Primary Prevention of Cardiovascular Disease in Diabetes: Treat as Secondary Prevention or Assess Individual Risks?

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Norwegian Postgraduate Course in Diabetes
University of Oslo
17 October 2000, Oslo, Norway
A Problematic Patient with Diabetes

- 52 years old men, Type 2 DM 4 years. Smoking 10/day. HbA1c 8.7% No retinopathy
- Blood pressure 164/98 mmHg. No chest pain.
- Biochemistry - Urea 6 mmol/l
  - Creatinine 105 μmol/l
  - Total cholesterol 5.3 mmol/l
  - HDL cholesterol 0.9 mmol/l
  - Tryglycercride 2.6 mmol/l
  - Albumin excretion rate 60mg/24hrs
Questions

• 1. What is his main future risk in terms of complications of diabetes
• 2. Quantify this risk as a figure (% risk over the next 10 year)
• 3. What evidence-based management should you administer?
• 4. How much is it going to cost to prevent 1 event using just one agent?
INTRODUCTION

• Diabetes and risk factors for cardiovascular disease
• Treating risk factors in diabetes - glucose, blood pressure and lipids
• Primary prevention and secondary prevention - an evidence base?
• The case of aspirin
• Levels of risk factors versus levels of risk
# Diabetic Complications in the UKPDS

(Type 2 DM, Age 53, BMI 27.5, SBP 135, Chol 5.4)

Any diabetes-related endpoint 46.0/1000 patient years

<table>
<thead>
<tr>
<th>Macrovascular disease</th>
<th>24.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMI</td>
<td>17.0</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Microvascular disease</th>
<th>11.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic renal failure</td>
<td>0.8</td>
</tr>
<tr>
<td>Photocoagulation</td>
<td>11.0</td>
</tr>
<tr>
<td>Blind one eye</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Systolic Blood Pressure and 10 year CHD mortality in 342815 non-diabetic and 5163 diabetic men aged 35-57

10 year CHD Mortality per 1000

Systolic blood pressure (mm Hg)

Diabetics
Non-diabetics

Stamler (1991)
Myocardial Infarction (cumulative)

fatal or non fatal myocardial infarction, sudden death
573 of 3867 patients (15%)

% of patients with an event

- Conventional
- Intensive

p=0.052

Risk reduction 16%
(95% CI: 0% to 29%)

Years from randomisation
Epidemiological analysis by HbA$_{1c}$ categories

- Microvascular disease
- Myocardial infarction

Incidence per 1000 patient-years

Updated mean HbA$_{1c}$ (%)
The graph shows the HbA1c levels over time for overweight patients in a cohort with median values. Different medications are compared, including Conventional, Insulin, Chlorpropamide, Glibenclamide, and Metformin. The x-axis represents years from randomisation, and the y-axis shows HbA1c levels in percentage. The graph indicates that Insulin and Metformin maintain lower HbA1c levels compared to Conventional, Chlorpropamide, and Glibenclamide over the years.
Myocardial Infarction

Overweight patients

- Conventional (411)
- Intensive (951)
- Metformin (342)

$M \lor C$
$p=0.010$

$M \lor I$
$p=0.12$
(Central) Obesity  ↓ Physical Activity  ↓

Hyperinsulinaemia  ⇌ Insulin Resistance

↑ Proinsulin  ↓ Microalbuminuria
↑ Fibrinogen  ↓ Small Dense LDL
↑ PAI-1  ↑ TG
↑ BP  ↓ HDL

IGT  Diabetes Mellitus
Blood Pressure: Tight vs Less Tight Control

cohort, median values

Less tight control Tight control

mmHg

Years from randomisation

0 2 4 6 8

UKPDS
Myocardial Infarction

- Less Tight Blood Pressure Control (390)
- Tight Blood Pressure Control (758)

% of patients with event

Risk reduction: 21% p=0.13
Stroke

- Less Tight Blood Pressure Control (390)
- Tight Blood Pressure Control (758)

% patients with event

Years from randomisation

risk reduction
44% p=0.013

ukpds
### Numbers Needed to Treat for 10 Years to Prevent

<table>
<thead>
<tr>
<th>Event</th>
<th>Glucose</th>
<th>BP*</th>
</tr>
</thead>
<tbody>
<tr>
<td>One patient developing diabetes-related endpoint</td>
<td>19.6*</td>
<td>6.3*</td>
</tr>
<tr>
<td>One diabetes-related death</td>
<td>91</td>
<td>15.1*</td>
</tr>
<tr>
<td>One myocardial infarction</td>
<td>37</td>
<td>20.4</td>
</tr>
<tr>
<td>One stroke</td>
<td>∞</td>
<td>19.6*</td>
</tr>
</tbody>
</table>

*Hypertensive subjects only (38%)

+p<0.05

UKPDS 38
Myocardial Infarction

hazard ratio

haemoglobin $A_{1c}$ (%)

systolic blood pressure (mmHg)

> 8  7-8  6-7  < 6  < 130  130-140  > 150

0  2  4  6  8
## Systolic Blood Pressure and Macrovascular Disease in the UKPDS

<table>
<thead>
<tr>
<th></th>
<th>( \Delta ) risk per 10mmHg updated mean SBP</th>
<th>( \Delta ) risk by reducing SBP by 10mmHg</th>
</tr>
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<tbody>
<tr>
<td>Myocardial Infarction</td>
<td>12 (7 to 16) %</td>
<td>21 (-7 to 41) %</td>
</tr>
<tr>
<td>Stroke</td>
<td>19 (14 to 24) %</td>
<td>44 (11 to 65) %</td>
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</tbody>
</table>

*UKPDS36, 2000*