Is hypertension still a problem?

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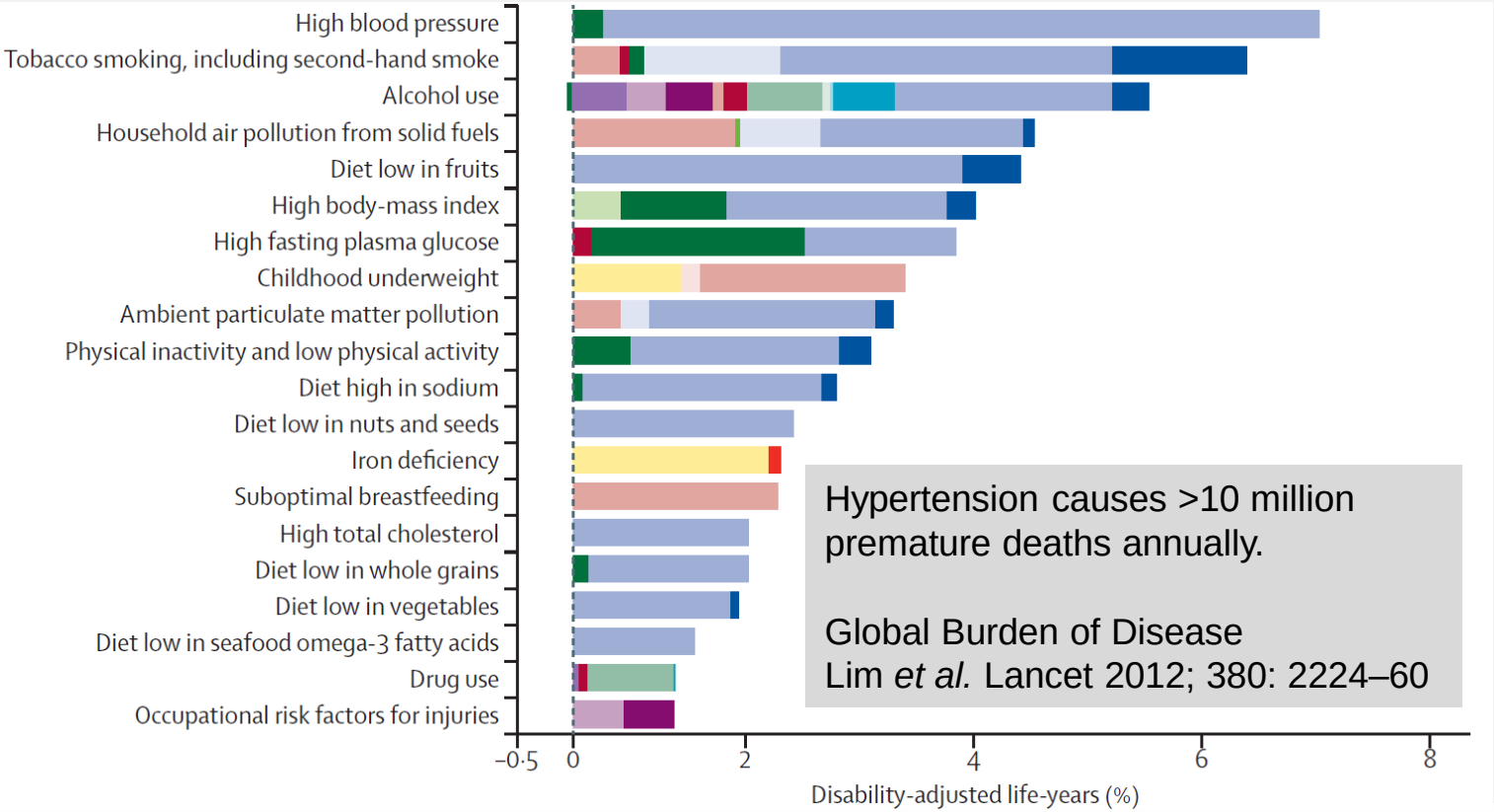
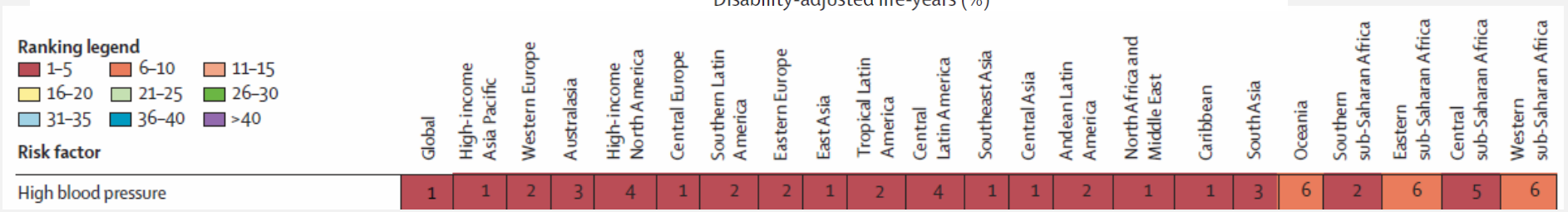
High blood pressure: worldwide the most significant risk factor causing deaths and disability

- 20 leading risk factors causing disability-adjusted life-years



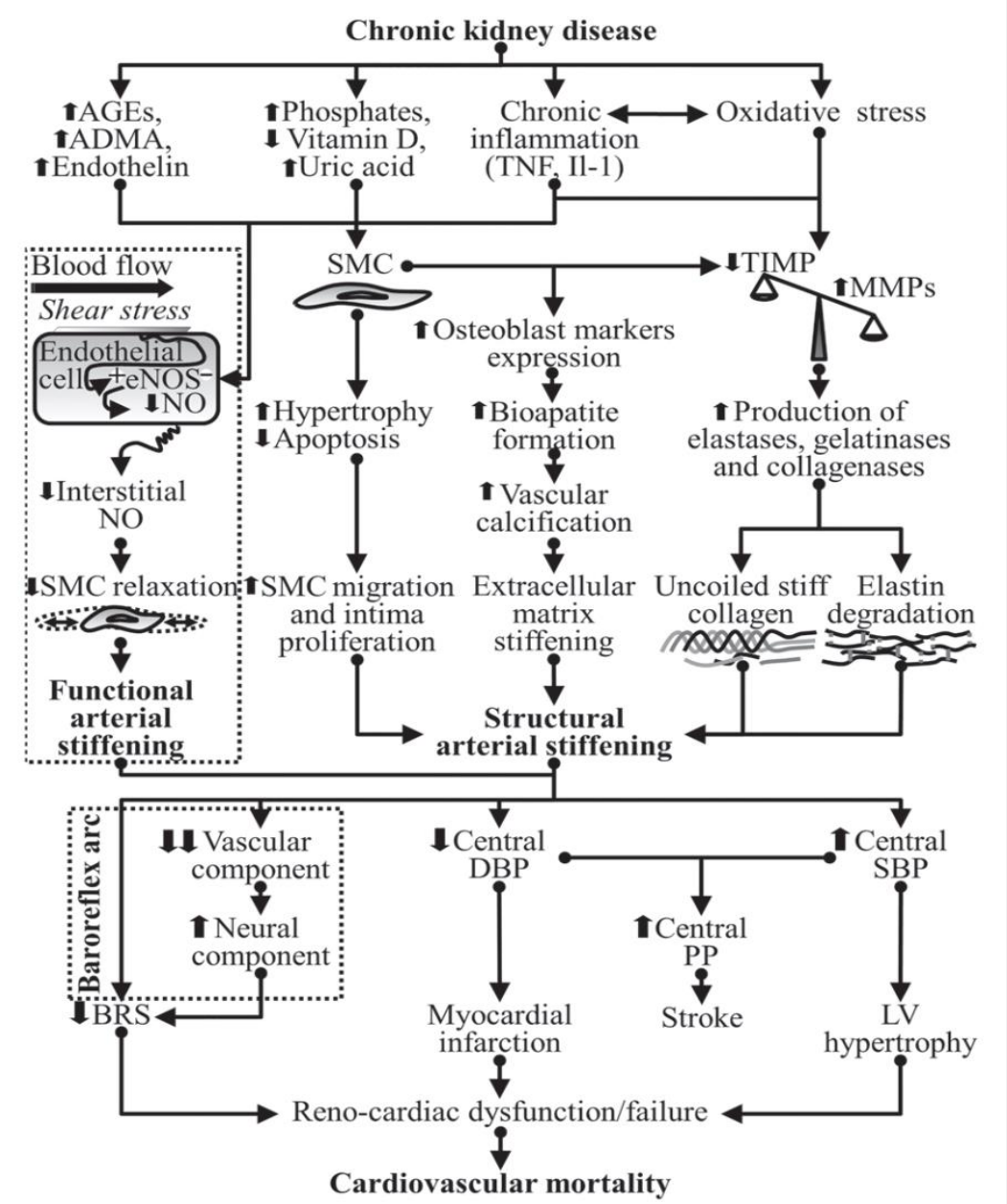
Hypertension causes >10 million premature deaths annually.

Global Burden of Disease
Lim *et al.* Lancet 2012; 380: 2224–60



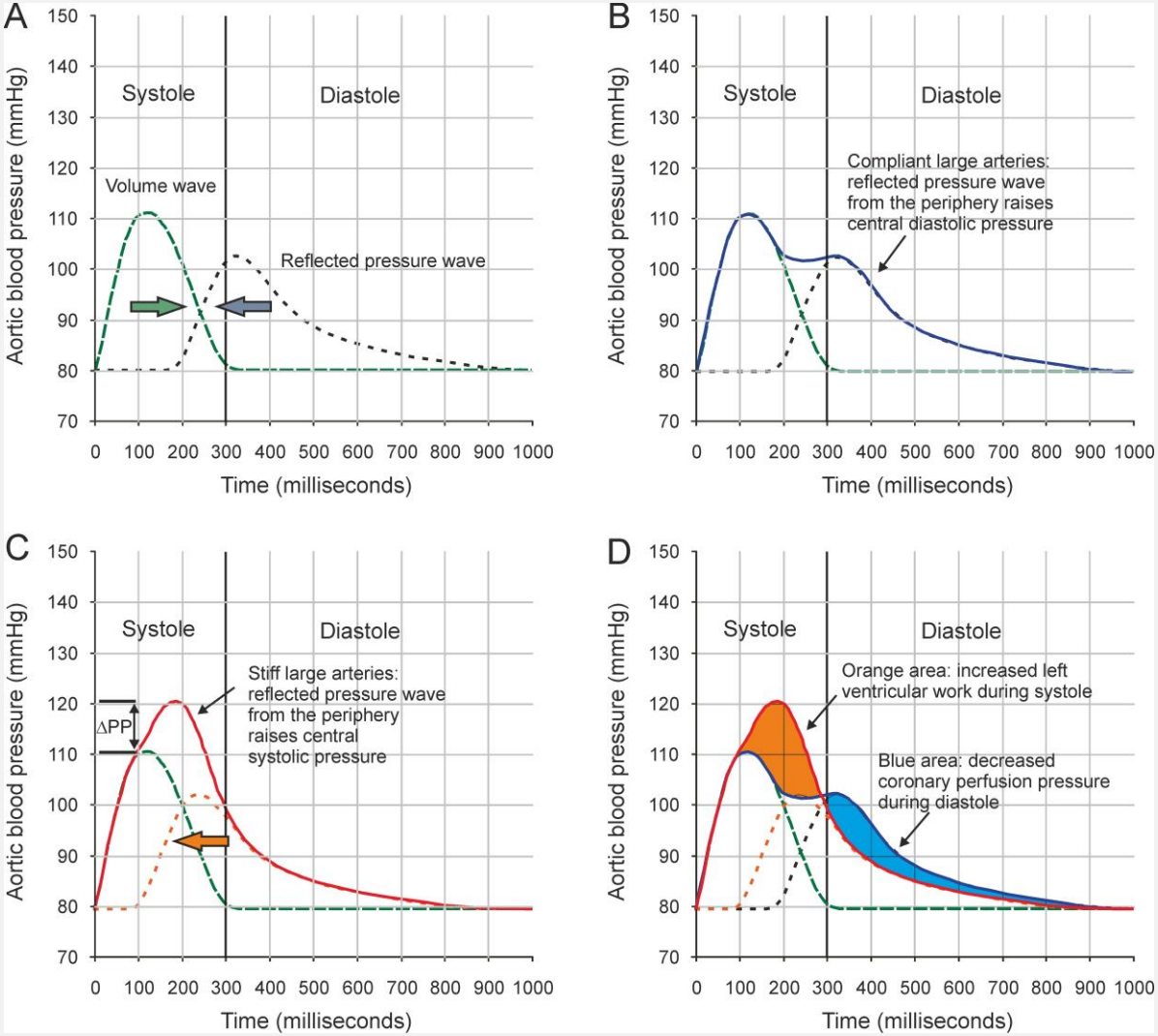
Premature vascular ageing in CKD patients

- ~85% of CKD patients are hypertensive
- CKD patients with normal BP better preserve their GFR than hypertensive CKD patients
- Lower BP target (<130/80) is associated with better renal outcomes in patients with proteinuric CKD
- Intensive BP control lowers mortality risk among trial participants with hypertension and CKD



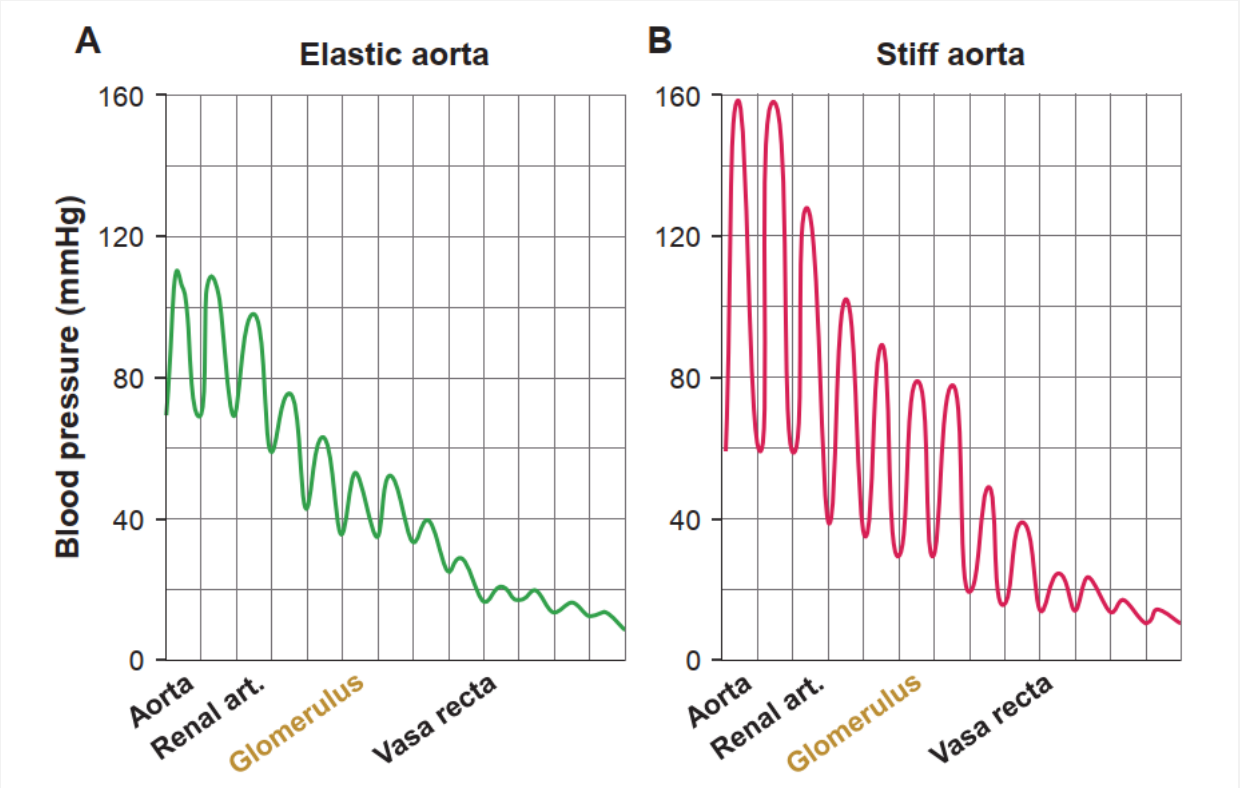
Stefanski et al. *Kidney Int* 1996, 50: 1321-1326. Anderson et al. *Ann Int Med* 2015; 162:258. Jafar et al. *Ann Intern Med* 2003; 139:244-252. Malhotra et al. JAMA Internal Medicine 2017; 177:1498-1505. Zanoli et al. *JASN* 30: 918–928, 2019.

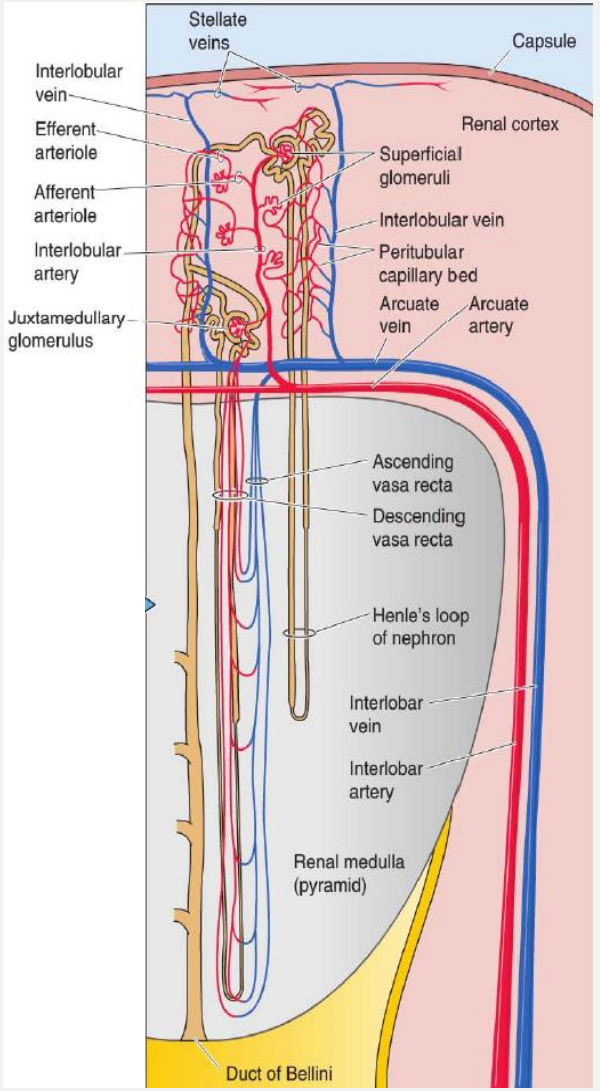
Volume wave, pressure wave, reflected pressure wave



Modified from O'Rourke and Hashimoto *J Am Coll Cardiol* 2007;50:1–13.

Pulsatile flow in small arteries





Hashimoto *Tohoku J. Exp. Med.*, 2014, 233, 1-8.

2018 ESC/ESH Guidelines: management of hypertension

Table 23 Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke[a]/TIA	
18 - 65 years	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	**Target to <140 to 130** *if tolerated*	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	70–79
65 - 79 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
≥80 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
Office DBP treatment target range (mmHg)	70–79	70–79	70–79	70–79	70–79	

CAD = coronary artery disease; CKD = chronic kidney disease (includes diabetic and non-diabetic CKD); DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

Williams et al. *J Hypertens* 36:1953–2041

2018 ESC/ESH Guidelines: management of hypertension

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Age group			Office DBP treatment target range (mmHg)
18 - 65 years		Target to 130 if to	to 130 if tolerated <120	70–79
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Office DBP treatment target range (mmHg)		70–	–79	

This phenotype is more than 100 years old

1896: Riva Rocci published work describing the use of sphygmomanometer in the *Gazzetta Medica di Torino*

1905: Nikolai Korotkov published work on auscultatory BP measurement (in 281 words) in *Izvestie Imp. Voiennomedicinskoi Akademii* (Reports of the Imperial Military Medical Academy).

CAD = coronary artery di… c and non- … = transient ischaemic attack.

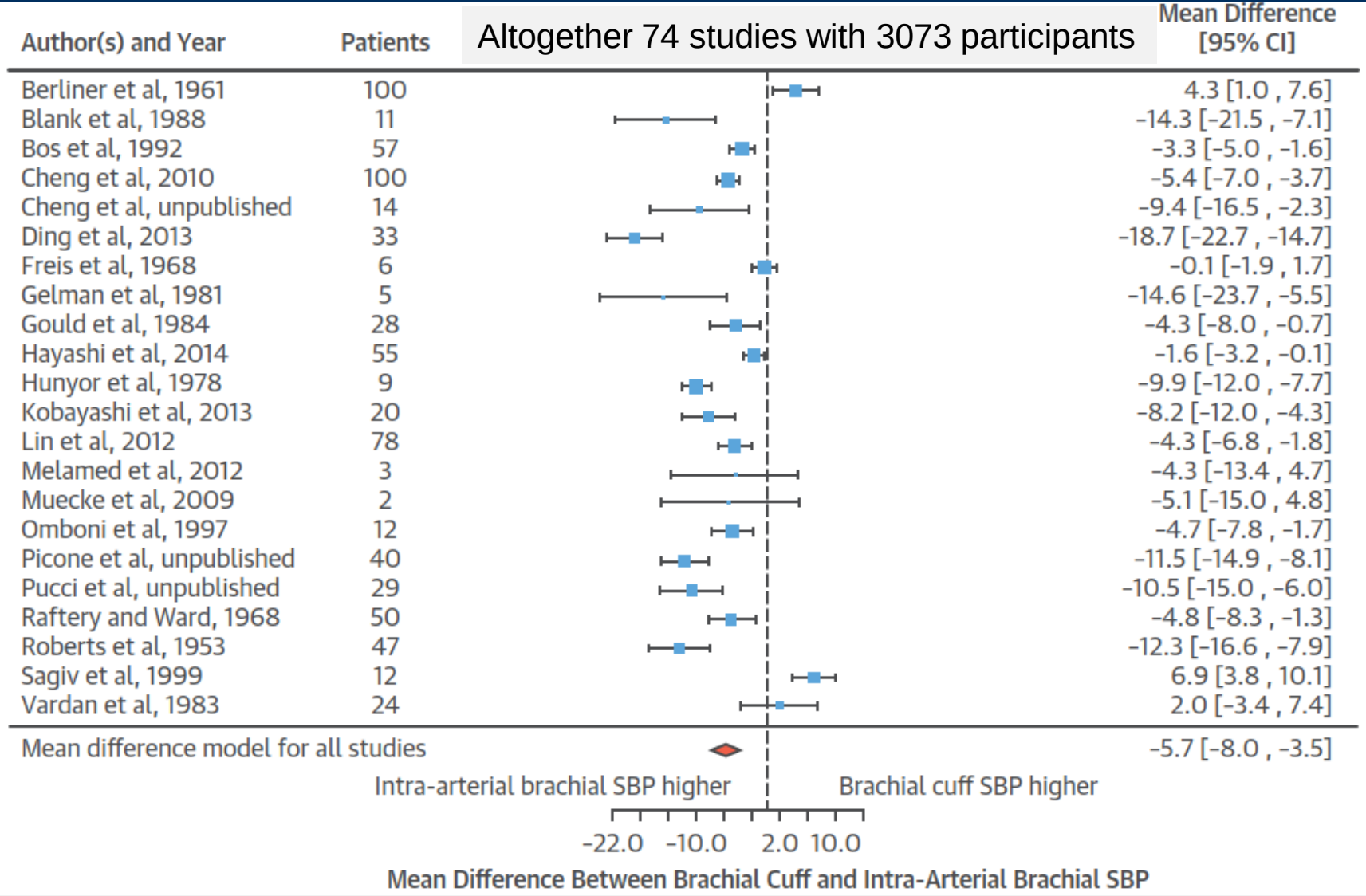
BP targets in renal patients

- **Strategies for treatment of hypertension in CKD (2018)**
  - Office SBP to 130–139 mmHg
  - Office DBP to 70-79 mmHg
- **BP goal <130/80 evidence-based in CKD (2019)**
  - Attention to measuring BP accurately, assessing patient preferences and concurrent medical conditions, and monitoring for adverse effects
- **CKD in diabetic patients, class I level A evidence (2020)**
  - Individualized treatment, SBP target <130 mmHg if tolerated, not <120 mmHg
  - Age >65 years: SBP goal 130-139 mmHg
  - DBP target <80 mmHg, not <70 mmHg

Williams et al. *European Heart Journal* (2018) 39, 3021–3104. Chang et al. *CJASN* (2019), 14:161-169.
Cosentino et al. *European Heart Journal* (2020) 41, 255-323 [CKD = eGFR<60 ml/min/1.72 m^2 or U-AlbCre≥3 mg/mmol].

Accuracy of cuff-measured BP

SBP underestimated by 6 mmHg



Picone et al. *Journal of the American College of Cardiology* 2017; 70(5): 572–586.

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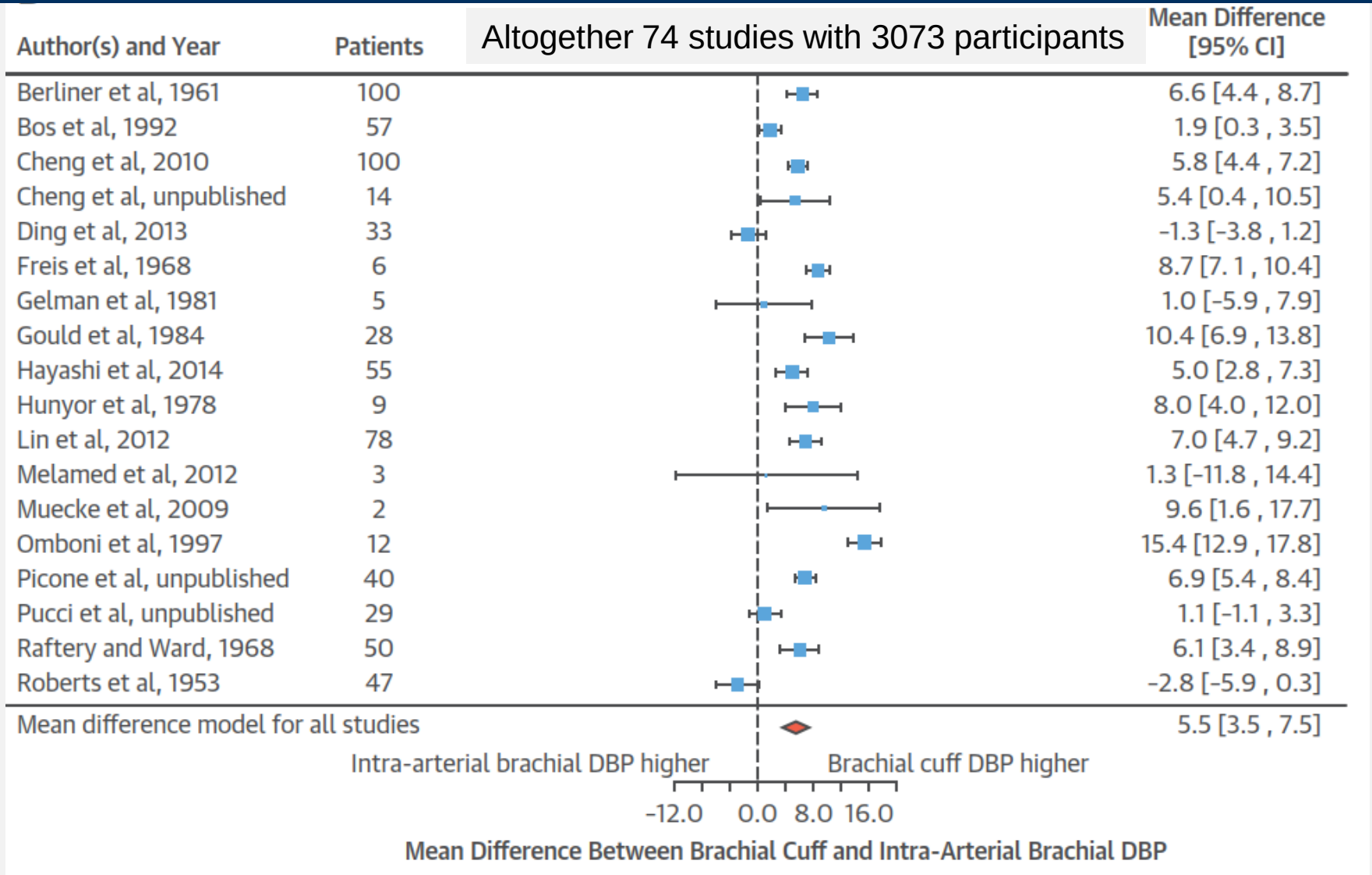

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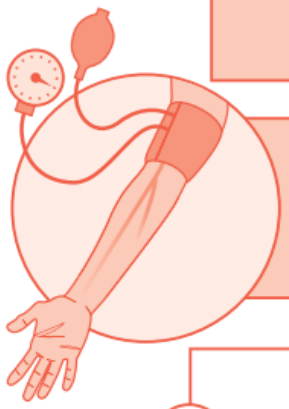
Accuracy of cuff-measured BP

Brachial PP underestimated by 12 mmHg

Altogether 74 studies with 3073 participants



Hypertension (elevated blood pressure (BP))
is the single largest risk factor for cardiovascular disease mortality

Non-invasive brachial (upper arm) cuff BP is the principal method for hypertension diagnosis and management

Does the cuff accurately measure BP?

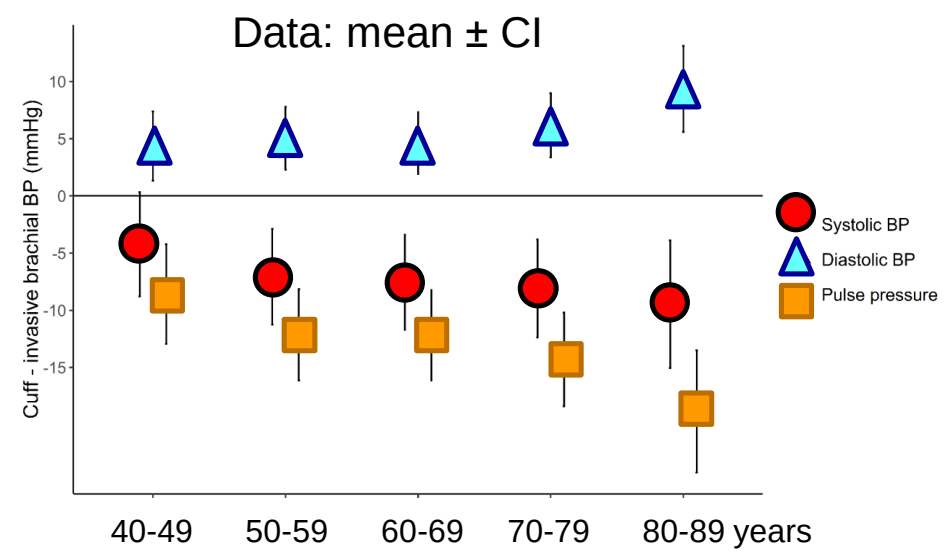
For patients with **Normal BP** <120/80 mm Hg	For patients with **Prehypertension** (≥120/80 to <140/90 mm Hg) or **Stage 1 hypertension** (≥140/90 to <160/100 mm Hg)	For patients with **Stage 2 hypertension** ≥160/100 mm Hg
Reasonable confidence can be placed in cuff BP readings	Cuff **overestimates** diastolic BP at brachial and aortic level Cuff **underestimates** systolic BP at brachial level Cuff variably **under- or overestimates** SBP at the aorta	Reasonable confidence can be placed in cuff BP readings

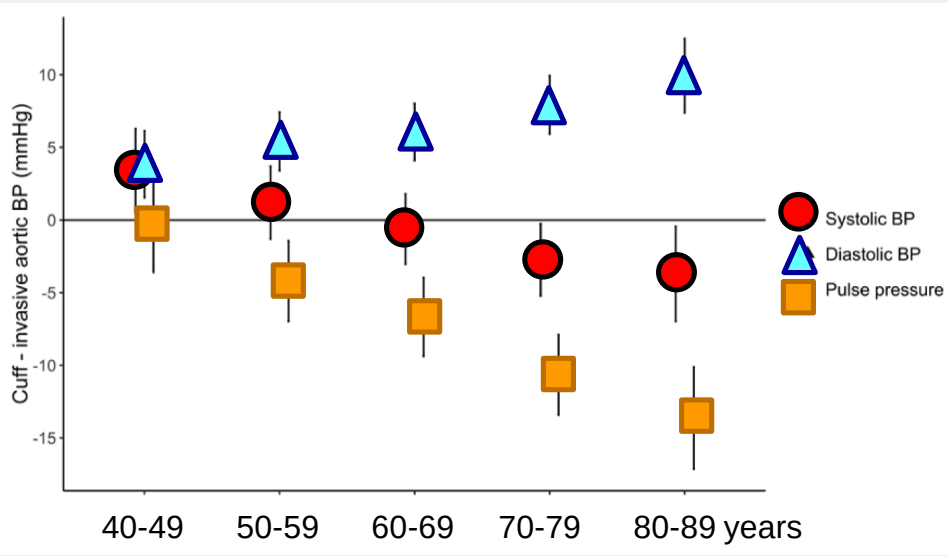
Improved accuracy is recommended

Picone et al. *Journal of the American College of Cardiology* 2017; 70(5): 572–586.

Age and cuff-based blood pressure

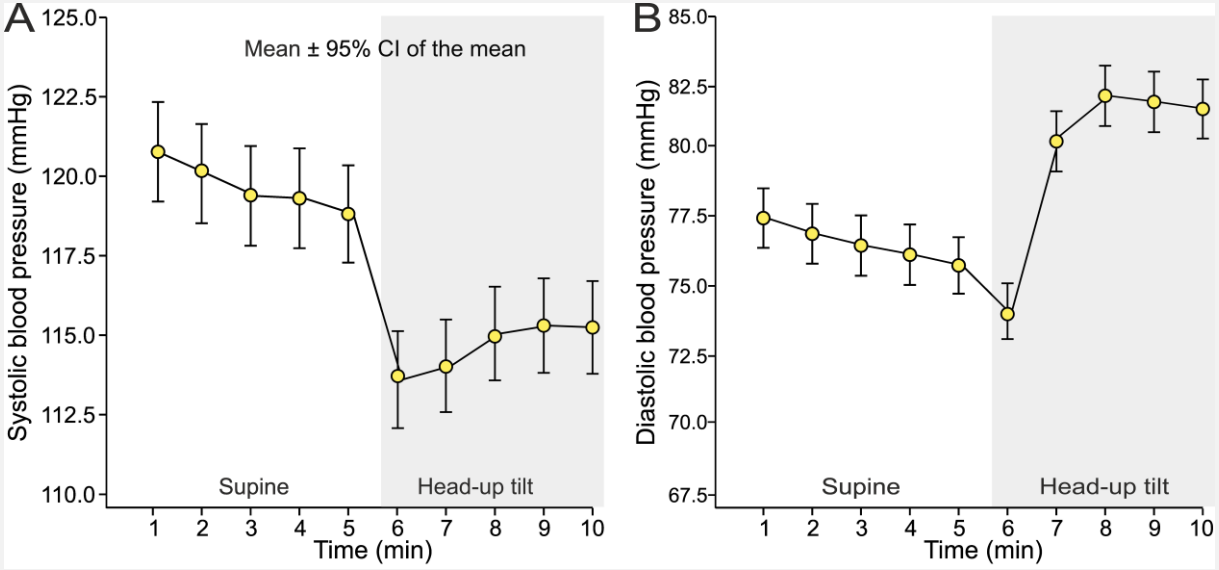
- 31 studies with 1674 patients undergoing coronary angiography
- 22 different cuff BP devices:
  19 oscillometric,
  1 automated auscultation,
  2 mercury sphygmomanometry
- Progressive increase in cuff pulse pressure underestimation with increasing age
- "*It is imperative that more personalized methods of BP measurement are developed*"





Picone et al. *Hypertension* 2020; 75: 844–850.

Upright Change in Aortic BP

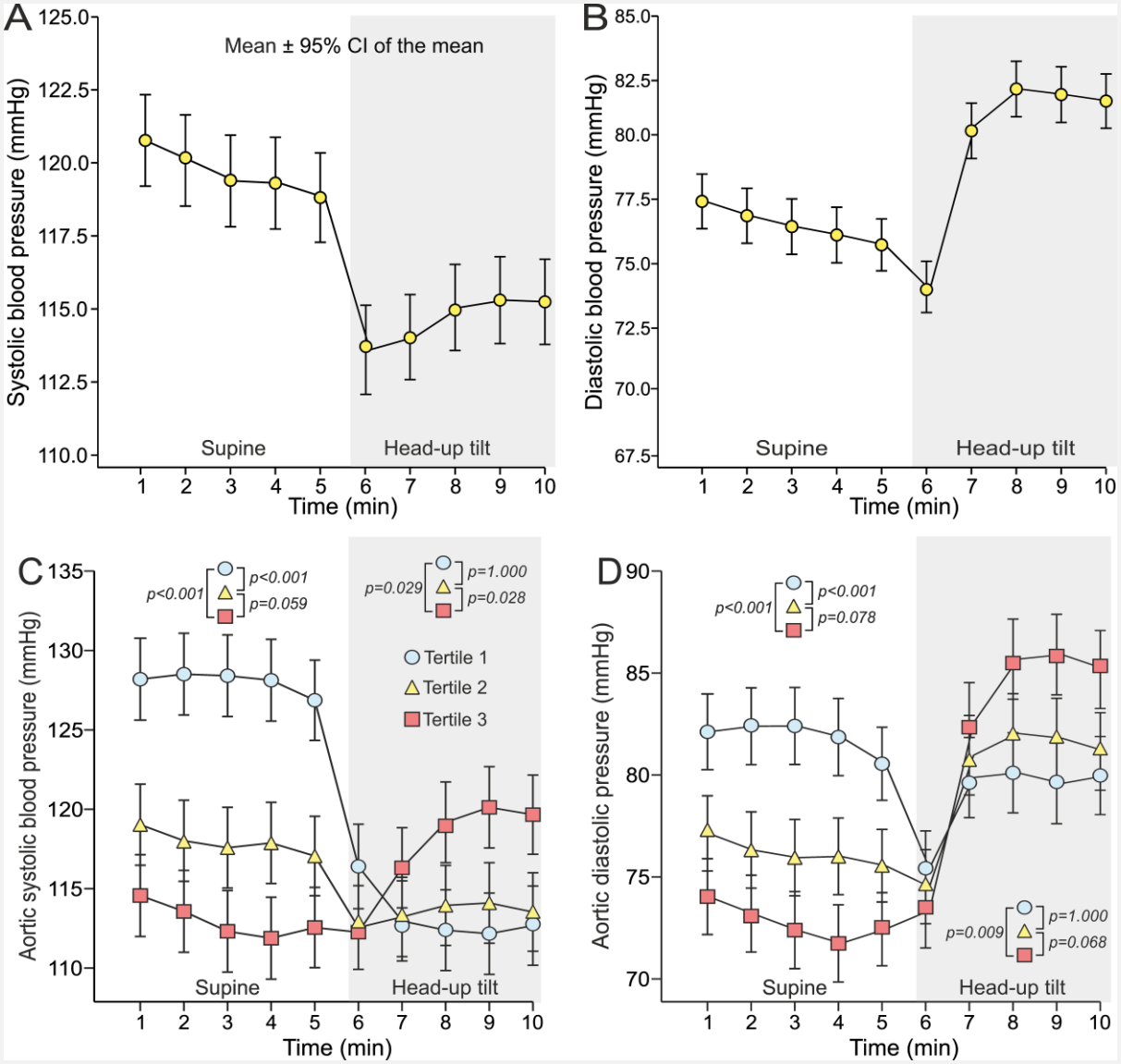


- 613 subjects without medications
  - 301 men
  - 312 women

- Divided to tertiles according to the supine-to-upright change in central SBP

Suojanen et al. *Manuscript in preparation*

Upright Change in Aortic BP



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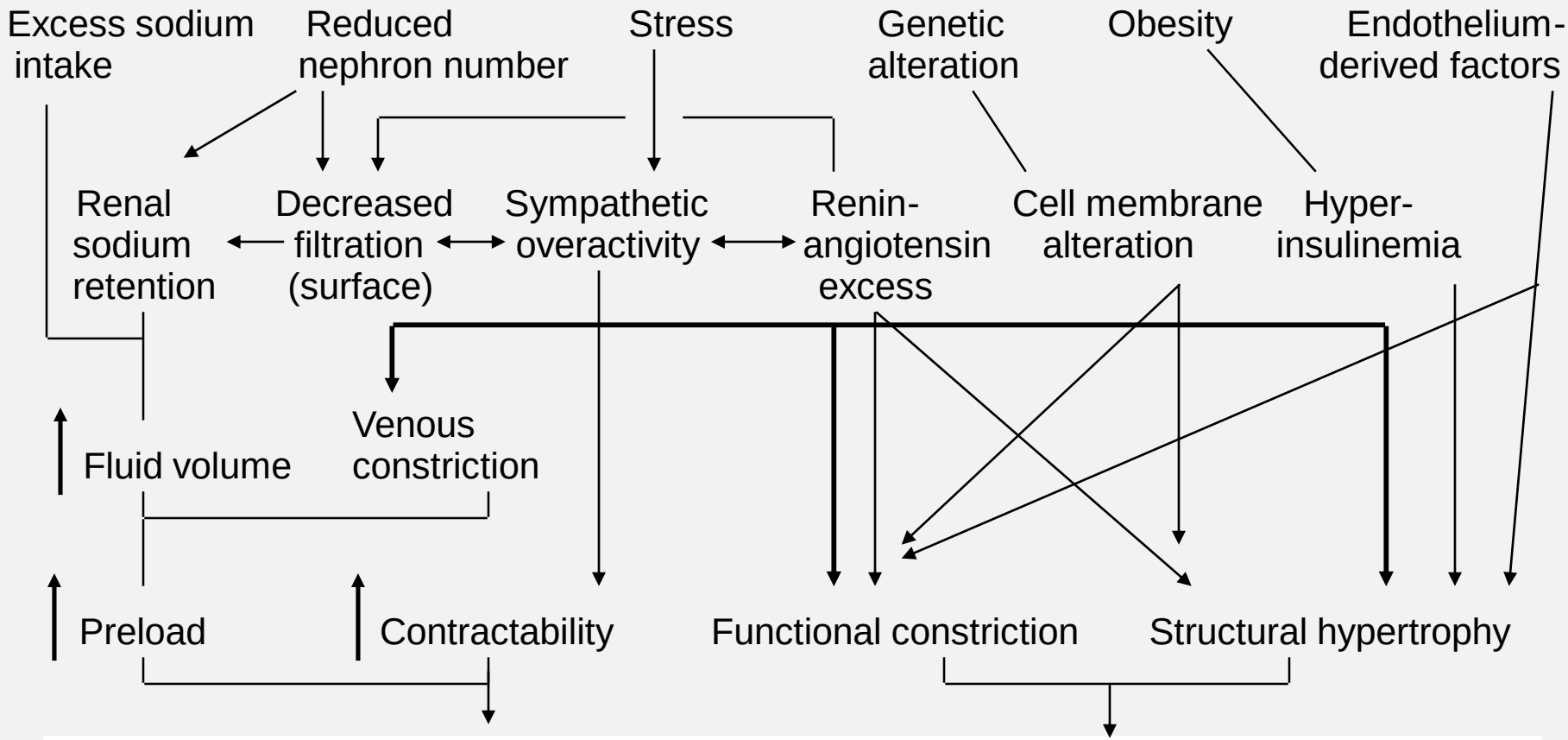
Control of circulation

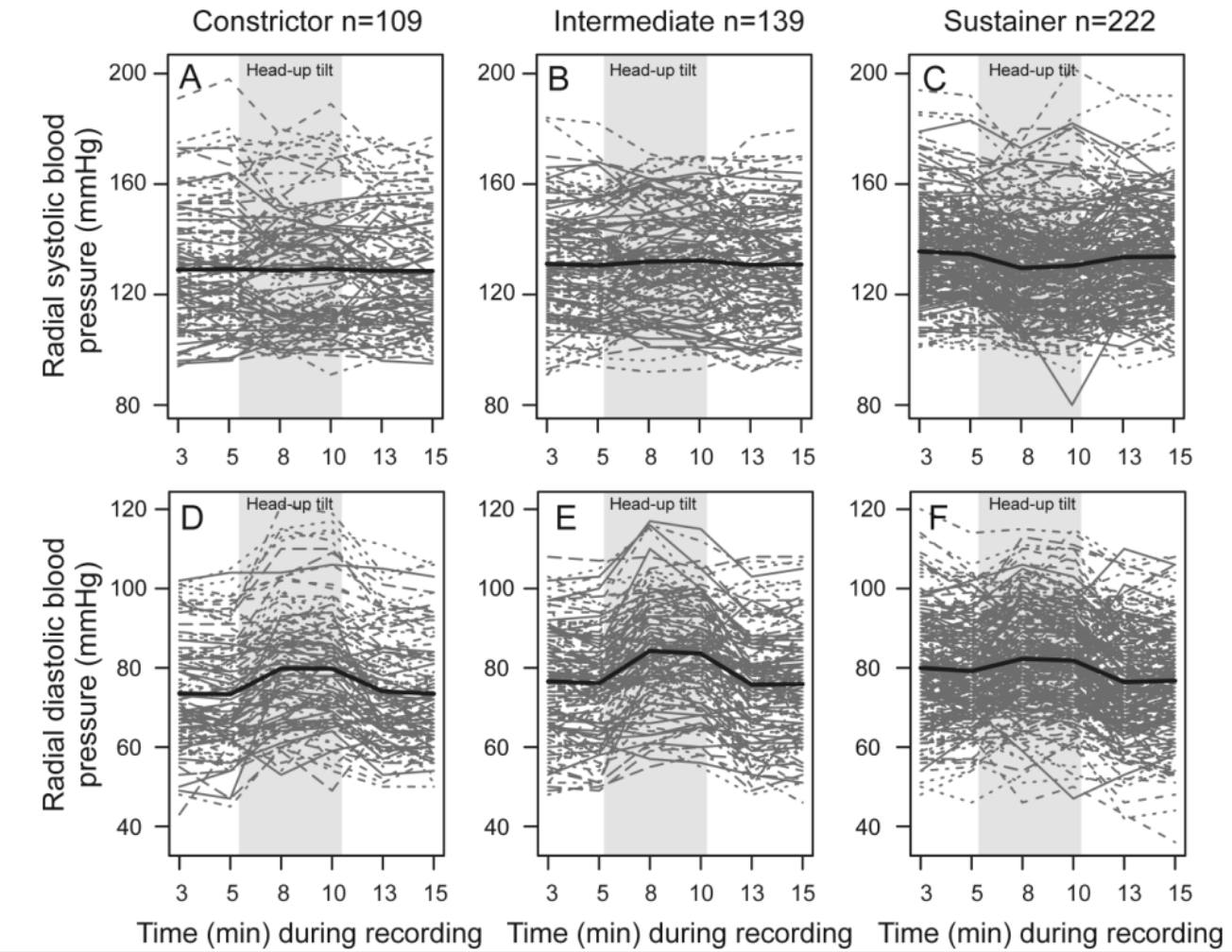


Blood pressure = Cardiac output x Peripheral resistance

Hypertension = Increased CO and/or Increased PR

Modified from norman Kaplan's *Clinical Hypertension, 11th edition.*

Cardiovascular response to upright posture

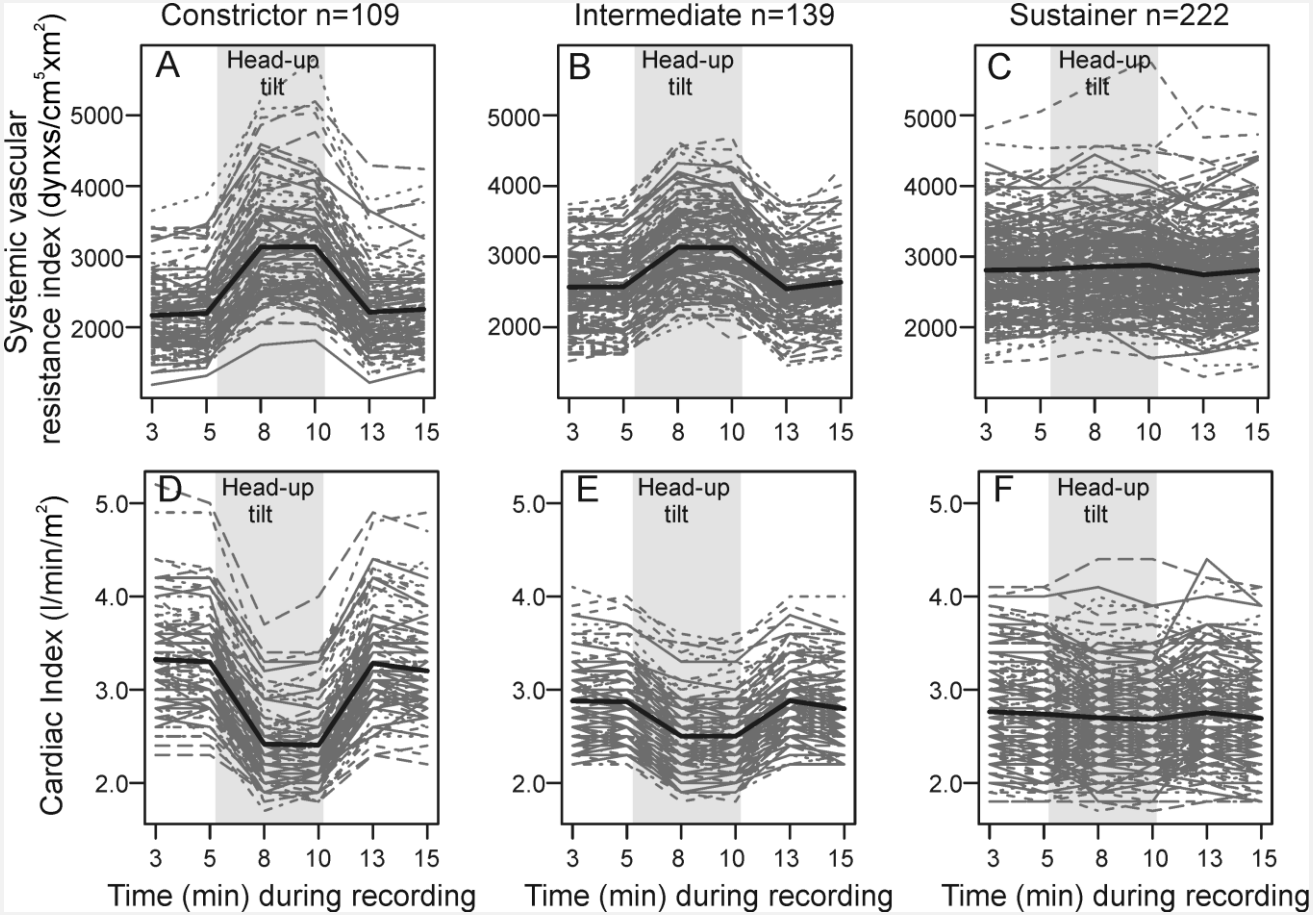


- 470 subjects
- Based on supine-to-upright changes in systemic vascular resistance (SVR) and cardiac output (CO), clustering to three phenotypes.

- Why these variables: SVR and CO are the principal determinants of blood pressure.

Tahvanainen et al. *BMC Cardiovascular Disorders* 2016, 16:101.

Cardiovascular response to upright posture: clustering to three phenotypes



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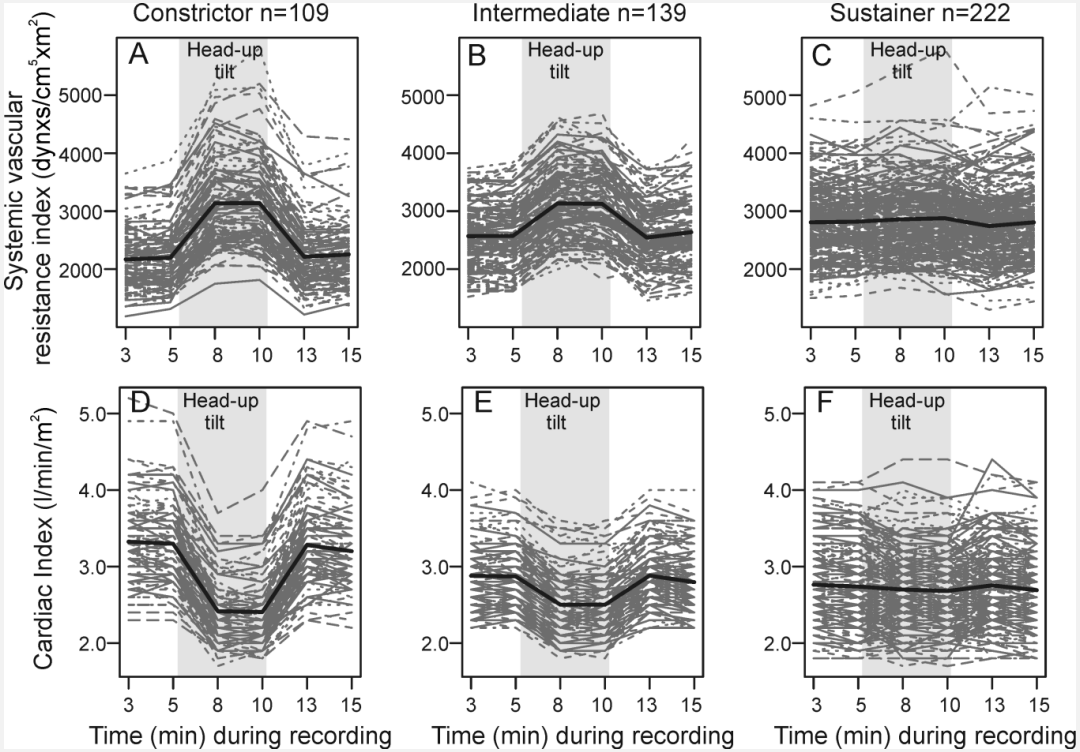
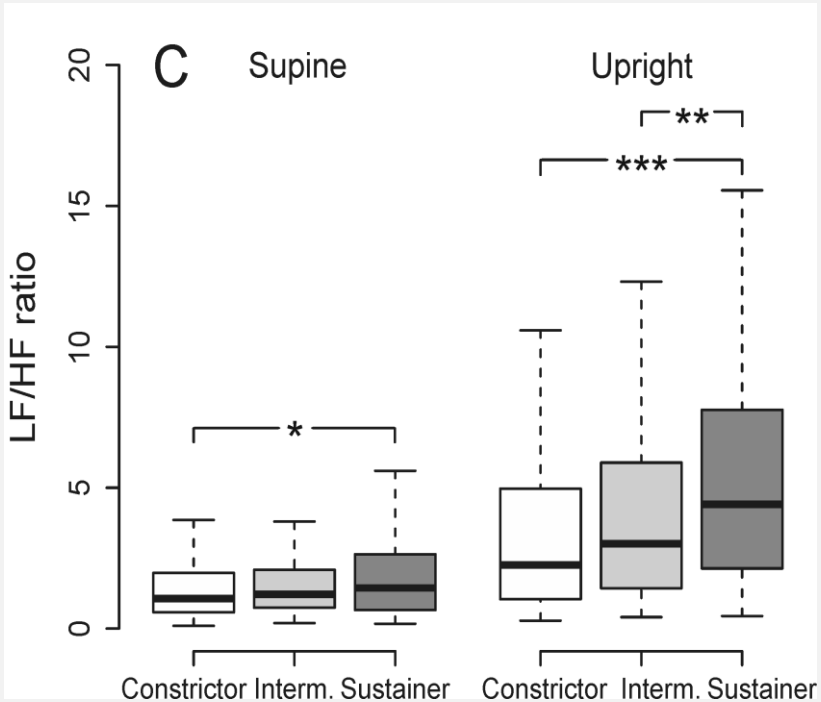
Sustainer phenotype: highest cardiac sympathovagal balance

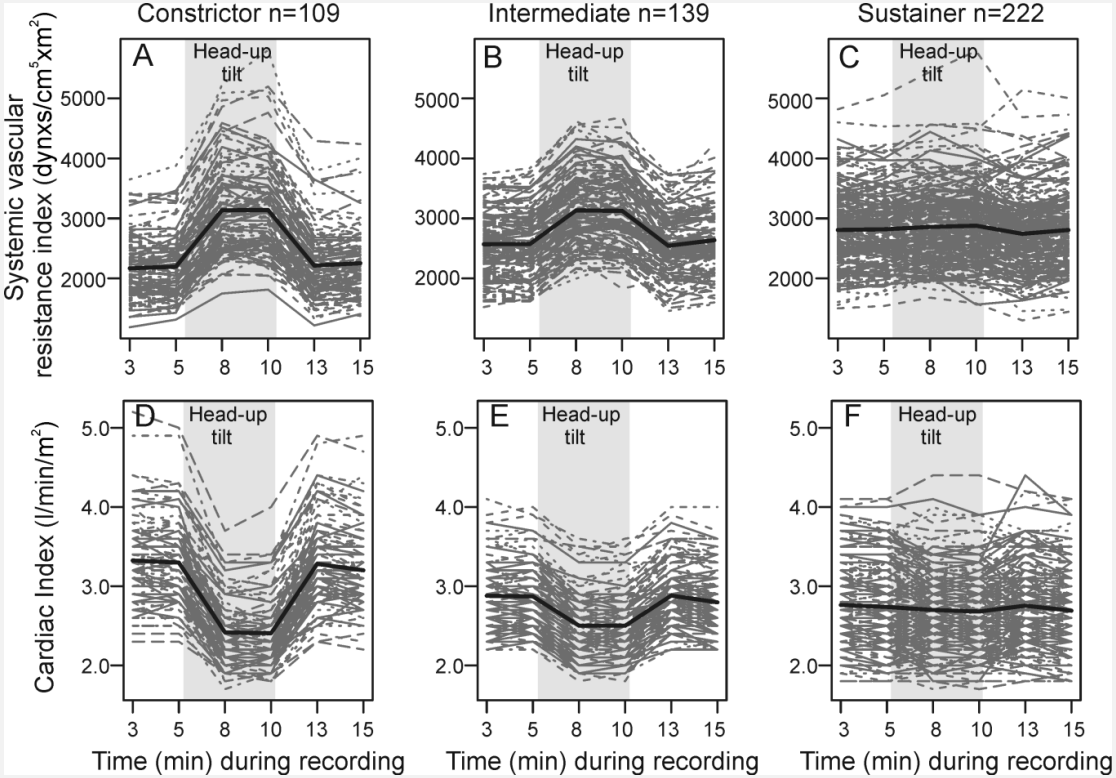


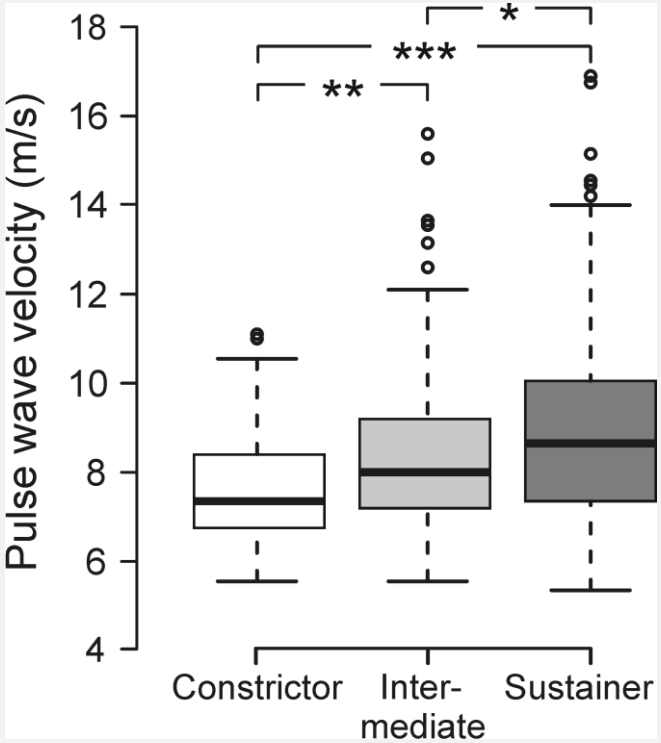


- "Sustainer" phenotype:
  - Lowest upright heart rate variability in HF power (lowest cardiac parasympathetic tone)
  - Increased supine and upright LF/HF ratio (sympathovagal balance)

Tahvanainen et al. BMC Cardiovascular Disorders 2016, 16:101.

Cardiovascular response to upright posture: associated with arterial stiffness

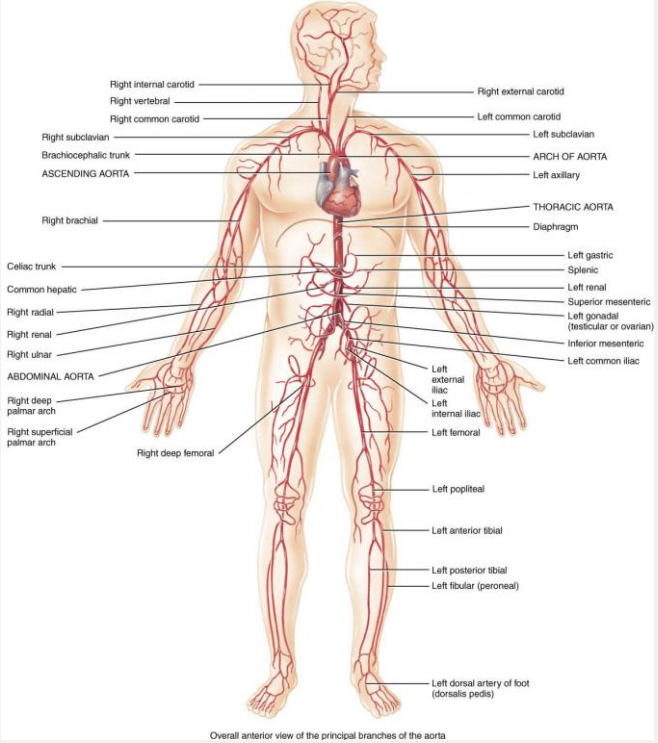




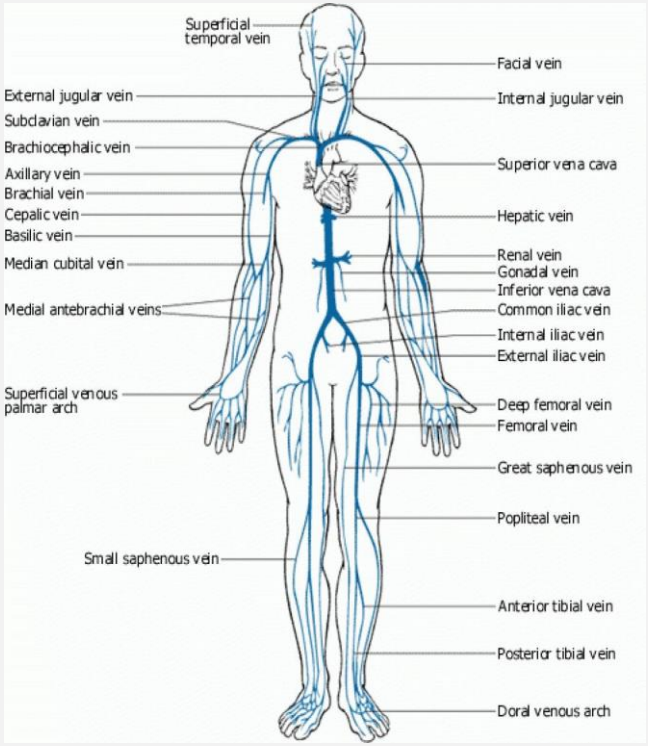
- In multivariate analysis, sustainer cluster, age, BMI and higher BP were explanatory factors for higher arterial stiffness

Tahvanainen et al. *BMC Cardiovascular Disorders* 2016, 16:101.

The arterial system is complex and blood flow is pulsatile



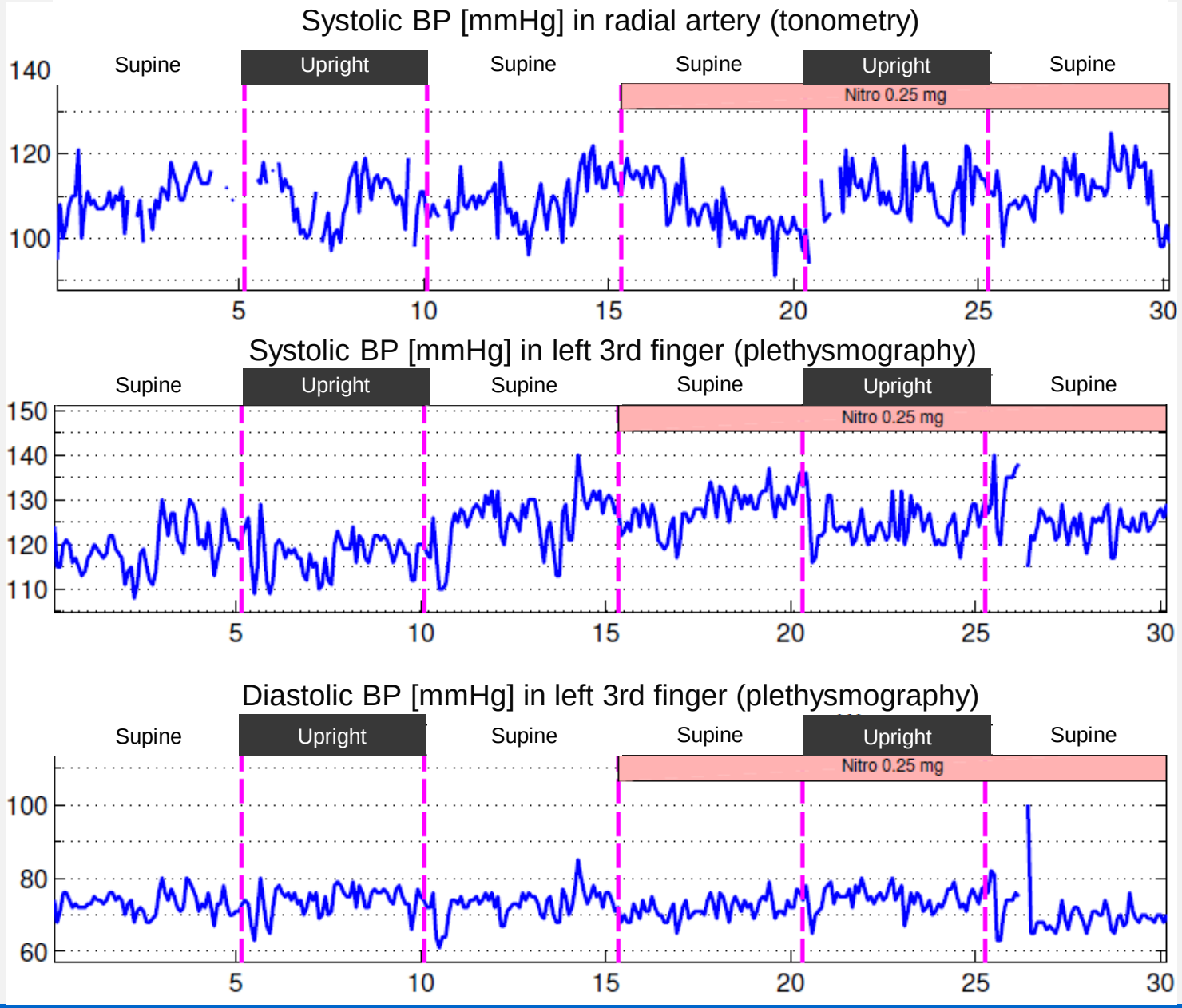
Overall anterior view of the principal branches of the aorta



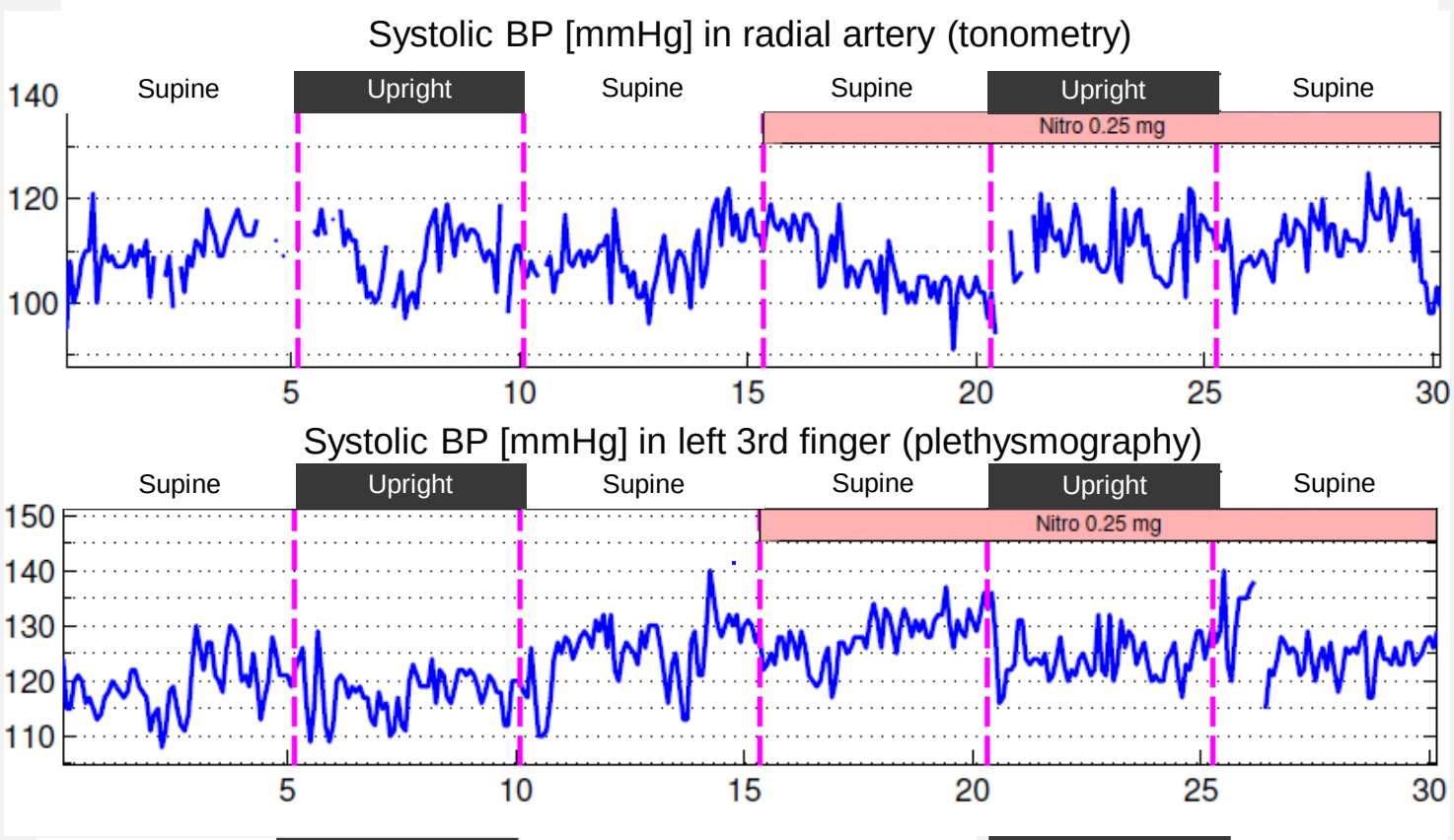
- A cohort of 92457 adults: mean resting heart rate is 65/min
- If 65/min is the mean heart rate for 24 hours, there are ~93600 systolic and diastolic blood pressure values within one day

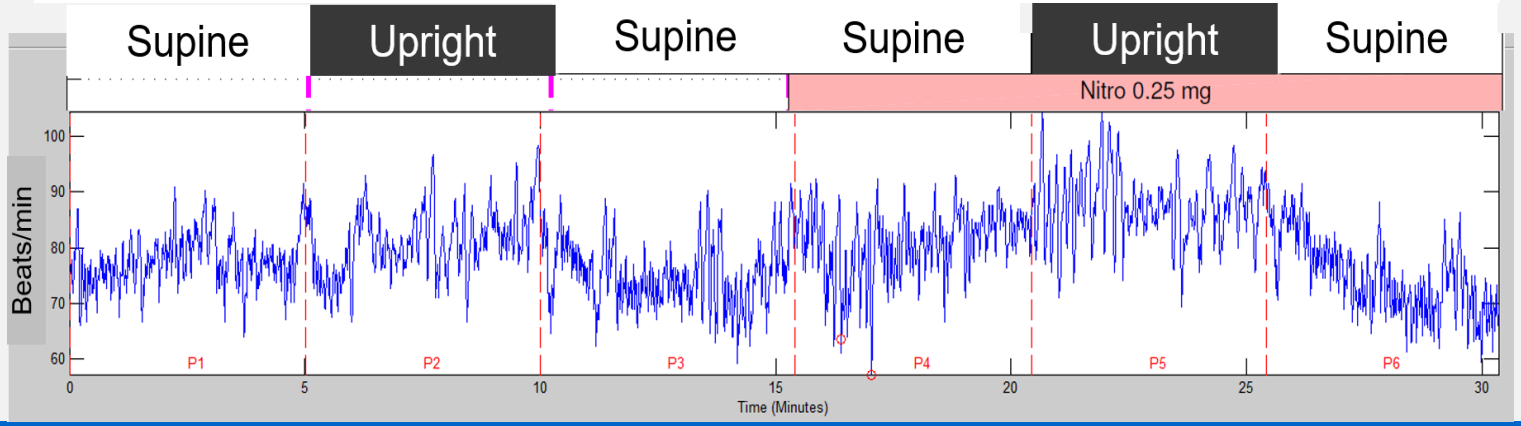
Quer et al. *PLoS ONE* 2020; 15(2): e0227709.

Blood pressure in a 26-year-old woman



BP and heart rate in a 26-year-old woman





May Measurement Month 2018

- 1 504 963 individuals were screened in 89 countries
  - Mean age 45.3 years; 52.4% female
- Hypertension: SBP > 140 mmHg or DBP > 90 mmHg, or taking antihypertensive medication
- 33.4% of the individuals had hypertension
  - 59.5% were aware of their diagnosis
  - 55.3% were taking antihypertensive medication
- Hypertensive subjects
  - Of those on medication, 60.0% were controlled
  - Of all hypertensives, 33.2% were controlled

Beaney et al. *European Heart Journal* (2019) doi:10.1093/eurheartj/ehz300.

Hypertension is still a problem

- The methods to measure blood pressure are not optimal
- Low BP targets in CKD seem warranted and rational
  - Individual tailoring of treatment based on common sense is essential
  - BP measurement in the upright position provides relevant information
- CKD is associated with premature vascular ageing and hypertension is a major factor contributing to this process
  - Uncontrolled hypertension increases cardiovascular morbidity and mortality and accelerates progression to ESRD
- Intensive BP control reduces the risk for adverse cardiovascular outcomes and mortality in CKD
  - Adverse effects should be closely monitored and concurrent medical conditions taken carefully into account