

TElmisartan in the management of abDominal aortic aneurysm (TEDY) trial

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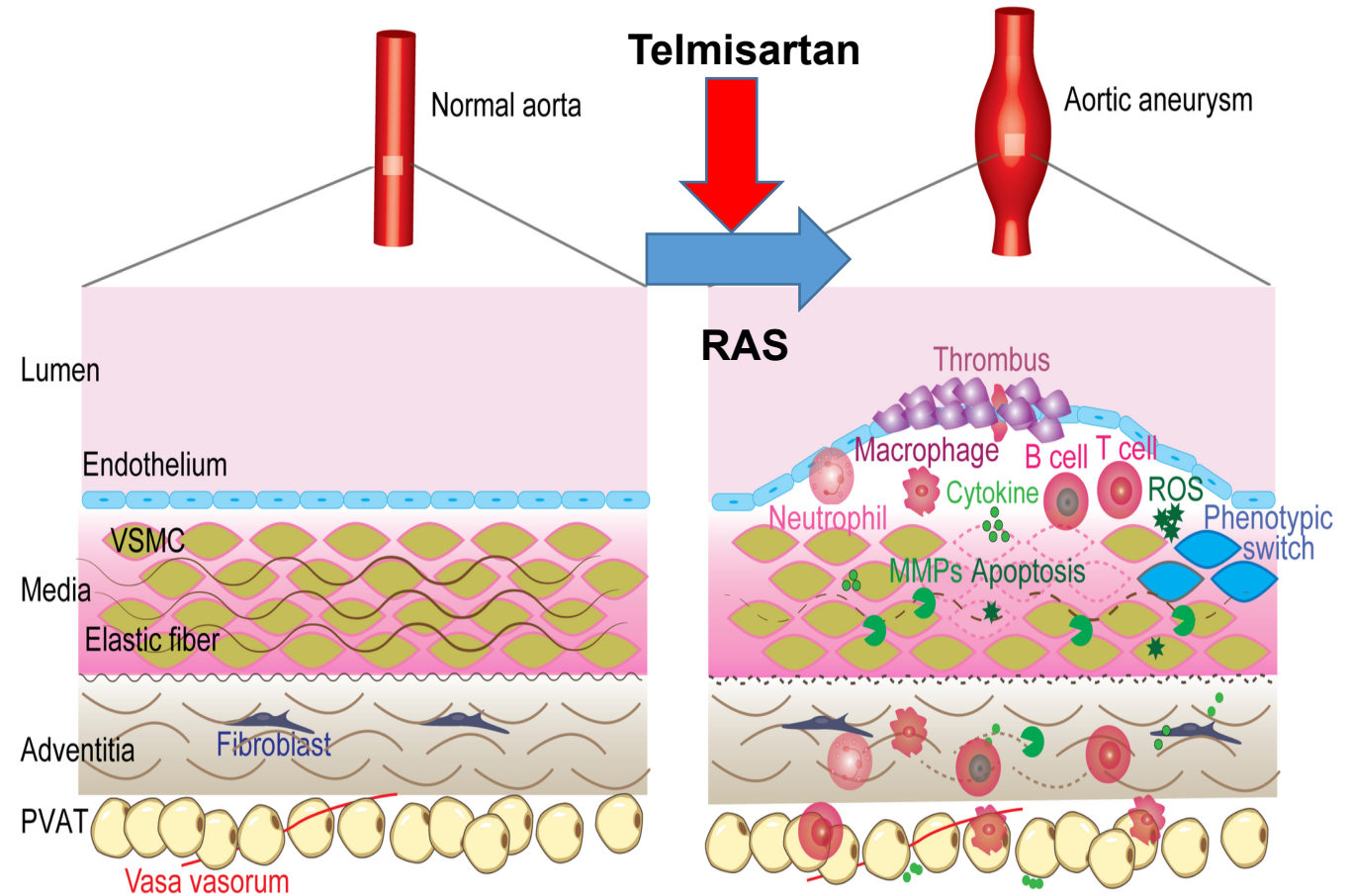


Jason Jenkins



Main hypothesis: Telmisartan blocks aortic expansion

- Telmisartan (ARB) prevents ECM remodelling/ inflammation/ aortic expansion in four mouse model studies
- Telmisartan activates PPAR γ which is also reported to limit aortic expansion in mouse models & aortic inflammation in patients



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TEDY Methods

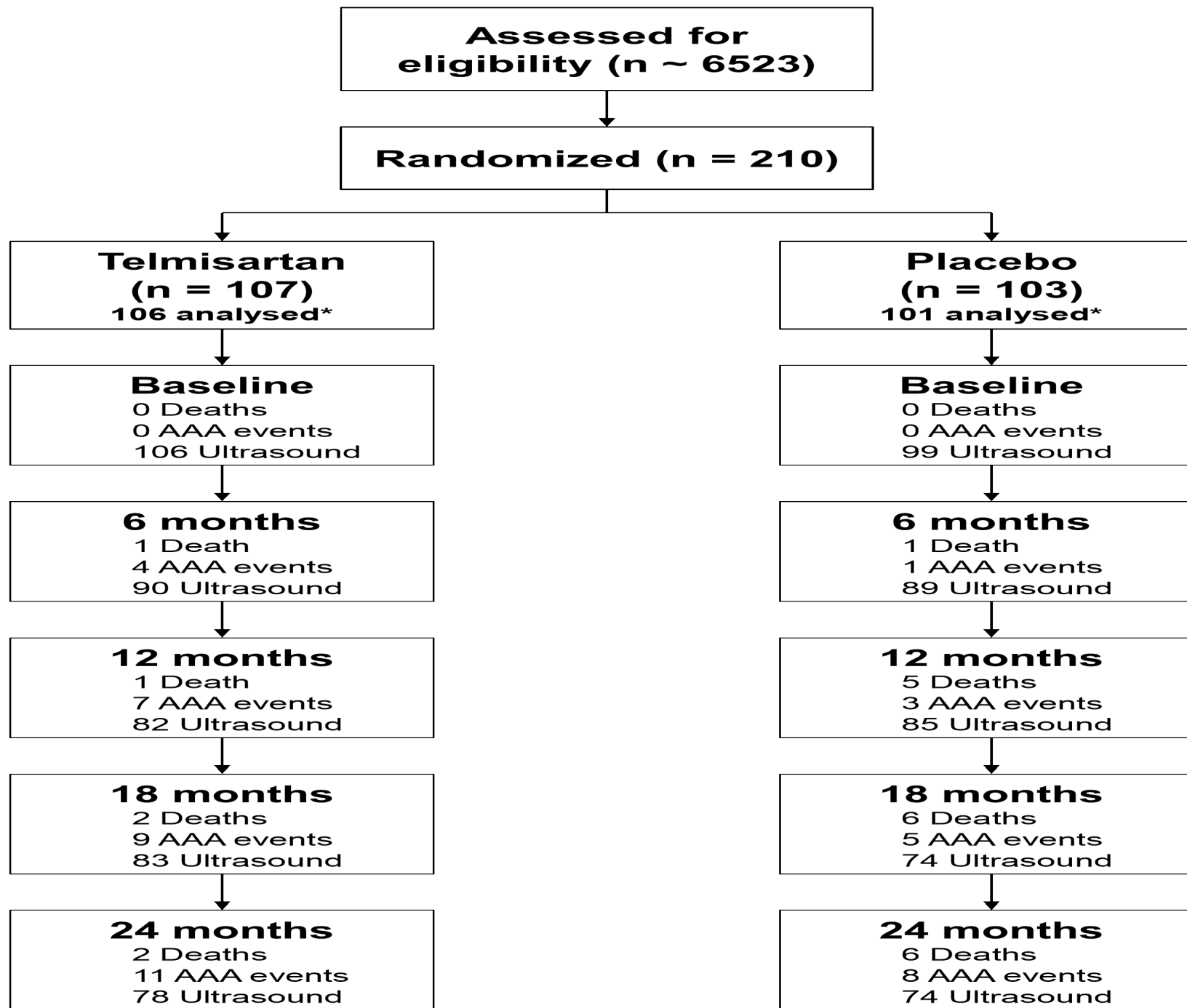
Hypothesis: 40 mg of telmisartan daily reduces AAA growth over 24 months

Design: Placebo-controlled parallel randomised trial

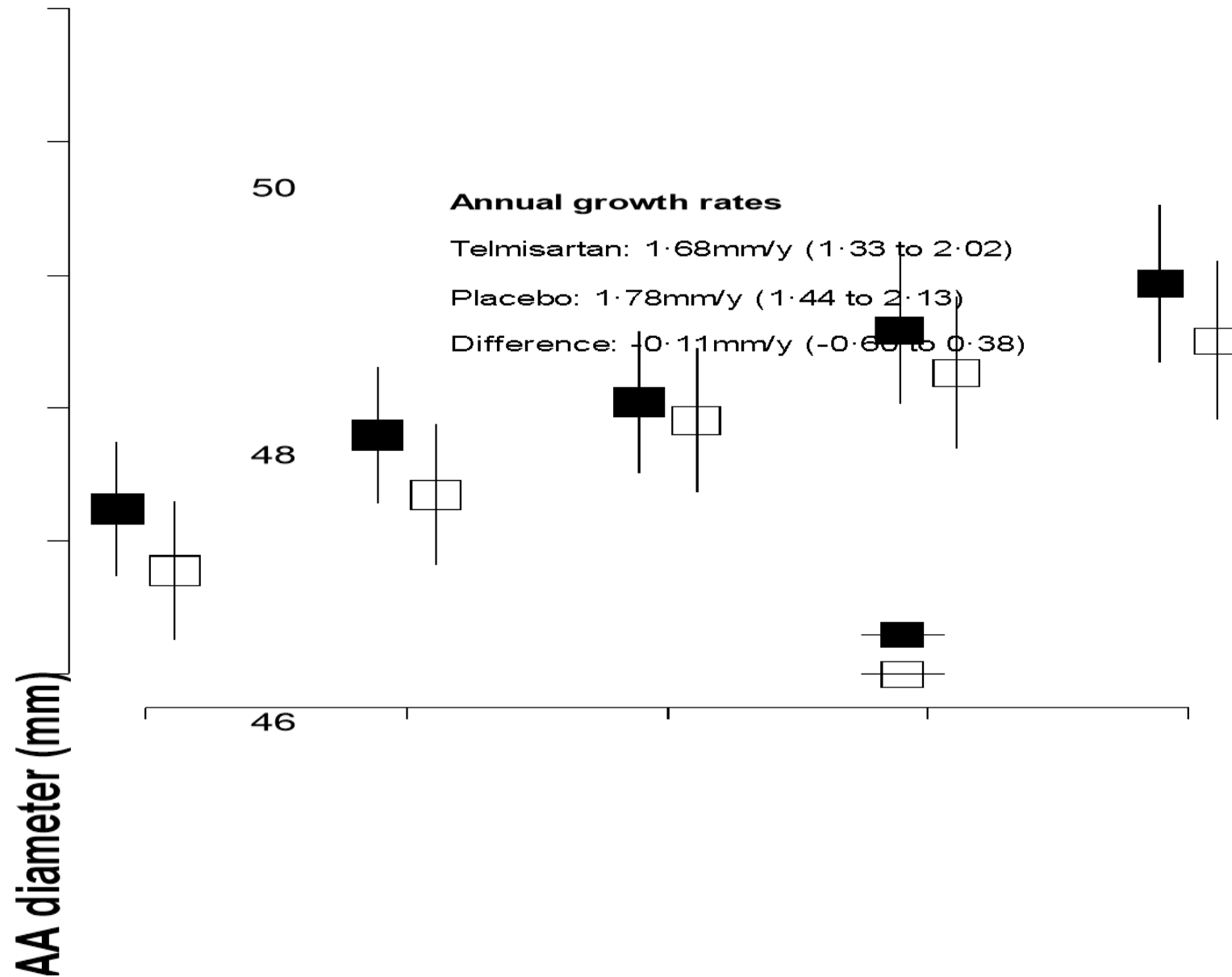
Primary outcome: Six monthly US images AP OTO diameter centrally read by single observer

Reproducibility coefficient 2.31, n=50

Secondary outcomes: CT orthogonal diameter & volume



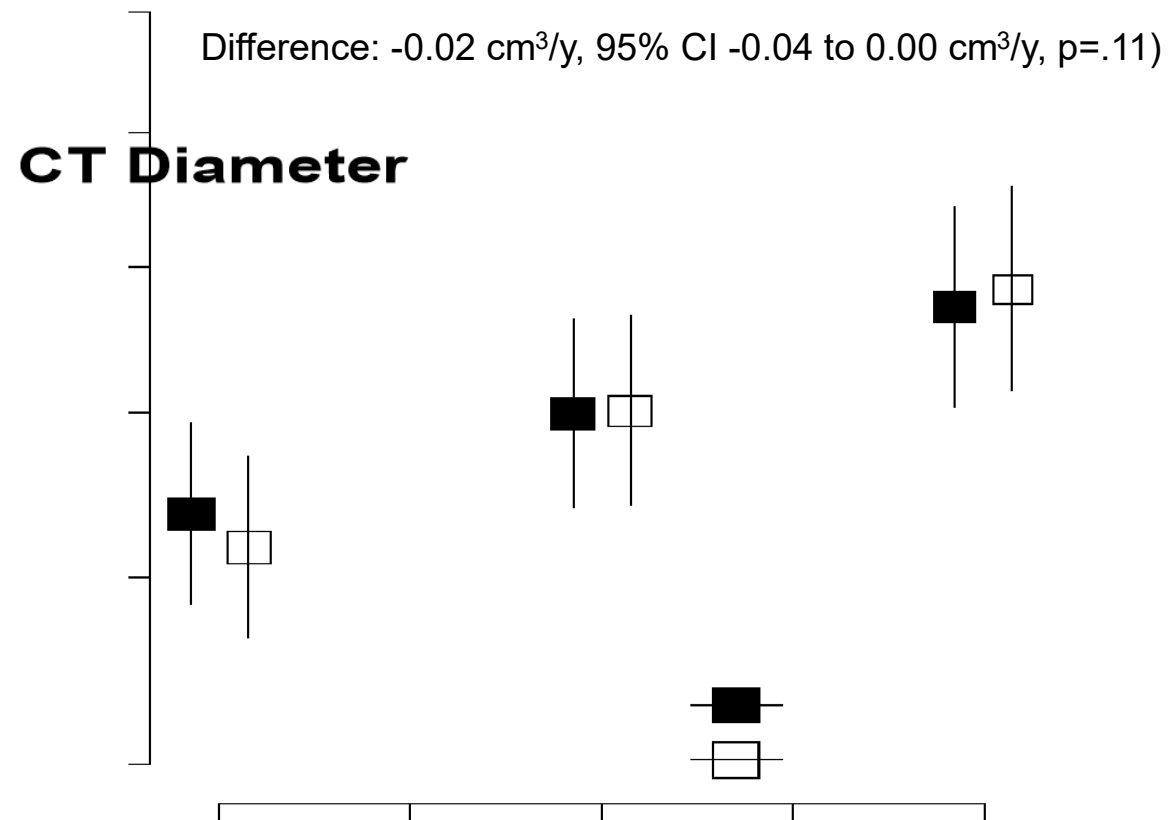
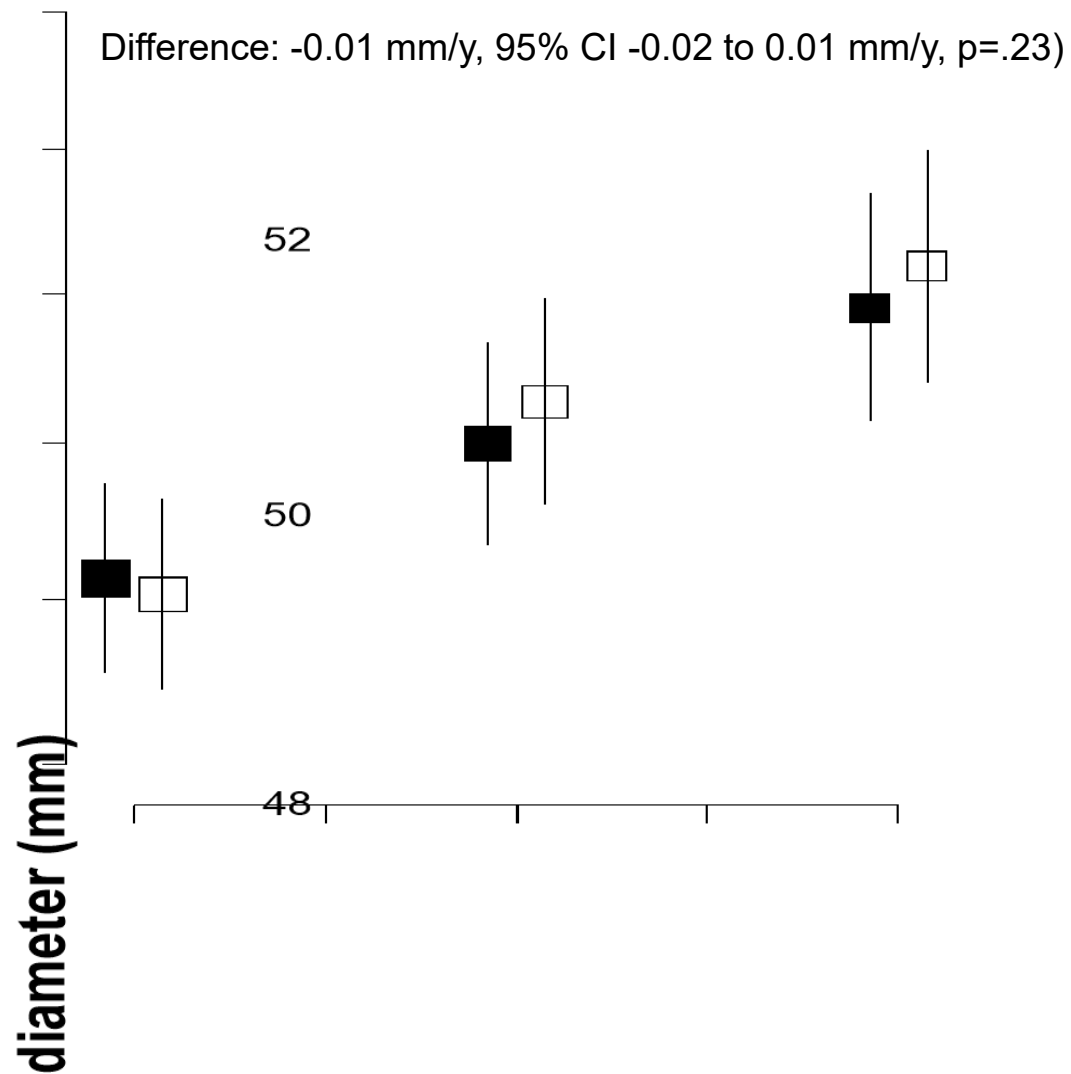
US-measured AAA growth



QRCPPD

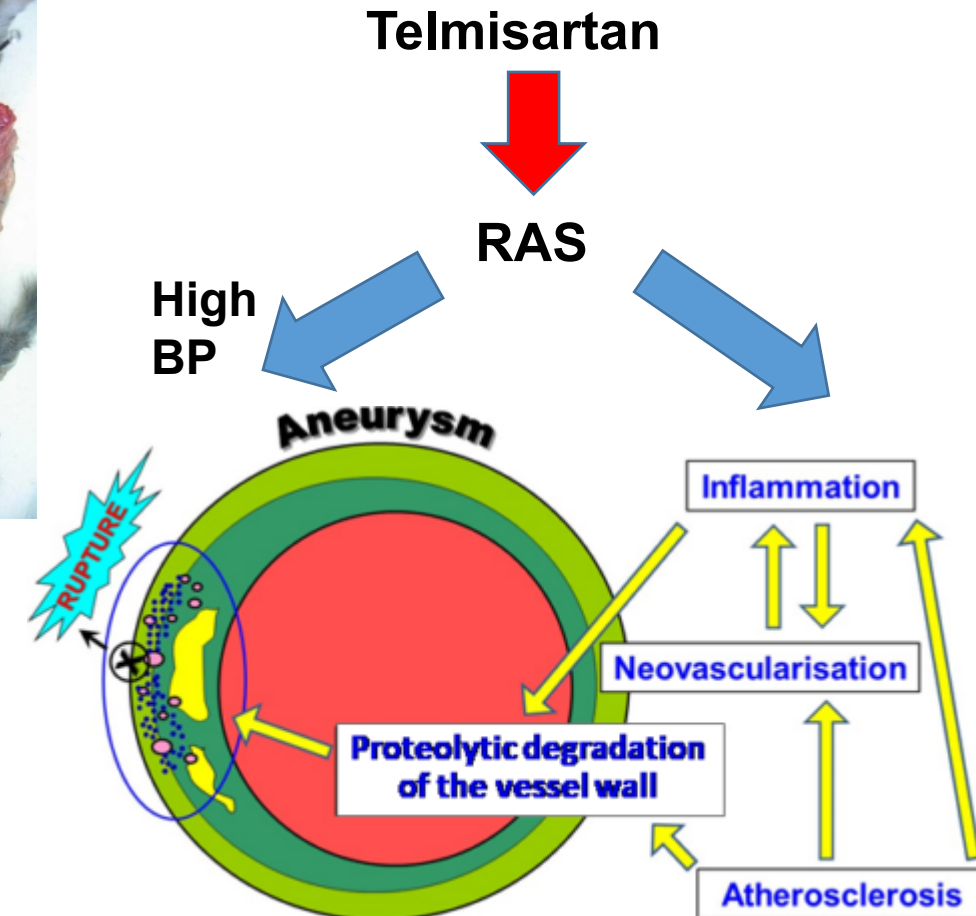
Queensland Research Centre for
Peripheral Vascular Disease

CT-measured AAA growth



Exploratory hypothesis: Telmisartan blocks aortic rupture

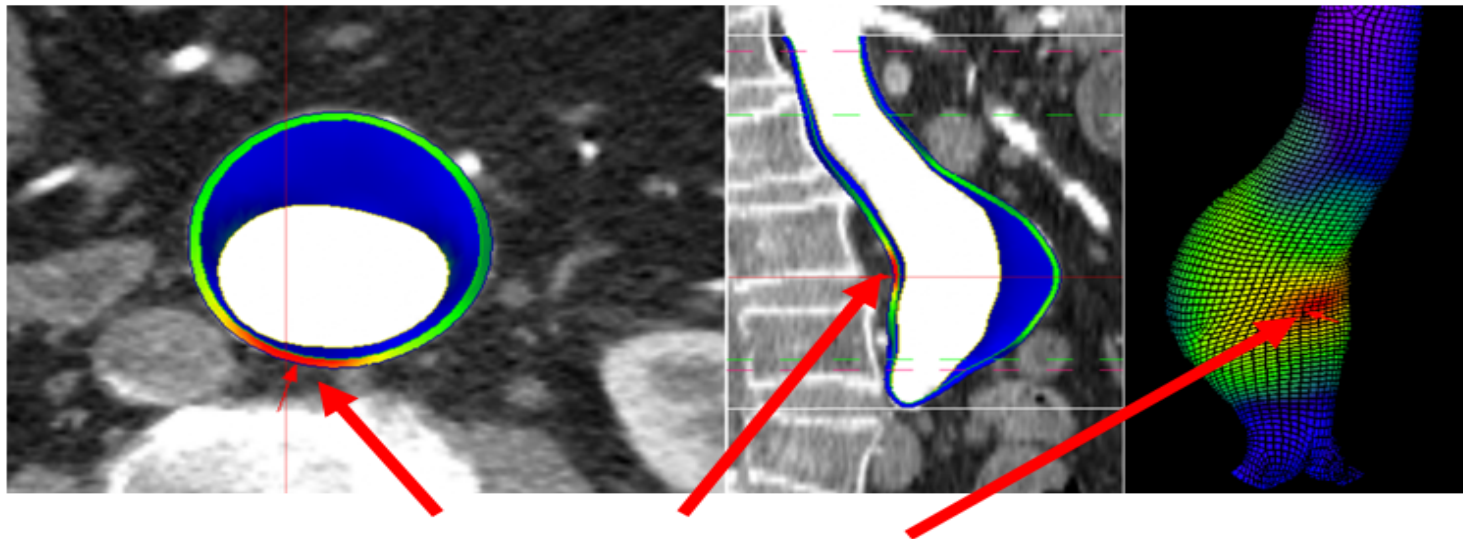
- High BP not associated with AAA growth but important risk factor for AAA rupture (HR 1.32, 95% CI 1.11, 1.56)
- Possible a drug may limit AAA rupture but not growth
- AngII infusion promotes aortic rupture
- Telmisartan limits AAA rupture in mouse models



Sweeting MJ, et al. Br J Surg. 2012;99(5):655-65.
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How to best measure AAA rupture risk

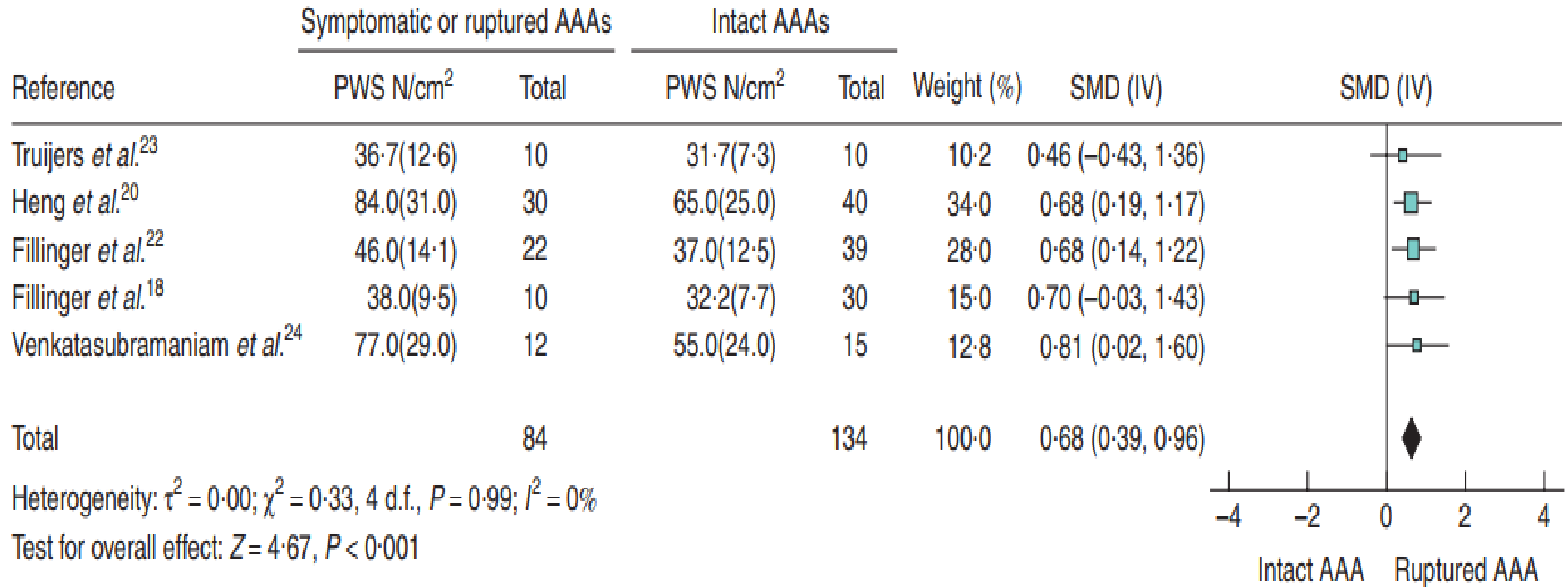
- Finite element analysis (FEA) can estimate the stress exerted on the AAA wall.
- Aortic peak wall stress (**PWS**)=**Maximum tensile stress** that arises in the AAA wall.
- Peak wall rupture index (**PWRI**)=Ratio between maximum **wall stress** and **wall strength**.



High wall stress

- Measured from CTA scans
- Semi-automated software (A4 Clinics)
- Limited engineering background required
- Can be performed <30min/scan.

PWS higher in ruptured compared to intact AAA

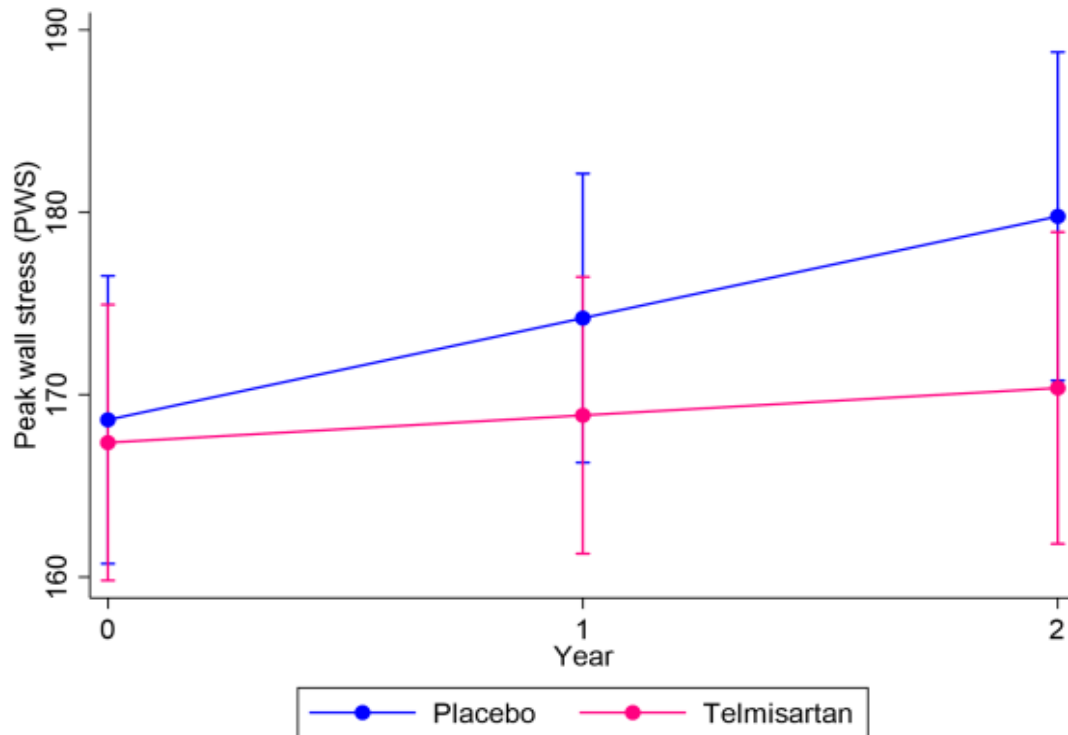


Sub-analysis of TEDY

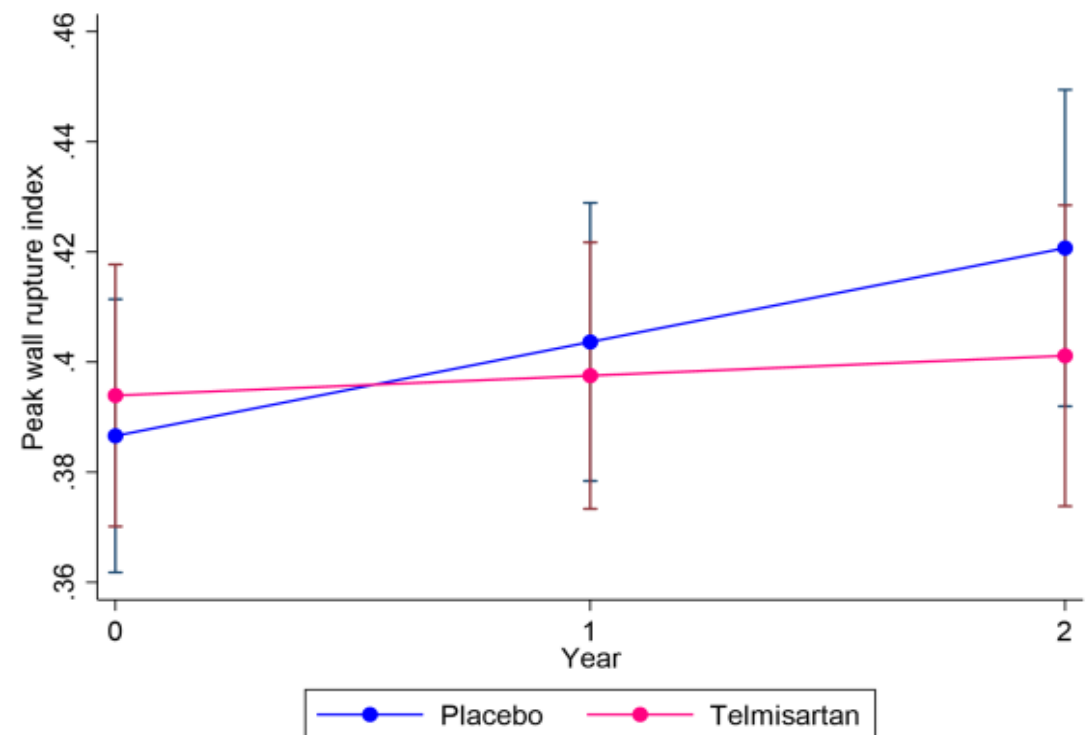
	Telmisartan (n=65)	Placebo (n=59)	P-value
Diameter (mm)	39.7 [37.2-43.6]	40.8 [36.6-43.0]	0.962
Age	73.7 [68.7-79.4]	75.3 [71.5-80.4]	0.155
Sex	56 (86)	53 (90)	0.531
Ever smoking	59 (91)	55 (93)	0.617
Hypertension	31 (48)	21 (36)	0.173
Dyslipidaemia	51 (78)	38 (64)	0.082
Diabetes	9 (14)	7 (12)	0.742
CVD	40 (62)	28 (47)	0.116
SBP (mmHg)	139 [125-147]	134 [125-150]	0.584
DBP (mmHg)	78 [72-85]	78 [70-85]	0.715

Telmisartan reduces increase in PWS/ PWRI

A



B



- Mean annual increases in PWS were **1.50 (95% CI -1.25, 4.25 kPa/ yr)** and **5.58 (95% CI 2.60, 8.56 kPa/ yr)**
- Mean annual increases in PWRI were **0.004 (95% CI -0.005, 0.012)** and **0.017 (95% CI 0.008, 0.026)/ yr.**
- Mean differences between groups were:
 - PWS : -4.08 (95% CI -8.13, -0.03 kPa/year) p=0.048
 - PWRI: -0.013 (95% CI -0.026, -0.001)/year p=0.033

Conclusions

- Telmisartan did not limit AAA growth
- A sub-analysis of TEDY suggested telmisartan limited increase in PWS and PWRI
- Interpretation: Telmisartan does not appear to limit AAA growth but could lower AAA rupture risk
- Limitations: Small sample size and exploratory analysis with negative primary outcome