

MEDI7011

Research Frontiers in Medical Science

# Blood pressure and vascular function: The role of regional changes of large artery stiffness in end-organ diseases.

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Macquarie University. On the land of the Wallumattagal clan of the Dharug Nation.



Define arterial stiffness and the *Windkessel* effect

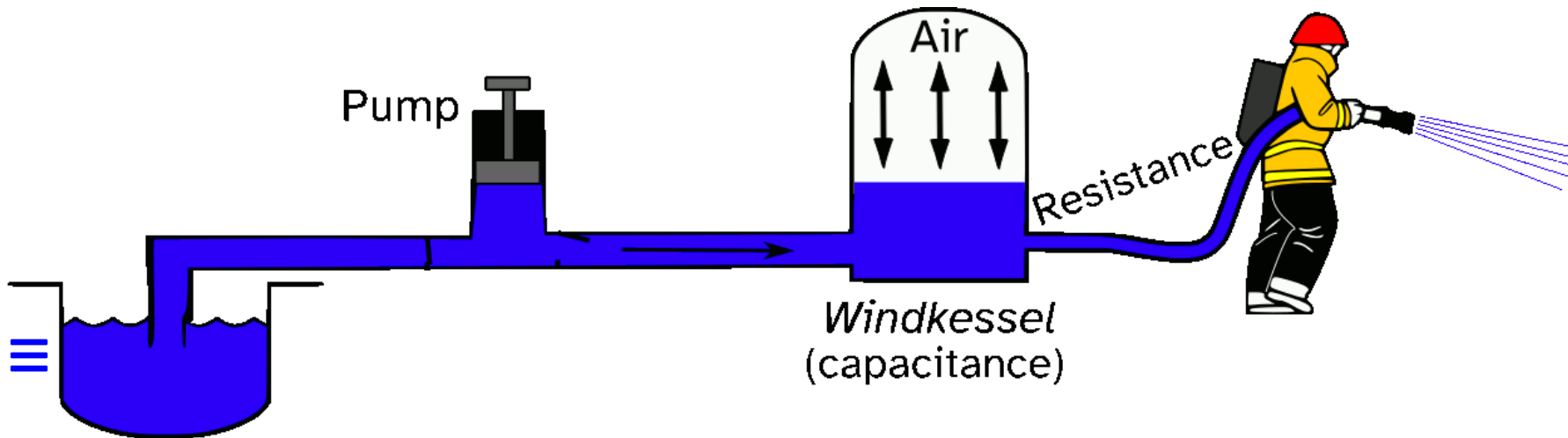
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# Define arterial stiffness and the *Windkessel* effect

Compliant arteries act as a capacitor, storing and releasing energy

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# Define arterial stiffness and the *Windkessel* effect

The heart: a pulsatile flow source

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**Heart rate (HR)** The number of beats of the heart per unit time (e.g. beats per minute bpm)

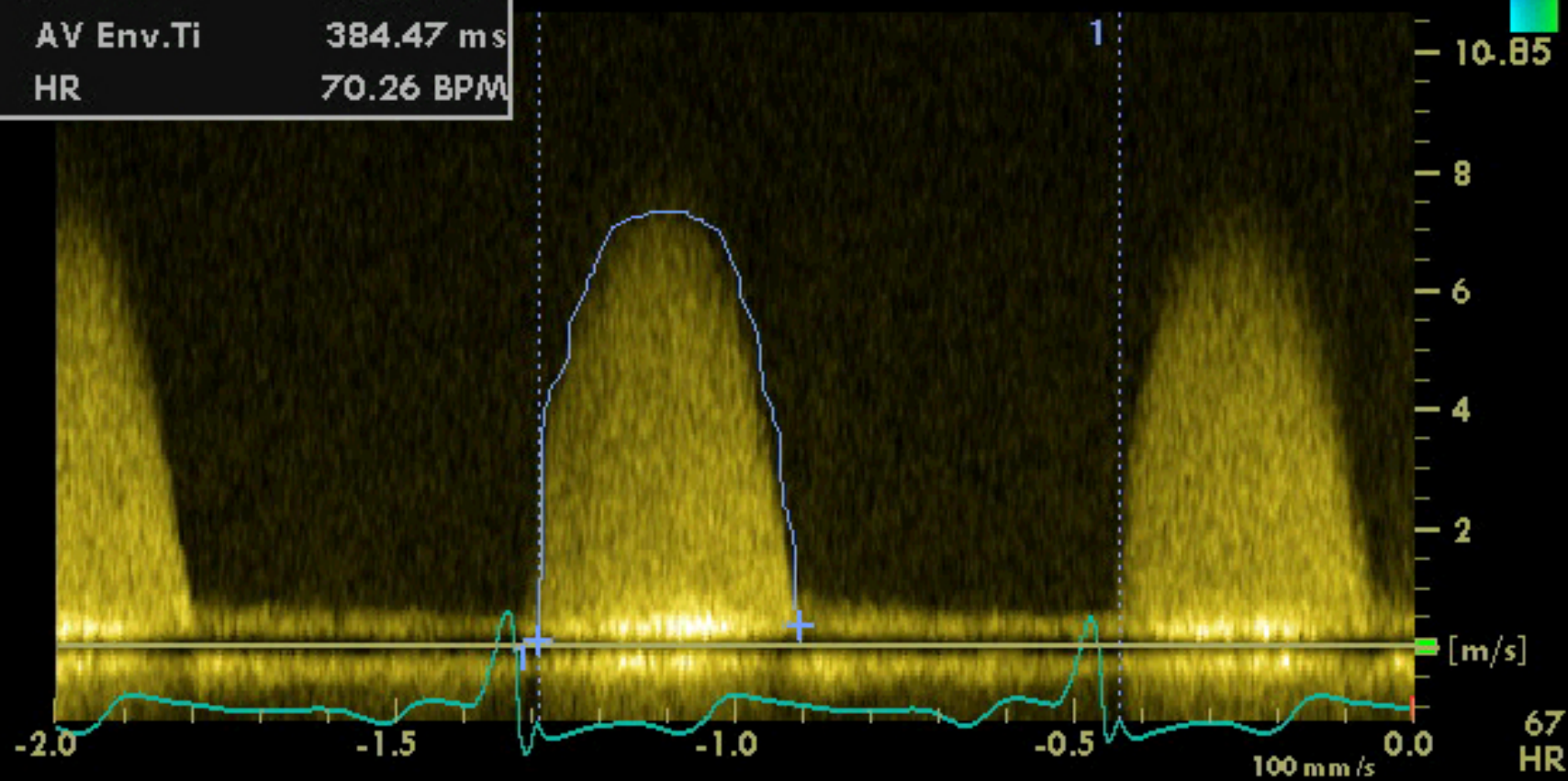
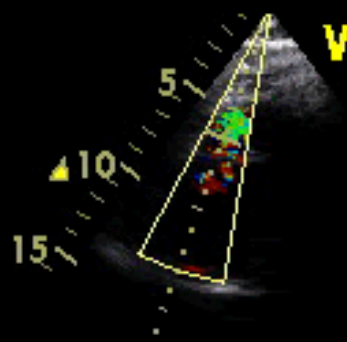
**Stroke volume (SV)** The volume of blood ejected by the left ventricle into the aorta in a single stroke (beat) of the heart

**Cardiac output (CO)** The average rate of blood being ejected by the left ventricle into the aorta

$$CO = SV \times HR$$



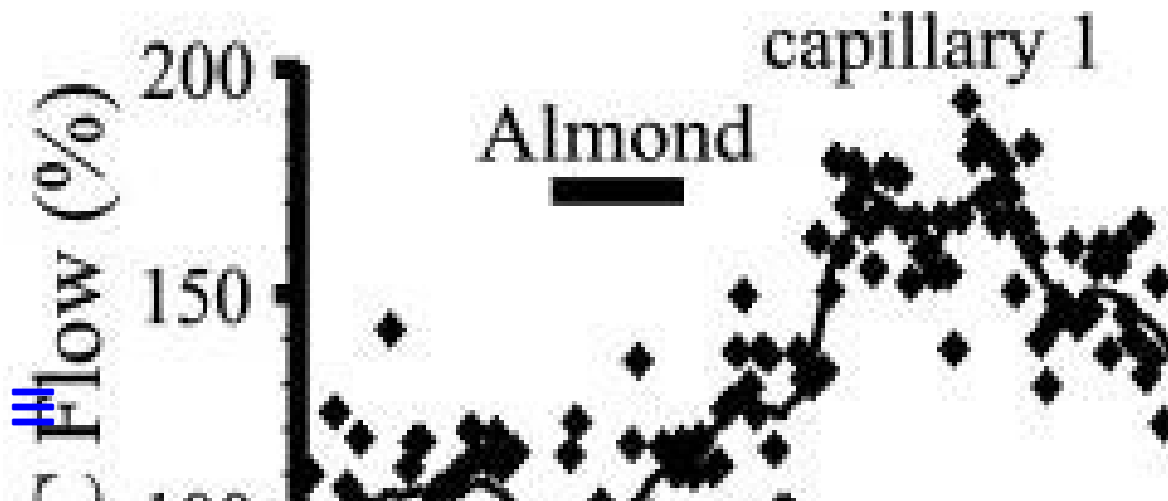
1	AV Vmax	7.32 m/s
	AV Vmean	5.87 m/s
	AV maxPG	214.41 mmHg
	AV meanPG	149.54 mmHg
	AV VTI	225.71 cm
	AV Env.Ti	384.47 ms
	HR	70.26 BPM



# Define arterial stiffness and the *Windkessel* effect

The capillaries: a non-pulsatile flow bed

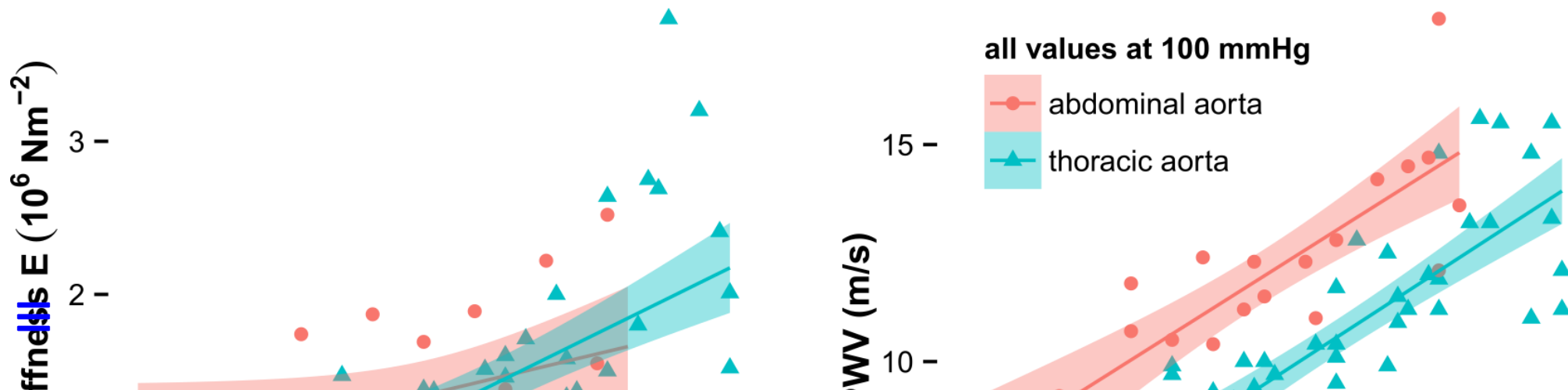
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# Define arterial stiffness and the *Windkessel* effect

Large arteries get stiffer with age

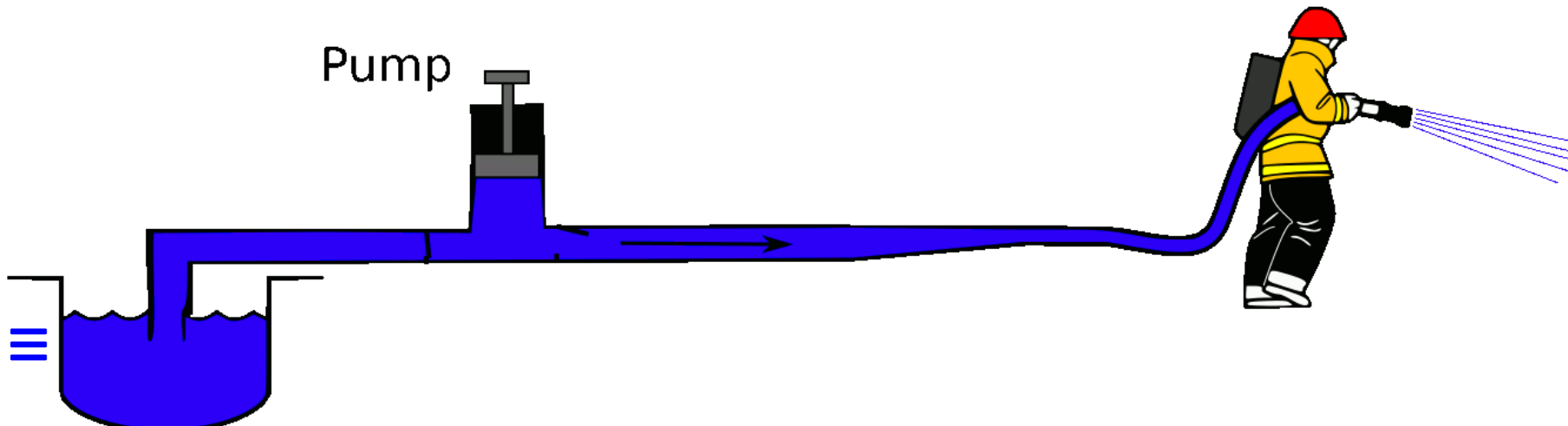
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# Define arterial stiffness and the *Windkessel* effect

Stiff arteries reduce the *Windkessel* effect

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# Compliant large arteries



# Stiff large arteries

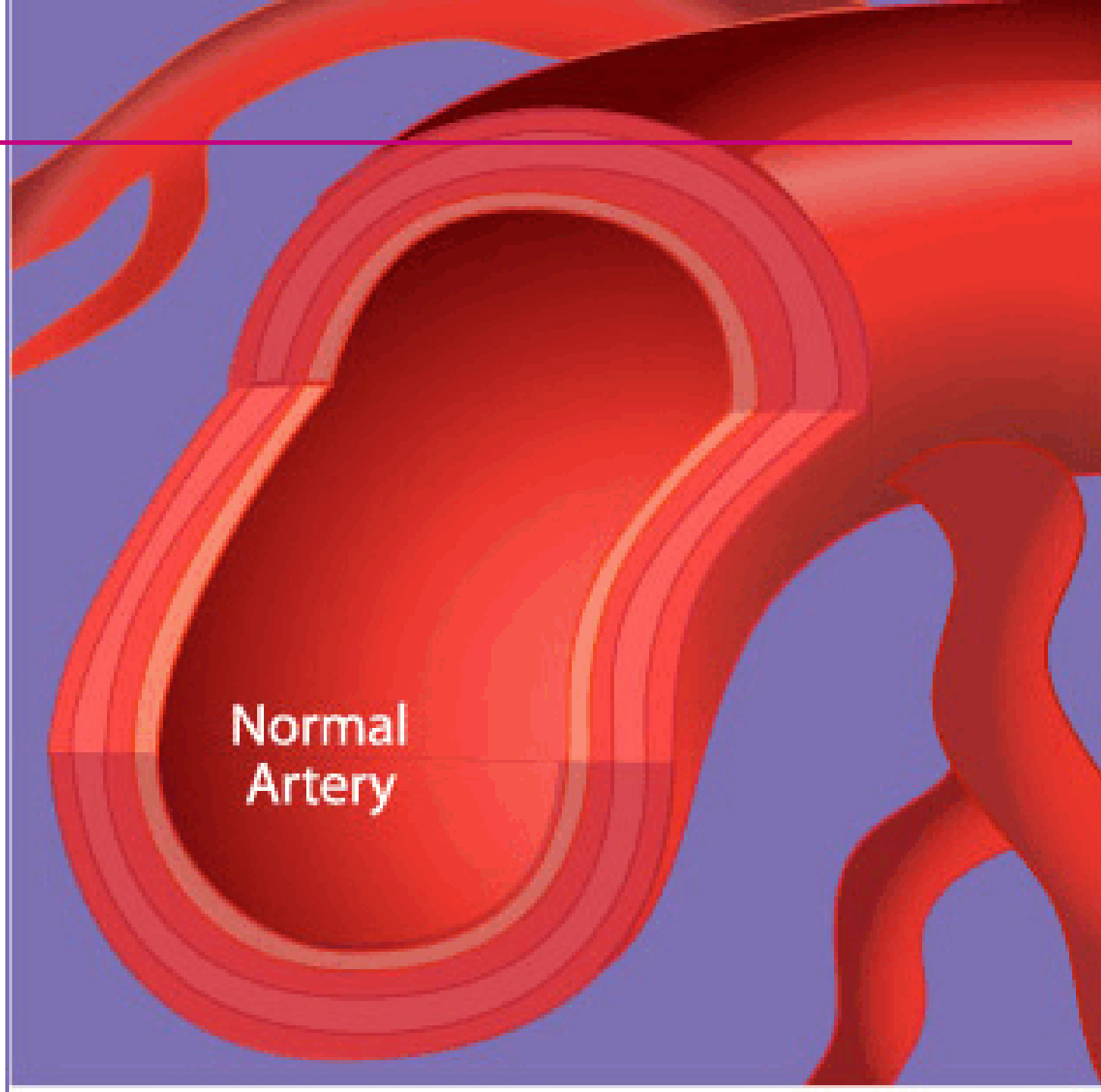
Source: [Weekly Media](#)



# Not Atherosclerosis

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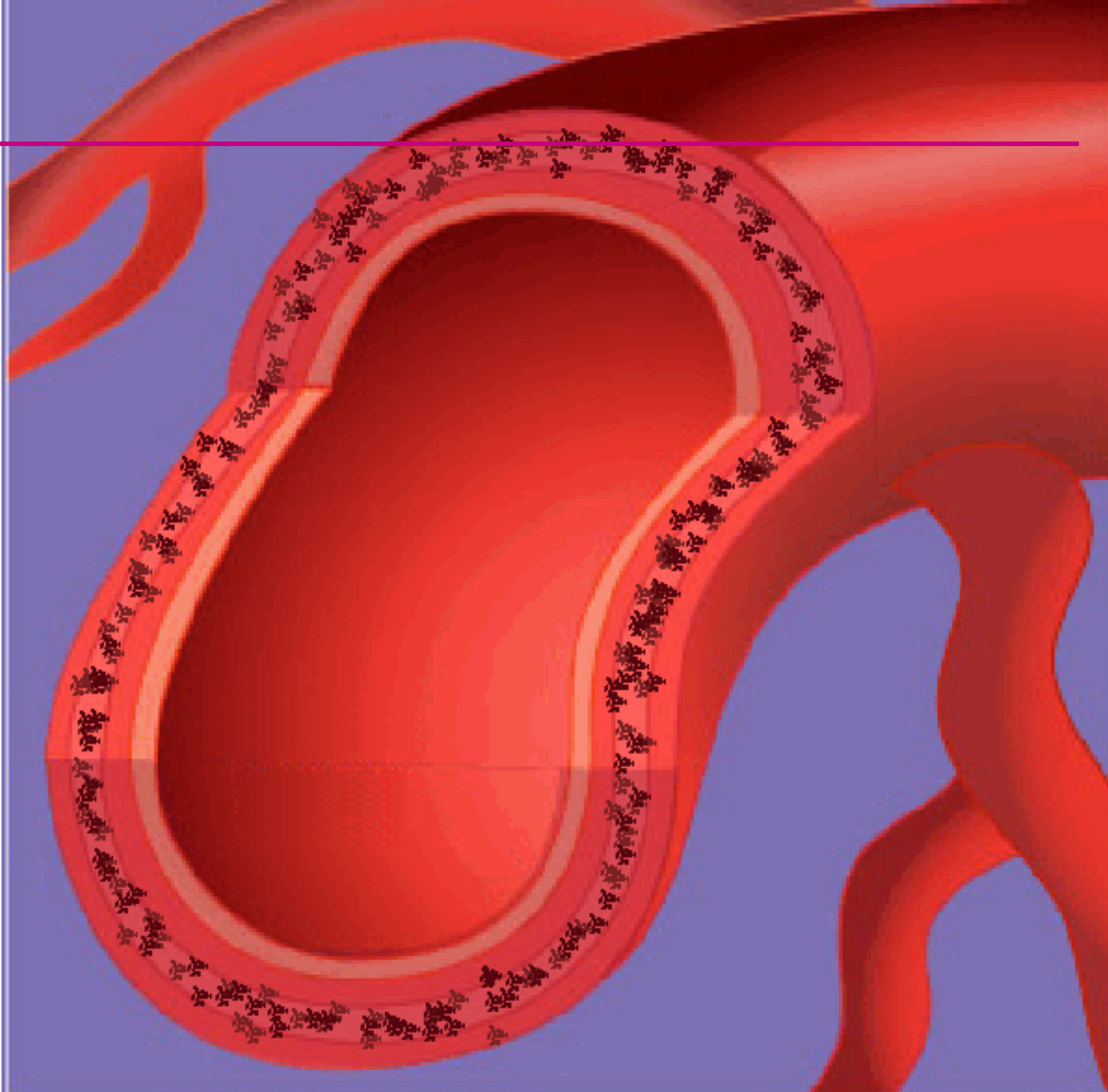
The reduction of the *Windkessel* effect is **not** due to **atherosclerosis**: Small artery flow restriction (or blockage) through isolated plaque formation in the *intimal layer*.



# Arteriosclerosis

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The loss of the *Windkessel* effect is due to **arteriosclerosis**: Stiffening of the arteries including changes in the *medial layer*.



# The clinical importance of large artery stiffness

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# The clinical importance of large artery stiffness

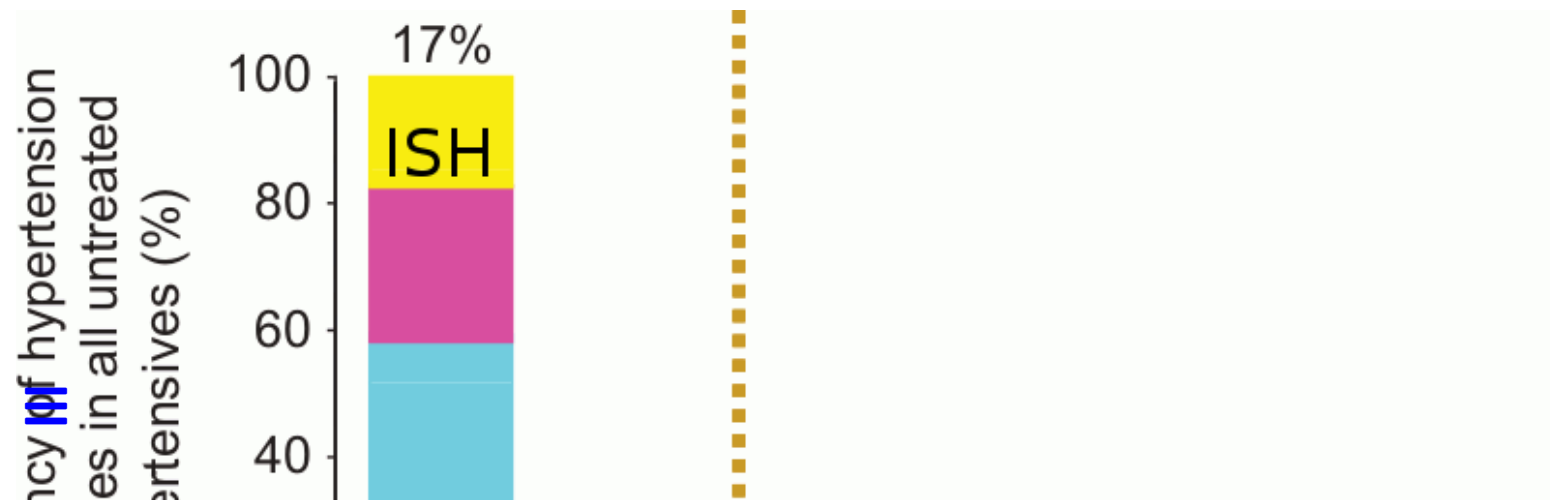
Major contributor to the predominant form of hypertension

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IDH: isolated diastolic hypertension

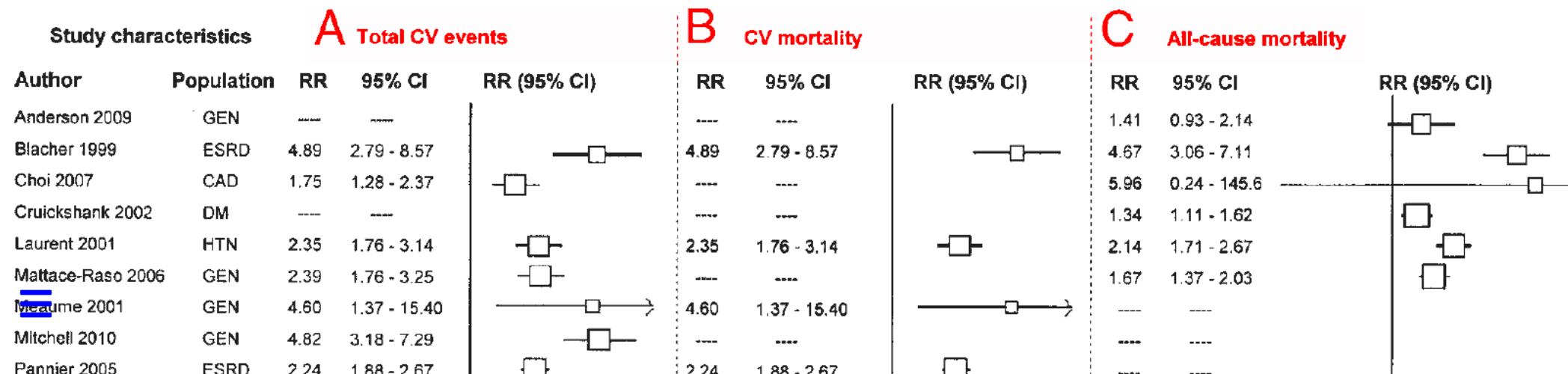
ISH: isolated systolic hypertension

Nilsson, PM et al. *Blood pressure and pulse wave velocity as metrics for evaluating pathologic ageing of the cardiovascular system*. Blood Press, 2013, 23:17--30.



# The clinical importance of large artery stiffness

## Independent predictor of cardiovascular mortality



How do large artery changes effect the end-organs?

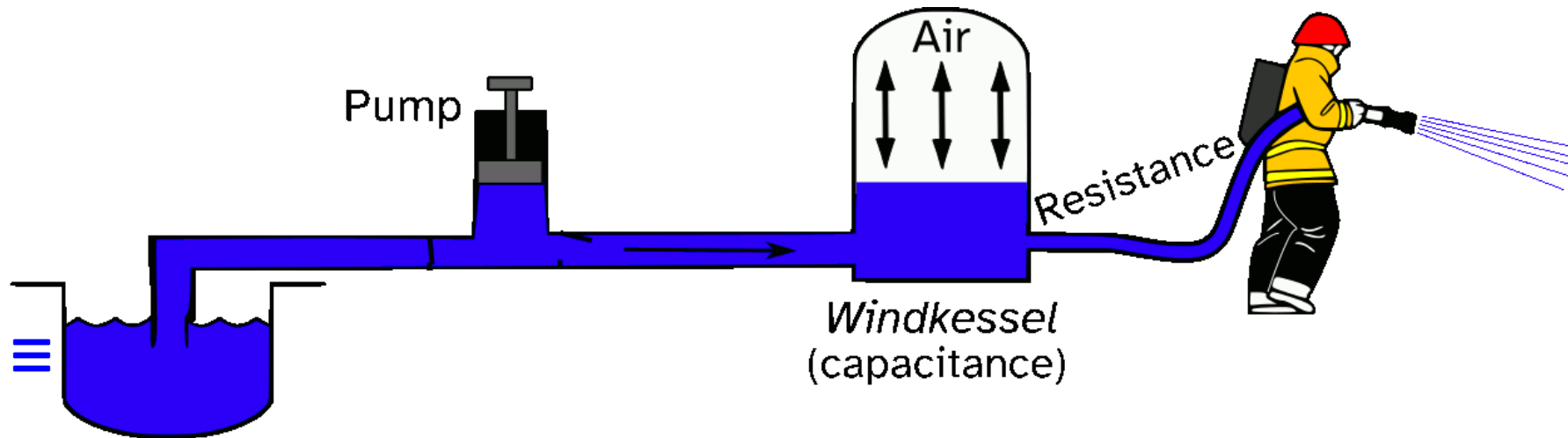




# How do large artery changes effect the end-organs?

## Pulse pressure transmission

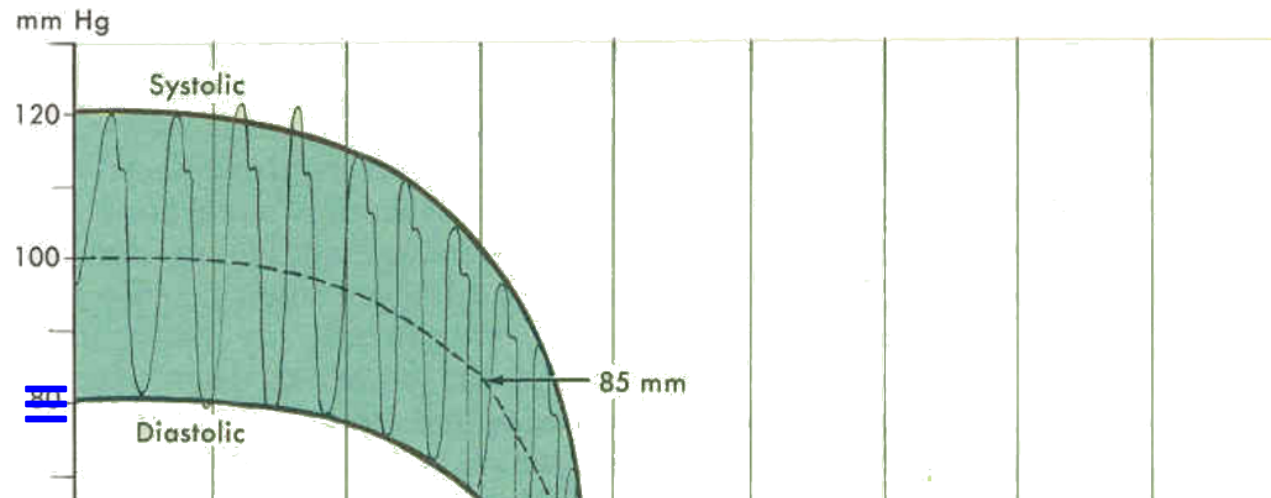
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# How do large artery changes effect the end-organs?

## Pulse pressure transmission

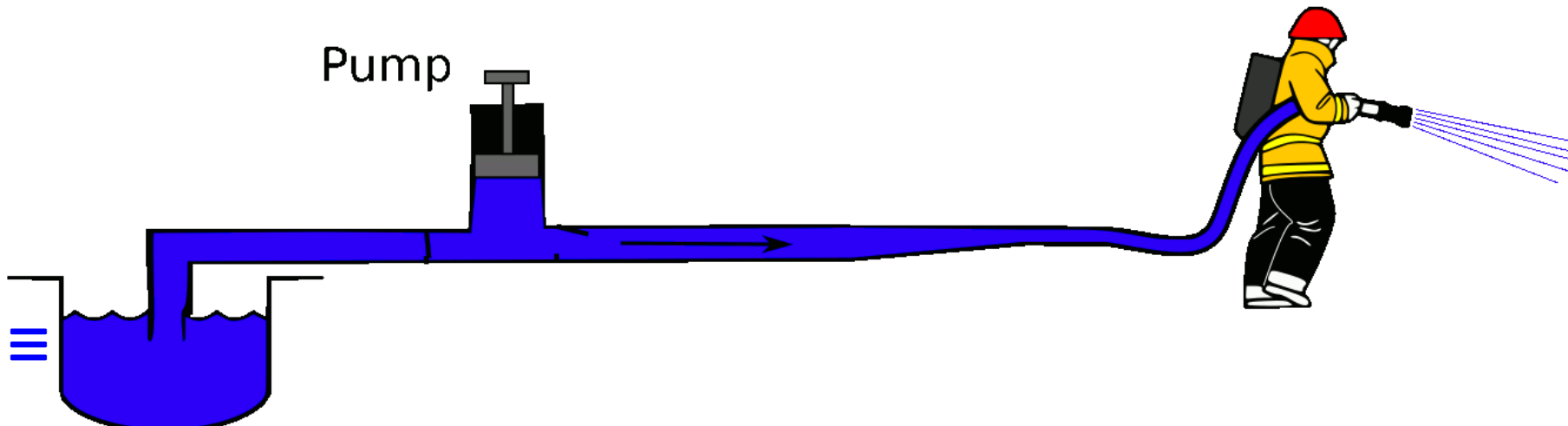
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# How do large artery changes effect the end-organs?

## Pulse pressure transmission

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# How do large artery changes effect the end-organs?

## Low resistance arterial beds

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Low resistance arterial beds may be particularly susceptible to the increased transmission of the pulse pressure.

Low resistance arterial beds include:

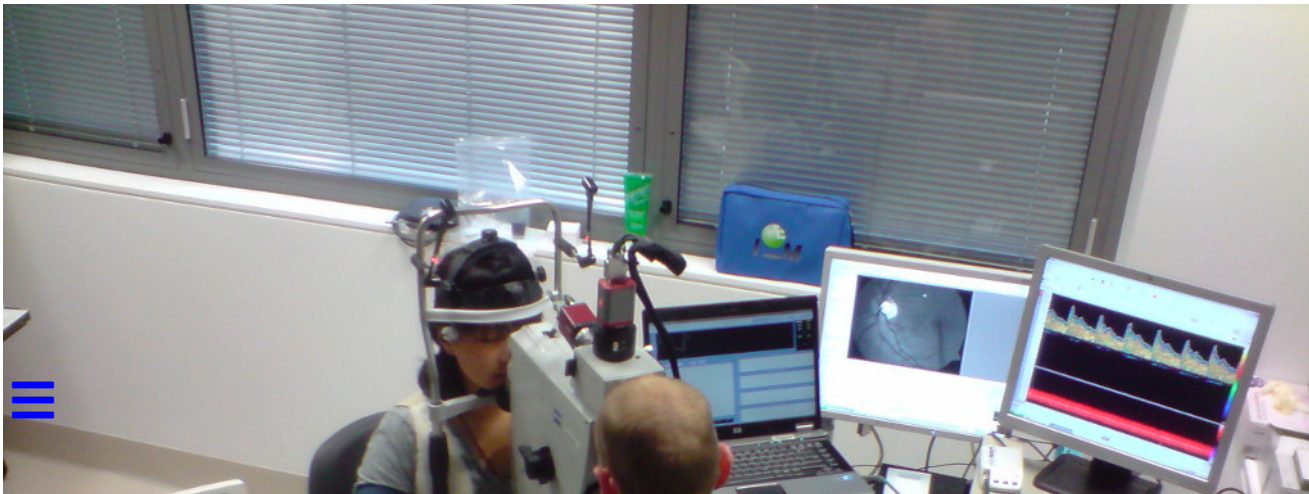
- the brain
- the kidneys



# How do large artery changes effect the end-organs?

## Measurement

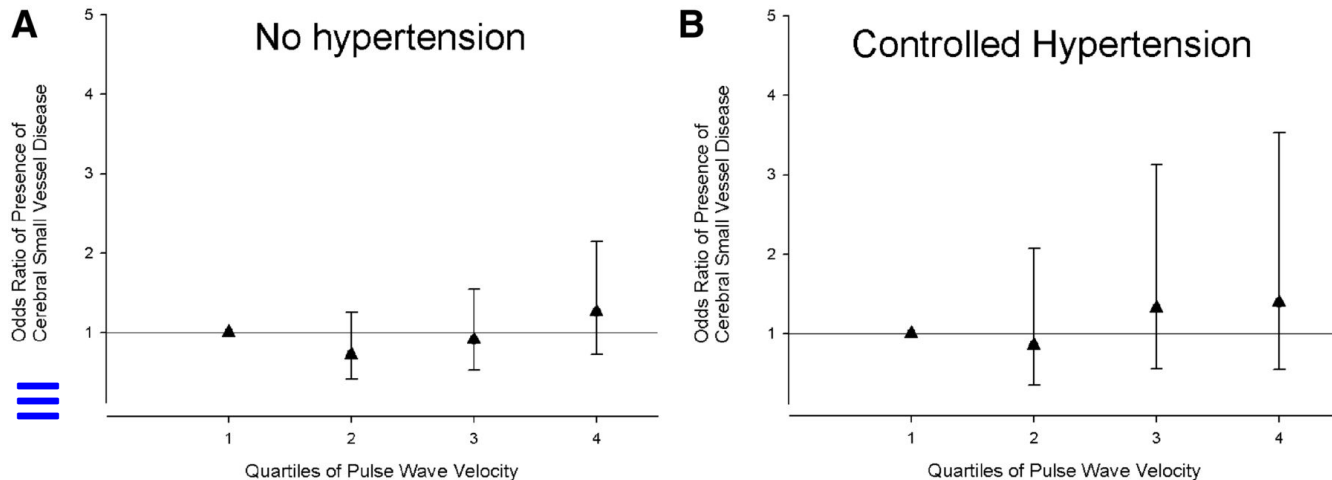
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# How do large artery changes effect the end-organs?

## Stiffness of large arteries is associated with cerebral small vessel disease

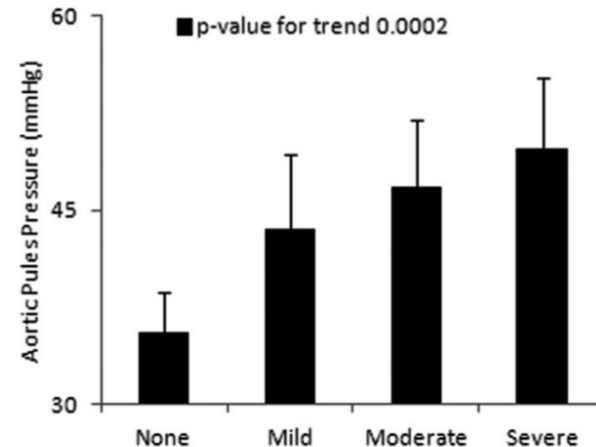
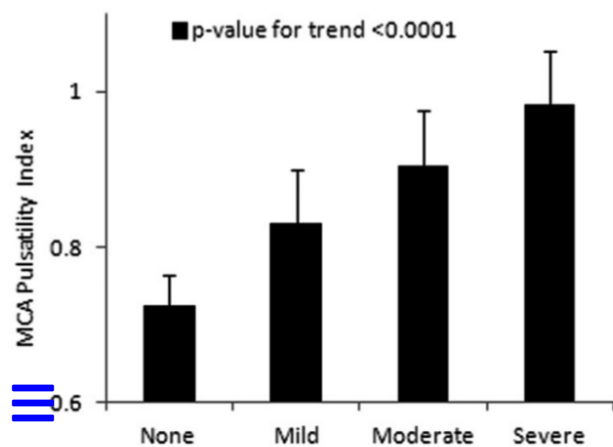
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# How do large artery changes effect the end-organs?

## Stiffness of large arteries is associated with dementia

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# Young middle-aged individuals are vulnerable to cognitive decline associated with arterial stiffness

## Original Contribution

### Effects of Arterial Stiffness on Brain Integrity in Young Adults From the Framingham Heart Study

Pauline Maillard, PhD; Gary F. Mitchell, MD; Jayandra J. Himali, PhD; Alexa Beiser, PhD; Connie W. Tsao, MD; Matthew P. Pase, PhD; Claudia L. Satizabal, PhD; Ramachandran S. Vasan, MD; Sudha Seshadri, MD; Charles DeCarli, MD

**Background and Purpose**—Previous work from the Framingham Heart Study suggests that brain changes because of arterial aging may begin in young adulthood and that such changes precede cognitive deficits. The objective of this study was to determine the association of arterial stiffness with measures of white matter and gray matter (GM) integrity in young adults.

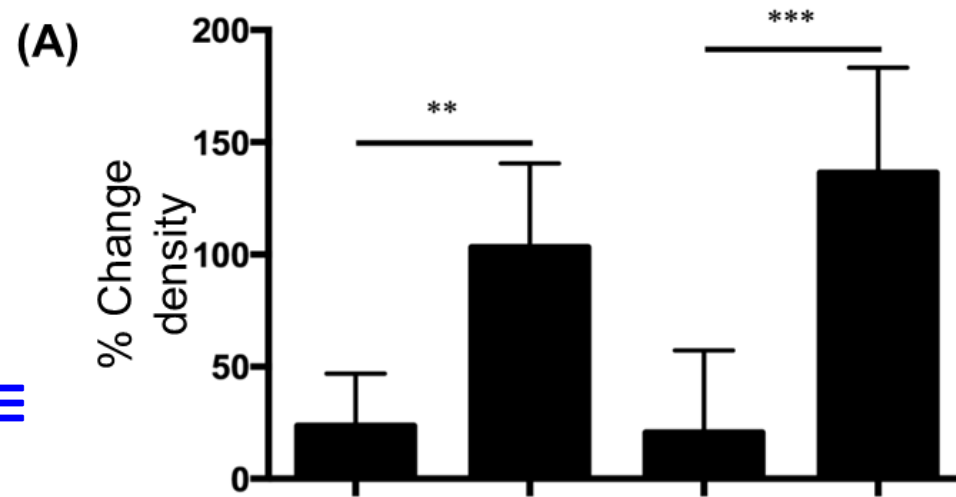
**Methods**—One thousand nine hundred three participants from the Framingham Heart Study Third Generation (mean age,  $46 \pm 8.7$  years) had complete tonometry measurements and brain magnetic resonance imaging (T1-weighted and diffusion tensor imaging). Tonometry measures included carotid-femoral pulse wave velocity, augmentation index, carotid-femoral pulse wave velocity, augmentation index, and carotid-femoral pulse wave velocity. Brain imaging measures included white matter integrity (fractional anisotropy) and GM integrity (cortical thickness).



# How do large artery changes effect the end-organs?

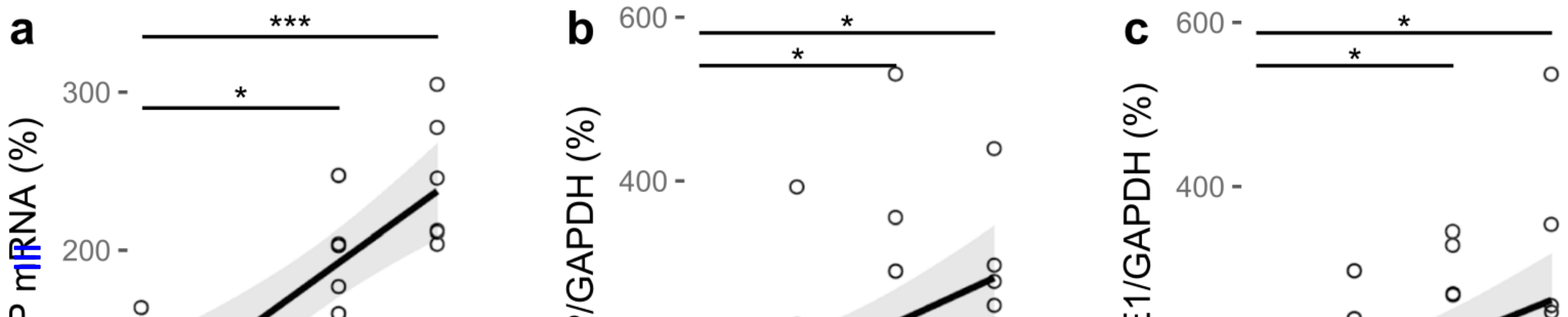
Plausible mechanistic link to Alzheimer's disease

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# How do large artery changes effect the end-organs?

Plausible mechanistic link to Alzheimer's disease



Can the stiffening of arteries be treated/prevented?

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# Can the stiffening of arteries be treated/prevented?

## Mechanism of anti-hypertensive drugs

antihypertensive drug class	action
Diuretics	Reduce blood volume through salt reduction.
Beta blockers	Reduce heart rate, reduce cardiac output.
ACE inhibitors	Reduce angiotensin production and reduce peripheral vasoconstriction.
ARB's	Block angiotensin, reduce peripheral vasoconstriction.
Calcium channel blockers	Prevent calcium entering smooth muscle, reduces heart contractility and peripheral vasoconstriction.
Alpha blockers	Vasodilator, reduces peripheral resistance.
Alpha-2 Receptor agonists	reduce sympathetic activity  reduced heart rate and peripheral resistance.
Peripheral adrenergic inhibitors	Block brain neurotransmitters, reduce smooth muscle contraction and peripheral resistance.
Vasodilators	Directly act on blood vessels to reduce peripheral resistance.



# No treatment options.

(Yet.)



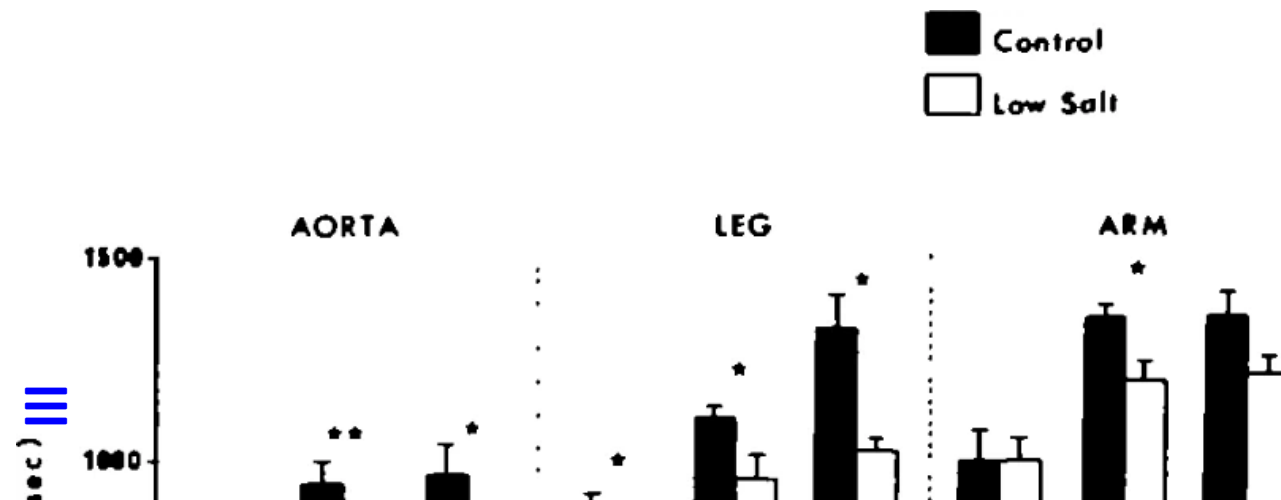
# Can it be prevented?



# Can the stiffening of arteries be treated/prevented?

Lifestyle factors: Effect of dietary salt

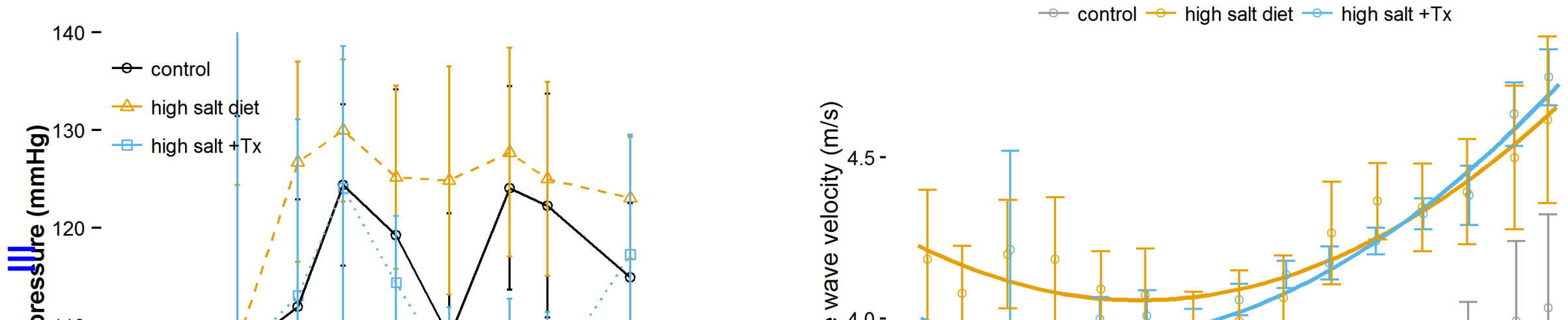
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# Can the stiffening of arteries be treated/prevented?

## Lifestyle factors: Effect of dietary salt

Connolly, K.; Spronck, B.; Georgevsky, D; Avolio, A. P. McEniery, C. M.; Wilkinson, I. B. & Butlin, M. *Large artery stiffness and the role of glycosaminoglycans with high dietary salt intake*. Unpublished, 2016.





Can the stiffening of large arteries be measured?

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# Can the stiffening of large arteries be measured?

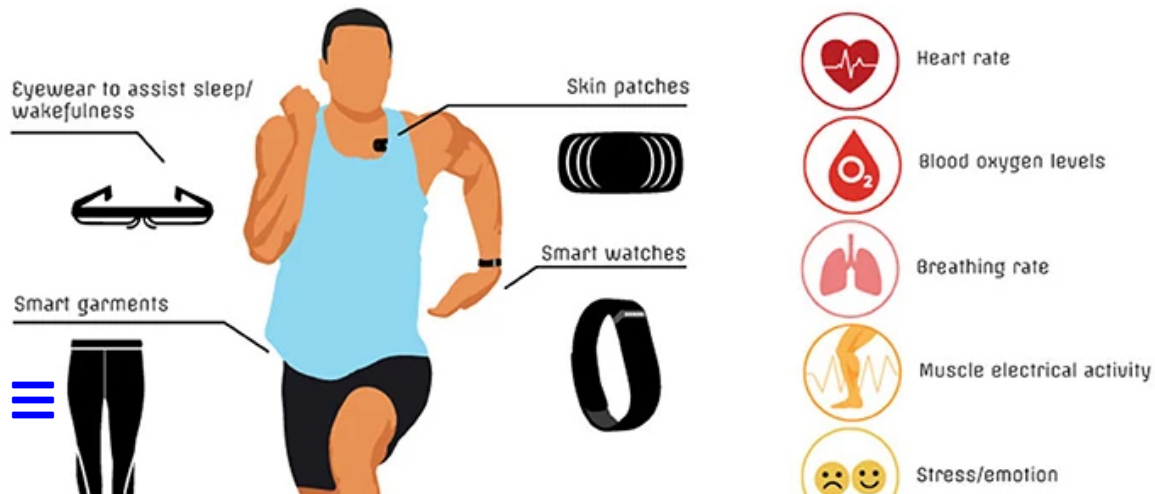
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# Can the stiffening of large arteries be measured?

## Wearable devices

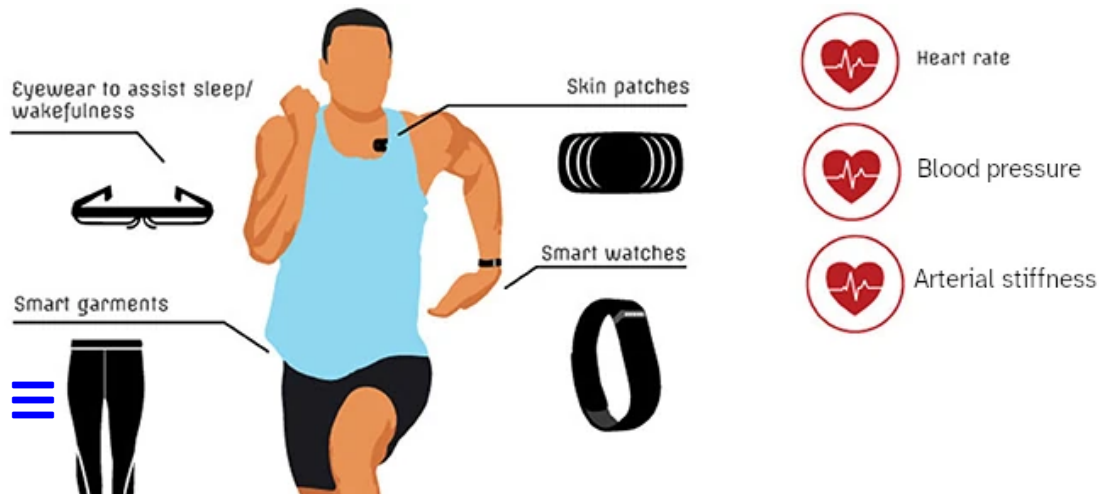
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# Can the stiffening of large arteries be measured?

## Wearable devices

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