

# **HbA<sub>1c</sub> as a Marker of Glycaemic Control in Diabetes Care**

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**What do we require of a marker of glycaemic control in diabetes care?**

# The Impact of Diabetes Acute Events

Significant morbidity and mortality from:

- Hypoglycaemia
- Hyperglycaemia / ketoacidosis

Need for:

- Real-time, near-patient and laboratory monitoring, for diagnosis and for day-to-day treatment adjustment
- Assessment of long-term risk of acute events

# The Impact of Diabetes

## Long-Term Events

- Average life-expectancy reduced by 7-10 years
  - premature vascular disease
- Commonest cause of blindness in Western world in people aged <65 years
- Commonest single cause of end-stage renal disease world-wide
- Commonest non-traumatic cause of amputation

# Long-Term Monitoring

Need test which:

- Relates glucose control to risk of long-term complications
- Allows estimate of risk of microvascular and macrovascular complications
- Allows setting of appropriate individual targets

→ must relate to DCCT / UKPDS HbA<sub>1c</sub>

# Audit and Research

## Research:

- Compare the effectiveness of new and old treatments

## Audit and Benchmarking

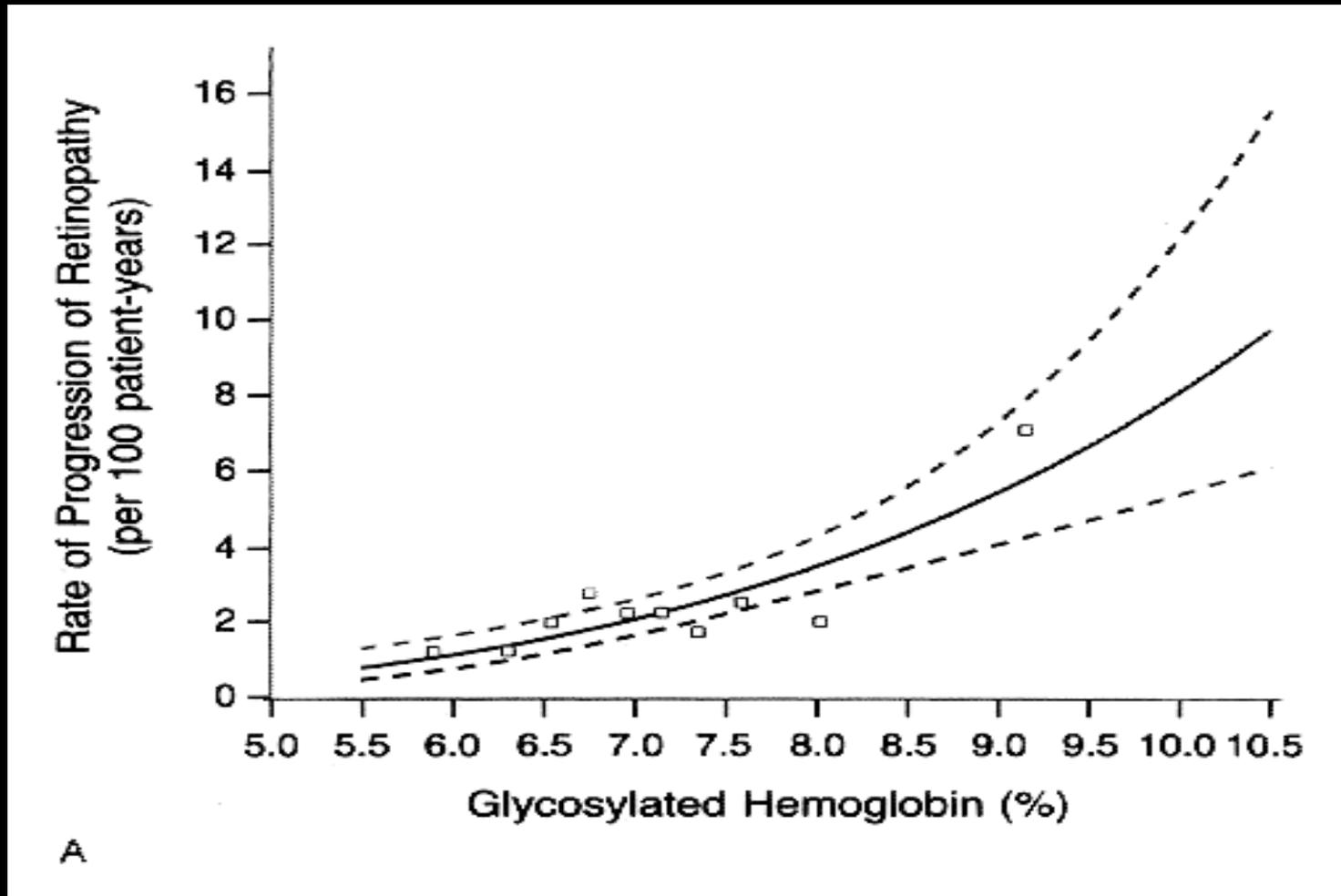
- Setting appropriate targets
- Monitoring and comparing achieved targets locally, nationally, internationally

# Reducing the Impact of Diabetes

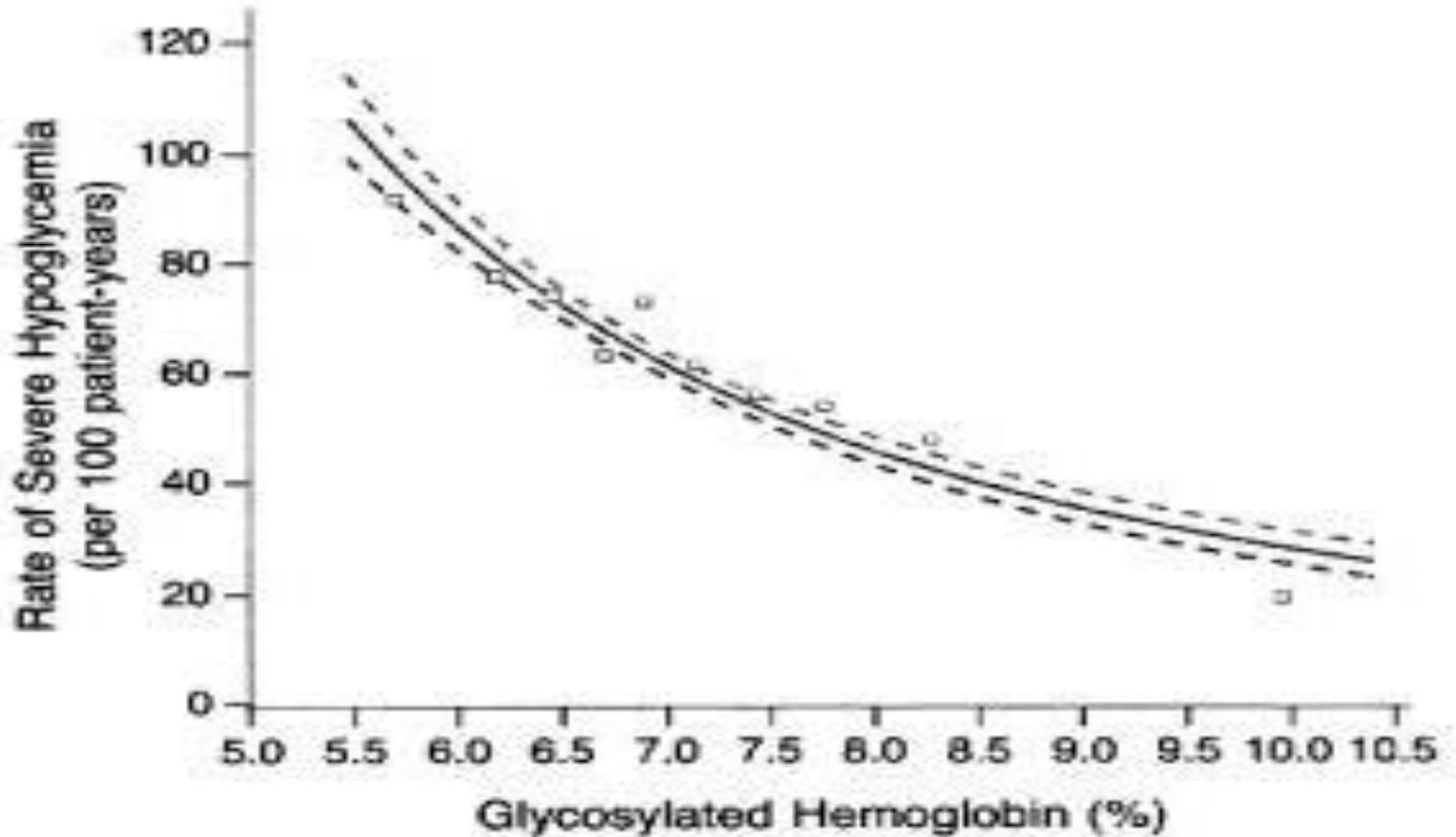
- **Diabetes Control and Complications Trial**
- **UK Prospective Diabetes Study**

# DCCT

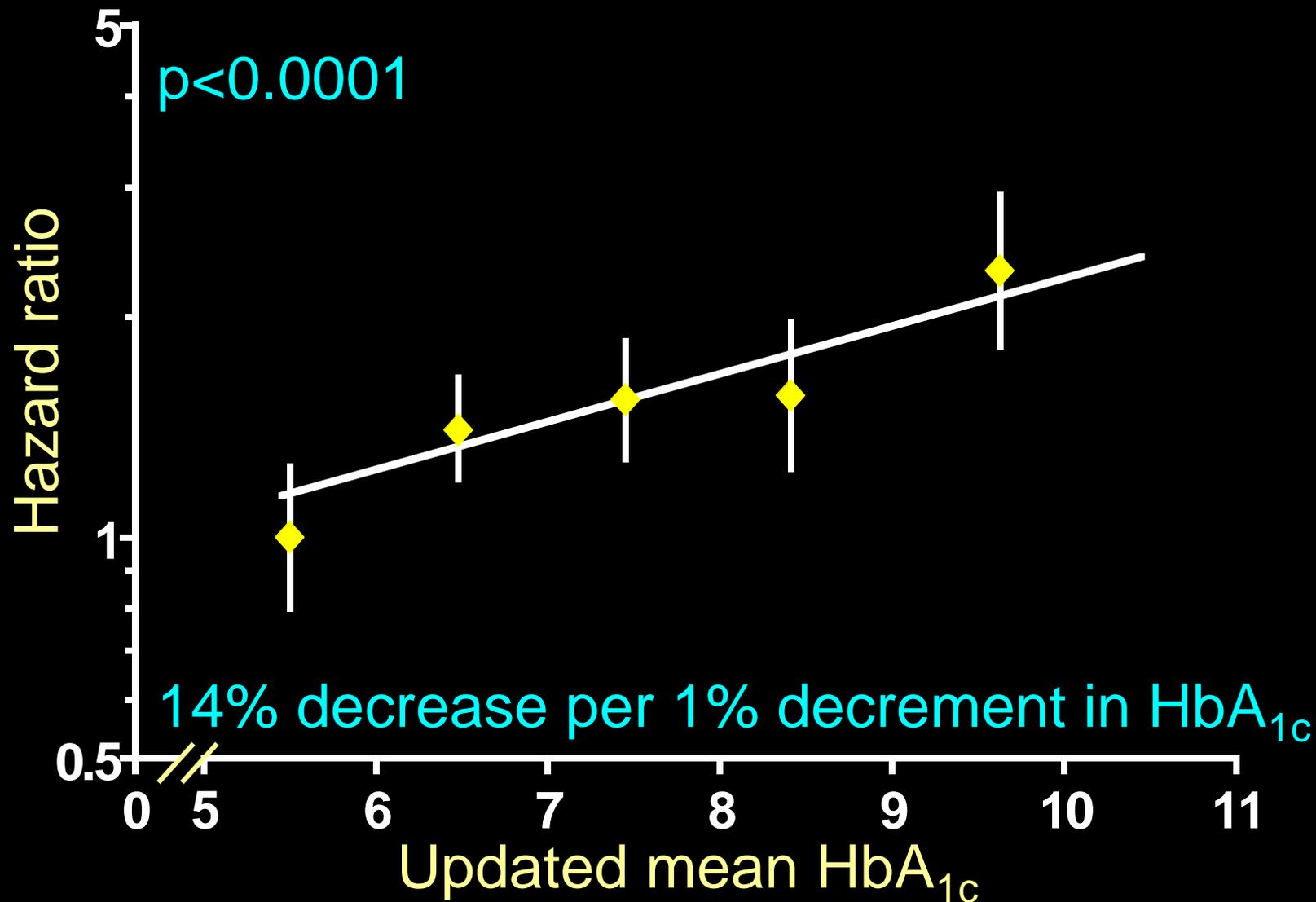
## Risk of Microvascular Complications



# Severe Hypoglycaemia and HbA<sub>1c</sub>

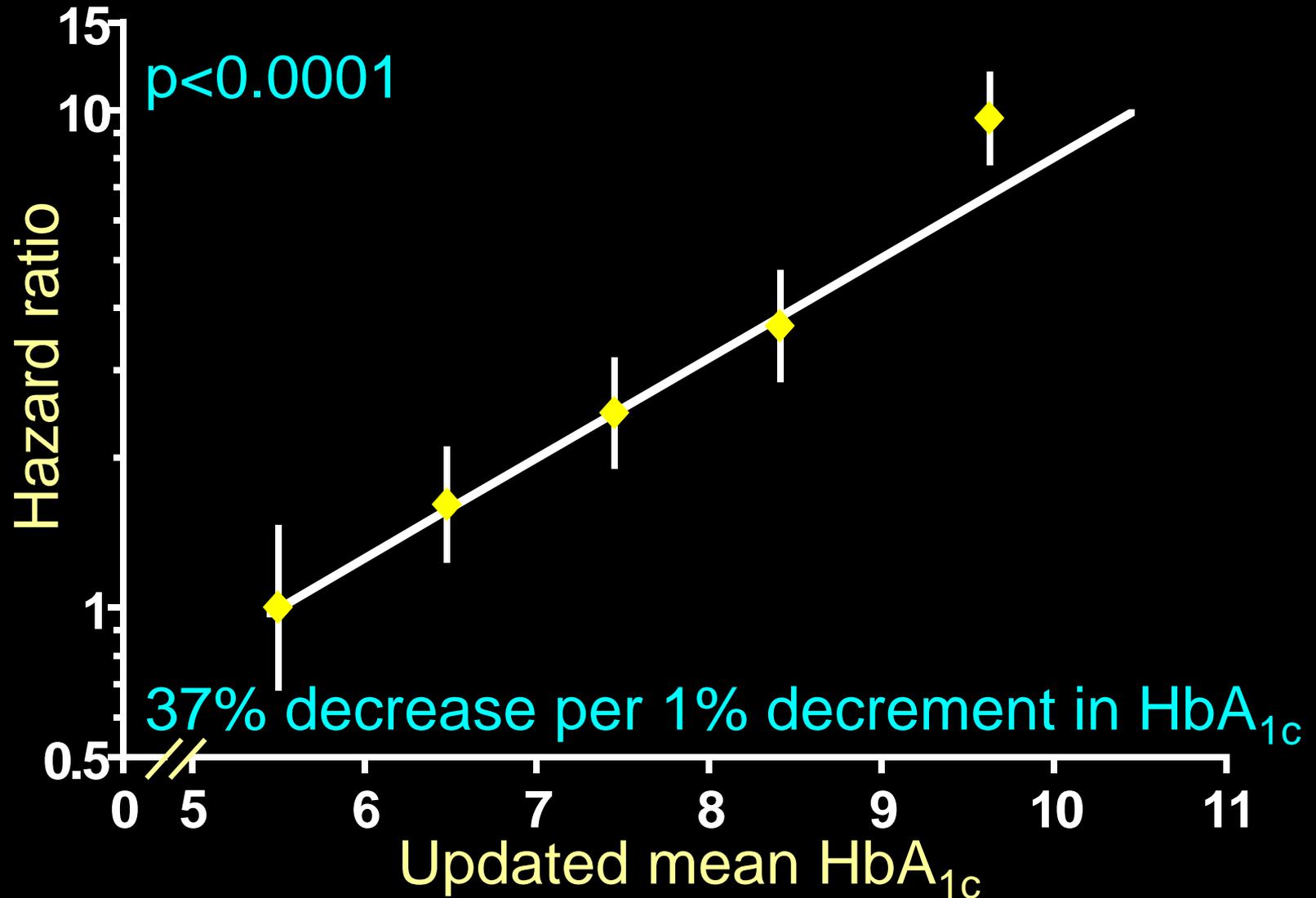


# Fatal and Non-Fatal Myocardial Infarction



UKPDS 35. *BMJ* 2000; 321: 405-12

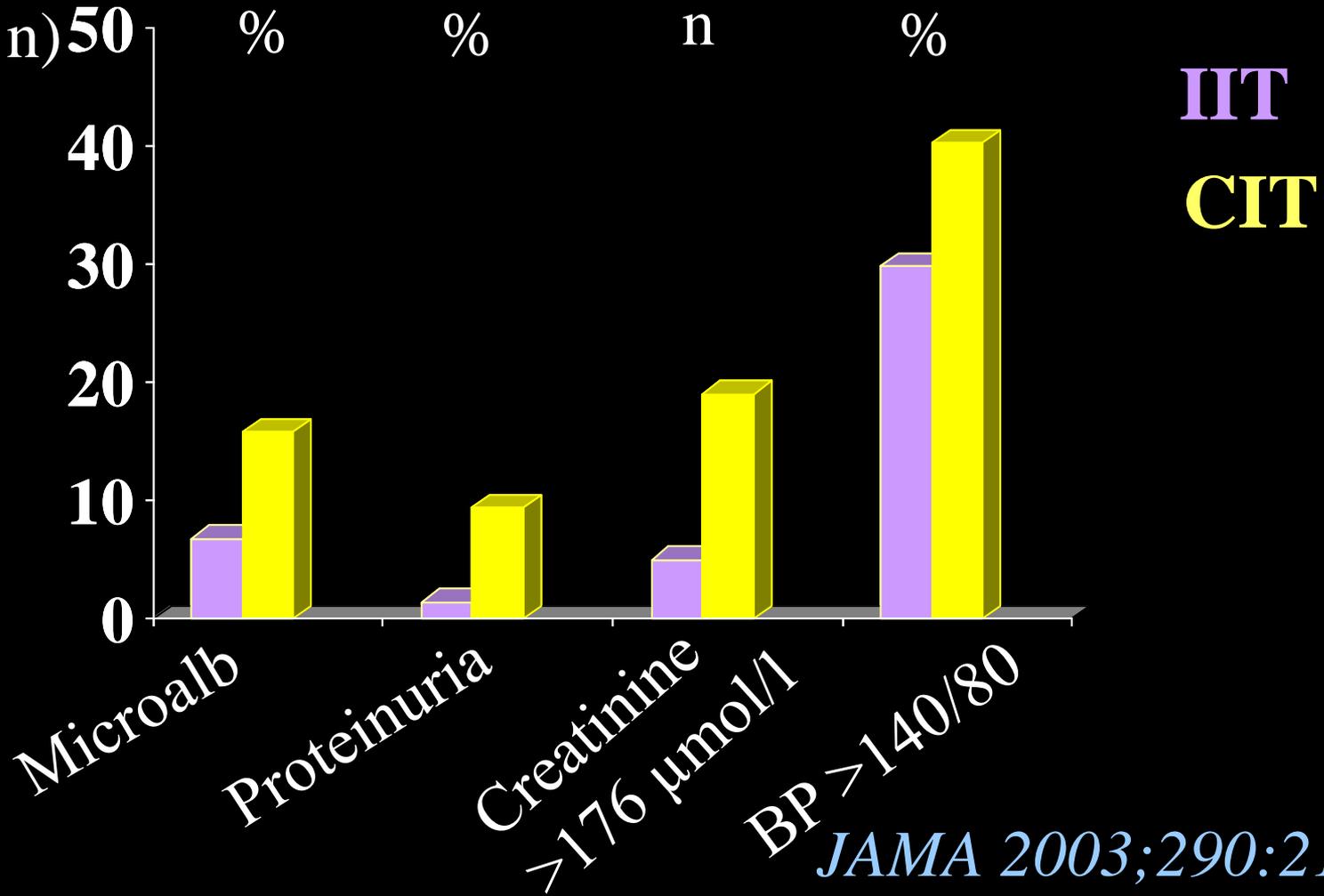
# Microvascular Endpoints



UKPDS 35. *BMJ* 2000; 321: 405-12

# EDIC 8-year Open Follow-Up

Prevalance  
(% or n)



*JAMA 2003;290:2159*

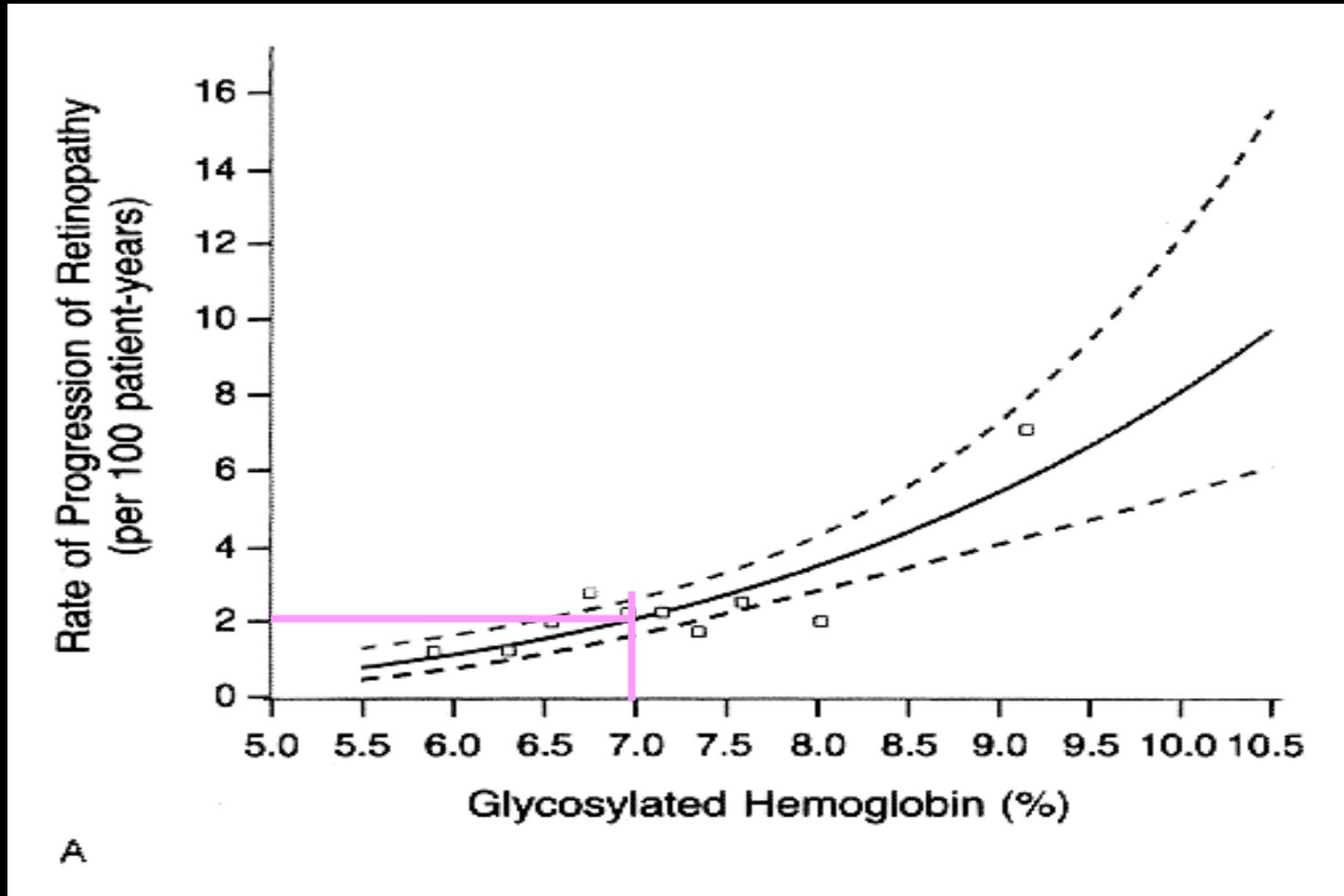
# HbA<sub>1c</sub> in Populations

- Relates glucose control to risk of long-term complications
- Allows estimate of risk of microvascular and macrovascular complications
- Allows setting of appropriate group targets

But is it good enough in individuals?

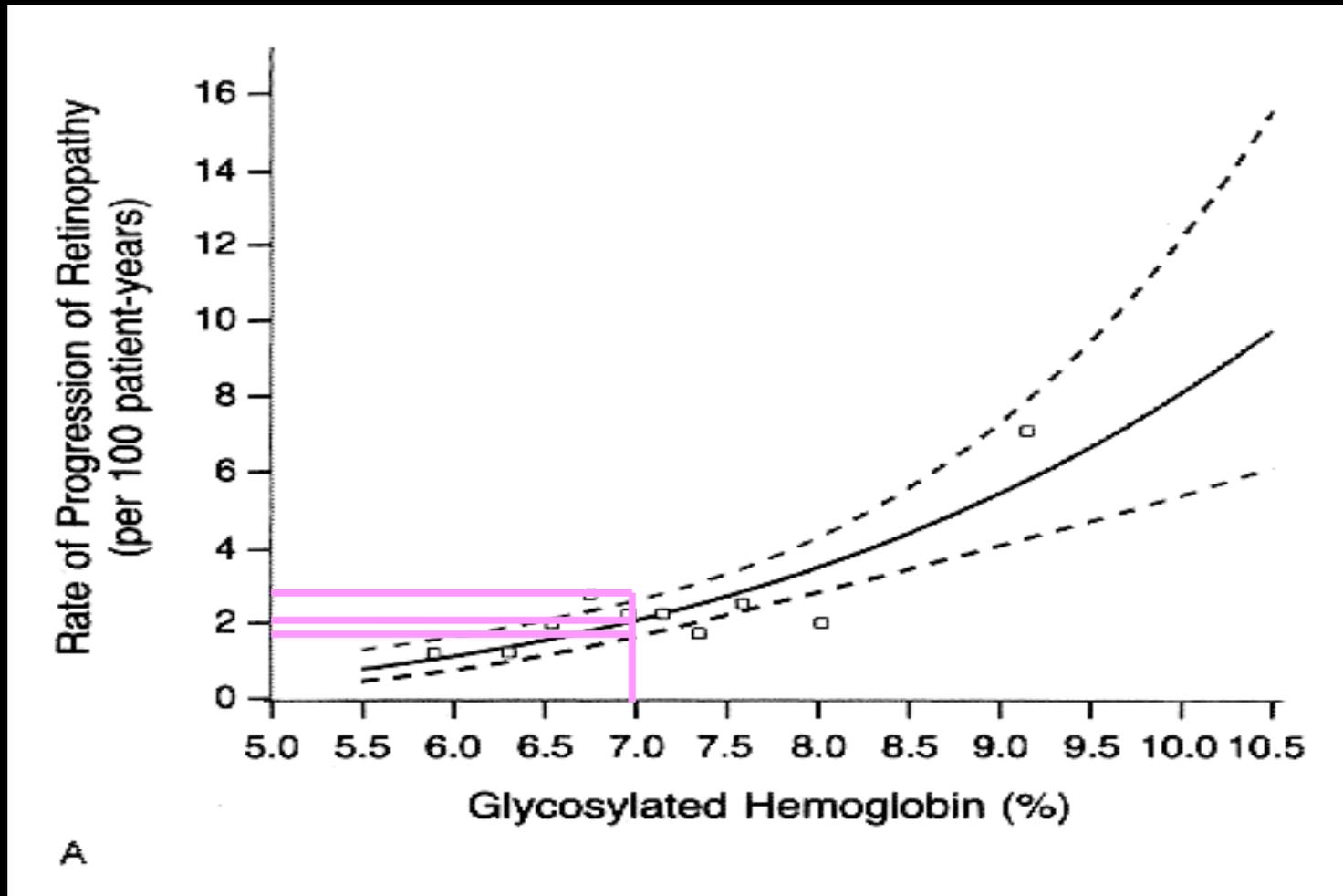
# DCCT

## Risk of Microvascular Complications



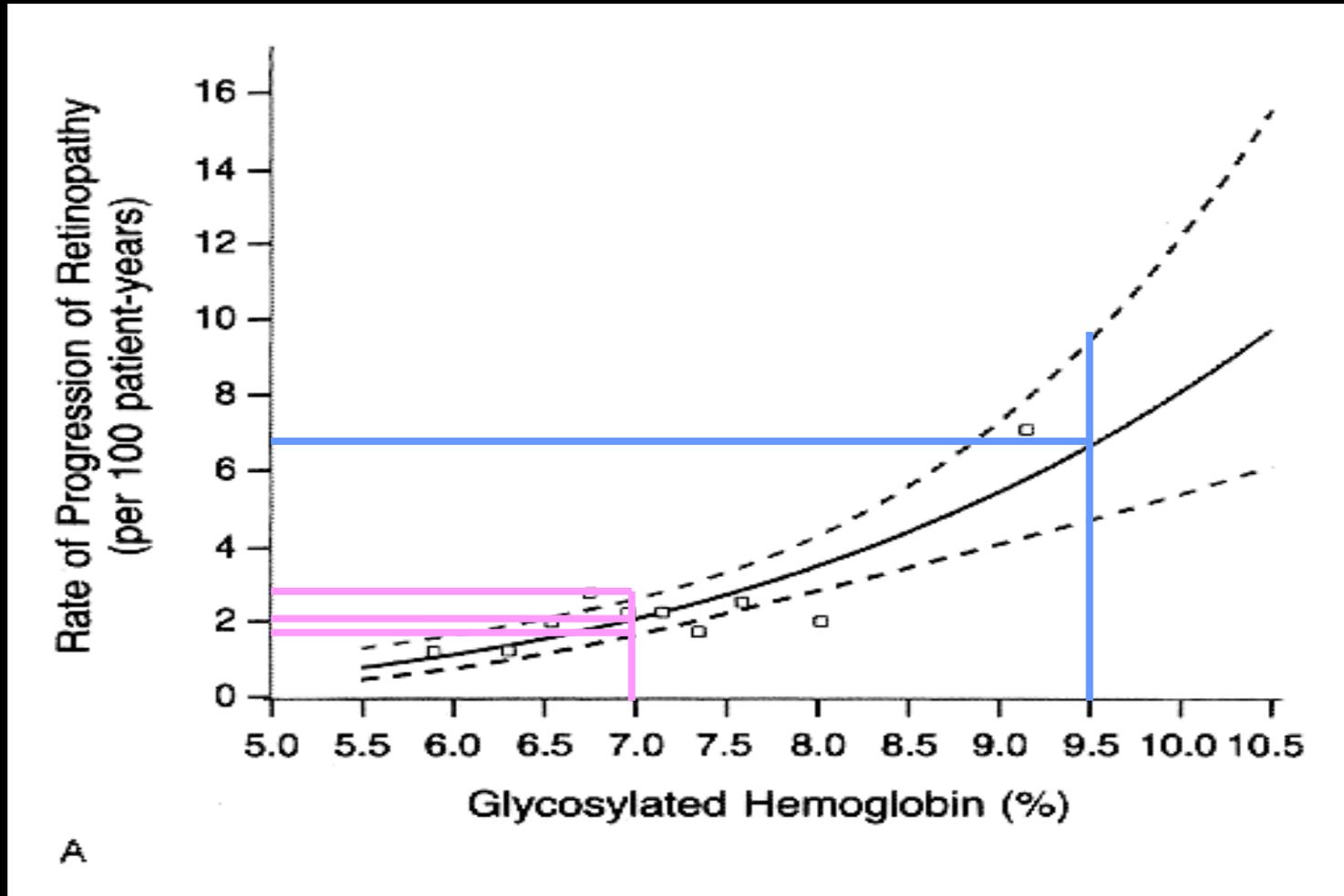
# DCCT

## Risk of Microvascular Complications



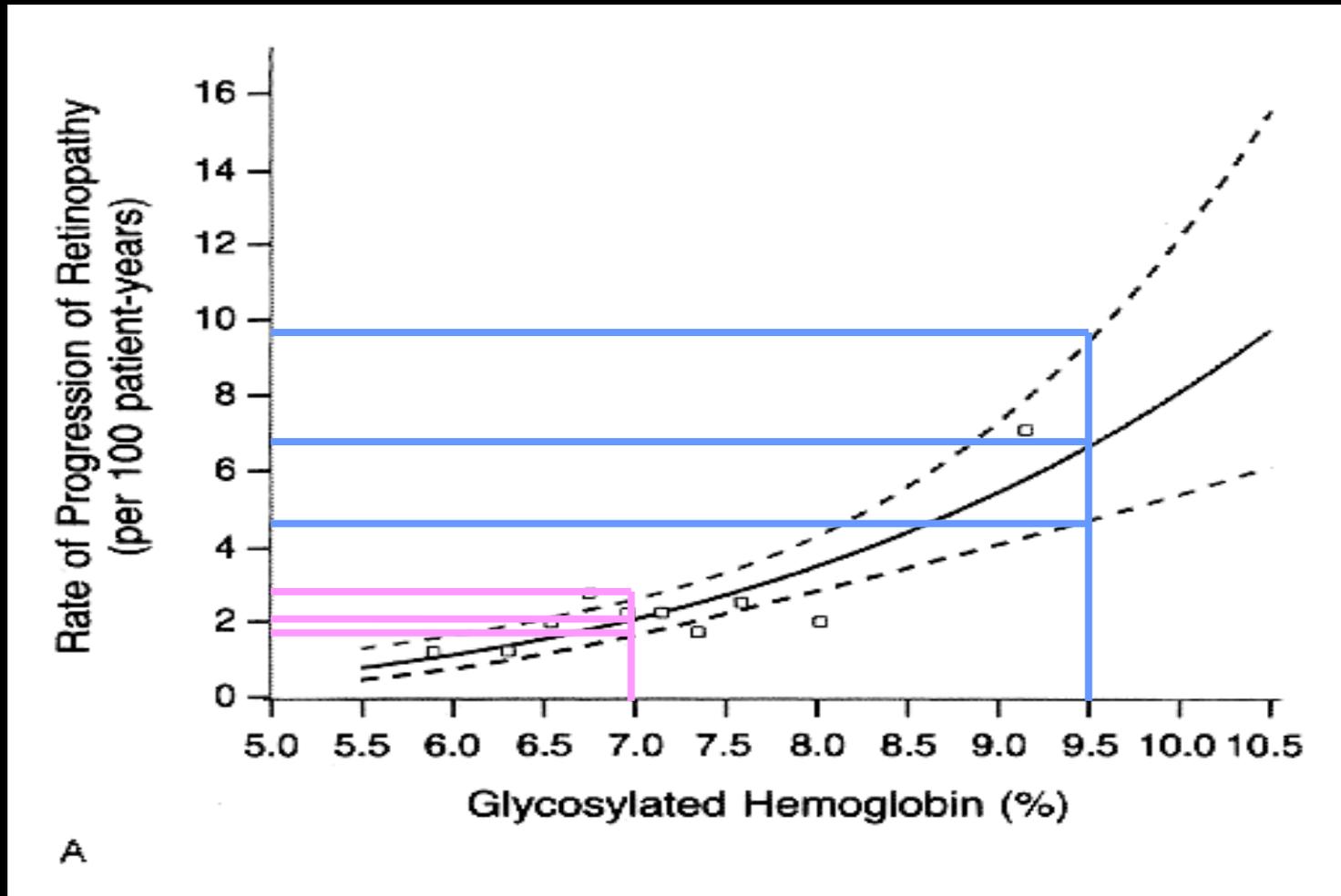
# DCCT

## Risk of Microvascular Complications



# DCCT

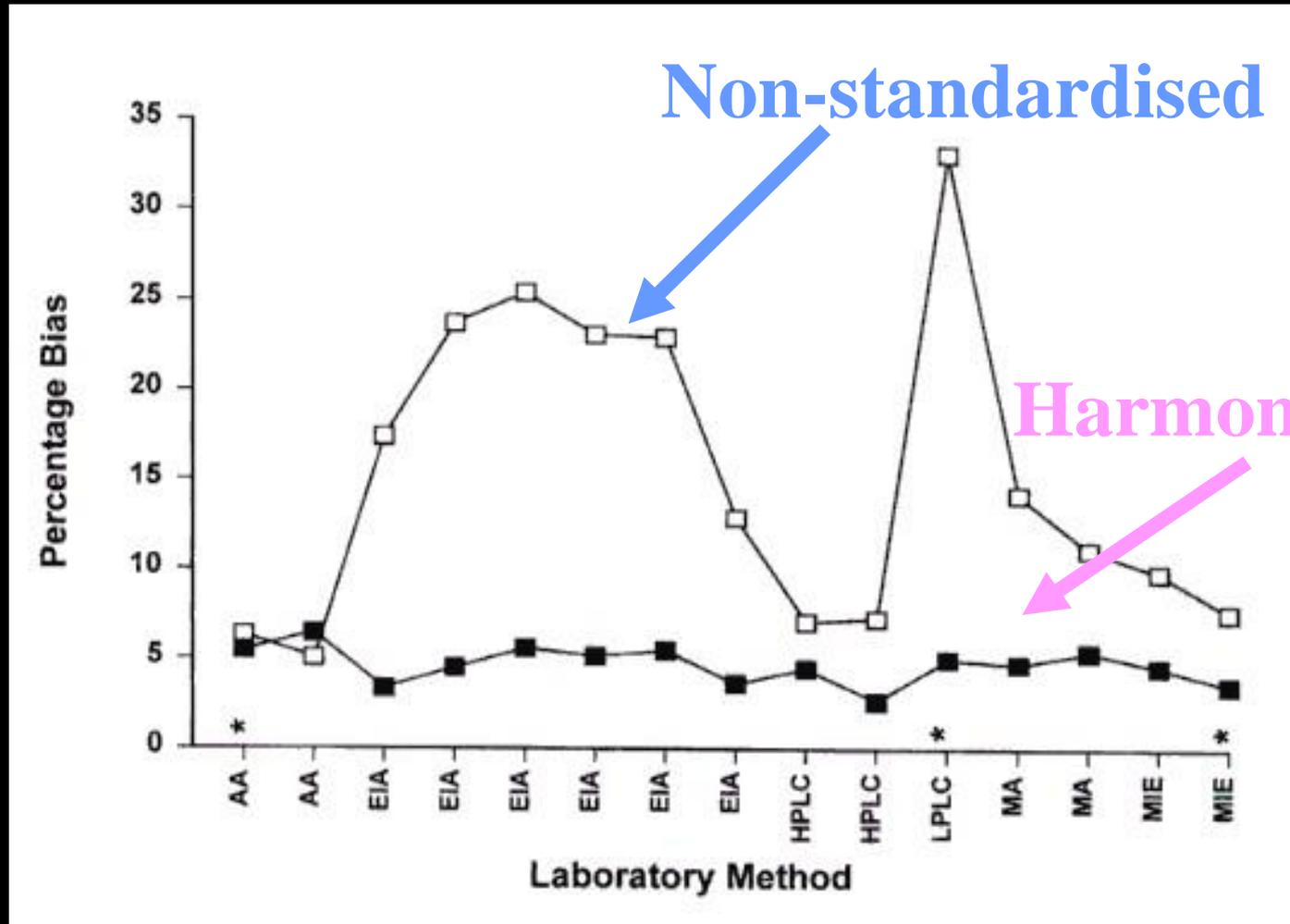
## Risk of Microvascular Complications



# But is the HbA<sub>1c</sub> Assay Reproducible?

Is HbA<sub>1c</sub> of 7.5 % the same in  
Nottingham  
as Newcastle  
as Oxford  
as Minneapolis?

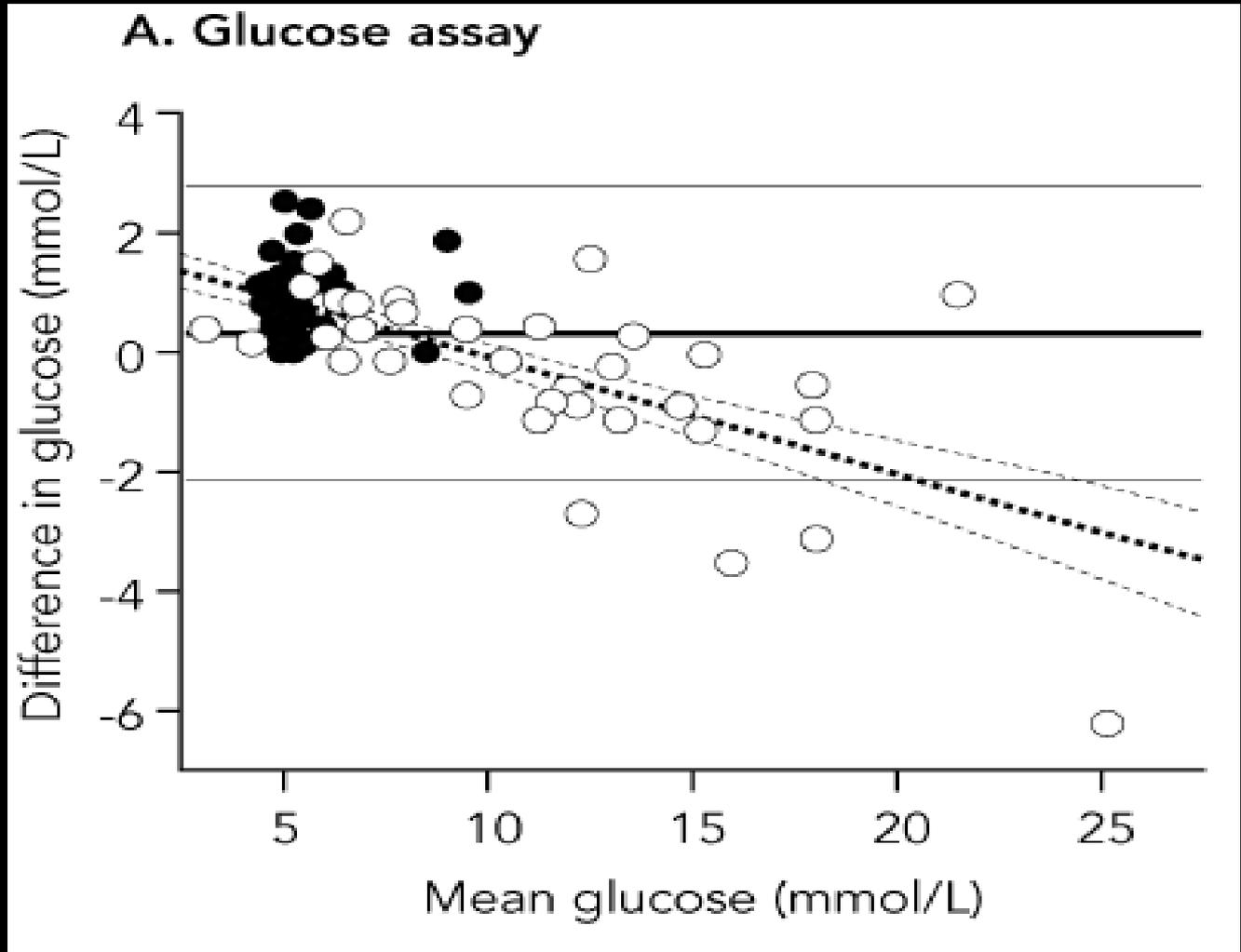
# Laboratory Measurement of HbA<sub>1c</sub>



# Point of Care vs Laboratory Glucose

Mean  
Difference  
0.36 mmol/l  
(-2.07 – 2.79)

P=0.007



# Variation Between Blood Glucose Meters

Range (mmol/l)	Average % Difference Between Meters			
	A vs B	A vs C	A vs D	A vs E
4 – 6	1.7	10.5	2.8	14.7
6 - 8	4.6	6.5	-1.4	10.3
8 - 11	2.6	6.9	4.0	8.9

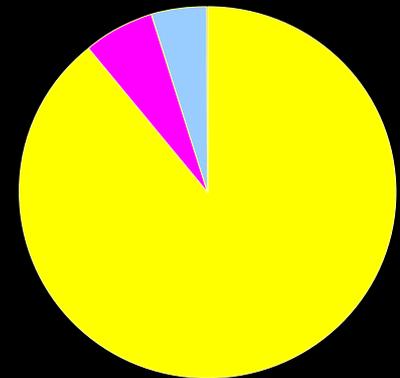
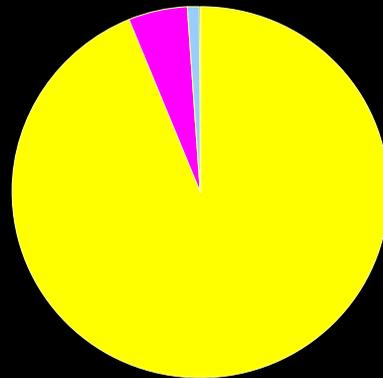
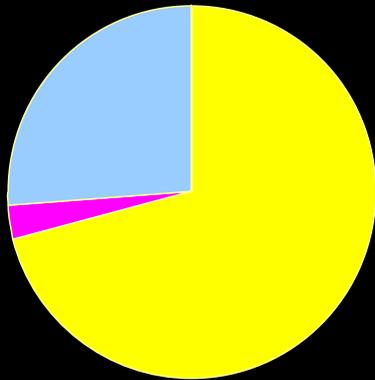
*Kimberly, Clin Chim Acta 2005; in press*

# Accuracy of CGMS

<3.9 mmol/l

3.9-10.0 mmol/l

>10 mmol/l



■ accurate

■ serious error

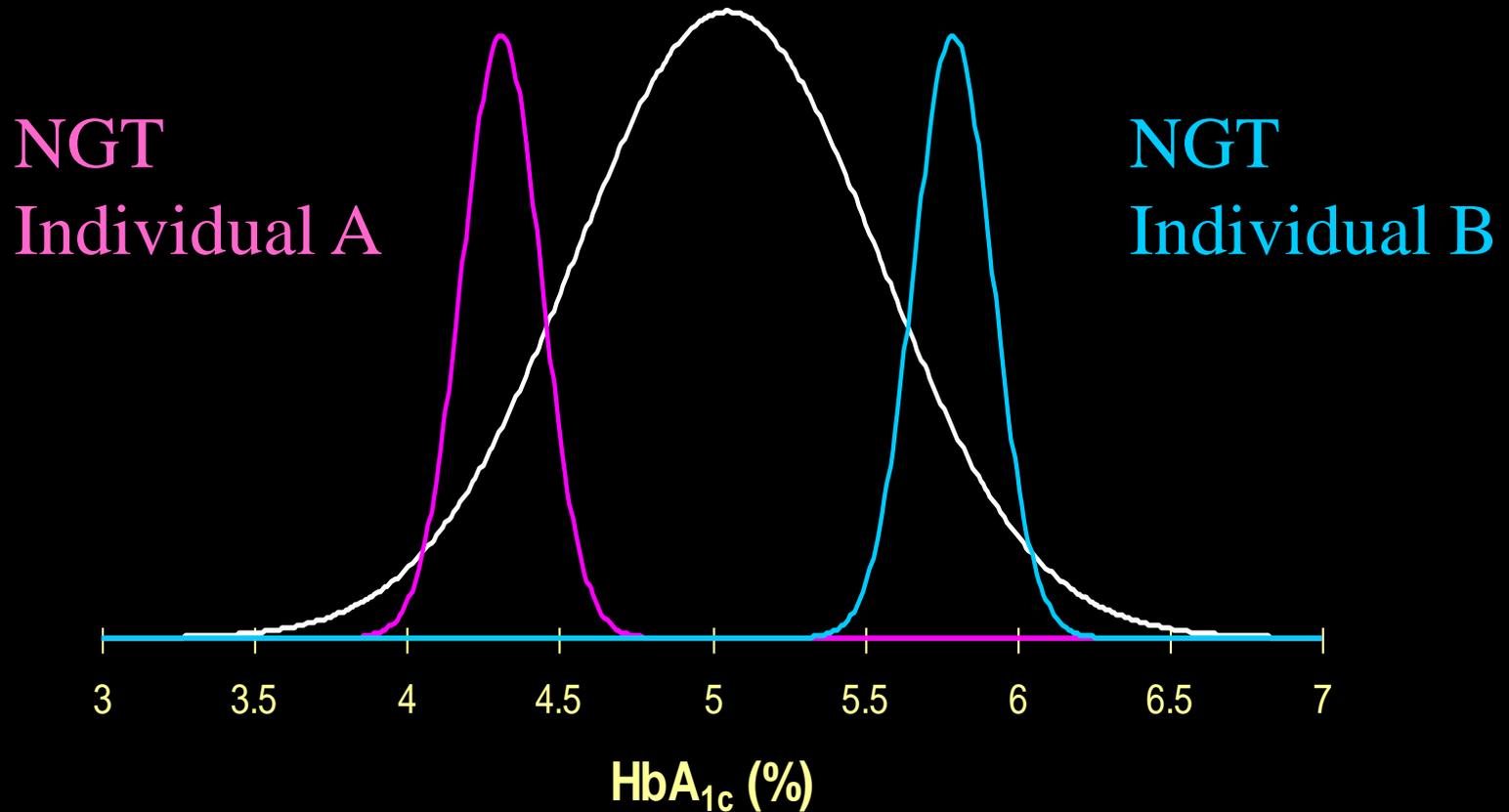
■ benign error

*Kovatchev Diabetes Care 2004;27:1922*

Precision of HbA<sub>1c</sub> assay as good as near-patient  
blood glucose testing and has much better  
quality control

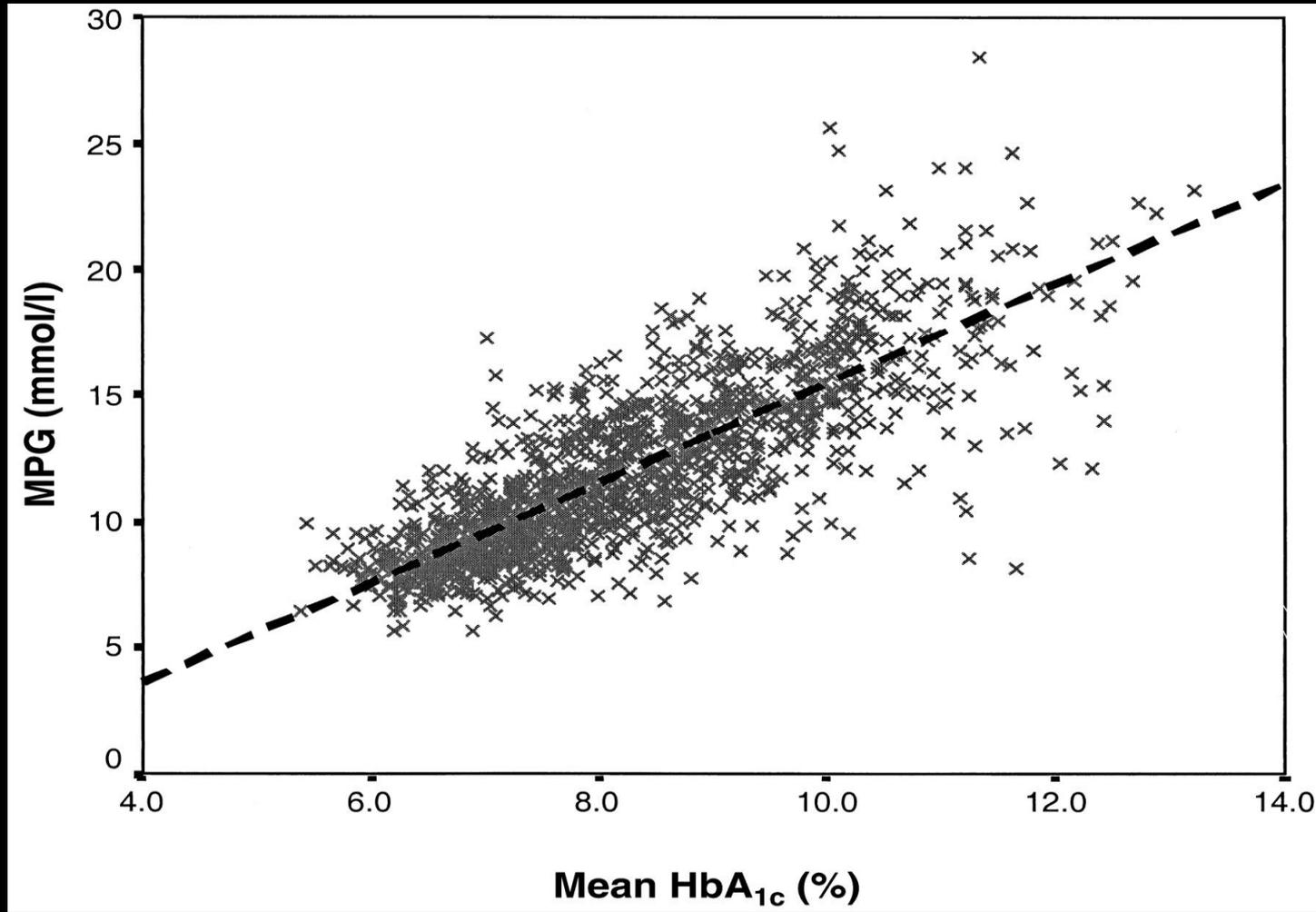
# Biological Variation of HbA<sub>1c</sub>

Non-diabetic distribution



*Kilpatrick ES et al. Diabetes Care. 1998; 21:261-4*

# Mean Plasma Glucose vs HbA<sub>1c</sub>



*Rohlfing CL et al Diabetes Care 2002;25:275-8*

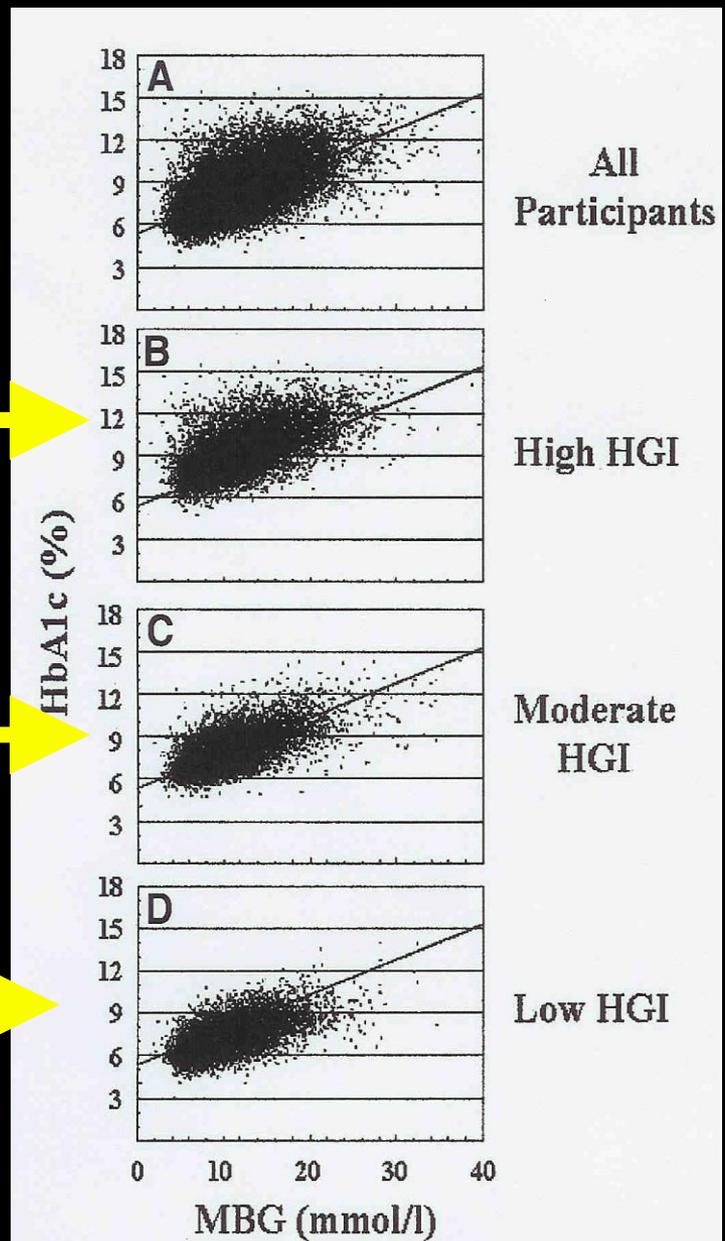
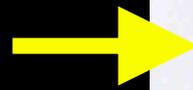
High HbA<sub>1c</sub> for MBG



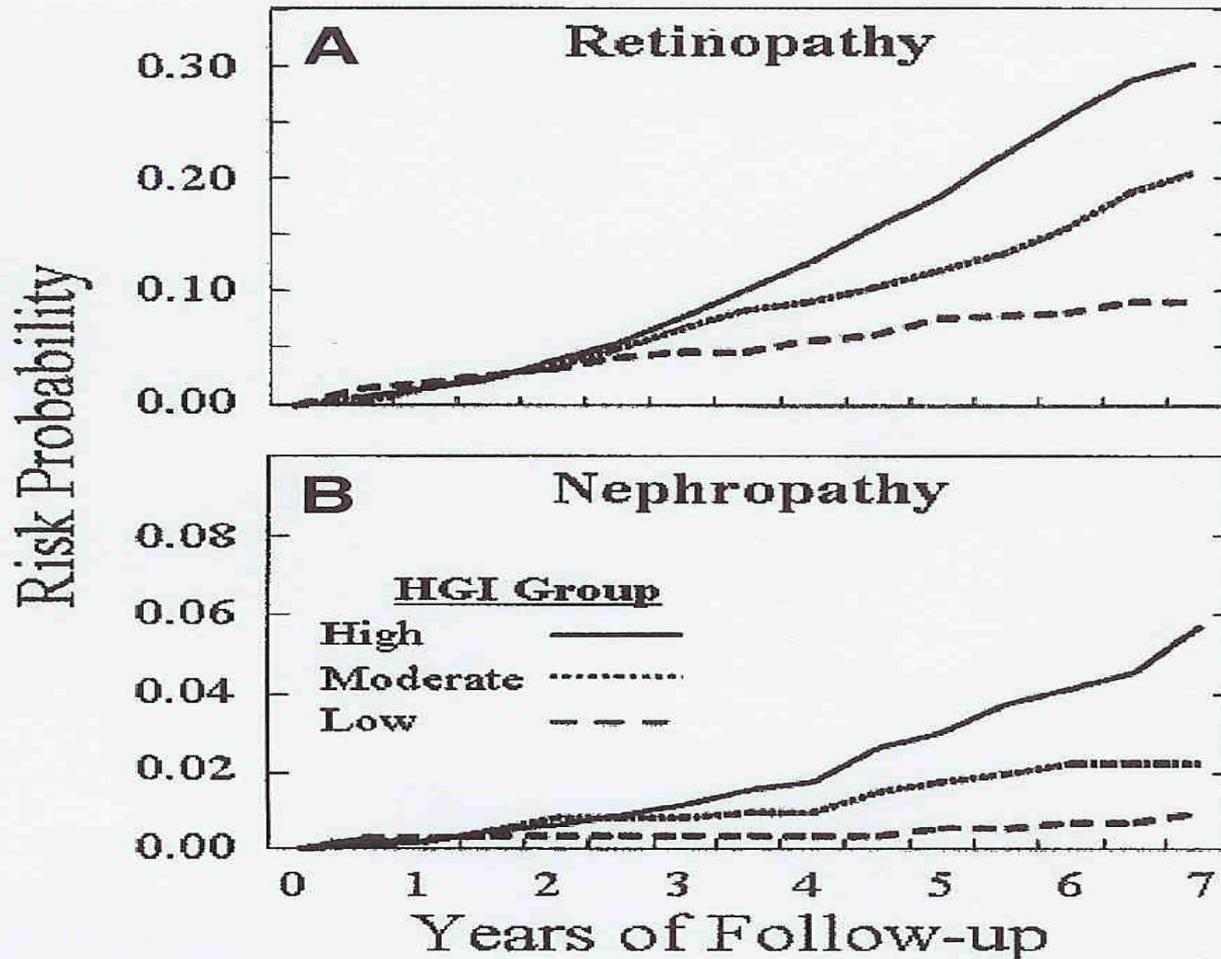
Medium HbA<sub>1c</sub> for MBG



Low HbA<sub>1c</sub> for MBG



# HGI and Risk of Complications



# HbA<sub>1c</sub> Limitations

- Haemoglobinopathies  
can screen for
- Anaemia  
can measure and usually correct
- Renal failure  
newer assays- no interference from carbamylation  
abnormal RBC turnover still a problem

# HbA<sub>1c</sub>

- Meets the requirements for a satisfactory marker for risk of complications in diabetes care:
  - Glucose
  - Non-glucose
- Most of its limitations have been/can be overcome