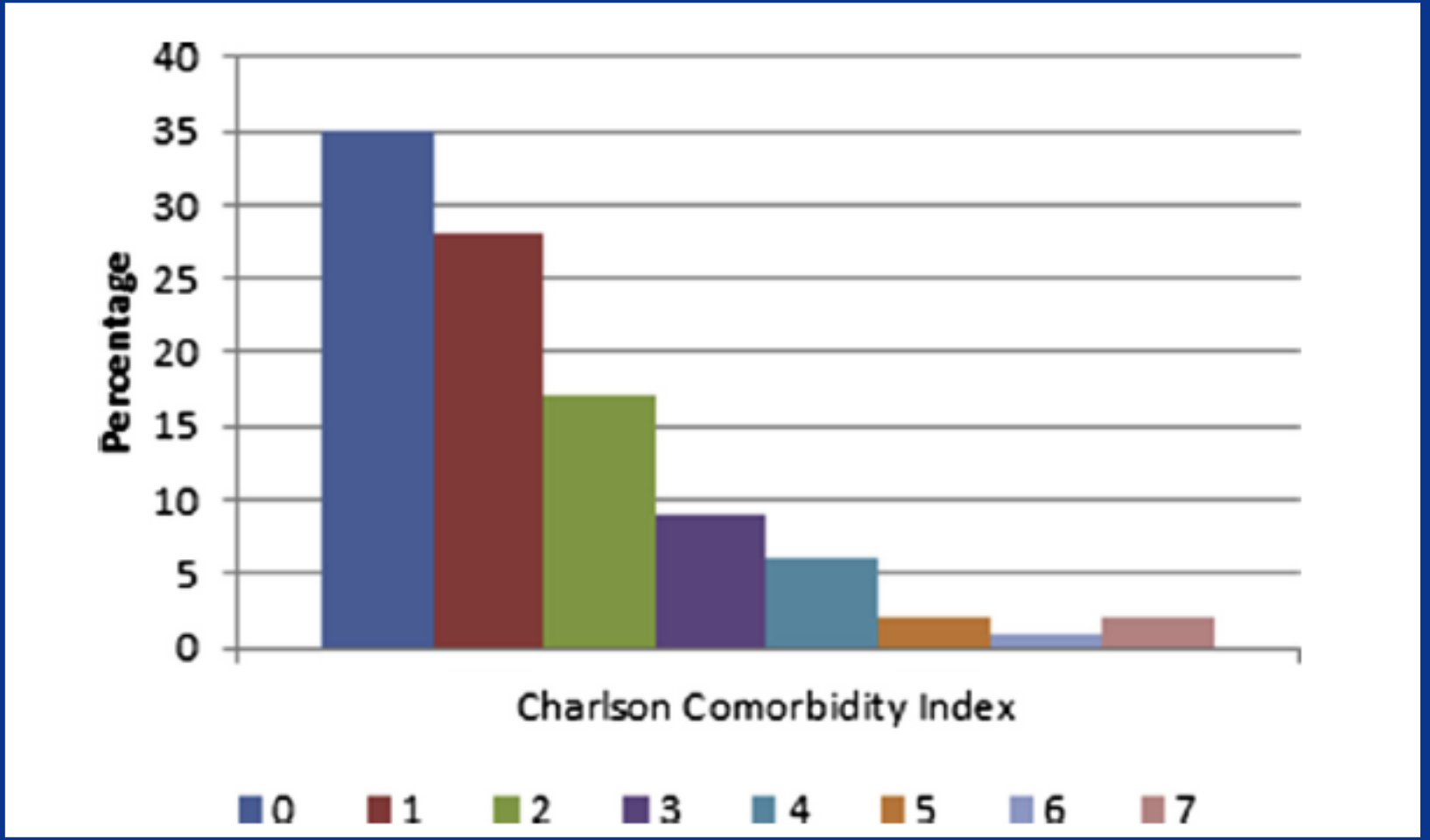
Fibrosis of the conducting system?



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Controversy in treatment…..

Table 4
Balancing the risks and benefits of treatments

Risks	Treatment	Benefits
Bradycardia Orthostatic hypotension Fatigue	Rate control	Reduced symptoms (palpitations, dyspnea) Reduced risk of tachycardia-mediated cardiomyopathy
Medication side effects and interactions Higher rates of hospitalizations	Rhythm control	Reduced symptoms
Procedural complications	Ablation	Reduced symptoms
Procedural complications Risk of pacemaker-mediated cardiomyopathy/heart failure (RV pacing)	AV-nodal ablation and permanent pacemaker placement	Reduced symptoms Reduced risk of tachycardia mediated cardiomyopathy
Increased risk of bleeding	Anticoagulation	Reduced risk of stroke
Procedural complications	Left atrial appendage closure device	Reduced risk of stroke

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Overview
What I will not cover
Atrial fibrillation
Hypertension

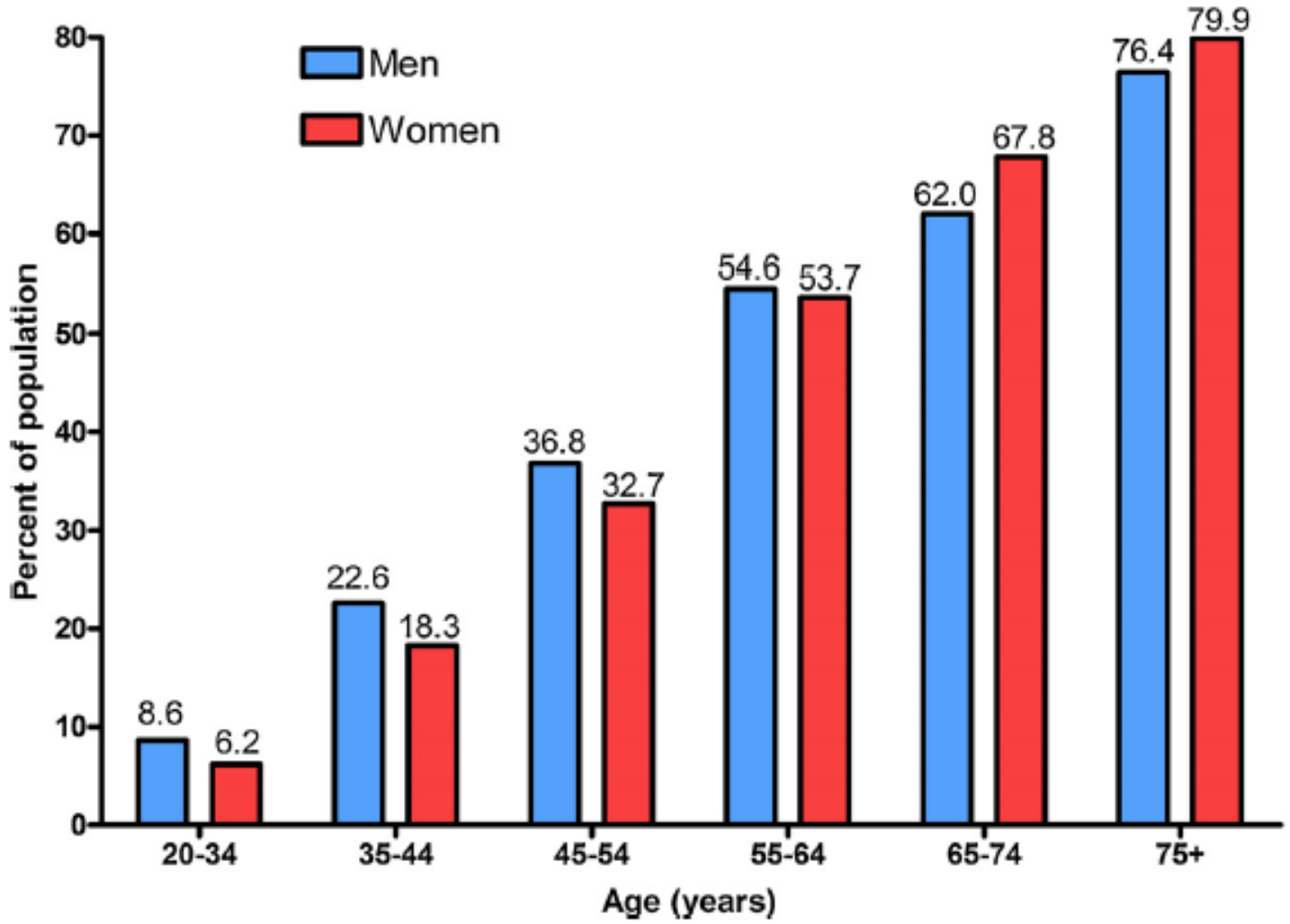
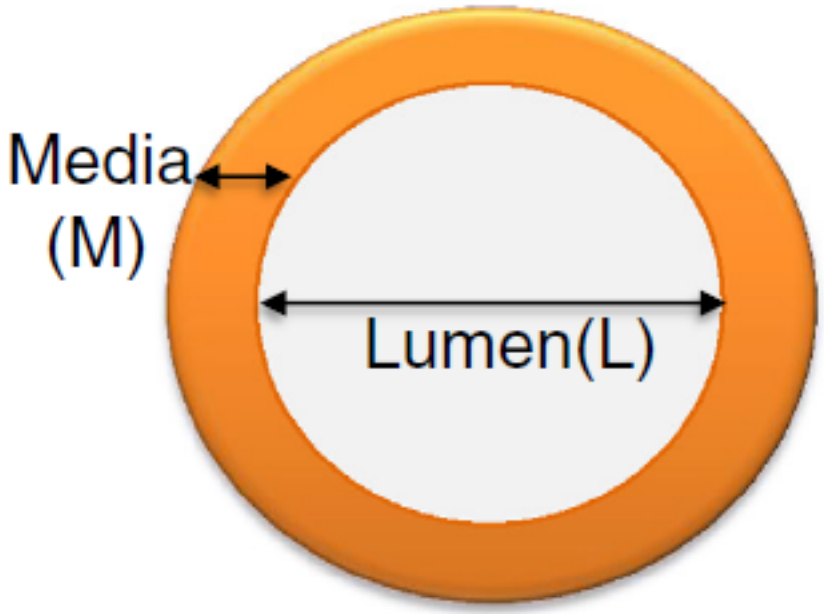


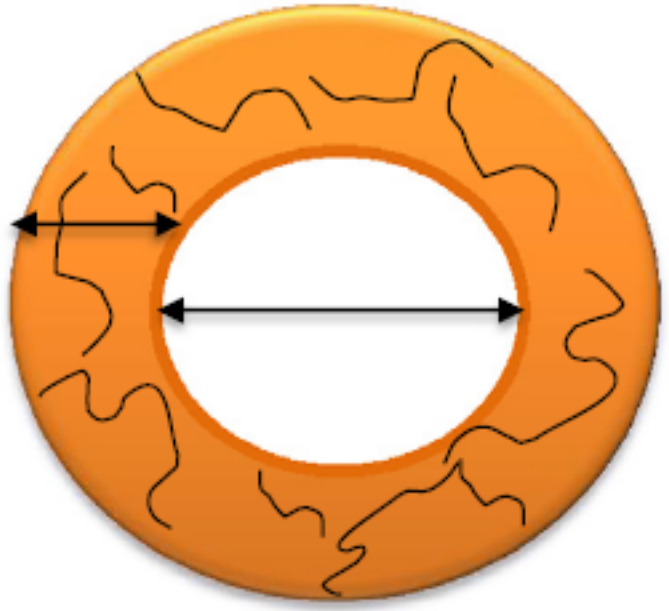
Fig. 1. Prevalence of hypertension among adults by age and sex according to the National Health and Nutrition Examination Survey: 2007–2012. Re-created from Chart 9.1 in Mozaffarian et al. (2015).

Young - Healthy



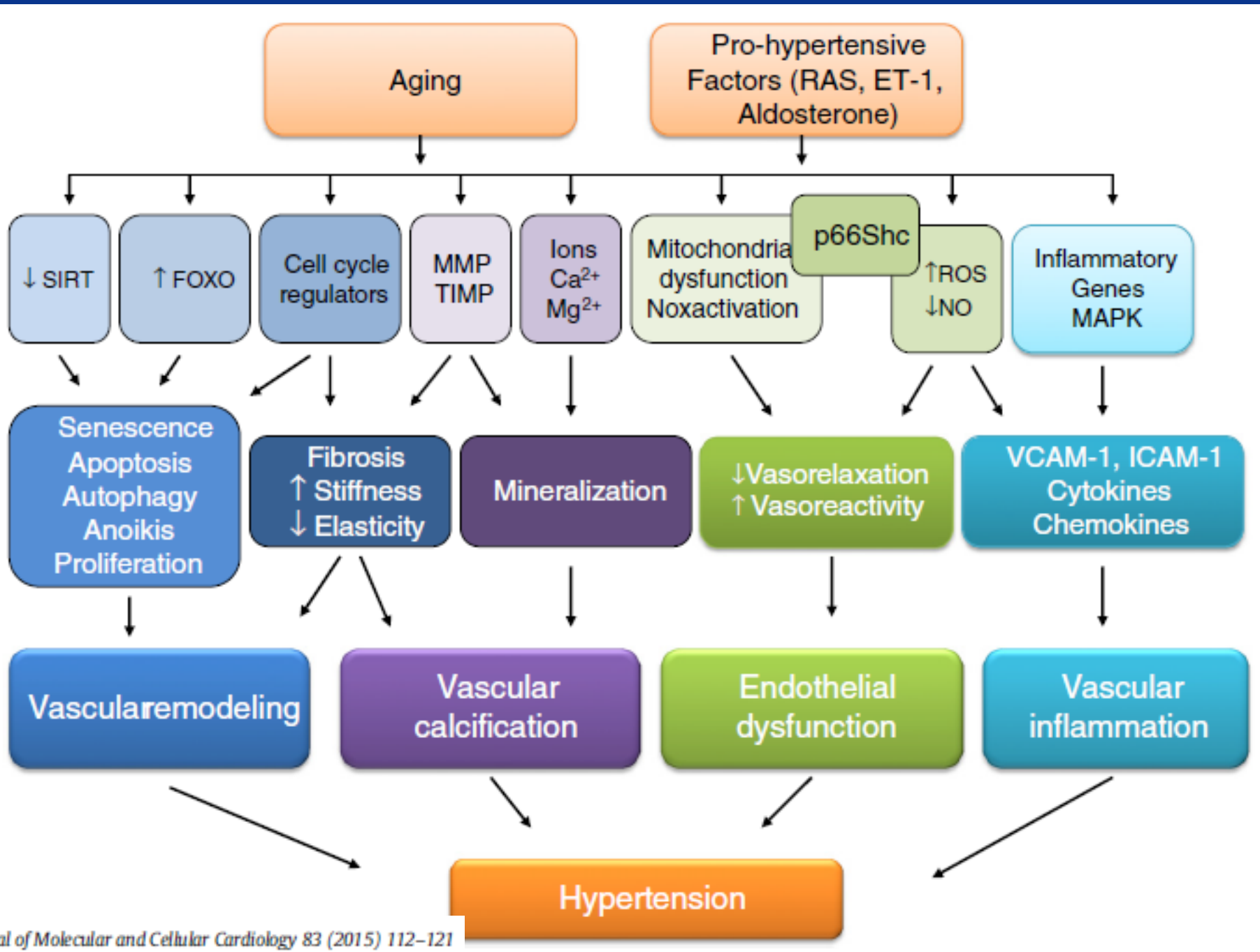
Normal Vascular Homeostasis

Aged - Hypertension



Endothelial dysfunction
↑ M:L ratio
Vascular remodelling
Increased stiffness
Vascular inflammation
Calcification

A. Harvey et al. / Journal of Molecular and Cellular Cardiology 83 (2015) 112–121

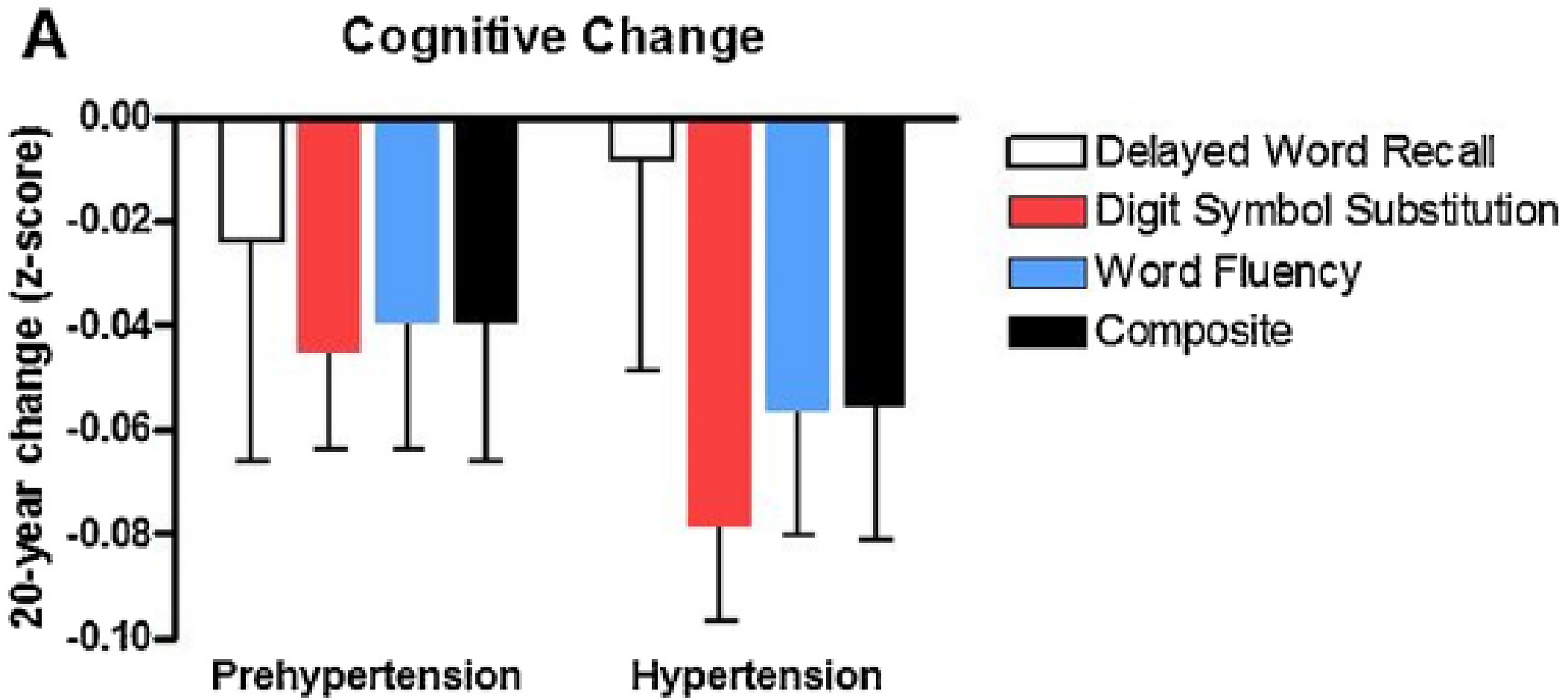


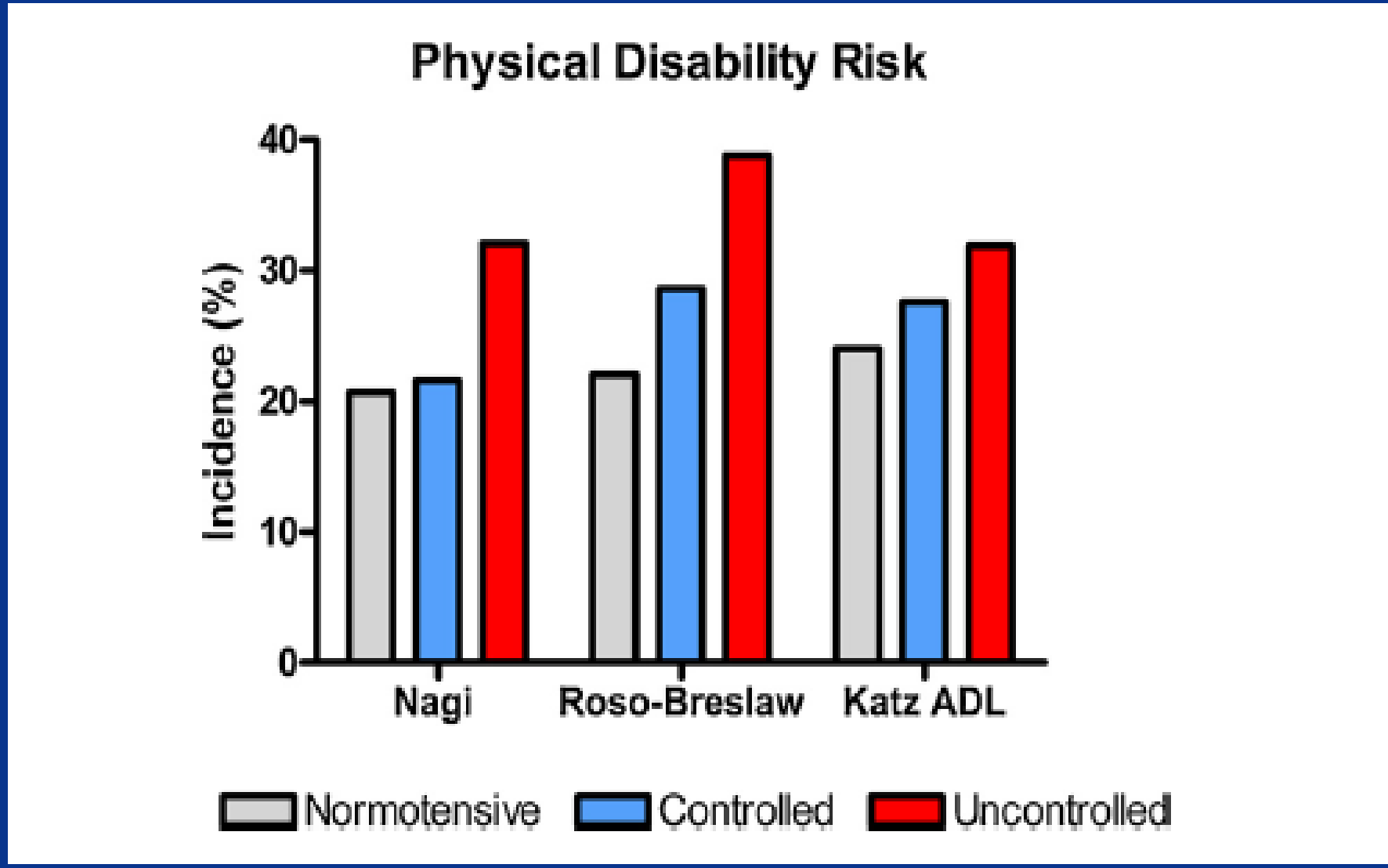
A. Harvey et al. / Journal of Molecular and Cellular Cardiology 83 (2015) 112–121

Table 1
Clinical differences between midlife and systolic hypertension

Clinical Differences	Midlife	Systolic
1. Age (y)	<55 (midlife)	>55 (older)
2. Prevalence (%)	30–35	65
3. BP Control	Relatively easy	Relatively difficult
4. SBP	Elevated	Elevated
5. DBP	High	Normal or low
6. PP	Mildly increased	Markedly increased
7. MBP	High	Slightly increased
8. Hemodynamic cause	Increased TPR	Increased aortic stiffness
9. Atherosclerosis	Yes	No
10. Therapy	ACEI, ARB, CCB, and so forth	Future vs. arteriosclerosis
11. SBP treatment target		
JNC 8	130–140 mm Hg	150 mm Hg
SPRINT	120 mm Hg	120 mm Hg

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; DBP, diastolic blood pressure; MBP, mean blood pres-


A
Cognitive Change
20-year change (z-score)
0.00
-0.02
-0.04
-0.06
-0.08
-0.10
Prehypertension
Hypertension
Delayed Word Recall
Digit Symbol Substitution
Word Fluency
Composite



T.W. Buford / Ageing Research Reviews 26 (2016) 96–111

Age and Ageing (1979), *8*, 115

Treatment of Hypertension in Patients under the Age of 65

The treatment of essential hypertension in patients under the age of 65 is firmly established on the basis of:

1. evidence of an association between hypertension and risks to life and health;
2. evidence of reduction in these risks by effective treatment in controlled trials.

There is however evidence that treatment in practice often falls far short of what is desirable.

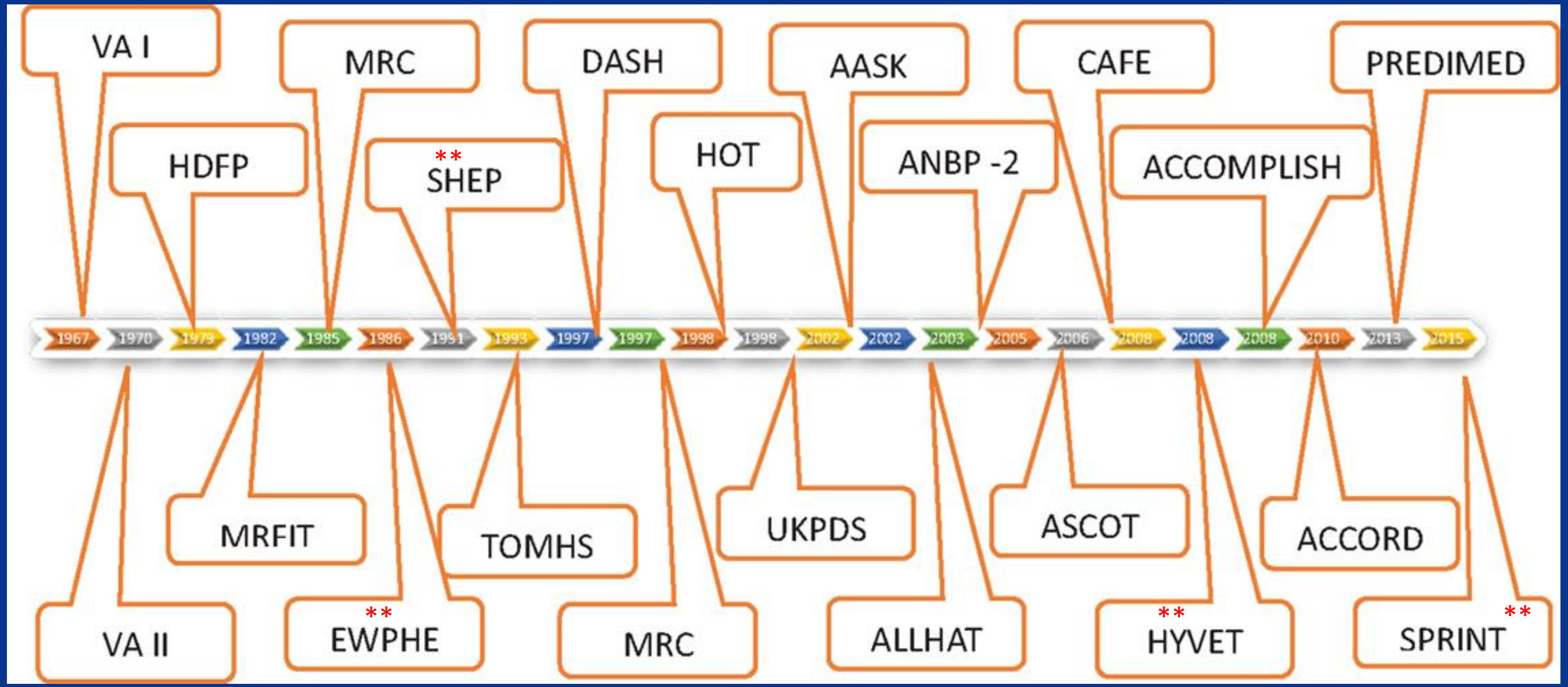
Treatment of Hypertension in Patients aged 65 and over

The case for treating essential hypertension in patients aged 65 and over is less firmly based. Not only is the evidence conflicting and insufficient, but there are doubts about the case for treatment a priori.

Survivorship
Autoregulation
Brain circulation

The prescribing of potent antihypertensive drugs to every elderly person with a high blood pressure will benefit a few, will harm many, and will be wholly irrelevant to the medical needs of most, especially of those in whom the high blood pressure is an incidental finding and is not the cause of the symptoms for which the patient has sought medical help.

We still do not know in which elderly patients hypertension is a disease and in which it is, like old age itself, an achievement. Doctors are advised to curtail antihypertensive therapy in the elderly until much more is known about its effects.

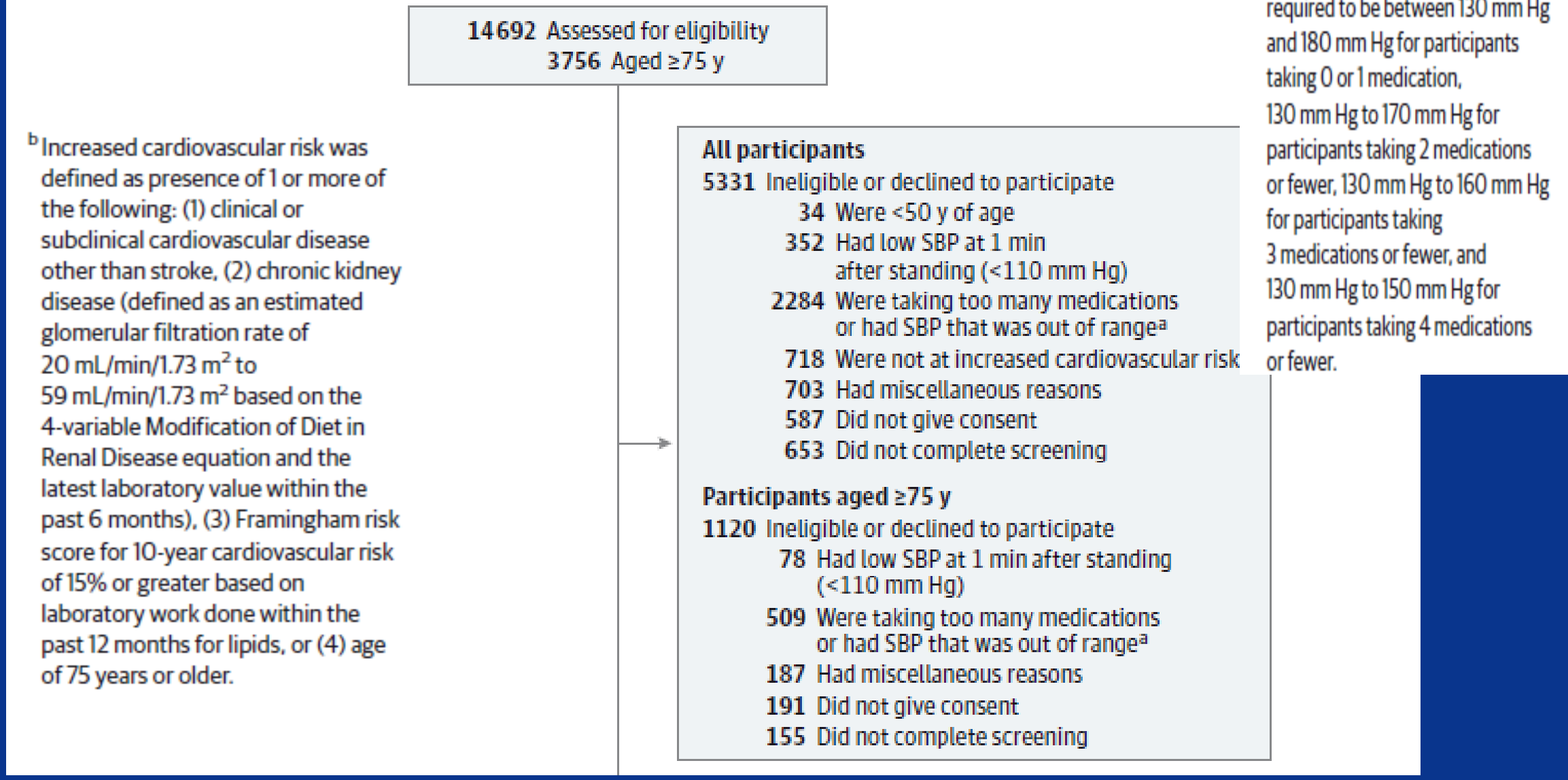


Major trials for treatment of hypertension

Table 1. Blood Pressure Management for People Older Than 80 Years as Recommended by Various National and

Source	Specific Recommendations	
	Patients >80 y	Frail Patients
Eighth Joint National Committee (JNC 8),[24] 2014	None	None
American Society of Hypertension and the International Society of Hypertension,[37] 2014	Some recent trials suggest that in patients ≥80 y, achieving an SBP of <150 mm Hg is associated with strong cardiovascular and stroke protection, and thus a target of <150/90 mm Hg is now recommended for patients in this age group (unless these patients have chronic kidney disease or diabetes, whereby <140/90 mm Hg can be considered)	
European Society of Hypertension and the European Society of Cardiology,[3] 2013	In individuals >80 y with an initial SBP ≥160 mm Hg, it is recommended to reduce SBP to 150-140 mm Hg if they are in good physical and mental health condition Continuation of well-tolerated antihypertensive treatment should be considered when a treated individual is >80 y	In frail older patients, it is recommended to leave decisions about antihypertensive therapy to the treating physician and based on monitoring of the clinical effects of treatment

Figure 1. Eligibility, Randomization, and Follow-up for Systolic Blood Pressure (SBP) Intervention Trial (SPRINT) Participants Aged 75 Years or Older



[b] Increased cardiovascular risk was defined as presence of 1 or more of the following: (1) clinical or subclinical cardiovascular disease other than stroke, (2) chronic kidney disease (defined as an estimated glomerular filtration rate of 20 mL/min/1.73 m^2 to 59 mL/min/1.73 m^2 based on the 4-variable Modification of Diet in Renal Disease equation and the latest laboratory value within the past 6 months), (3) Framingham risk score for 10-year cardiovascular risk of 15% or greater based on laboratory work done within the past 12 months for lipids, or (4) age of 75 years or older.

[a] Systolic blood pressure was required to be between 130 mm Hg and 180 mm Hg for participants taking 0 or 1 medication, 130 mm Hg to 170 mm Hg for participants taking 2 medications or fewer, 130 mm Hg to 160 mm Hg for participants taking 3 medications or fewer, and 130 mm Hg to 150 mm Hg for participants taking 4 medications or fewer.

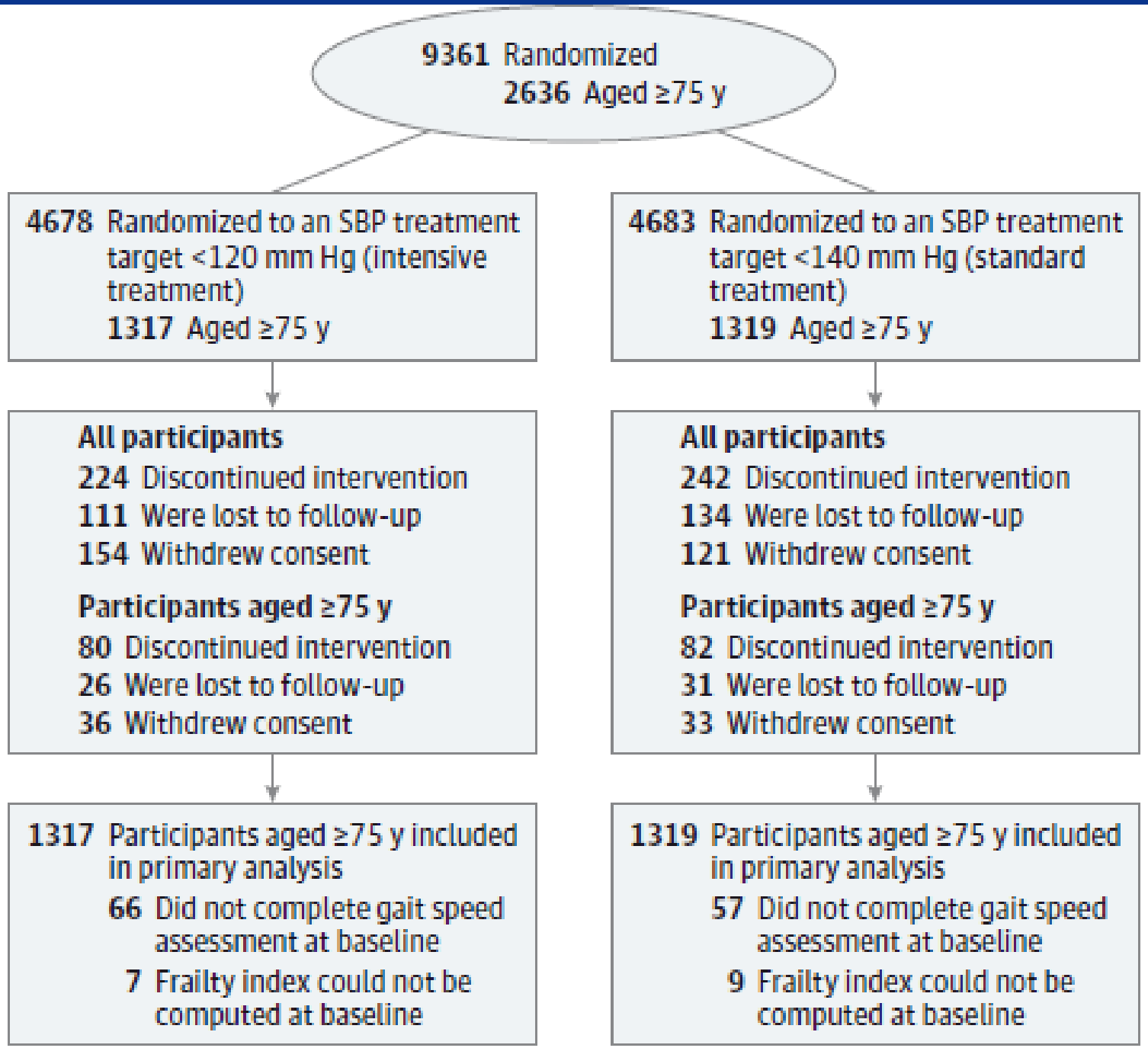

9361 Randomized
2636 Aged ≥75 y
4678 Randomized to an SBP treatment target <120 mm Hg (intensive treatment)
1317 Aged ≥75 y
4683 Randomized to an SBP treatment target <140 mm Hg (standard treatment)
1319 Aged ≥75 y
All participants
224 Discontinued intervention
111 Were lost to follow-up
154 Withdrew consent
Participants aged ≥75 y
80 Discontinued intervention
26 Were lost to follow-up
36 Withdrew consent
All participants
242 Discontinued intervention
134 Were lost to follow-up
121 Withdrew consent
Participants aged ≥75 y
82 Discontinued intervention
31 Were lost to follow-up
33 Withdrew consent
1317 Participants aged ≥75 y included in primary analysis
66 Did not complete gait speed assessment at baseline
7 Frailty index could not be computed at baseline
1319 Participants aged ≥75 y included in primary analysis
57 Did not complete gait speed assessment at baseline
9 Frailty index could not be computed at baseline

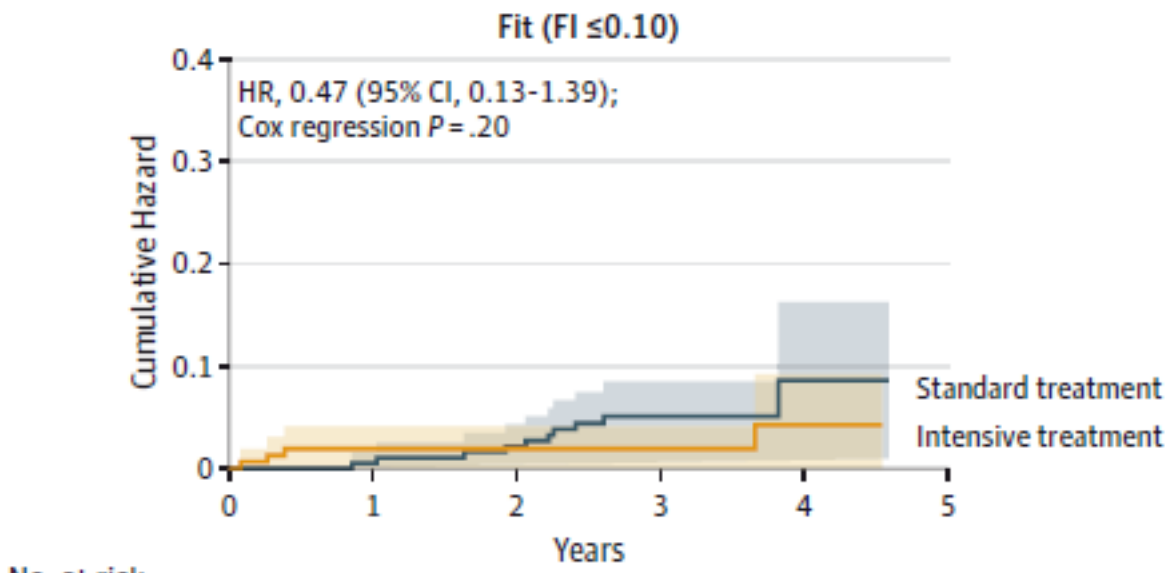
Table 1. Baseline Characteristics of Participants Aged 75 Years or Older

	Intensive Treatment (n = 1317)	Standard Treatment (n = 1319)
Female sex	499 (37.9)	501 (38.0)
Age, mean (SD), y	79.8 (3.9)	79.9 (4.1)
Race/ethnicity, No. (%)		
White	977 (74.2)	987 (74.8)
Black	225 (17.1)	226 (17.1)
Hispanic	89 (6.8)	85 (6.4)
Other	26 (2.0)	21 (1.6)
Seated blood pressure, mean (SD), mm Hg		
Systolic	141.6 (15.7)	141.6 (15.8)
Diastolic	71.5 (11.0)	70.9 (11.0)
Orthostatic hypotension, No. (%)	127 (9.6)	124 (9.4)
Gait speed		
Median (IQR), m/s	0.90 (0.77-1.05)	0.92 (0.77-1.06)
Speed <0.8 m/s, No. (%)	371 (28.2)	369 (28.0)
Frailty index, median (IQR)[c]	0.18 (0.13-0.23)	0.17 (0.12-0.22)
Frailty status, No. (%)		
Fit (frailty index ≤0.10)	159 (12.1)	190 (14.4)
Less fit (frailty index >0.10 to ≤0.21)	711 (54.0)	745 (56.5)
Frail (frailty index >0.21)	440 (33.4)	375 (28.4)
Montreal Cognitive Assessment score, median (IQR)[d]	22.0 (19.0-25.0)	22.0 (19.0-25.0)

Table 3. Incidence of Cardiovascular, Renal, and Mortality Outcomes by Treatment Group

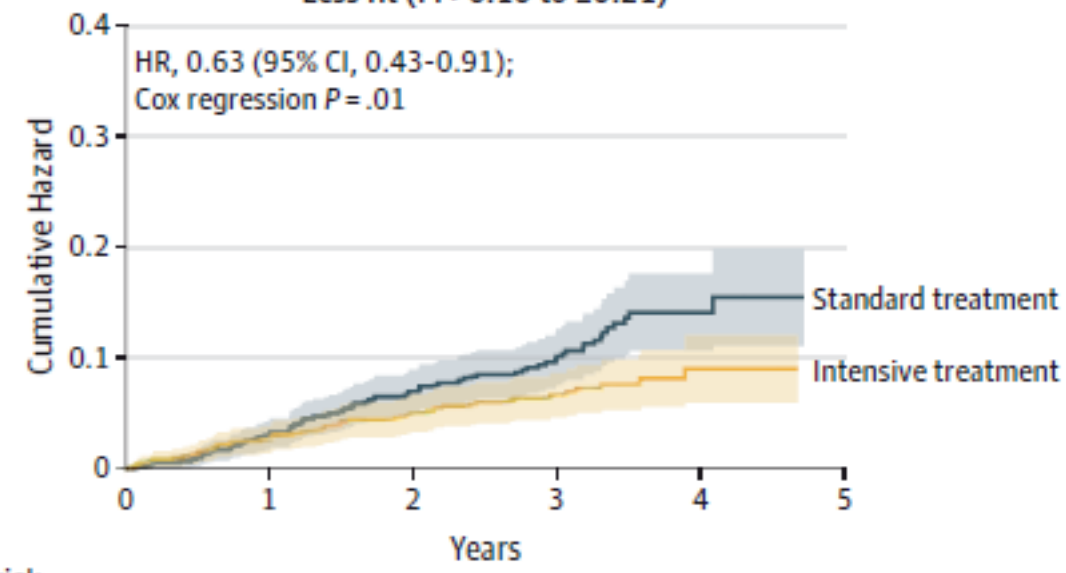
	Intensive Treatment		Standard Treatment		
	No. With Outcome Events (n = 1317)[a]	% (95% CI) With Outcome Events/y	No. With Outcome Events (n = 1319)[a]	% (95% CI) With Outcome Events/y	*P* Value
All participants					
Cardiovascular disease primary outcome[c]	102	2.59 (2.13-3.14)	148	3.85 (3.28-4.53)	.001
Myocardial infarction (MI)[d]	37	0.92 (0.67-1.27)	53	1.34 (1.02-1.75)	.09
ACS not resulting in MI[d]	17	0.42 (0.26-0.68)	17	0.42 (0.26-0.68)	.94
Stroke[d]	27	0.67 (0.46-0.97)	34	0.85 (0.61-1.19)	.22
Heart failure[d]	35	0.86 (0.62-1.20)	56	1.41 (1.09-1.83)	.03
Cardiovascular disease death[d]	18	0.44 (0.28-0.70)	29	0.72 (0.50-1.03)	.09
Nonfatal MI	37	0.92 (0.67-1.27)	53	1.34 (1.02-1.75)	.09
Nonfatal stroke	25	0.62 (0.42-0.91)	33	0.83 (0.59-1.16)	.15
Nonfatal heart failure	35	0.86 (0.62-1.20)	55	1.39 (1.06-1.81)	.03
All-cause mortality	73	1.78 (1.41-2.24)	107	2.63 (2.17-3.18)	.009
Primary outcome plus all-cause mortality	144	3.64 (3.09-4.29)	205	5.31 (4.63-6.09)	<.001

Figure 2. Kaplan-Meier Curves for the Primary Cardiovascular Disease Outcome in Systolic Blood Pressure Intervention Trial (SPRINT) in Participants Aged 75 Years or Older by Baseline Frailty Status



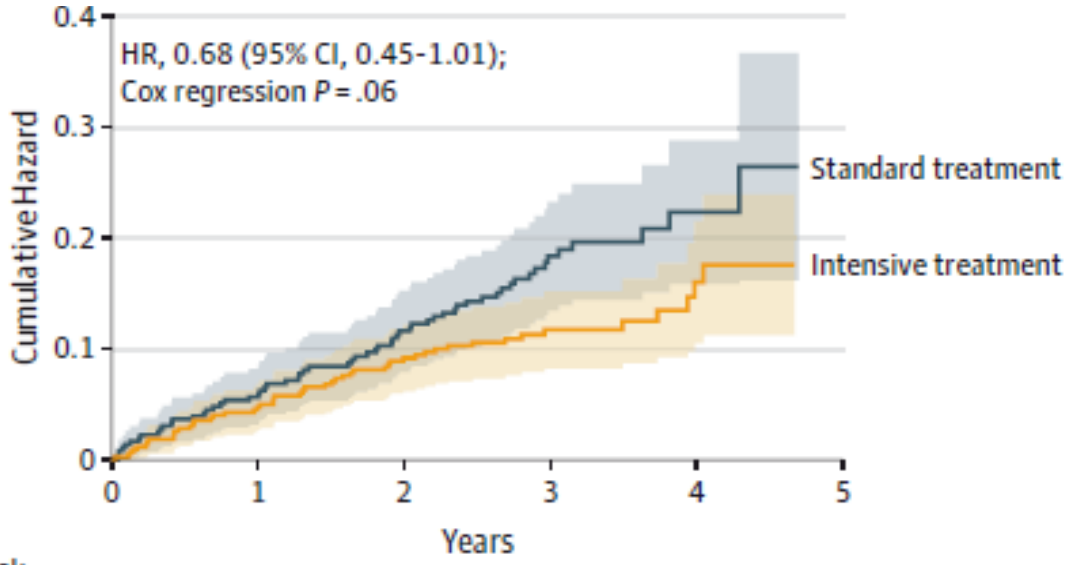
No. at risk

Type of treatment					
Standard	190	186	182	94	19
Intensive	159	151	150	107	16



No. at risk

Type of treatment					
Standard	745	697	653	390	91
Intensive	711	677	644	378	93



No. at risk

Type of treatment					
Standard	375	338	305	177	49
Intensive	440	398	371	223	71

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

Dena Ettehad, Connor A Emdin, Amit Kiran, Simon G Anderson, Thomas Callender, Jonathan Emberson, John Chalmers, Anthony Rodgers, Kazem Rahimi

Lancet 2016; 387: 957–67

1. **Blood pressure lowering below current recommended levels decreased risk of heart disease**
2. **No threshold below which lowering blood pressure did not decrease risk**
3. **There was consistency between studies in the effect of treatment**
4. **Drugs specific to outcomes worked-tailoring**

Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis

Lancet 2016; 387: 435–43

Xinfang Xie, Emily Atkins, Jicheng Lv, Alexander Bennett, Bruce Neal, Toshiharu Ninomiya, Mark Woodward, Stephen MacMahon, Fiona Turnbull, Graham S Hillis, John Chalmers, Jonathan Mant, Abdul Salam, Kazem Rahimi, Vlado Perkovic, Anthony Rodgers

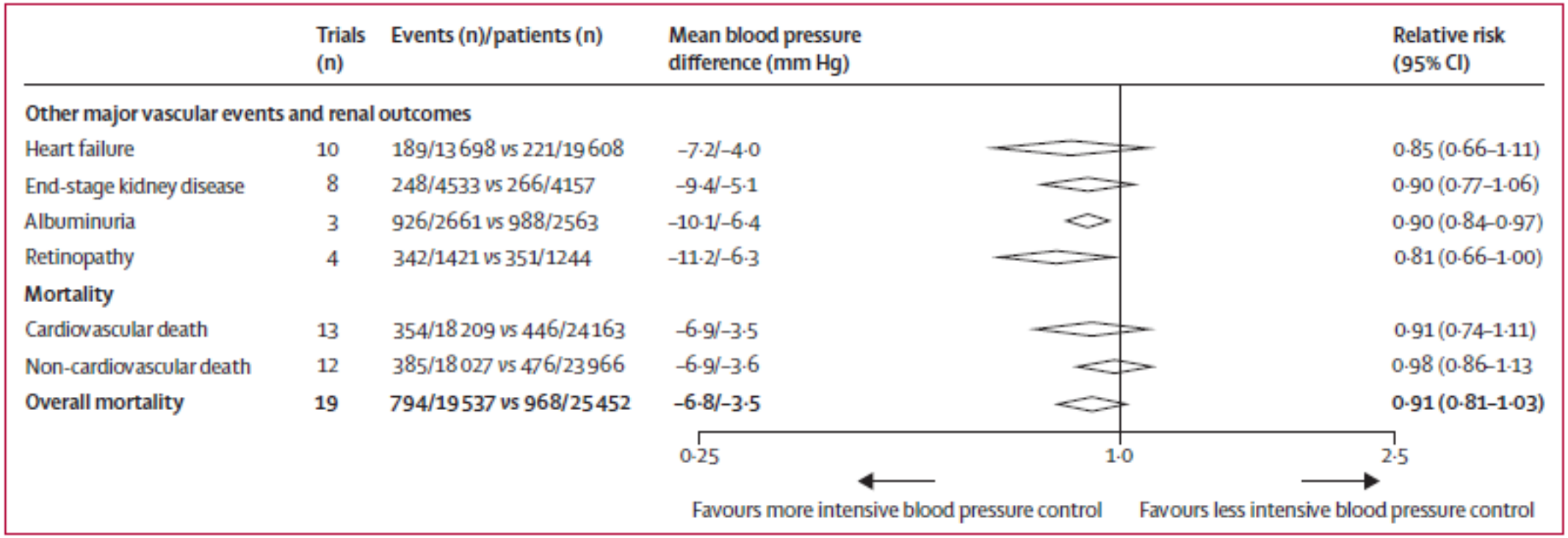
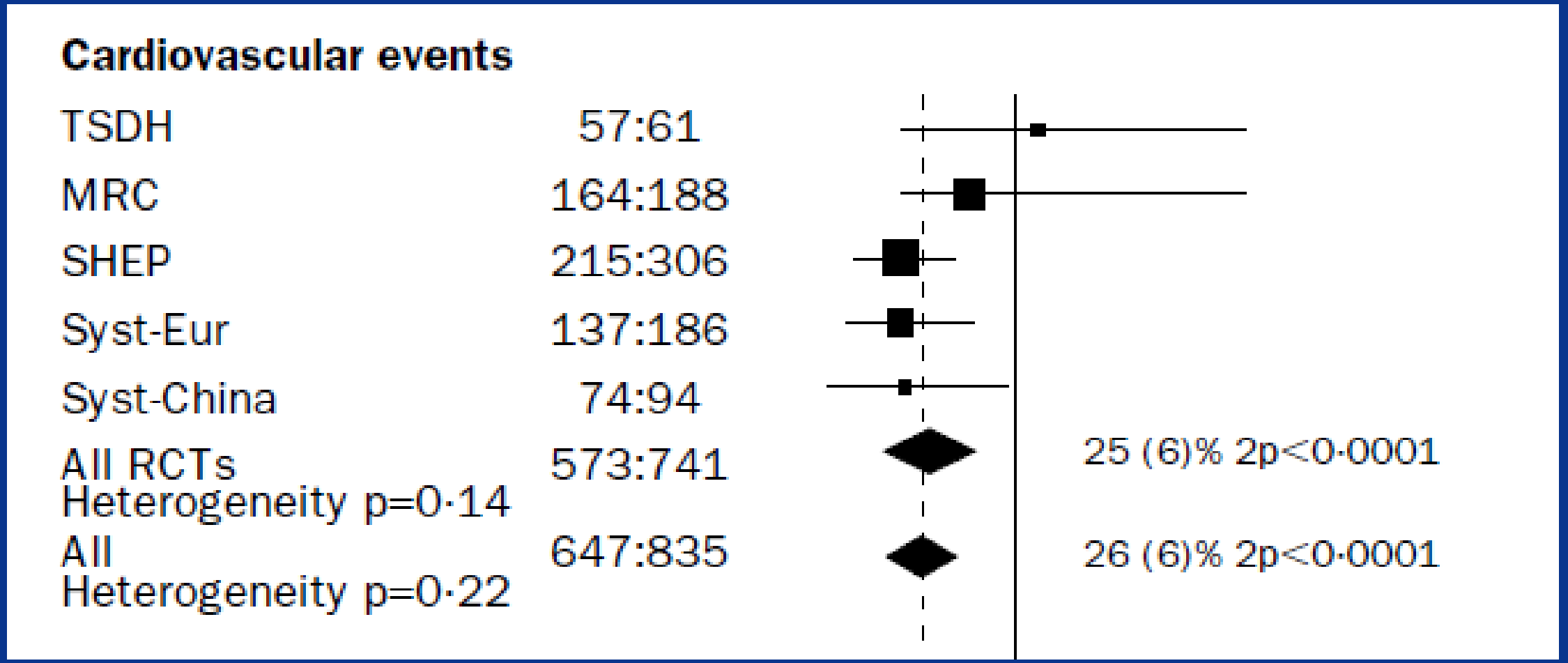


***Figure 3*: Effect of intensive versus less intensive blood pressure lowering on the risk of other major vascular events, renal outcomes, and mortality**
Weights are from random-effects analysis. Diamonds represent the 95% CI for pooled estimates of effect.

Word of caution……



Lancet 2000; **355:** 865–872

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Treatment of Hypertension in Patients 80 Years of Age or Older

Selected age-associated changes in the cardiovascular system

Difficult to separate aging and disease
Changes in vasculature greater than changes in heart
Common, costly, with unsettled clinical issues

Overview
What I will not cover
Atrial fibrillation
Hypertension

Thank you for your attention.