



# An Introduction to Diabetes

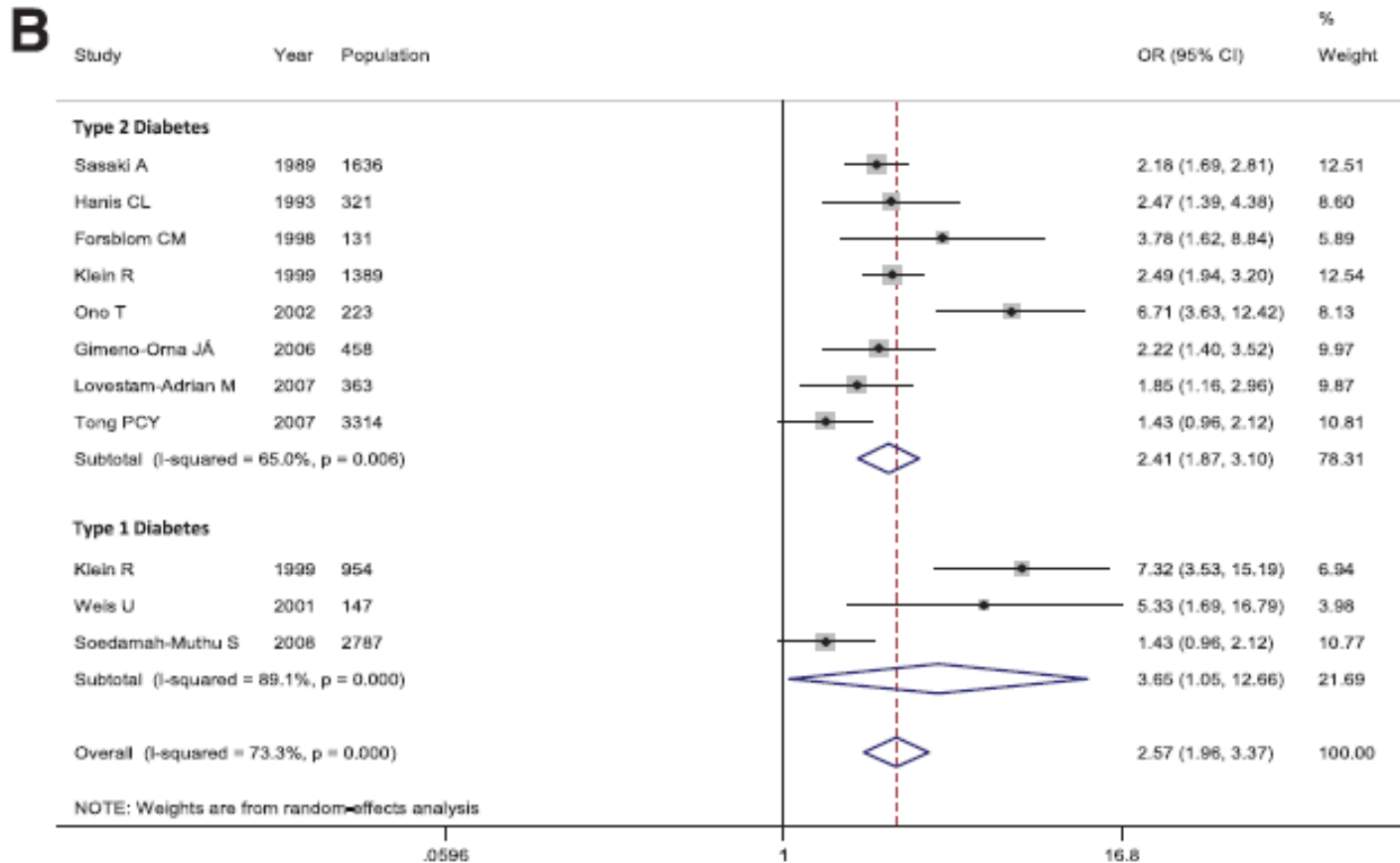
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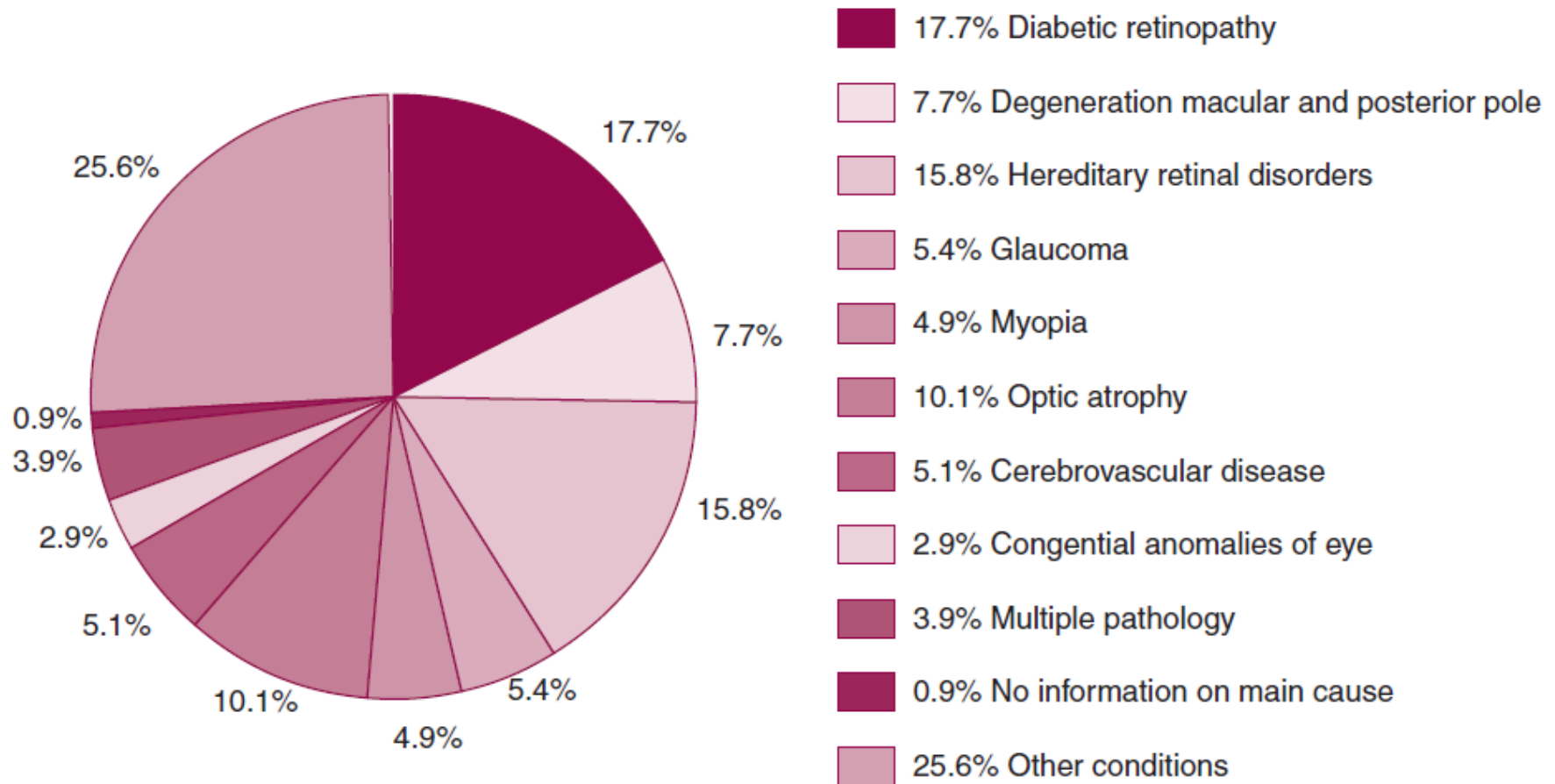


# Why is This an Important Subject?

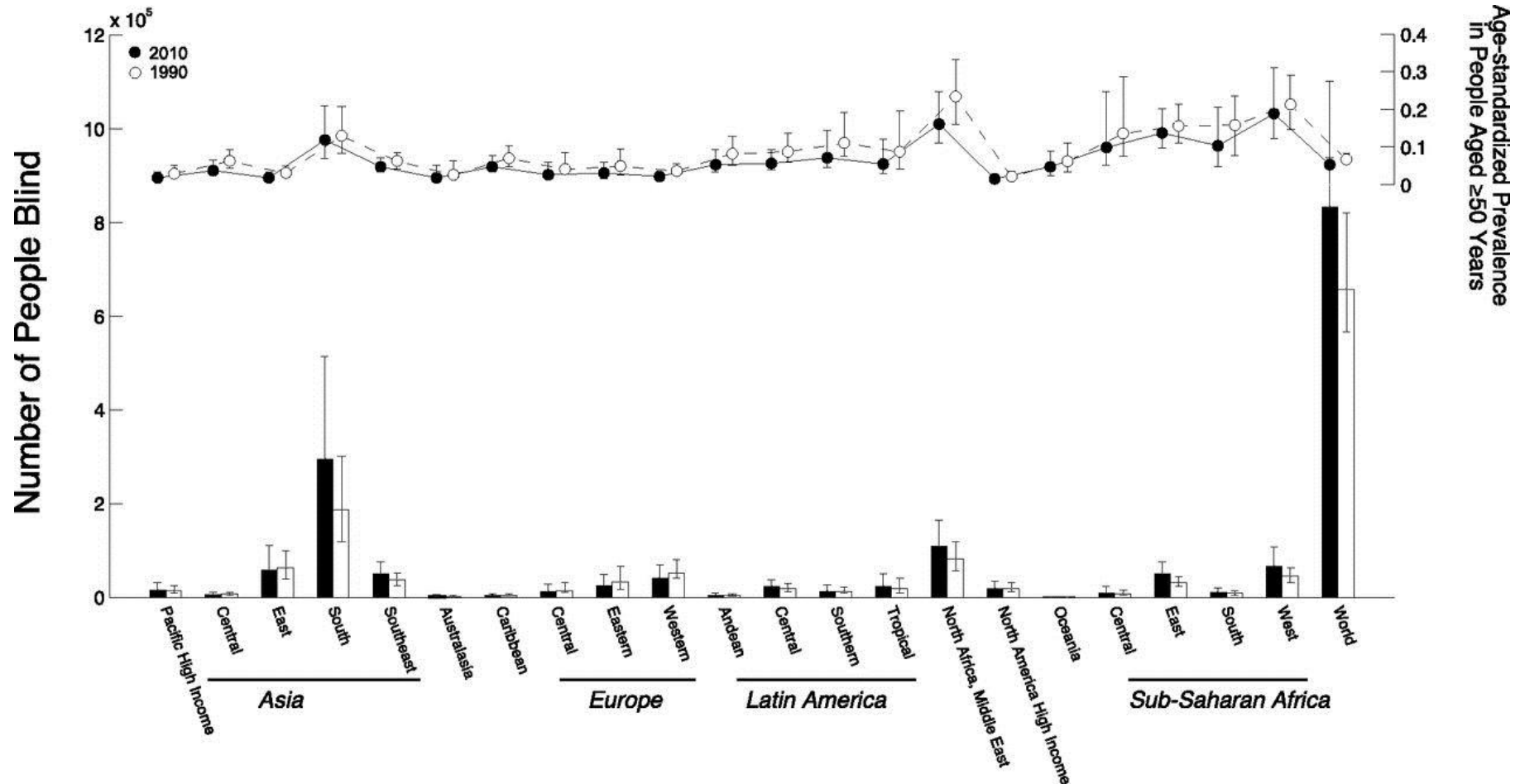


Because the presence of any form of retinopathy is associated with an increased all-cause mortality rate

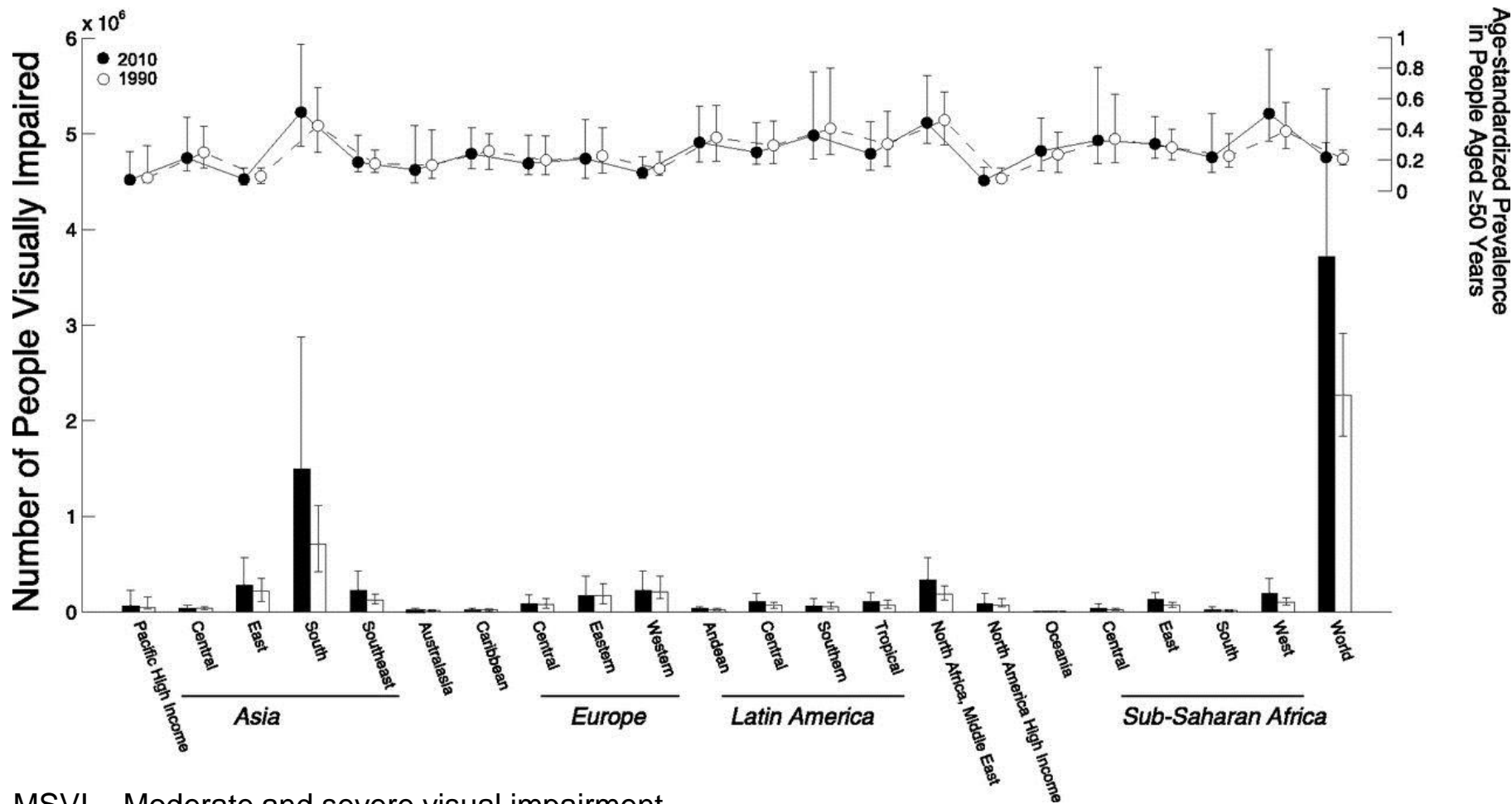
# Causes of Blindness in England and Wales 1999-2000



# Number of People with Blindness Due to DR in 1990 and 2010



# Number of People with MSVI Due to DR in 1990 and 2010



MSVI – Moderate and severe visual impairment

# What is Diabetes Mellitus?

A complex metabolic disorder characterised by chronic hyperglycaemia resulting from defects in insulin secretion or insulin action, or both

First described in 1550 BC

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# Two Main Types

- Type 1
    - Autoimmune destruction of the  $\beta$  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
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# 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
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# Other Types

- Gestational diabetes
  - Drug induced diabetes
  - Genetic disorders
  - Pancreatic disease
-

# How is the Diagnosis Made?

Test	Value
HbA1c	>48mmol/mol (6.5%)
Fasting glucose	>7.0mmol/l (126mg/dl)
2-hour glucose after a 75g oral glucose load	>11.1mmo/l (200mg/dl)
Random glucose	>11.1mmol/l (200mg/dl)

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

# Familial Risks

	Type 1	Type 2
If neither parent has it	1 in 250	10%
If mother has it	1 in 50 - 100	20 – 30 %
If father has it	1 in 12	20 – 30 %
If 1 sibling has it	1 in 15 – 30	40%
If 1 sibling and 1 parent has it	1 in 10	
If both parents have it	1 in 3	70%
If an identical sibling has it		80 – 100%

# Epidemiology

- The 2008/9 National Diabetes Audit found the prevalence of diabetes to be 4.13% in England and Wales. This rose to 6.6% in 2012 (a 59% increase in 4 years!)
- ~90% of whom have Type 2 diabetes
- Lifetime risk of developing diabetes is about 10%

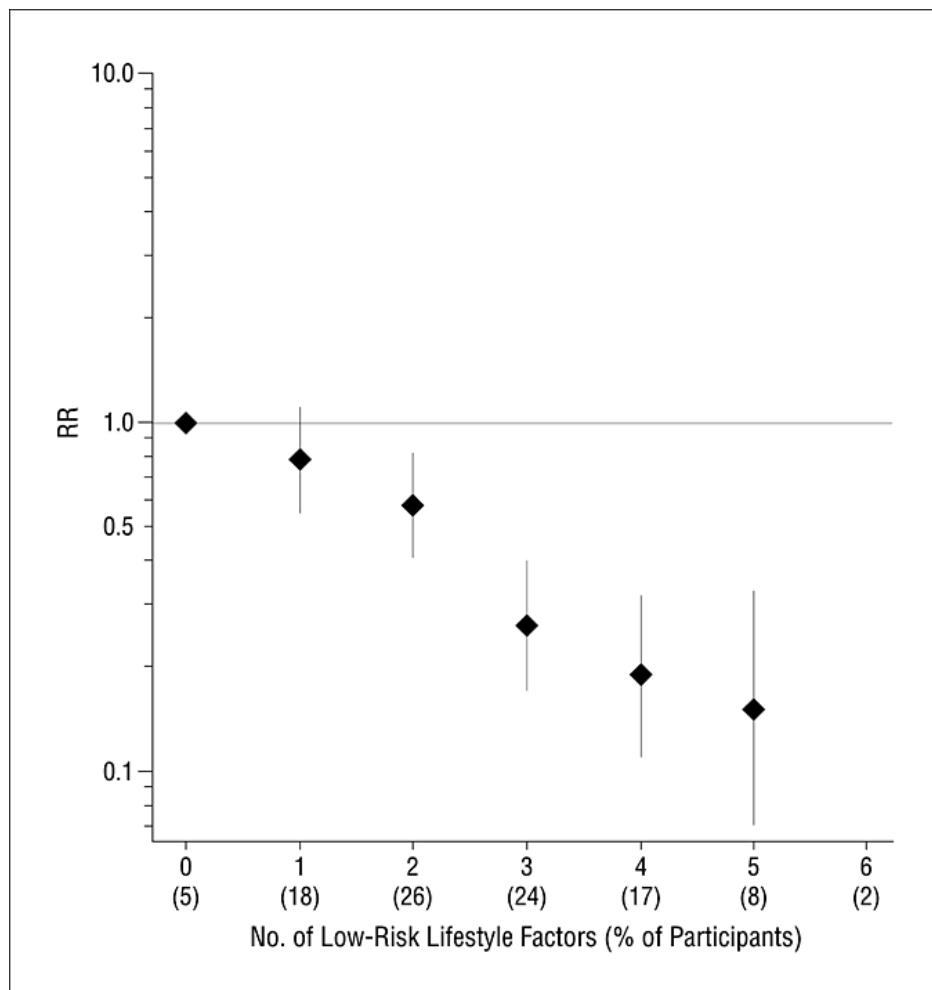
# The Global Burden

WHO Region	Prevalence (%)		Number (millions)		Percentage increase
	1980	2014	1980	2014	
<b>Africa</b>	3.1%	7.1%	4	25	229%
<b>Americas</b>	5%	8.3%	18	62	166%
<b>Eastern Mediterranean</b>	5.9%	13.7%	6	43	232%
<b>Europe</b>	5.3%	7.3%	33	64	137%
<b>SE Asia</b>	4.1%	8.6%	17	96	210%
<b>Western Pacific</b>	4.4%	8.4%	29	131	191%
<b>Total</b>	<b>4.7%</b>	<b>8.5%</b>	<b>108</b>	<b>422</b>	<b>194%</b>

# The Global Burden

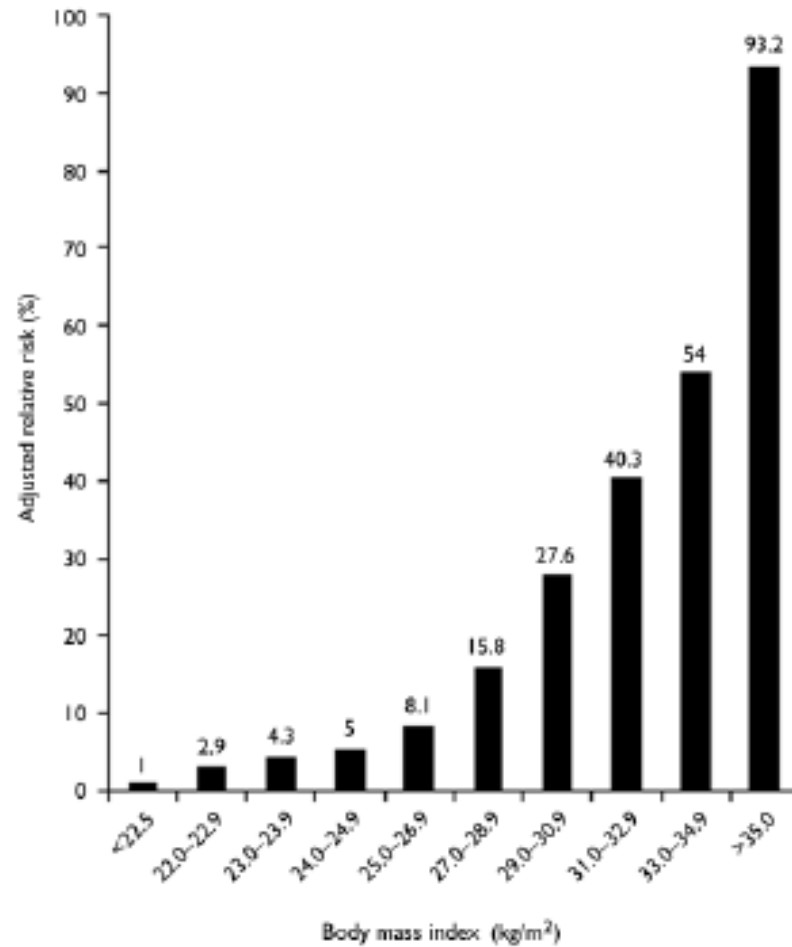
- Diabetes related healthcare costs account for about 10% of all health expenditure in developed nations
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# Relative Risk of Developing Diabetes



- Lower with more lifestyle factors
  - Moderate physical activity
  - Healthy diet
  - Never smoked
  - Moderate alcohol use
  - BMI < 25 Kg/m<sup>2</sup>
  - Waist circumference less than 88 cm for women or 92 cm for men

# BMI and Diabetes





# Clinical Features

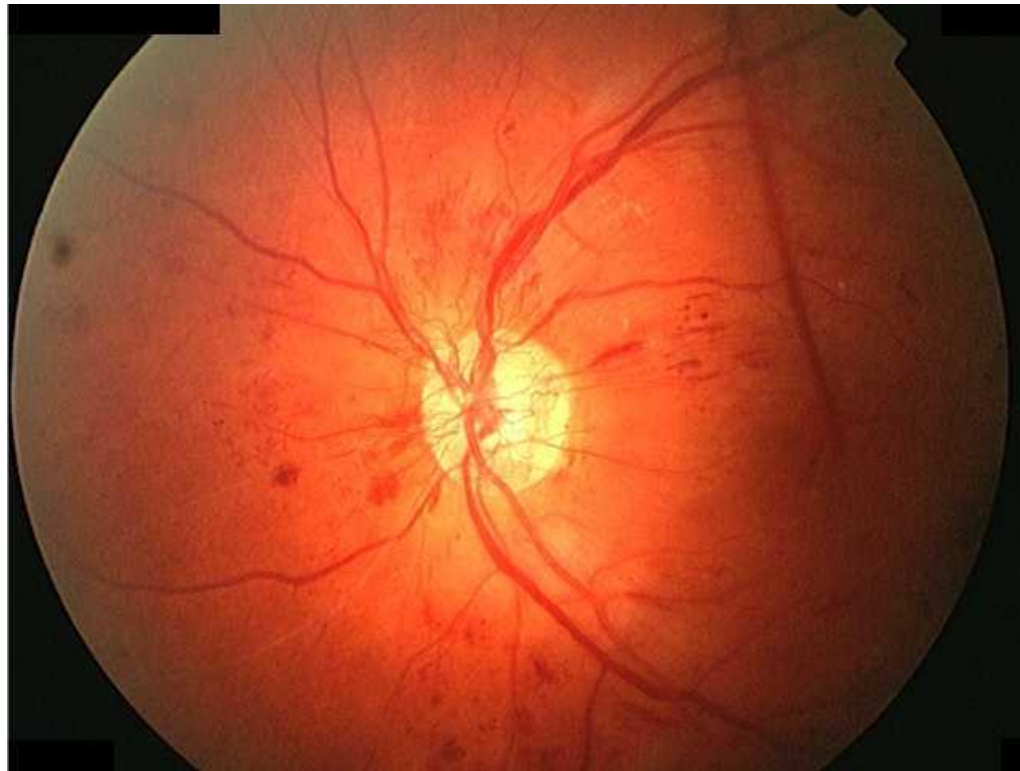
	Type 1	Type 2
<b>Age at Onset (years)</b>	<b>&lt; 40</b>	<b>&gt; 40</b>
<b>Duration of Symptoms</b>	<b>Days or Weeks</b>	<b>Years</b>
<b>Body Weight</b>	<b>Normal or Low</b>	<b>Normal or High</b>
<b>Ketones</b>	<b>Yes</b>	<b>No</b>
<b>Insulin Mandatory?</b>	<b>Yes</b>	<b>No</b>
<b>Autoantibodies</b>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

# Why is it Important?

- Poorly controlled diabetes leads to accelerated cardiovascular morbidity and mortality
- A combination of microvascular and macrovascular disease

# Microvascular Disease

- Diabetic retinopathy – the commonest cause of blindness in the developed world



# Diabetes and Eyes: Some History

- In the 1970's and 1980's diabetes was the leading cause of severe visual impairment
- People with diabetes were 25 times more likely to have a VA of 20/200 in their best eye due to
  - Haemorrhage
  - Tractional detachment of the macula due to proliferative diabetic retinopathy
  - Macular oedema
  - Cataract
  - Glaucoma

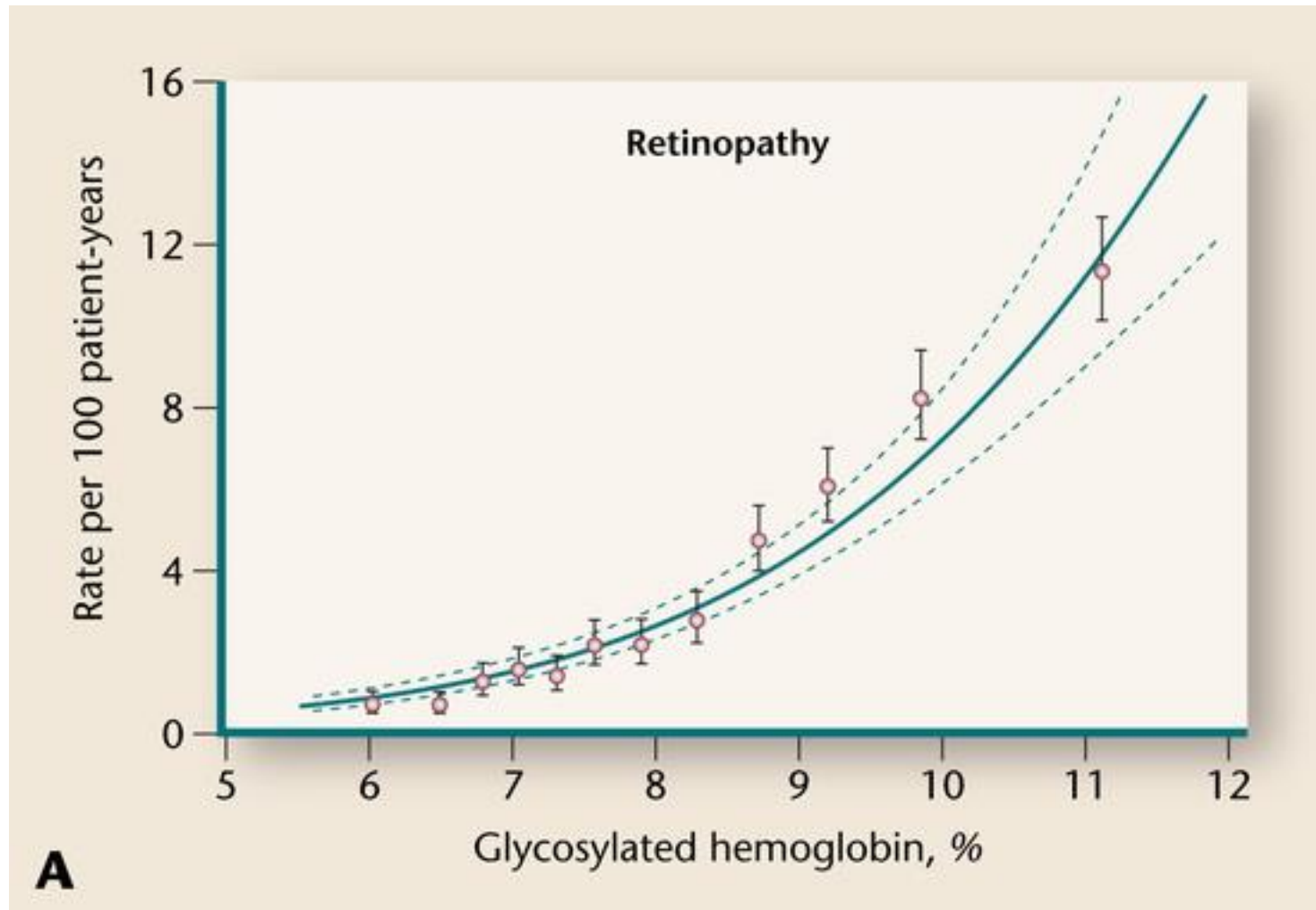
# Some History

- There was no definitive evidence that achieving good glycaemic control would actually result in less diabetic retinopathy
- Also, technology was not of a standard to allow easy optimisation of control
- In the early 1970's the efficacy of photocoagulation had not yet been demonstrated
- Vitrectomy was in its developmental stages

# WESDR

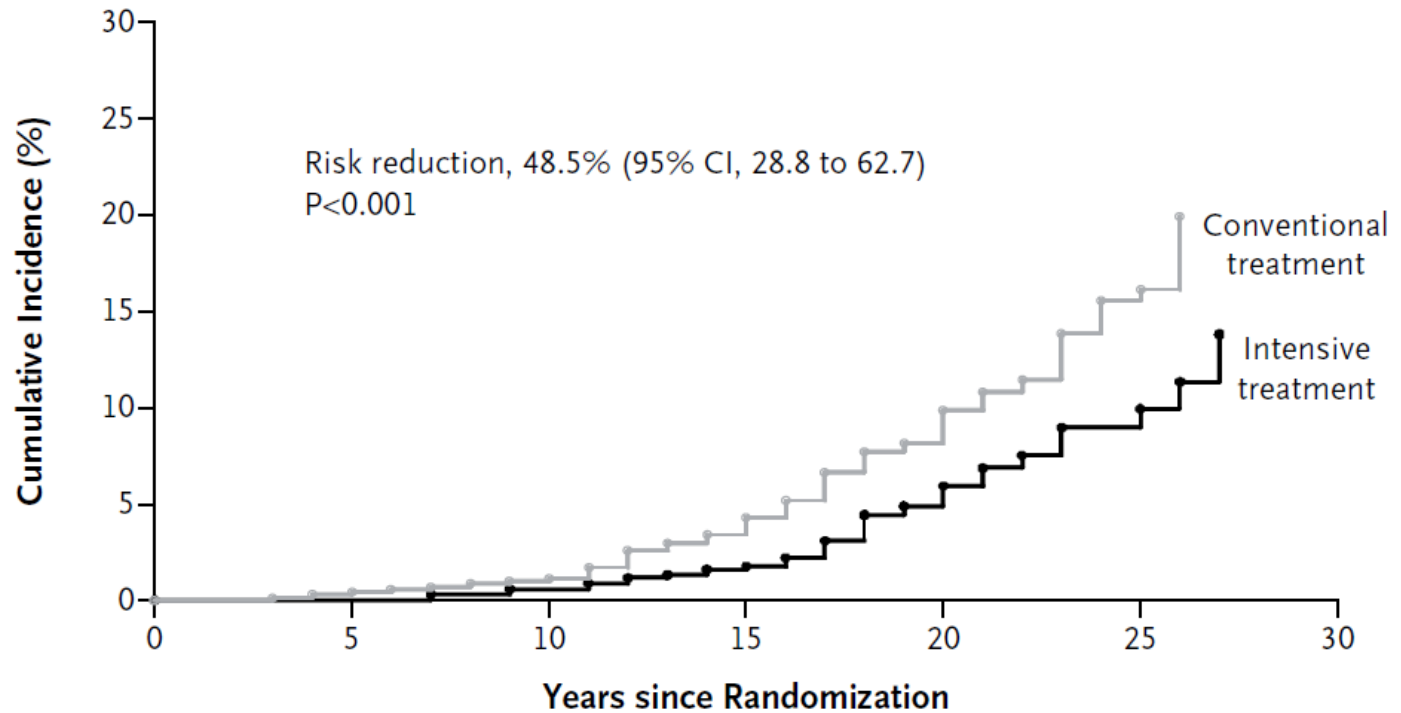
- It was the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) cohort data that first demonstrated a relationship between glycaemic control and the risk of retinopathy

# Retinopathy and Glycaemic Control



# The Effects Last for a LONG Time

## A Any Diabetes-Related Ocular Surgery



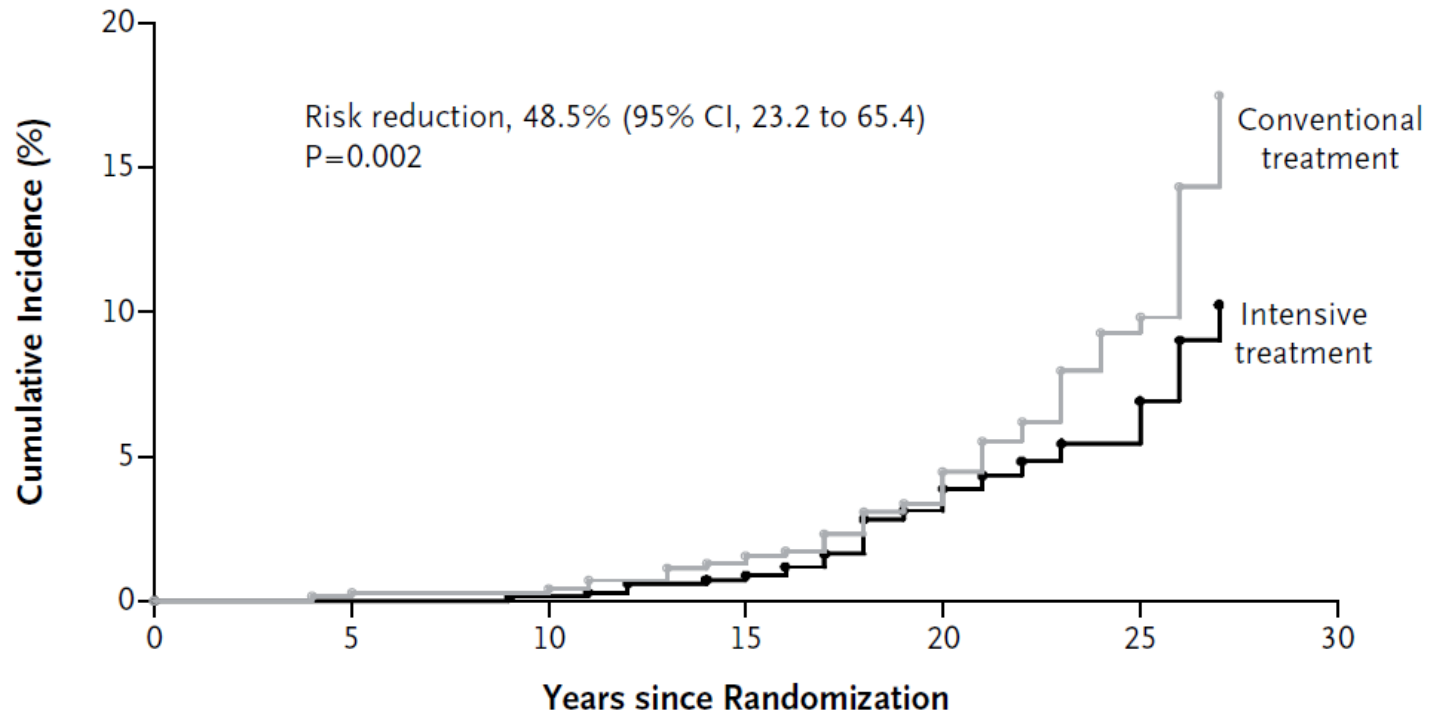
### No. at Risk

Intensive treatment	711	705	688	668	629	184
Conventional treatment	730	721	699	662	596	150



# The Effects Last for a LONG Time

## B Cataract-Extraction Surgery

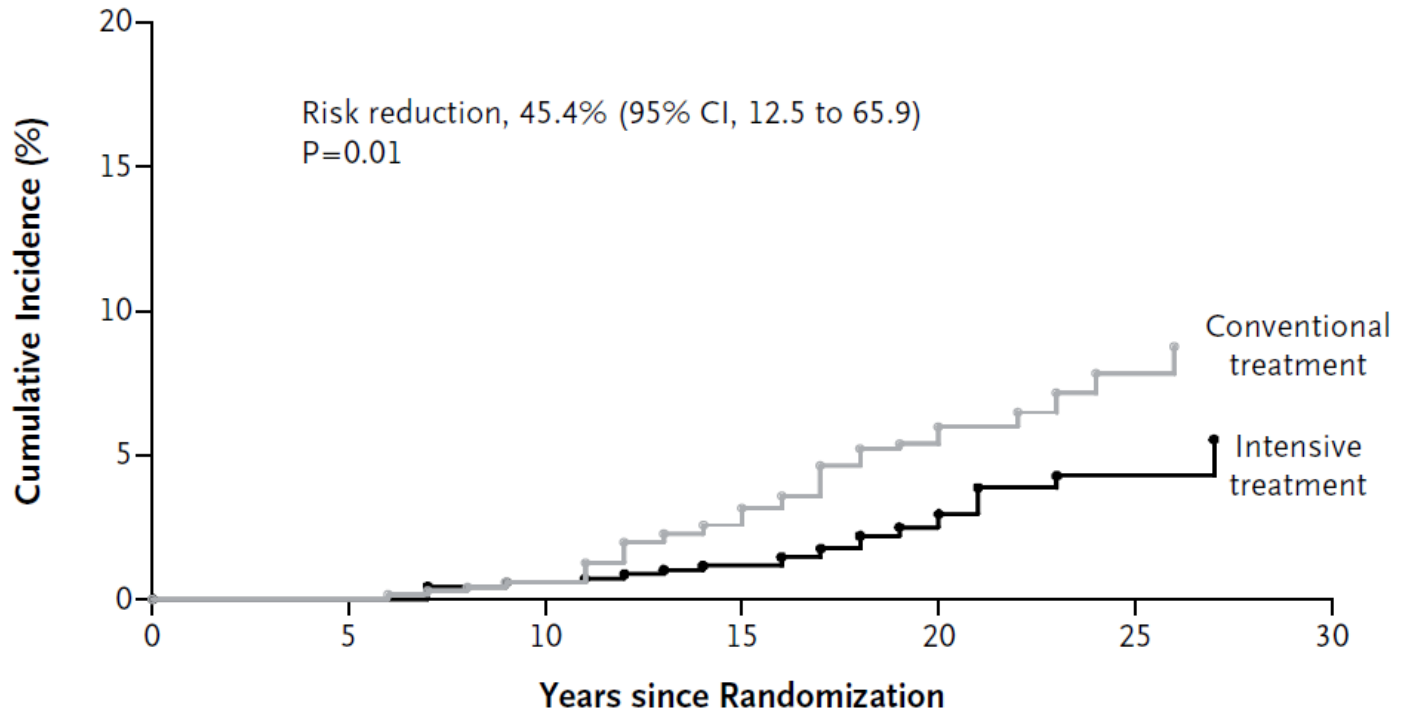


### No. at Risk

Intensive treatment	711	705	691	674	640	191
Conventional treatment	730	722	704	677	626	164

# The Effects Last for a LONG Time

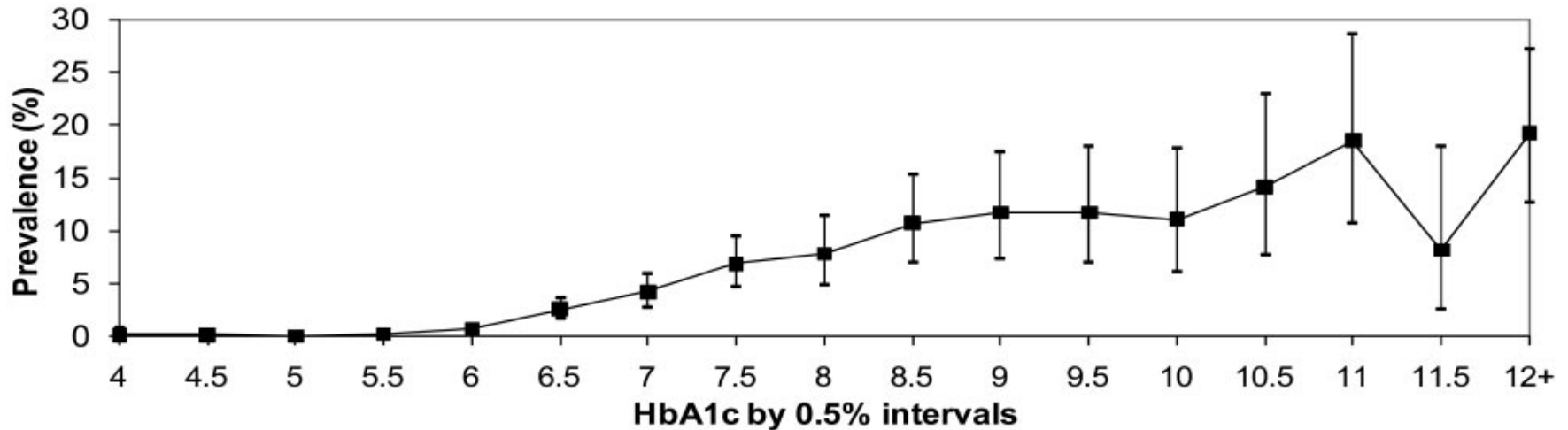
## C Vitrectomy, Retinal-Detachment Surgery, or Both



### No. at Risk

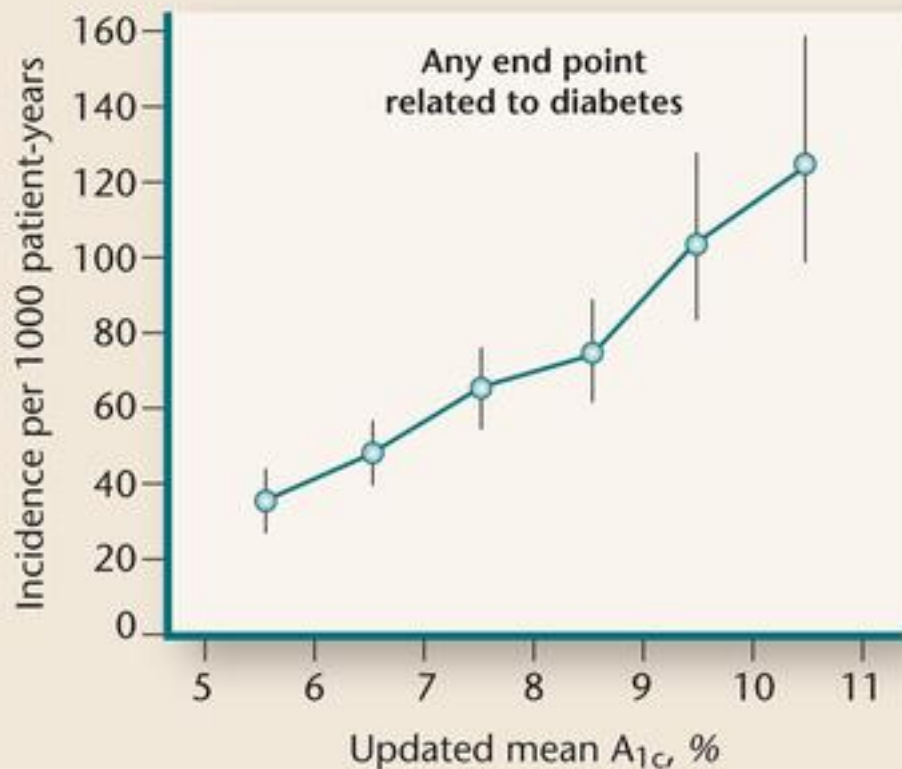
Intensive treatment	711	705	688	671	645	191
Conventional treatment	730	723	702	668	615	159

# Epidemiology of Retinopathy



Cross sectional data from 44,623 individuals

# Glycaemic Control is Important



## Reduction in risk per 1% reduction in A<sub>1c</sub>

Overall: 21%\*

Diabetes mortality: 21%\*

MI: 14%

Stroke: 12%†

Microvascular: 37%\*

Heart failure: 16%†

Cataract extraction: 19%\*

Amputations or PVD death: 43%\*

\*  $P < 0.0001$ .

†  $P < 0.05$ .

# Taking The Right Medication

- Taking glucose lowering medication is important
- So are the other medications
  - Such as ACE inhibitors (drugs that end in 'pril' – e.g. ramipril, enalapril, lisinopril)
  - Or ARB's (drugs that end in 'artan' – e.g. losartan, candesartan, valsartan)
  - Lipid lowering agents

# Microvascular Disease

- Neuropathy

Large fiber Neuropathy	Small fiber Neuropathy	Proximal motor Neuropathy	Acute mono Neuropathies	Pressure Palsies
Sensory loss: 0-+++ (Touch, vibration) Pain: +-+++ Tendon reflex: N↓↓↓ Motor deficit 0-+++	Sensory loss: 0-+ (thermal, allodynia) Pain+-+++ Tendon reflex: N-↓ Motor deficit: 0	Sensory loss: 0-+ Pain: +-+++ Tendon reflex: ↓↓ Proximal Motor deficit: +-+++	Sensory loss: 0-+ Pain: +-+++ Tendon reflex: N Motor deficit: +-+++	Sensory loss in Nerve distribution: +-+++ Pain: +-+++ Tendon reflex: N Motor deficit: +-+++

# Microvascular Disease

- Combinations of neuropathy and ischaemia



# Microvascular Disease

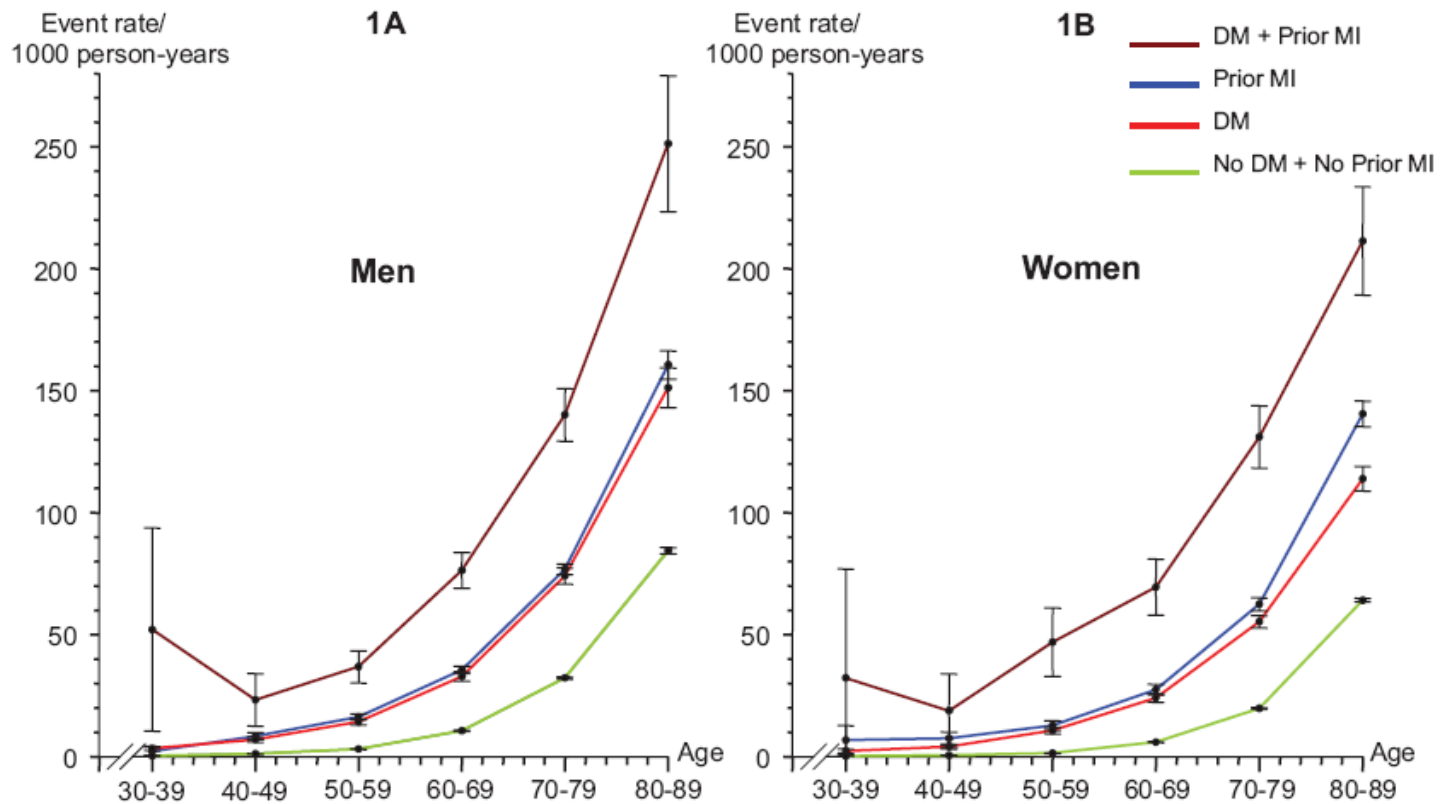
- Nephropathy
    - Diabetes is the commonest cause of End Stage Renal Disease in the developed world
-



# Macrovascular Disease

- Stroke
  - Myocardial infarction
-

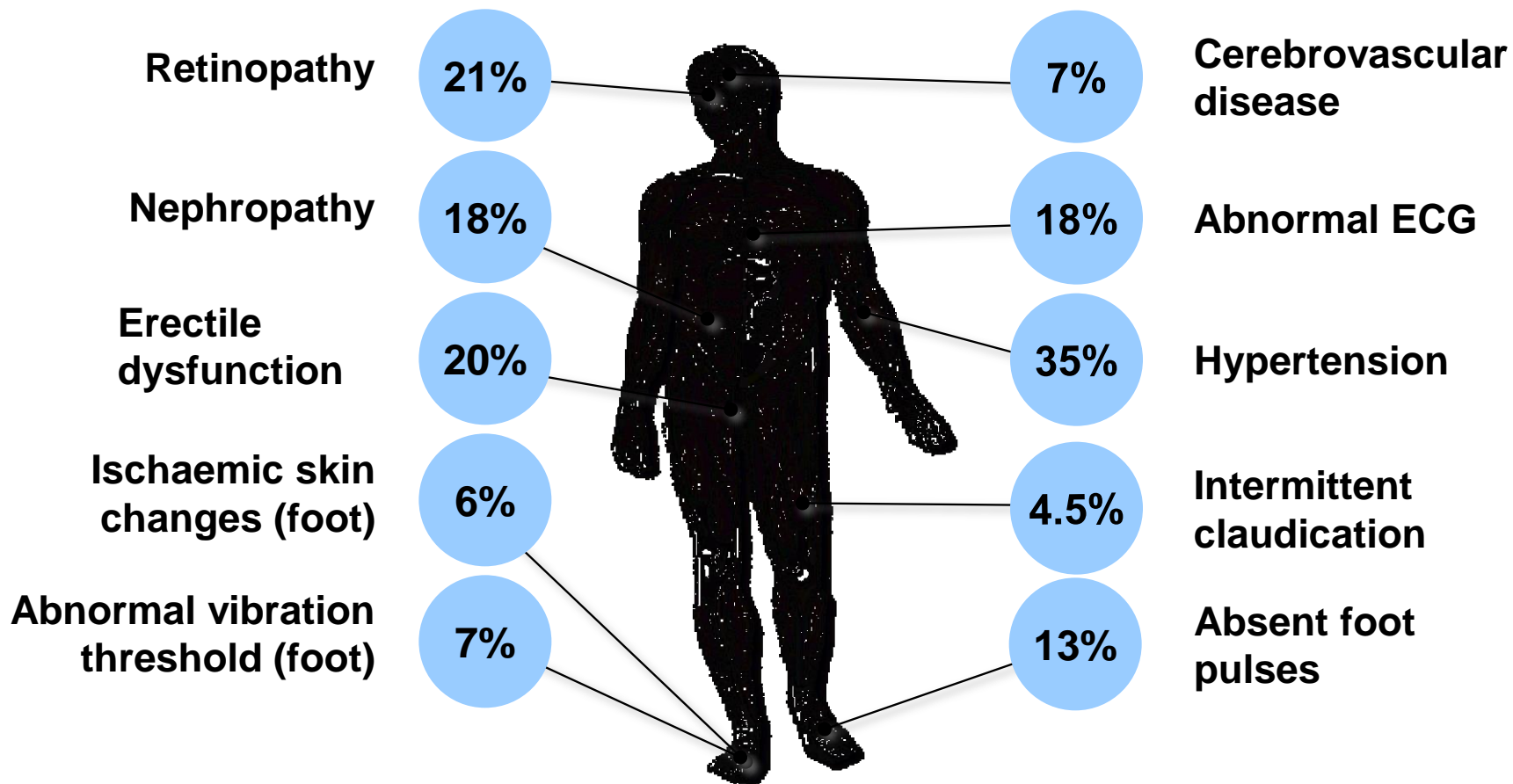
# Data From 3.3M Danes



**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

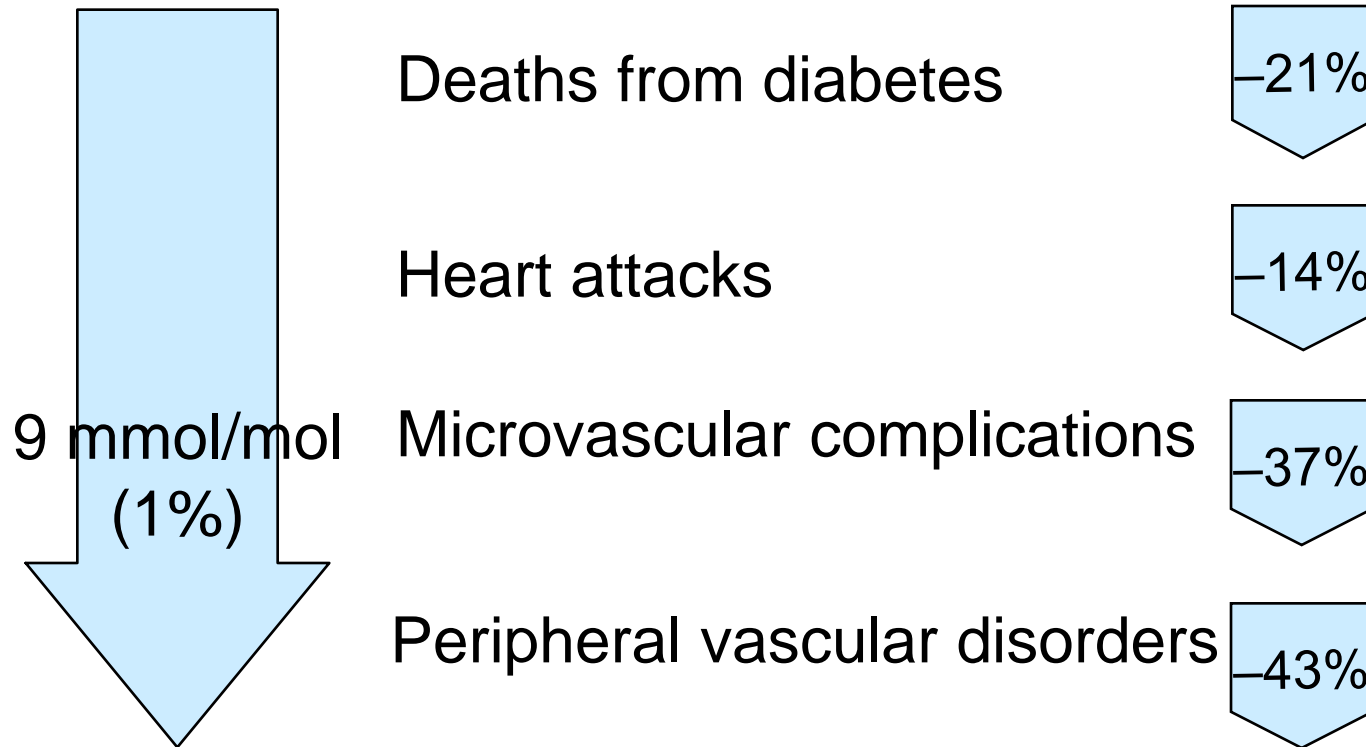
# Vascular Complications Of Type 2 Diabetes At The Time Of Diagnosis



# Lessons from UKPDS: Better Control Means Fewer Complications

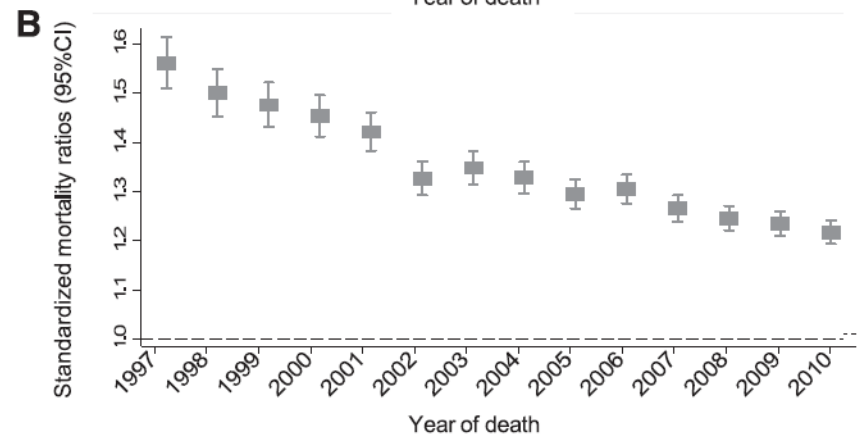
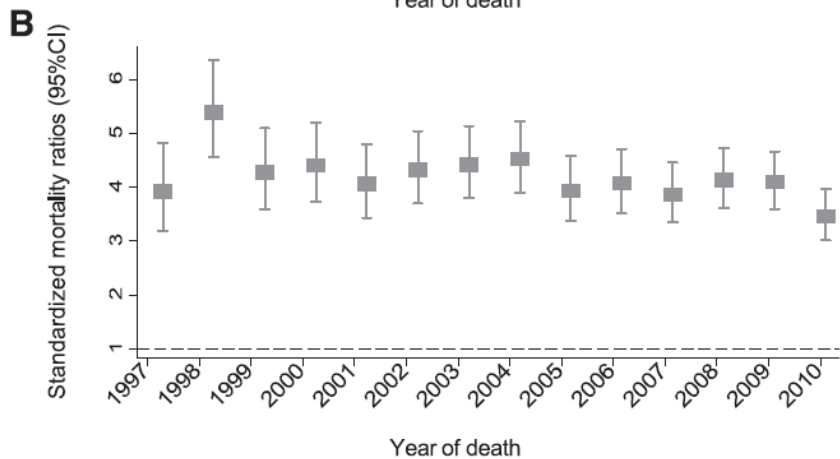
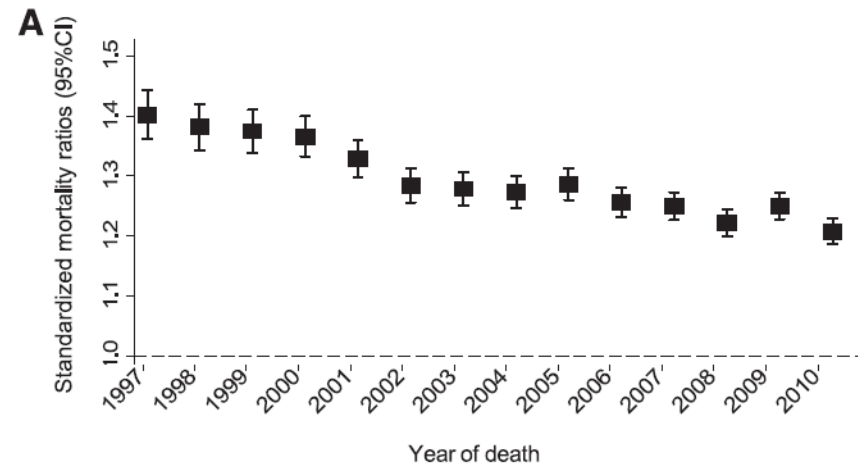
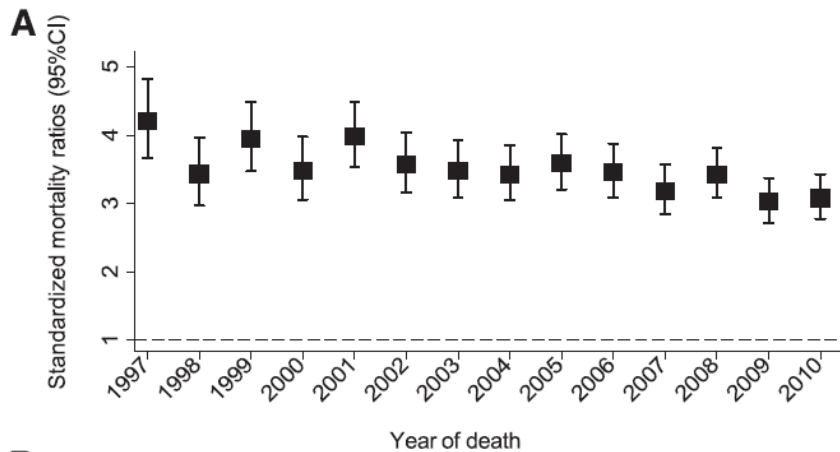
Every 9mmol/mol (1%)  
reduction in HbA<sub>1c</sub>

REDUCED  
RISK\*



\*p<0.0001

# Diabetes Related Mortality is Falling



Type 1

A = Men B = Women

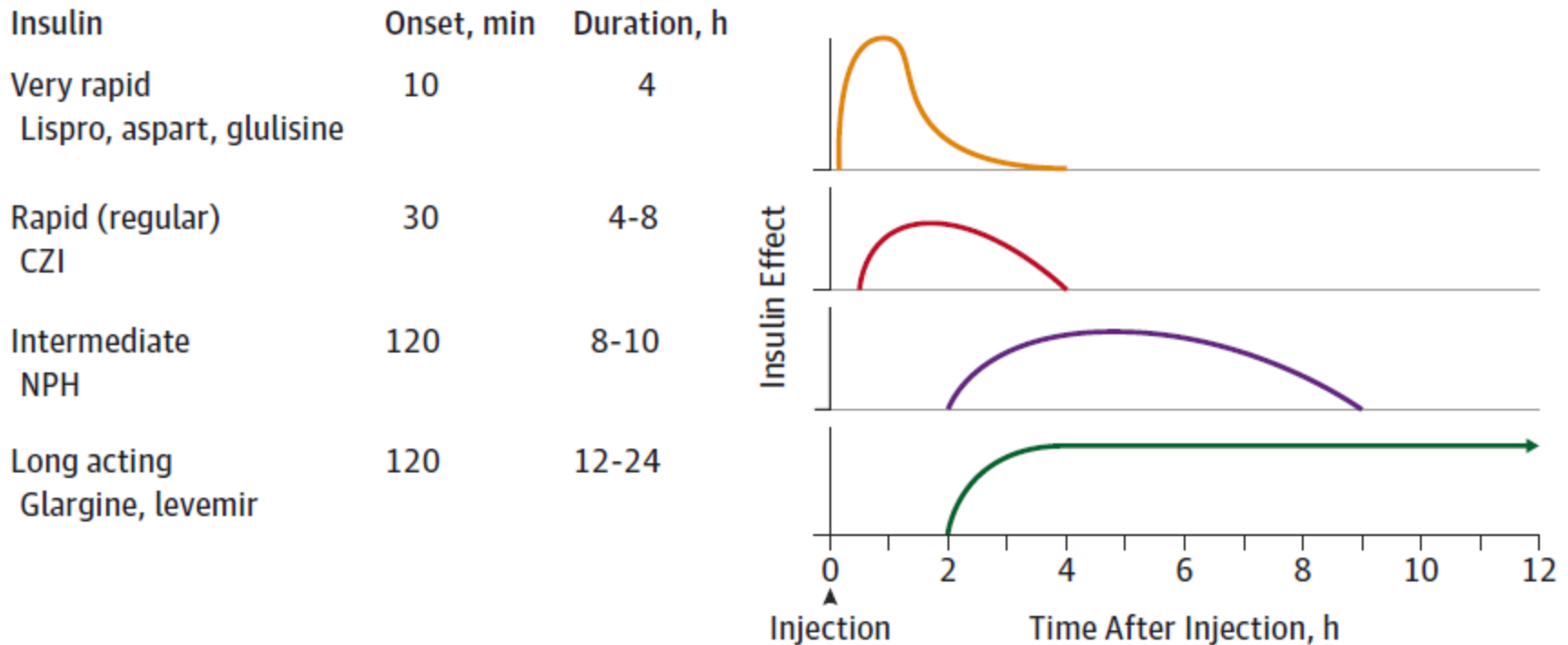
Type 2

# Non-Insulin Hypoglycaemic Agents

- $\alpha$  glucosidase inhibitors
  - Metaglinides
  - Metformin
  - Sulphonylureas
  - Thiazolidindiones
  - GLP – 1 analogues
  - DPP IV inhibitors
  - SGLT 2 inhibitors
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# Insulin Durations

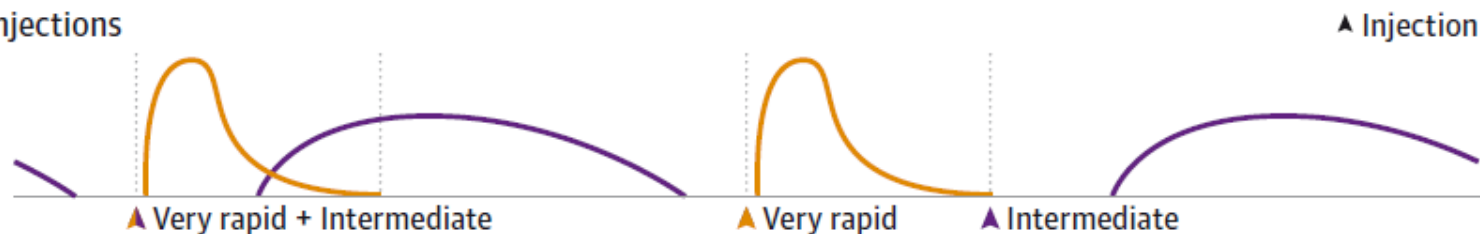
Figure 1. Insulin Activity Profiles



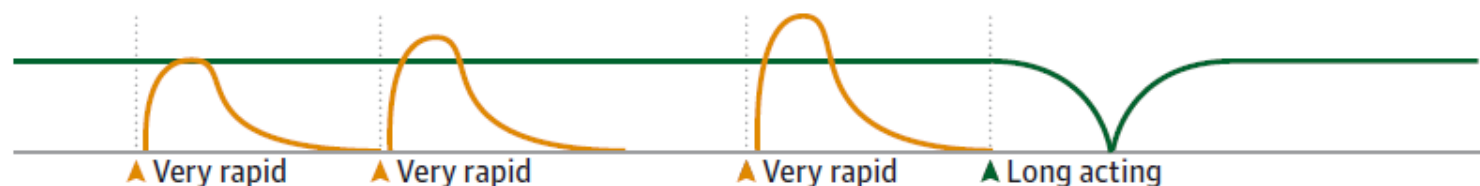
# Insulin Regimens

Figure 2. Three Examples of Insulin Regimens for Type 1 Diabetes

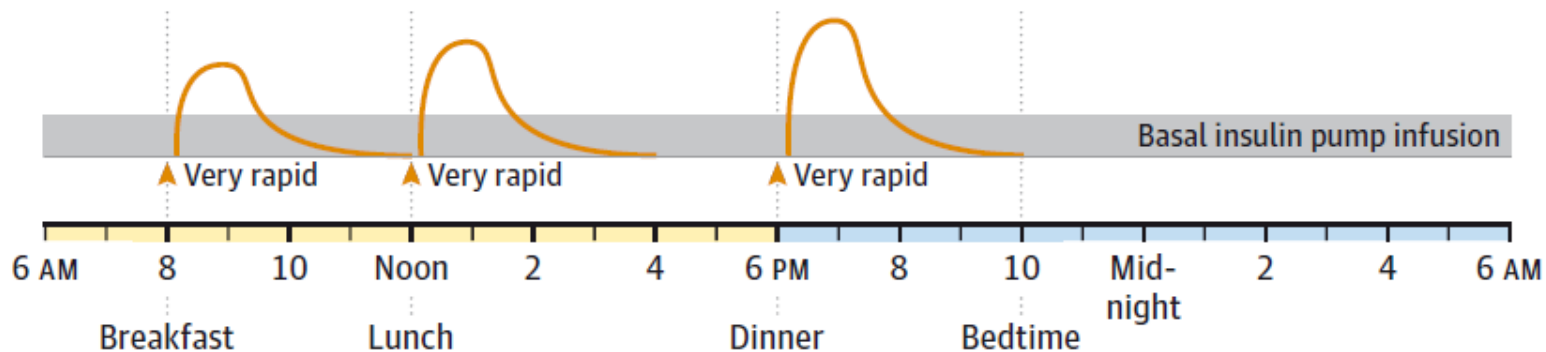
## 3 Daily injections



## 4 Daily injections



## Insulin pump regimen



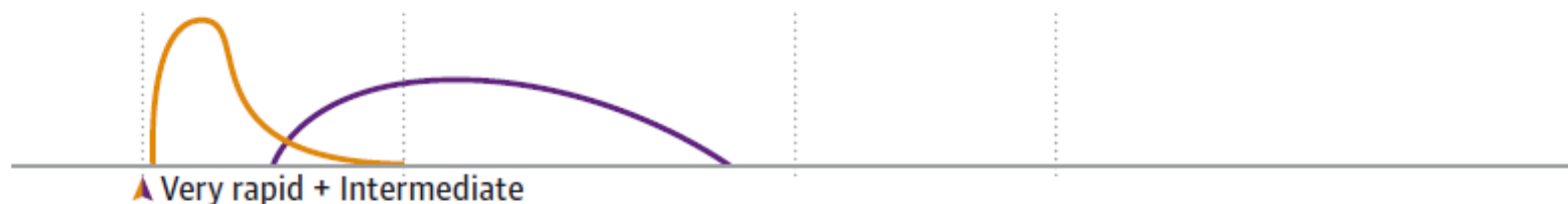


# Insulin Regimens

Figure 3. Three Examples of Single Injection Regimens for Type 2 Diabetes

Combined very rapid plus intermediate insulin

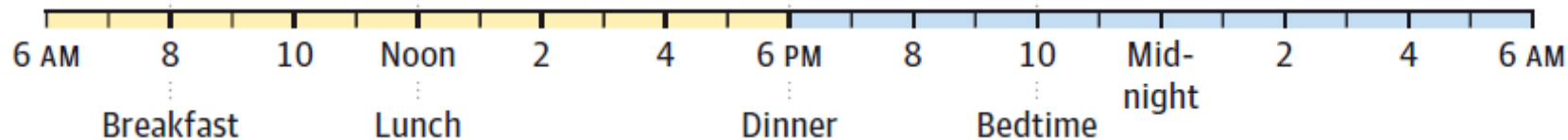
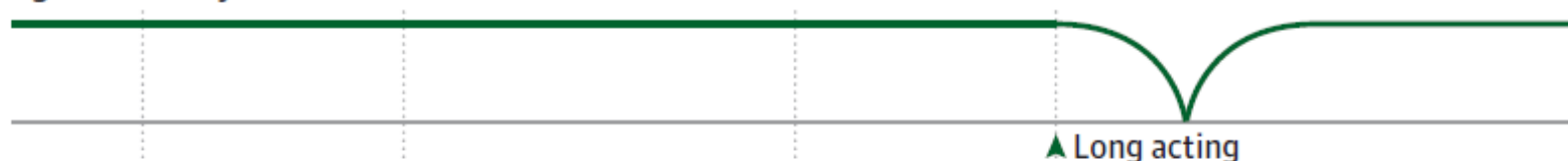
▲ Injection



Intermediate insulin only



Long-acting insulin only



# In Summary

- Diabetes is very common, and type 2 diabetes is becoming commoner
  - Good glycaemic control is important to help reduce the risk of developing the microvascular and macrovascular complications – or to reduce the risk of progression
  - Regular screening for complications is essential
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# What Can YOU Do?

- Ask them if they take all their medication every day
  - Ask them to stop smoking
  - Ask them to see their doctor if they have any concerns or problems sooner rather than later
-



# An Introduction to Diabetes

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