Longitudinal changes in aortic reservoir function independently predict declining renal function among healthy individuals

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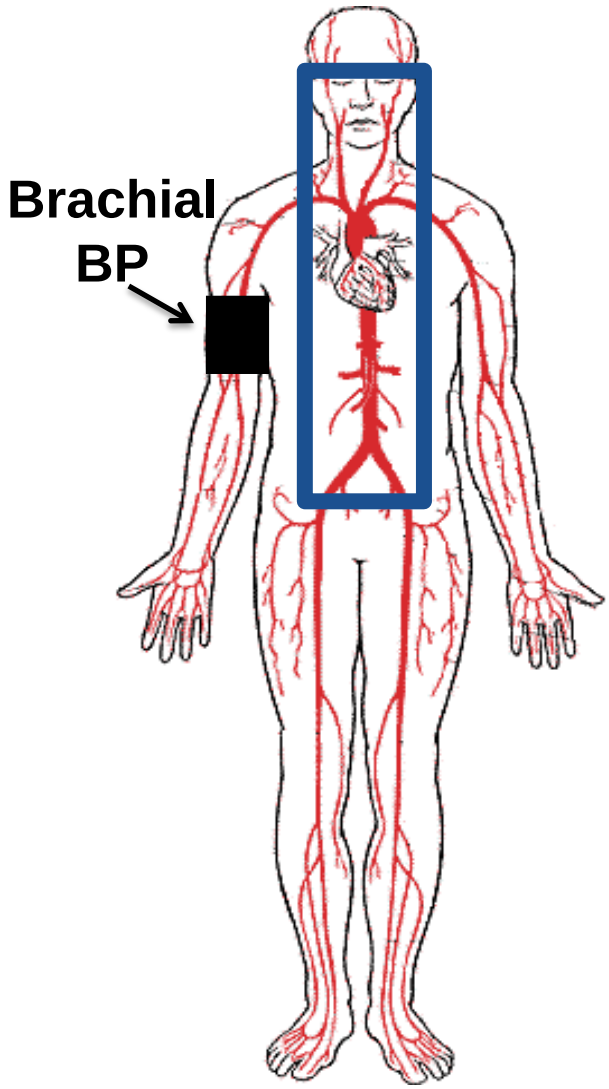
Haemodynamics and renal function

High blood pressure (BP) is associated with poor renal function and vice versa

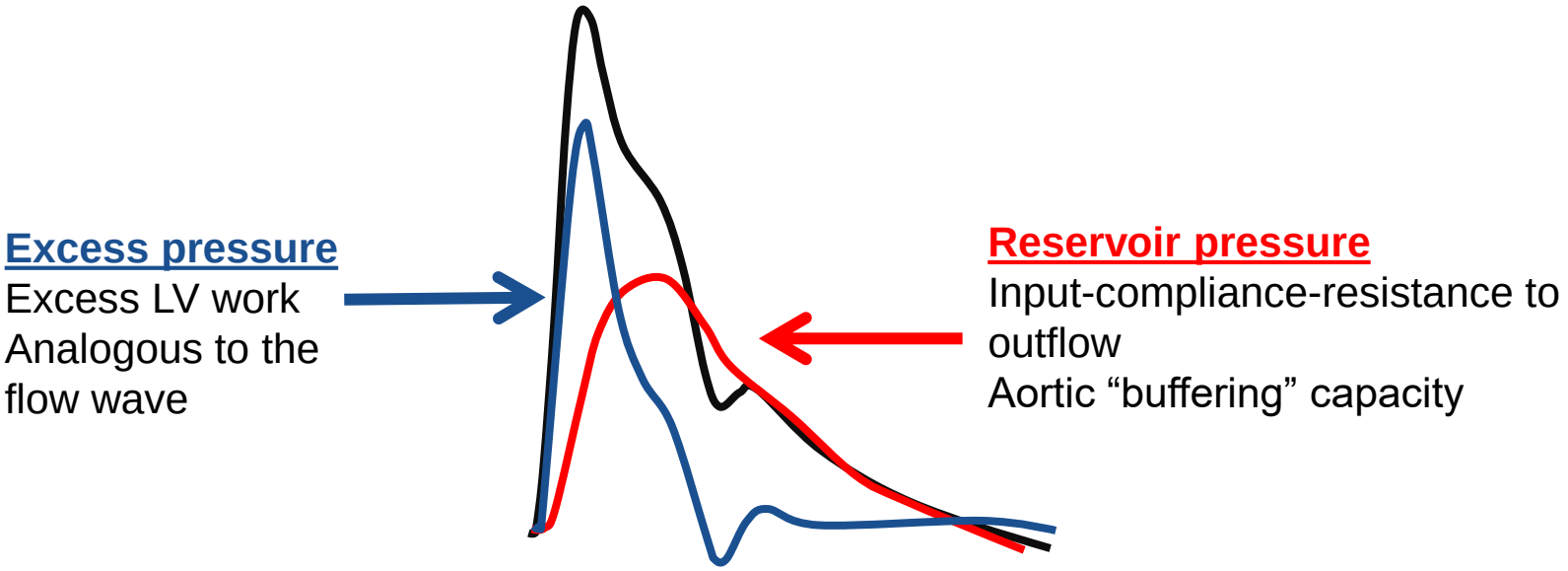
Renal function may be more closely related central haemodynamics (including central BP)

- Central BP indices[1] are associated with renal function.



[1]Safar ME et al. Hypertension 2002; 39: 735-738

Reservoir-excess pressure paradigm



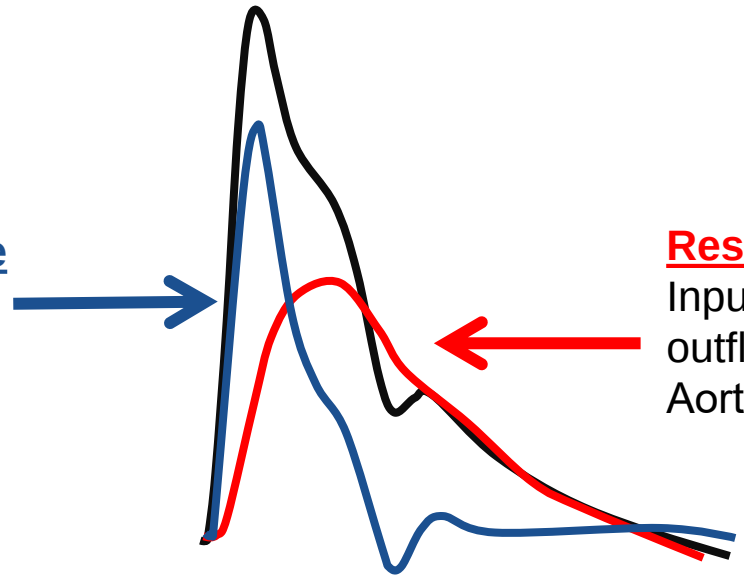
Physiologically plausible

- Describe age- and exercise- related changes in central BP (invasive pressure and flow velocity)[1, 2]
- Theoretical principles supported by in vivo human study[3]

[1]Davies et al. Am J Physiol Heart Circ 2009; 298:H580-6
[2]Schultz et al. Hypertension 2013; 62: 175-82
[3]Schultz et al. ATVB 2014; 34: 1597-603

Reservoir-excess pressure paradigm

Excess pressure
Excess LV work
Analogous to the flow wave



Reservoir pressure
Input-compliance-resistance to outflow
Aortic “buffering” capacity

Clinically relevant

- Cardiovascular events and mortality[1-4]
- Grey matter atrophy[5]
- Exercise induced albuminuria[6]

[1]Davies JE et al. Hypertension 2014; 64: 60-68
[2]Hametner et al. Int J Cardiol 2013; 15: 171(1): 31-6
[3]Narayan et al. Hypertension 2015; 65: 629-35
[4]Cheng et al. Int J Cardiol 2016; 215: 338-95

[5]Climie RE et al. Cadiovasc Diabetol 2014; 13: 143
[6]Climie RE et al. Am J Physiol Heart Circ 2015; 308: H1136-42

To our knowledge no studies have examined the
longitudinal changes in reservoir characteristics
and the association of these changes with **renal function**.

Aim and Hypothesis

AIM

To determine the association between the change in aortic reservoir characteristics and the change in renal function in healthy individuals

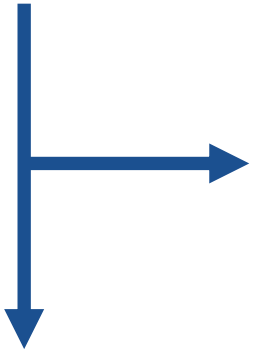
HYPOTHESIS

The change in aortic reservoir characteristics will be associated with the change in renal function

Flow of study participants

Powered for exercise haemodynamics[1]

Baseline
(January to December 2011)
n=40



Lost to follow up n=6
Moved interstate n=1

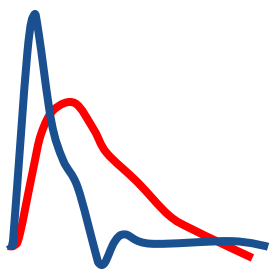
Follow up
(June to November 2014)
n=33
Mean follow up time (3.0±0.3 years)

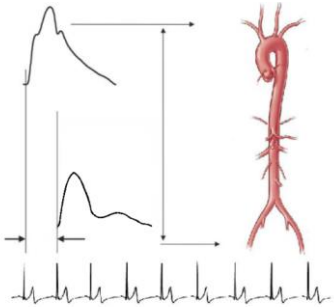
<u>Exclusion criteria</u>
A clinical history of cardiovascular disease or severe pulmonary disease
Arrhythmia
Pregnancy

1. Holland D et al, Am J Hypertens 2008, 21:1100–1106.

Study Protocol

Visit 1

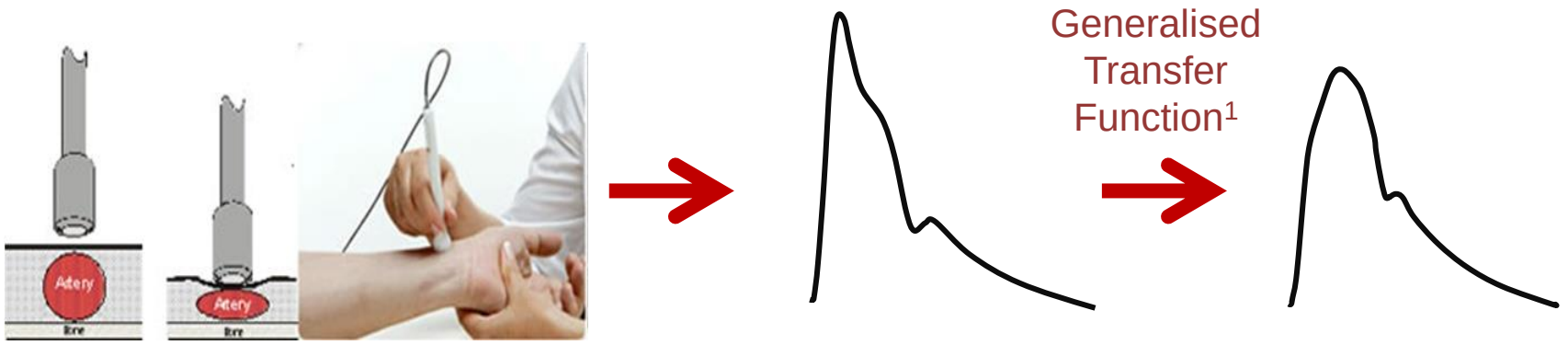




Within in 10 days

Visit 2

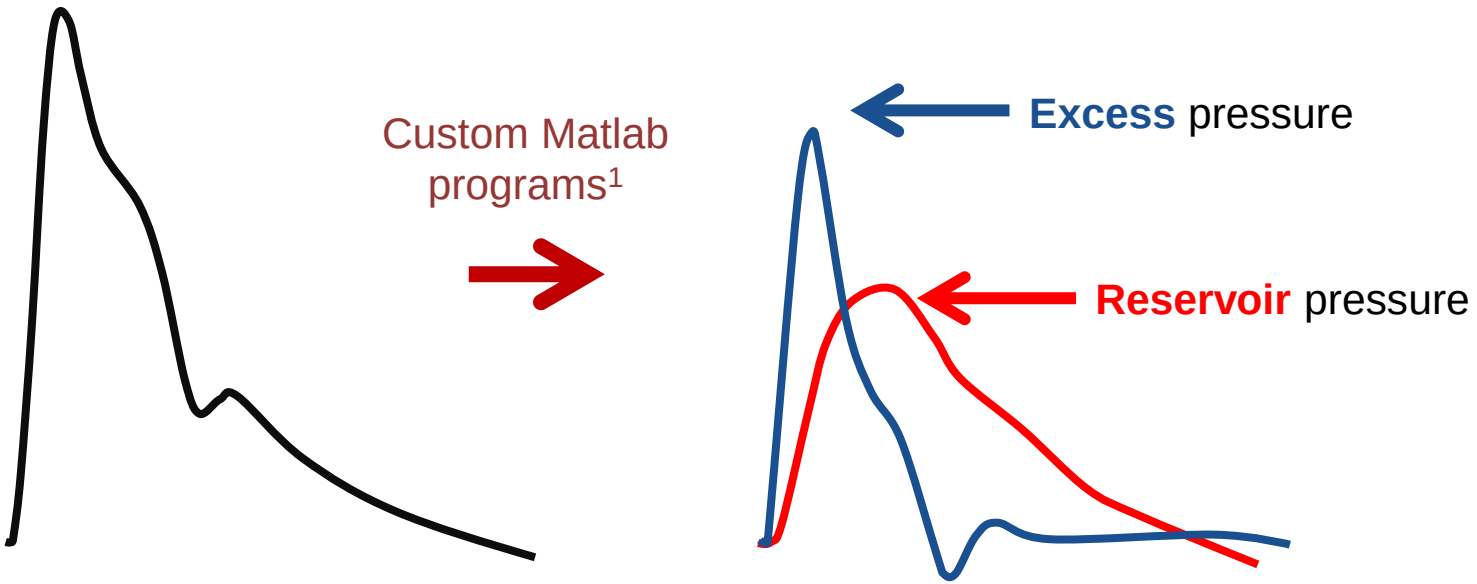
Central blood pressure



Radial waveform calibrated with brachial cuff systolic and diastolic BP

1. Sharman JE et al. *Hypertension* 2006; 47: 2103-1208

Reservoir characteristics



Radial waveforms ensemble averaged

Reservoir pressure derived based on previous equations

Excess pressure = total measured pressure wave – reservoir pressure

1.Davies JE et al. Hypertension 2014; 64: 60-68

Participant Characteristics (n=33)

	Baseline	Follow up	Change	P Value
Age (years)	54±9	57±9	3±0	<0.001
Body mass index (kg/m^2)	25.3±3.5	25.3±3.8	-0.02±1.4	0.95
Daytime systolic BP (mmHg)	136±14	137±13	1±10	0.56
In-clinic systolic BP (mmHg)	115±9	119±13	5±11	0.017
Current smoker, n (%)	2 (6)	1 (3)	-1 (3)	0.99

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Current smoker, n (%)	2 (6)	1 (3)	-1 (3)	0.99
Glucose (mmol/L)	4.7±0.4	5.1±0.5	0.4±0.5	<0.001
Insulin (IU/mL)	2.5±4.7	9.2±8.9	6.8±6.1	<0.001
Total cholesterol (mmol/L)	5.5±1.1	5.6±1.1	0.06±1.0	0.75

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Total cholesterol (mmol/L)	5.5±1.1	5.6±1.1	0.06±1.0	0.75
eGFR (mL/min/1.73m^2)	107.8±4.0	98.9±3.4	-8.85±2.2	<0.001

The change in reservoir characteristics

	Baseline	Follow up	Change	P Value
Reservoir pressure integral (Pa.s)	11126±1729	11229±1555	103±1649	0.73
Excess pressure integral (Pa.s)	451±104	519±180	67±154	**0.022**

The change in reservoir characteristics

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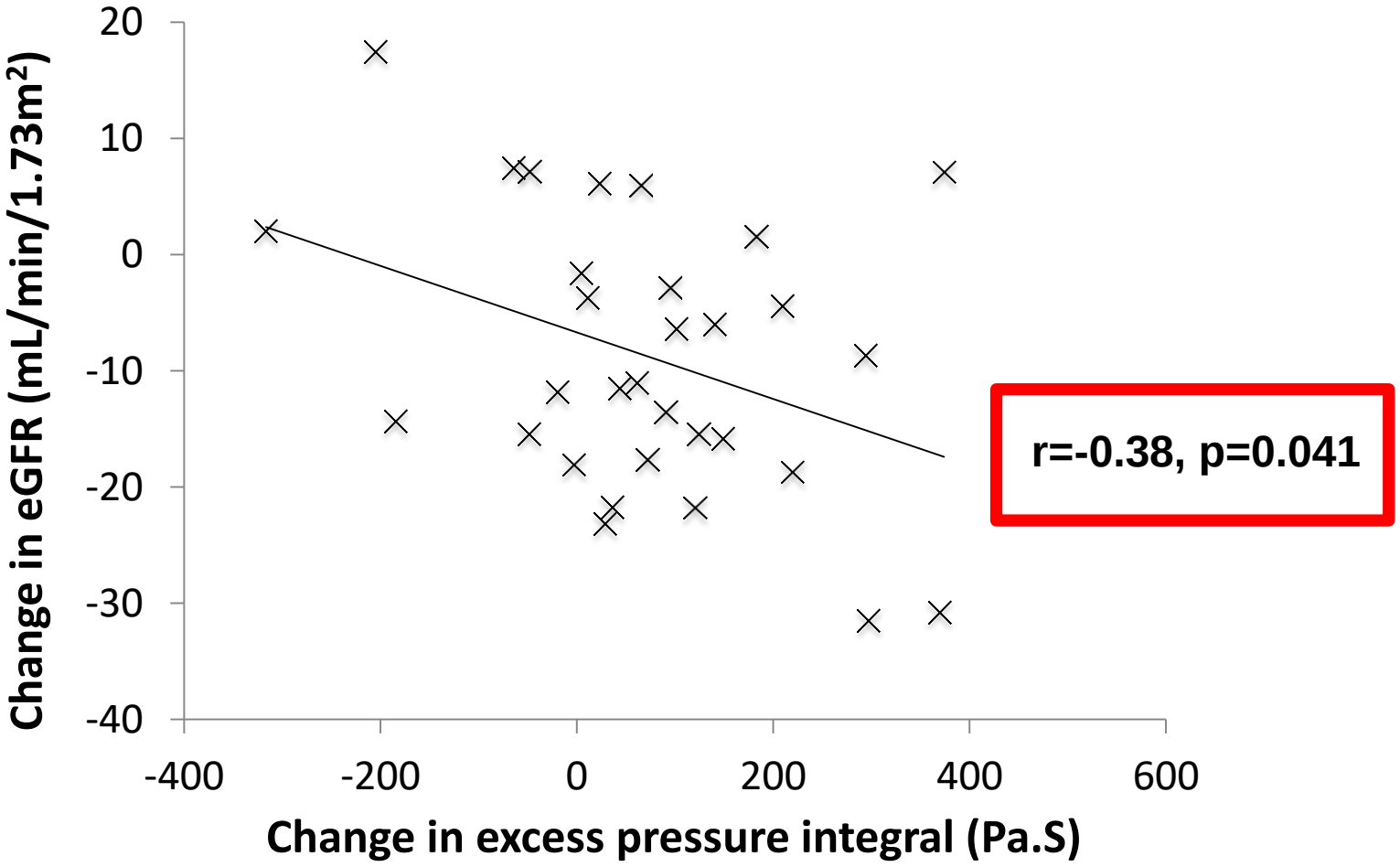
Other central haemodynamics				
Central systolic BP (mmHg)	103±10	108±14	6±10	**0.003**
Central pulse pressure (mmHg)	37±5	42±9	5±6	**<0.001**
Augmented pressure (mmHg)	8±5	12±7	4±4	**<0.001**
Augmentation index (%)	21±11	27±11	6±7	**<0.001**
Aortic PWV (m/s)	6.5±1.4	7.3±1.2	0.9±1.3	**0.001**

Association of change in excess pressure and change in renal function

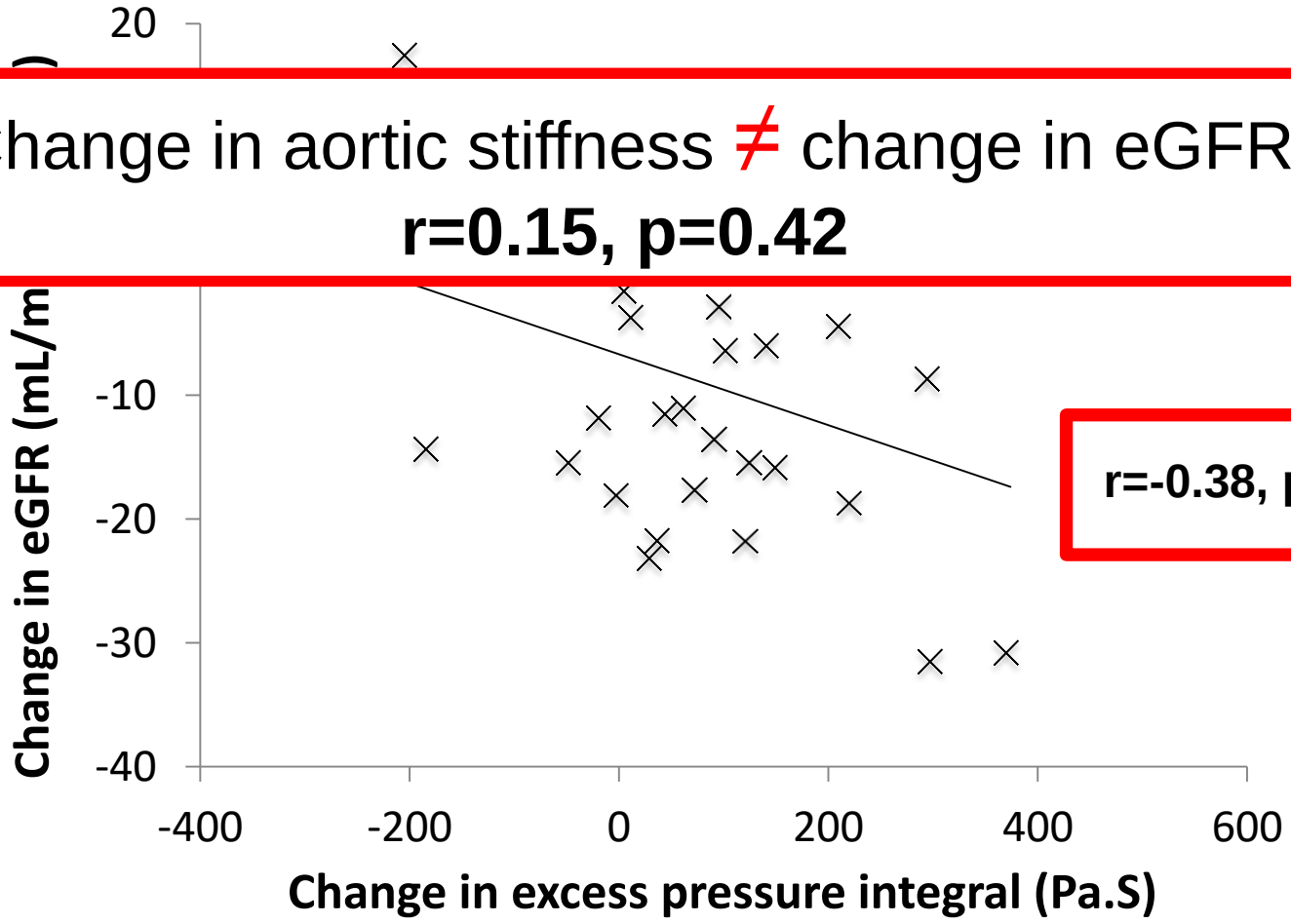


Independent of age at follow up, change in BMI and ambulatory daytime systolic BP (β =-0.03, p=0.046)

Association of change in excess pressure and change in renal function

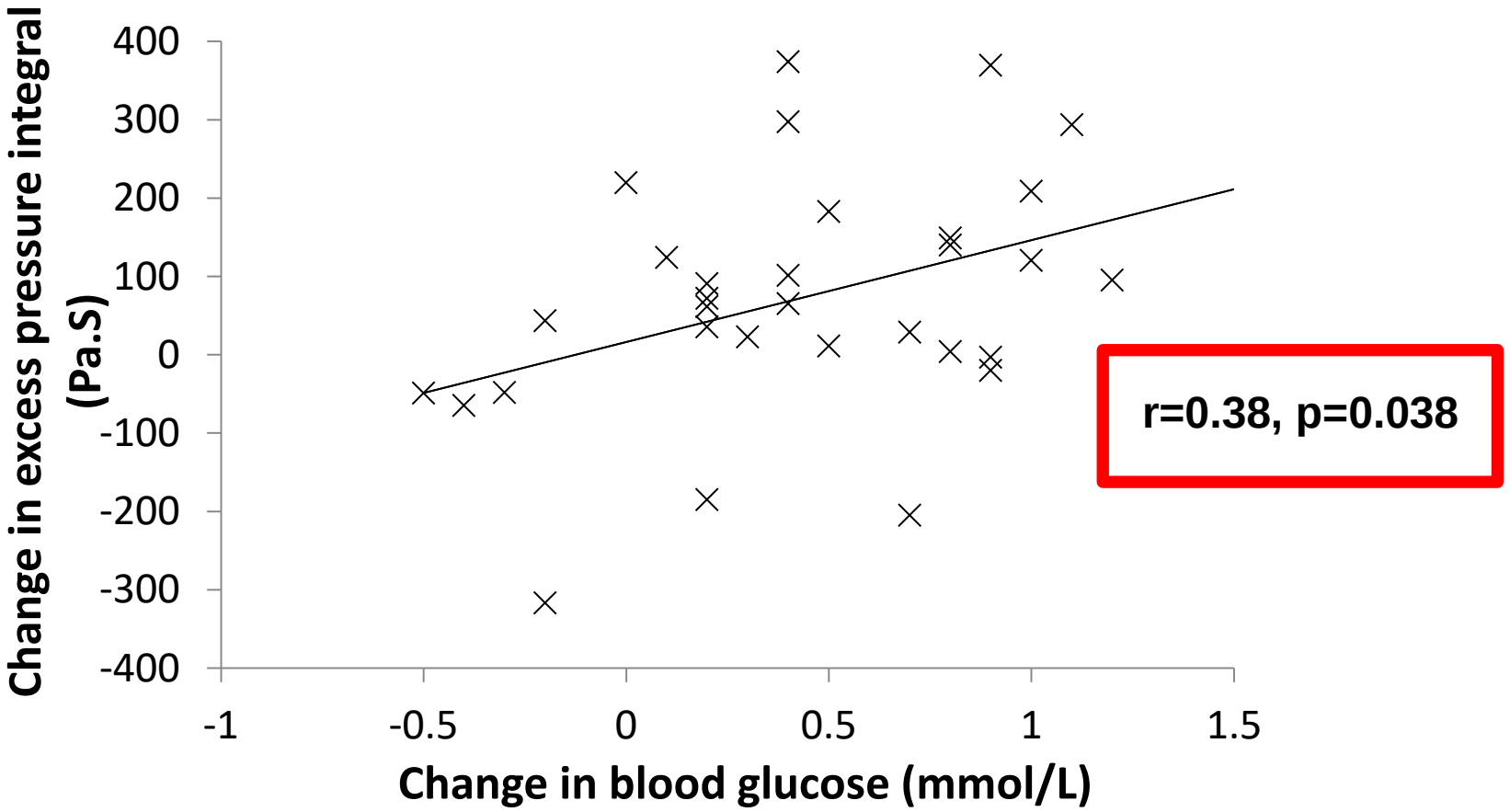
Change in aortic stiffness ≠ change in eGFR

r=0.15, p=0.42



Independent of **hypertension status (ambulatory daytime systolic BP≥135/85 and/or using antihypertensives)** (β =-0.03, p=0.020)

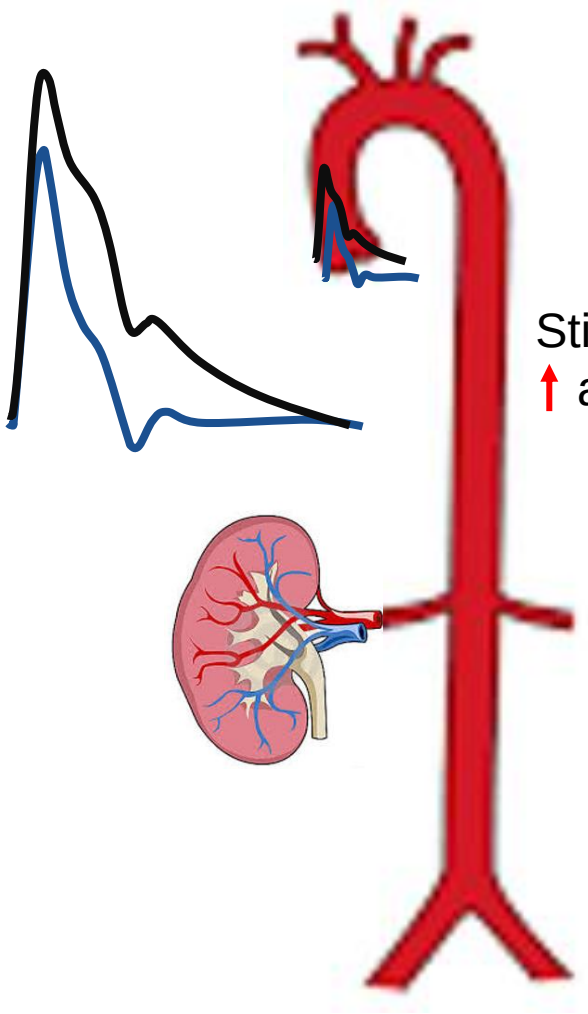
Association of change in glucose and change in excess pressure



- Independent of age at follow up, change in BMI, 24 hour daytime systolic BP (β =140.33, p=0.035).
- No significant interaction (p>0.05 for product term).
- The addition of glucose did not alter the relationship between excess pressure and eGFR but it did render it borderline significant (p=0.057).

Potential mechanism of kidney damage

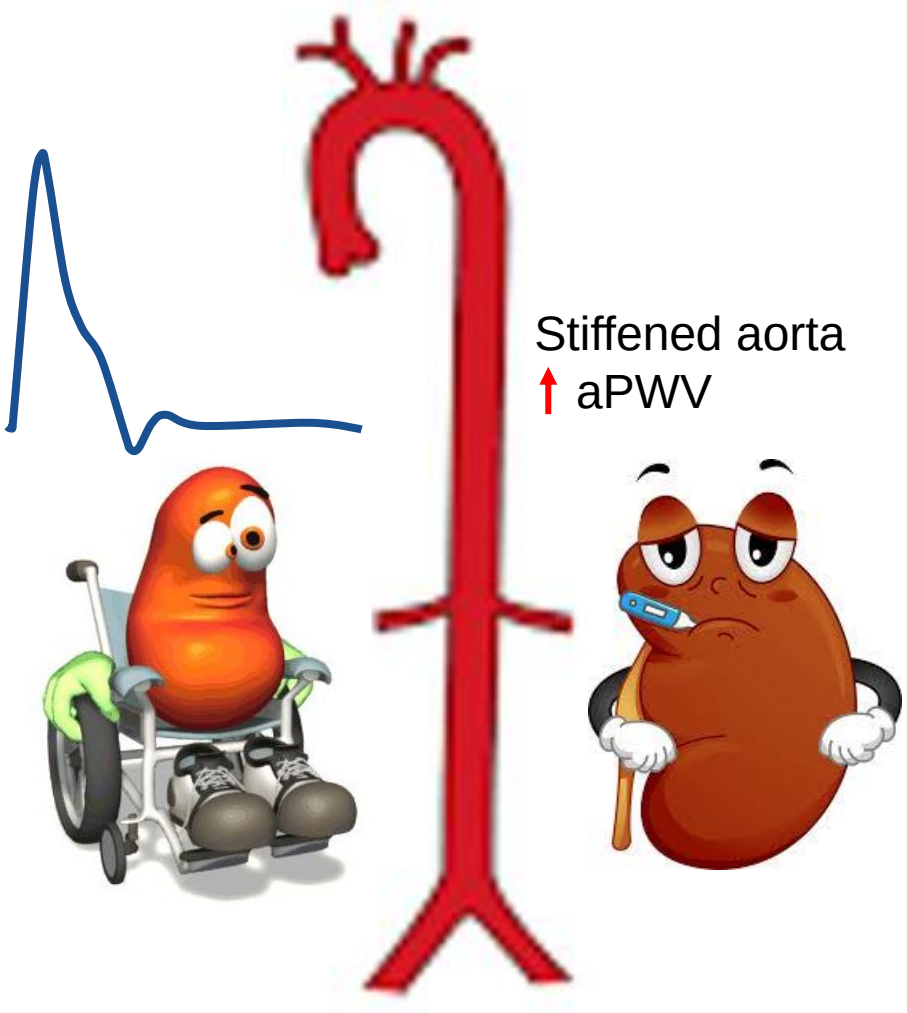
↑ **Pressure /**
Excess pressure



Stiffened aorta
↑ aPWV

Potential mechanism of kidney damage

↑ **Excess pressure**



Stiffened aorta
↑ aPWV

Conclusions

- First longitudinal pilot data of reservoir characteristics
- Excess pressure is associated with a decline in renal function among healthy people over a 3 year follow up period

Larger cohort, with more detailed analysis of metabolic and haemodynamic changes is required

Thank you

Diabetes Australia Research Trust

Study participants

ARTERY Society travel grant