A randomised trial of routine blood pressure lowering among 11140 patients with type 2 diabetes
Background

- Most people with diabetes will die or be disabled by vascular complications
- Blood pressure levels are a critical determinant of vascular risk
- Treating hypertension in people with diabetes reduces risk (UKPDS)
- Many people with diabetes don’t have hypertension, but might benefit from blood pressure lowering
Blood pressure and vascular risk in diabetes

*Best evidence: 2000*
Blood pressure lowering in diabetes

Unresolved issues: 2000

Among patients with type 2 diabetes, does routine BP lowering therapy:

- Produce additional benefits when systolic pressure is lowered below 145 mmHg?
- Produce similar benefits for hypertensive and non-hypertensive patients?
- Produce benefits additional to those produced by other treatments, including ACE inhibitors?
Design features

- Randomised placebo-controlled trial
- Fixed combination of perindopril and indapamide (single tablet once a day)
- Primary outcomes: major vascular events
- 11,140 patients with type 2 diabetes from 20 countries
- 4.3 years average follow-up
- Adherence at end of follow-up
  > 73% (active) vs 74% (placebo)
Blood pressure reduction

∆ 2.2 mmHg (95% CI 2.0-2.4); p<0.001

∆ 5.6 mmHg (95% CI 5.2-6.0); p<0.001

Mean Blood Pressure (mmHg)

Systolic

Diastolic

Follow-up (Months)

Average BP during follow-up
140.3 mmHg
134.7 mmHg

Placebo

Perindopril-Indapamide

77.0 mmHg
74.8 mmHg
ADVANCE BP reduction in context:
UK Prospective Diabetes Study
Main results
Mortality and morbidity
All-cause mortality

Relative risk reduction
14%: 95% CI 2-25%
p=0.025
 Deaths

**Cardiovascular**

Relative risk reduction 18%; p=0.027

**Non-cardiovascular**

Relative risk reduction 8%; p=0.41
Combined primary outcomes
*Major macro or microvascular event*

Relative risk reduction
9%: 95% CI: 0 to 17%
p=0.041
Other outcomes

- 14% reduction in coronary heart disease
- 21% reduction in renal disease
- For all outcomes, similar benefits:
  - In those with or without hypertension
  - In the presence or absence of treatment with:
    - ACE inhibitors and other BP lowering drugs
    - Statins and other lipid lowering drugs
    - Aspirin and other antiplatelet drugs

Very good control of all risk factors in both groups by the end of follow-up
Blood pressure lowering in diabetes: unresolved issues 2000

Among patients with type 2 diabetes, does routine BP lowering therapy:

1. Produce additional benefits when systolic pressure is lowered below 145 mmHg? YES

2. Produce similar benefits for hypertensive and non-hypertensive patients? YES

3. Produce benefits additional to those produced by other treatments, including ACE inhibitors? YES
Global projections for diabetes (millions) 2007-2025

World
2007 = 246 million
2025 = 380 million
Increase +55%

Potential global benefits of treatment 2010-2015

If the benefits observed in ADVANCE were applied to just half the world’s diabetic population

Approximately 1.5 million deaths could be avoided over this period