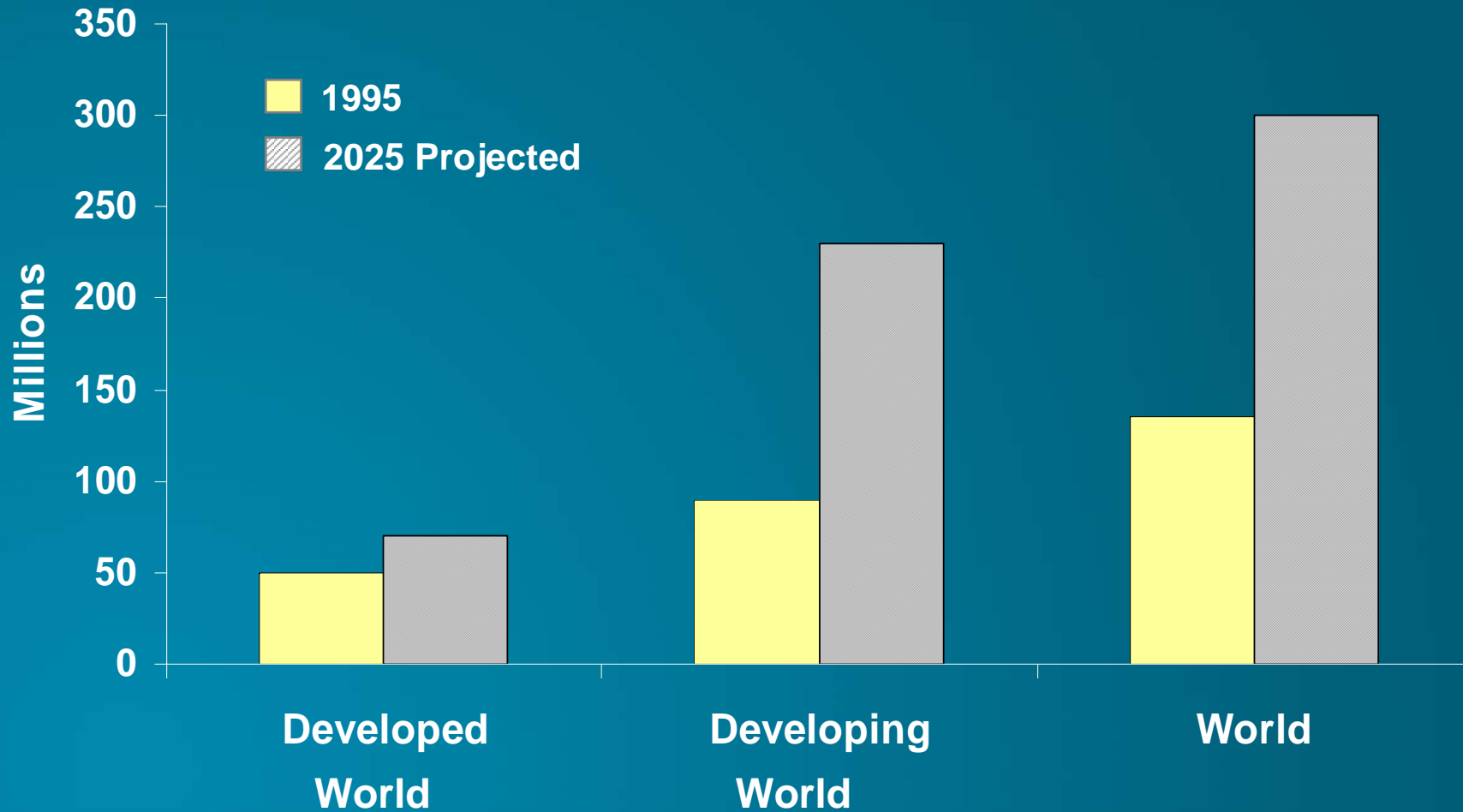


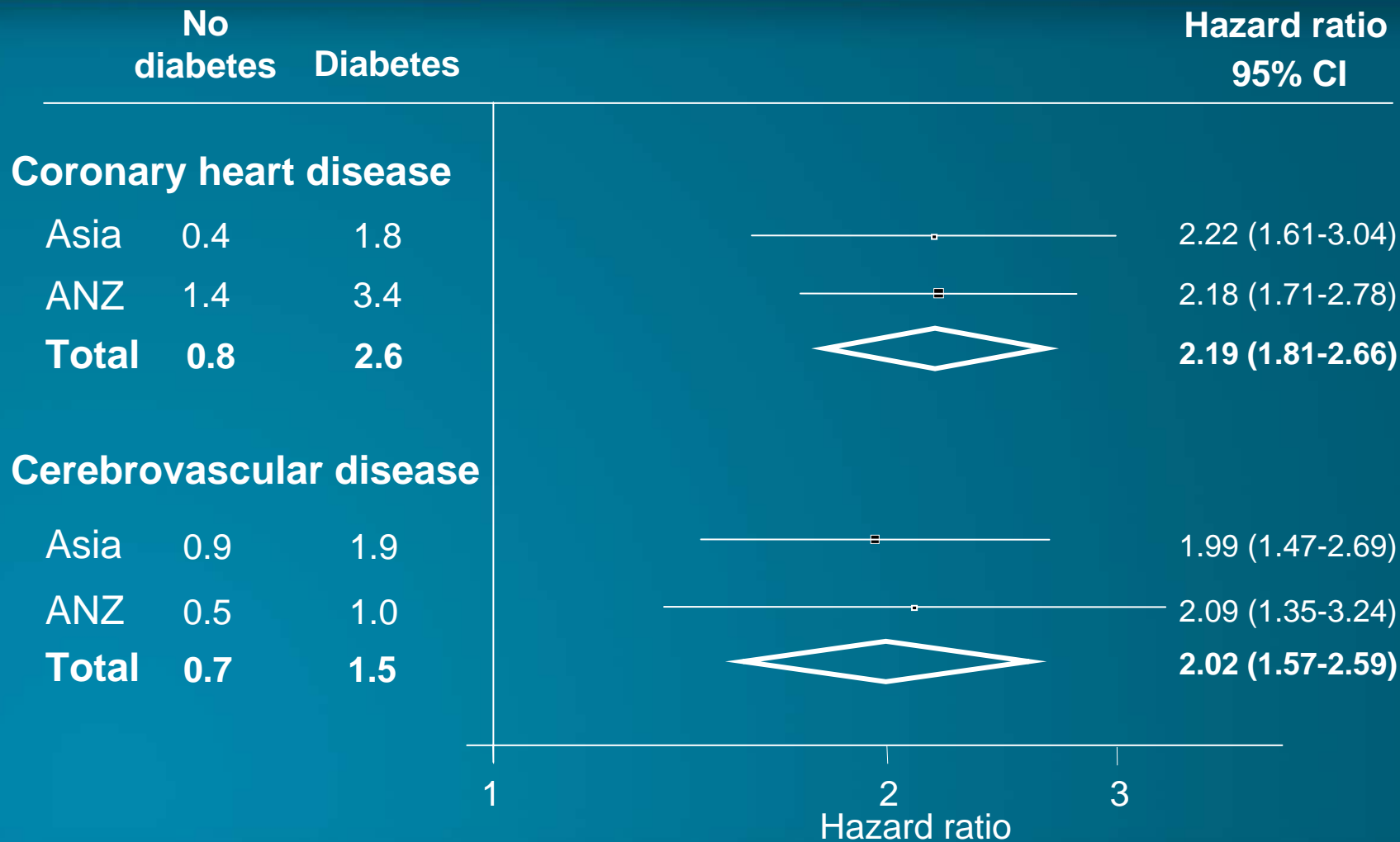


A factorial randomised trial of blood pressure lowering and intensive glucose control for the prevention of vascular disease among high risk patients with type 2 diabetes

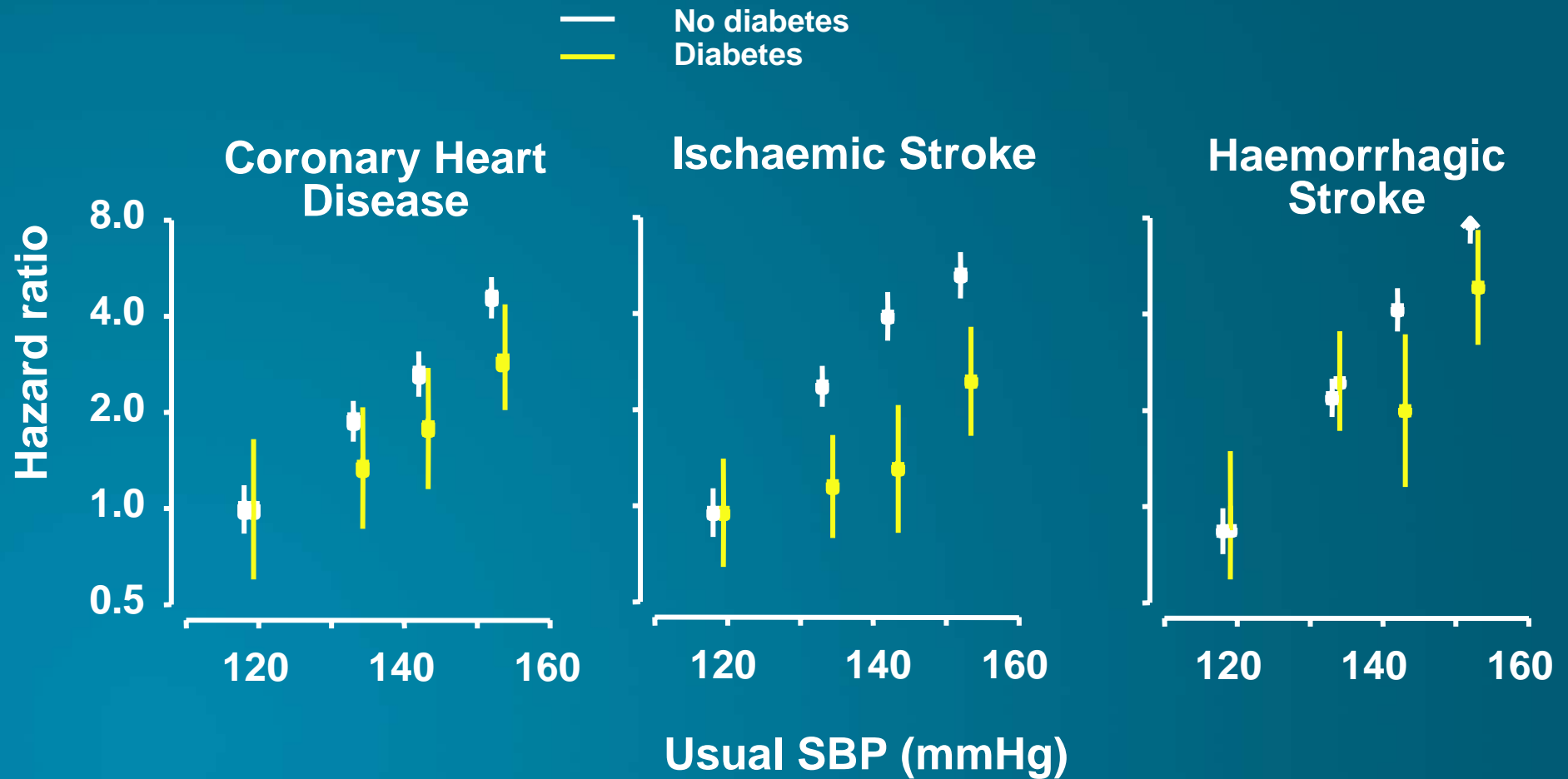
# Global distribution of diabetes



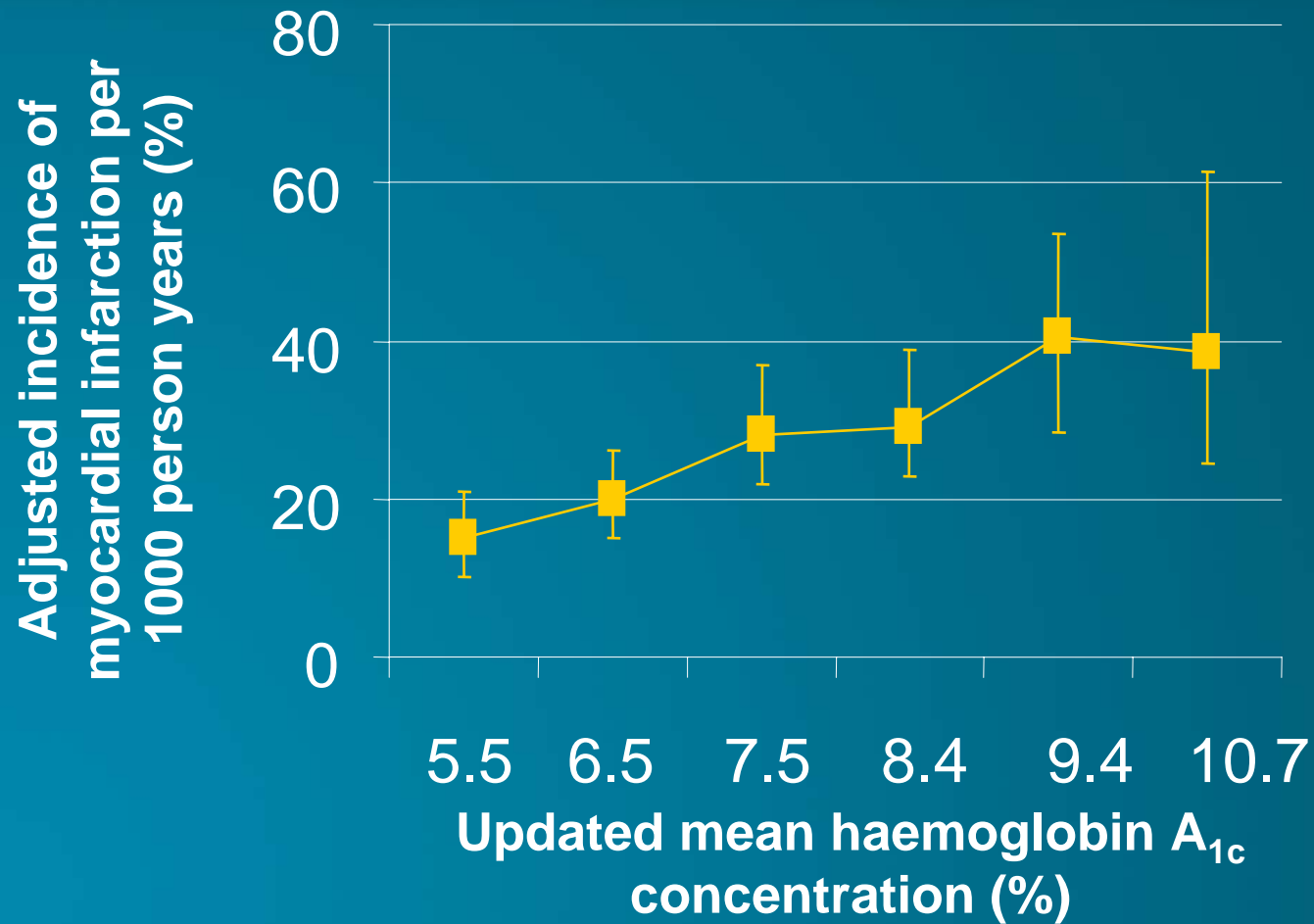
# Risks associated with diabetes



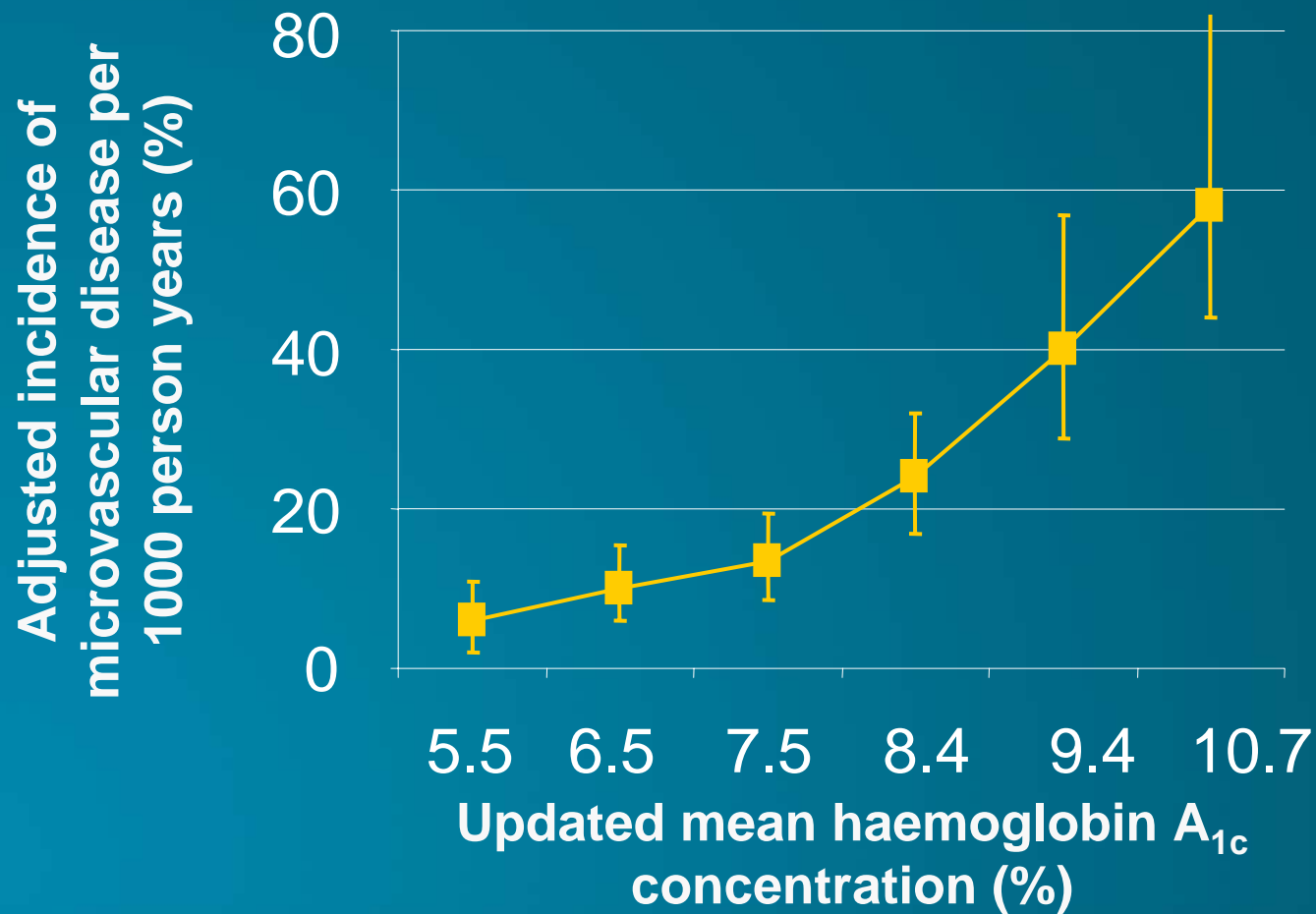
# Blood pressure and cardiovascular death



# Usual haemoglobin A1c and myocardial infarction



# Usual haemoglobin A1c and microvascular disease



# Unresolved issues in 2000

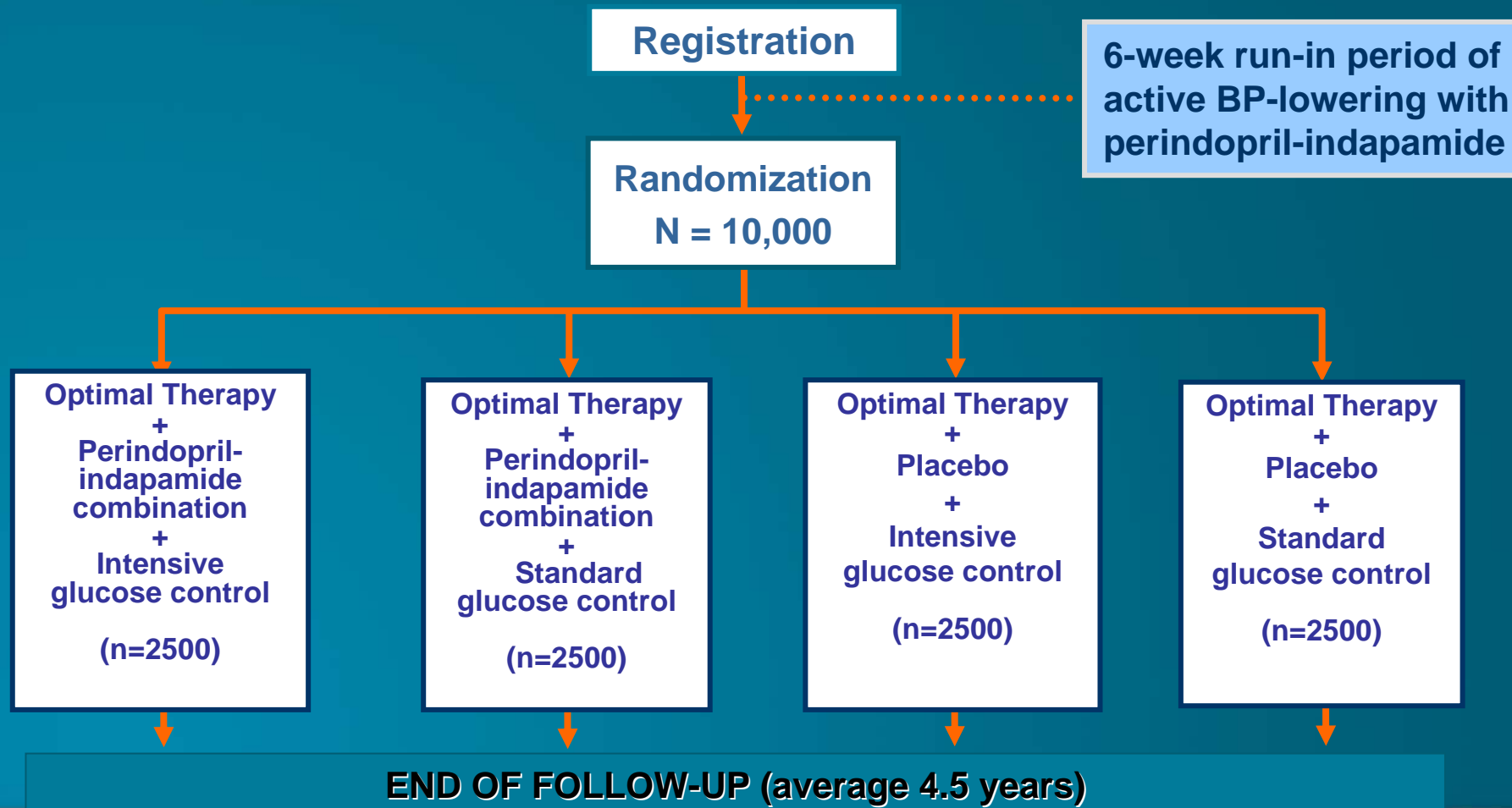
1. Would benefits of BP-lowering extend to patients with diabetes **across a broader range of BP?**
2. Would benefits of BP-lowering with *Per-Ind* be manifest **on top of optimal therapy** with other BP-lowering drugs, including blockers of the RAS?
3. Would **intensive glucose control** with *Gliclazide MR*-based regimen decrease **macrovascular disease?**

# Unresolved issues in 2000

4. Would ***even more intensive glucose control*** targeting a 6.5% level of HbA<sub>1c</sub> of further reduce microvascular disease?
5. Would the ***effects of BP lowering and tighter glucose control be additive?***



# Study design



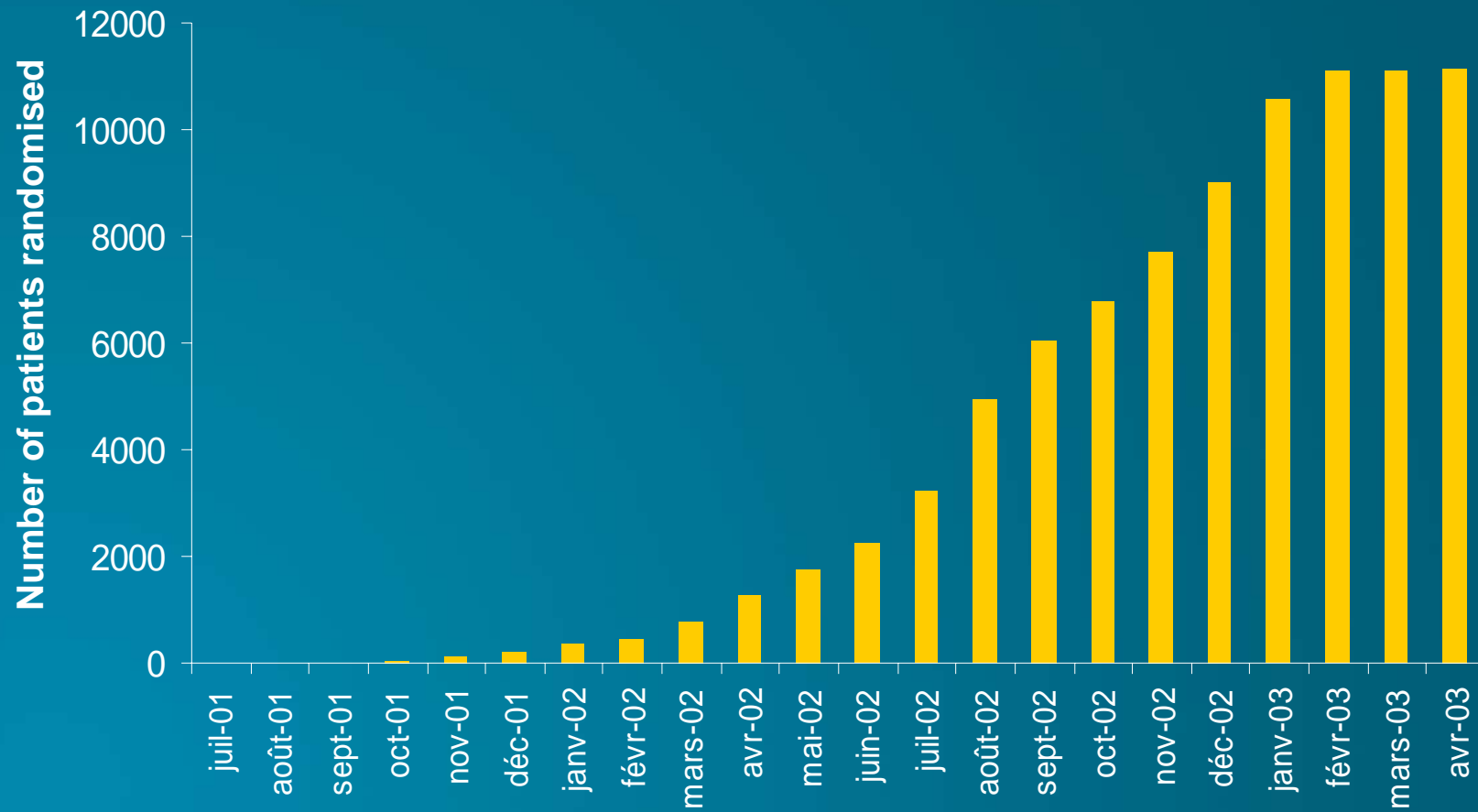
# Inclusion criteria

- ▶ Type 2 diabetes
- ▶ Age 55 years or older
- ▶ Elevated risk of vascular disease
  - ▶ Age  $\geq$  65 years
  - ▶ History of major macrovascular disease
  - ▶ History of major microvascular disease
  - ▶ First diagnosis of diabetes > 10 years prior to entry
  - ▶ Other major risk factor

# Primary outcomes

- ▶ For both treatment comparisons
- ▶ Macrovascular
  - ▶ Composite of non-fatal stroke, non-fatal MI, and cardiovascular death
- ▶ Microvascular
  - ▶ Composite of new or worsening nephropathy or retinopathy

# ADVANCE Randomisations



# Randomised participants - countries

<i>Australia</i>	<i>978</i>	<i>Italy</i>	<i>21</i>
<i>Canada</i>	<i>436</i>	<i>Lithuania</i>	<i>118</i>
<i>China</i>	<i>3,293</i>	<i>Malaysia</i>	<i>236</i>
<i>Czech Republic</i>	<i>209</i>	<i>Netherlands</i>	<i>630</i>
<i>Estonia</i>	<i>155</i>	<i>New Zealand</i>	<i>507</i>
<i>France</i>	<i>196</i>	<i>Philippines</i>	<i>136</i>
<i>Germany</i>	<i>327</i>	<i>Poland</i>	<i>604</i>
<i>Hungary</i>	<i>434</i>	<i>Russia</i>	<i>164</i>
<i>India</i>	<i>471</i>	<i>Slovakia</i>	<i>458</i>
<i>Ireland</i>	<i>442</i>	<i>United Kingdom</i>	<i>1,325</i>

**TOTAL = 11,140**

# Participant characteristics at baseline

Number of centres	215
Number randomized	11140
Female, %	43
Mean Age, years	66
Mean SBP/DBP, mmHg	145/81
History of hypertension, %	69
Current BP lowering therapy, %	75
History of vascular disease, %	39
Current smoking, %	14
Mean BMI, kg/m <sup>2</sup>	28

# Substudies

- ▶ ADVANCE Echocardiography Study
  - ▶ This study will examine the effects of the study treatments on heart function, in about 500 patients
- ▶ ADVANCE Retinopathy Measurements (AdRem) Study
  - ▶ This study will examine the effects of the study treatments on eye disease, in about 2000 patients

# ADVANCE Echocardiography Study

**LV Hypertrophy**

1.4cm

LV

1.4cm



**Mitral Doppler**

**Tissue Doppler**

E'





# AdRem

## ADVANCE Retinopathy Measurements Substudy

