An Introduction to Diabetes

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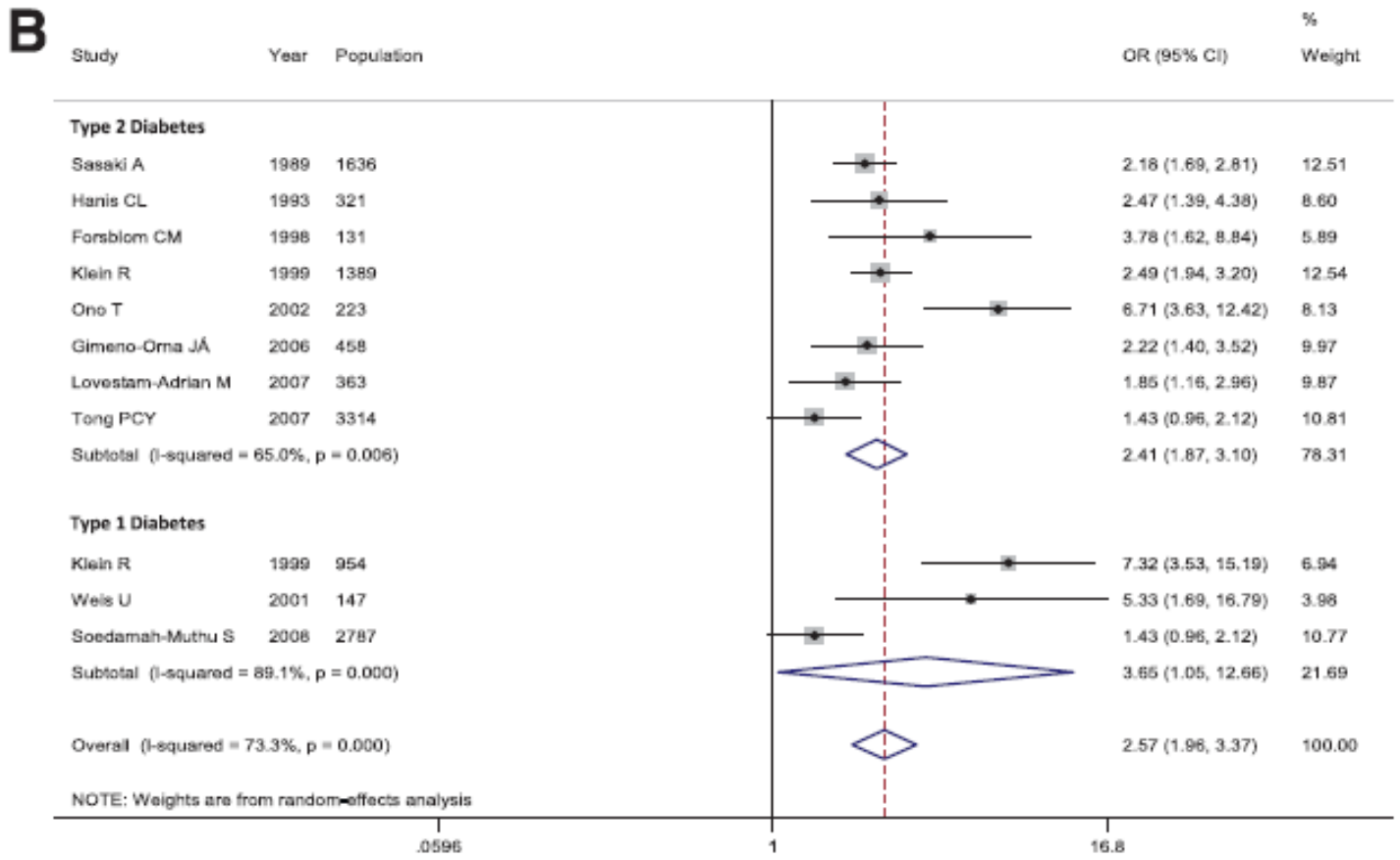
Why is This an Important Subject?



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

Kramer CK Diabetes Care 2011;34(5):1238-1244

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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

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

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

ADA Diabetes Care 2015;38(Suppl 1):S8-S16

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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%

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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 NHS Information Centre, National Diabetes Audit Executive Summary 2010
http://www.idf.org/atlasmap/atlasmap Last accessed 1st October 2014

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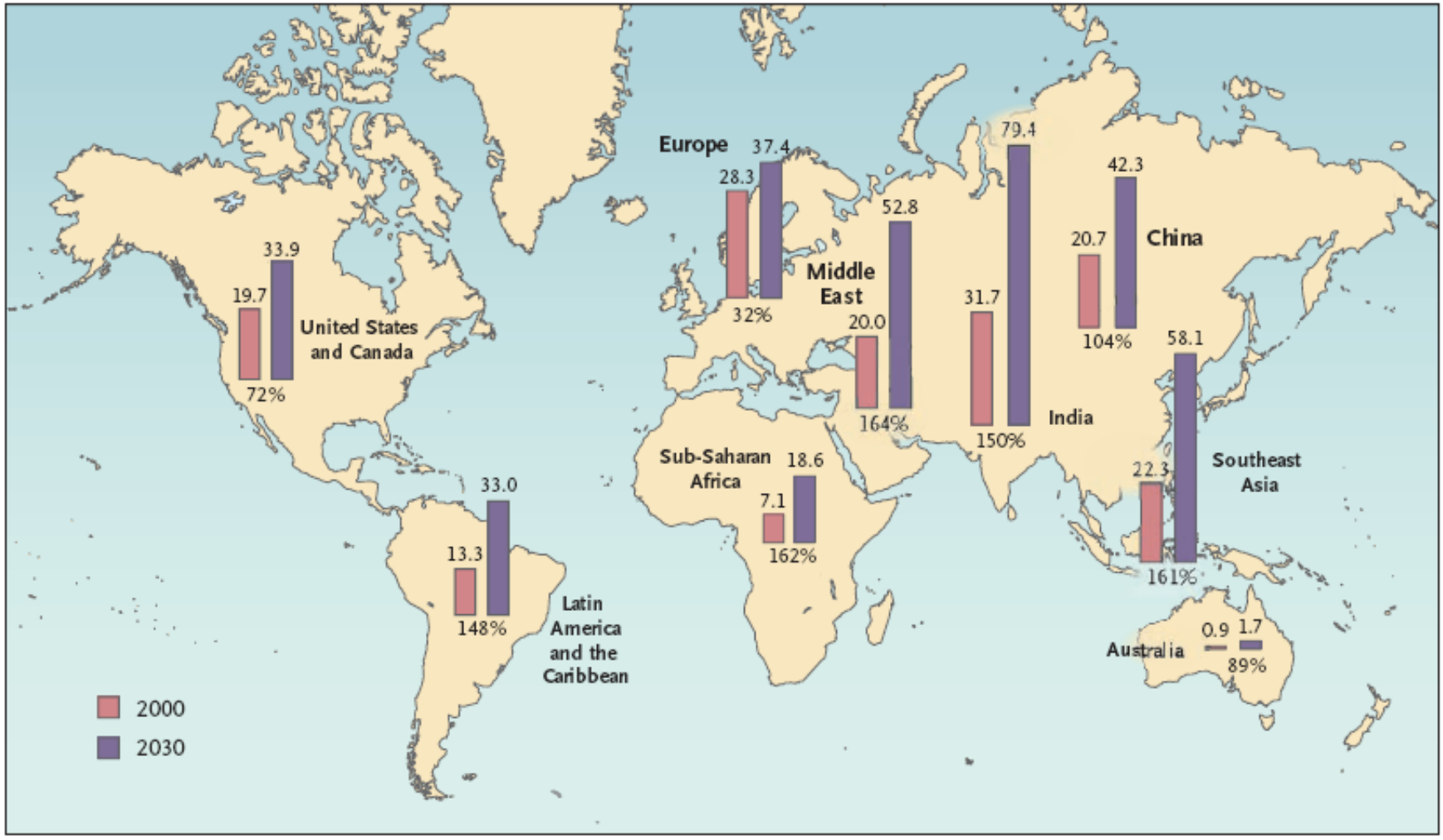
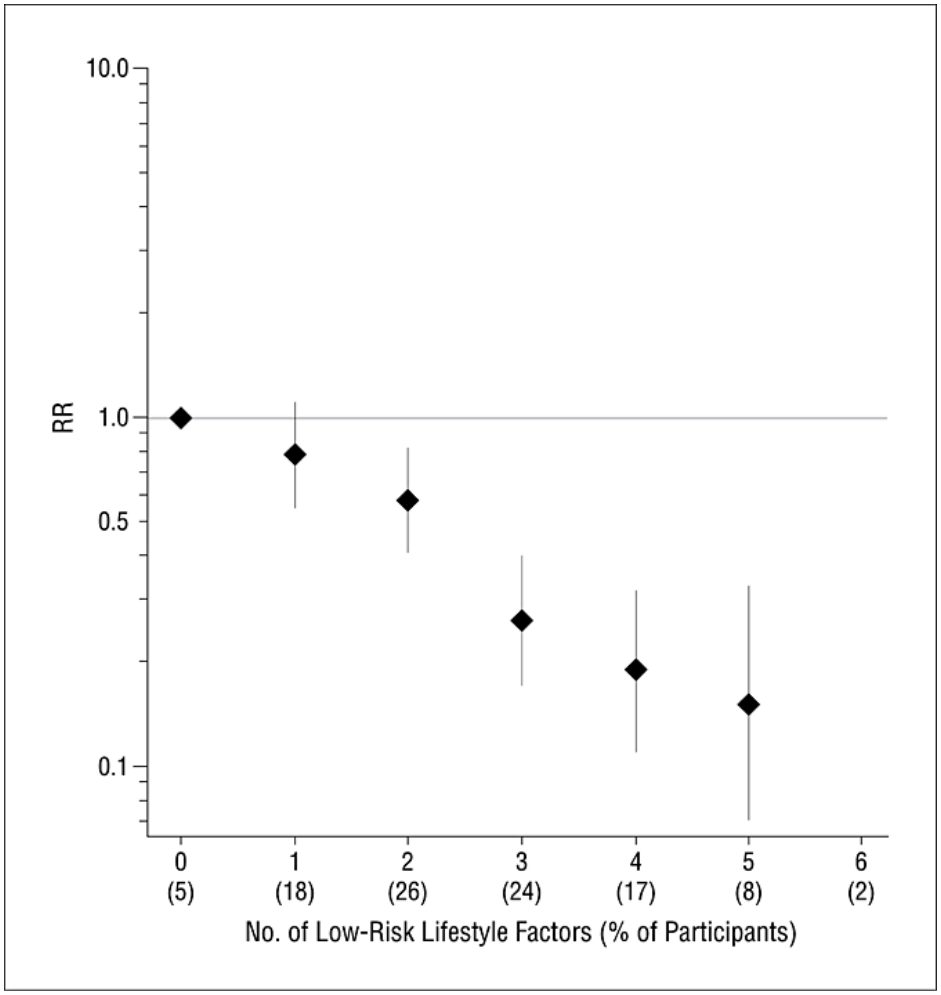
The Global Burden



The Global Burden

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

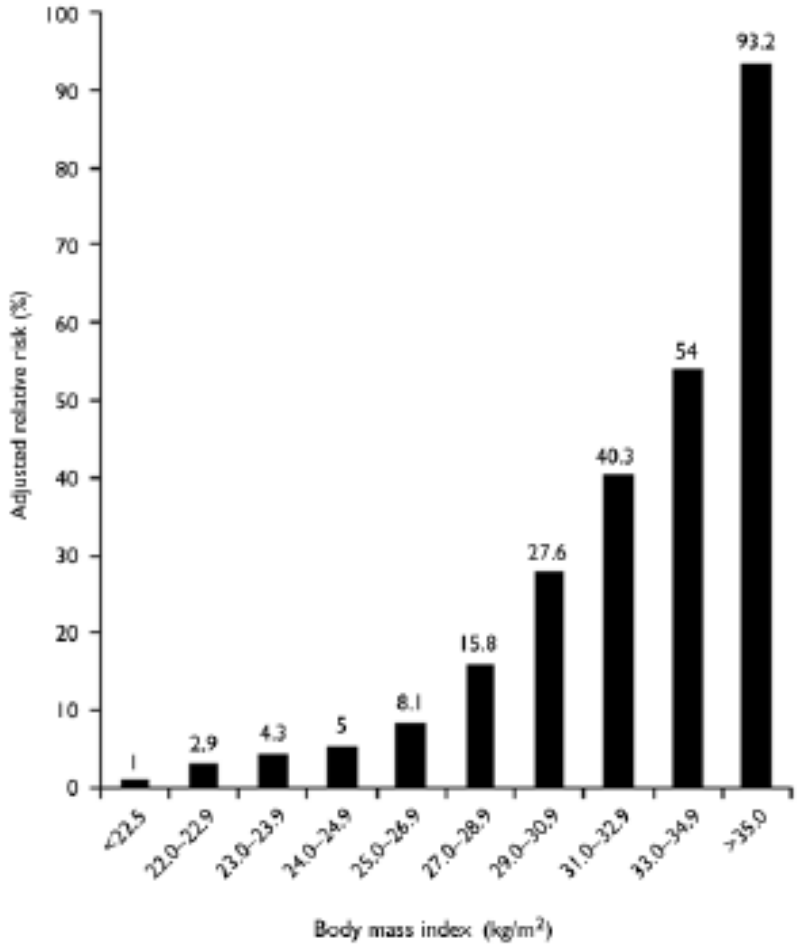
Relative Risk of Developing Diabetes



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

Mozaffarian D. Arch Intern Med 2009;169(8):798-807

BMI and Diabetes



Colditz et al Ann Internal Med 1995; 122:481-486

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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%

Why is it Important?

- Poorly controlled diabetes leads to accelerated cardiovascular morbidity and mortality

- A combination of microvascular and macrovascular disease

Thom T et al Circulation 2006;113(6):e85-151

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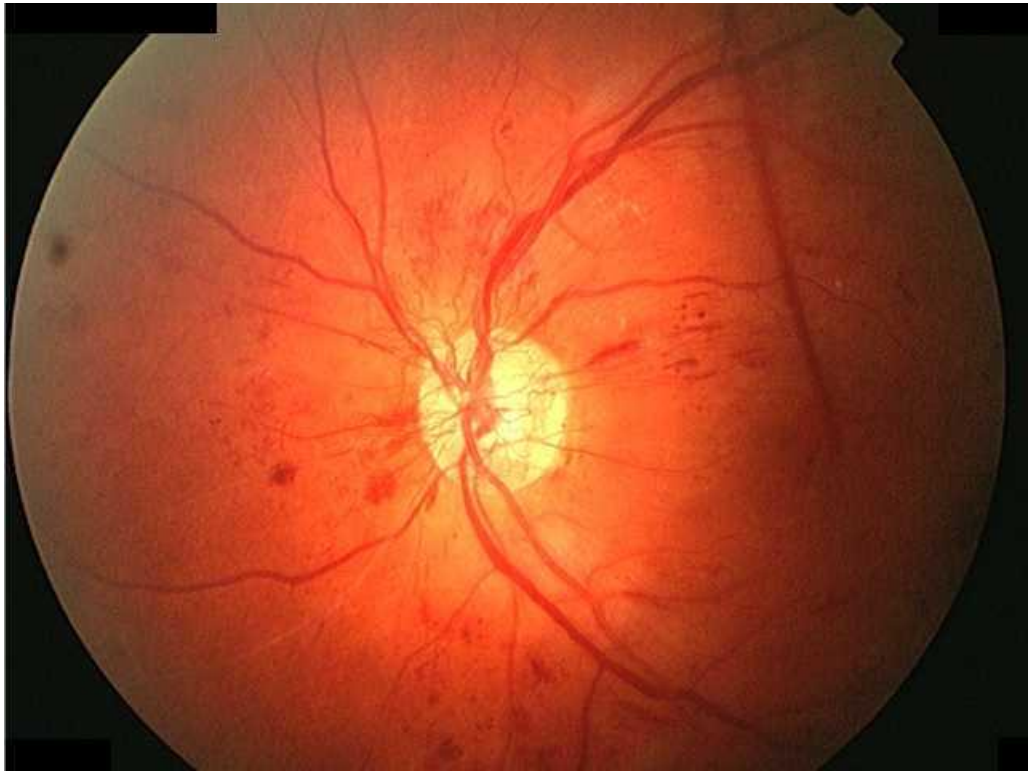
Microvascular Disease

- 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

Klein R & Klein BE Diabetes 2010;59(8):1853-1860

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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

Klein R & Klein BE Diabetes 2010;59(8):1853-1860

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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

Klein R et al JAMA 1988;260:2864-2871

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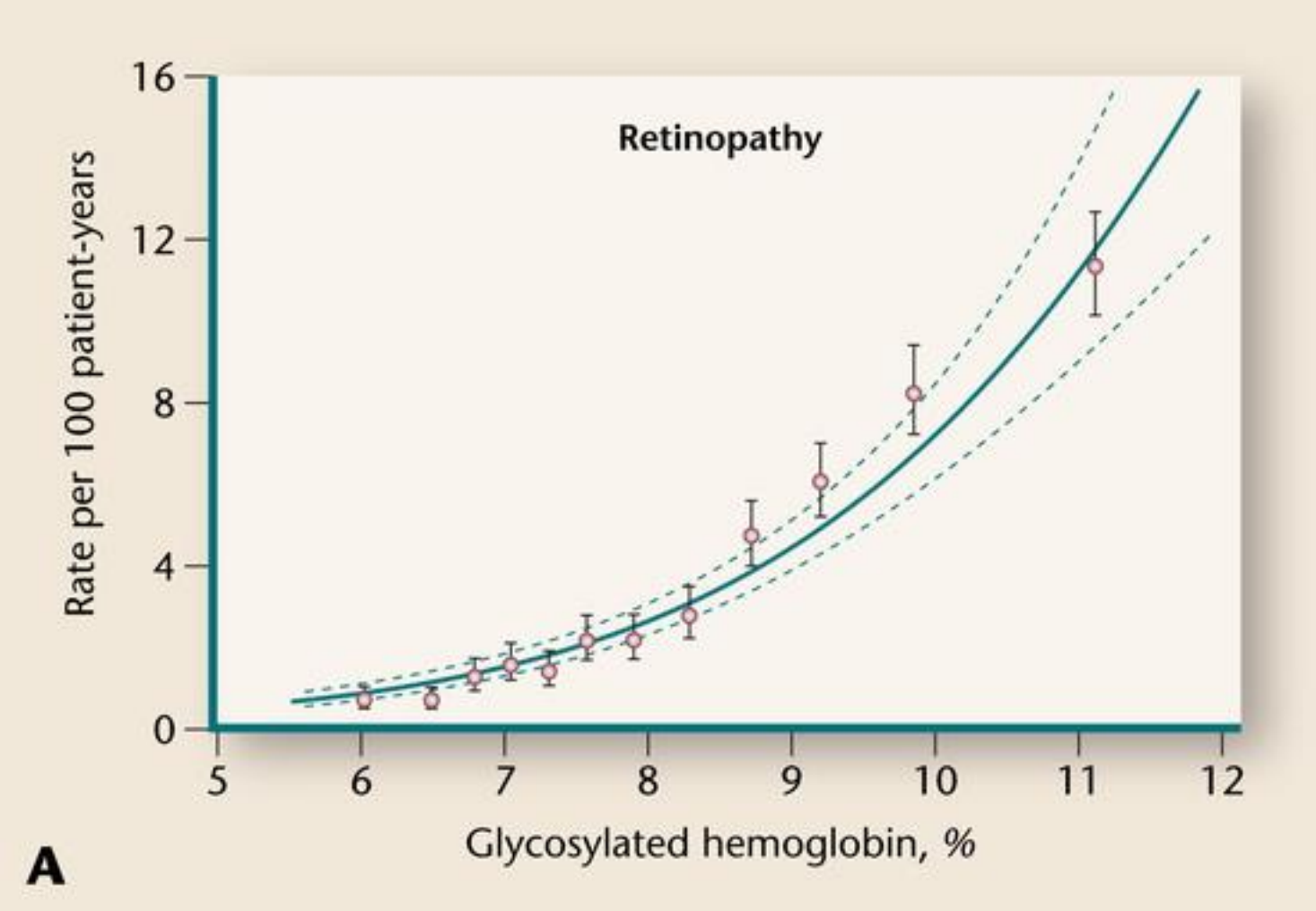
Retinopathy and Glycaemic Control

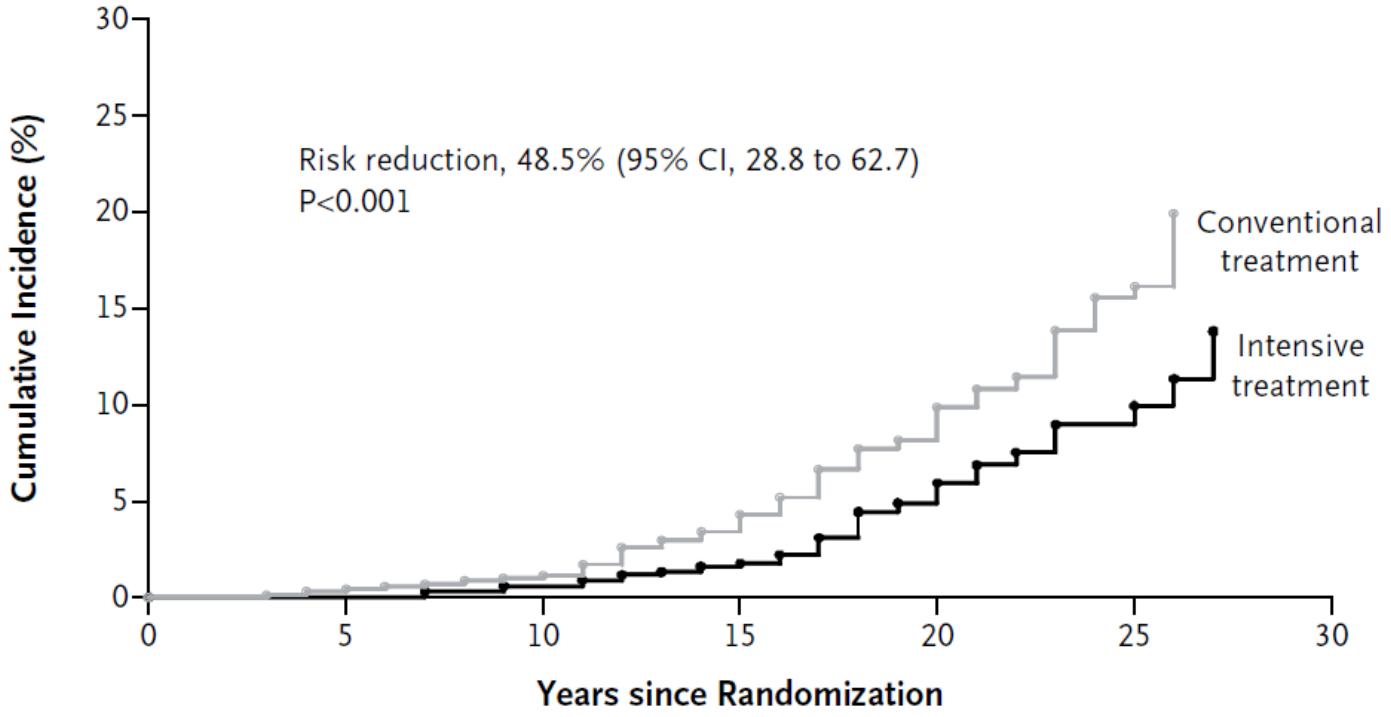


DCCT Research Group NEJM 1993;329(14):977-986

Specsavers

The Effects Last for a LONG Time

A Any Diabetes-Related Ocular Surgery



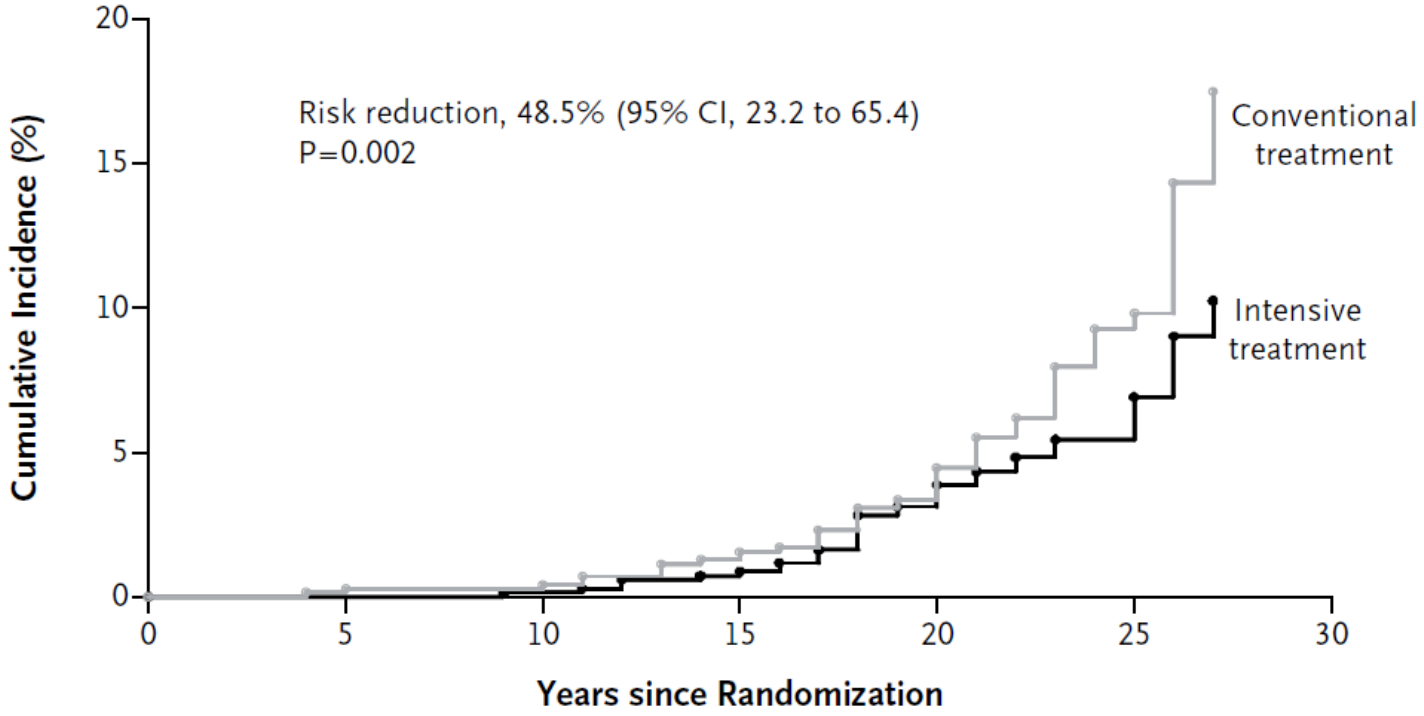
No. at Risk						
Intensive treatment	711	705	688	668	629	184
Conventional treatment	730	721	699	662	596	150

DCCT Research Group NEJM 2015;372(18):1722-1733

Specsavers

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

DCCT Research Group NEJM 2015;372(18):1722-1733

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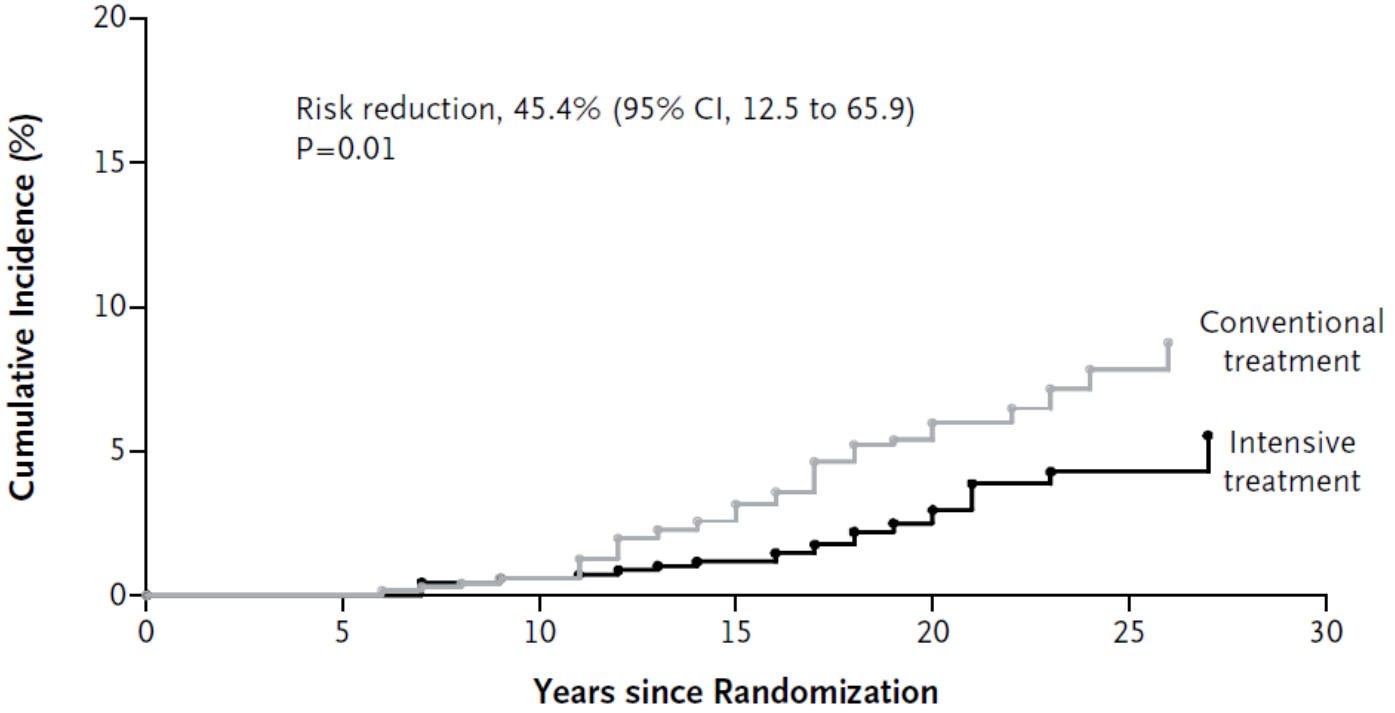
The Effects Last for a LONG Time

C Vitrectomy, Retinal-Detachment Surgery, or Both



No. at Risk

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DCCT Research Group NEJM 2015;372(18):1722-1733

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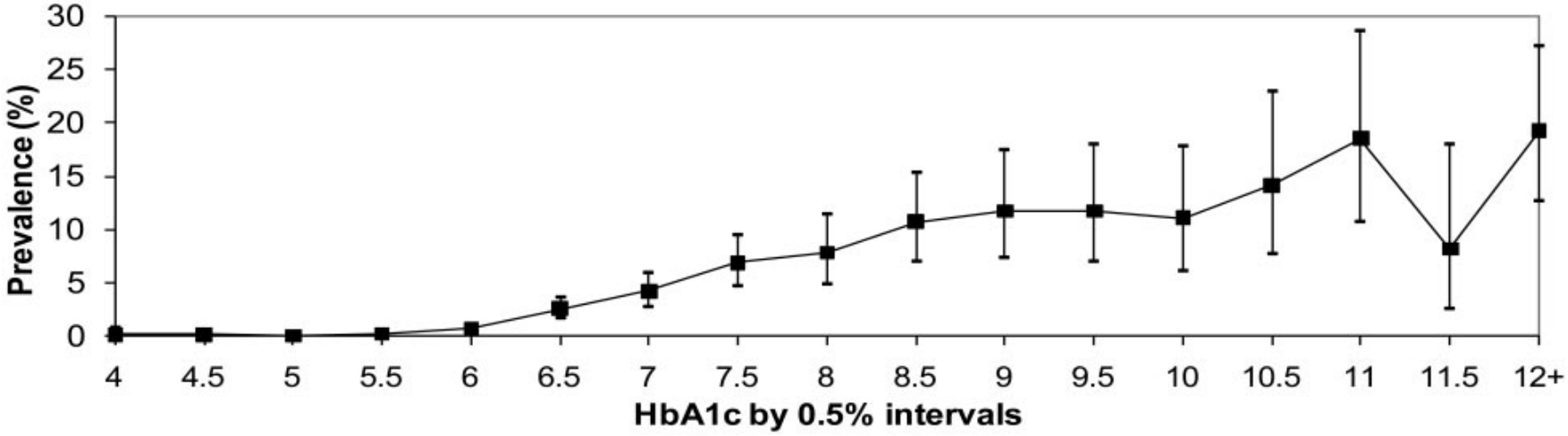
Epidemiology of Retinopathy



Cross sectional data from 44,623 individuals

Colagiuri S et al Diabetes Care 2011;34(1):145-150

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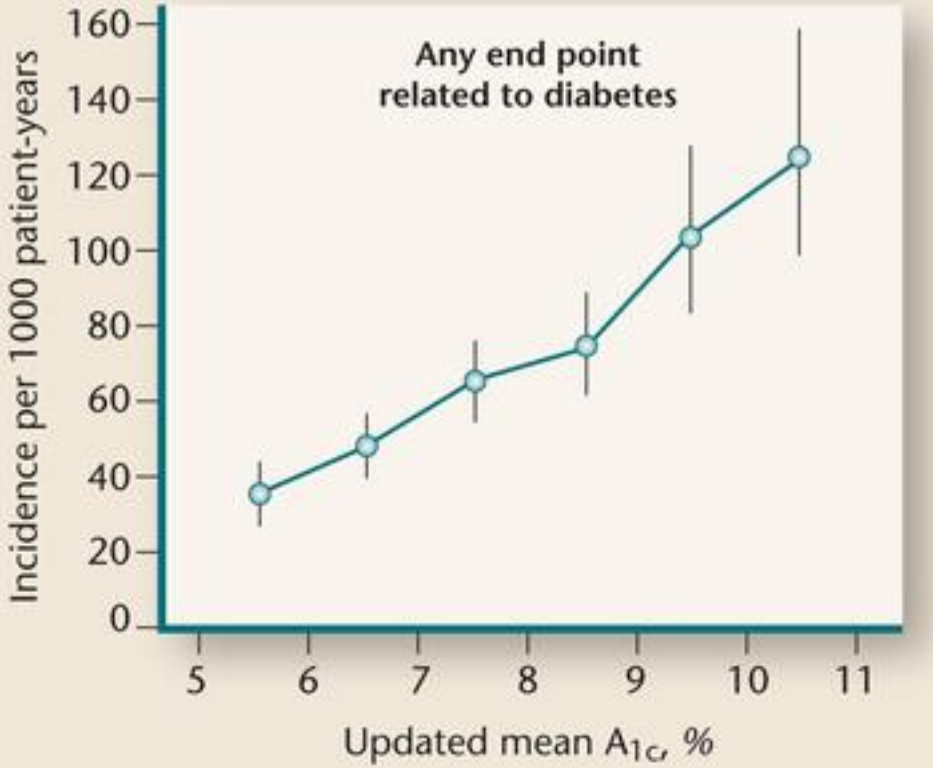
Glycaemic Control is Important



Reduction in risk per 1% reduction in A_{1c}

- 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

Taking The Right Medication

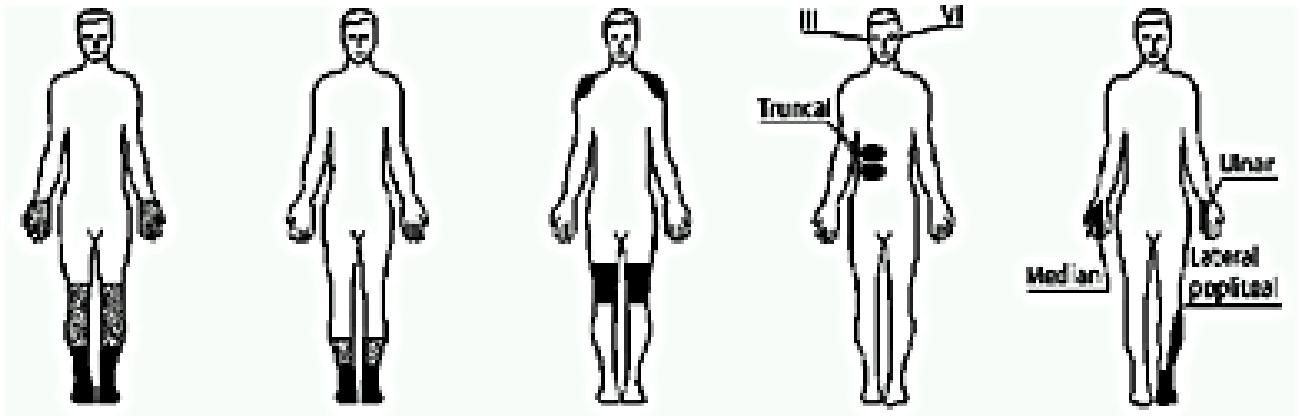
- Taking glucose lowering medication is important

- 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

Wang B et al Lancet Diabetes Endocrinol 2015;3(4)263-274
FIELD Study Investigators Lancet 2005;366(9500):1849-1861
ACCORD – EYE NEJM 2010;363(3):233-244

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

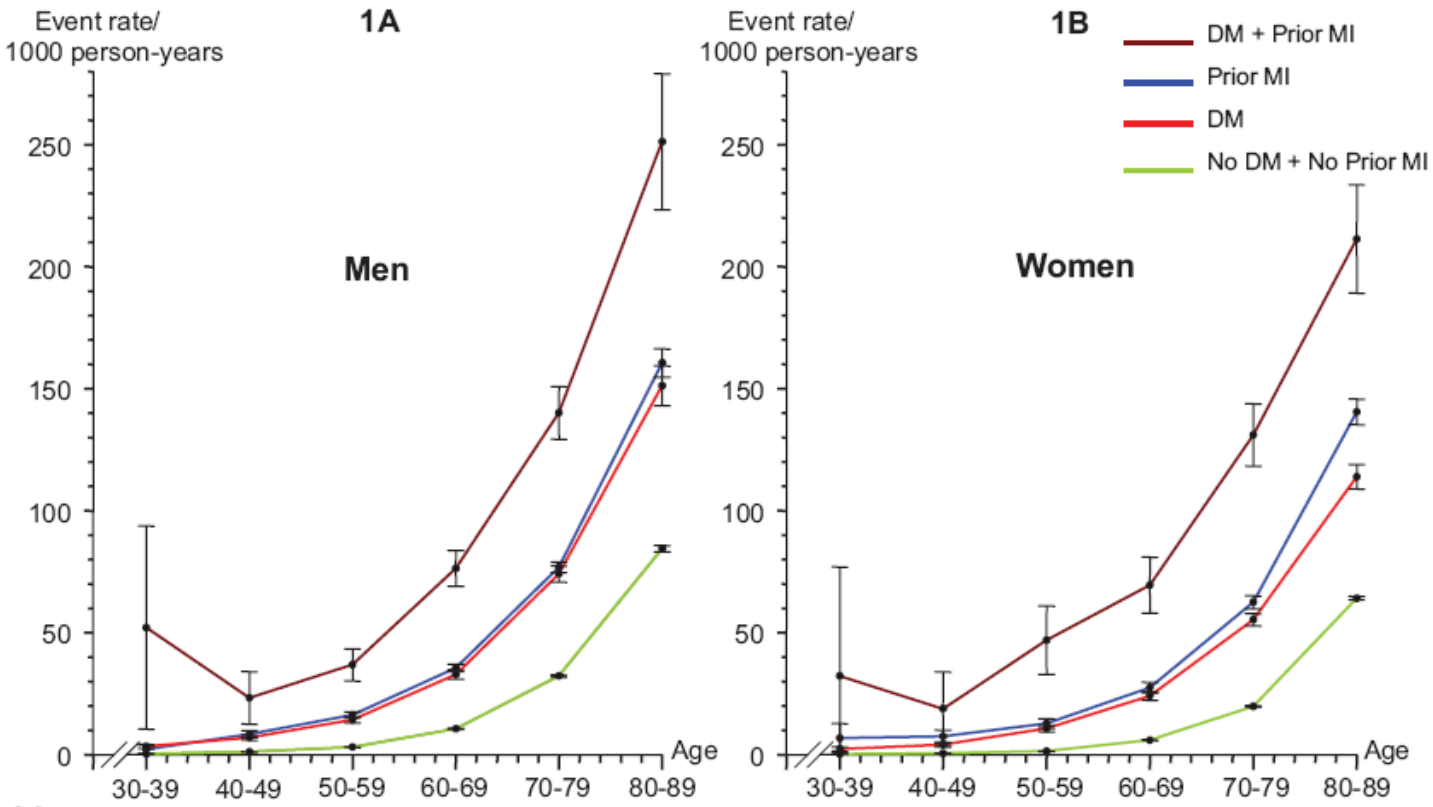
Microvascular Disease

- 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

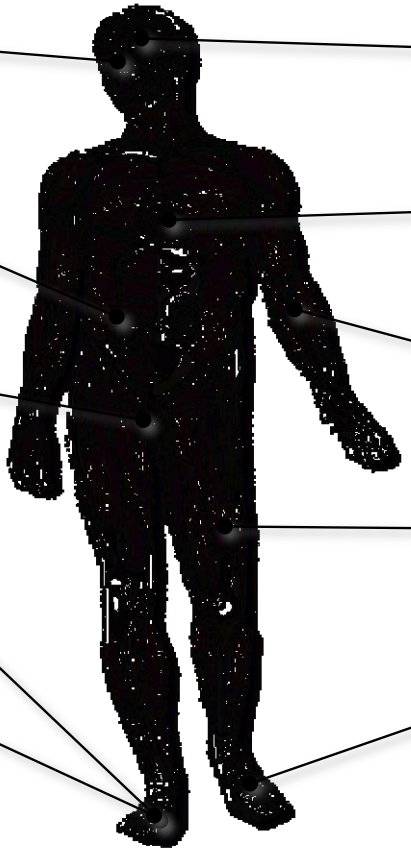


Numbers at risk:

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

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

Vascular Complications Of Type 2 Diabetes At The Time Of Diagnosis



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

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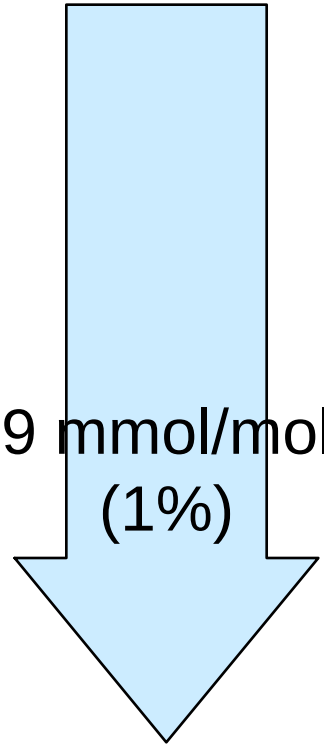
Lessons from UKPDS: Better Control Means Fewer Complications

Every 9mmol/mol (1%) reduction in HbA_{1c}

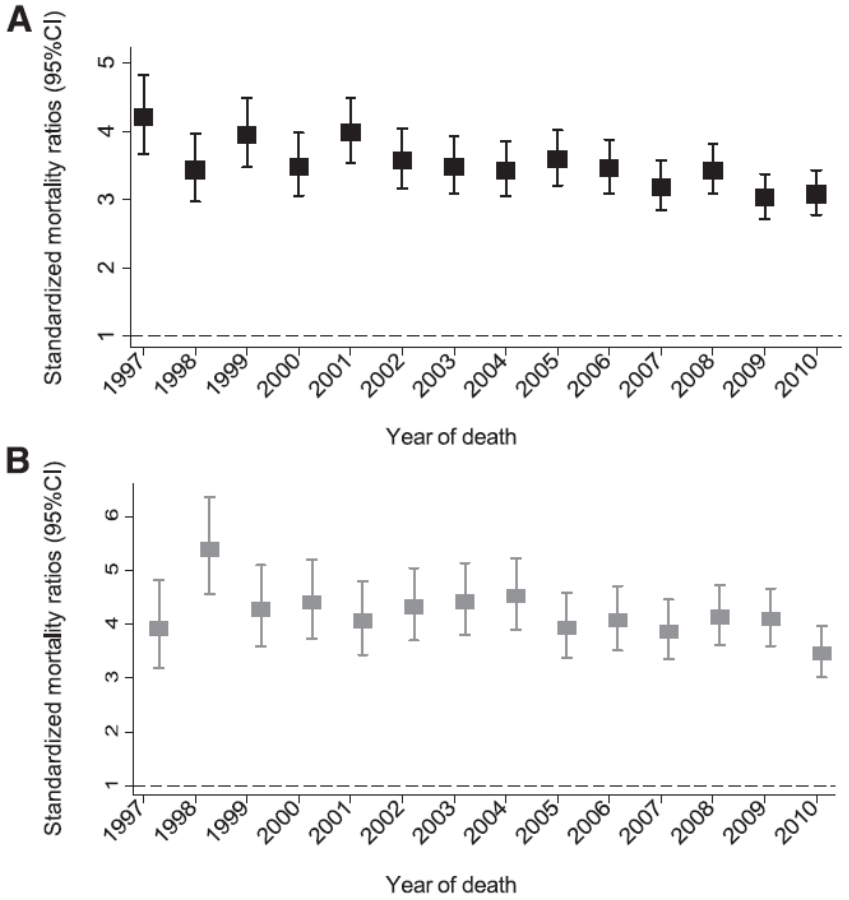


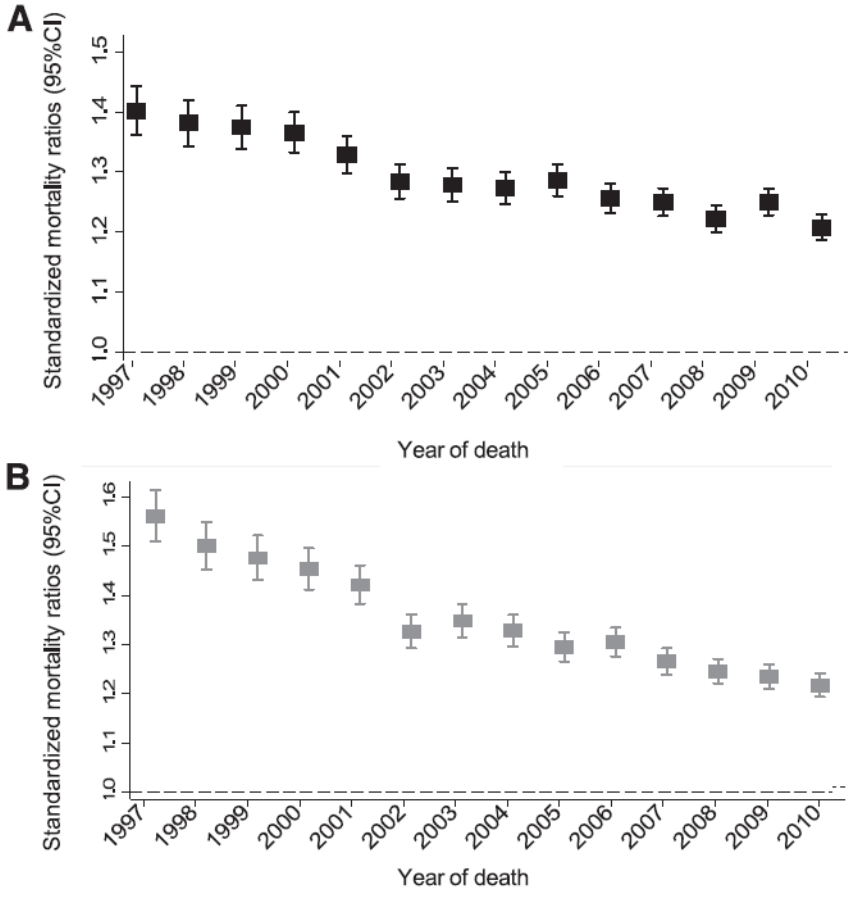
	REDUCED RISK*
Deaths from diabetes	–21%
Heart attacks	–14%
Microvascular complications	–37%
Peripheral vascular disorders	–43%

*p<0.0001

UKPDS 35. BMJ 2000;321:405–12

Diabetes Related Mortality is Falling





Type 1 A = Men B = Women Type 2

Harding JL et al Diabetes Care 2014;37(9):2579-2586

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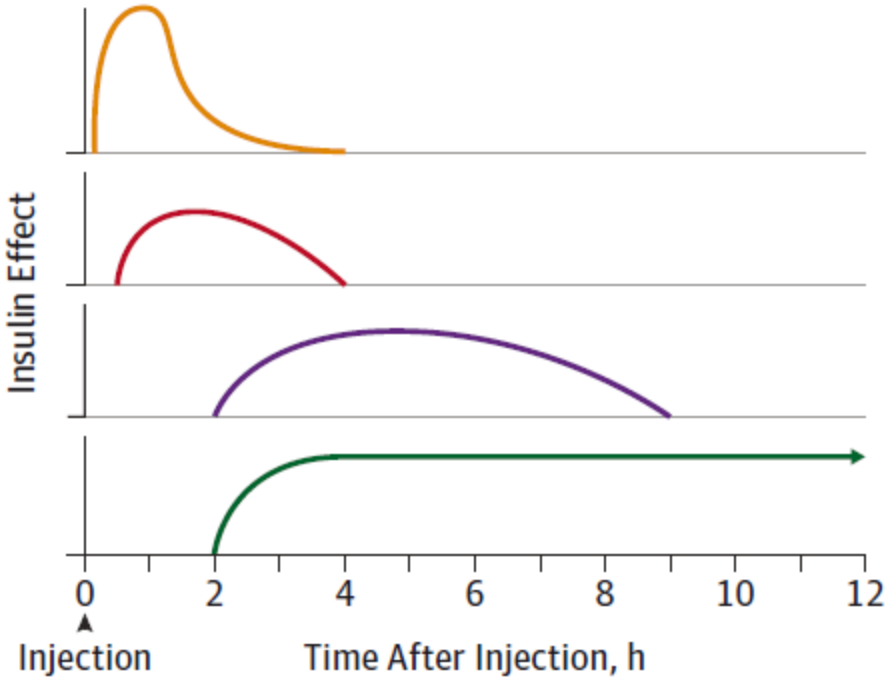
Non-Insulin Hypoglycaemic Agents

- α glucosidase inhibitors
- Metaglinides
- Metformin
- Sulphonylureas
- Thiazolidindiones
- GLP – 1 analogues
- DPP IV inhibitors
- SGLT 2 inhibitors

Insulin Durations

Figure 1. Insulin Activity Profiles

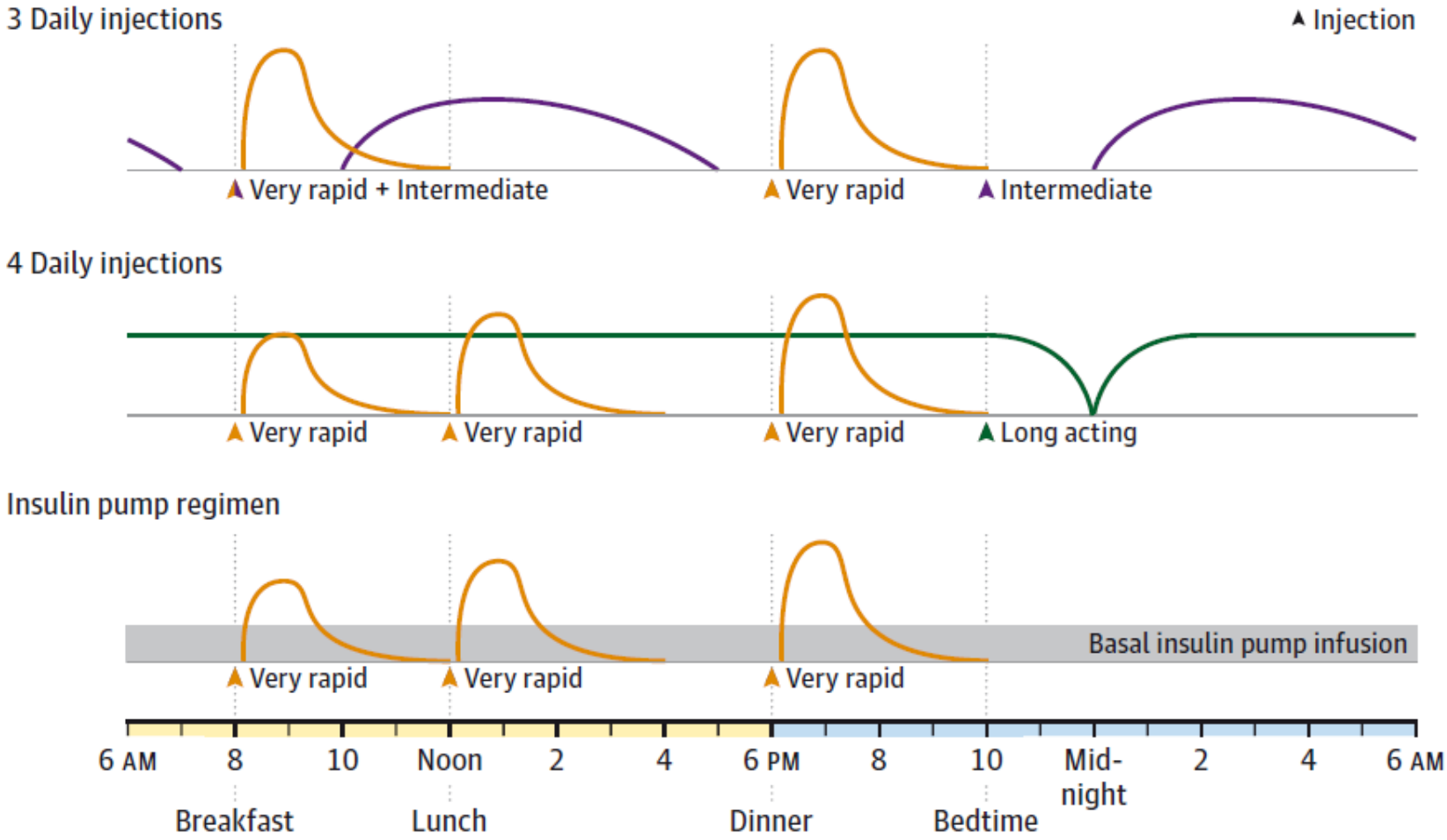
Insulin	Onset, min	Duration, h
Very rapid Lispro, aspart, glulisine	10	4
Rapid (regular) CZI	30	4-8
Intermediate NPH	120	8-10
Long acting Glargine, levemir	120	12-24



Nathan DM JAMA 2015;314(10):1052-1062

Insulin Regimens

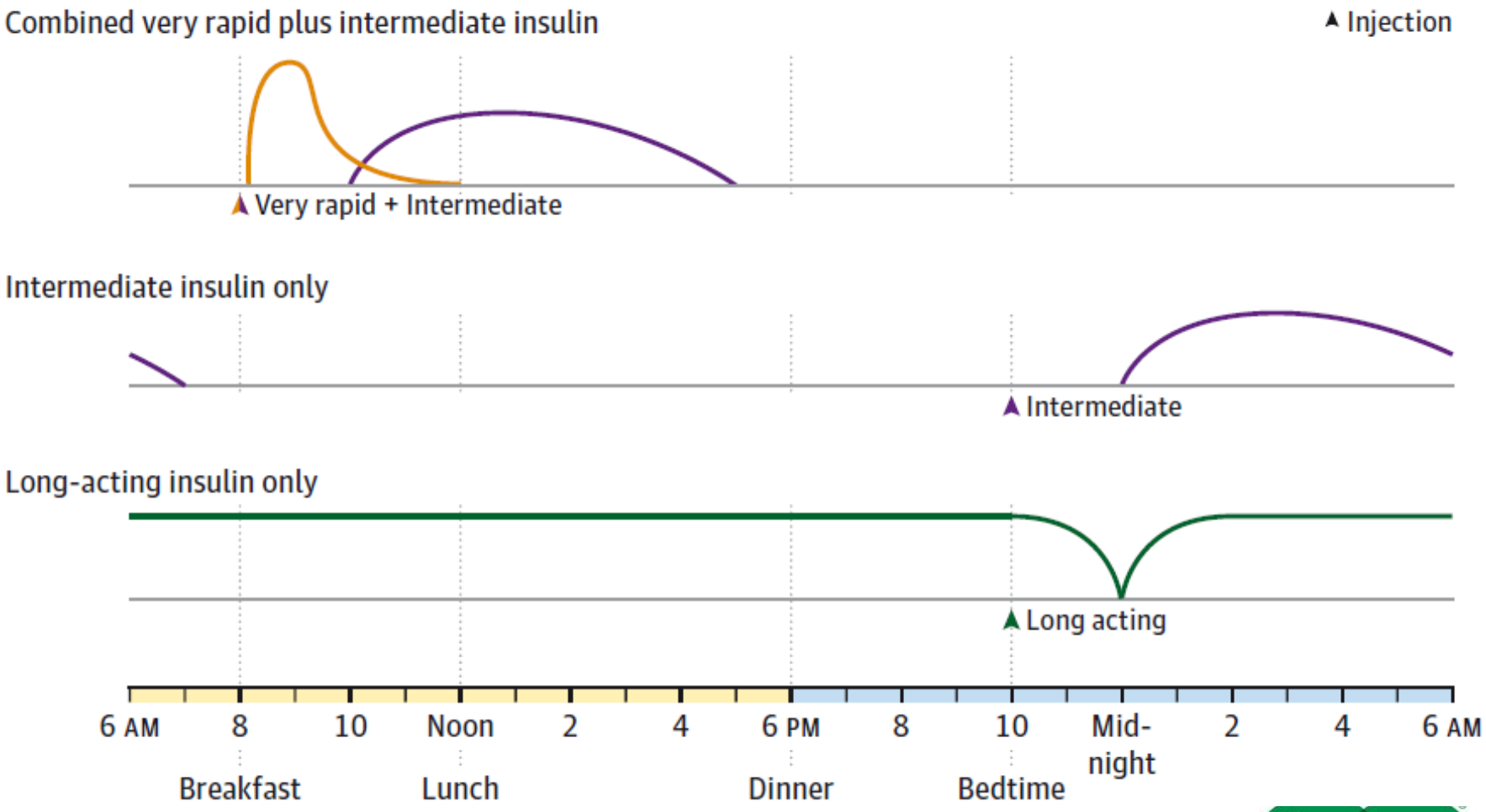
Figure 2. Three Examples of Insulin Regimens for Type 1 Diabetes



Nathan DM JAMA 2015;314(10):1052-1062

Insulin Regimens

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



Nathan DM JAMA 2015;314(10):1052-1062

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

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

www.norfolkdiabetes.com