# Reiterating the benefit of ACE/ARB: DM + ASCVD

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# Disclosures

Nil

# Objectives

Indications for ACE/ARB in:

- Diabetes
- ASCVD

Rates of ACE/ARB utilization

Evidence for ACE/ARB in DM + ASCVD

Practical reminders

# ACE/ARB indication: diabetes

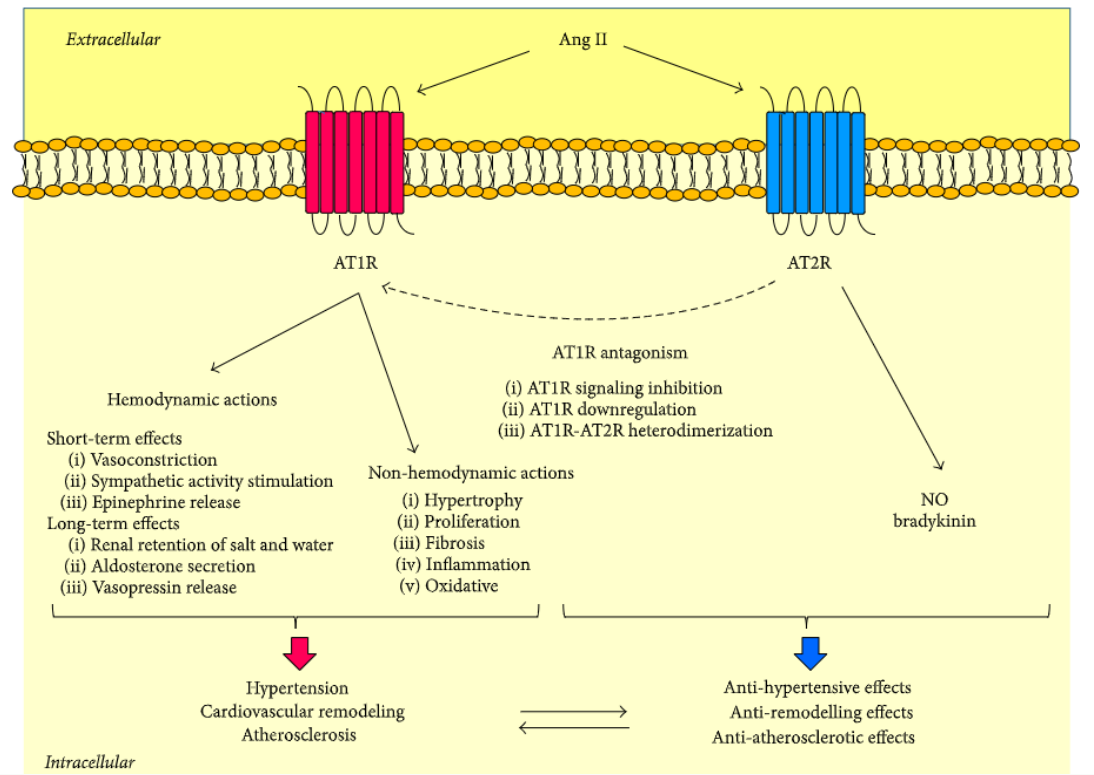
Robust trial (and meta-analysis) data supporting slowing of DM nephropathy

- As measured by creatinine doubling, albuminuria progression
- Uncertainty of benefit in absence of 'hypertension' or baseline microalbuminuria

**10.12** An ACE inhibitor or angiotensin receptor blocker, at the maximum tolerated dose indicated for blood pressure treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin-to-creatinine ratio ≥300 mg/g creatinine **A** or 30–299 mg/g creatinine. **B** If one class is not tolerated, the other should be substituted. **B**

Hermans MP *Am J Med* 1992; Lacourciere Y *Kidney Int* 2000; Parving HH *NEJM* 2001; Lewis EJ *NEJM* 2001

# ACE/ARB indication: ASCVD




## ESC guidelines: chronic coronary syndromes

| ACE inhibitors | | |
|---|---|---|
| ACE inhibitors (or ARBs) are recommended if a patient has other conditions (e.g. heart failure, hypertension, or diabetes).[328–330] | I | A |
| ACE inhibitors should be considered in CCS patients at very high risk of cardiovascular events.[331,332,335,336] | IIa | A |

| | | |
|---|---|---|
| ACE inhibitor treatment is recommended in CCS patients with diabetes for event prevention.[482] | I | B |

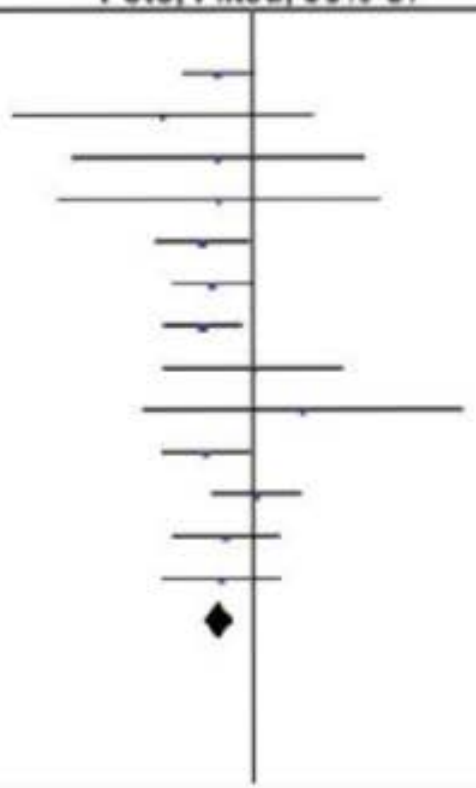
Bernardi S et al. *J Diabetes Res.* 2016; Knuuti J et al. *Eur Heart J.* 2019

# ACE/ARB indication: normotensive ASCVD

| Study or Subgroup | ACEi or ARB Events | Total | Placebo Events | Total | Peto odds ratio Peto, Fixed, 95% CI |
|---|---|---|---|---|---|
| 1.5.1 SBP < 130 mmHg | | | | | |
| ACTIVE-I | 269 | 1360 | 313 | 1376 | 0.84 [0.70, 1.01] |
| CAMELOT | 10 | 357 | 16 | 360 | 0.63 [0.29, 1.37] |
| DIABHYCAR | 12 | 159 | 17 | 191 | 0.84 [0.39, 1.79] |
| DREAM | 10 | 1031 | 12 | 1041 | 0.84 [0.36, 1.95] |
| EUROPA | 127 | 1932 | 159 | 1896 | 0.77 [0.60, 0.98] |
| HOPE | 205 | 1563 | 223 | 1419 | 0.81 [0.66, 0.99] |
| PROFESS | 198 | 1872 | 252 | 1892 | 0.77 [0.63, 0.94] |
| PROGRESS | 41 | 274 | 42 | 282 | 1.01 [0.63, 1.60] |
| RENAAL | 15 | 88 | 11 | 81 | 1.30 [0.57, 3.00] |
| SAVE | 173 | 956 | 207 | 941 | 0.78 [0.63, 0.98] |
| SOLVD | 179 | 1197 | 175 | 1190 | 1.02 [0.81, 1.28] |
| TRACE | 129 | 525 | 143 | 524 | 0.87 [0.66, 1.14] |
| TRANSCEND | 93 | 732 | 100 | 683 | 0.85 [0.63, 1.15] |
| **Subtotal (95% CI)** | | 12046 | | 11876 | **0.84** [0.77, 0.90] |
| Total events | 1461 | | 1670 | | |

Heterogeneity: $Chi^2 = 6.80$, $df = 12$ ($P = 0.87$); $I^2 = 0\%$

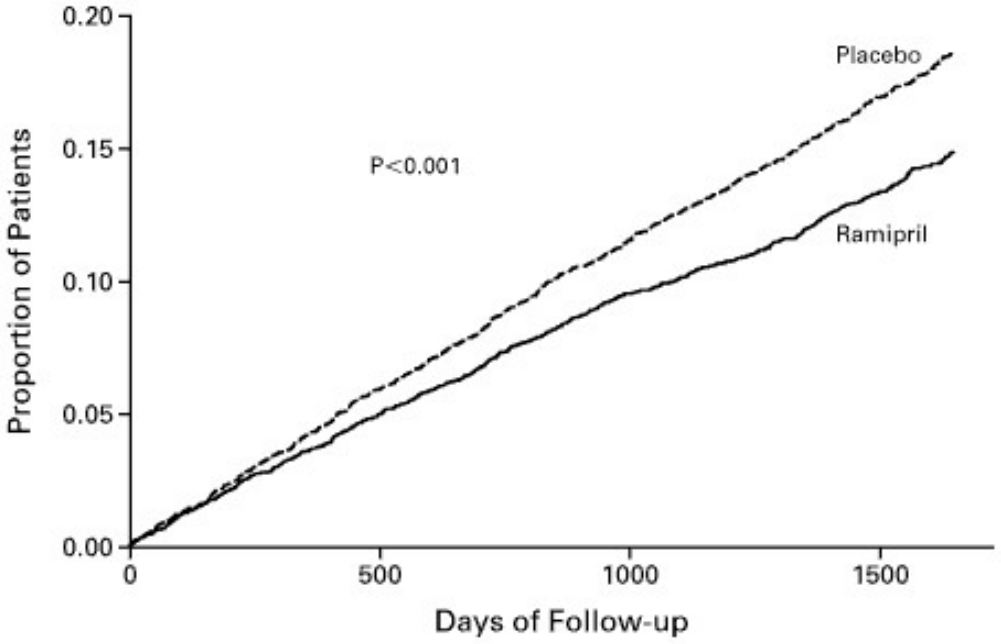
Test for overall effect: $Z = 4.58$ ($P < 0.00001$)




McAlister F et al. *Eur Heart J.* 2012

# ACE/ARB indication: DM + ASCVD

Extrapolation of large trials involving participants with DM and either high CV risk or established ASCVD




**10.44** In patients with known atherosclerotic cardiovascular disease, particularly coronary artery disease, ACE inhibitor or angiotensin receptor blocker therapy is recommended to reduce the risk of cardiovascular events. **A**

HR 0.78 (95%CI 0.70-0.86)

Yusuf S et al. *N Engl J Med* 2000; ADA Standard 10 2022

# Indications: COORDINATE patients

Slowing in progression of nephropathy +/- retinopathy

First-line anti-hypertensive

Reduction in MACE, even when normotensive

Reduction in mortality in context of HFrEF

# Under-prescription

In DM from NAMCS:

- 64% had hypertension although only 38% of these received ACE/ARB
- 11% had IHD although only 40% received ACR/ARB
- Overall usage was ~ 32% of eligible patients
    - NHANES suggest ~45% of eligible patients
- More likely to receive prescription: specialty care, ASCVD

Ibrahim SL et al. *Prev Med Rep* 2016; Rosen AB et al. *J Gen Intern Med* 2006; Winkelmayer WC et al. *Am J Kidney Dis* 2005

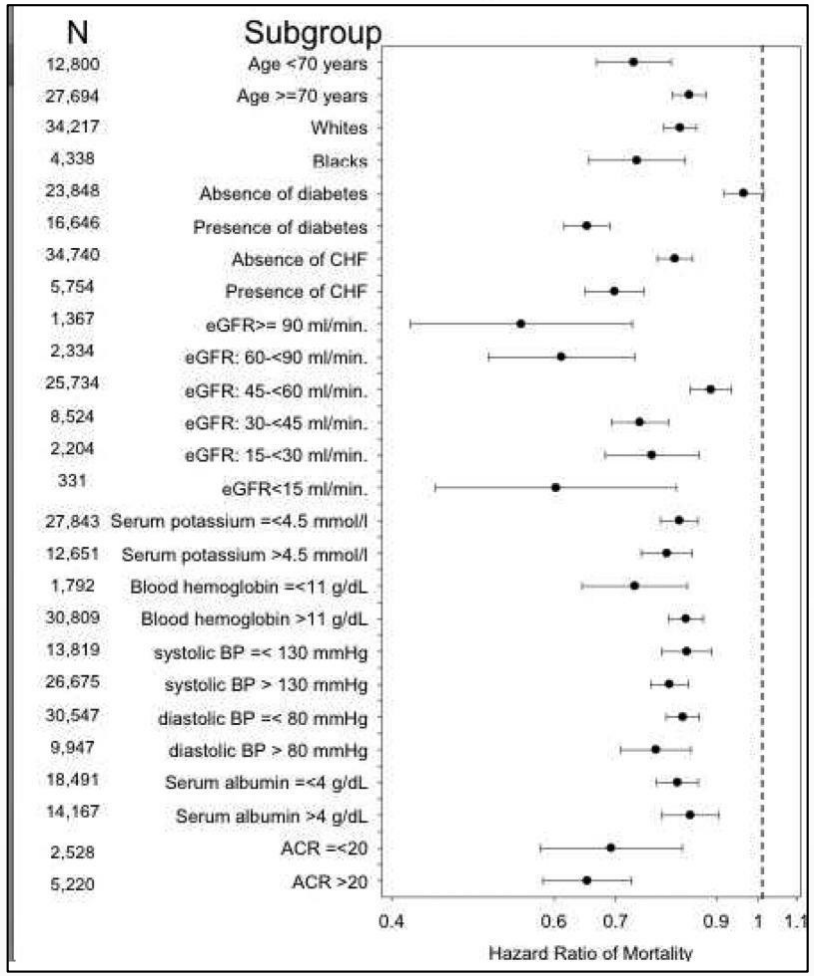
# Barriers to prescription

Polypharmacy

Perception of net clinical benefit/risk

- reduced GFR/increased age

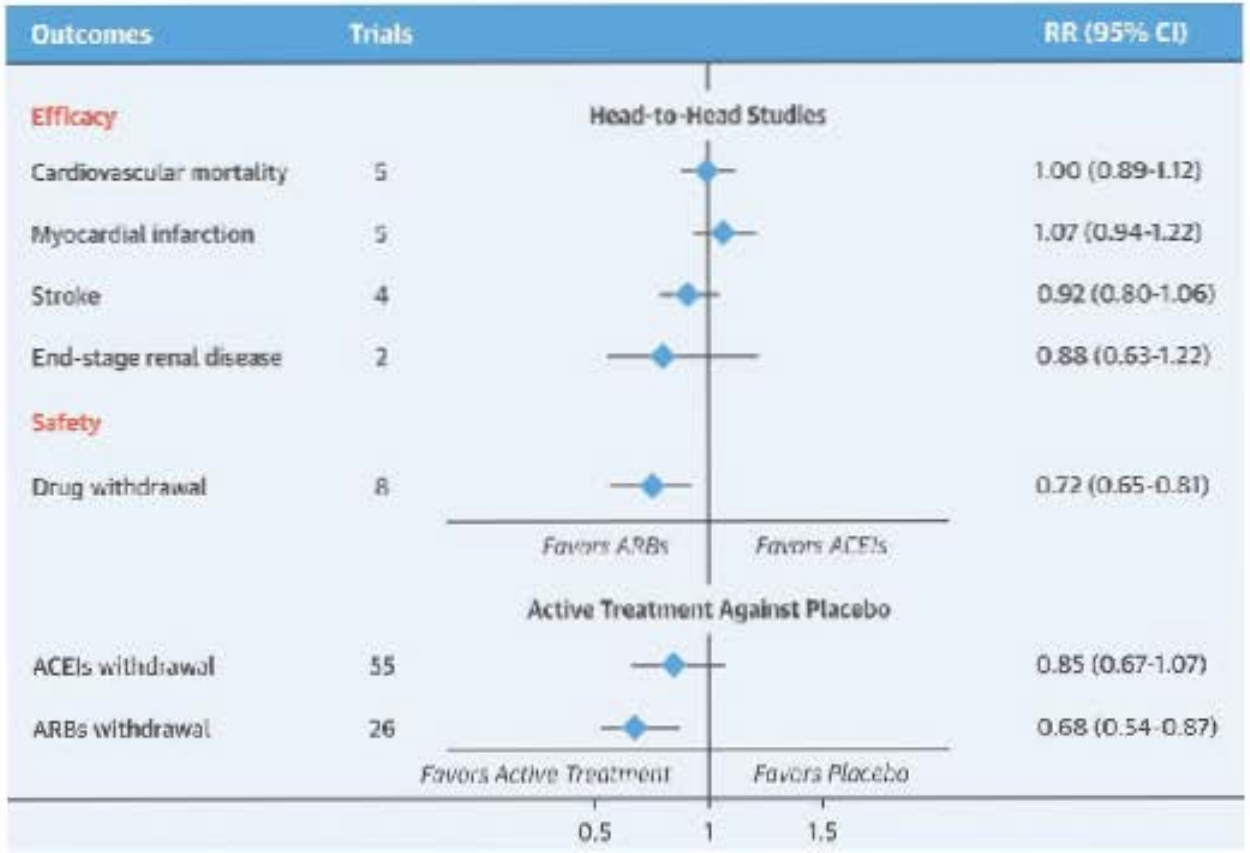
Interdisciplinary boundaries/inertia




Molnar MZ et al. *J Am Coll. Cardiol.* 2014

# ACE vs. ARB

- No convincing data to suggest either is superior.
- In setting of most being generic, guidelines now comfortable with either.
- Some argue the improved tolerance with ARB should allow it to be first line
- Aim for ‘maximally tolerated’




Messerli, F.H. et al. J Am Coll Cardiol. 2018;71(13):1474-82.

COORDINATE-Diabetes

Mann JF *Lancet* 2008; Xie X *Am J Kidney Dis* 2016; Ricci F *Int J Cardiol* 2016; Potier L *Heart* 2017; Savarese G *JACC* 2013

# Practical reminders

- Check baseline K/Cr.
- Re-check K/Cr in 1 week after commencing (and with uptitration)
    - Allow Cr <20% increase
    - Allow eGFR <15% increase
    - Allow K <5.5
- Cough may settle within 1 month. If not -> ARB.
- Re-check K/Cr annually
- ACE angioedema cross reactivity ~2.5%
- Make space in their current anti-HTN regimen

# Summary

- Participants in COORDINATE likely to benefit from ACE/ARB due to:
    - ASCVD risk reduction (highly likely)
    - Nephroprotection in context of albuminuria (probably)
    - Hypertension treatment (probably)
- Re-evaluate a prior history of intolerance