

Importance of postprandial glycaemia (PPG) for the cardiovascular risk: the DECODE Study

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In asymptomatic population, which indicator of glycaemia is most important?

PPG?

The highest
glucose level

FPG?

The lowest
glucose level

HbA_{1c}?

The long-term average glycaemic exposure

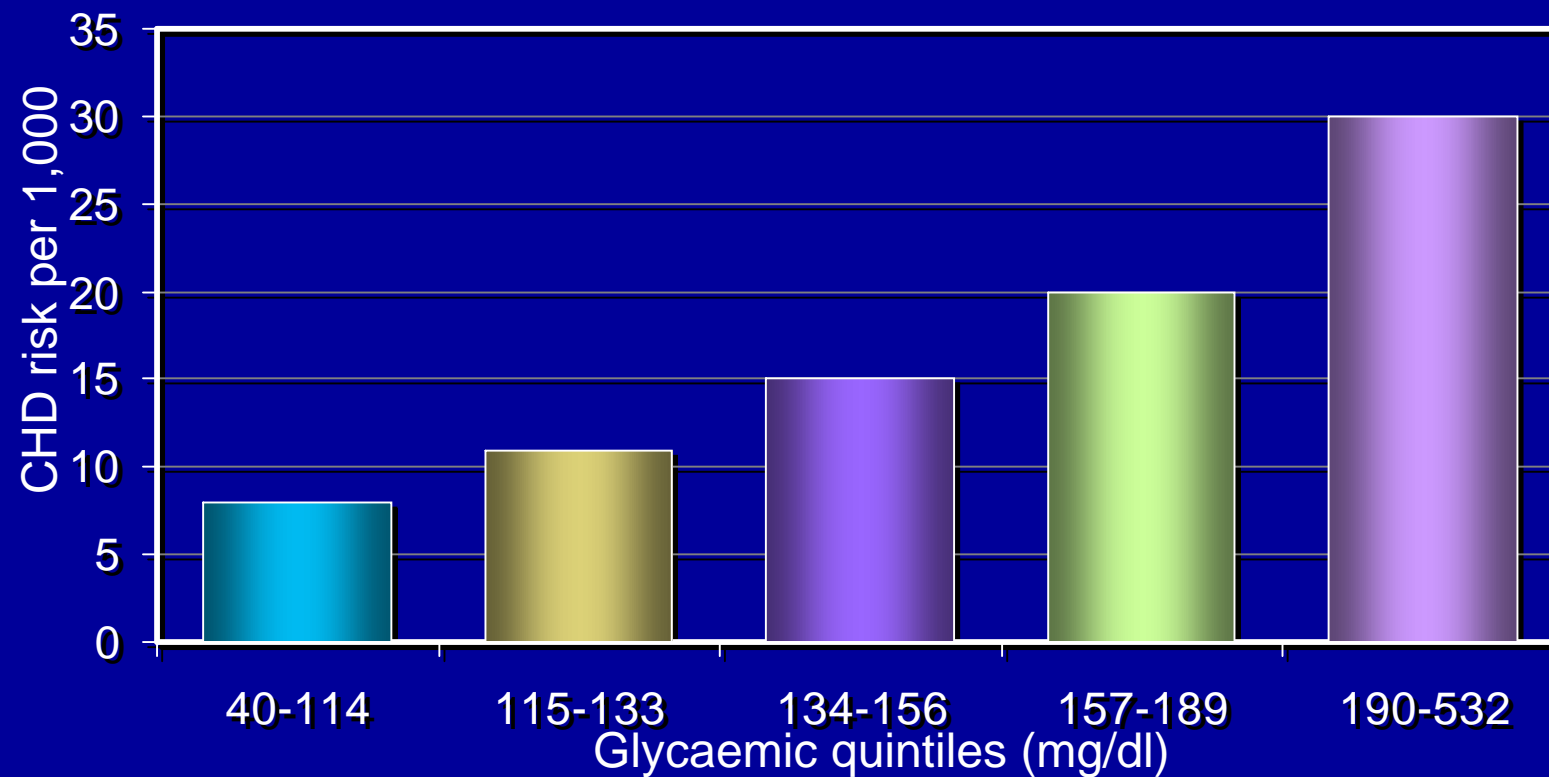
Epidemiology of PPG: Evidence for its importance

- ◆ What is the evidence that fasting PG is a risk factor in its own right?
- ◆ What is the evidence that PPG is a risk factor in its own right?

**What is the evidence that PPG
is a risk factor in its own right?**

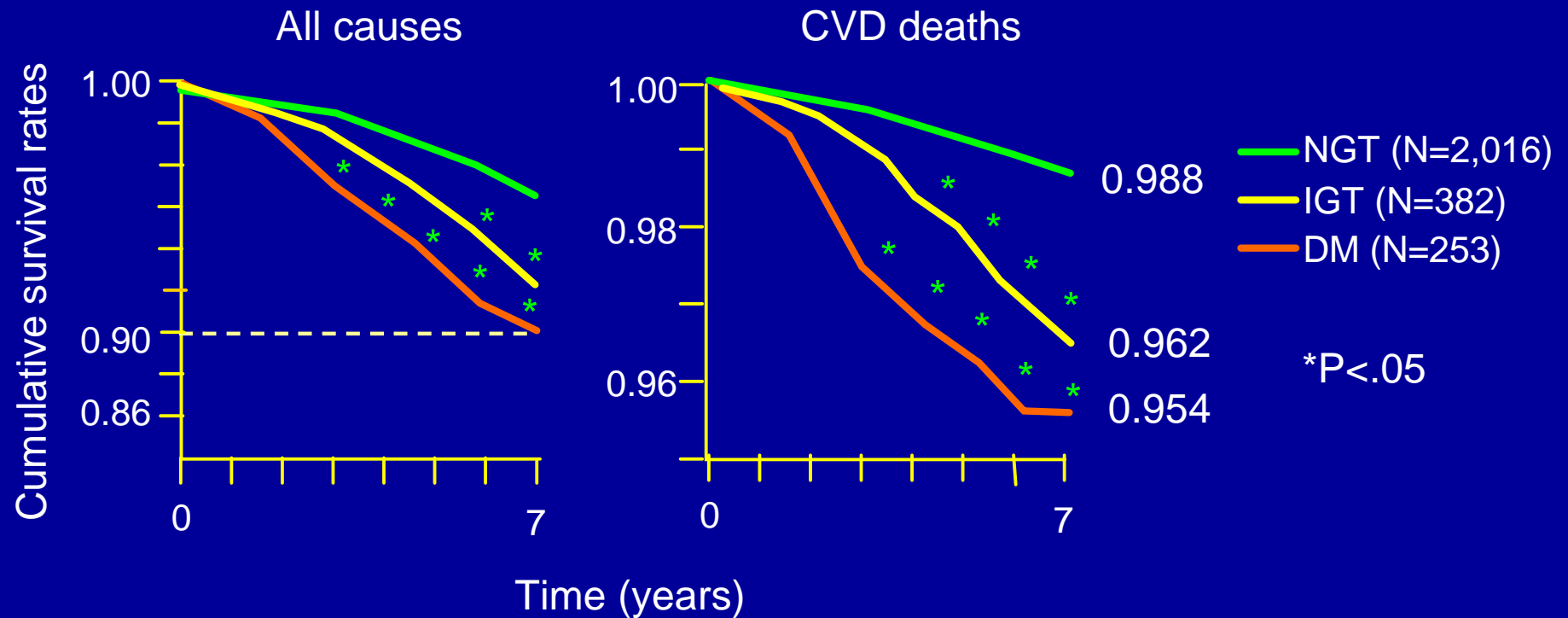
Honolulu Heart Program: PPG predicted risk of death within 12 years

1h postprandial serum glucose



$P < .001$ comparing quintile 1 to 5 N=8,006 men

Glucose tolerance, from IGT to overt diabetes, was a risk factor for death from CVD: Funagata Study, Japan



The DECODE Study

Diabetes

Epidemiology:

Collaborative analysis

Of

Diagnostic criteria in

Europe

DECODE:

Participating centres

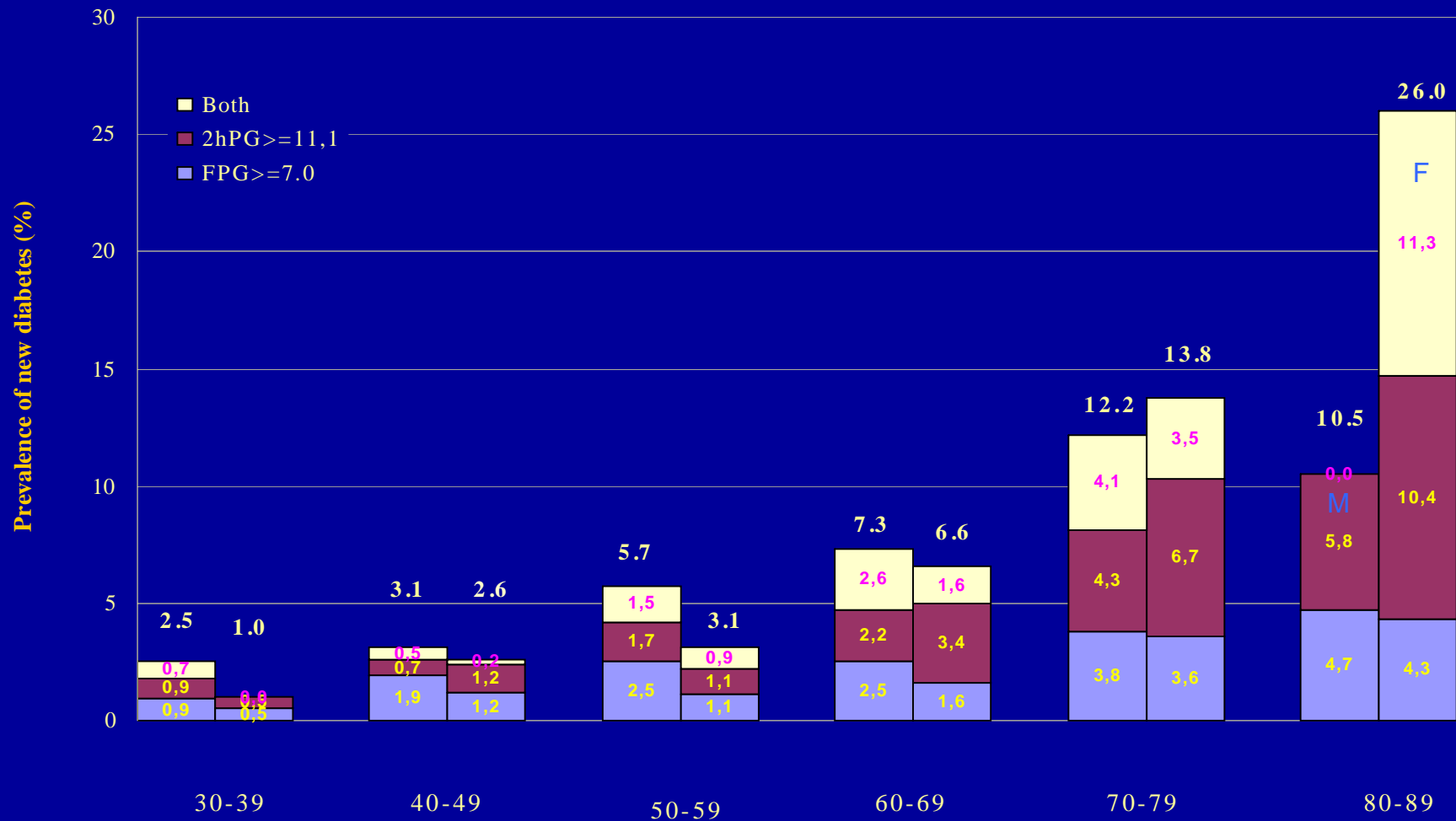
- ◆ **Denmark (Glostrup), Finland (FIN-MONICA, Helsinki policemen, Oulu, Piëksämäki, Vantaa, East-West Finland), Iceland (Reykjavik), Sweden (Uppsala, Umeå)**
- ◆ **France (Paris), England (Ely, London, Newcastle), Italy (Cremona), Malta, Poland (Kracow), Spain (Canary Islands, Catalonia, Madrid), the Netherlands (Zutphen, Hoorn)**
- ◆ **N=39,000**

The overall prevalence of diabetes is the same, whether assessed by fasting glucose (≥ 7.0 mmol/L) or 2-hour post-challenge glucose (≥ 11.1 mmol/L), but the majority of diabetic subjects will remain undiagnosed if fasting glucose is measured only

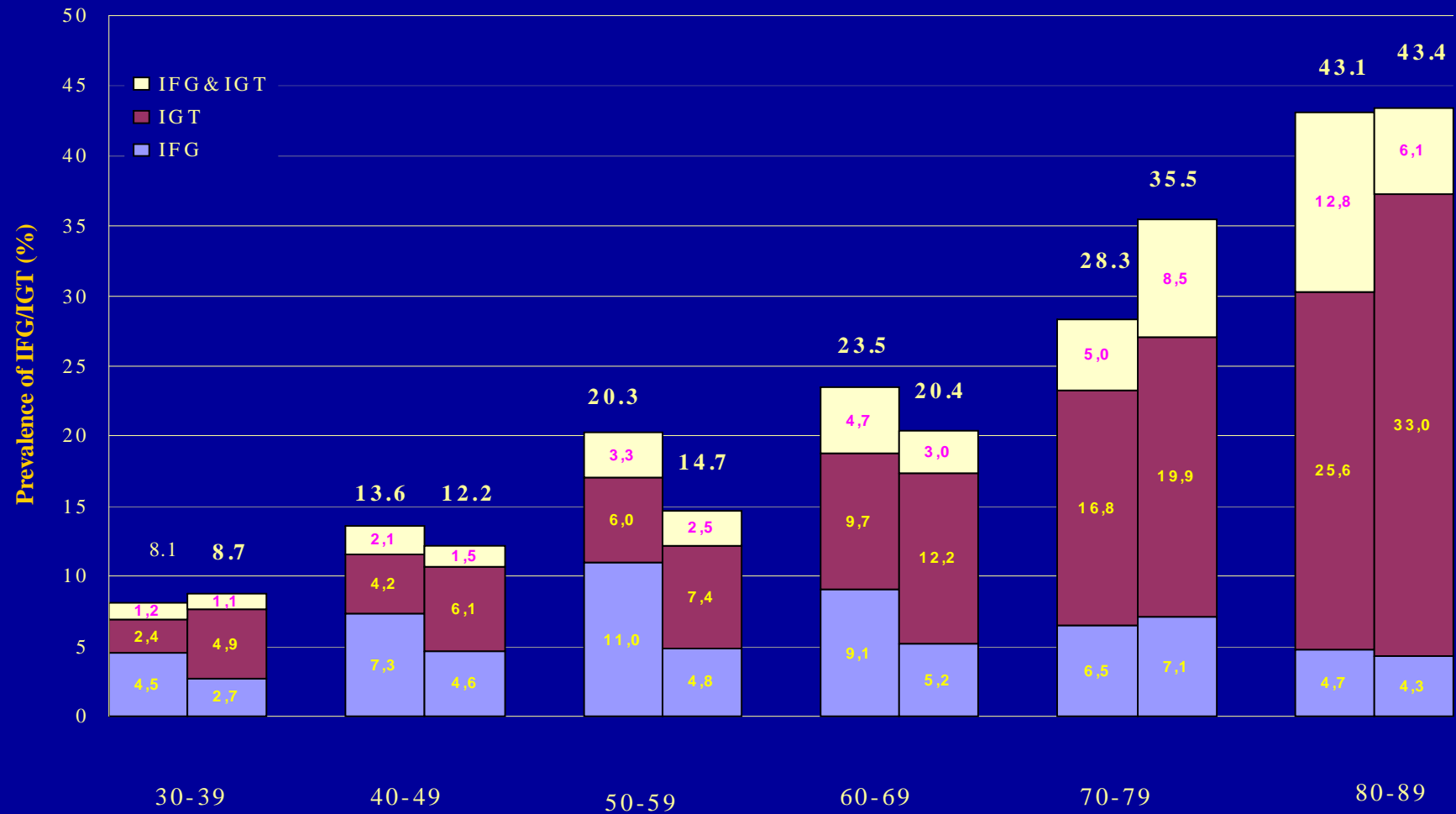
2-Hour Plasma Glucose (mmol/L)

		<7.8	7.8-11.0	≥ 11.1	Total
Fasting plasma glucose (mmol/L)	<6.1	21,968	2562	316	24,846
	6.1-6.9	2020	893	206	3119
	≥ 7.0	276	378	489	1143
	Total	24,264	3833	1011	29,108

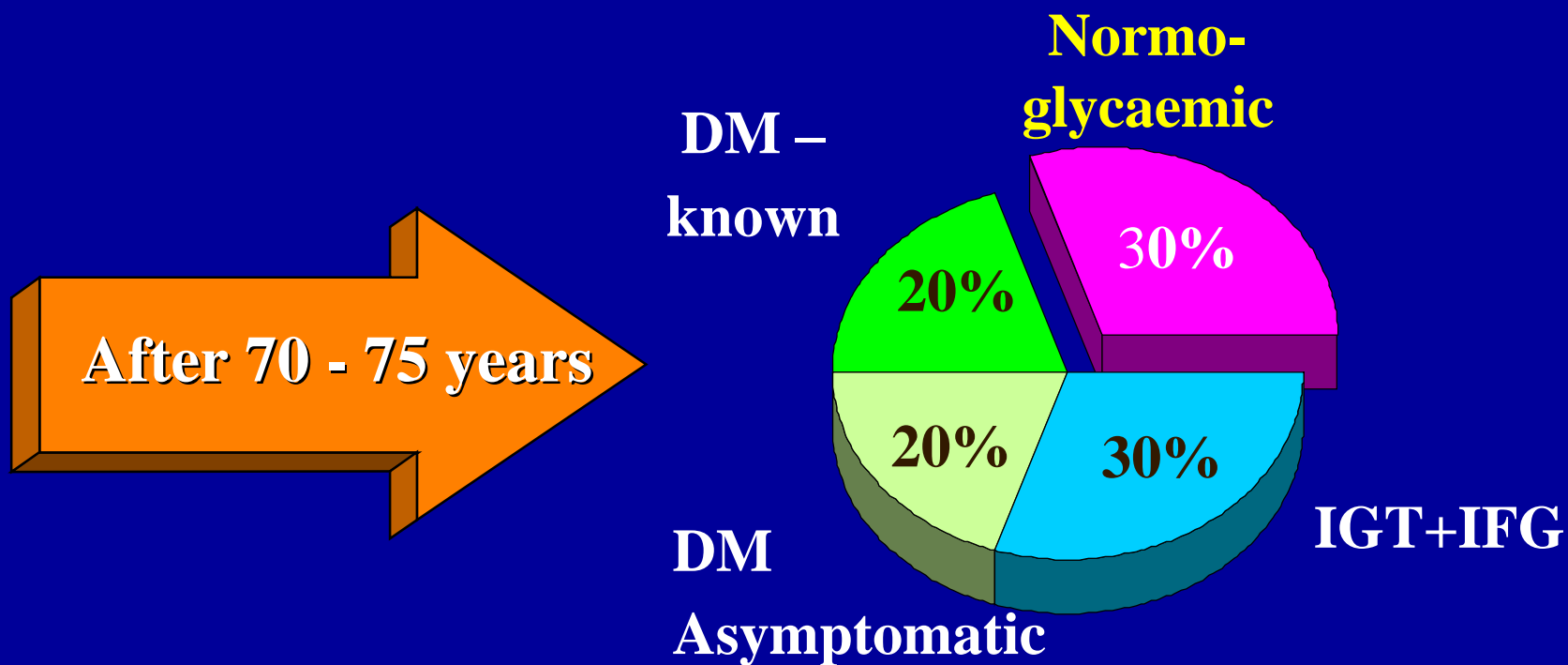
Prevalence of previously undiagnosed diabetes (%) in Europe by age-group, DECODE



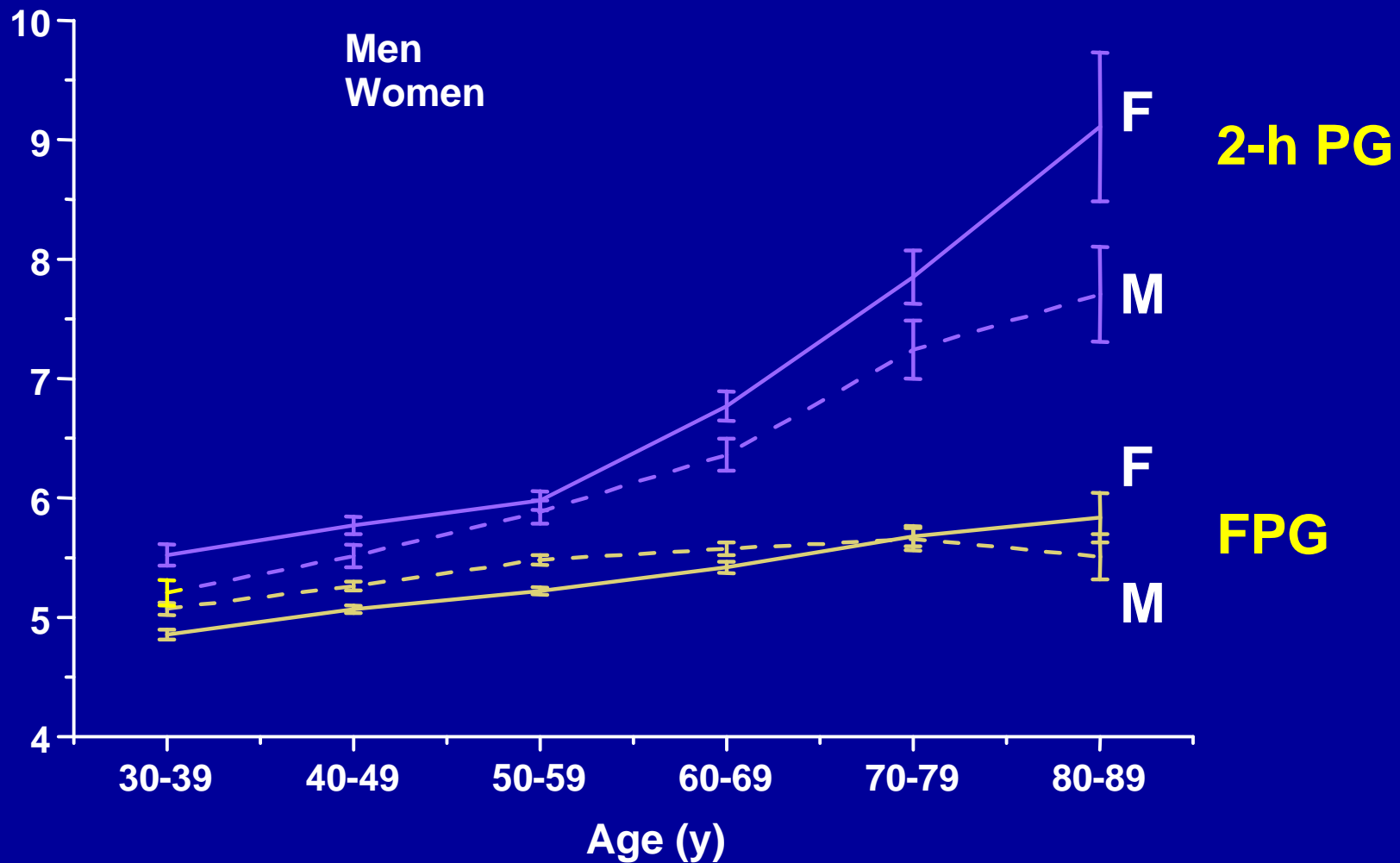
Prevalence of IFG/IGT (%) in Europe by age-group, DECODE



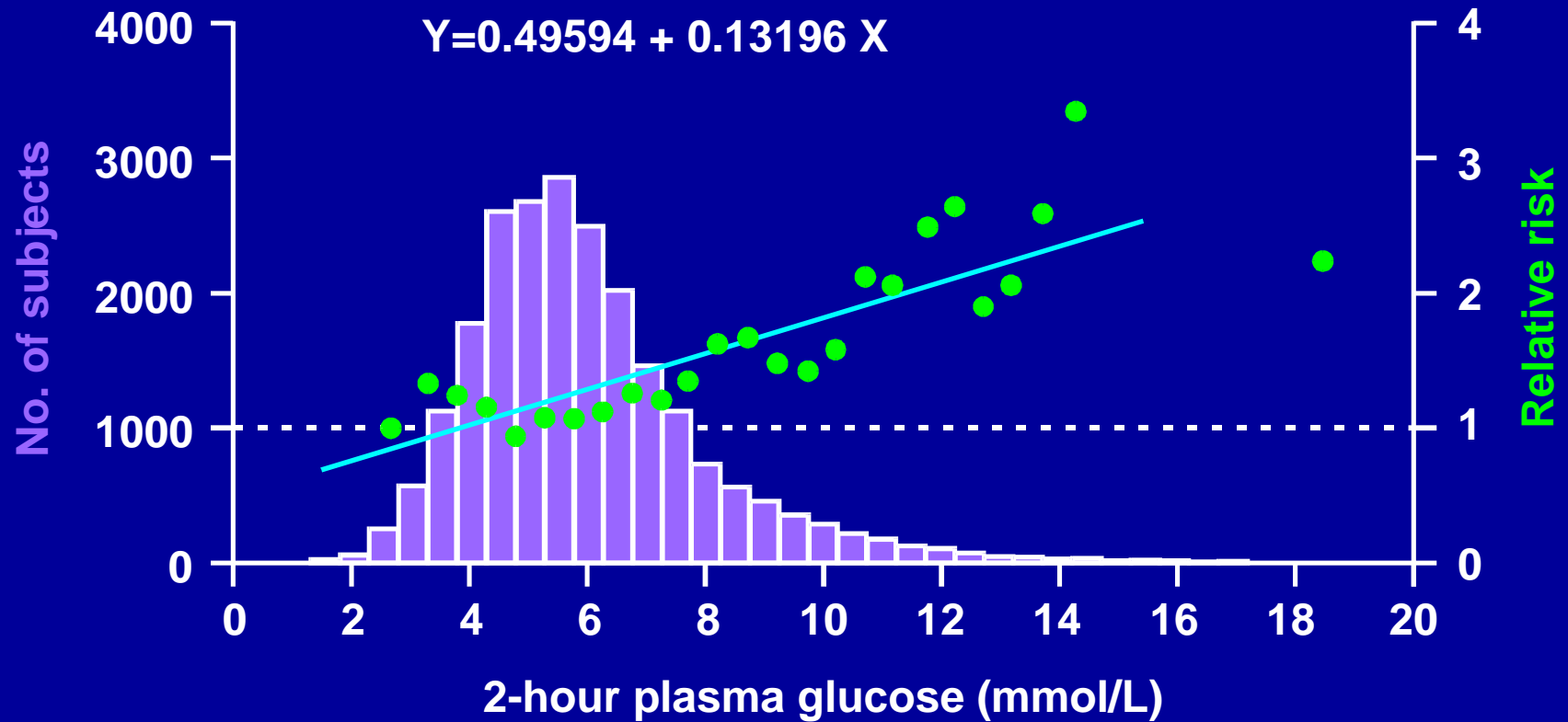
Lifetime Risk of Hyperglycaemia (i.e. the prevalence in the elderly) in Europeans is very high



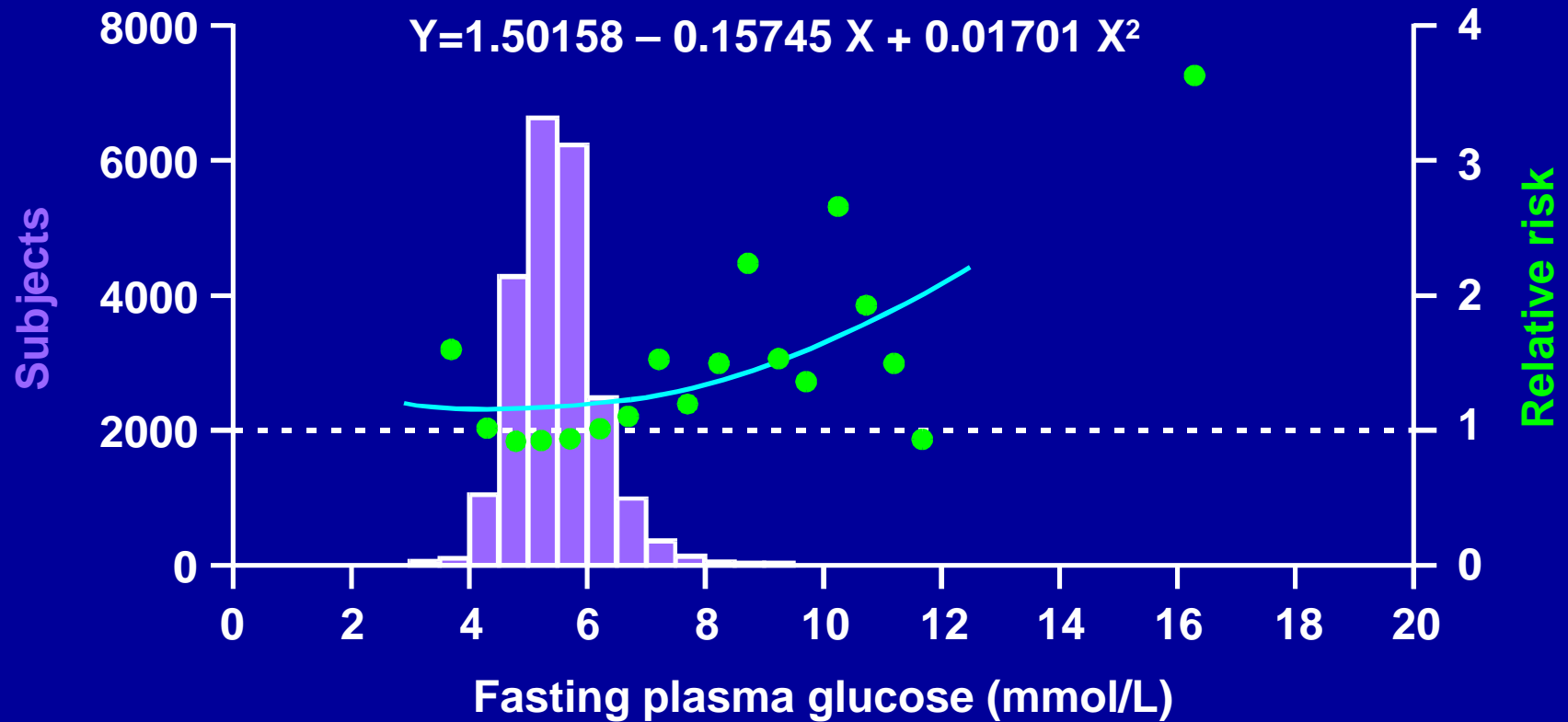
2-hour plasma glucose concentration is increasing with age, but fasting glucose is not: DECODE



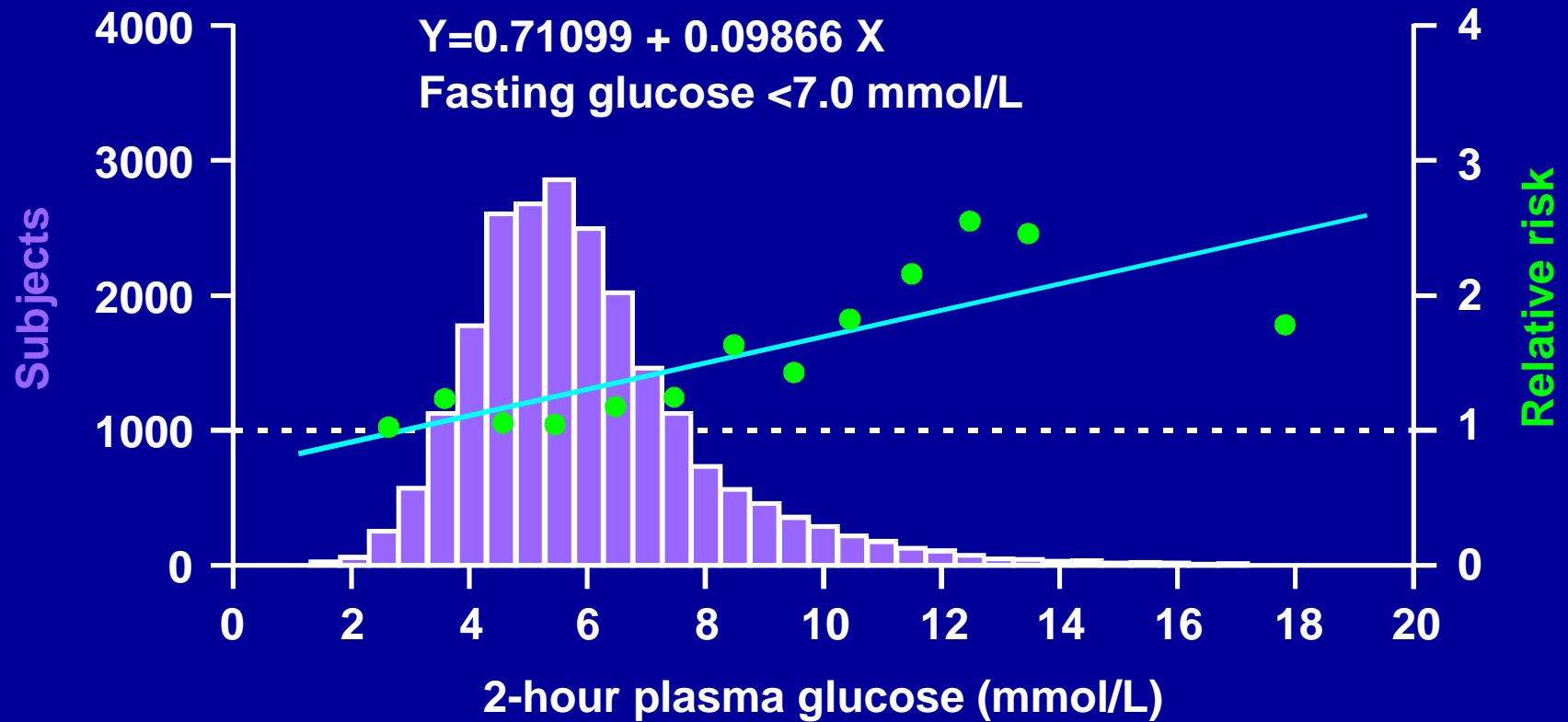
All-cause mortality has a linear relationship with 2-hour plasma glucose: DECODE



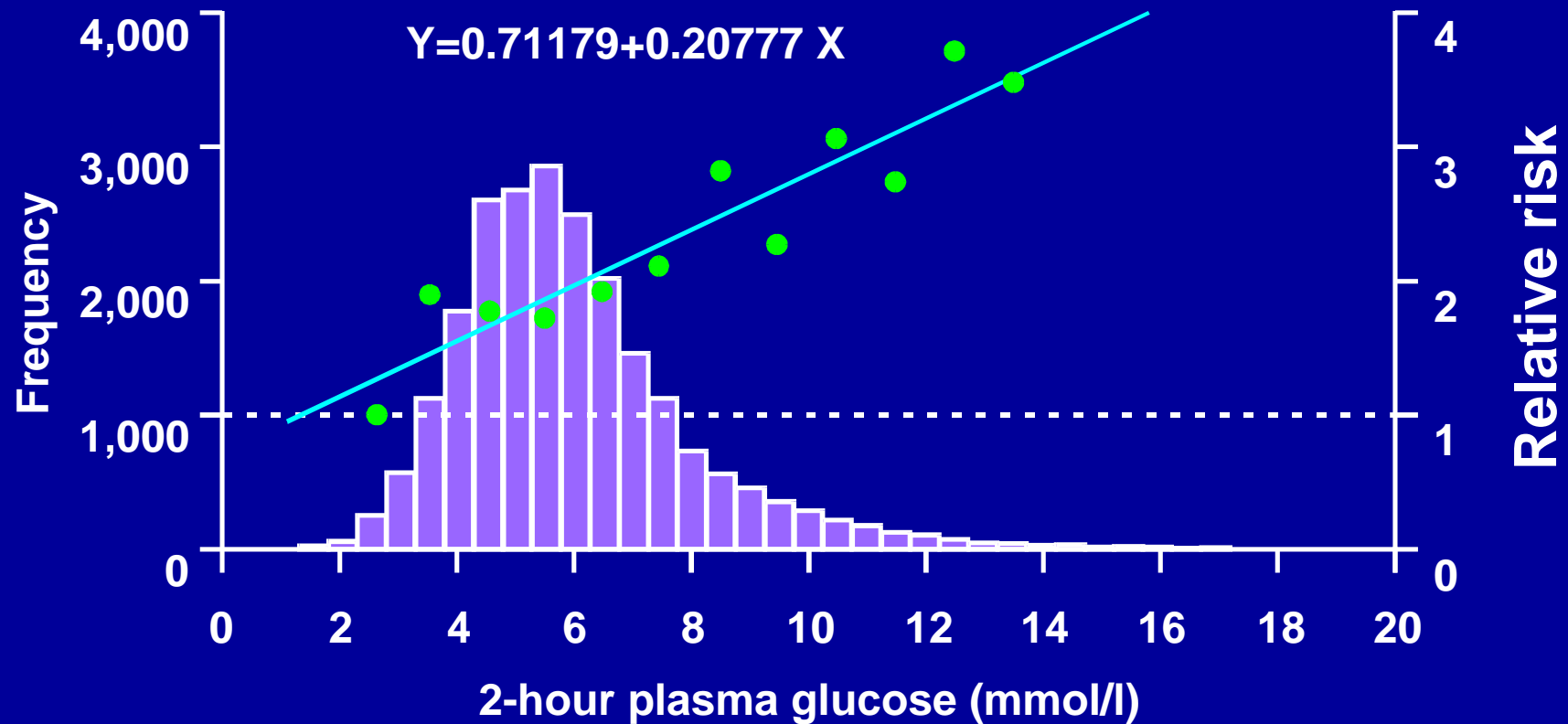
All-cause mortality is increased after fasting plasma glucose of 7.0 mmol/L: DECODE



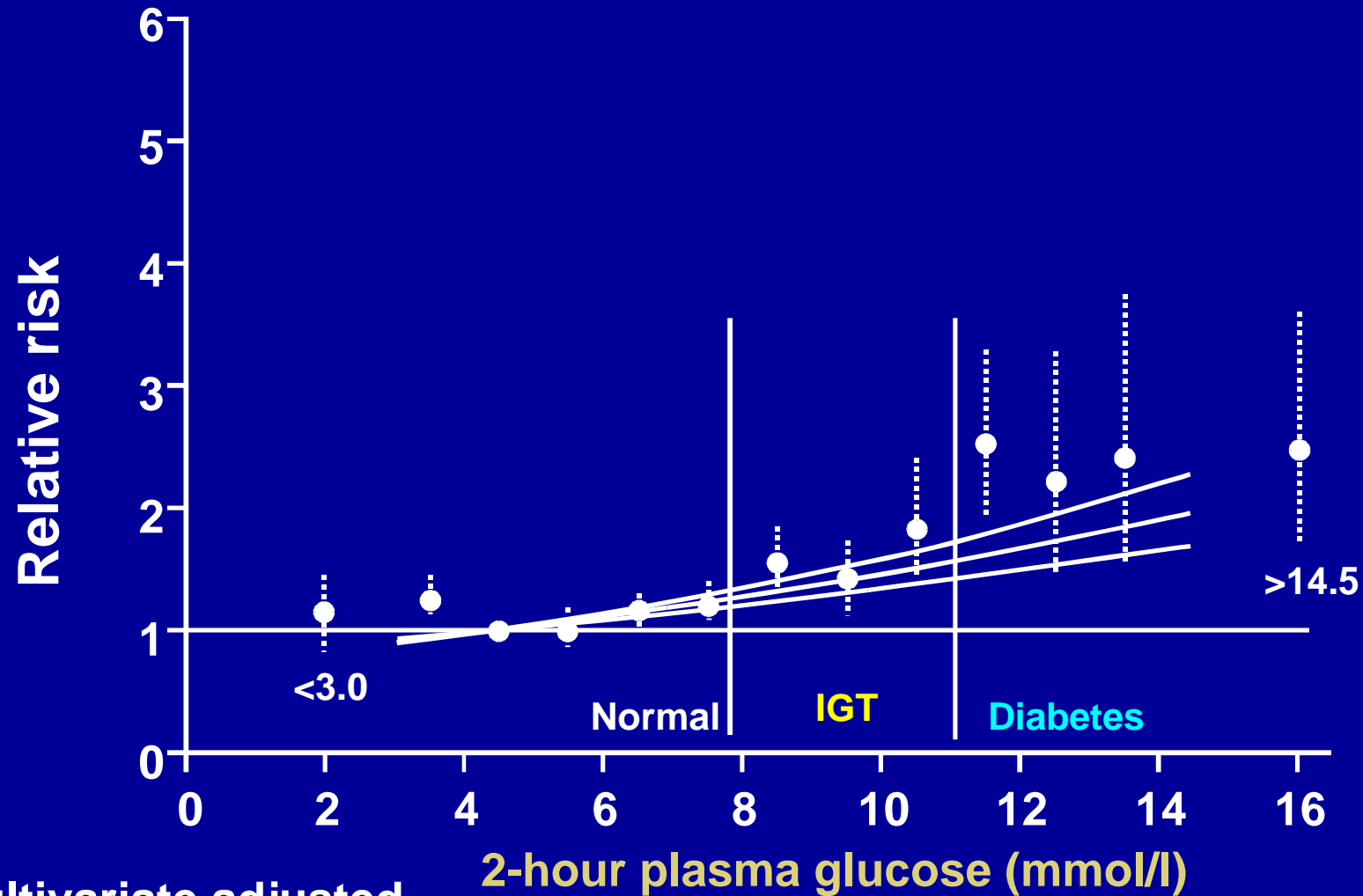
All-cause mortality increases linearly also in people with nondiabetic fasting glucose level (<7.0 mmol/L): DECODE



Relative risk of death from CVD is linear by 2- hr PG - DECODE

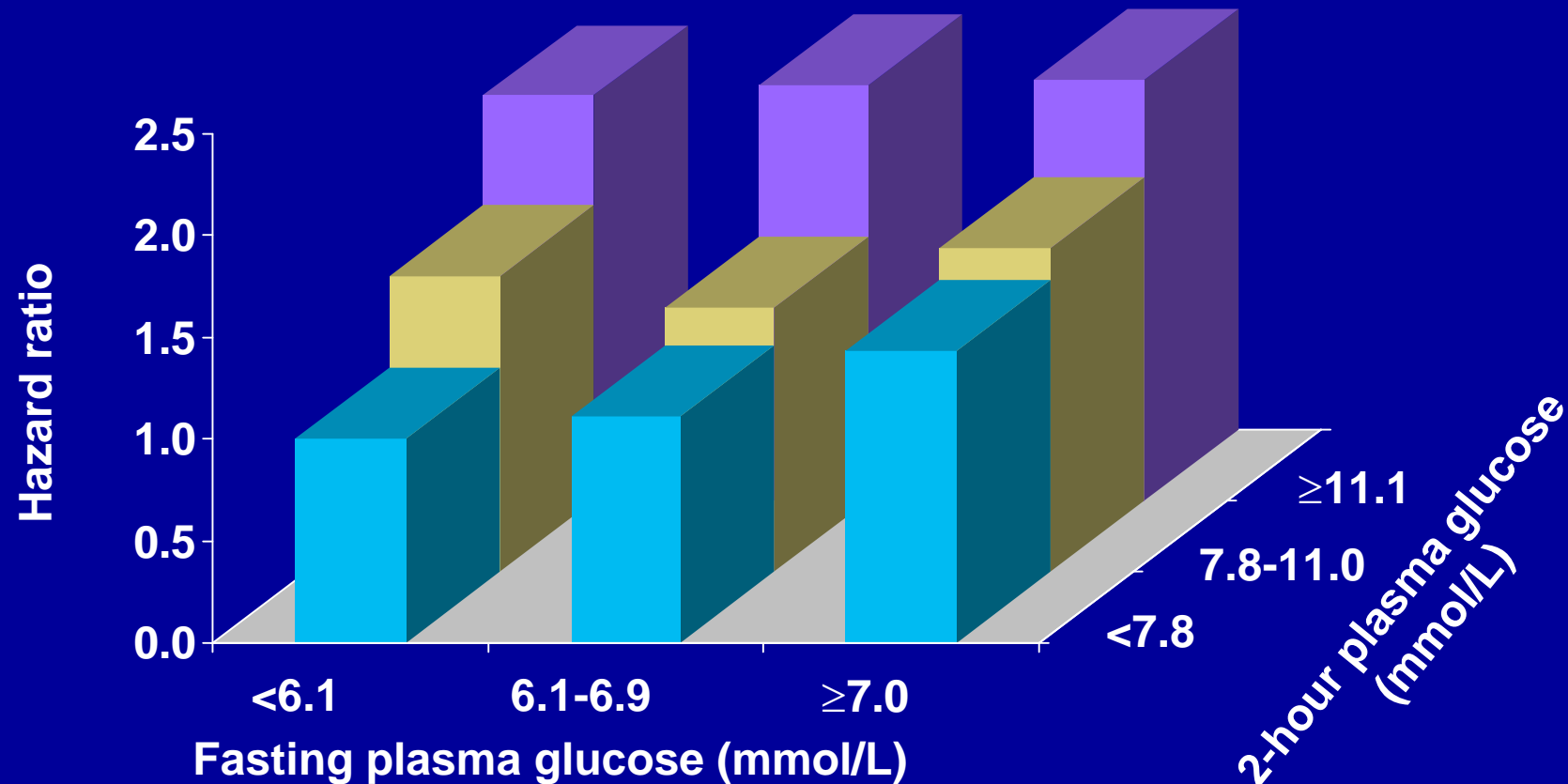


Relative risk of **non-CVD** mortality by 2-hr post-load glucose starts to increase already before the cut-point for diabetes - DECODE



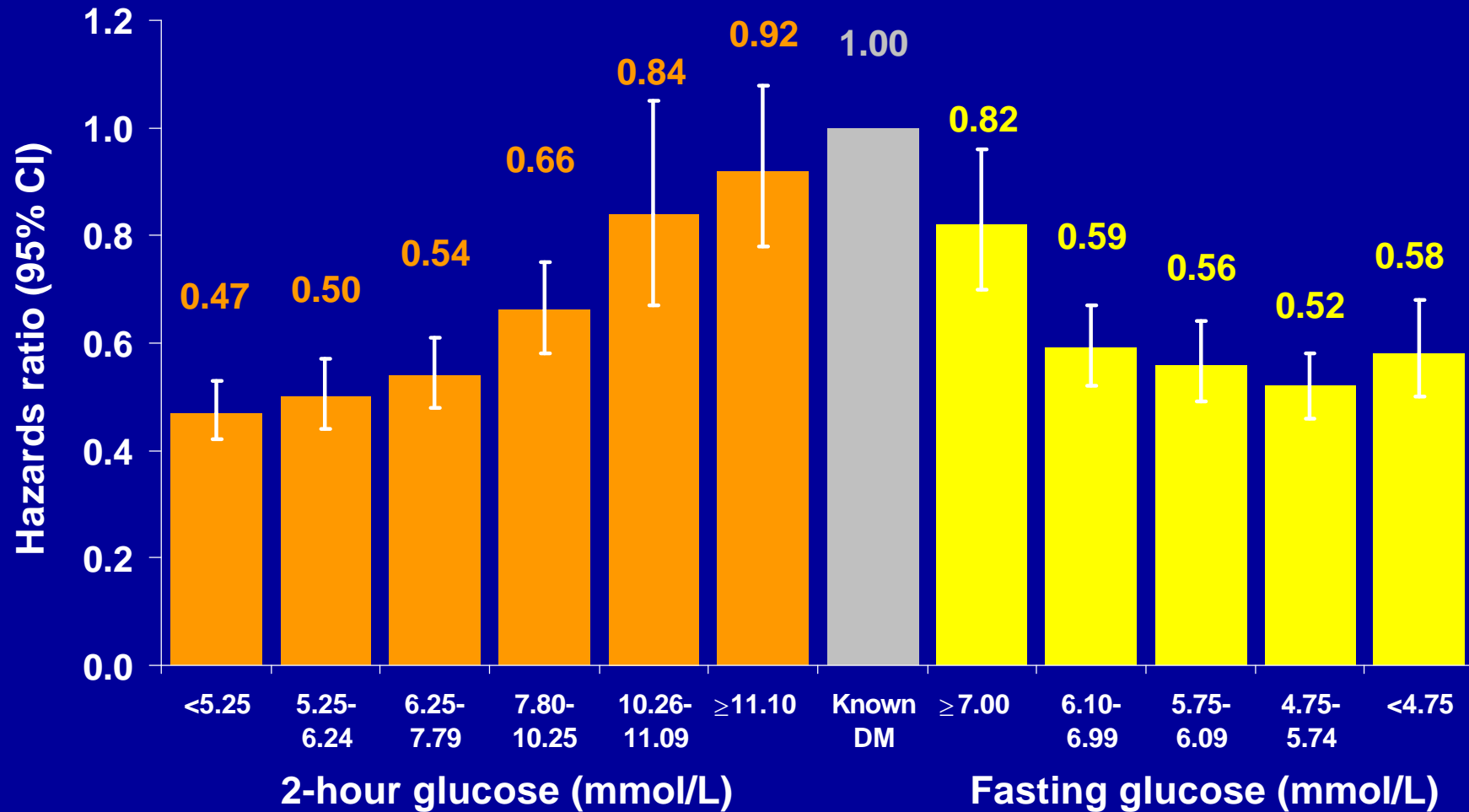
Multivariate adjusted

All-cause mortality AT ANY LEVEL OF FASTING GLUCOSE is primarily determined by 2-hour plasma glucose: DECODE



Adjusted for age, center, sex, cholesterol, BMI, SBP, smoking.
Adapted from DECODE Study Group. *Lancet*. 1999;354:617-621.

All-cause mortality in asymptomatic people with elevated 2-hour plasma glucose is almost as high as in patients treated for diabetes: DECODE



Relative risk (95% CI) of cause-specific mortality is significantly increased in subjects with IGT: DECODE

Mortality	RR, Multivariate Adjusted	RR, Adjusted Also for FPG
CVD	1.34 (1.14-1.57)	1.32 (1.12-1.56)
CHD	1.28 (1.02-1.59)	1.27 (1.03-1.58)
Stroke	1.26 (0.88-1.80)	1.21 0.84-1.74)
All-cause	1.40 (1.27-1.54)	1.37 (1.25-1.51)

Multivariate adjusted: for age, center, sex, cholesterol, BMI, BP, smoking.

Relative risk* for mortality in asymptomatic diabetic patients according to FPG becomes non-significant after adjusting for 2-hour glucose - DECODE

Mortality	FPG ≥7.0 mmol/l	FPG ≥7.0 mmol/l adjusted for 2-hour glucose
CVD	1.48 (1.15–1.91)	1.21 (0.88–1.65)
CHD	1.43 (1.02–2.02)	1.09 (0.71–1.67)
Stroke	1.93 (1.17–3.18)	1.65 (0.88–3.08)
All-cause	1.65 (1.43–1.19)	1.21 (1.01–1.44)

*Relative to FPG ≤6.0 mmol/l

Adjusted for age, center, sex, cholesterol, BMI, SBP, smoking

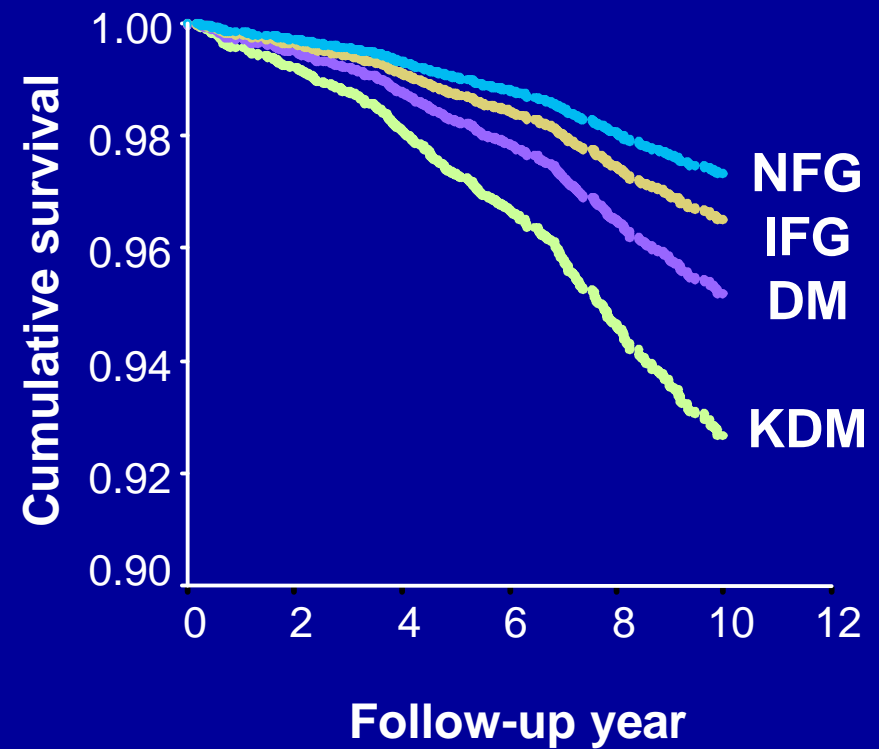
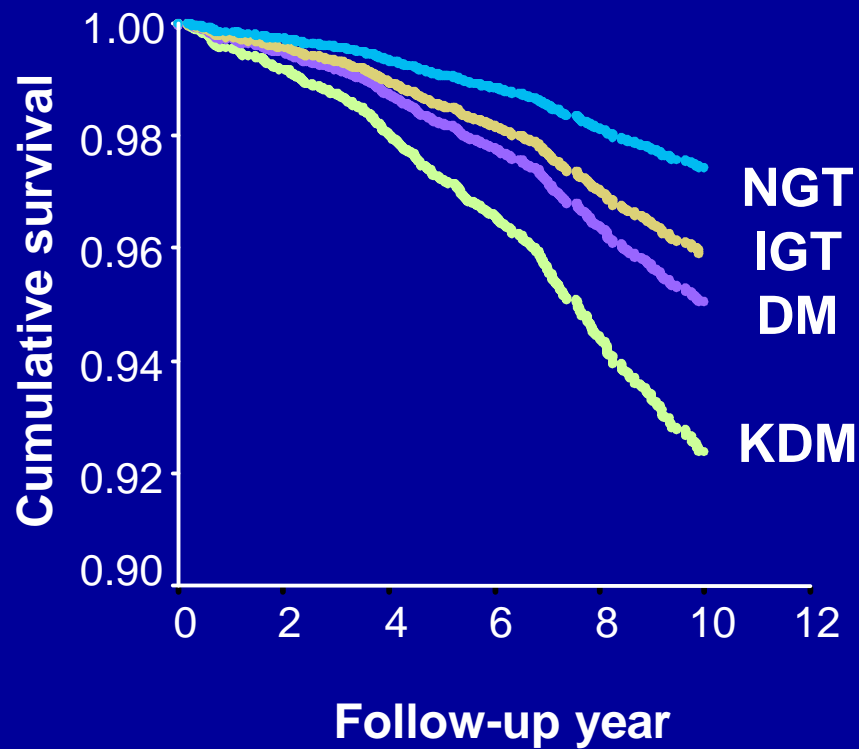
Relative risk* for mortality in diabetic patients according to 2-hour glucose is not modified by fasting glucose - DECODE

Mortality	2-hour glucose ≥ 11.1 mmol/l	2-hour glucose ≥ 11.1 mmol/l adjusted for FPG
CVD	1.55 (1.20–2.01)	1.40 (1.01–1.92)
CHD	1.64 (1.18–2.28)	1.56 (1.03–2.36)
Stroke	1.74 (1.01–2.99)	1.29 (0.66–2.54)
All-cause	1.92 (1.66–2.22)	1.73 (1.45–2.06)

*Relative to 2-hour glucose < 7.8 mmol/l

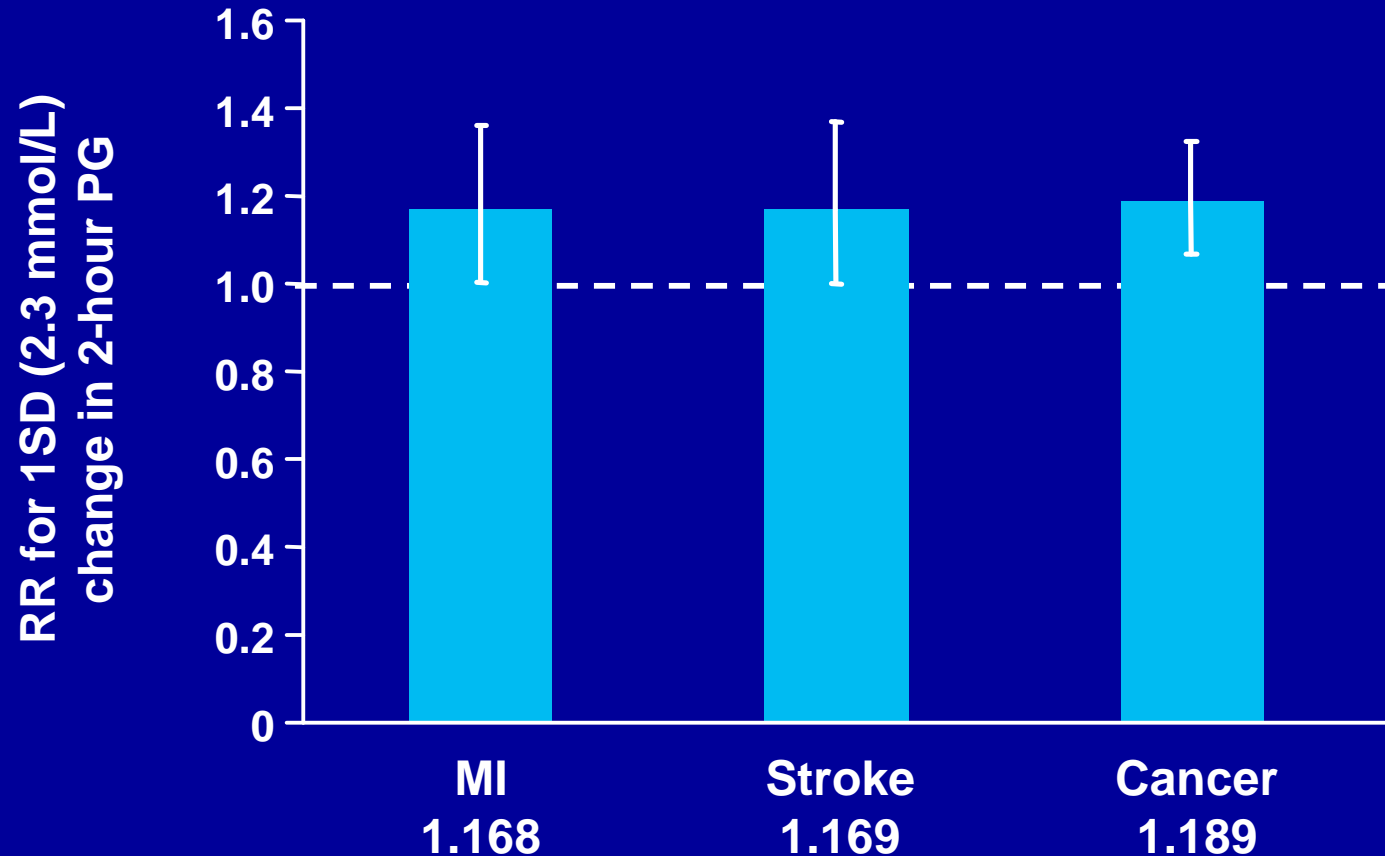
Adjusted for age, center, sex, cholesterol, BMI, SBP, smoking

CVD mortality in Finnish people aged 45 to 64 years at baseline by abnormalities in glucose regulation



NGT=normal glucose tolerance; NFG=normal fasting glucose; IGT=impaired glucose tolerance; IFG=impaired fasting glucose; DM=diabetes mellitus; KDM=previously diagnosed diabetes.

2-hour post-challenge plasma glucose is a significant risk factor for the incidence of MI, stroke, and cancer



Adjusted for age, center, sex, cholesterol, BMI, SBP, smoking.
Source: Finnish DECODE centers.

Relative hazards* of all-cause mortality corresponding to a 2 SD increase in **FPG, 2-hr PG and HbA1c - all simultaneously in the same model - DECODE**

Parameter	Hazards ratio* (95% CI)	P – value**
Fasting PG	0.86 (0.64 - 1.16)	> 0.10
HbA1c	1.23 (0.95 - 1.58)	> 0.10
2-hr PG	1.35 (1.01 - 1.80)	< 0.05

* Adjusted for age, center, sex, cholesterol, BMI, SBP, smoking

** Compared with models with and without the parameter of interest

2h-postchallenge glucose levels increase the risk of CVD events - independently of standard CVD risk factors, fasting glucose, or HbA_{1c} - Framingham Offspring Study:

	<u>Adjusted for CVD risk factors</u>			FG+PPG	FG+HbA _{1c}	PPG+HbA _{1c}
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
FPG (per 0.7 mmol/l increase)						
Relative Risk	1.088**			0.868*	1.024	
95% CI	1.02-1.16			0.76-0.998	0.92-1.14	
2hPG (per 1 SD, 2.1 mmol/l increase)						
Relative Risk		1.18***		1.42***		1.23**
95% CI		1.10-1.27		1.17-1.72		1.07-1.43
HbA_{1c} (per 0.71% increase)						
Relative Risk			1.151*		1.115	0.929
95% CI			1.02-1.30		0.92-1.35	0.77-1.13
c-statistic	0.752	0.749	0.740	0.741	0.745	0.741

* P<.05; ** P<.01; *** P<.001

Meigs JB, et al. Diabetes Care 2002;25:1845-1850.

Summary and conclusions

- **Post-challenge (-prandial) hyperglycaemia increases strongly with age, whereas fasting hyperglycaemia does not.**
- **More than half of people with asymptomatic diabetes remain undetected if post-challenge glucose measurement is not done.**
- **The effect of post-load glucose on mortality starts to increase at a level well below the cut-point for diabetes, 11.1**
- **Screening for asymptomatic hyperglycemia may be important, especially in groups known to be at high risk for diabetes, in order to identify individuals at risk of premature death**