



SFKF

Lunchwebinar  
6 December 2022



# NYHETER OM HYPERTONI OCH VASKULÄRT ÅLDRANDE

Peter M Nilsson, MD, PhD, Professor  
Klinisk Forskningsenhet, VO Internmedicin  
Ints. Kliniska vetenskaper, LU, SUS Malmö

# Disposition

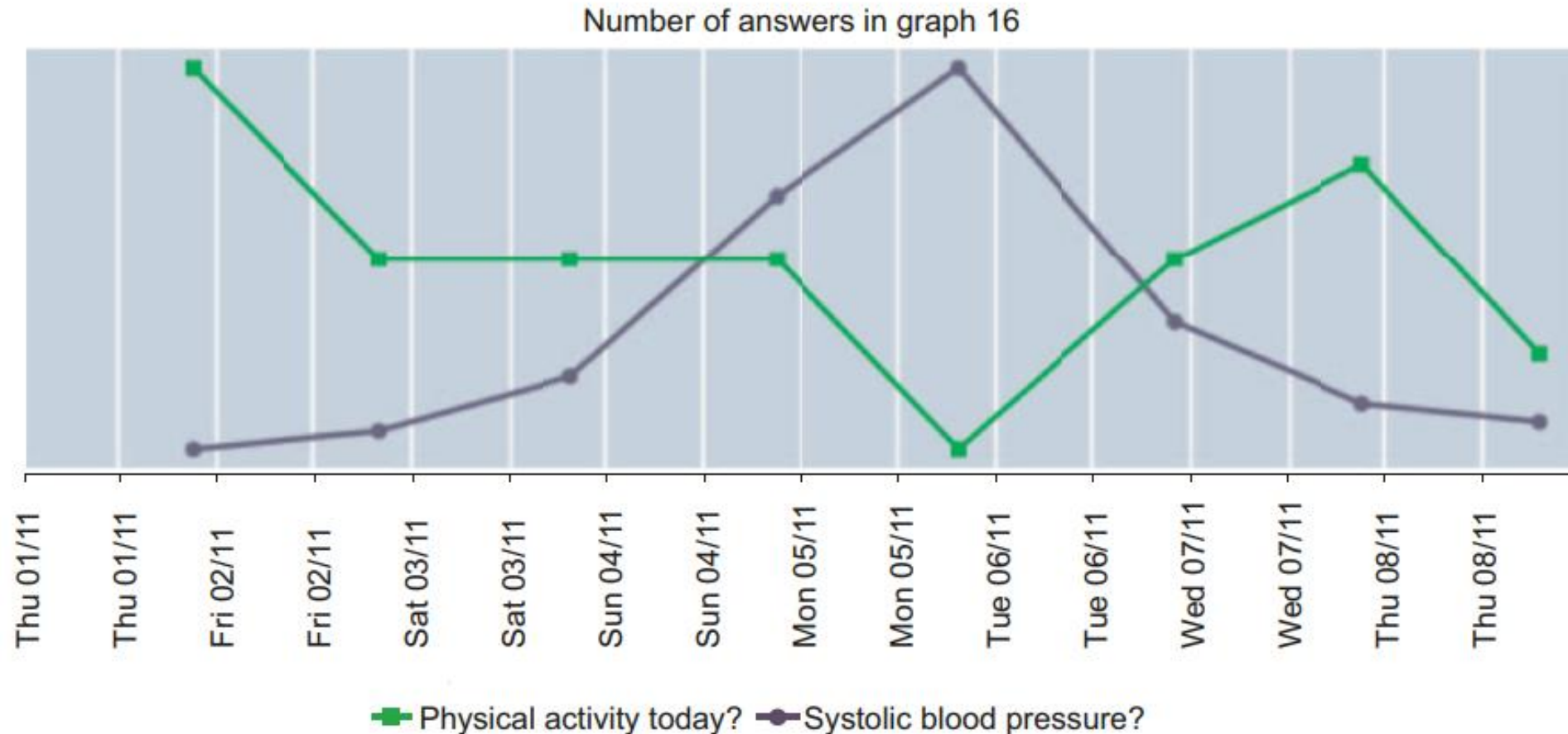
- Nyheter om hypertoni och tidpunkt för medicinering
- Nyheter om vaskulärt åldrande, artärstyvhet (PWV)
- Programmering tidigt i livet för kardiovaskulär hälsa

# PERHIT Study. Recruitment of treated HT patients from Swedish PHC.

## Home-BP measurements and registration of activities

**Combination graph (click "Change displayed questions" to choose questions)**

Change displayed questions



PERHIT

# PERson-centredness in Hypertension management using Information Technology: a randomized controlled trial in primary care



Ulrika Andersson  
Lunds universitet

	Visit	Intervention [n (%)]	Control [n (%)]	P value
BP <140/90 mmHg	Baseline	171/482 (35.5)	165/467 (35.3)	0.963
	8 weeks	226/463 (48.8)	181/454 (39.9)	<b>0.006</b>
	12 months	208/442 (47.1)	172/420 (41.0)	0.071
SBP <140 mmHg	Baseline	191/482 (39.6)	182/467 (39.0)	0.837
	8 weeks	254/463 (54.9)	198/454 (43.6)	<b>&lt;0.001</b>
	12 months	225/442 (50.9)	195/420 (46.4)	0.189
DBP <90 mmHg	Baseline	331/482 (68.7)	299/467 (64.0)	0.130
	8 weeks	331/463 (71.5)	314/454 (69.2)	0.440
	12 months	325/442 (73.5)	299/420 (71.2)	0.443

BP, blood pressure. Bold text indicates significant *P*-values.

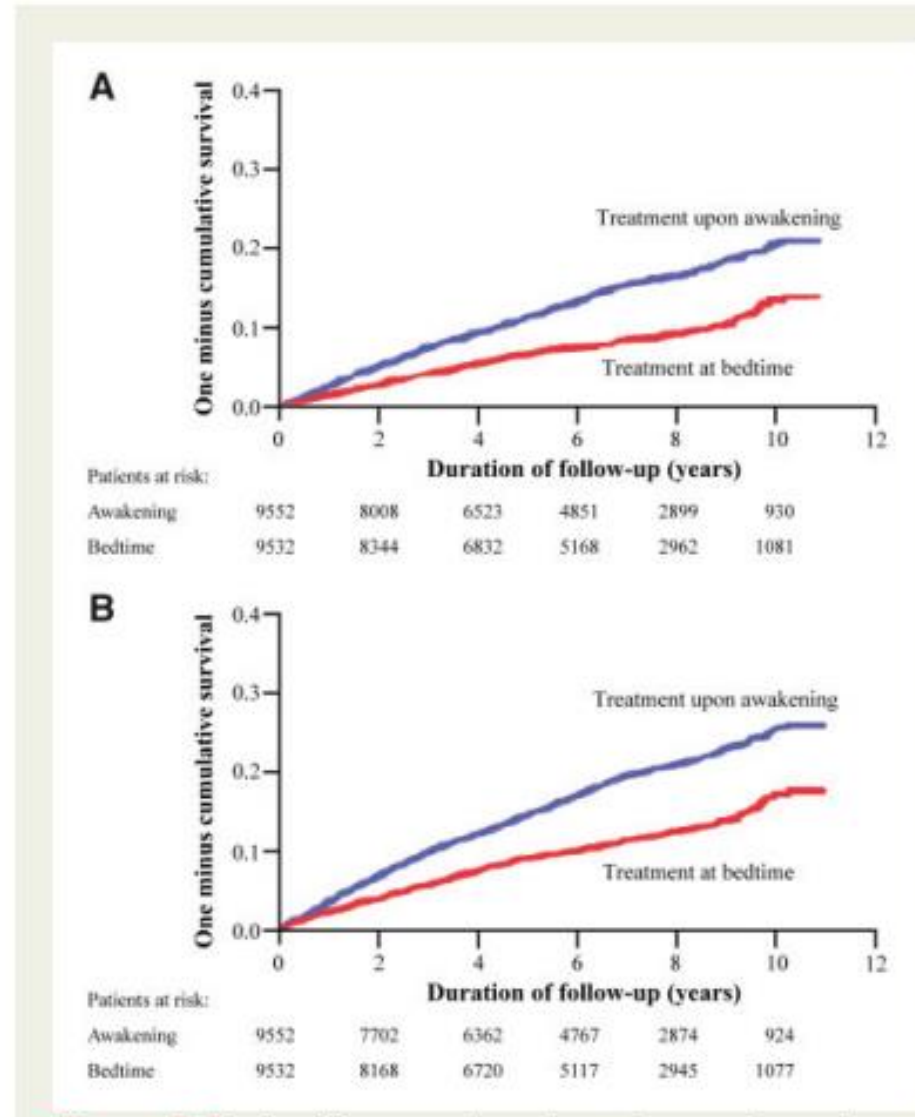
A total of **862** HT patients from PHC completed the trial, **442 in the intervention group** and **420 in the control group**. The primary outcome (BP <140/90 mmHg) at 8 weeks was achieved by 48.8% in the intervention group and 39.9% in the control group ( $P < 0.006$ ).

# Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial

Cardiovascular disease outcome as a function of hypertension treatment-time regimen (either upon **awakening** or at **bedtime**).

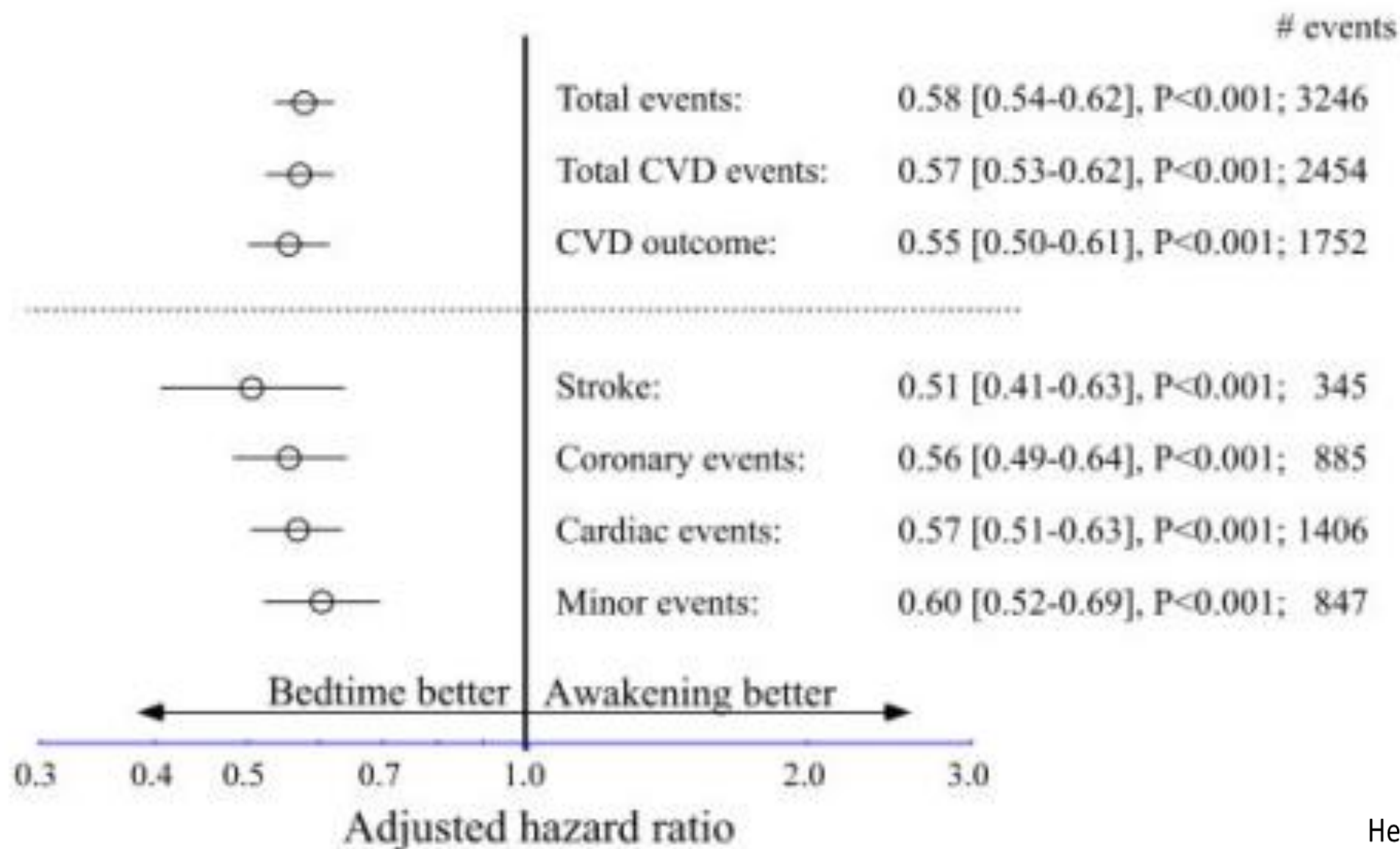
(A) Cardiovascular disease outcome: composite of cardiovascular disease death, myocardial infarction, coronary revascularization, heart failure, and stroke; log-rank: 140.1,  $P < 0.001$ .

(B) Total cardiovascular disease events: composite of cardiovascular disease death, myocardial infarction, coronary revascularization, heart failure, stroke, angina pectoris, peripheral artery disease, and transient ischaemic attack; log-rank: 174.0,  $P < 0.001$



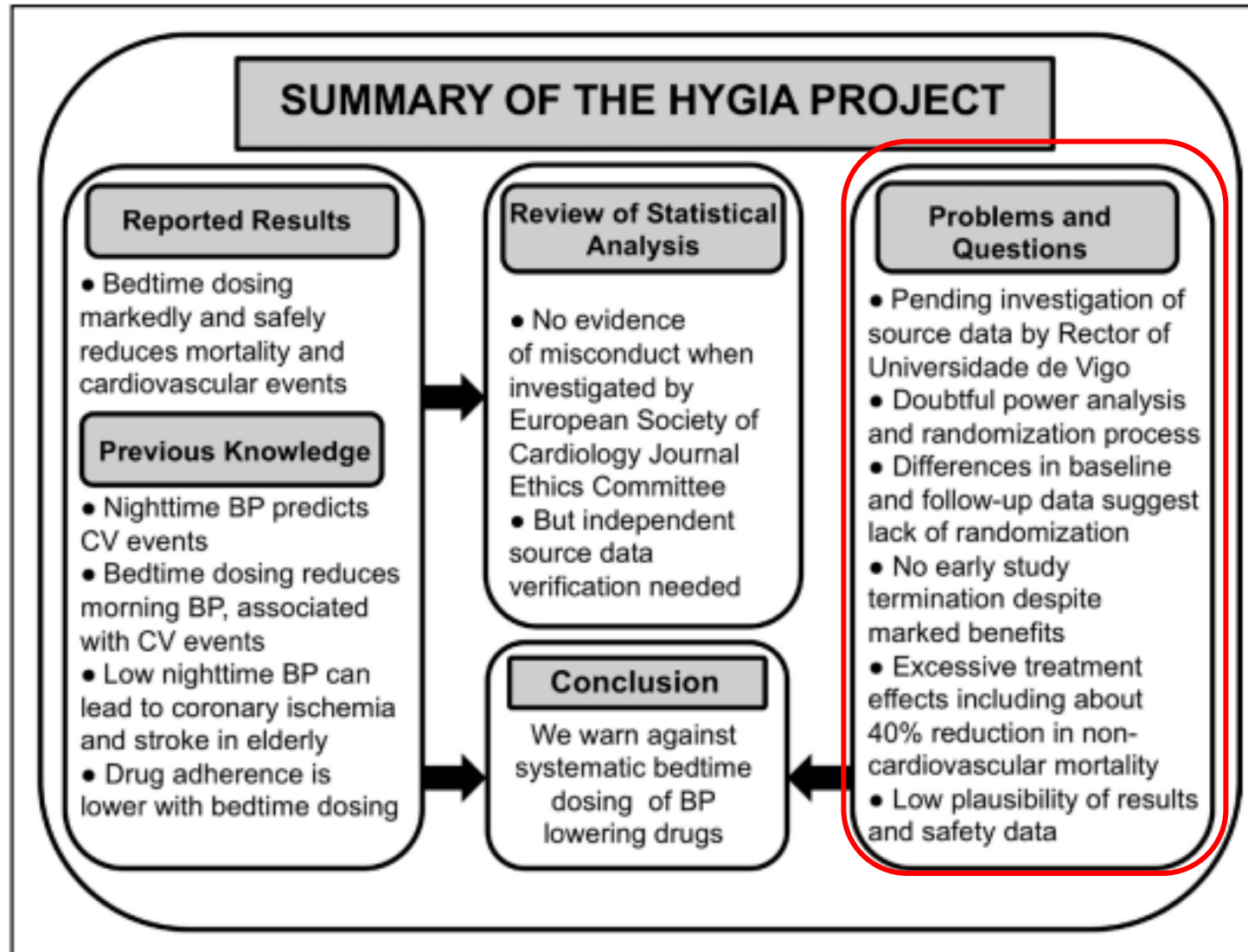
Ramon Hermida  
University of Vigo  
Spain

Hermida *et al*  
Eur Heart J 2020





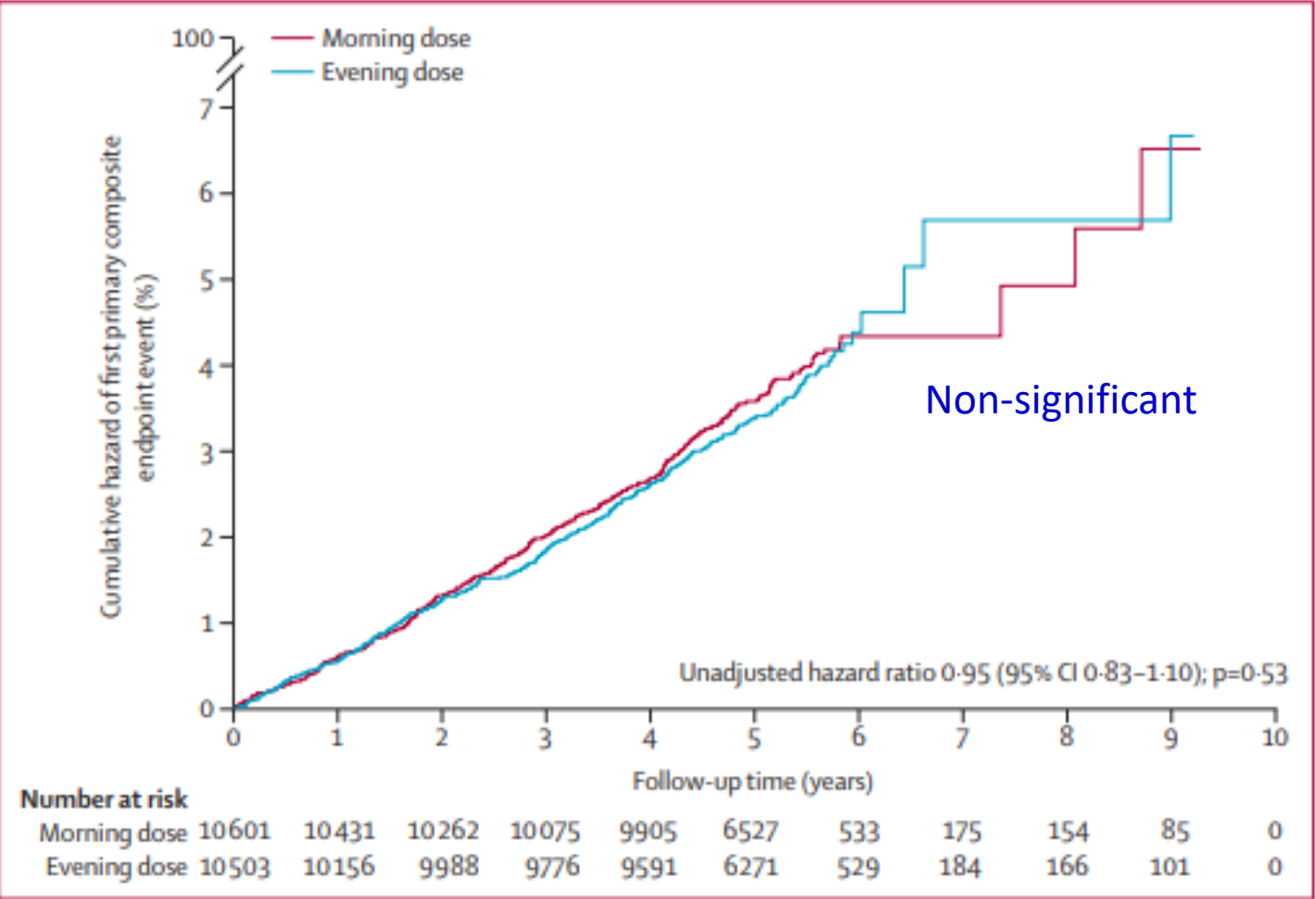
# Missing Verification of Source Data in Hypertension Research: The HYGIA PROJECT in Perspective



Mattias Brunström  
Umeå universitet



Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study): a prospective, randomised, open-label, blinded-endpoint clinical trial





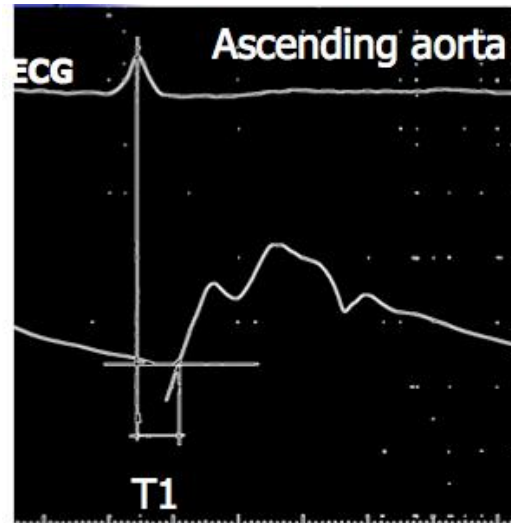
## TIME study: Adverse events

	Evening dosing group (n=9574)*	Morning dosing group (n=10 054)*	Between-group difference (95% CI)†
Dizziness or light-headedness	3511 (36.7%)	4007 (39.9%)	-3.2% (-4.6 to -1.8)
Excessive visits to the toilet during the day or night	3825 (40.0%)	3660 (36.4%)	3.6% (2.2 to 4.9)
Sleep problems	4017 (42.0%)	4125 (41.0%)	0.9% (-0.5 to 2.3)
Upset stomach or indigestion	2639 (27.6%)	3050 (30.3%)	-2.8% (-4.1 to -1.5)
Diarrhoea	1803 (18.8%)	2170 (21.6%)	-2.8% (-3.9 to -1.6)
Feeling generally less well	3079 (32.2%)	3311 (32.9%)	-0.8% (-2.1 to 0.6)
Muscle aches	3724 (38.9%)	4352 (43.3%)	-4.4% (-5.8 to -3.0)
Other (not specified)	2970 (31.0%)	2686 (26.7%)	4.3% (3.0 to 5.6)

Numbers reported are the number of participants who indicated that they had experienced each prespecified symptom. \*Number of participants who submitted at least one completed study follow-up form. †Difference in percentage: evening dosing group minus morning dosing group.

**Table 3: Prespecified adverse events (symptoms) in safety analysis population (n=19 628)**

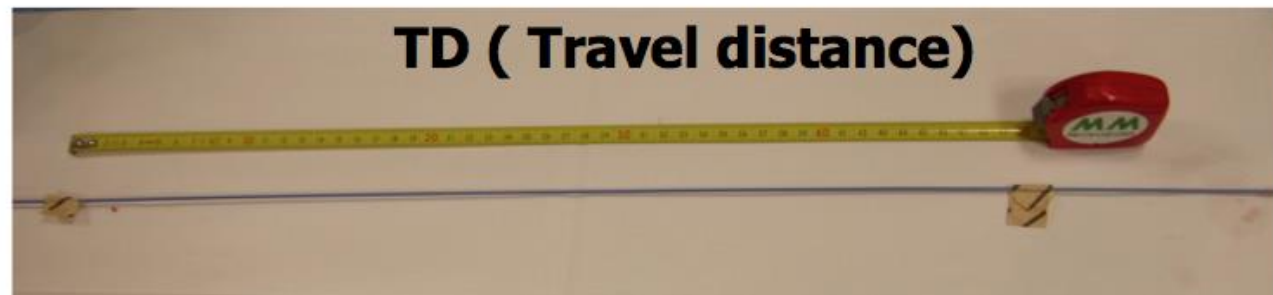
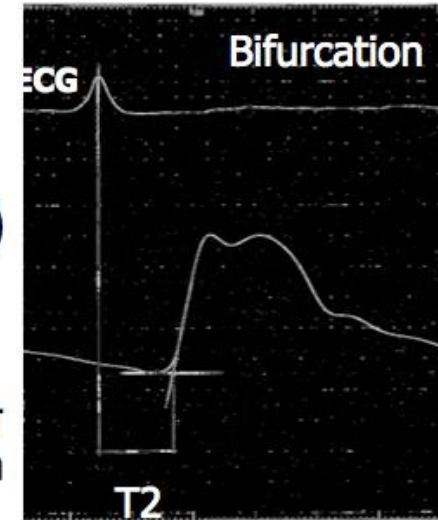
# The Gold standard for measuring arterial stiffness: **Aortic PWV**



$$\text{Velocity} = \text{TD} / \text{TT}$$

$$\text{TT (Travel time)} = \text{T2} - \text{T1}$$

intersecting tangents for footpoints determination



Between observer reproducibility: BlandAltman: Diff. 0.06 m/sec, 95% CI 0.82 / -0.69 m/sec Weber AJH 2007; 20:256  
Comparison between manual and computed TT measurement: 0.9 msec, SD 4.3 msec

# Carotid femoral (cf) PWV

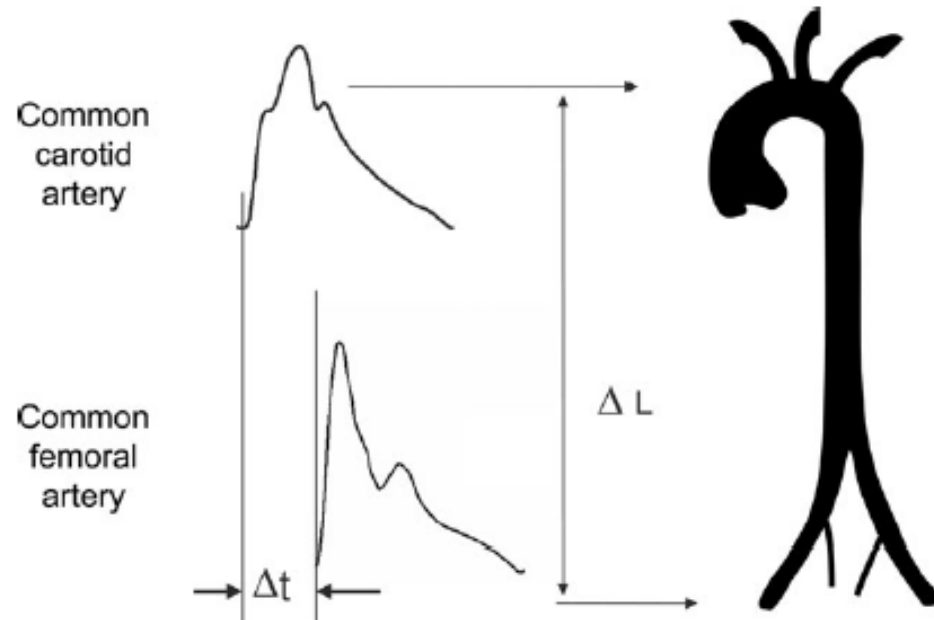


European Heart Journal (2006) 27, 2588–2605  
doi:10.1093/eurheartj/ehl254

Special article

## Expert consensus document on arterial stiffness: methodological issues and clinical applications

Stephane Laurent<sup>1\*</sup>, John Cockcroft<sup>2</sup>, Luc Van Bortel<sup>3</sup>, Pierre Boutouyrie<sup>1</sup>, Cristina Giannattasio<sup>4</sup>, Daniel Hayoz<sup>5</sup>, Bruno Pannier<sup>6</sup>, Charalambos Vlachopoulos<sup>7</sup>, Ian Wilkinson<sup>8</sup>, and Harry Struijker-Boudier<sup>9</sup> on behalf of the European Network for Non-invasive Investigation of Large Arteries

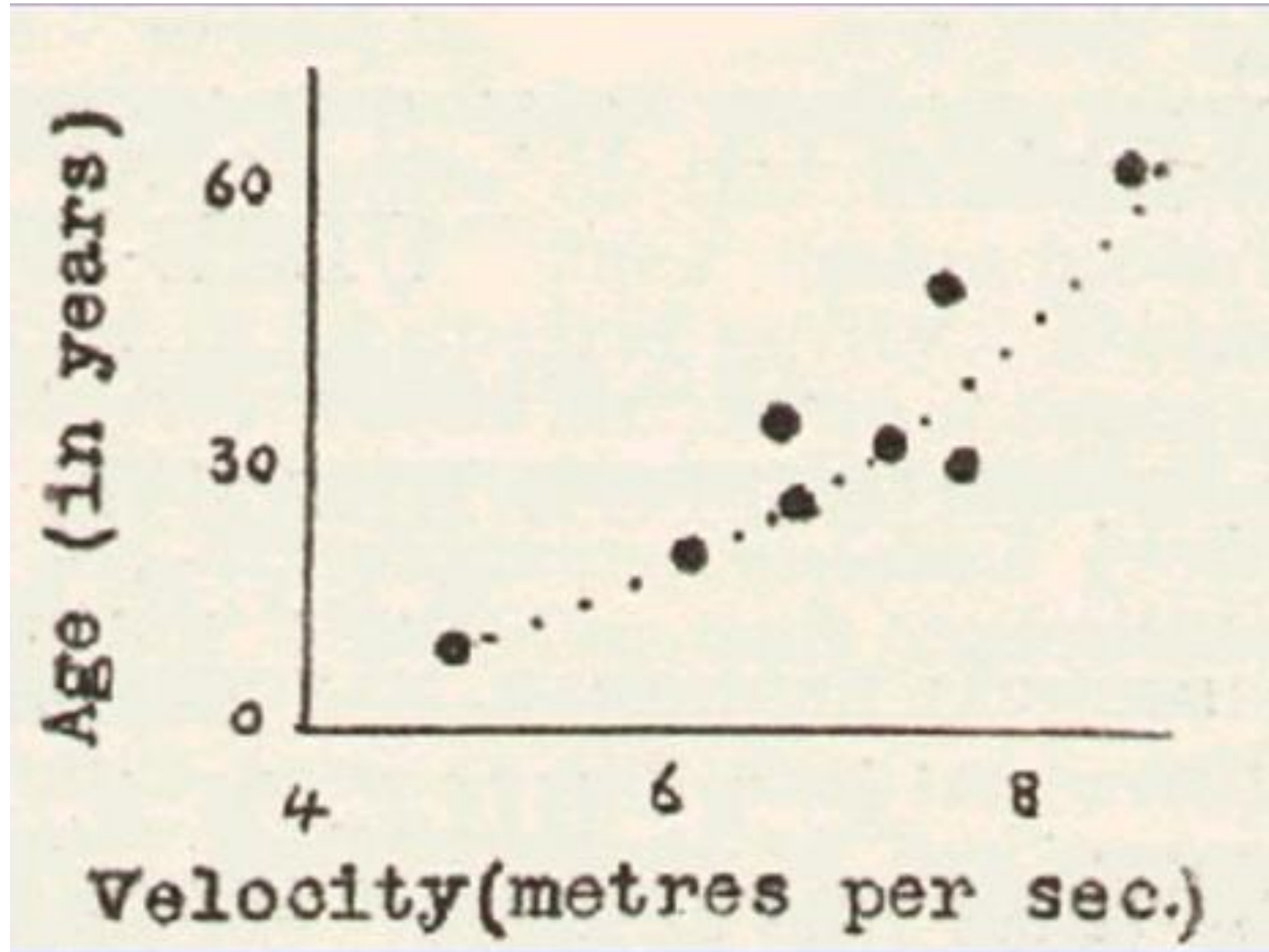


**Figure 1** Measurement of carotid-femoral PWV with the foot to foot method.



$$PWV = \sqrt{\frac{E_{inc} \cdot h}{2r\rho}}$$

Moens Korteweg equation



**Study Data**

Spi/Dp (Mp):

26 Jan 2015 13:48:30

125/73 (-)

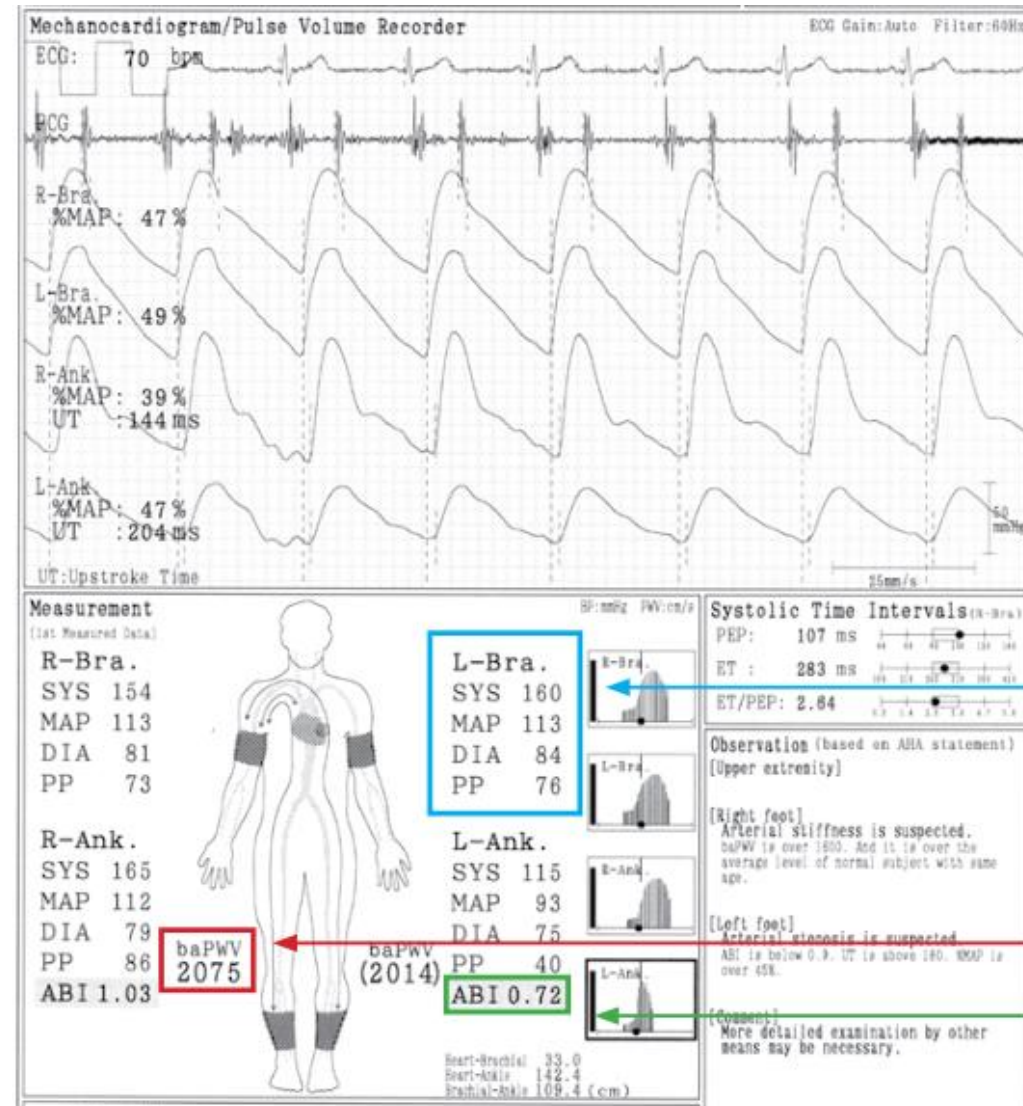
Distance: 450 mm

Algorithm: Intersecting tangent





# Brachial ankle PWV



# Large-Artery Stiffness in Health and Disease

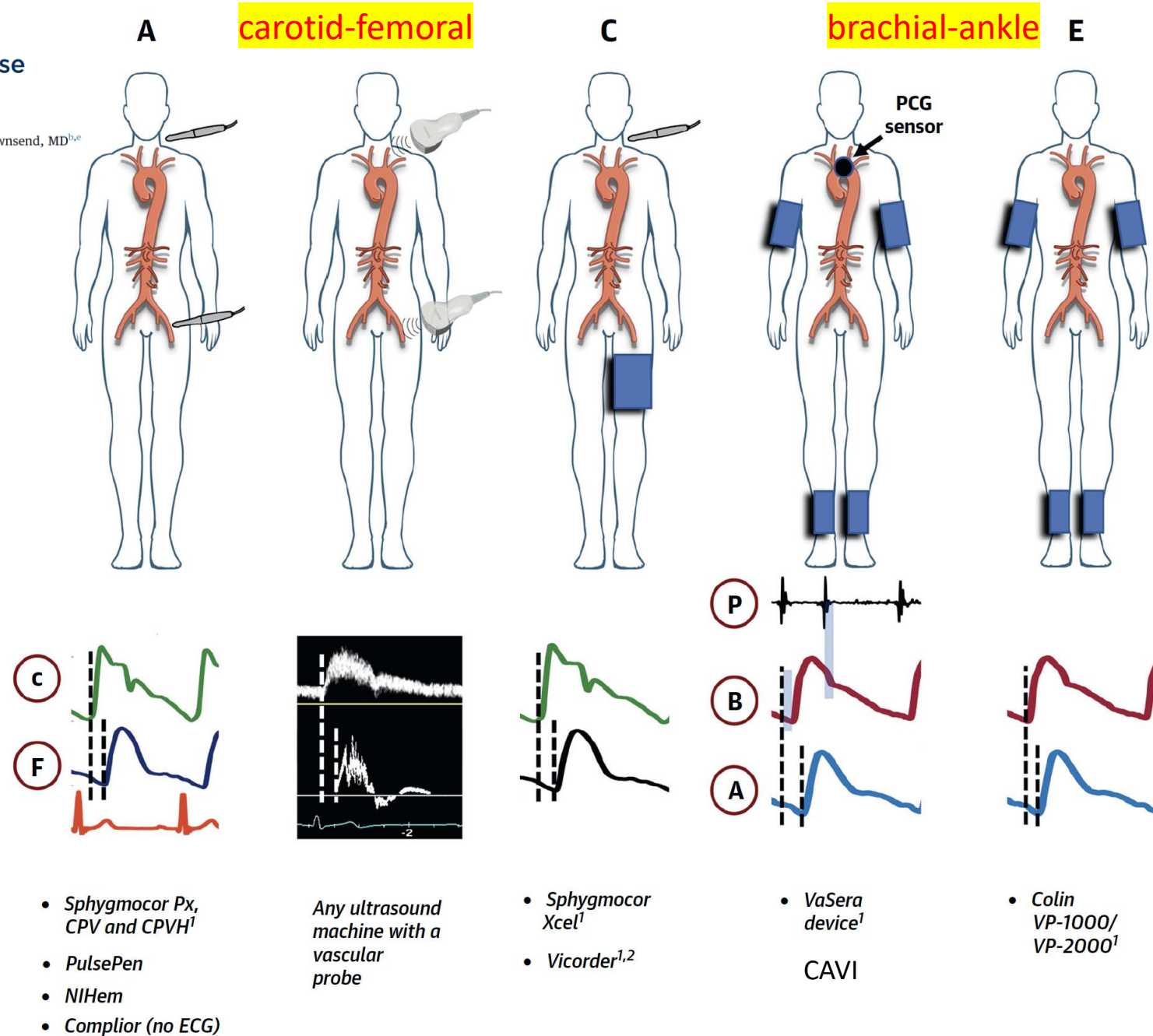
## JACC State-of-the-Art Review

Julio A. Chirinos, MD, PhD,<sup>a,b</sup> Patrick Segers, PhD,<sup>c</sup> Timothy Hughes, PhD,<sup>d</sup> Raymond Townsend, MD<sup>b,e</sup>

JACC VOL. 74, NO. 9, 2019

SEPTEMBER 3, 2019:1237-63

**FIGURE 10** Methods of Measurement of Carotid-Femoral PWV, CAVI, and ba-PWV by Various Devices





**Stéphane LAURENT,  
MD, PhD, FESC**

Emeritus Professor of  
Pharmacology at Paris  
University  
Paris Cardiovascular  
Research Center  
(P.A.R.C.C.) INSERM  
U970

# The SPARTE study 2011-2021

Strategy for **P**reventing cardiovascular complications  
based on **ARTE**rial stiffness

First randomized clinical trial aiming at  
demonstrating that arterial stiffness  
is a surrogate end-point

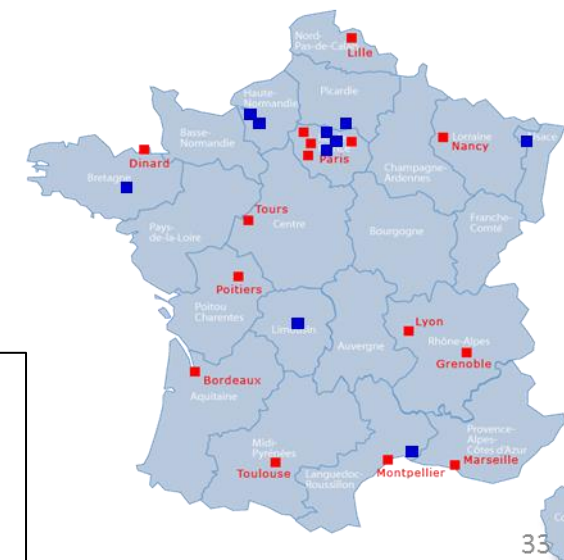
## Population

Hypertensive patients 55-75 yrs

Moderate to very high CV risk (fatal and non fatal CVD)



25 centers in France



# **SPARTE study: primary hypothesis**

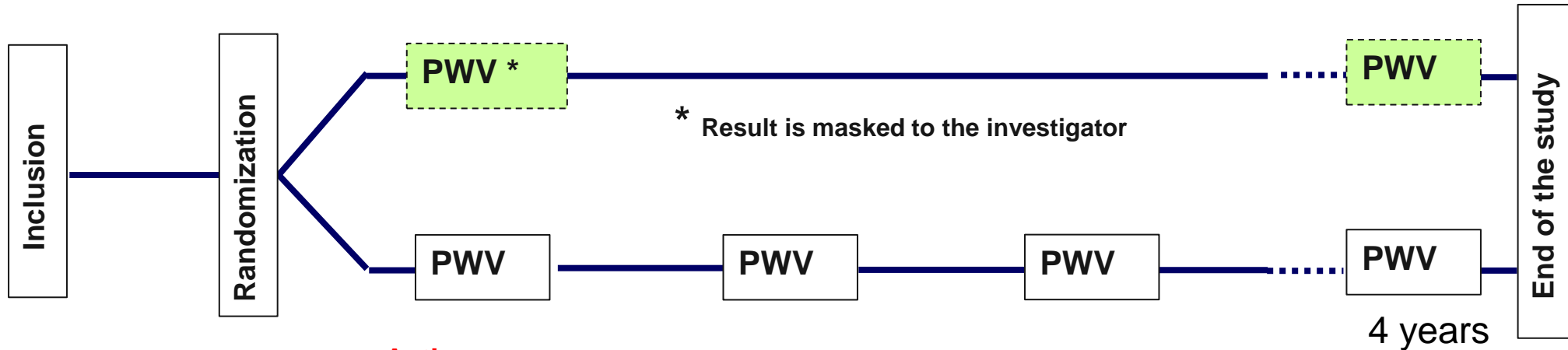
**Strategy for Preventing cardiovascular complications based on ARTERial stiffness**

A therapeutic strategy aiming at  
implementing the international guidelines  
+ normalising BP  
**+ normalising arterial stiffness**  
...reduces CV and renal events to a significantly greater extent  
than the sole implementation of international guidelines

# The SPARTE study: a PROBE design

Laurent et al. Hypertension 2012  
Laurent et al. Art Res 2020

Control group, PWV measured at M0, M24, and M48



## Active group

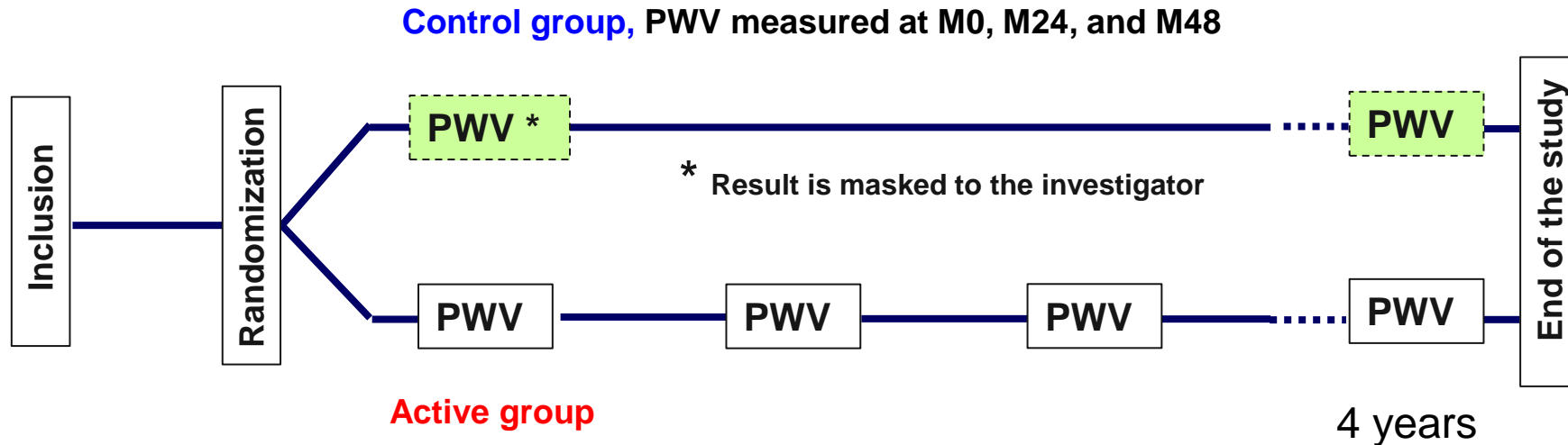
- PWV measured every 6 months
- Objective: PWV < 10 m/s

Blinded endpoint: cardiovascular events



## The SPARTE study: a PROBE design

Laurent et al. Hypertension 2012  
Laurent et al. Art Res 2020



## Active group

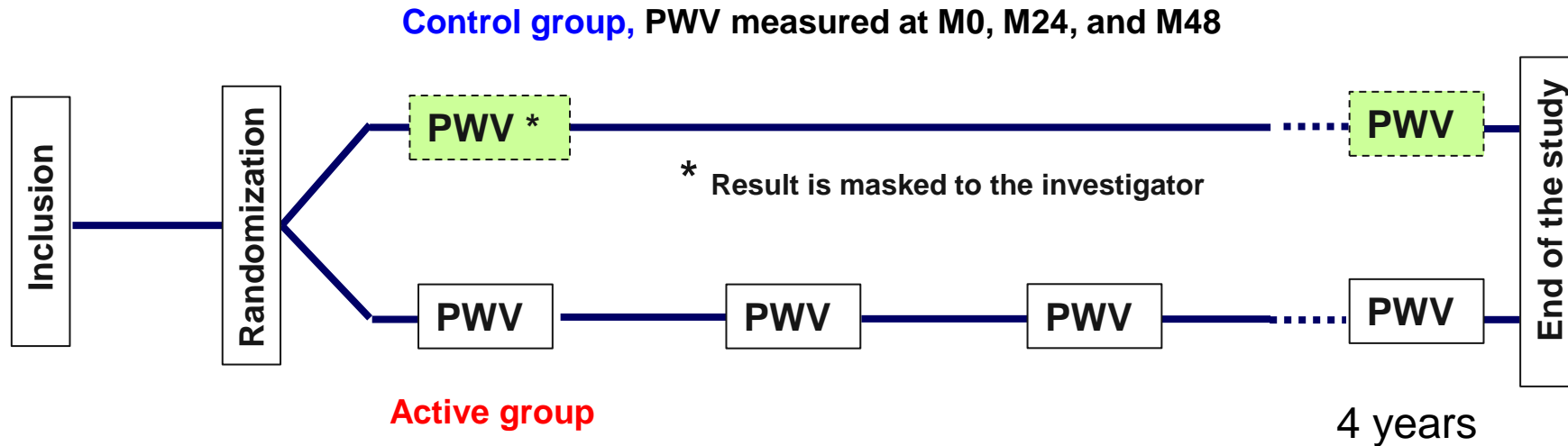
- PWV measured **every 6 months**
- Objective: PWV < 10 m/s
- **Specific therapeutic strategy**

- **High recommended dose of ACEI or ARB**
- **CCB + ARB or CCB + ACEI combinations**
- **Triple combinations RASI + CCB + DIU**
- **Aldosterone antagonists**
- **Vasodilating BB**

Blinded endpoint: cardiovascular events

# The SPARTE study: a PROBE design

Laurent et al. Hypertension 2012  
Laurent et al. Art Res 2020



## Active group

- PWV measured every 6 months
- Objective: PWV < 10 m/s
- Specific therapeutic strategy
- **ABPM at M0, M6 and M48**

Blinded endpoint: cardiovascular events

## The SPARTE study: number of patients to be included

**Selected population:** moderate to very high CV risk (fatal and non fatal CVD) > 20% at 10 years

### Combined end-point

Stroke + CHD (MI, PCI, CABG) + PAD (PCI, bypass surgery, amputation) + CHF hospitalization  
+ aortic dissection + doubling of serum creatinine + dialysis + sudden death

### Incidence of combined CV events

10% per year

### Effect of the therapeutic strategy

20% reduction in the active group

**Duration of the study:** 4 years

**Nb of patients:** 750 patients per group

Nb of composite events during 4 years follow-up.					
	Events			Risk	
nb per group	Control	Active	$\Delta$ (Co-Ac)	Power	Alpha
250	100	80	20	0.46	0.05
500	200	160	40	0.75	0.05
<b>750</b>	<b>300</b>	<b>240</b>	<b>60</b>	<b>0.90</b>	<b>0.05</b>
1000	400	320	80	0.96	0.05
1250	500	400	100	0.98	0.05
1500	600	480	120	0.99	0.05

 OPEN ACCESS

RESEARCH ARTICLE

 PDF/EPUB

**ORIGINAL ARTICLE**

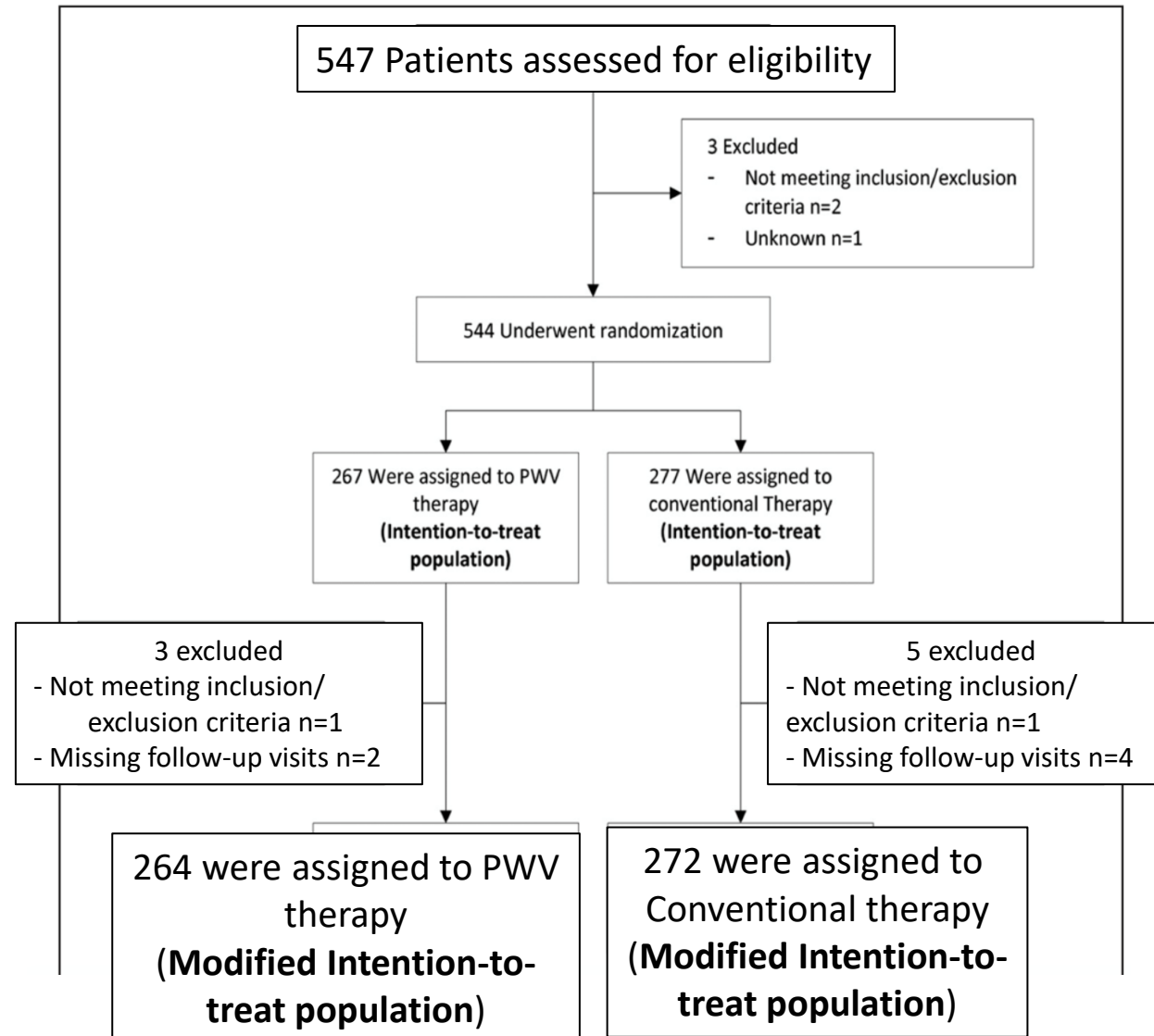
Laurent et al. *Hypertension* 2021; 78:983-995

# SPARTE Study

## Normalization of Arterial Stiffness and Cardiovascular Events in Patients With Hypertension at Medium to Very High Risk

Stephane Laurent<sup>ID</sup>, Gilles Chatellier, Michel Azizi, David Calvet, Gabriel Choukroun, Nicolas Danchin, Pascal Delsart, Xavier Girerd, Philippe Gosse<sup>ID</sup>, Hakim Khettab<sup>ID</sup>, Gerard London, Jean-Jacques Mourad<sup>ID</sup>, Bruno Pannier, Helena Pereira, Dominique Stephan, Paul Valensi<sup>ID</sup>, Pedro Cunha, Krzysztof Narkiewicz, Rosa-Maria Bruno<sup>ID</sup>, Pierre Boutouyrie, on behalf of SPARTE Investigators\*

# Flow chart





## Baseline characteristics

Characteristic	PWV group (n=264)	Conventional group (n=272)
Criterion for increased cardiovascular risk, n (%)		
Age, y	65.0 (6.0)	65.2 (5.5)
ESH-ESC cardiovascular risk		
Medium cardiovascular risk	34 (12.8%)	38 (14.0%)
High cardiovascular risk	157 (59.5%)	160 (58.8%)
Very high cardiovascular risk	73 (27.7%)	74 (27.2%)
Type 2 diabetes, n (%)	96 (36.4%)	102 (37.5%)
Dyslipidemia, n (%)	218 (82.9%)	224 (82.4%)
Cardiovascular disease, n (%)	66 (25.0%)	60 (22.1%)
Smokers, current (%)	26 (9.8%)	28 (10.5%)
Female sex, n (%)	102 (38.6%)	97 (35.7%)

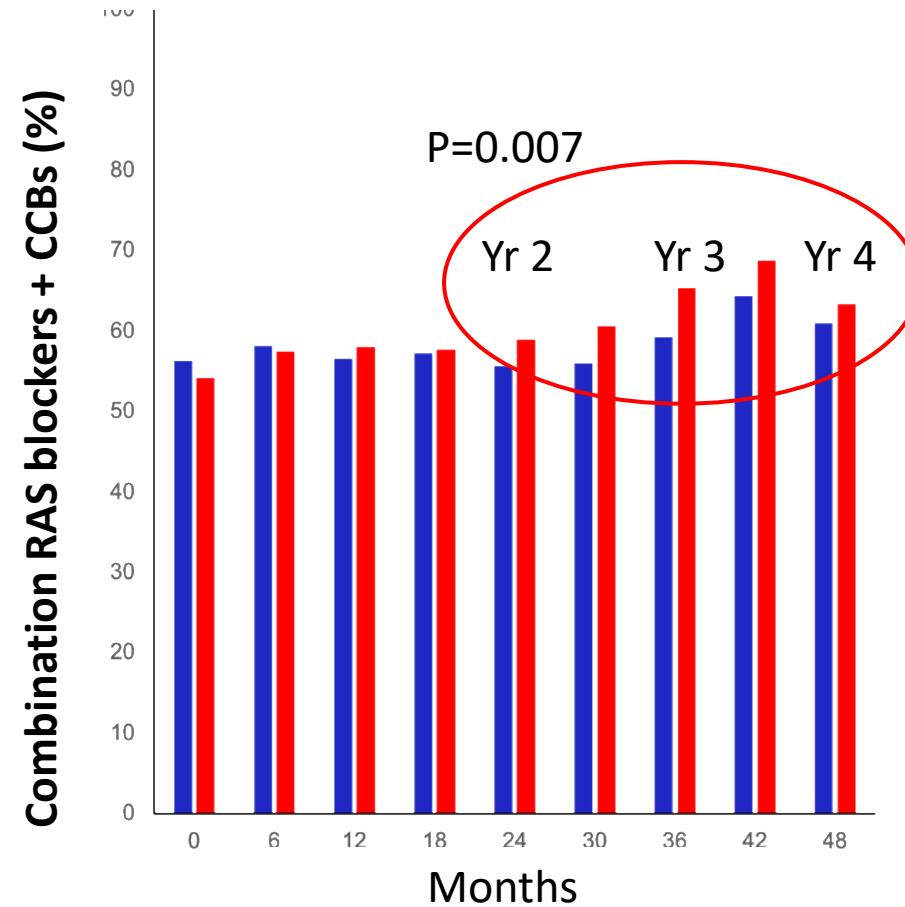
## Baseline characteristics

Characteristic	PWV group (n=264)	Conventional group (n=272)
Baseline office blood pressure		
Systolic, mm Hg	133.6 (17.1)	134.2 (15.5)
Diastolic, mm Hg	76.4 (10.4)	77.5 (10.4)
SBP <140 mmHg and DBP <90 mmHg, n (%)	177 (67.0%)	182 (67.2%)
Ambulatory blood pressure monitoring		
Day SBP, mm Hg	134.9 (12.8)	133.0 (11.5)
Day DBP, mm Hg	79.6 (9.1)	78.4 (8.5)
Pulse wave velocity, m/s	9.9 (2.3)	10.0 (2.5)
Pulse wave velocity >10 m/s, n (%)	107 (42.0%)	106 (41.4%)
Central blood pressure		
Central SBP, mm Hg	126.6 (16.2)	128.1 (16.4)
Central DBP, mm Hg	77.6 (11.2)	78.0 (10.3)
Central PP, mm Hg	49.4 (12.5)	50.1 (13.4)

## Baseline characteristics

Characteristic	PWV group (n=264)	Conventional group (n=272)
Use of antihypertensive agents, n (%)	261 (99.6%)	270 (99.3%)
Use of diuretics, n (%)	144 (54.5%)	153 (56.3%)
Use of ACE inhibitor, n (%)	87 (33.0%)	89 (32.7%)
Use of ARB, n (%)	152 (57.6%)	153 (56.3%)
Use of CCB, n (%)	154 (58.3%)	171 (62.9%)
Use of betablockers, n (%)	84 (31.8%)	79 (29.0%)
Use of lipid-lowering agents, n (%)	189 (72.1%)	183 (67.3%)
Lipid-lowering agents, n/patient	1.1 (0.3)	1.1 (0.3)
Use of antidiabetic agents, n (%)	90 (34.4%)	99 (36.7%)
Antidiabetic agents, n/patient	1.9 (0.9)	1.8 (0.8)
Use of antiplatelet agents, n (%)	138 (53.3%)	134 (49.4%)

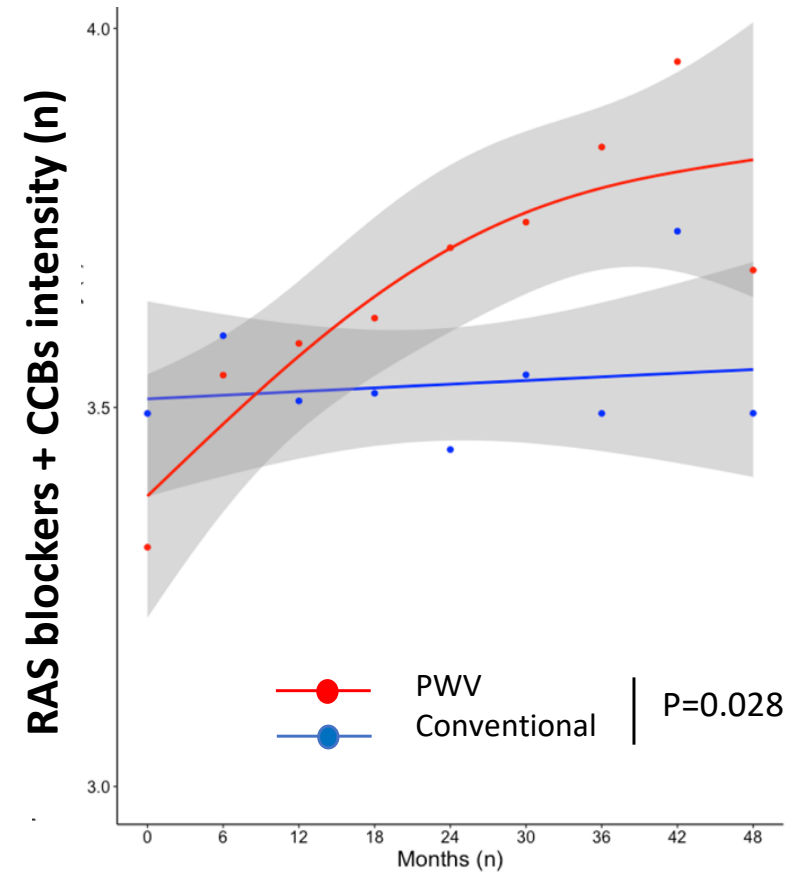
## More RASb + CCB combinations in the PWV group



■ Conventional ■ PWV-based

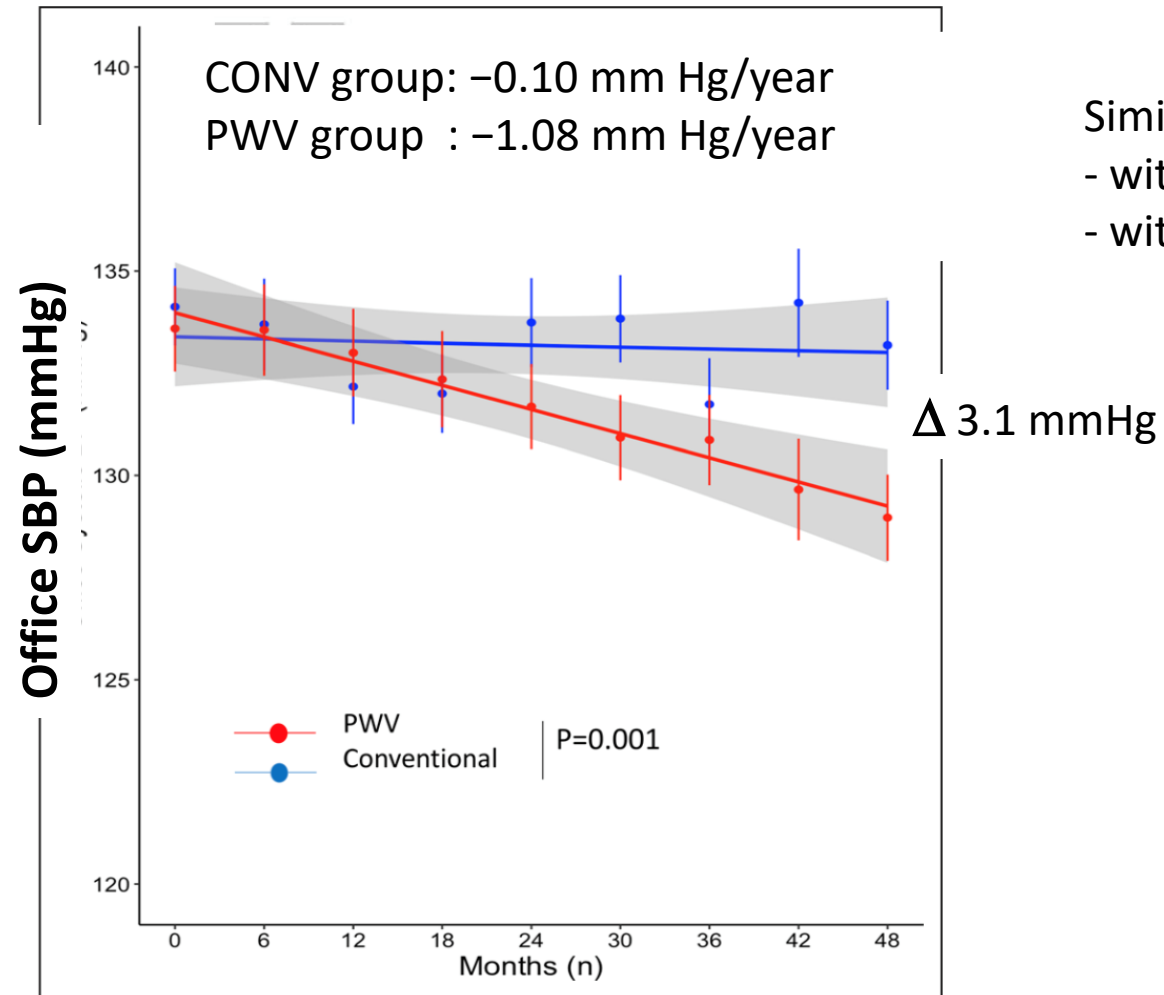
## Higher doses within the RASb + CCB combinations in the PWV group

Treatment intensity score was calculated by assigning to each administered drug a coefficient indicating the dosage (1=low, 2=average, 3=high).





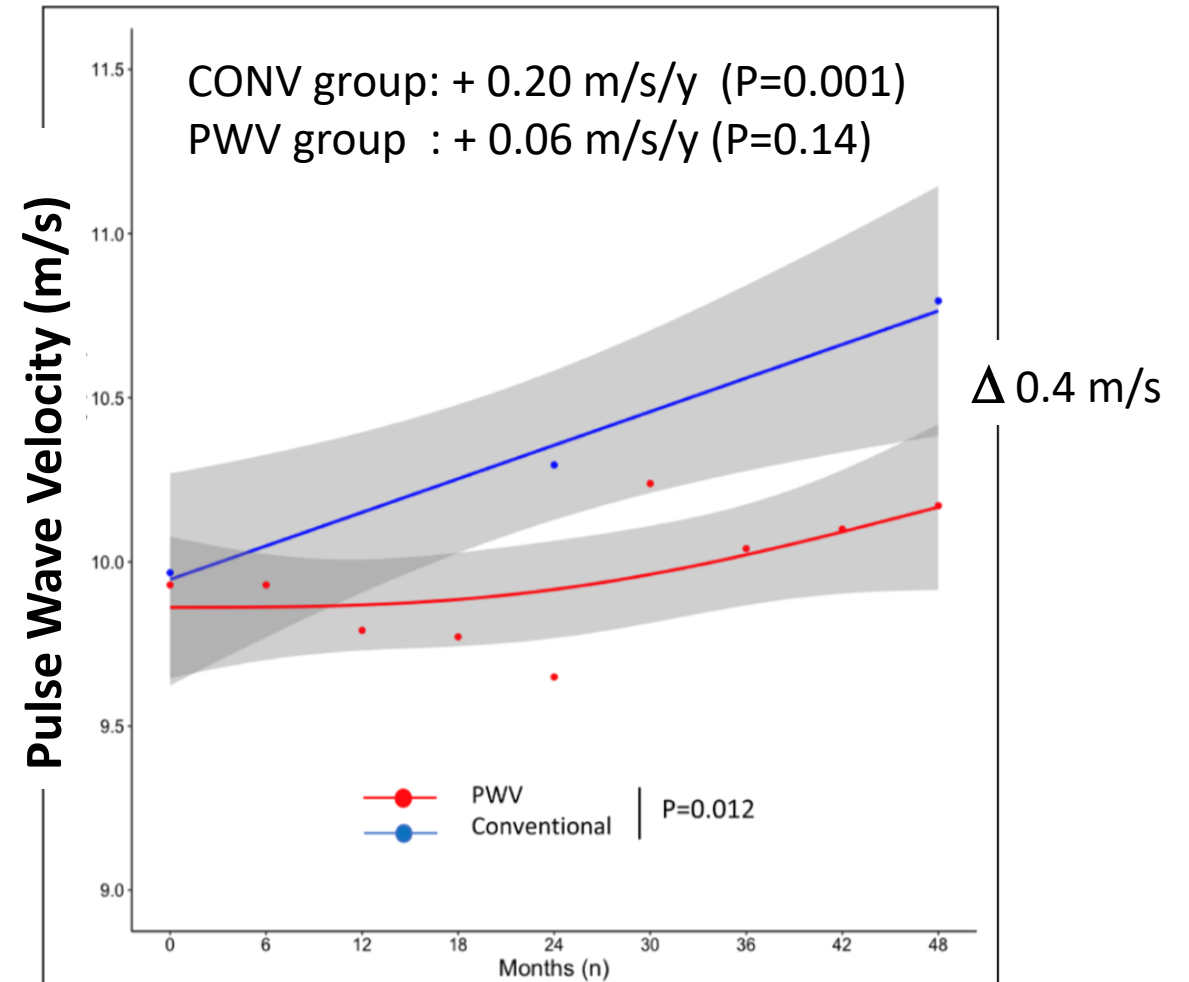
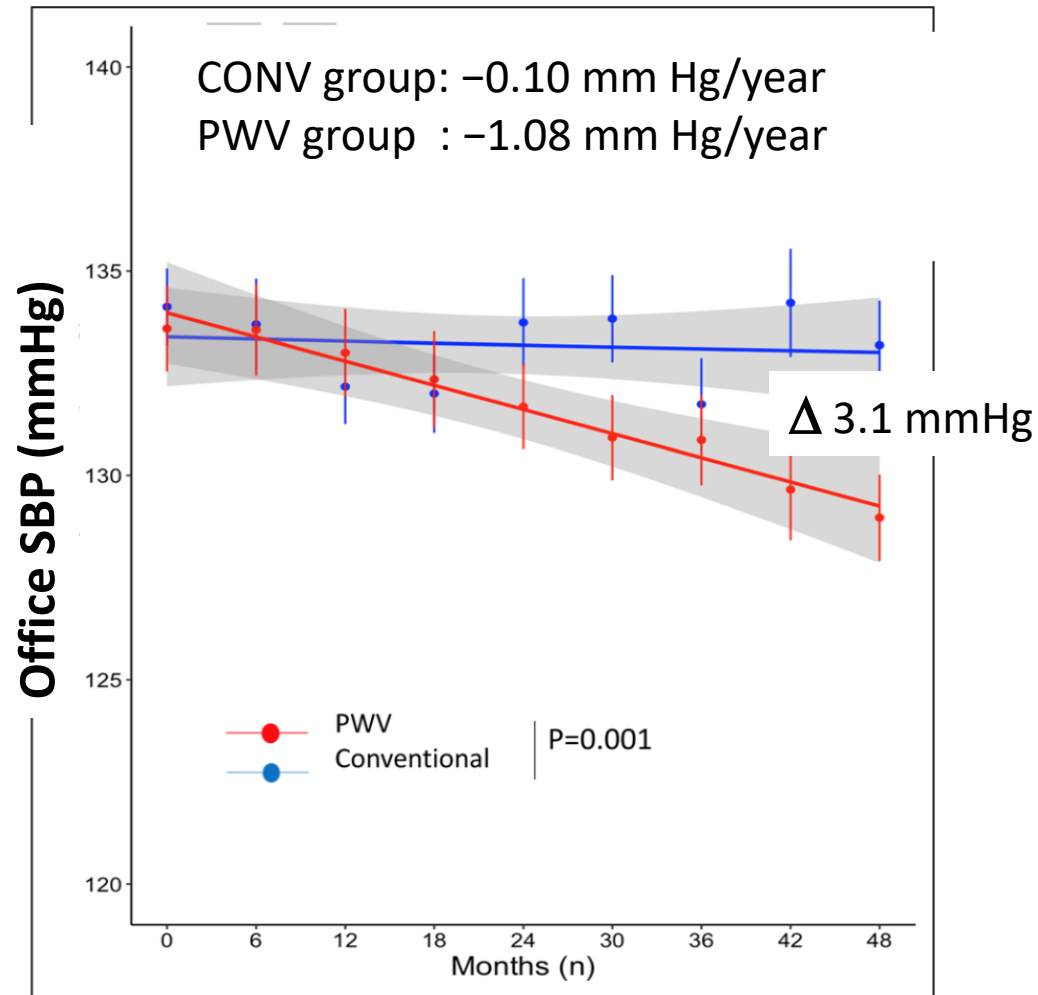
## Office BP was reduced to a greater extent in the PWV group...



Similar results

- with office DBP,
- with SBP and DBP at ABPM

## Office BP was reduced to a greater extent in the PWV group... ... and PWV did not raise



# Primary end-point: no significant difference between PWV and CONV groups

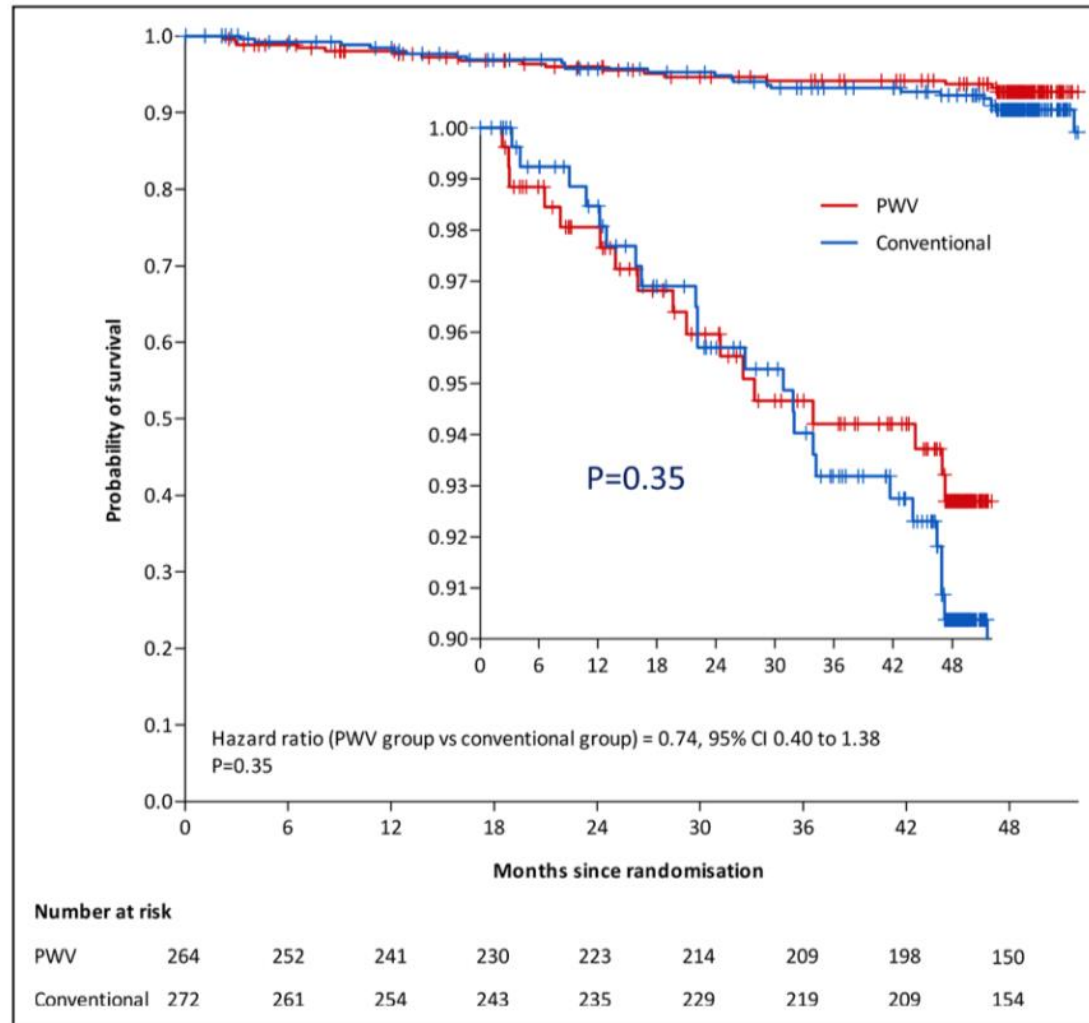
Stroke + CHD (MI, PCI, CABG)

+ PAD (PCI, bypass surgery, amputation)

+ CHF hospitalization + aortic dissection

+ doubling of serum creatinine

+ dialysis + sudden death



HR 0.74 (0.40-1.38)

$P=0.35$

PWV, n=17

CONV, n=24

## Discussion

- ❑ Lack of sufficient statistical power
  - 3 times less inclusion than initially planned
  - 2.5 to 5 times less yearly incidence of primary end-point  
(Cardio-SIS, ACCORD and STENO2 )
  - twice less CVD (SCORE or FRS)
    - Cohort effect
    - Close follow-up in hypertension centers

## Discussion

### ☐ Lack of sufficient statistical power

- 3 times less inclusion than initially planned
- 2.5 to 5 times less yearly incidence of primary end-point (Cardio-SIS, ACCORD and STENO2 )
- twice less CVD (SCORE or FRS)
  - Cohort effect
  - Close follow-up in hypertension centers

### ☐ Intensification of treatment : 2018 ESH-ESC Guidelines

### ☐ Further reduction of BP is possible in already controlled HT

### ☐ Targeting BP to 130-139 / 80-85 mmHg is not sufficient. PWV meas. is needed

## Destiffening drugs : old ones and new ones

- ☐ Anti-hypertensive drugs

- ☐ **Anti-diabetic drugs**

- ☐ **Lipid lowering drugs**

- ☐ **Anti-inflammatory drugs**

- ☐ **Anti-platelet agents**

...

All new drug should benefit from a RCT  
on its effects on arterial stiffness ...

... with long enough follow-up (> 6 months)

... and adjustment on BP



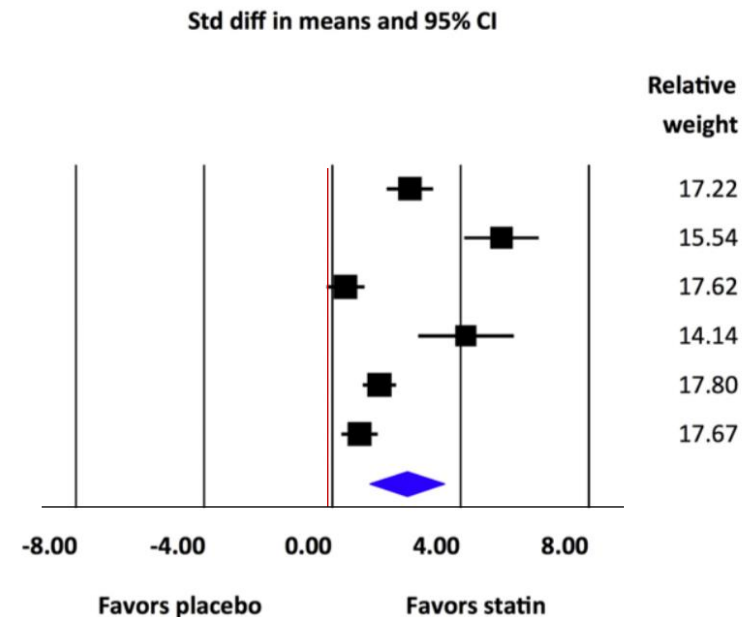
# Effects of statin therapy on arterial stiffness: A systematic review and meta-analysis of RCTs

Sikarin Upala<sup>a,b</sup>, Kamonkiat Wirunsawanya<sup>c</sup>, Veeravich Jaruvongvanich<sup>c,d</sup>, Anawin Sanguankeo<sup>i</sup>

6 RCTs, n=303, FU 1-6 M  
PWV  
Mean age 48

Upala et al. Int J Cardiol 2016

Study name	Statistics for each study			
	Std diff in means	Lower limit	Upper limit	p-Value
Kanaki 2013	2.417	1.688	3.146	0.000
Lunder 2011	5.275	4.102	6.448	0.000
Oh 2014	0.412	-0.184	1.009	0.175
Orr 2009	4.165	2.670	5.661	0.000
Pirro 2007	1.468	0.940	1.996	0.000
Wallace 2010	0.847	0.268	1.425	0.004
	2.309	1.149	3.468	0.000



\*. Cross-sectionnal studies

- 2.3 m/s PWV (-1.15 to -3.43) # 15 years of ageing\*

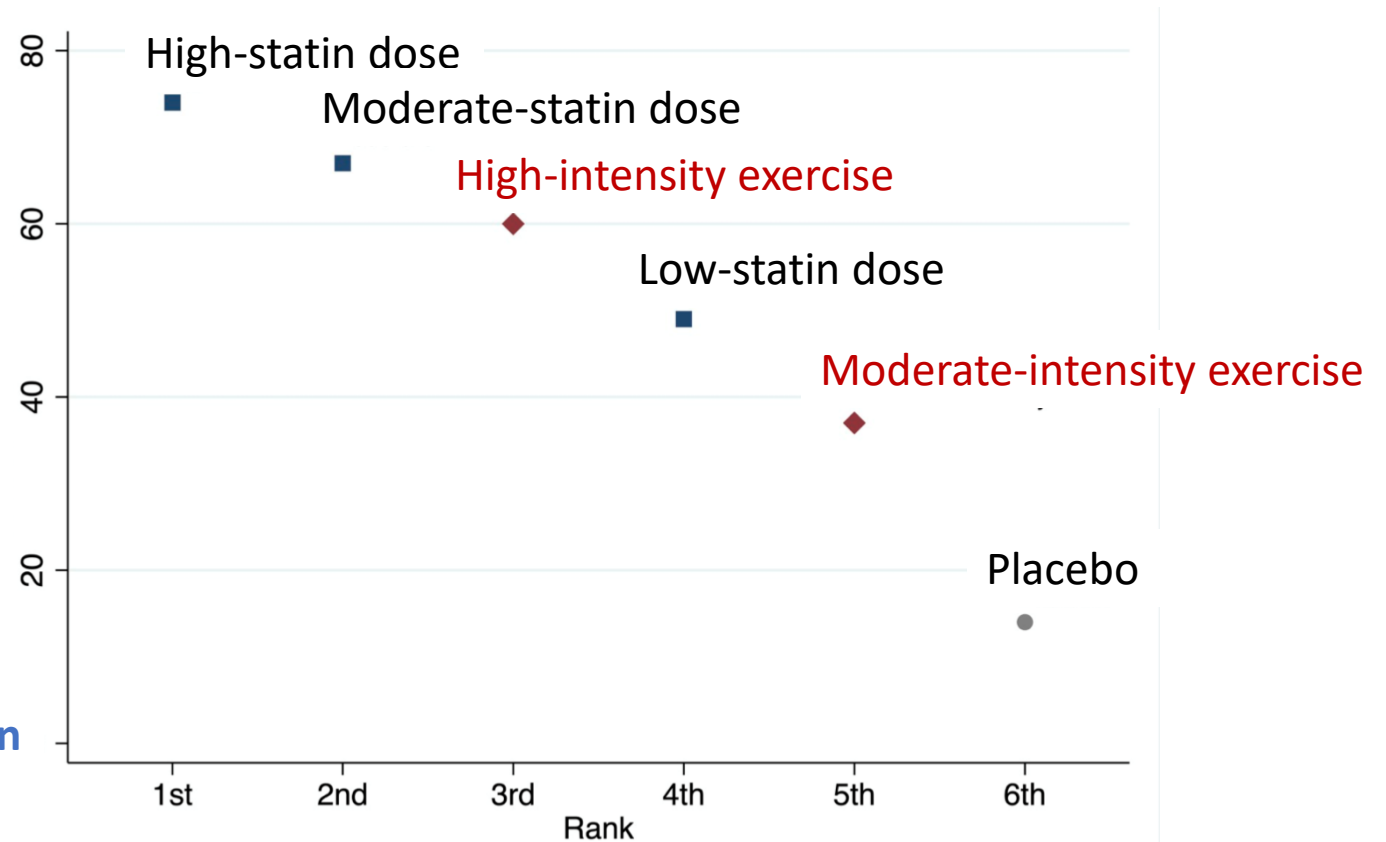
# Comparative effect of physical exercise versus statins on improving arterial stiffness in patients with high cardiometabolic risk: A network meta-analysis

Cevaro-Retondo I et al. Plos Medicine 2021

Best intervention

- Network meta-analysis
- 22 studies, including 18 RCTS and 4 non RCT
- 1,307 patients with high cardiometabolic risk
- cf-PWV
- Score of intervention

Worse intervention



# Birth weight and risk of adult disease



8.5 lbs



5.5 lbs

## *Low Birth Weight (LBW) →*

- hypertension
- type 2 diabetes
- hyperlipidaemia
- insulin resistance
- metabolic syndrome
- vascular dysfunction
- coronary heart disease (CHD)

## *High Birth Weight (HBW) →*

- obesity
- type 2 diabetes
- cardiovascular risk

**LBW:** caused by (1) impaired fetal growth, or (2) preterm delivery

**HBW:** caused by (1) maternal obesity, or (2) gestational diabetes

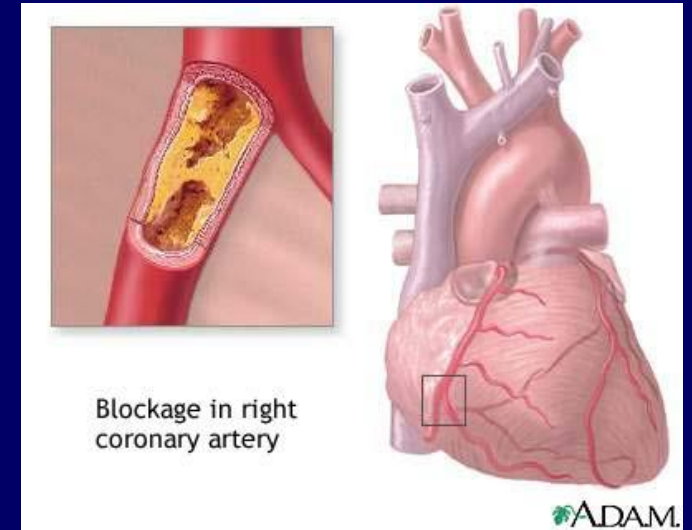
# Programming

A specific stimulus that during a critical time period might cause permanent changes in the organism

# Vascular Function & Structure in Children Born too Small or too Early *Mechanisms*

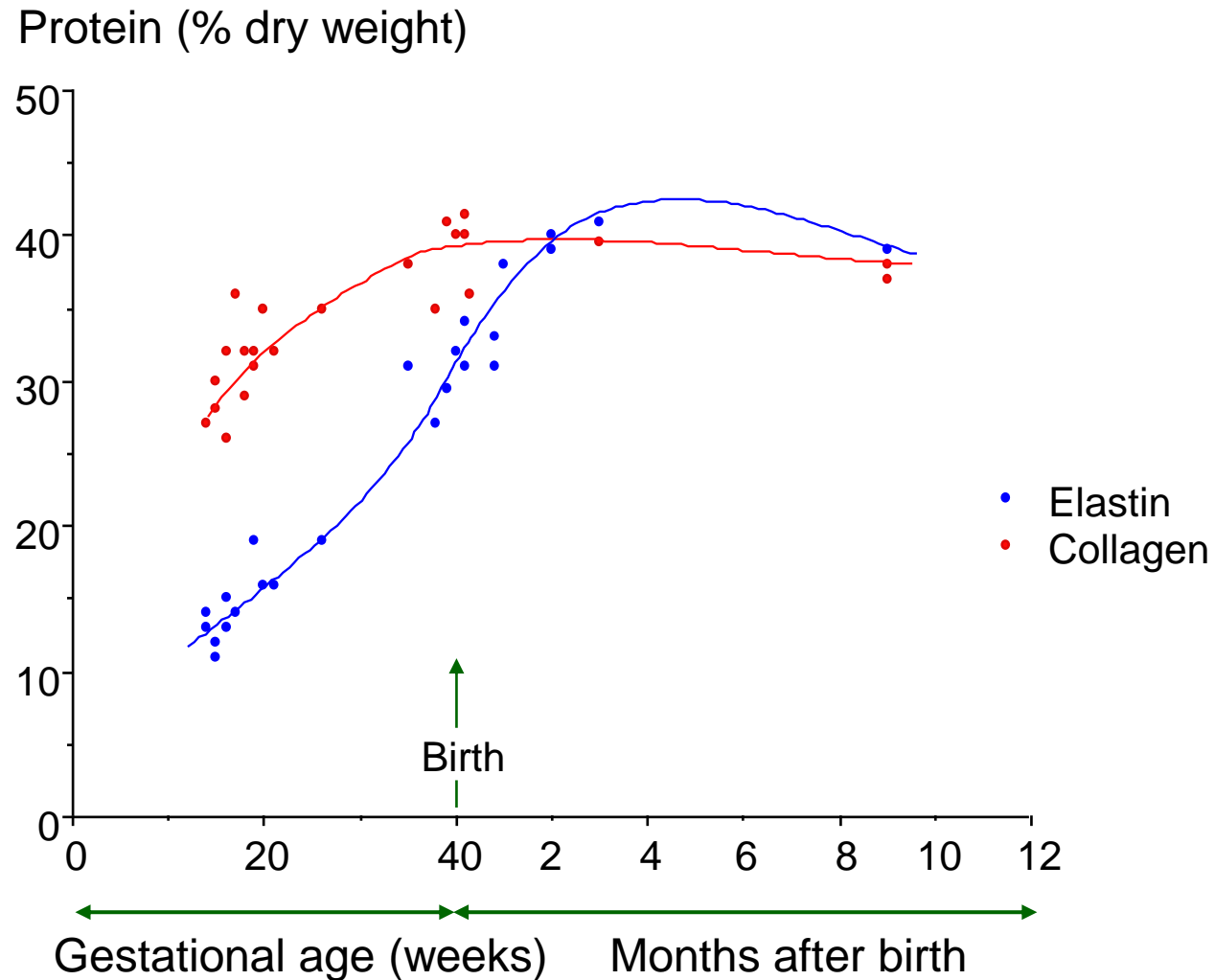


Early Mechanisms?



Capillary rarefaction  
Less elastin content of arterial wall  
Increased heart rate

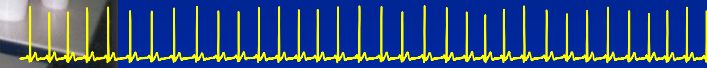
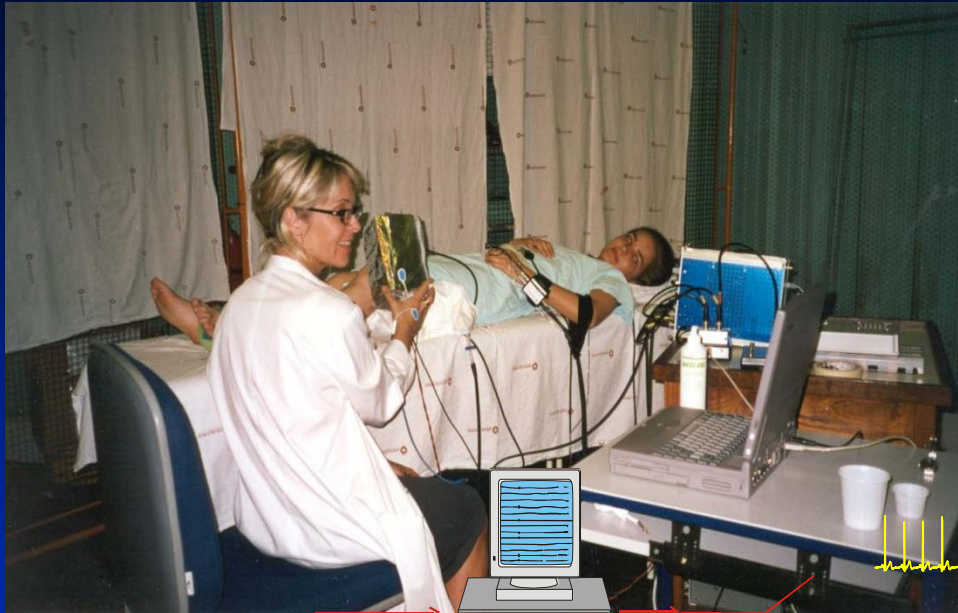
# Impaired synthesis of **elastin** in walls of aorta and large conduit arteries during early development as an initiating event in pathogenesis of systemic hypertension



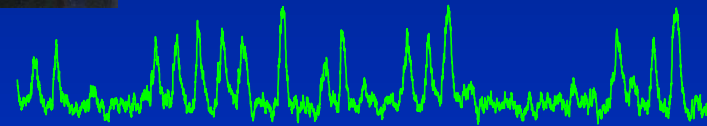


# The Microneurographic Technique

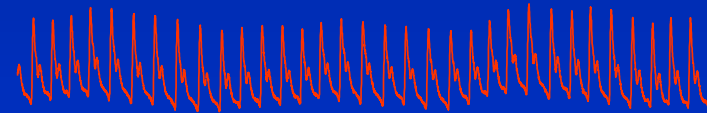
( Vallbo & Hagbarth, 1967, *Electroencephalogr. Clin. Neurophysiol.*)



ECG

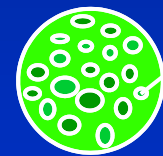


MSA

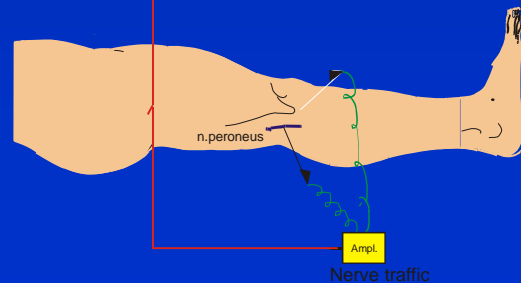


BP

ECG  
Nerve (MSA)  
Blood Pressure

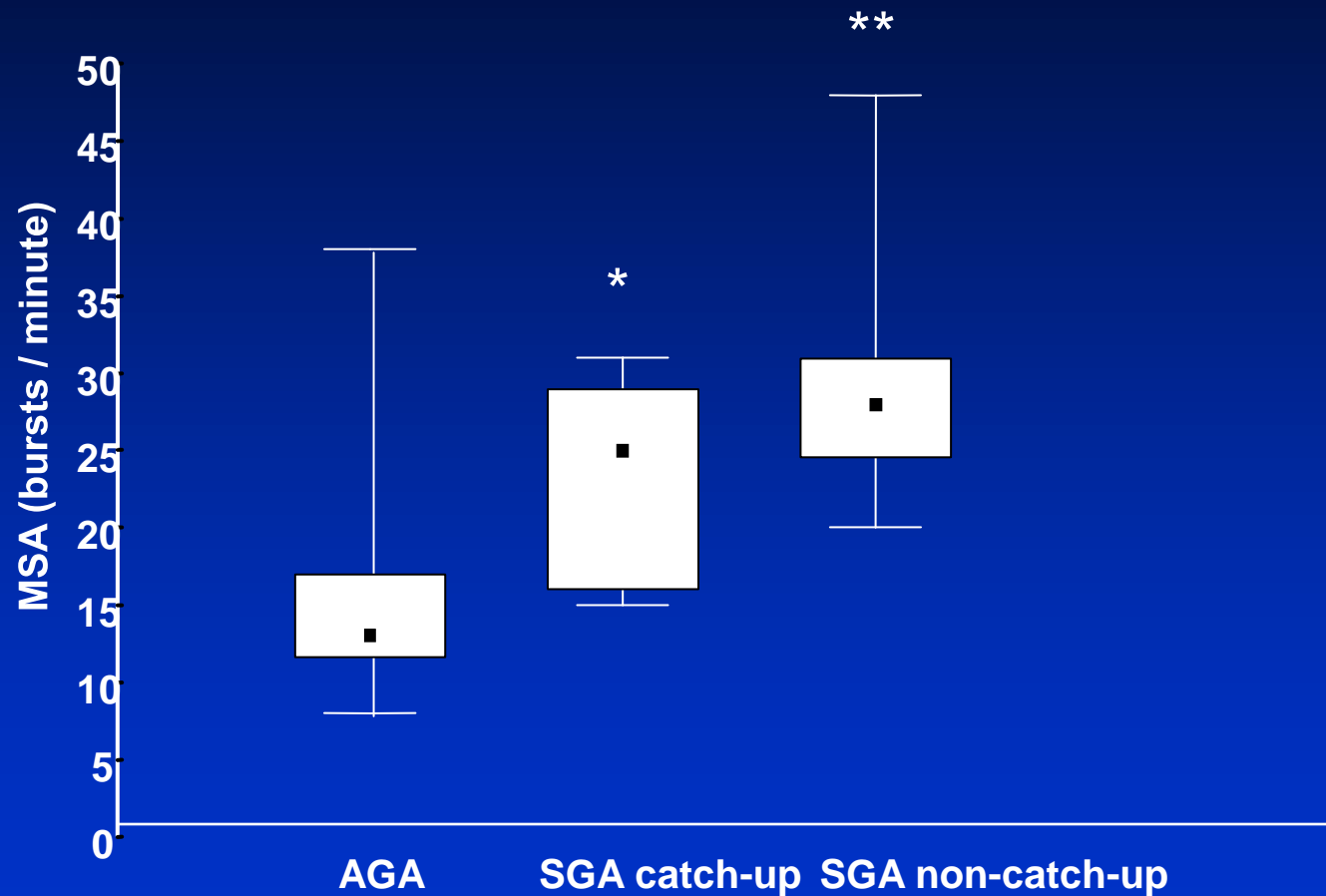


muscle  
fascicle



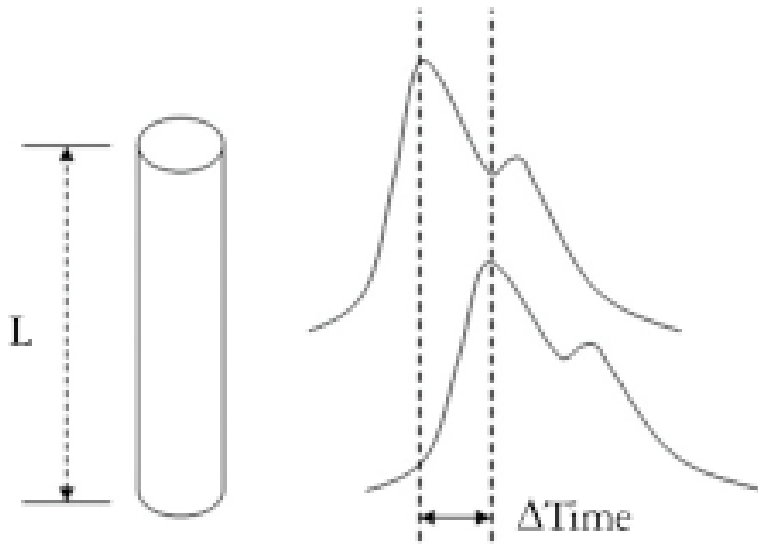
Sympathetic Nervous Activation

Sympathetic nerve activity is **increased in young adults born SGA** as compared to young individuals born AGA

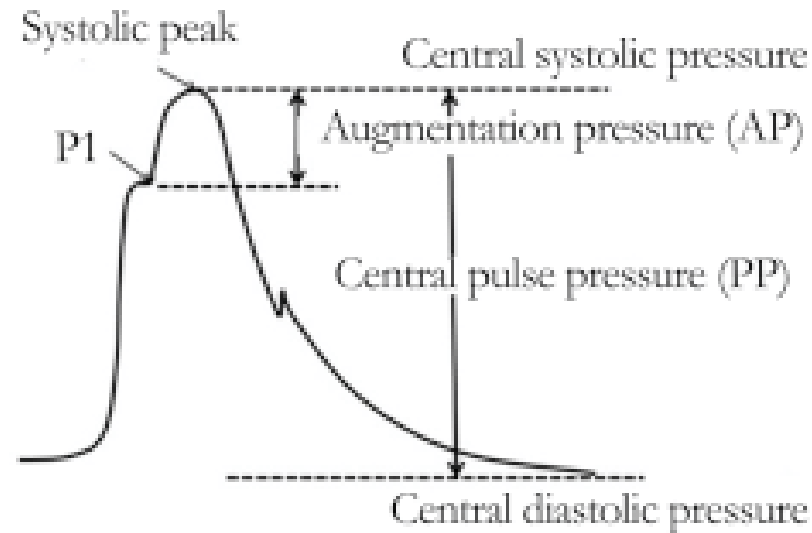


**AGA:** Appropriate for Gestational Age  
**SGA:** Small for Gestational Age

# Pulse wave velocity (PWV) and Augmentation Index (Aix)



$$PWV \text{ (m/sec)} = L / \Delta\text{Time}$$



$$Aix \text{ (\%)} = AP / \text{central PP} \times 100 \text{ (\%)}$$



# The Impact of Being Born Preterm or Small for Gestational Age on Early Vascular Aging in Adolescents



Katharina Stock, MD<sup>1</sup>, Anna Schmid, MD<sup>1</sup>, Elke Griesmaier, MD, PhD<sup>1</sup>, Nina Gande, MD<sup>1</sup>, Christoph Hochmayr, MD<sup>1</sup>, Michael Knoflach, MD<sup>2</sup>, Ursula Kiechl-Kohlendorfer, MD, MSc<sup>1</sup>, and the Early Vascular Aging (EVA) Study Group\*

Perof. Ursula Kiechl-Kohlendorfer  
University of Innsbruck, Austria

**Table II. Unadjusted characteristics of the study cohort and subgroups**

Characteristics	Study cohort			Subgroups				
	Term (n = 847)	Preterm (n = 83)	P value, Term vs Preterm	Term-AGA	Term-SGA	Preterm-AGA (n = 81)	P value	
				Term-AGA (n = 755)	Term-SGA (n = 92)		Term-AGA vs Term-SGA	Term-AGA vs Preterm-AGA
Perinatal characteristics								
Gestational age, wk, mean (SD)	39.8 (1.2)	34.8 (2.2)	<.001*	39.8 (1.2)	40.2 (1.3)	34.8 (2.3)	.002*	<.001*
Birth weight, g, mean (SD)	3359 (445)	2486 (651)	<.001*	3434 (398)	2734 (295)	2512 (635)	<.001*	<.001*
MAP, mmHg, mean (SD)	89 (7)	91 (8)	.005†	89 (7)	87 (8)	91 (8)	.100†	.008†
cIMT max, mm, mean (SD)	0.429 (0.056)	0.421 (0.054)	.198*	0.430 (0.057)	0.421 (0.046)	0.421 (0.054)	.261*	.163*
cIMT mean, mm, mean (SD)	0.381 (0.048)	0.372 (0.046)	.099†	0.382 (0.048)	0.377 (0.044)	0.372 (0.046)	.312†	.079†
PWV, m/s, mean (SD)	6.13 (1.18)	6.07 (0.91)	.824*	6.07 (1.09)	6.67 (1.73)	6.10 (0.91)	.011*	.756*

PWV, m/s	6.13	6.07	0.8	6.07	6.67	6.10	0.011	0.8
----------	------	------	-----	------	------	------	-------	-----

N= 930 adolescents, mean **16 years**  
**AGA:** Appropriate for Gestational Age  
**SGA:** Small for Gestational Age



# Arterial health during early childhood following abnormal fetal growth

Rasmus F.W. Olander<sup>1,2\*</sup>, Johnny K.M. Sundholm<sup>1,2</sup>, Sanna Suonsyrjä<sup>1,2</sup> and Taisto Sarkola<sup>1,2</sup>



Dr. Rasmus Olander  
University of Helsinki

N = 90 (SGA, N=23, LGA, N=19, AGA N=48), mean age 5.8 years

Dependent	Adjusted R <sup>2</sup>	Model p-value	Predictor	$\beta$	SE	B	p-value
Carotid-femoral PWV (m/s) C-f PWV Complior	0.224	<0.001	Birth weight, Z-score	0.024	0.031	0.083	0.444
			Height (cm)	0.043	0.016	0.300	0.010
			MAP (mmHg)	0.032	0.014	0.258	0.025
			Heart rate (bpm)	0.011	0.007	0.175	0.112

We report *no abnormalities* in arterial health, including PWV and BP, nor in adiposity, blood glucose or lipids during early childhood following abnormal fetal growth.

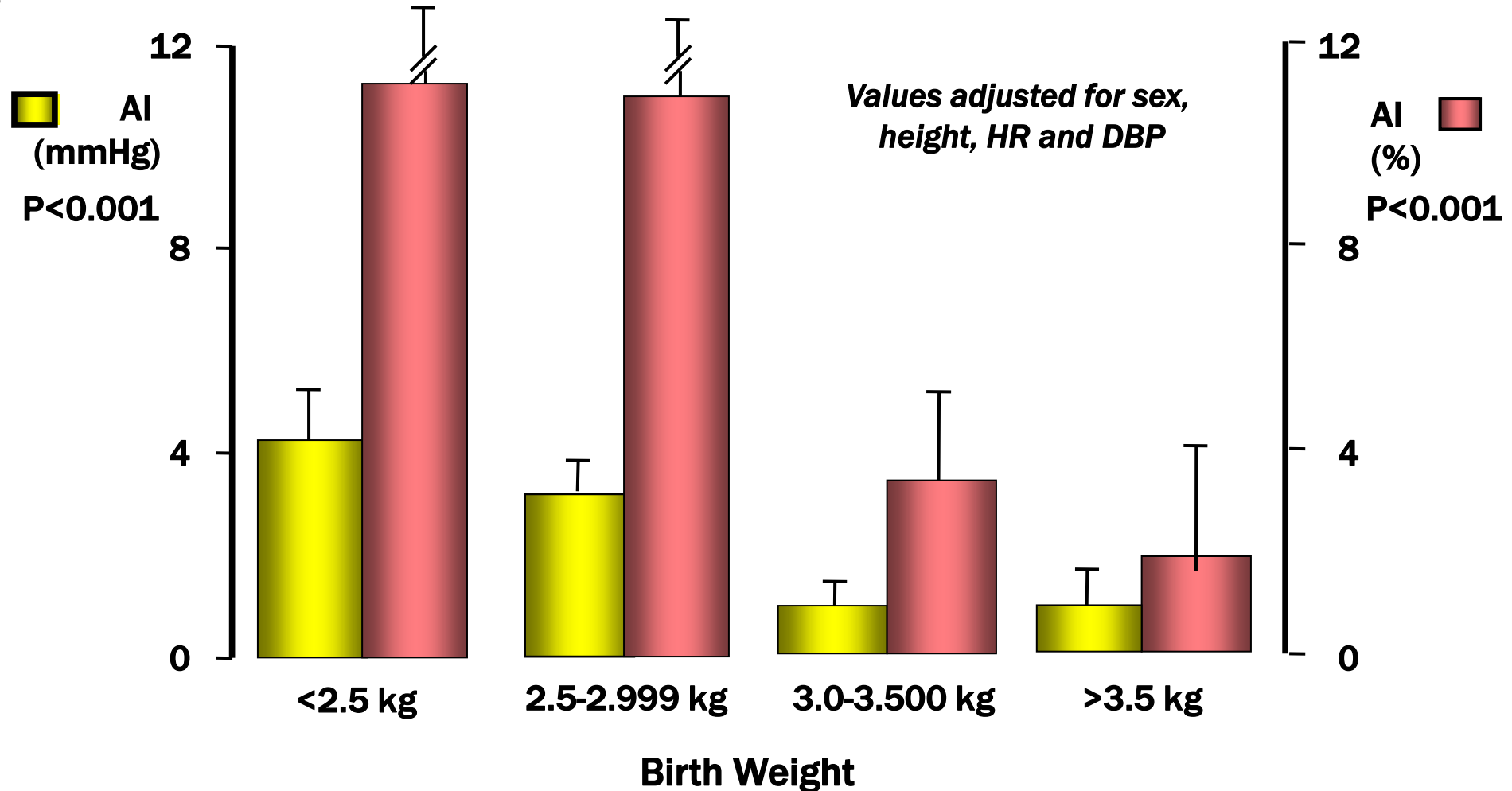
**...but Aix was NOT measured!**

Olander *et al.* BMC Pediatrics (2022) 22:40.



Prof. Empar Lurbe  
Valencia, Spain

# Augmentation Index (Aix) grouped by birth weight







Dr. Johannes Sperling  
Lund University

# Does early life programming influence arterial stiffness and central hemodynamics in adulthood?



Multiple regression – dependent variable **Augmentation Index** in relation to BW in different age groups

	Age 18-27 (n=620)			Age 27-44 (n=623)			Age 63-84 (n=326)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
	1	2	3	1	2	3	1	2	3
	$\beta$	$\beta$	$\beta$	$\beta$	$\beta$	$\beta$	$\beta$	$\beta$	$\beta$
<i>Early life</i>									
<b>Birth Weight (gram)</b>	<b>-0.06</b>	<b>-0.08</b>	<b>-0.08</b>	<b>-0.16*</b>	<b>-0.12*</b>	<b>-0.12*</b>	<b>-0.15*</b>	<b>-0.11*</b>	<b>-0.11*</b>
Gestational Age (weeks)	0.05	0.08	0.09	0.1*	0.07	0.07	0.02	-0.002	-0.01
<i>Adult data</i>									
Glucose (mmol/l)	0.02	-0.02	-0.02	0.004	-0.01	-0.01	0.03	0.06	0.06

**Model 1:** Age, sex and gestational age

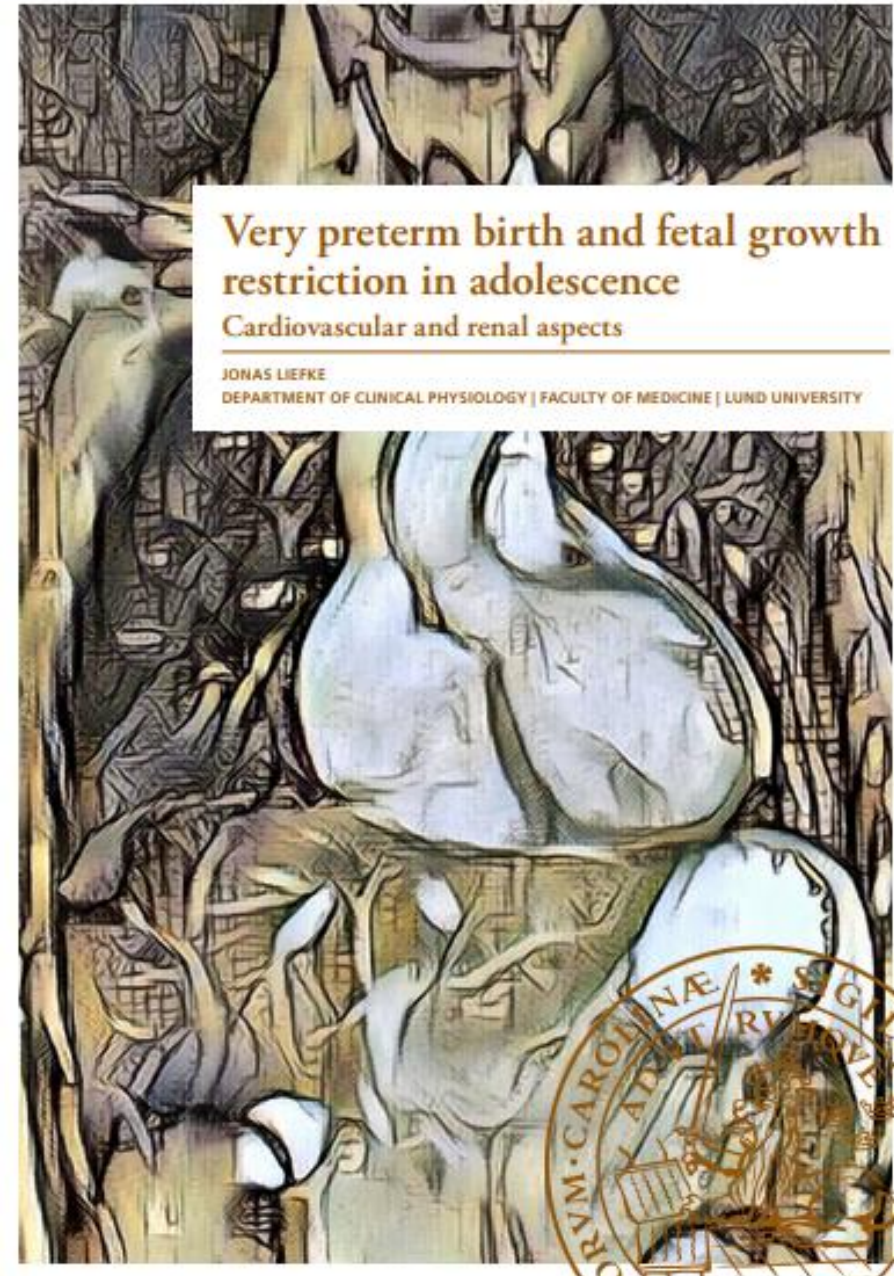
**Model 2:** + MAP, HR, smoking, anti-hypertensive treatment and BMI.

**Model 3:** + glucose.

P<0.05 is considered significant. \*Significant association.



Jonas Liefke, doktorand,  
Klin Fys, Lund  
Disputation den 7/12 2022



# Summary

---

- In the **TIME study**, final evidence was shown that the timing of intake of antihypertensive drugs (morning vs. bedtime) does not matter for risk of CVD events, thus the patient can choose what is most practical for the individual
- In the **SPARTE study**, a strategy to control arterial stiffness (PWV) was partly supported as compared to usual care based on guidelines, but a larger study is needed for evaluation of protection from developing CVD events
- **Early life programming** (prematurity, fetal growth, birth weight) provides new insights into the the early influences on vascular structure and function, leading to increased risk in adult life