# Diabetes Prevention & Management of Complications

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# The Planet is Changing

**How do old and new relate?**
**A guide to the new values expressed as mmol/mol is:**

| DCCT – $HbA_{1c}$ (%) | IFCC – $HbA_{1c}$ (mmol/mol) |
|---|---|
| 6.0 | 42 |
| 6.5 | 48 |
| 7.0 | 53 |
| 7.5 | 59 |
| 8.0 | 64 |
| 9.0 | 75 |

IFCC (mmol/mol) = (current value (%) * 10.93) - 23.50 (reported to a whole number)

# Who is From One of These Places?

- Asia
- Africa
- North or South America
- Australia or Polynesia
- Europe

# Why is This Important?

- Most of you are from a genetically susceptible population
- Many of you may know someone with diabetes
- You may be the person they turn to for advice

# Why is it Important?

- Diabetes has an impact on almost every branch of medicine
- More than 10% of inpatients have diabetes
- It is becoming more prevalent
- The global economic burden of diabetes is enormous

# The Impact of Diabetes in the UK

- The prevalence of people with known diabetes increased in one health district from 2.3 to 3.4% between 1996 and 2005, while the proportion known to have diabetic complications fell from half to one third
- Glucose-lowering therapies and test strips accounted for 6.9% of the total UK drug bill in 2008
- Adjusted costs for these prescriptions rose (in England) from £290m in 2000 to £591m in 2008
- Insulin accounted for 48.4% of these costs and test strips for a further 23.6%

Gale EAM Diabetic Medicine 2010;27(9):973-976

# The Impact of Diabetes in the UK

- The glitazones accounted for 11.7% of scripts by cost, but 2.8% by volume. Metformin accounted for 10.7% by cost, but 52.8% by volume
- Use of insulin secretagogues (mainly sulphonylureas), fell from 16.2 to 3.7% by cost between 2000 and 2008 and from 33.7 to 19.5% by volume
- Patients with Type 1 diabetes had a mean HbA1c of 8.8% in 2000 as against 8.7% in 2008. Insulin-treated patients with Type 2 diabetes had an HbA1c of 8.5% in 2000 as against 8.4% in 2008

Gale EAM Diabetic Medicine 2010;27(9):973-976

# The Impact of Diabetes in the UK

- Reductions in HbA1c were seen in some treatment groups and may reflect earlier diagnosis and / or more aggressive escalation of therapy
- Systolic blood pressure fell by approximately 8 mmHg ()5%) in those with Type 2 diabetes and total cholesterol fell from 5.6 to 4.2 mmol / l ()25%) over the same period
- The costs for acute hospital care for diabetes rose from 8.7 to 12.3% of revenue between 1994 and 2004

Gale EAM Diabetic Medicine 2010;27(9):973-976

# Some Definitions

- Type 1
- Type 2
- Others (not mentioned any more)

# Two Main Types

- Type 1
  - Autoimmune destruction of the β cells of the Islets of Langerhans in the pancreas. This leads to an absolute insulin deficiency. Insulin treatment is therefore mandatory
  - Previously known as IDDM or juvenile onset diabetes

# Two Main Types

- Type 2
  - Impaired insulin action (insulin resistance) and eventually, impaired insulin secretion as well
  - Usually treated with oral medication initially, then may move onto insulin
  - Formerly known as NIDDM or maturity onset diabetes

# How is the Diagnosis Made (1)?

| Glucose criteria (mmol/L) | | | |
|---|---|---|---|
| | *Fasting** | *Random* | *OGTT (2 hr value)* |
| **Diabetes mellitus** | ≥ 7.0 | ≥ 11.1** | ≥ 11.1 |
| **Impaired fasting glucose** | 5.6 – 6.9 | | |
| **Impaired glucose tolerance** | | | 7.9 – 11.0 |
| **Normal** | ≤ 5.5 | | ≤ 7.8 |

* includes fasting value on OGTT (oral glucose tolerance test) or no calorie intake for ≥8 hours.
** with classic symptoms or hyperglycaemic crisis.

Davies PH et al Brit J Diab Vasc Dis 2010;10(6):261-264

# How is the Diagnosis Made (2)?

| $HbA_{1c}$ criteria: IFCC assay[11] | | |
|---|---|---|
| | DCCT aligned – $HbA_{1c}$ (%) | IFCC- $HbA_{1c}$ (mmol/mol) |
| **Diabetes mellitus** | ≥ 6.5 | ≥ 48 |
| **Pre-diabetes** | 5.7 – 6.4 | 39-47 |
| **Normal** | ≤ 5.6 | ≤ 38 |

*Please note the above values may not apply in the following clinical circumstances*

- **Abnormal red cell turnover conditions:** such as anaemias from haemolysis, spherocytosis or iron deficiency (such as in pregnancy)
- **Haemoglobinopathies:** certain ones will affect diagnostic criteria (eg HbS, HbC, HbF, HbE). With Sickle cell trait, specific $HbA_{1c}$ assays will overcome this problem.
- **Rapid onset diabetes:** such as most Type 1 diabetes mellitus and some Type 2: the $HbA_{1c}$ can be within the normal range despite marked hyperglycaemia
- **Near patient testing:** using current $HbA_{1c}$ tests are not deemed to be sufficiently accurate for diagnosis
- In these and other cases where there is doubt as to the use of $HbA_{1c}$, the glucose criteria below must be used. Renal failure concerns can be overcome if specific assays are used.

Davies PH et al Brit J Diab Vasc Dis 2010;10(6):261-264

# How is the Diagnosis Made (3)?

| Diagnosis of Diabetes Mellitus: Summary of ADA criteria[12]<br>*Any one criterion is sufficient even if others normal* |
|---|
| 1: $HbA_{1c}$: ≥ 6.5% (≥ 48 mmol/mol) using an IFCC standardised assay |
| 2: Fasting glucose: ≥ 7.0 mmol/L |
| 3: OGTT 2 hour value: ≥ 11.1 mmol/L |
| 4: Random glucose ≥ 11.1 mmol/L with classic symptoms or hyperglycaemic crisis. |
| ***In the absence of classic symptoms or hyperglycaemic crisis, criteria 1 - 3 need repeating.*** |

So, in summary, making the diagnosis of diabetes is not as straightforward as it used to be

Davies PH et al Brit J Diab Vasc Dis 2010;10(6):261-264

# Clinical Features

| | Type 1 | Type 2 |
|---|---|---|
| Age at Onset (years) | < 40 | > 40 |
| Duration of Symptoms | Days or Weeks | Years |
| Body Weight | Normal or Low | Normal or High |
| Ketones | Yes | No |
| Insulin Mandatory? | Yes | No |
| Autoantibodies | Yes | No |
| Complications at Diagnosis | No | Up to 20% |
| Family History? | No | Yes |
| Other Autoimmune Diseases? | Yes | No |
| Percentage of cases | 10% | 90% |

# Familial Risks – Type 1

- If neither parent = 1 in 250
- If mother has it = 1 in 50 – 100
- If father has it = 1 in 12
- If 1 sibling has it = 1 in 15 – 30
- If 1 sibling and 1 parent has it = 1 in 10
- If both parents have it = 1 in 3

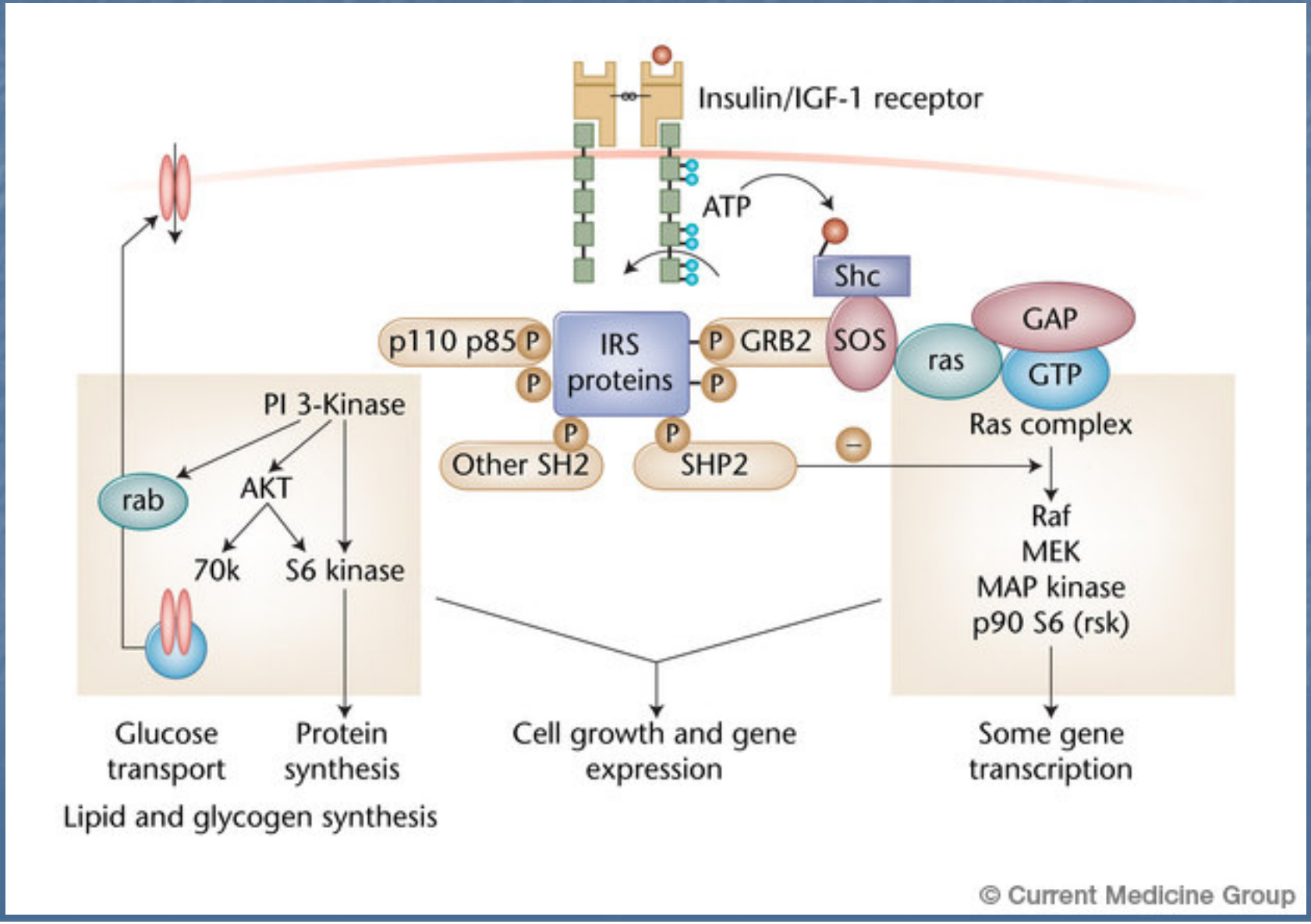
# Familial Risks – Type 2

- If neither parent has type 2 diabetes = 10%
- If 1 parent has it = 20 - 30%
- If 1 sibling has it = 40%
- If both parents have it = 70%
- If an identical twin has it = 80-100%

# So, Can Diabetes Be prevented?

Yes – but only if you chose your parents very carefully

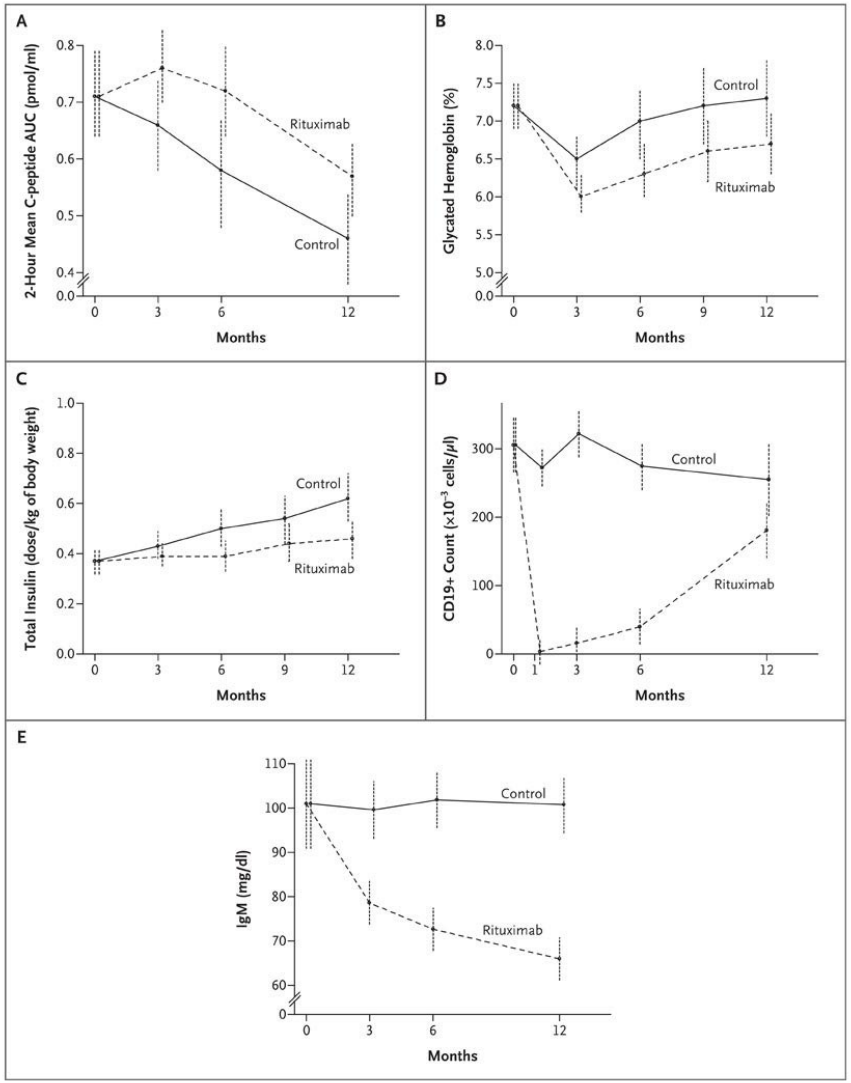
# The Insulin Signalling Cascade



# Is Type 1 Diabetes Preventable?

- Not at the moment
  - Lots of people are doing work on trying to modulate the immune system
  - No luck as yet

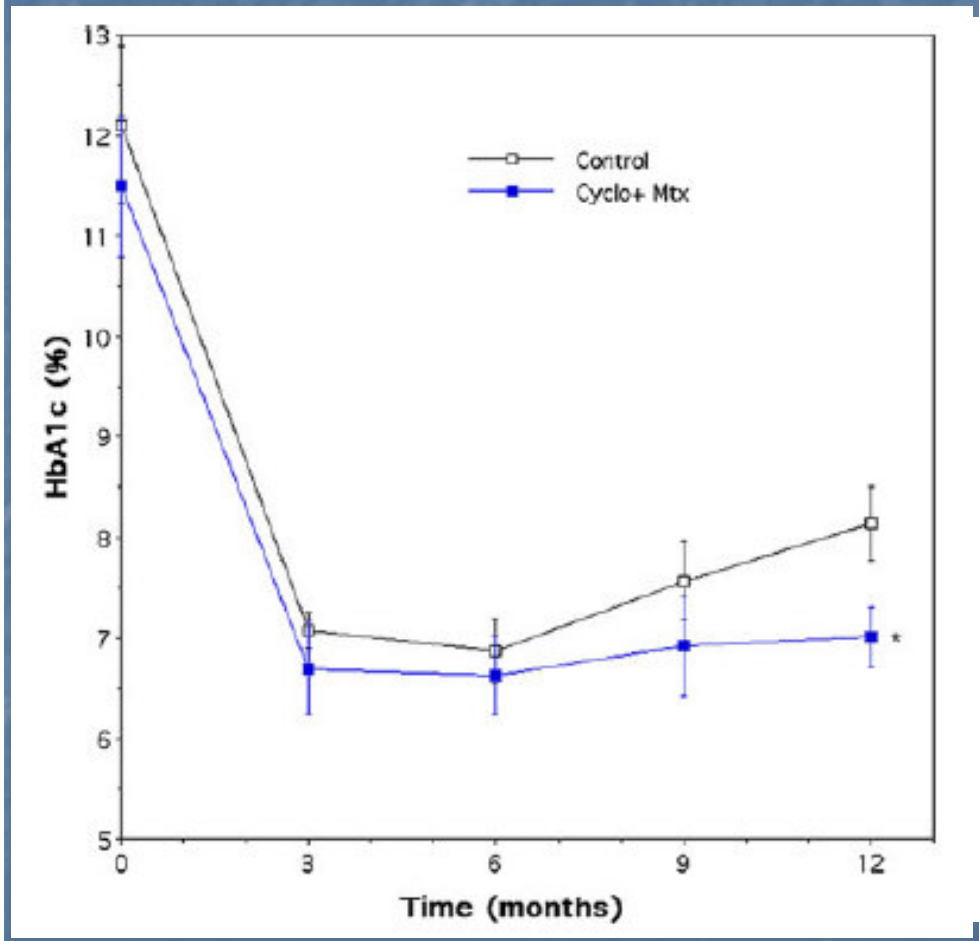
# Rituximab

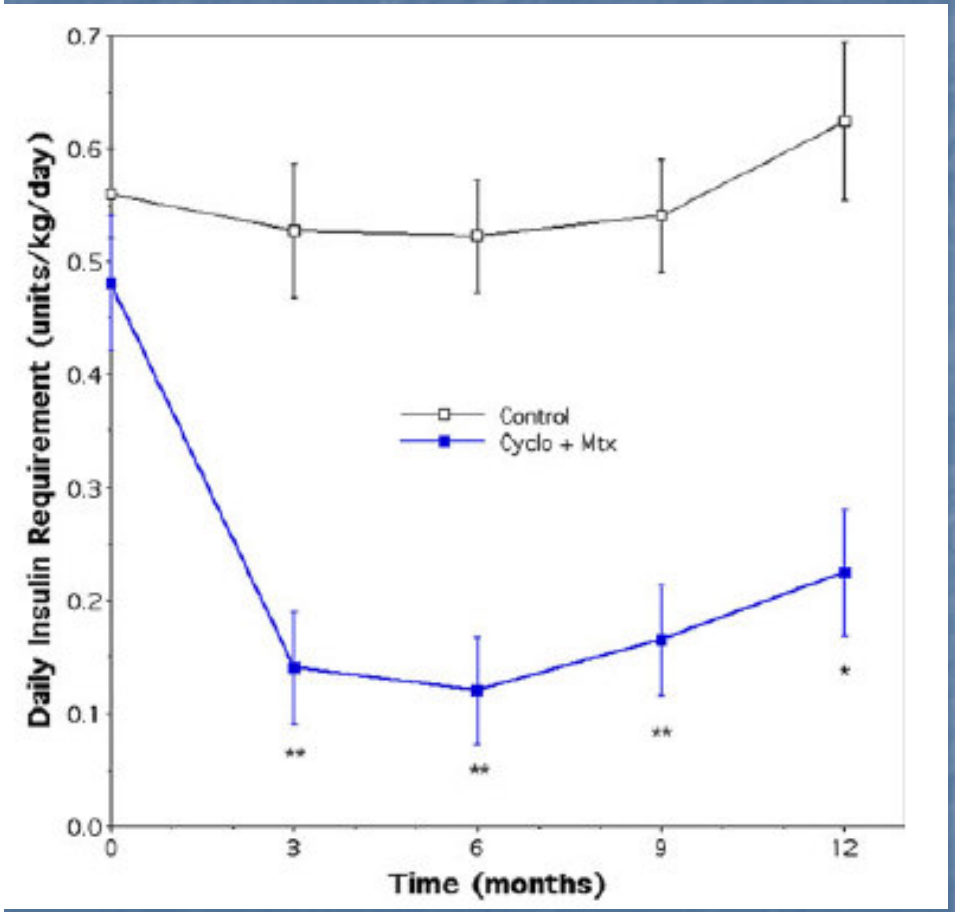



- 87 people with newly diagnosed type 1 diabetes
- Given 4 doses of rituximab over 3 weeks
- Followed up for a year

Pescovitz MD et al NEJM 2009;361(22):2143-2152

# Ciclosporin and Methotrexate



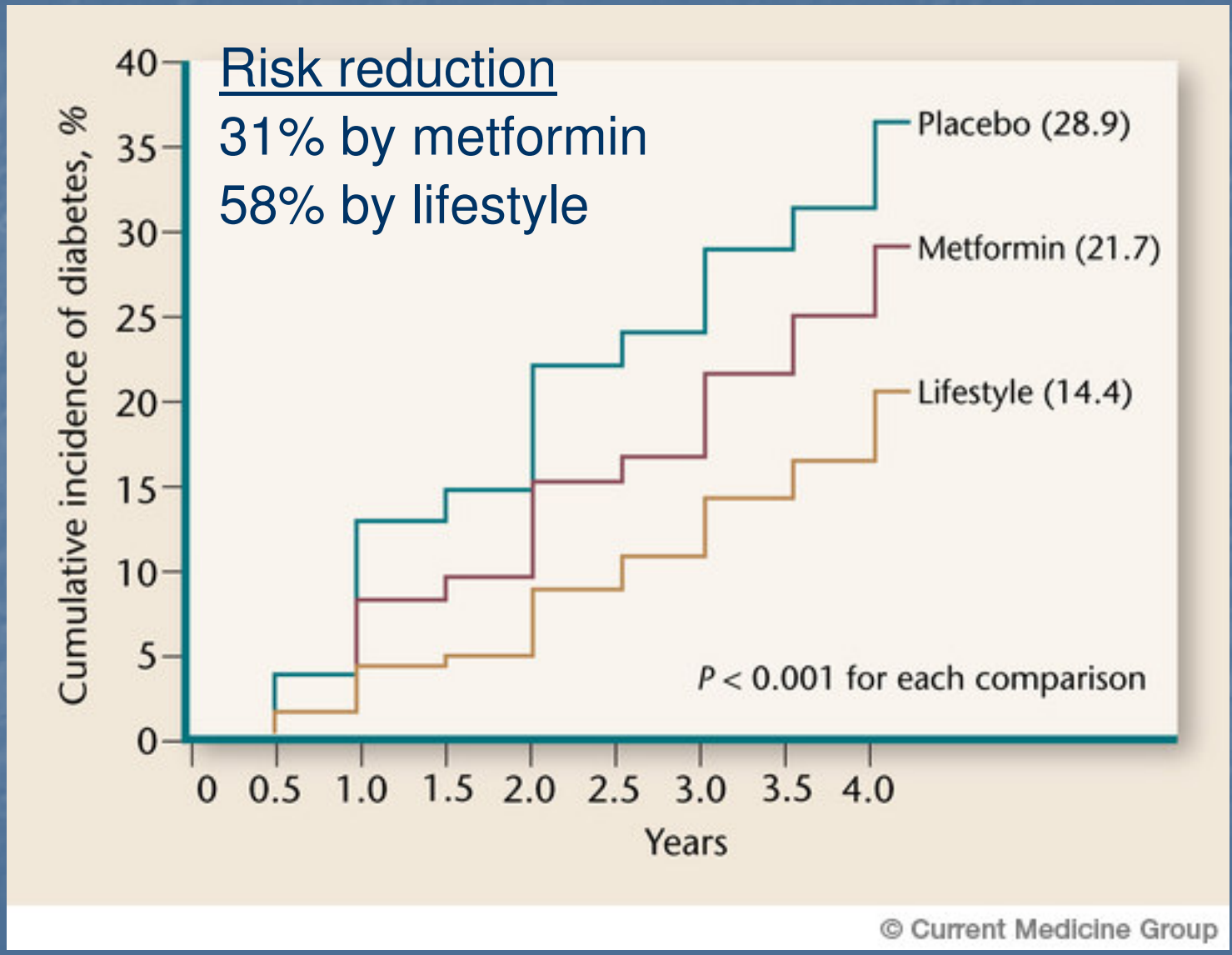

10 children with new onset T1DM given standard treatment or immunosuppressant's

Sobel DO et al Acta Diabteologia 2010;47(3):243-250

# Is Type 2 Diabetes Preventable?

- Absolutely
  - At least 3 studies have shown that TLC can make a difference

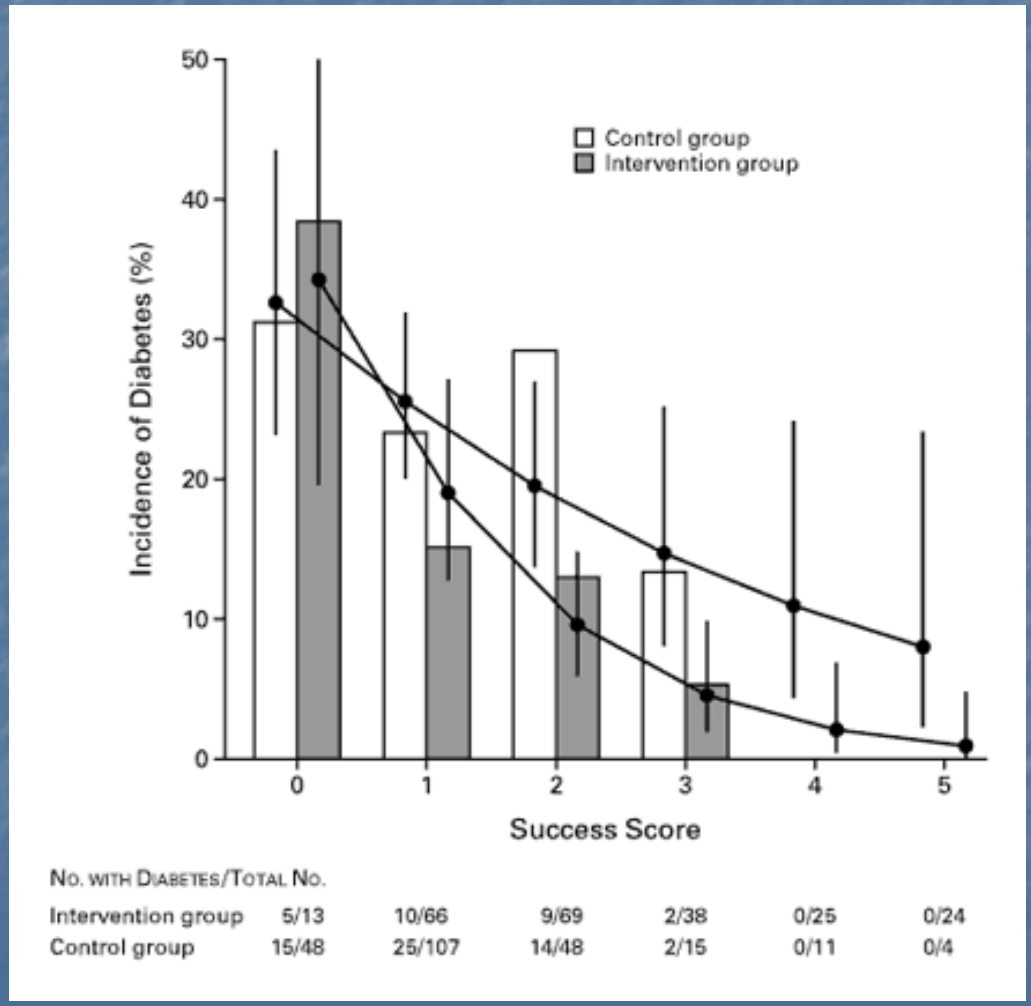
# Incidence of Diabetes






The DPP Research Group, *NEJM* 2002;346:393-403

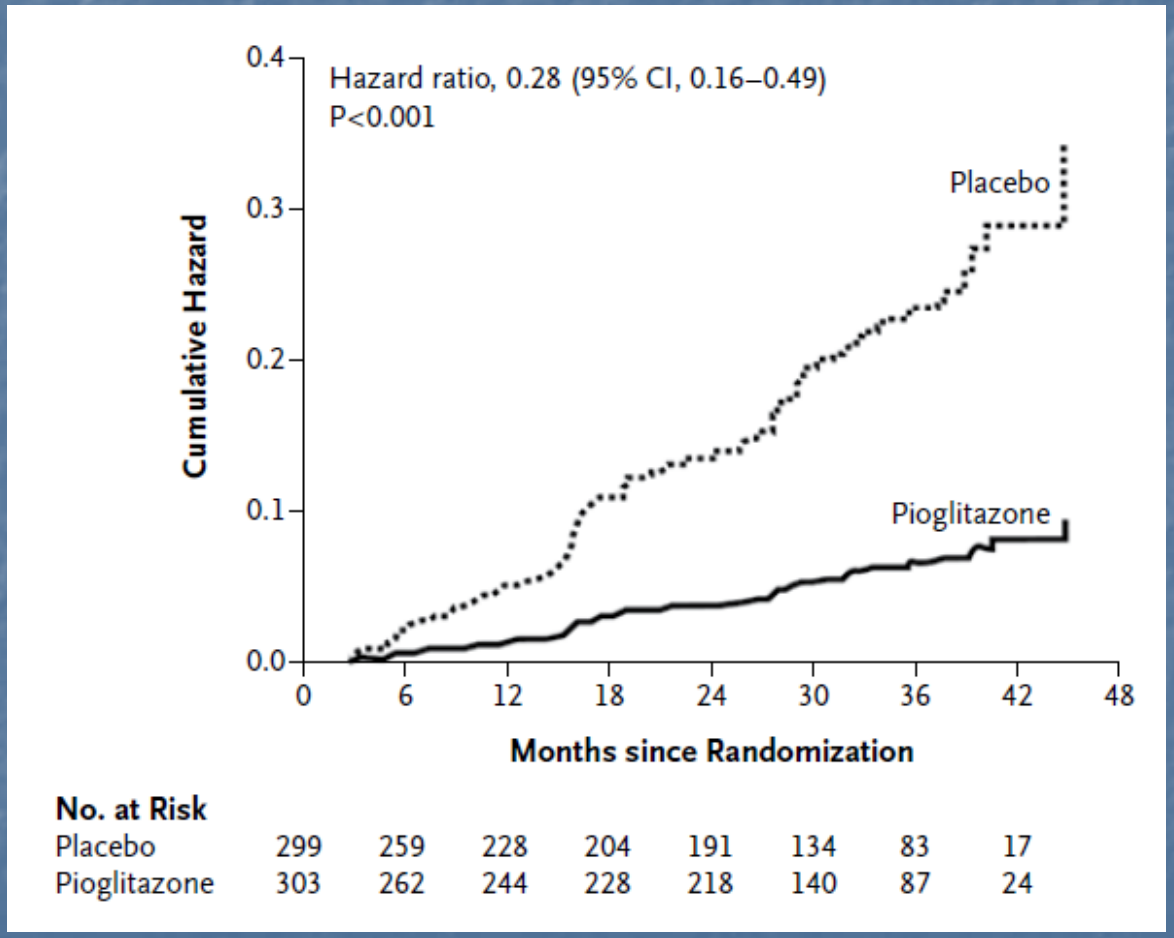
# Study Number 2




| No. with Diabetes/Total No. | | | | | | |
|---|---|---|---|---|---|---|
| Intervention group | 5/13 | 10/66 | 9/69 | 2/38 | 0/25 | 0/24 |
| Control group | 15/48 | 25/107 | 14/48 | 2/15 | 0/11 | 0/4 |

The Finnish DPS Group, *NEJM* 2001;344:1343-1350

# What About Other Drugs?




**1800 people randomised to pioglitazone or placebo**

DeFronzo RA et al NEJM 2011;364(12):1104-1115

# Welcome to the UEA-IFG Study:
# Delivering a Diabetes Prevention Programme
# In Central, North and South Norfolk, UK


[About the study]

[Want to know more?]

[Meet the study team]

[What's a T2Trainer?]

[Useful links and maps]

[Book appointment *]



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## Do you live in Norfolk, UK?
## Are you aged between years old?


Would you like to take part in the
UEA-IFG study in Norfolk, UK?

**Click on the map to check if you're eligible**

*** ***Our last Screening Appointments are on Fri 18th Dec 2009. If this is your first contact with us, please get in touch with us before 30th November 2009.*** ***

* In order to access these pages you must be eligible for the study and have a username and password

# Change in BMI Over Time

| BMI ($kg/m^2$) | 1993/1994 | 2004/2005 | % change |
|---|---|---|---|
| <25 | 38.5 | 32.1 | -20 |
| 25-29 | 41.2 | 39.0 | -5.6 |
| ≥30 | 20.3 | 28.9 | 29.8 |

Elderly Mexican Americans

Beard HA et al Diabetes Care 2009;32(12):2212-2217

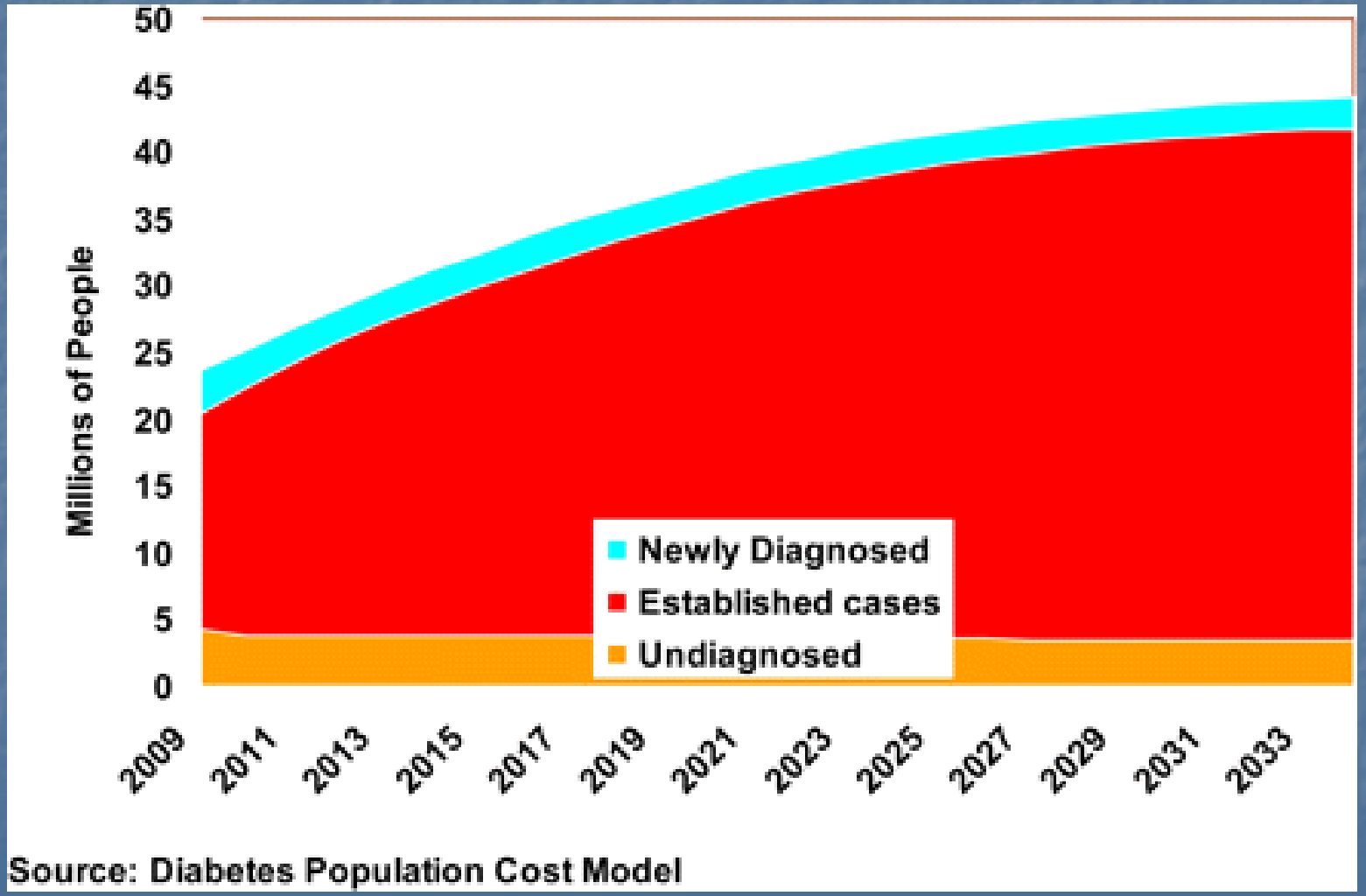
# Number with Diabetes

| BMI ($kg/m^2$) | 1993/1994 | 2004/2005 | % change |
|---|---|---|---|
| <25 | 18.8 | 23.6 | 4.8 |
| 25-29 | 16.9 | 40.3 | 23.4 |
| ≥30 | 27.3 | 46.9 | 19.6 |

Elderly Mexican Americans

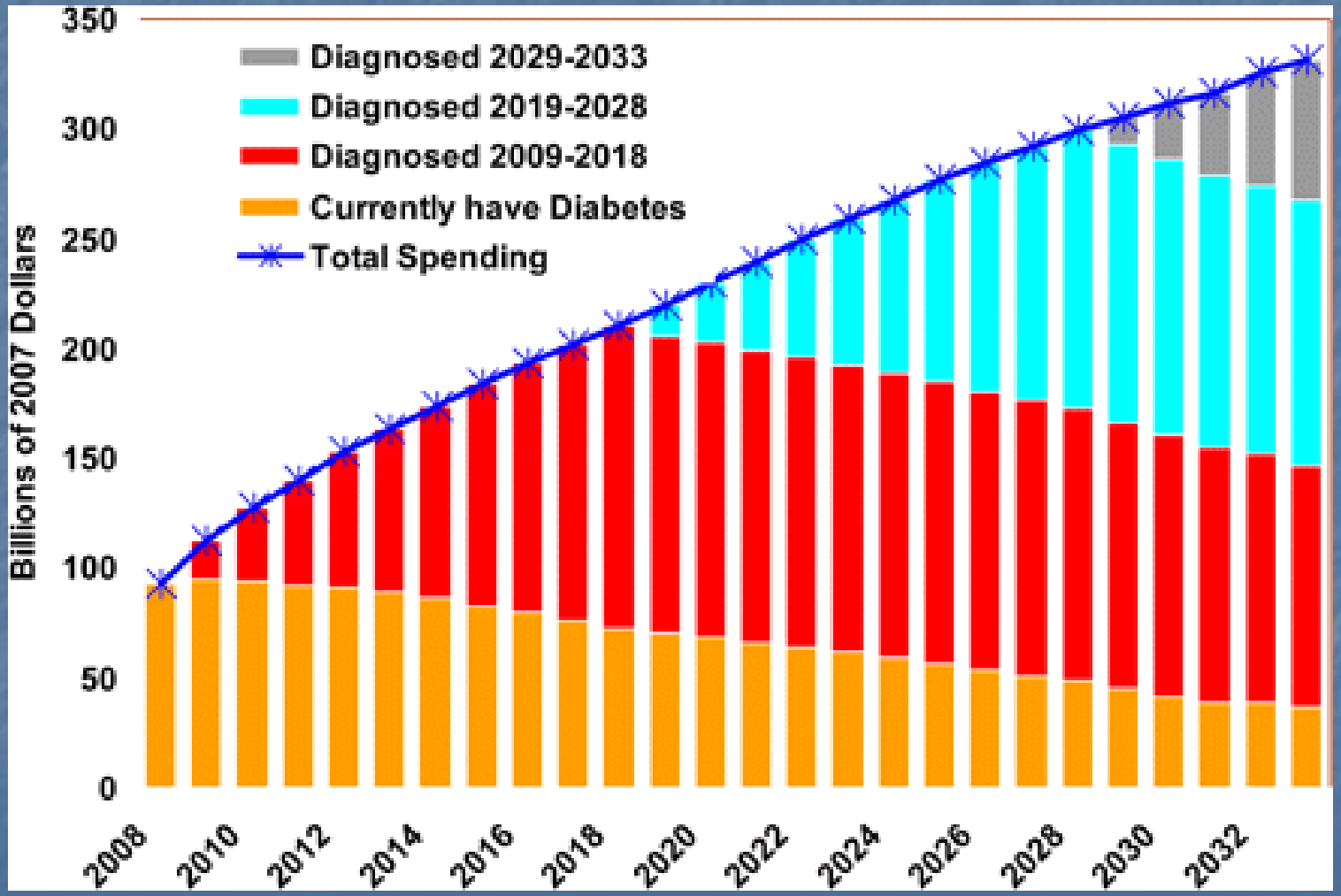
Beard HA et al Diabetes Care 2009;32(12):2212-2217

# Numbers Predicted to Have Diabetes in the USA



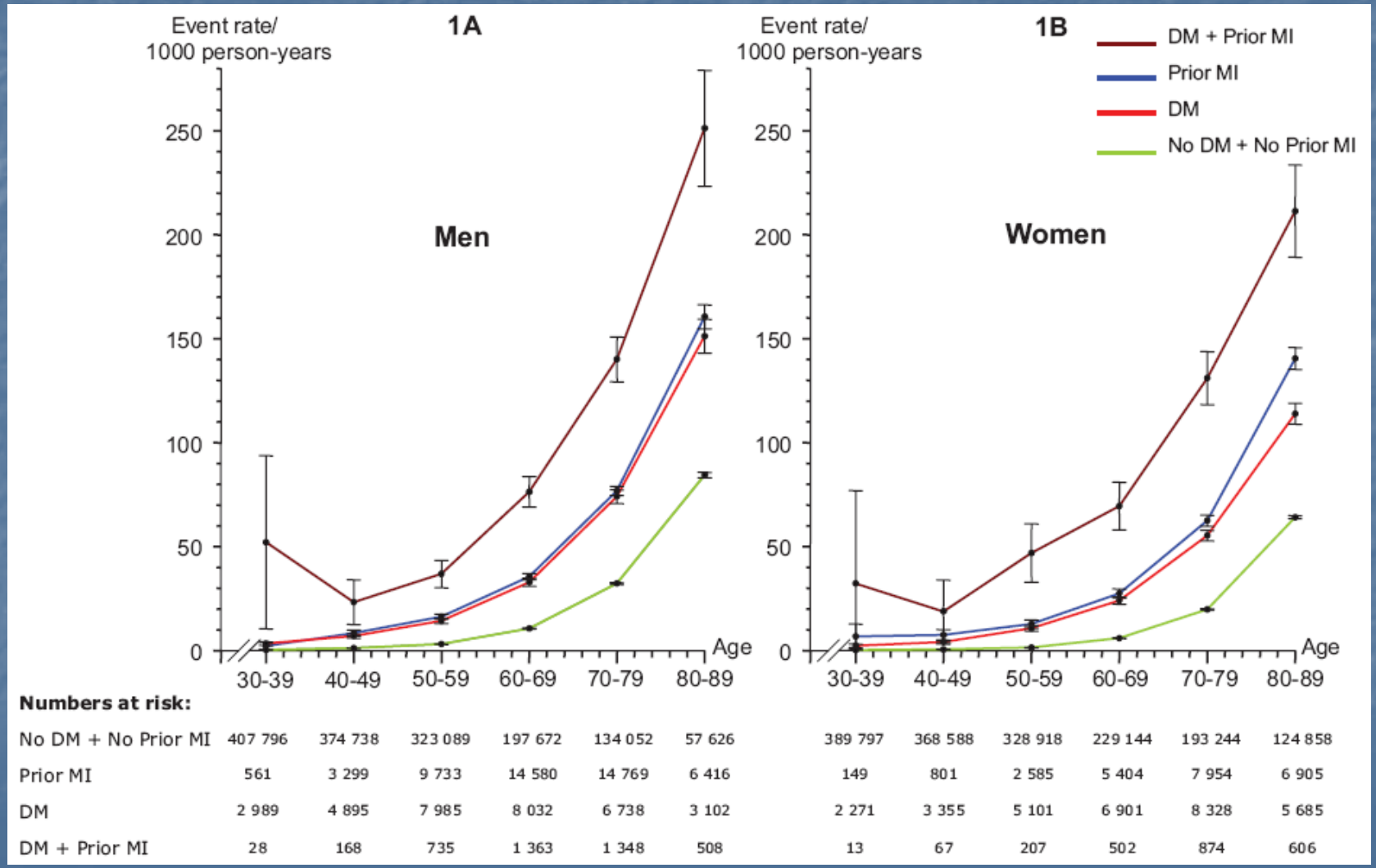

Huang et al et al Diabetes Care 2009;32(12):2225-2229

# Associated Costs




Huang et al et al Diabetes Care 2009;32(12):2225-2229

# Data From 3.3M Danes

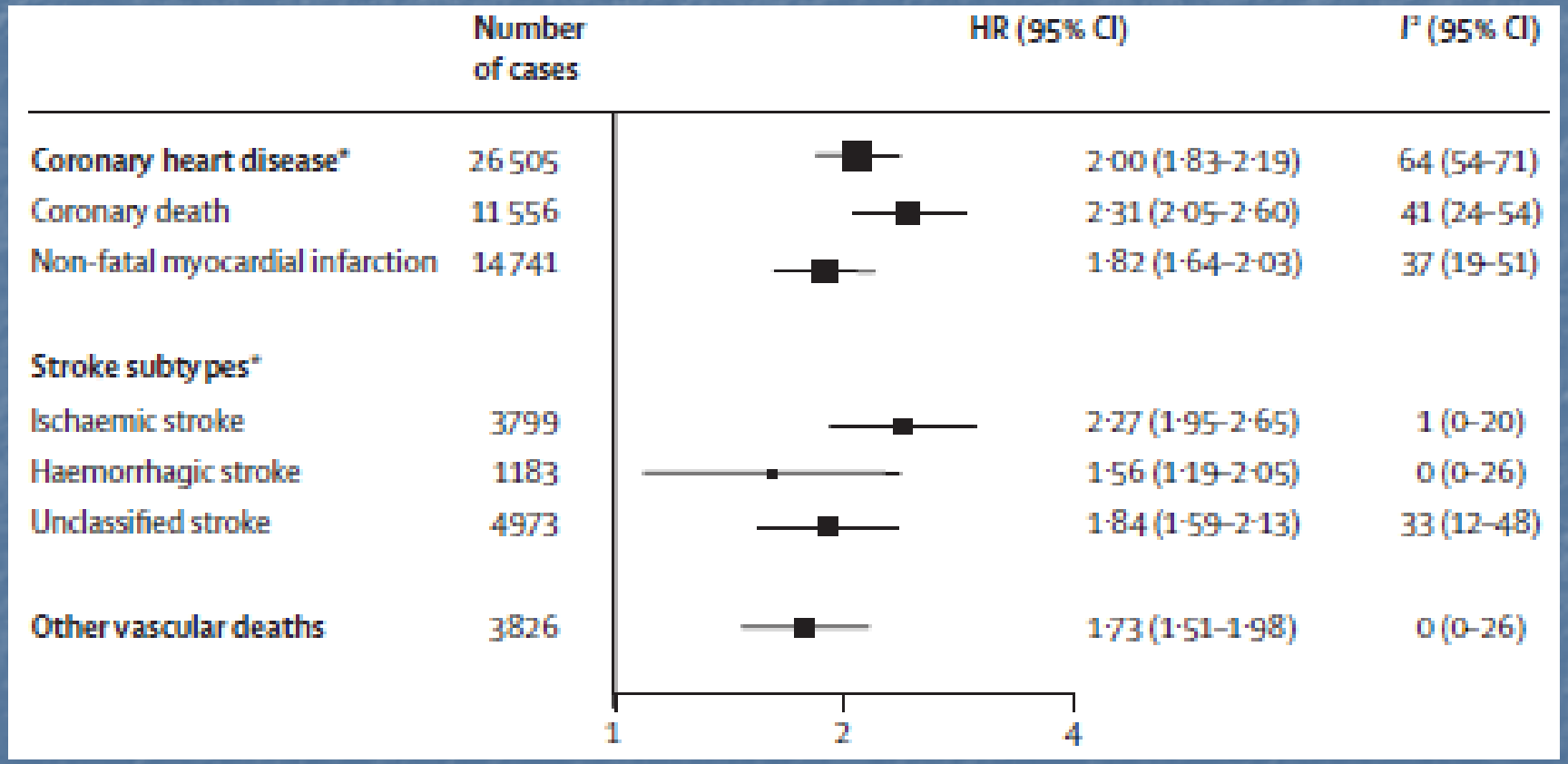



**Numbers at risk:**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No DM + No Prior MI | 407 796 | 374 738 | 323 089 | 197 672 | 134 052 | 57 626 | 389 797 | 368 588 | 328 918 | 229 144 | 193 244 | 124 858 |
| Prior MI | 561 | 3 299 | 9 733 | 14 580 | 14 769 | 6 416 | 149 | 801 | 2 585 | 5 404 | 7 954 | 6 905 |
| DM | 2 989 | 4 895 | 7 985 | 8 032 | 6 738 | 3 102 | 2 271 | 3 355 | 5 101 | 6 901 | 8 328 | 5 685 |
| DM + Prior MI | 28 | 168 | 735 | 1 363 | 1 348 | 508 | 13 | 67 | 207 | 502 | 874 | 606 |

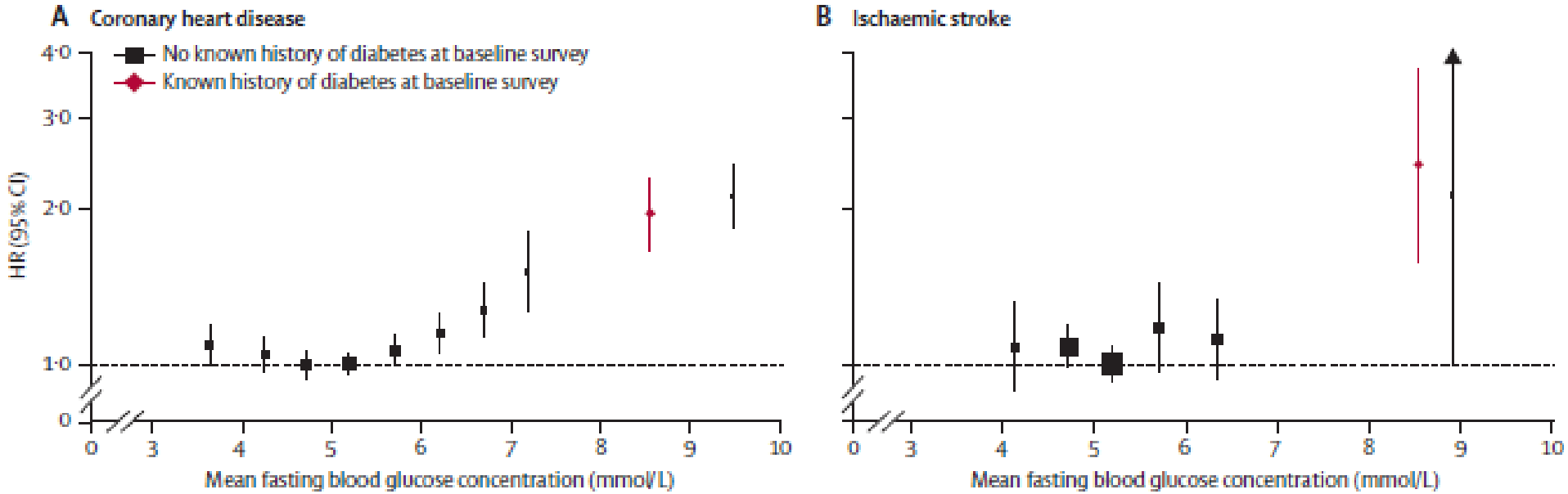
Schramm TK et al Circulation 2008;117:1945-1954

# Data from 700,000 People



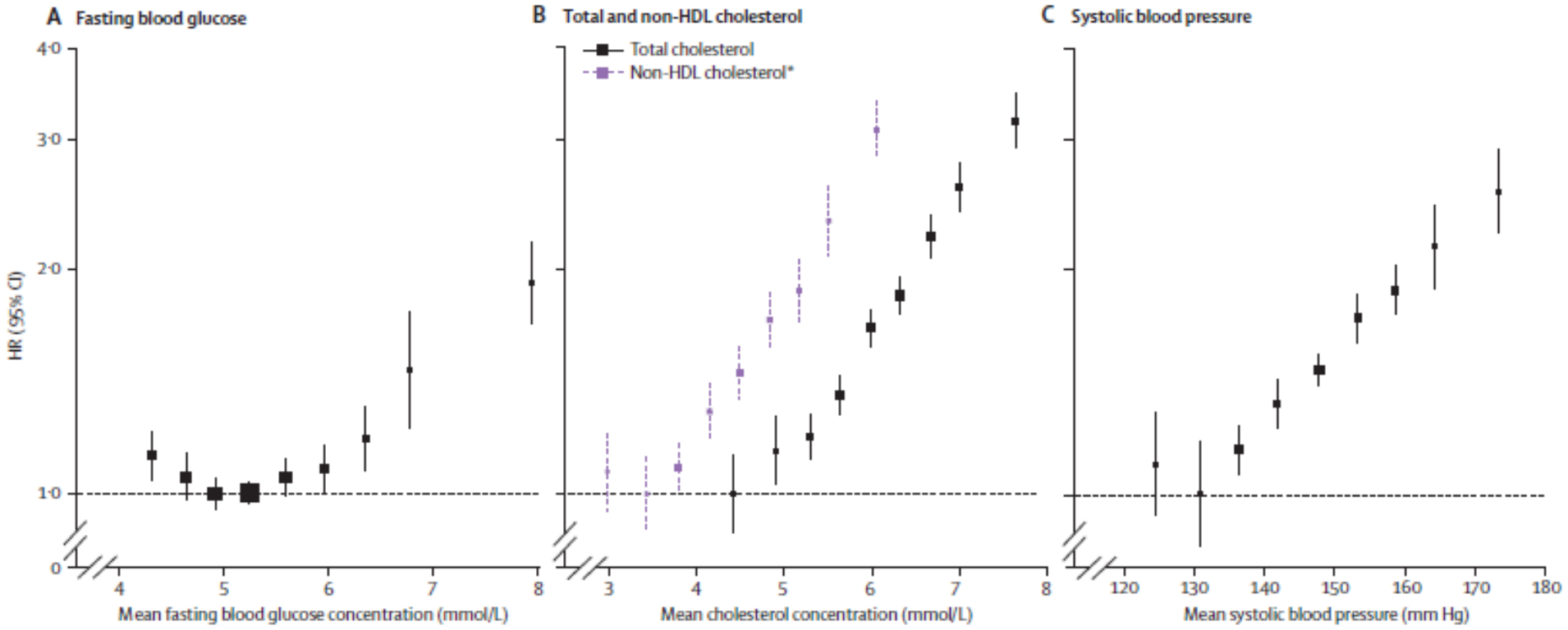

Emerging Risk Factors Collaboration Lancet 2010;375(9733):2215-2222

# Data from 700,000 People



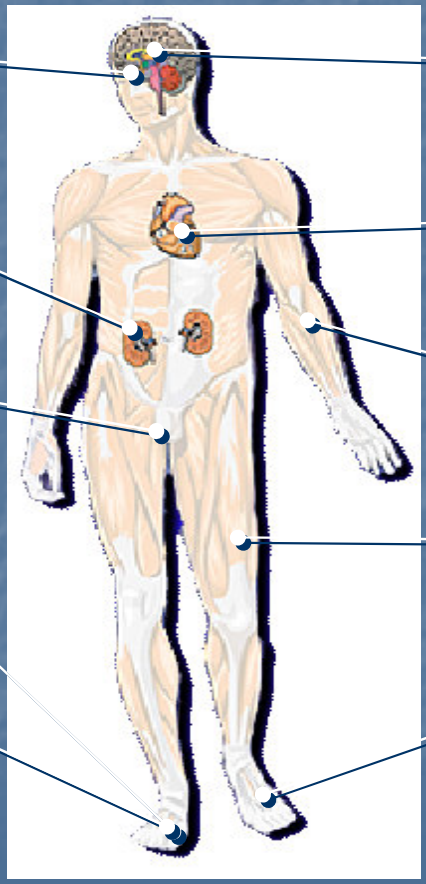

Emerging Risk Factors Collaboration Lancet 2010;375(9733):2215-2222

# Risk of Developing CHD




Emerging Risk Factors Collaboration Lancet 2010;375(9733):2215-2222

# Vascular Complications Of Type 2 Diabetes At The Time Of Diagnosis

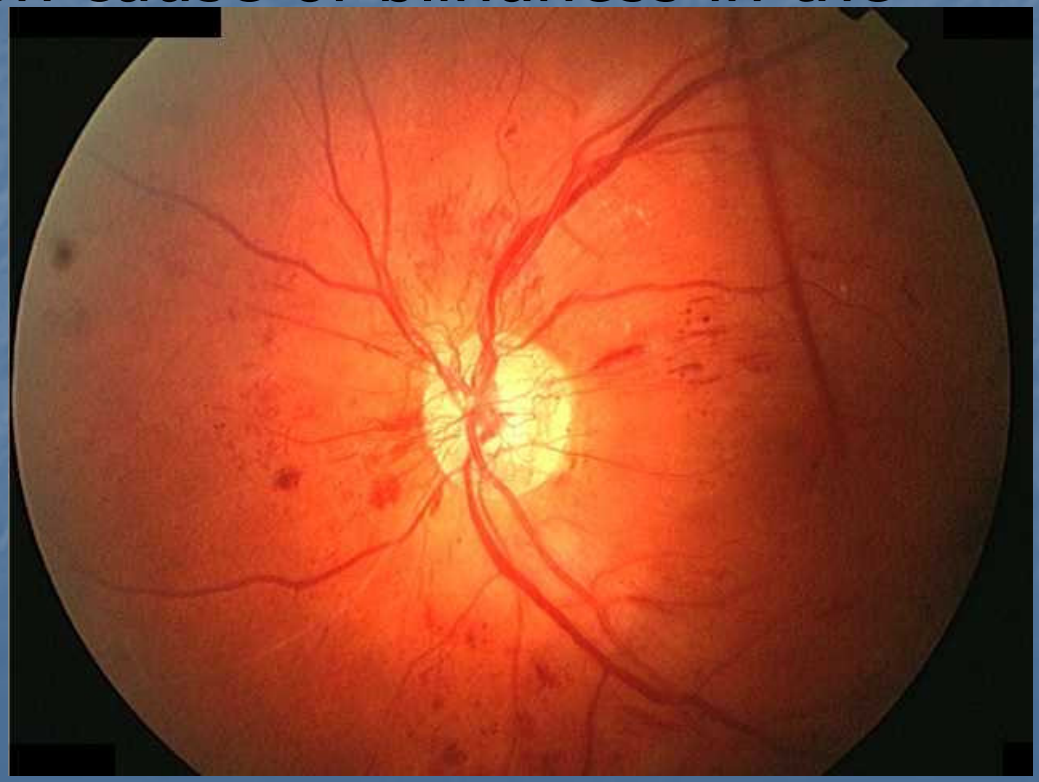


- Retinopathy[1] — 21%
- Nephropathy[2] — 18%
- Erectile dysfunction[1] — 20%
- Ischaemic skin changes (foot)[1] — 6%
- Abnormal vibration threshold (foot)[1] — 7%
- Cerebrovascular disease[3] — 7%
- Abnormal ECG[1] — 18%
- Hypertension[1] — 35%
- Intermittent claudication[3] — 4.5%
- Absent foot pulses[1] — 13%

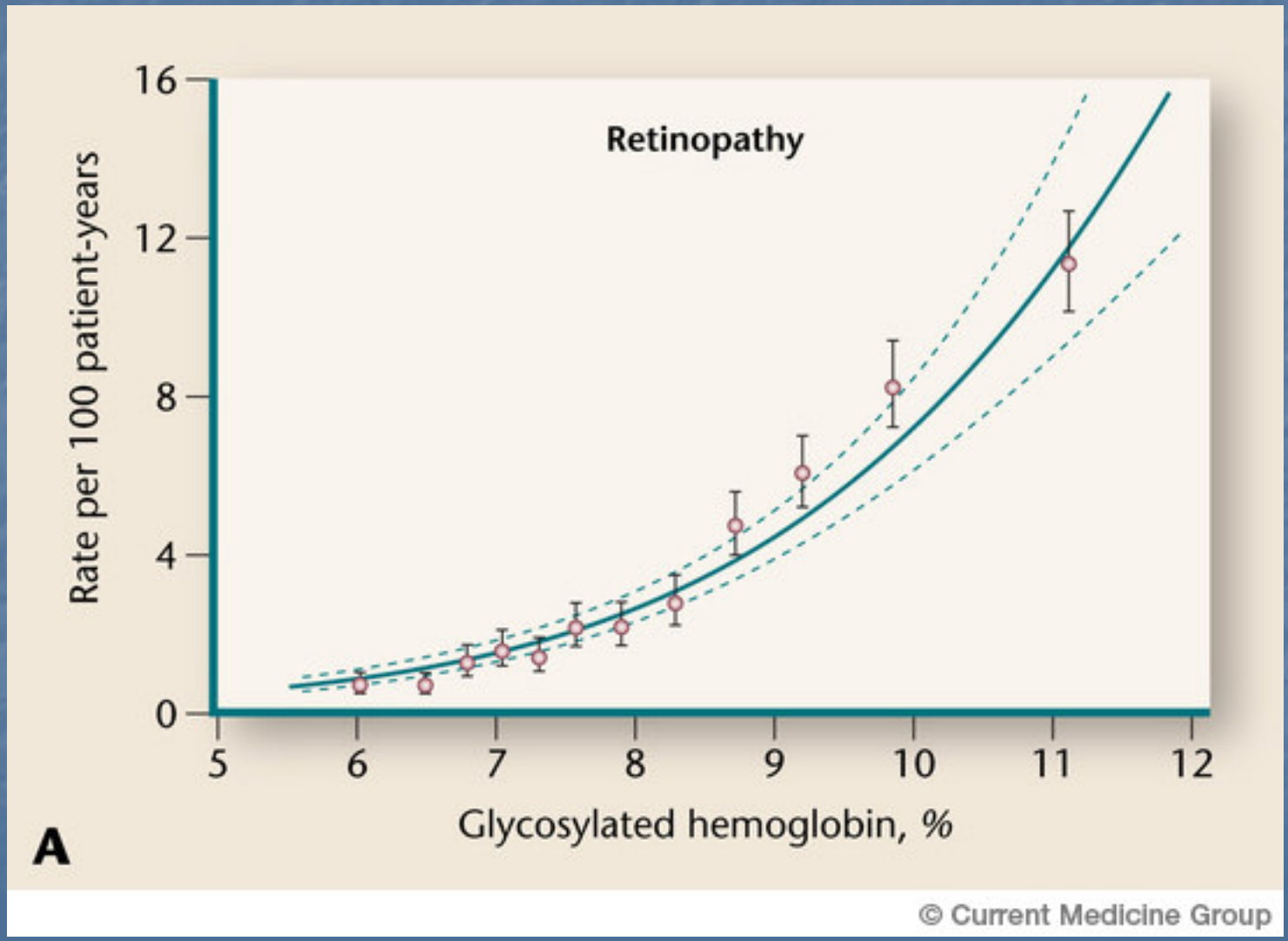
1. UKPDS Group. *Diabetes Res* 1990; **13**: 1–11. 2. The Hypertension in Diabetes Study Group. *J Hypertension* 1993; **11**: 30–17. 3. Wingard DL *et al. Diabetes Care* 1993; **16**: 1022–5.

# OK, so You Die – So What?

- Diabetes remains:
  - The most common cause of blindness in the developed world



# Retinopathy and Glycaemic Control




DCCT Research Group NEJM 1993;329(14):977-986

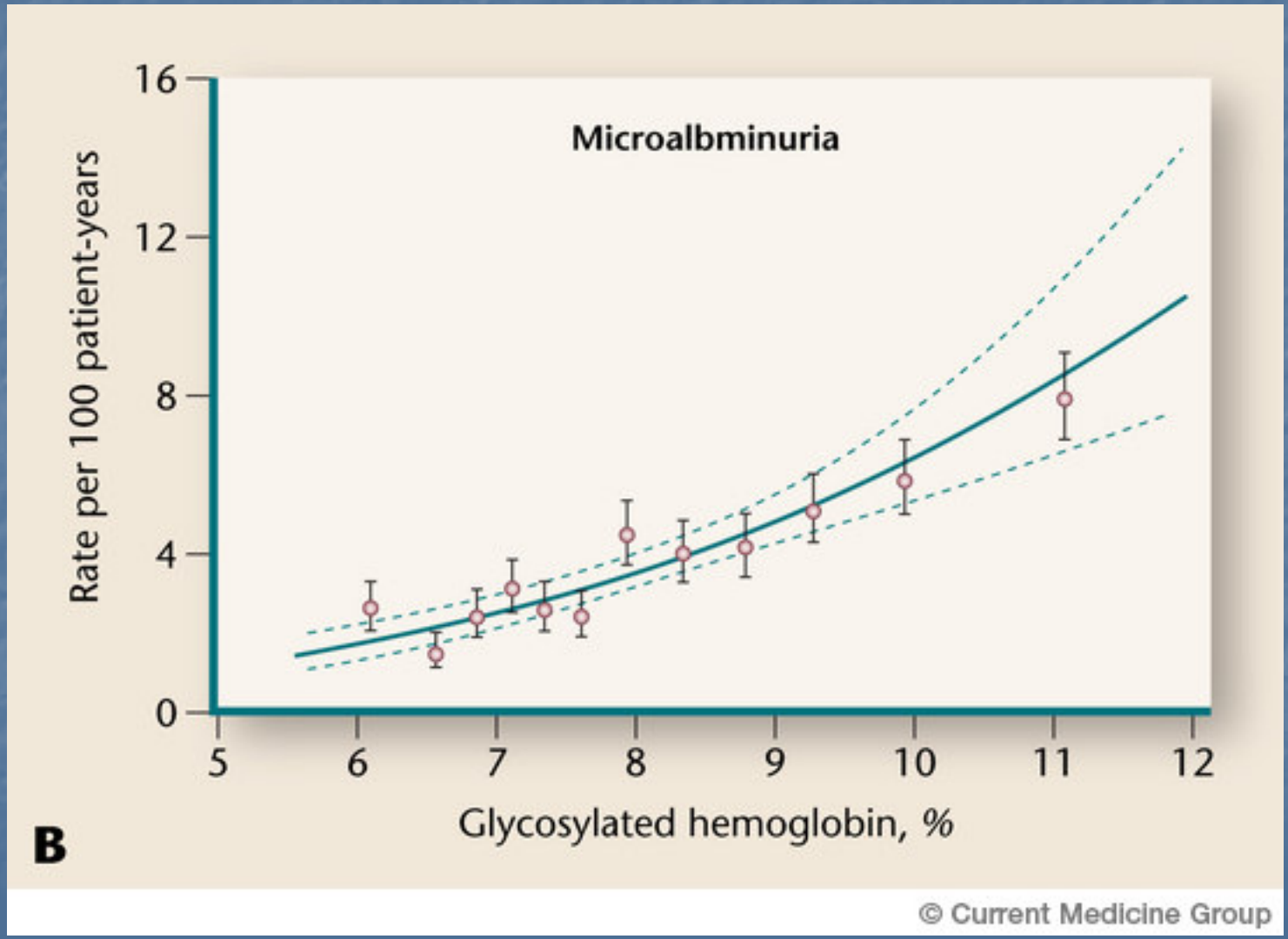
# OK, So You Go Blind Before You Die

- It is the most common cause for non-traumatic lower limb amputations in the world – in the UK, 50% of these occur in the 4% of the population who have diabetes

# OK, So You're Blind and Limp

- Diabetes is the most common cause of end stage renal disease in the world

# Nephropathy and Glycaemic Control

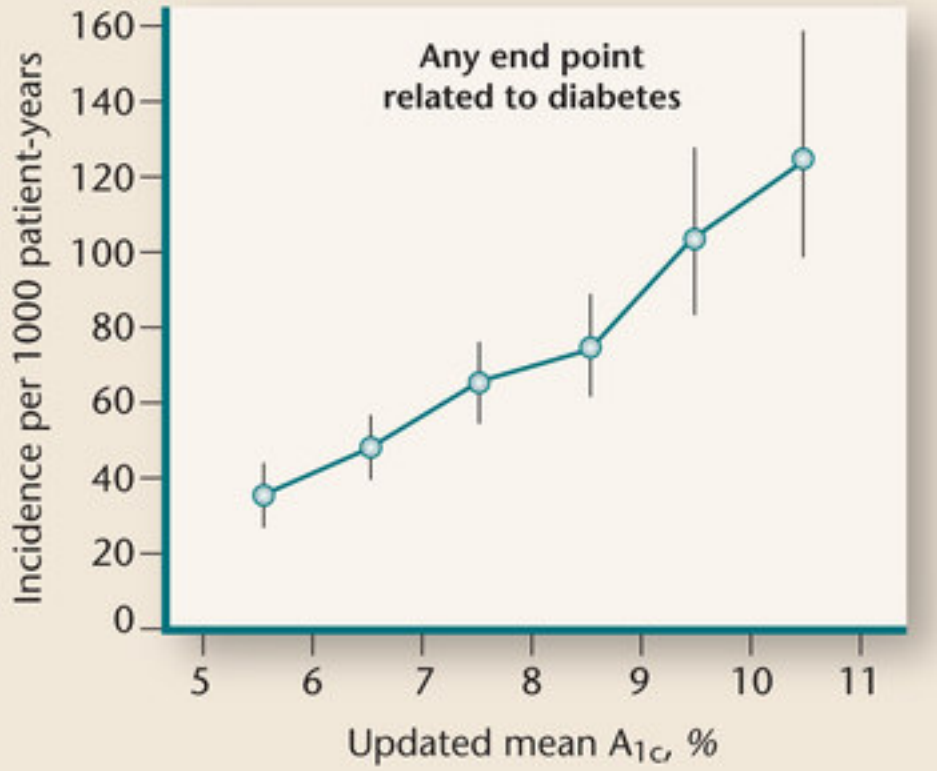



DCCT Research Group NEJM 1993;329(14):977-986

# Blind, Limp and on Dialysis

- You have a 2 – 3 fold increased risk of macro-vascular risk
  - i.e. strokes and heart attacks

# Glycaemic Control is Important




**Reduction in risk per 1% reduction in $A_{1c}$ (9 mmol/mol)**

- Overall: 21%*
- Diabetes mortality: 21%*
- MI: 14%
- Stroke: 12%†
- Microvascular: 37%*
- Heart failure: 16%†
- Cataract extraction: 19%*
- Amputations or PVD death: 43%*

* $P < 0.0001$.
† $P < 0.05$.



UKPDS Lancet 1998;352(9131):837-853

# Numbers Needed to Treat

- Primary prevention over 5 years
  - Statin – 40 – 70
  - BP lowering drugs – 80 – 160
  - Aspirin – > 300

Ridker PM et al Circulation: Cardiovascular Quality and Outcomes. 2009;2:616-623

# Blind, Limp, on Dialysis and Someone Wiping your Bottom

It’s all preventable

A little bit of exercise

A little bit less to eat

Any Questions?