Diabetes and the Eye – A Nurses Perspective

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NNUH

What is Diabetes?

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

First described in 1552 BC in the Ebers papyrus

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

Diabetes and the Eye - Some History

- In the 1970's and 1980's diabetes was the lading 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 (PDR)
  - Macular oedema
  - Cataract
  - Glaucoma

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

Some History

- There was no definitive evidence that achieving good glycaemic control would actually result in less DR
- 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

The Relationship Between Glycaemic Control and Retinopathy

- In 1978 Kelly M West wrote "The extent to which the level of hyperglycaemia determines the risk of retinopathy is not at all clear. This is the most important issue at hand and deserves high priority in epidemiologic research"

West KM. 1978. *Epidemiology of Diabetes and Its Vascular Lesions* . Elsevier, NY

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

DCCT and UKPDS

- It was then the DCCT and UKPDS that showed that improving glycaemic control substantially reduced the risk of developing retinopathy
  - 76% reduction in the progression of retinopathy in the primary prevention cohort of the DCCT
  - 54% reduction in the progression of DR in the secondary prevention cohort of the DCCT
  - 21% reduction in the progression of DR in the UKPDS
  - 29% reduction in the need for laser photocoagulation in the UKPDS

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

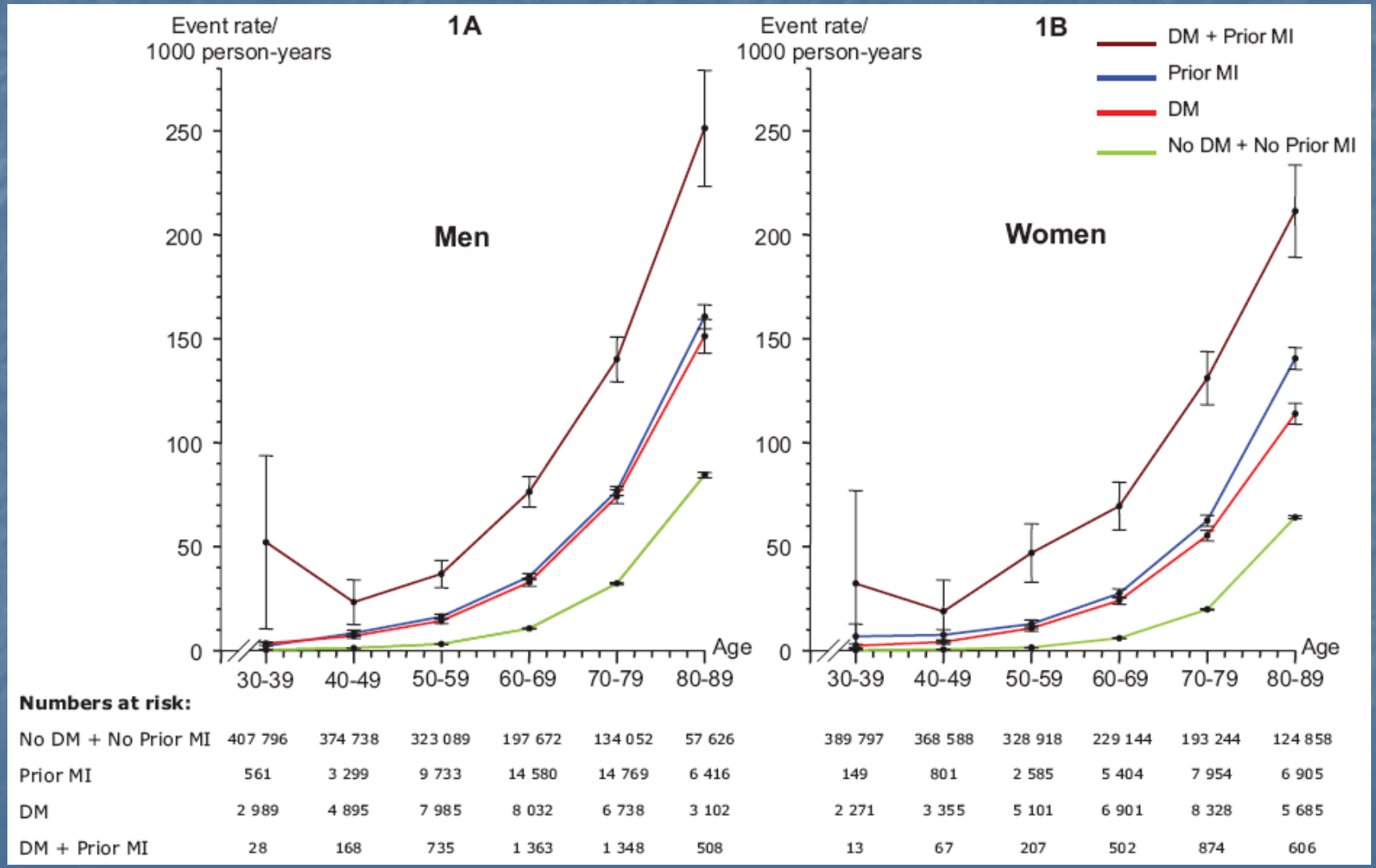
UKPDS 33 Lancet 1998;352:837-853

What Are the Other Risks??

- 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

Data From 3.3M Danes

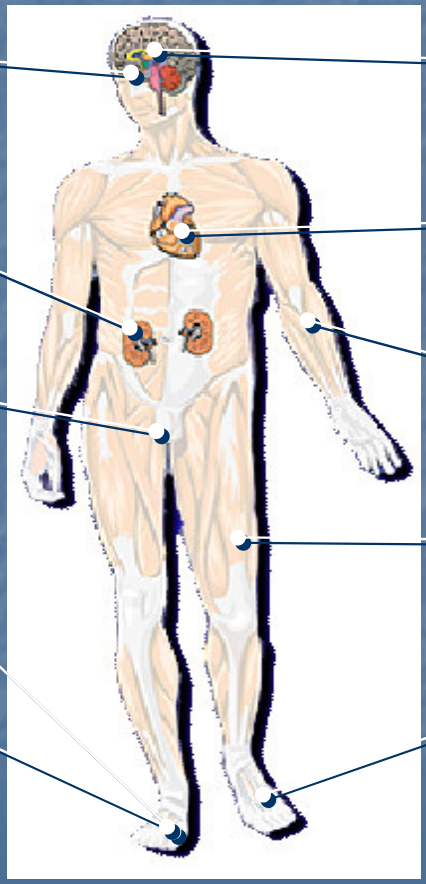


Numbers at risk:

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

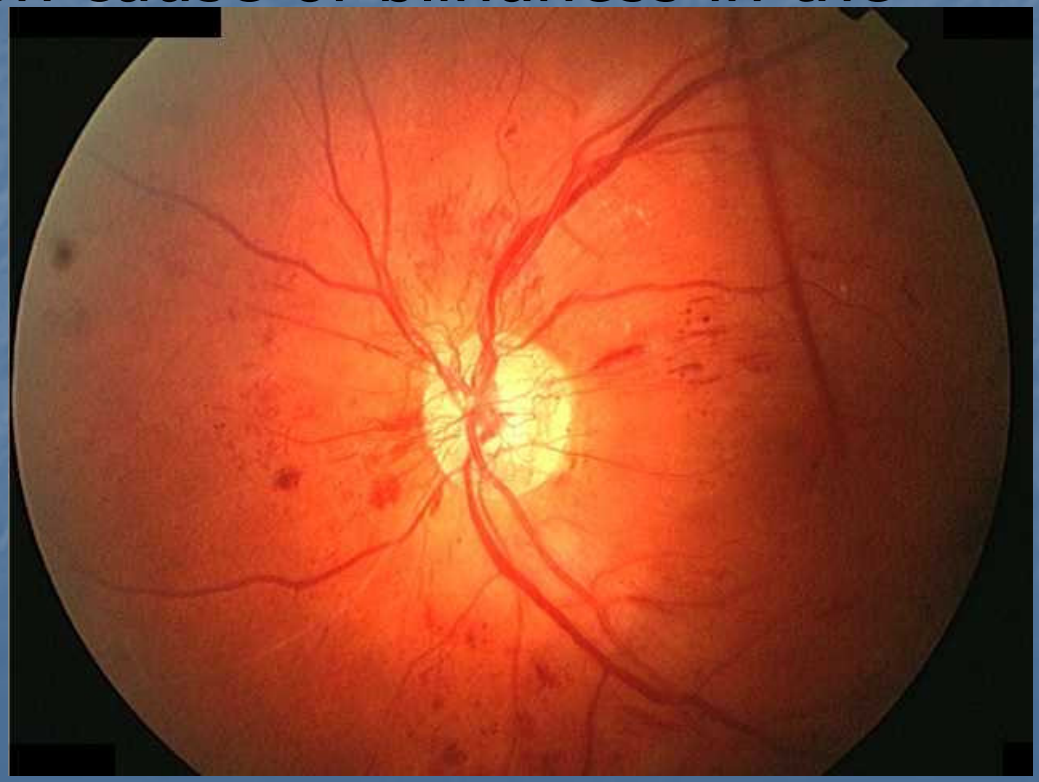


Retinopathy[1]	39%	7%	Cerebrovascular disease[3]
Nephropathy[2]	18%	18%	Abnormal ECG[1]
Erectile dysfunction[1]	20%	35%	Hypertension[1]
Ischaemic skin changes (foot)[1]	6%	4.5%	Intermittent claudication[3]
Abnormal vibration threshold (foot)[1]	7%	13%	Absent foot pulses[1]

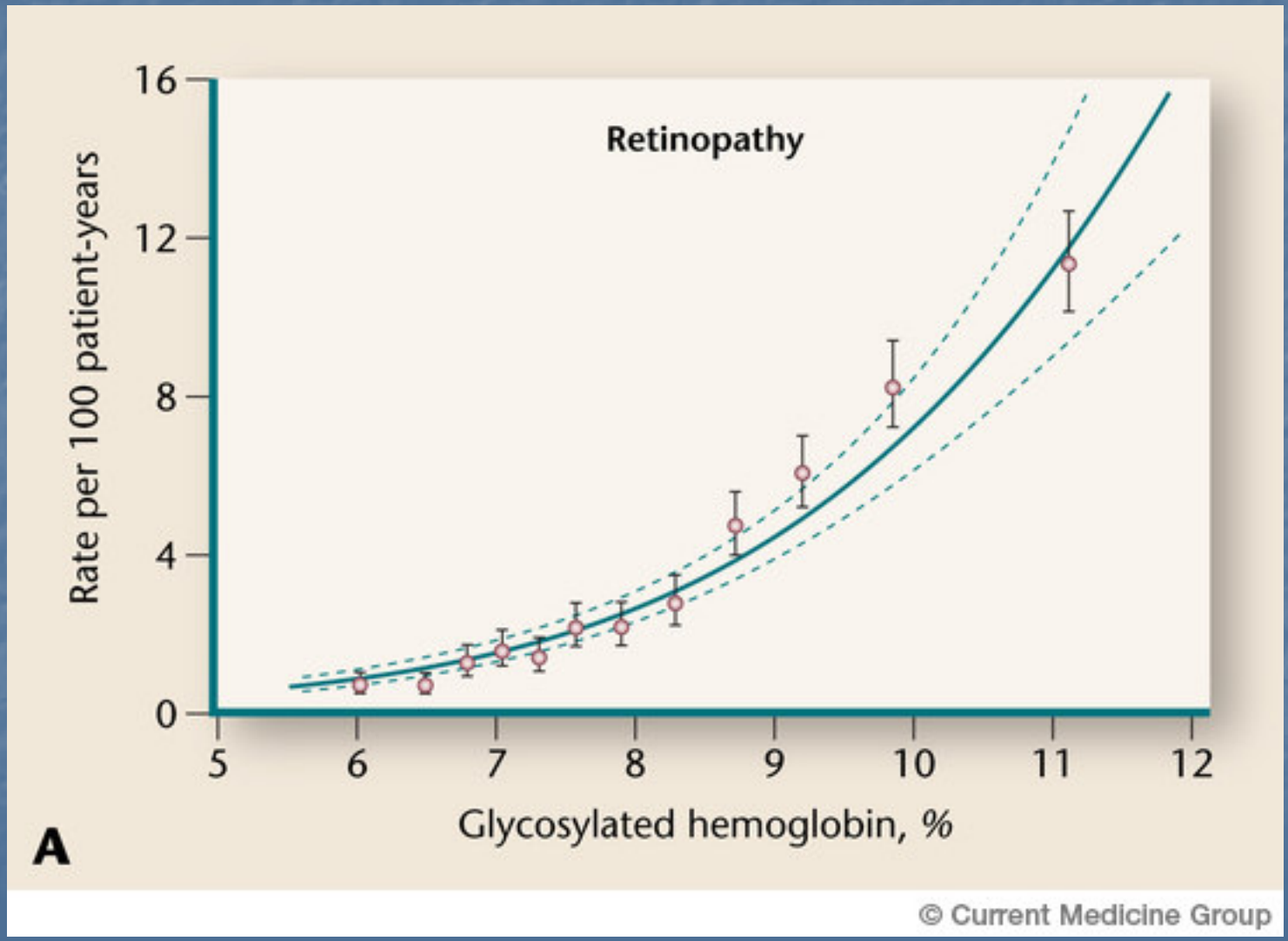
1. UKPDS 33 Lancet 1998352(9193):837-853. 2. The Hypertension in Diabetes Study Group. *J Hypertension* 1993; **11**: 30–17. 3. Wingard DL *et al. Diabetes Care* 1993; **16**: 1022–5.

OK, so You Die – So What?

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

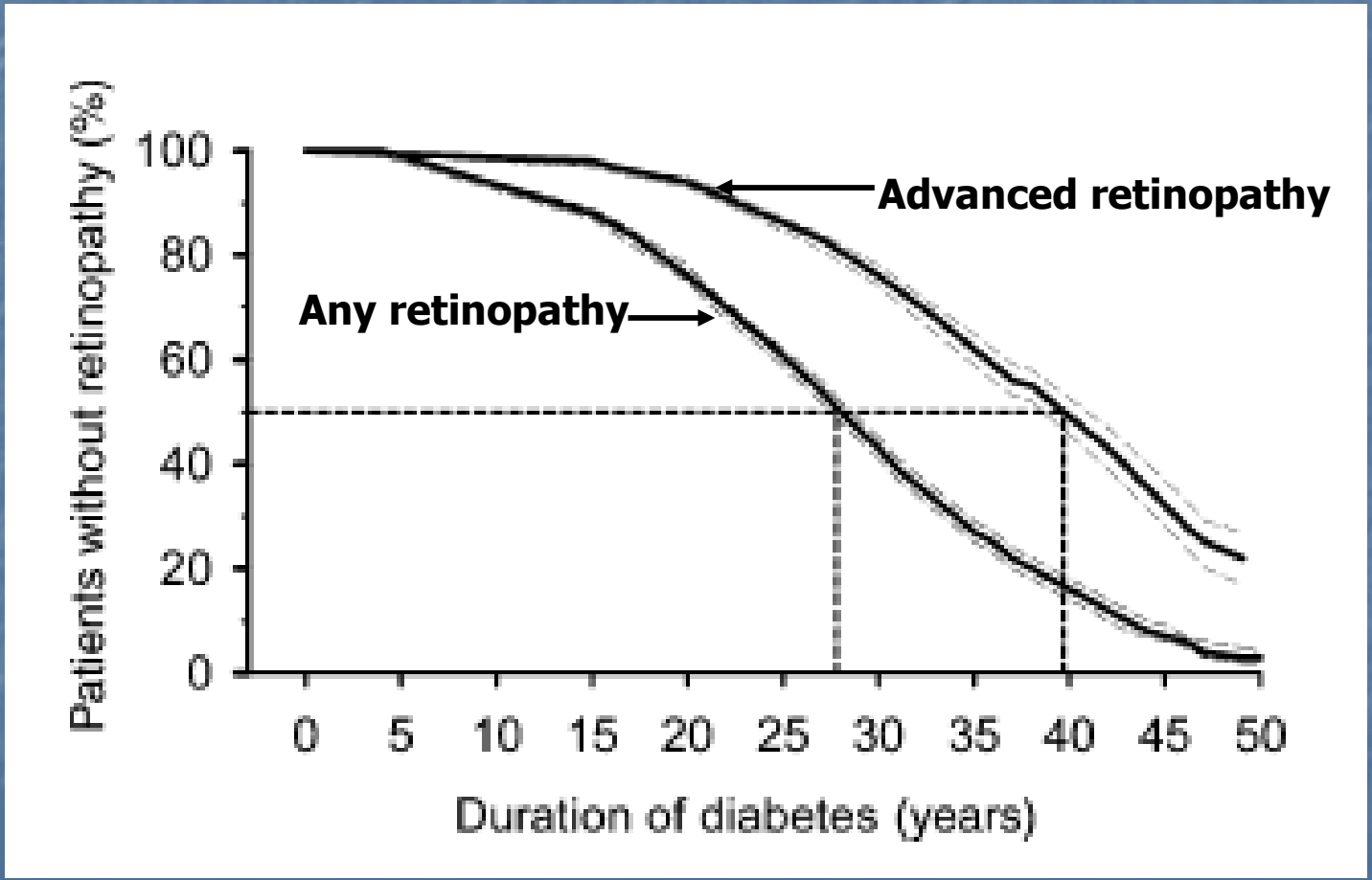


Retinopathy and Glycaemic Control



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

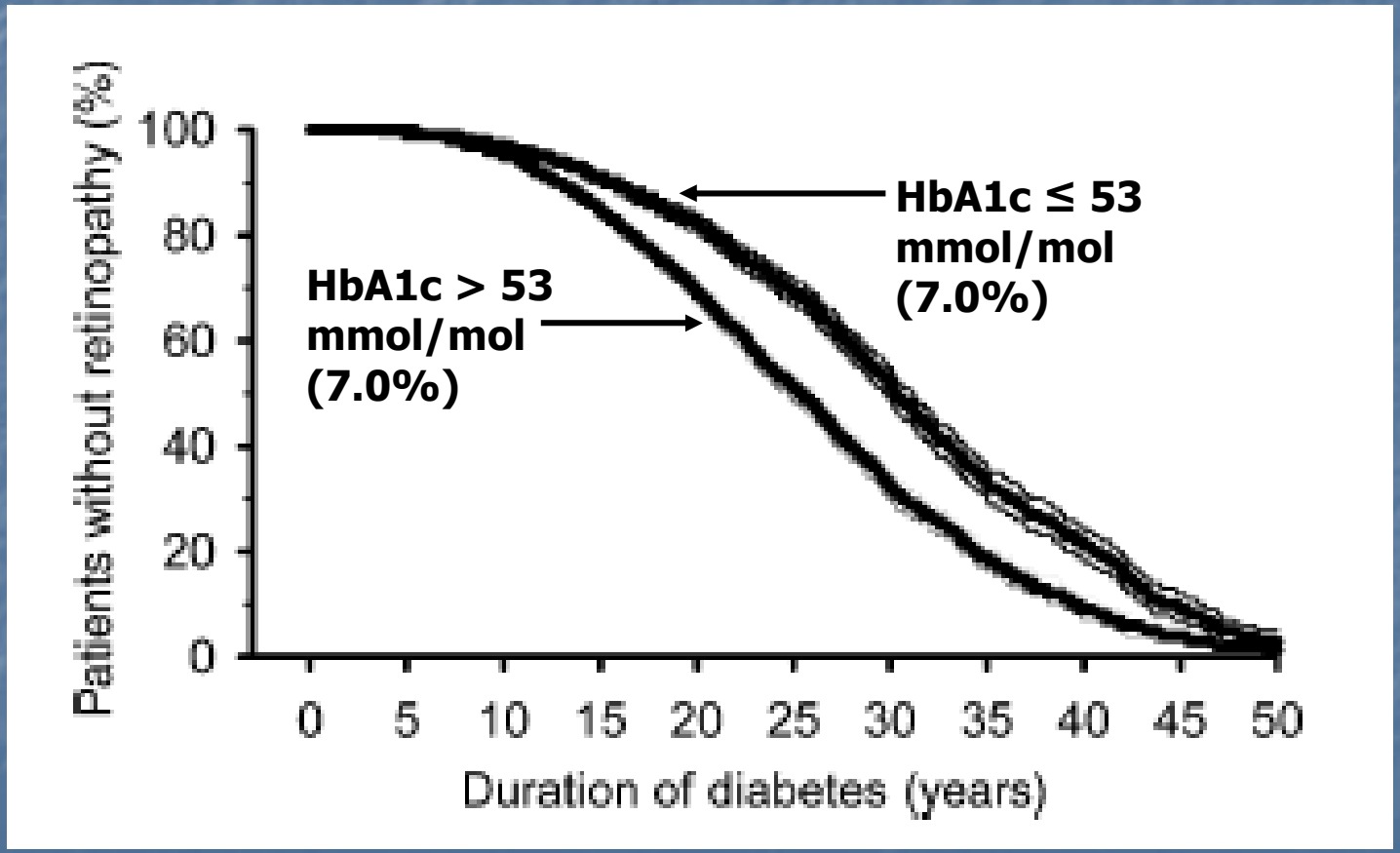
Retinopathy and Duration of Diabetes



8784 people with type 1 diabetes

Hammes HP et al Diabetologia 2011;54(8):1977-1984

Retinopathy and Severity of Diabetes



Hammes HP et al Diabetologia 2011;54(8):1977-1984

Prevalence?

- Data from Wisconsin suggests that up to 70% of people with type 1 have retinopathy, and 40% of people with type 2
- Of those with type 1, up to 50% will have proliferative disease within 20 years of diagnosis

Klein R et al Am J Epidimiol 1984;119(1):54-61

Things That Made the Most Difference

Table 2 Multiple logistic regression analysis, any retinopathy

Variable	OR	95% CI	*p* value[a]
Male sex	1.19	1.05–1.34	0.0057
Age at onset <5 years	0.41	0.335–0.502	<0.0001
HbA_{1c} >7.0% (53 mmol/mol)	2.23	1.93–2.57	<0.0001
Dyslipidaemia	Removed		
Hypertension	Removed		
Smoking	1.3	1.13–1.48	0.0002

Hammes HP et al Diabetologia 2011;54(8):1977-1984

Things That Made the Most Difference

Table 3 Multiple logistic regression analysis, severe retinopathy

Variable	OR	95% CI	*p* value[a]
Male sex	1.25	1.06–1.148	0.0094
Age at onset <5 years	0.66	0.51–0.86	0.015
HbA_{1c} >7.0% (53 mmol/mol)	1.52	1.26–1.84	<0.0001
Dyslipidaemia	1.58	1.31–1.90	<0.0001
Hypertension	1.70	1.34–2.16	<0.0001

Hammes HP et al Diabetologia 2011;54(8):1977-1984

Achieving Good Glycaemic Control – the Effects of Insulin on the Eye

- Tight glycaemic control using insulin is unequivocally associated with a long-term decreased risk of the development and progression of diabetic retinopathy in patients with either type 1 or type 2 diabetes mellitus
- If achieved early, this effect is maintained independently of glycaemic control
- There is a legacy effect of glycaemic control

Silva PS et al Nat Rev Endocrinol 2010;6(9):494-507

Other Preventative Strategies?

- The use of RAAS blockers (Euclid, Direct)
- Direct showed an NNT of 18 to prevent, and NNT of 21 to protect against progression
- Older agents such as enalapril and losartan also slow progression in type 1
- Lowering TG levels using fibrates also reduces the need for laser

Chaturvedi N et al Lancet 1998;351(9095):28-31

Chaturvedi N et al Lancet 2008;372(9647):1394-1402

Sjolie AK et al Lancet 2008;372(9647):1385-1393

Maure M NEJM 2009;361(1):40-51

Keech AC et al Lancet 2007;370(9600):1687-1697

What About 'Early Worsening'?

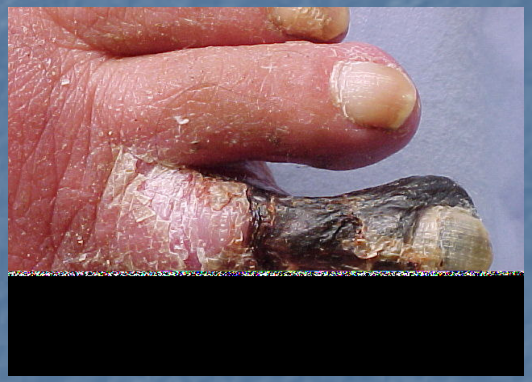
- In the first 2 years following the initiation of intensive insulin therapy, diabetic retinopathy can transiently worsen
- However, over the long term, intensive glycaemic control is associated with improved retinopathy and visual outcomes
- Early worsening has been shown to be more common in patients with poorly controlled, long-standing diabetes mellitus with moderate or more advanced non-proliferative diabetic retinopathy

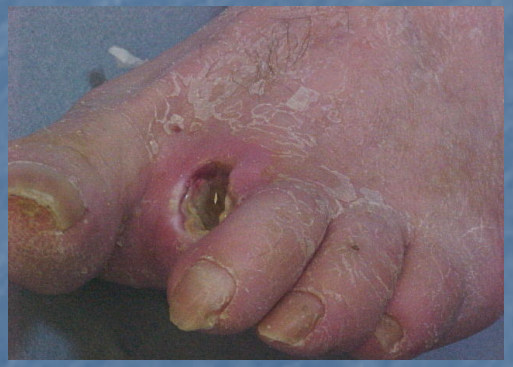
Early Worsening

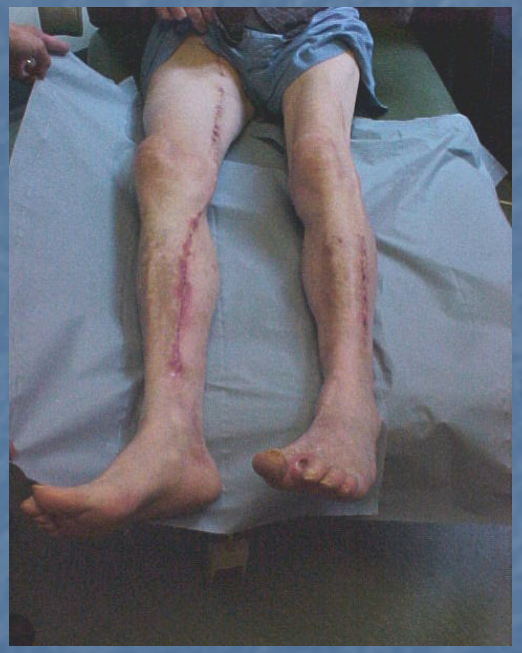
- Thus, this subgroup requires careful ophthalmologic monitoring before initiation of intensive treatment and for at least 6-12 months following initiation of intensive treatment, at a minimum of 3-monthly intervals

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



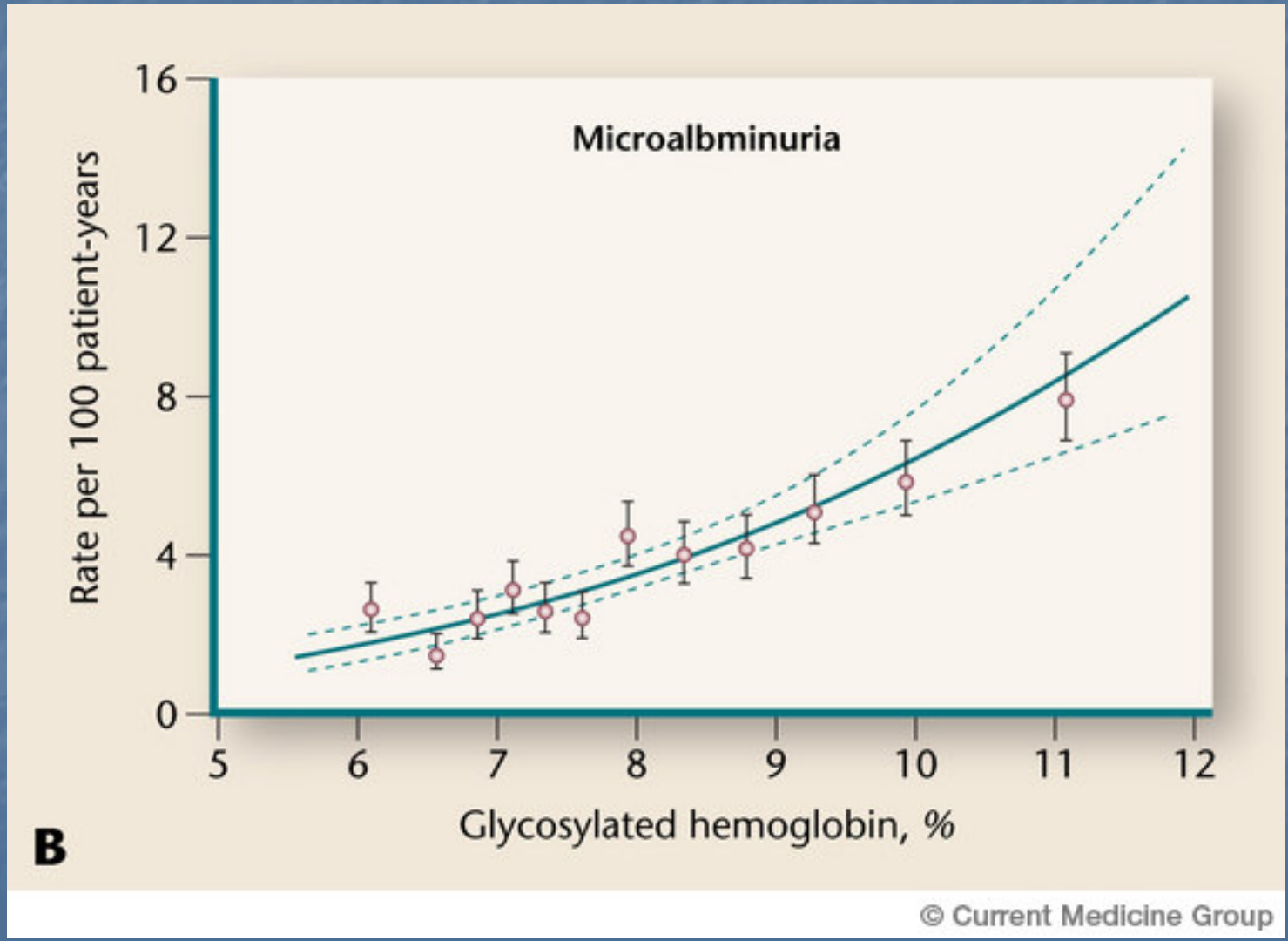




OK, So You're Blind and Limp

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

Nephropathy and Glycaemic Control

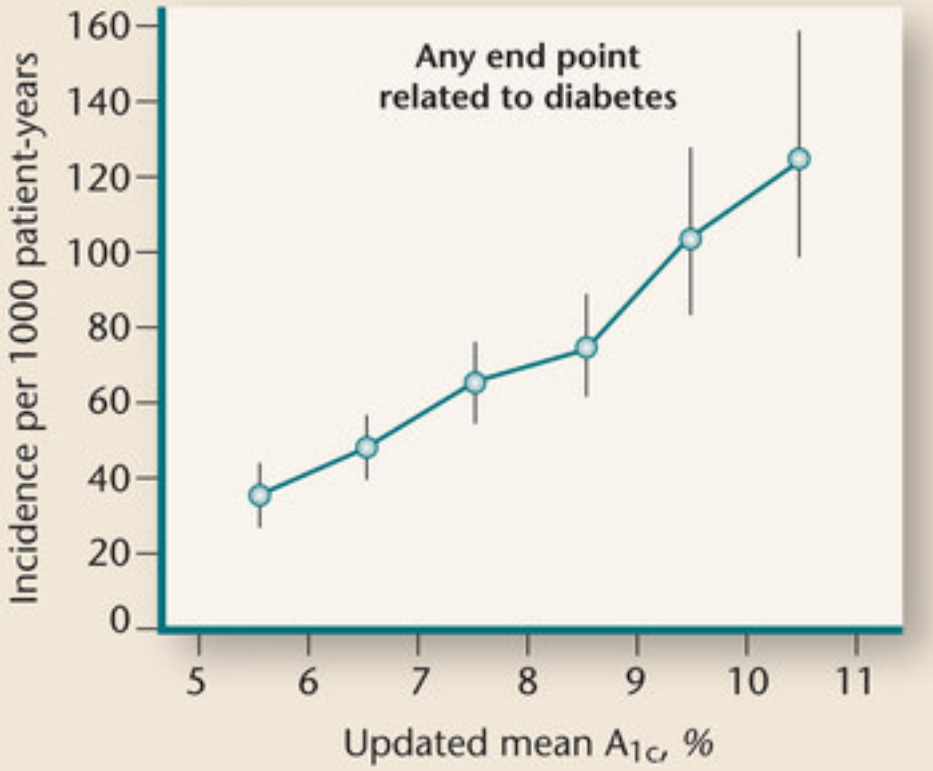


DCCT Research Group NEJM 1993;329(14):977-986

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

Blind, Limp, on Dialysis and Someone Wiping your Bottom

It’s all preventable

Overview

- The National Screening Committee grading system

Grading and disease management in national screening for diabetic retinopathy in England and Wales

S. Harding, R. Greenwood*, S. Aldington†, J. Gibson‡, D. Owens§, R. Taylor¶, E. Kohner**, P. Scanlon††, G. Leese‡‡. The Diabetic Retinopathy Grading and Disease Management Working Party

Diabet. Med. 20, 965–971 (2003)

Grading Classification

Retinopathy (R)		
Level 0	None	
Level 1	Background	Microaneurysm(s) Retinal haemorrhage(s) ± any exudate
Level 2	Preproliferative	Venous beading Venous loop or reduplication Intraretinal microvascular abnormality (IRMA) Multiple deep, round or blot haemorrhages (CWS—careful search for above features)
Level 3	Proliferative	New vessels on disc (NVD) New vessels elsewhere (NVE) Preretinal or vitreous haemorrhage Preretinal fibrosis ± tractional retinal detachment
Maculopathy (M)		Exudate within 1 disc diameter (DD) of the centre of the fovea Circinate or group of exudates within the macula Retinal thickening within 1 DD of the centre of the fovea (if stereo available) Any microaneurysm or haemorrhage within 1 DD of the centre of the fovea only if associated with a best VA of ≤ (if no stereo) 6/12
Photocoagulation (P)		Focal/grid to macula
Unclassifiable (U)		Peripheral scatter

Management of Each Grade

Retinopathy (R)	R0	Annual screening
	R1	Annual screening
	R2	Refer to hospital eye service
	R3	Fast-track referral to hospital eye service
Maculopathy (M)	M1	Refer hospital eye service
Photocoagulation (P)	P1	New screenee→refer hospital eye service Quiescent post treatment→annual screening
Other lesions (OL)		Refer to hospital eye service or inform primary physician
Ungradable/unobtainable (U)		Poor view but gradable on biomicroscopy→refer hospital eye service Unscreenable→discharge, inform GP (option to recall for further photos if purely technical failure)

So What Can *YOU* Do?

- Be active
  - Ask if they take their medications every day
  - Ask if they experience any side effects
  - Ask if they have mentioned any of these things to their doctors
  - TELL THEM TO STOP SMOKING

  - Be their advocate

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