Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Consulting Fees/Honoraria	• Abbott Ventures, Inc. • Ardelyx, Inc. • Boston Scientific, Inc. • Medtronic Vascular, Inc. • Rainbow Medical, Inc. • Nephera, Inc.
• Royalty Income	• Ardian, Inc.
• Ownership/Founder/Salary	• Cibiem, Inc. • Rox Medical, Inc.

Two Approaches to Hypertension

- Modify….
  - Regulation of the circulatory system
  - Physical properties of the circulatory system

Mechanical Means of Reducing BP

Create a Central (Iliac) Arterio-Venous Anastomosis

- Alter Cardiac output
  - Modify the efficiency of the heart
  - Reduce venous volume, and effective arterial volume
- Add Compliance into a Rigid Arterial Tree
- Reduce dynamic Vascular Resistance

Korsheed *et al*

Nephrol Dial Transplant (2011) 26: 3296–3302
doi: 10.1093/ndt/gfq851
Advance Access publication 11 February 2011

NDT
Nephrology Dialysis Transplantation

Original Articles

Effects of arteriovenous fistula formation on arterial stiffness and cardiovascular performance and function

Shvan Korsheed[1], Mohamed. T. Eldehni[1], Stephen G. John[1], Richard J. Fluck[1] and Christopher W. McIntyre[1,2]

Conclusions. AVF formation resulted in a sustained reduction in arterial stiffness and BP as well as an increase in LVEF. Overall, post-AVF adaptations might be characterized as potentially beneficial in these patients and supports the widespread use of native vascular access, including older or cardiovascular compromised individuals.

Central AV Anastomosis for the treatment of Hypertension
Proposed Mechanisms

Shunt via ROX Coupler

↓ renal hypoperfusion
→ ↓ sympatho-excitation
→ ↓ sodium and water retention

Venous oxygenation and increased pulmonary blood flow

Activation of pulmonary arterial mechanoreceptors

↓ SVR
↑ CO

↑ arterial compliance
↓ reflected pulse wave
↓ effective arterial volume
↑ tissue oxygen delivery
→ ↓ chemoreceptor activity
→ ↓ sympatho-excitation due to cerebral/renal hypoperfusion

Venous baroreceptor activation

↑ RAP
→ ANP release → vasodilatation
→ Bainbridge reflex
→ ↑ heart rate
→ peripheral sympatho-inhibition

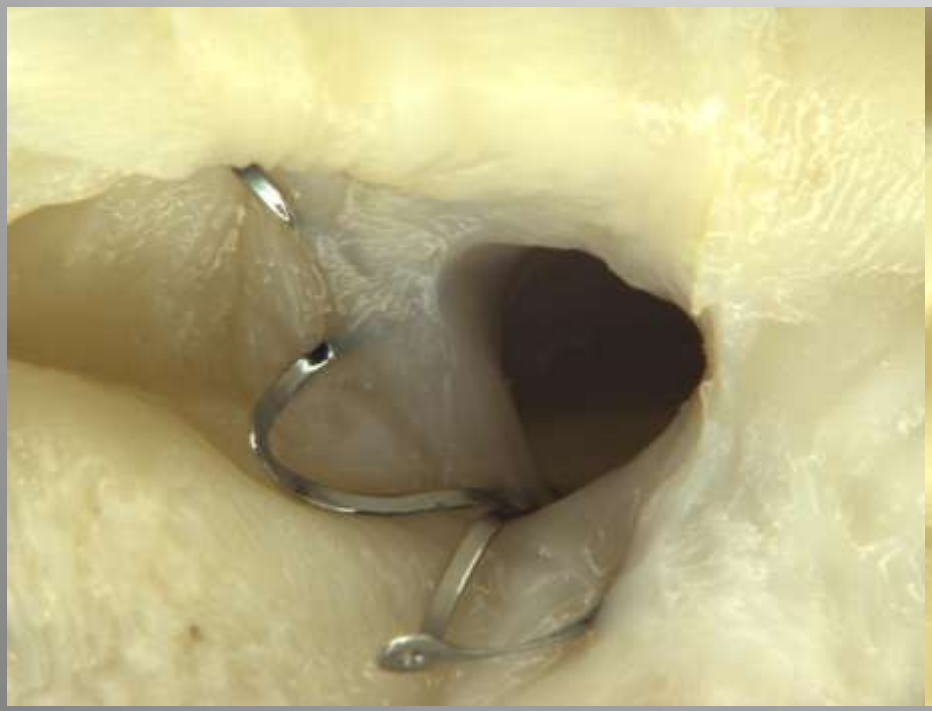
BP

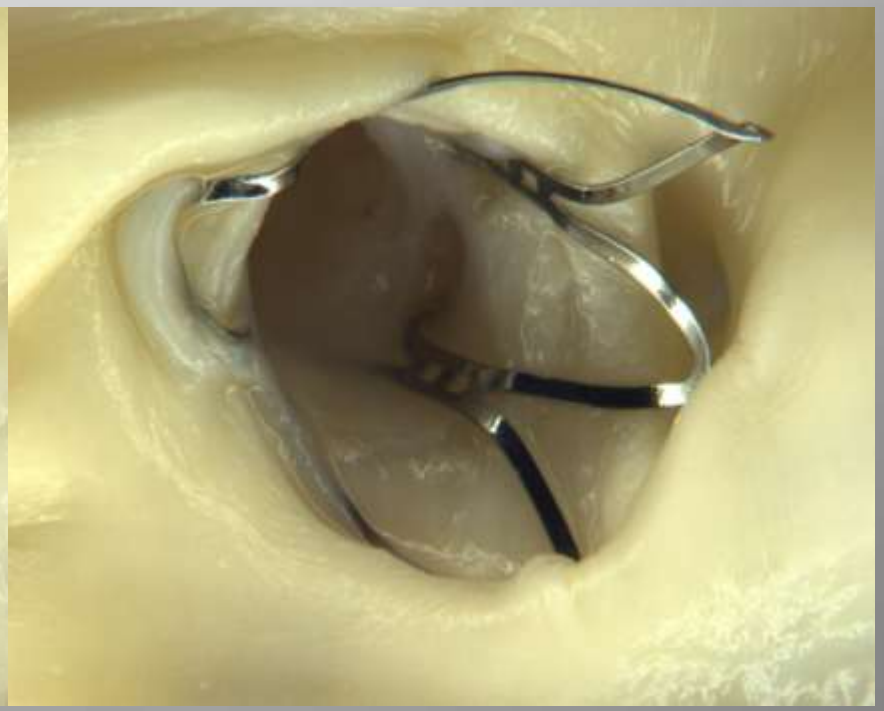
A. Burchell, M.Lobo, P. Sobotka, J. Paton. In Press

The ROX Coupler
Central A-V Anastomosis

ROX Coupler

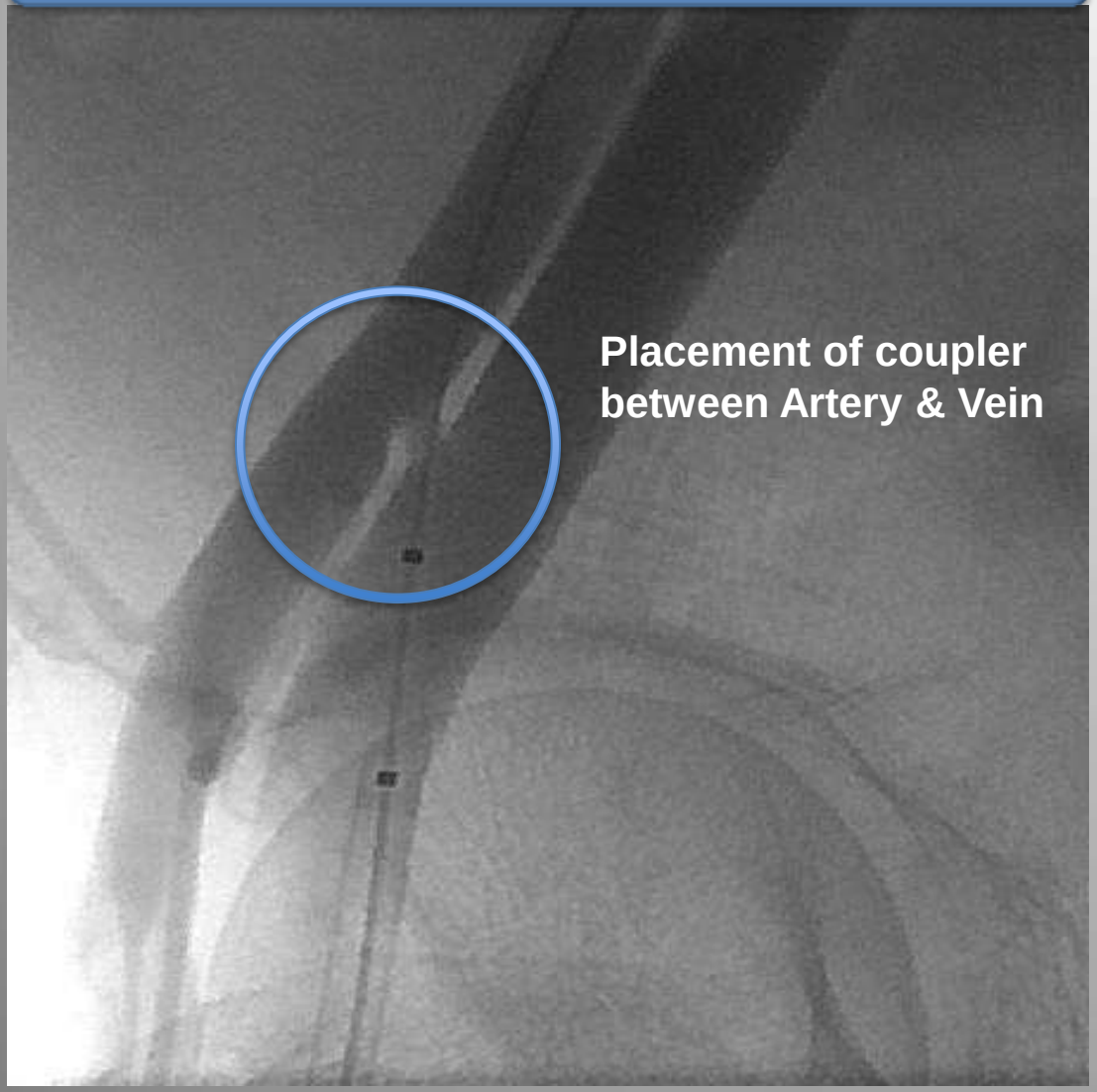
- Fixed Size A-V Anastomosis
- No Change in Size or Flow over time





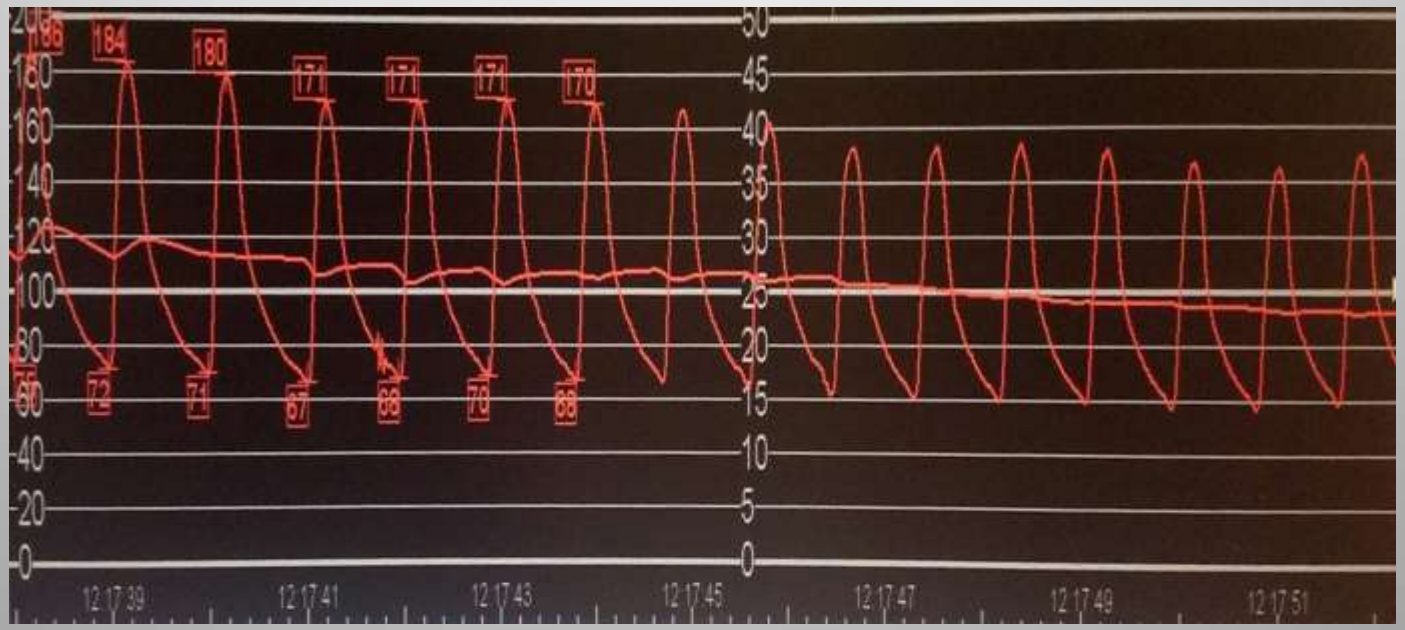
Immediately effective, Reversible Interventional Treatment for HTN
A unique solution for ISH?

Post - *FLOW* Procedure



- ✓ Femoral Arterial 4Fr & Venous 11Fr Access
- ✓ Create anastomosis between the iliac artery and iliac vein
- ✓ Lowers peripheral vascular resistance and restores compliance into the vascular system
- ✓ Under 1 hour procedure in standard cath lab
- ✓ No sedation required
- ✓ Procedure is **fully reversible** – retain all other treatment options

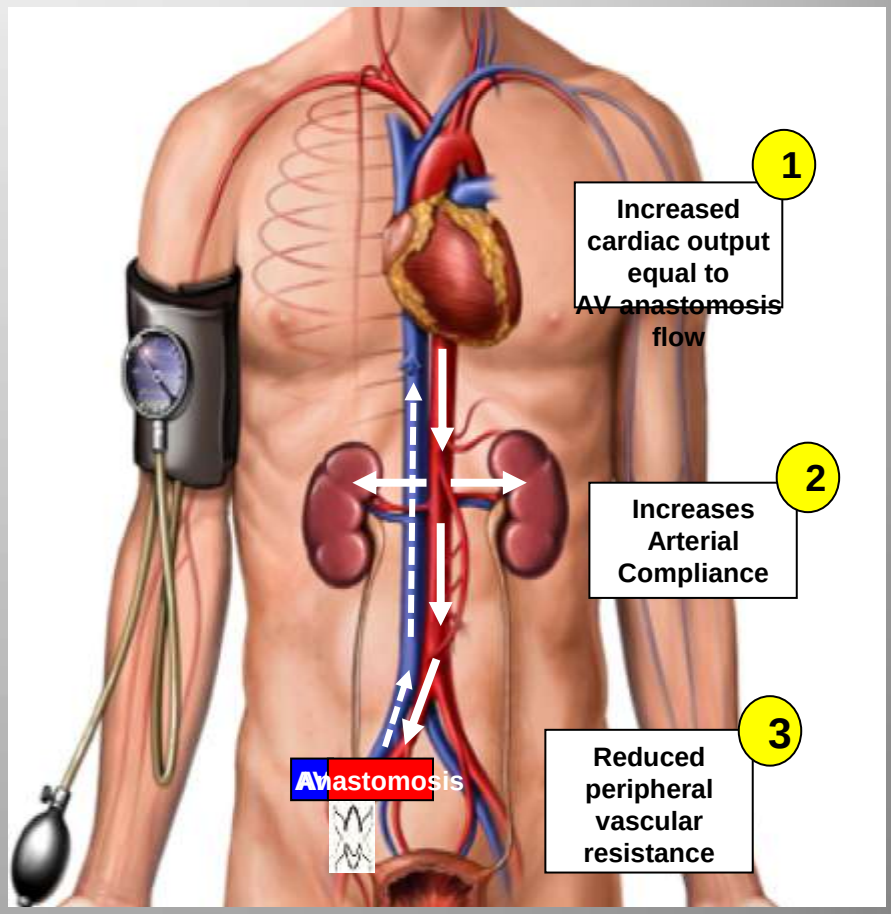
Immediate Reduction of BP



No SHAM effect
No Hawthorne effect
No Placebo effect
No Migration to Mean

Central AV Anastomosis to Treat HTN

- Impact on BP is Immediate
  - No sham/placebo effect
  - Patient/Clinician Satisfaction
- Only therapy addressing Compliance
- Treatment is Reversible
- Standard Cath Techniques Required

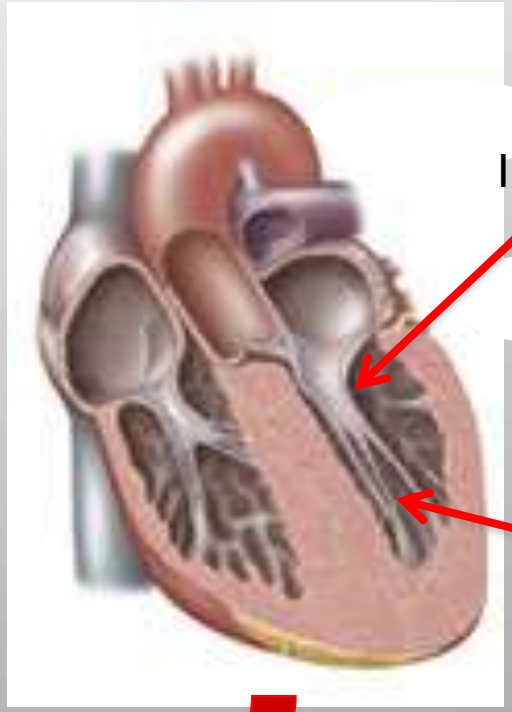


ROX Coupler HTN Experience

- Initial trials in COPD
  - Target to reduce pulmonary vascular resistance and improve the patient experience with end stage lung disease
- Revealed a predictable reduction in BP in patients with hypertension and no effect in normotensive patients

LVH Regression and Improved Diastolic Function

- Independently verified by two echo cardiologists
- Significant improvement in cardiac function post ROX procedure (n=5)



Improved left ventricular function (E'1 – E'0)

p=0.035

Improved diastolic function (E/A ratio)

p=0.047

Significant decrease in septal thickening

-2.90mm, p=0.007

Sofie Brouwers, et al. ESC 2012

Potential Issues

- Effects of chronically elevating Cardiac Output by <1l/m
  - High output failure only reported >3l/m
  - If PCWP rises, stent may be covered
- Turbulence and late venous stenosis
  - Clinically apparent with edema and loss of bp effect
  - Treatment: venous stent

URGENCY TO TREAT- REDUCE NOW!

Stroke
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association | American Stroke Association

Probability of stroke: a risk profile from the Framingham Study.

P A Wolf, R B D'Agostino, A J Belanger and W B Kannel

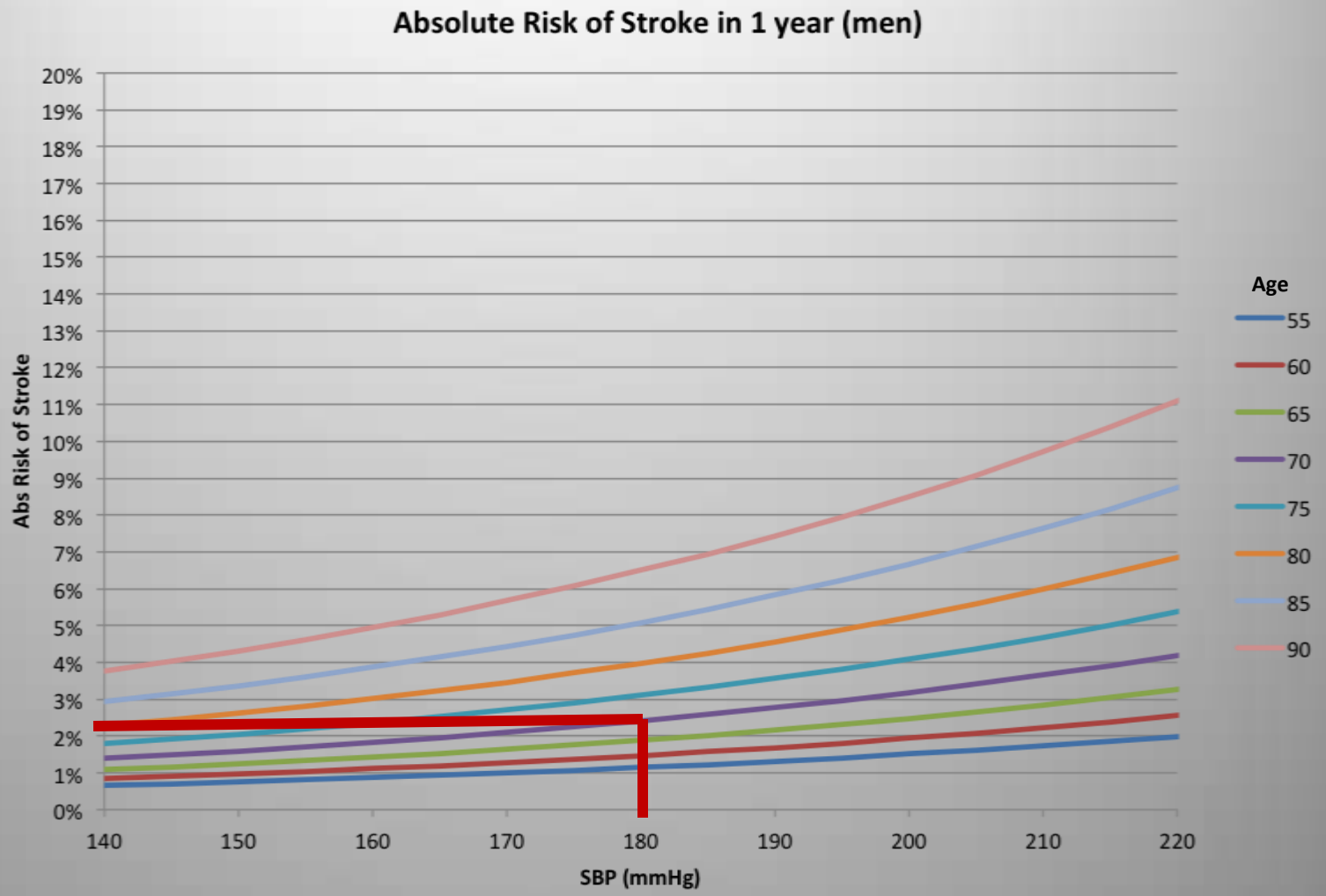
Stroke. 1991;22:312-318
doi: 10.1161/01.STR.22.3.312
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628

This model allows estimation of absolute risk of stroke at 1 year based on severity of hypertension

Example Patient A – Base Case with LVH

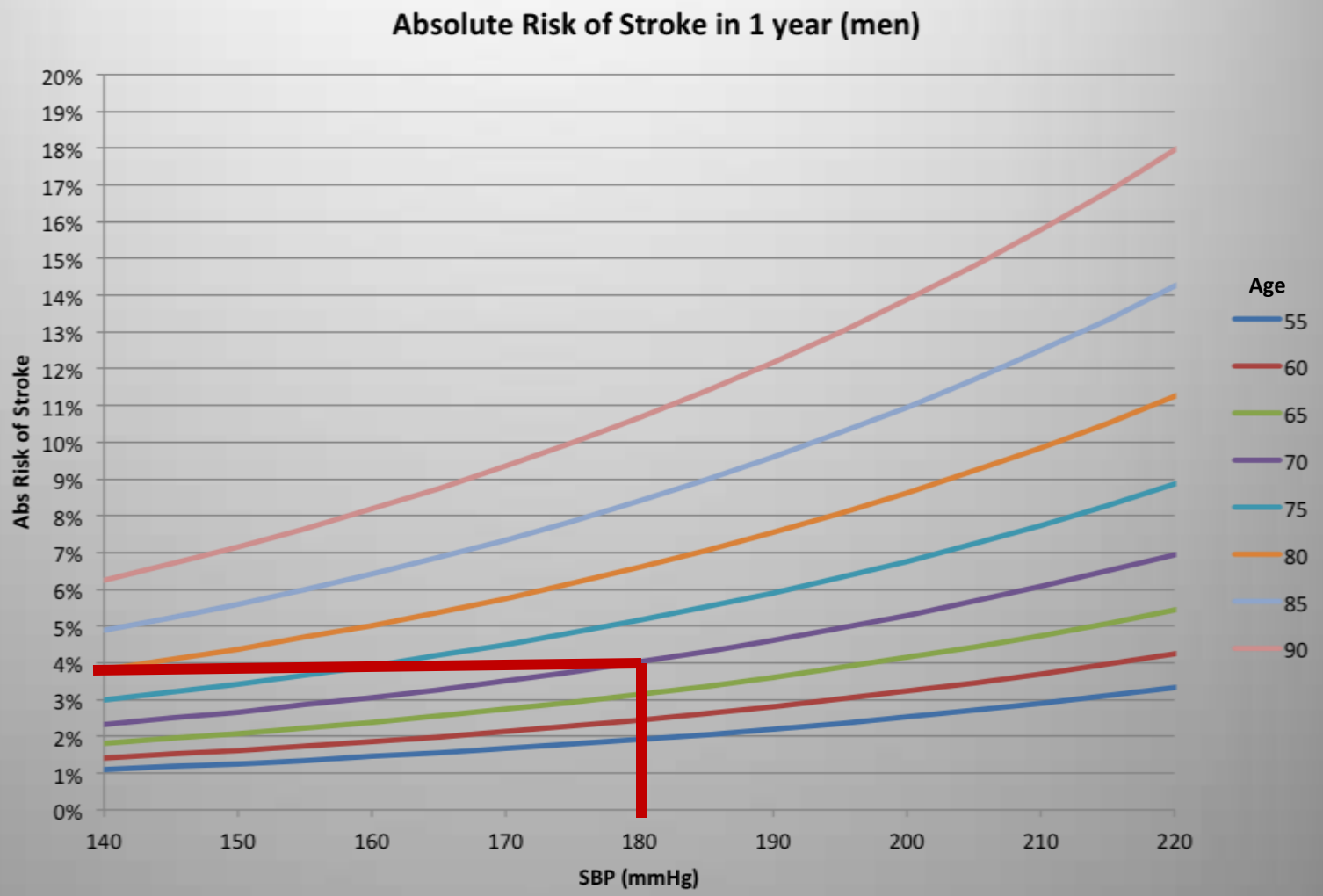
Hyp Rx	Yes
DM	No
Cigs	No
CVD	No
AF	No
LVH	Yes



Wolf et al 1991

Example Patient B – Add CVD

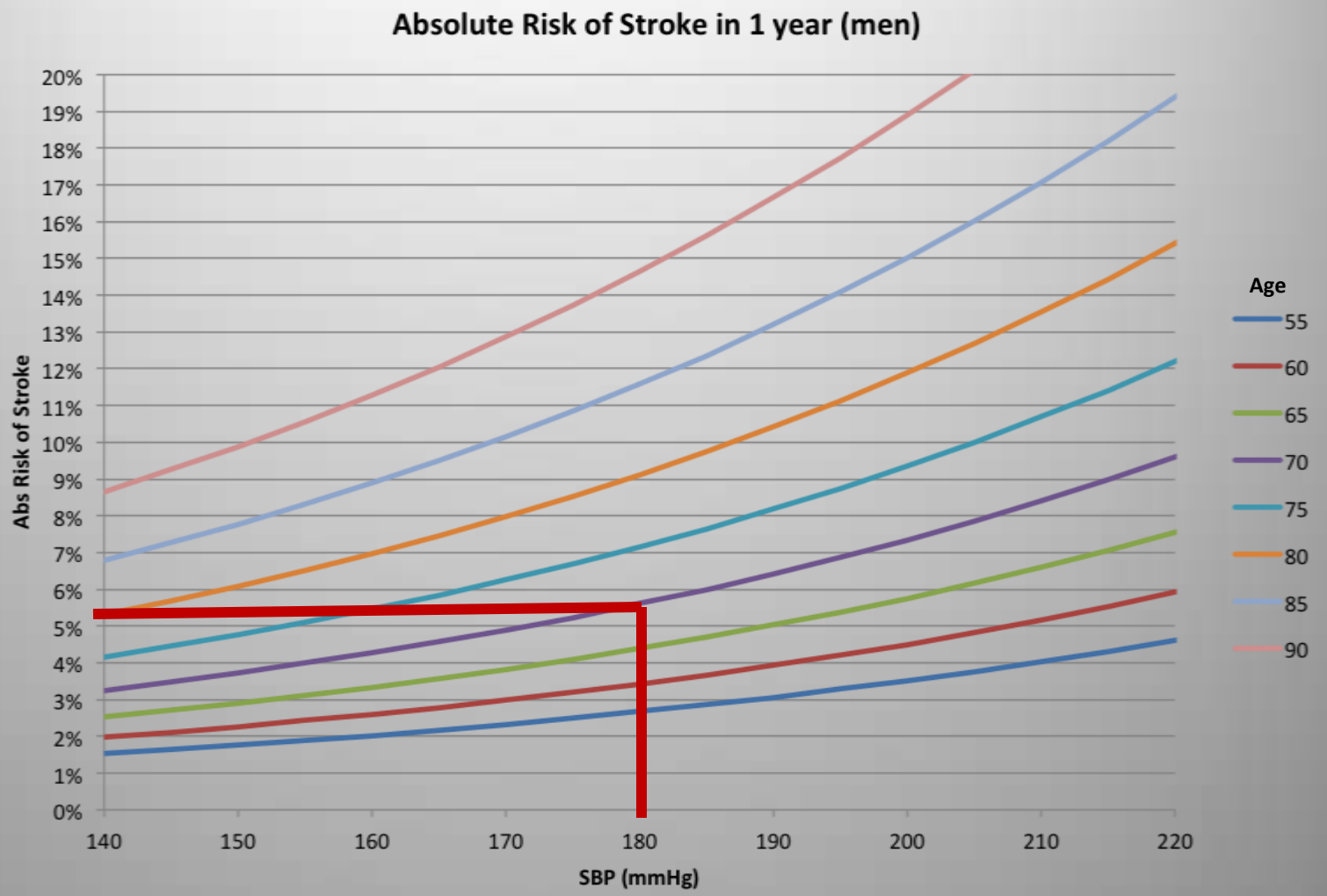
Hyp Rx	Yes
DM	No
Cigs	No
CVD	Yes
AF	No
LVH	Yes



Wolf et al 1991

Example Patient C – Add DM

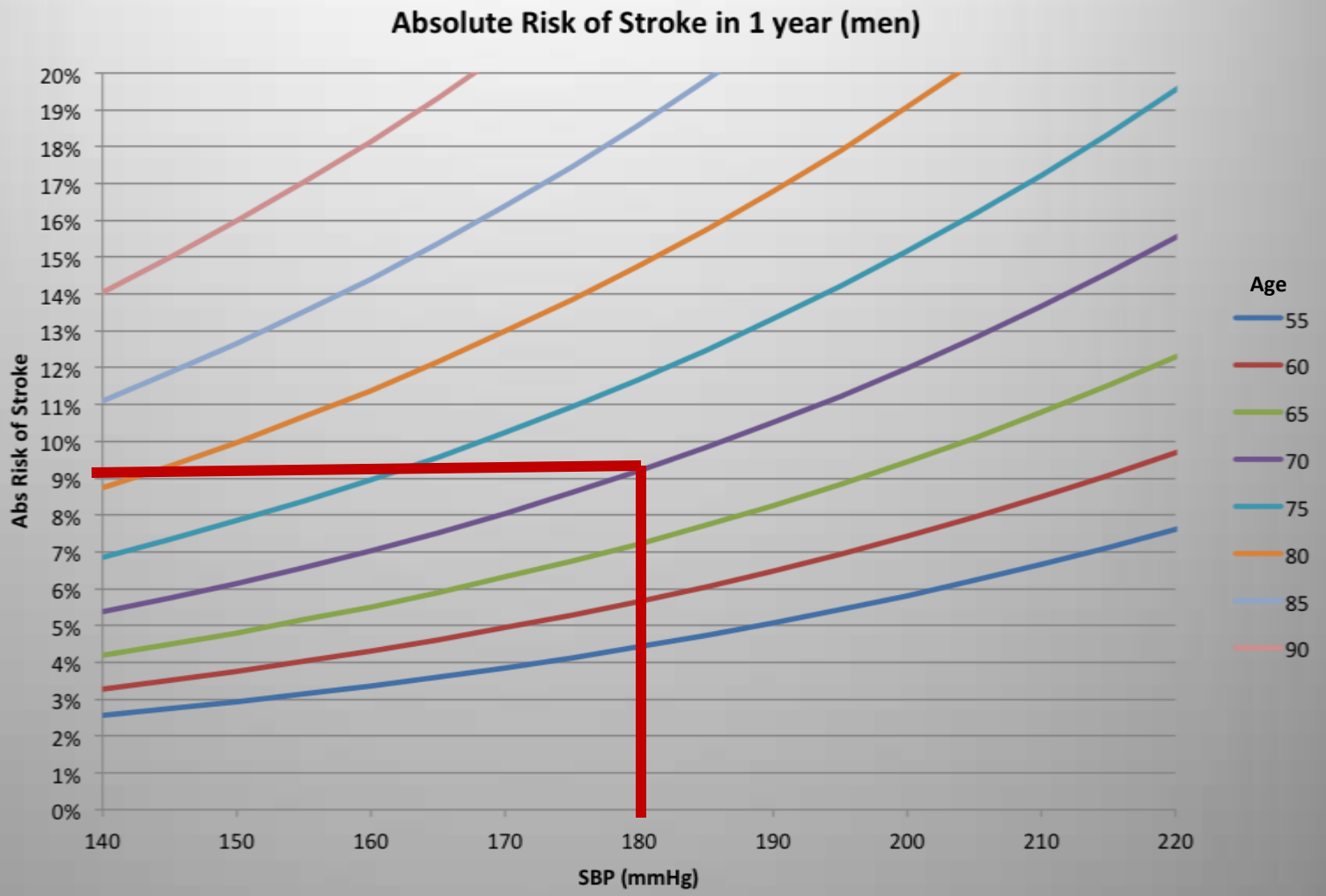
Hyp Rx	Yes
DM	Yes
Cigs	No
CVD	Yes
AF	No
LVH	Yes



Wolf et al 1991

Example Patient D – Add Cigarettes

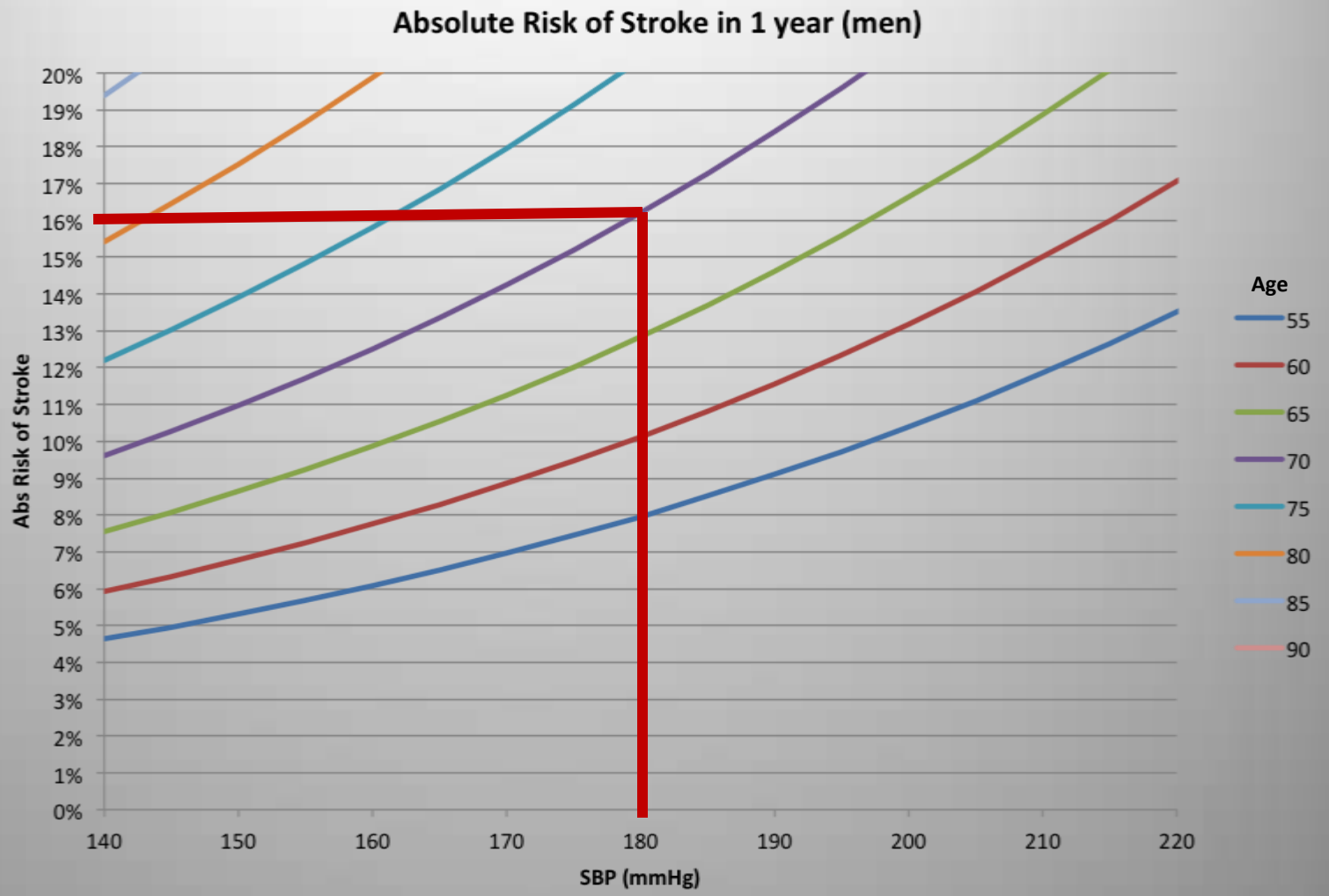
Hyp Rx	Yes
DM	Yes
Cigs	Yes
CVD	Yes
AF	No
LVH	Yes



Wolf et al 1991

Example Patient E – Add AF

Hyp Rx	Yes
DM	Yes
Cigs	Yes
CVD	Yes
AF	Yes
LVH	Yes



Wolf et al 1991

There’s No Time to Waste!

- **Treat to target is the goal** of antihypertensive therapy
- Delay in reaching target blood pressure causes **measurable risk of cardiovascular events**, especially stroke
- **Effective and prompt treatment of HTN can reduce CV risk and end organ disease**

Rox Central AV Anastomosis

- Randomized, open label Clinical Trial in rHTN anticipated completion 1Q2014
  - NCT01642498
  - Primary endpoints: 6 mo. ABPM (blinded endpoint) and oBP (open) endpoint trial
- Clinical Trial in additional disease spaces are being structured

Terminal Thoughts