

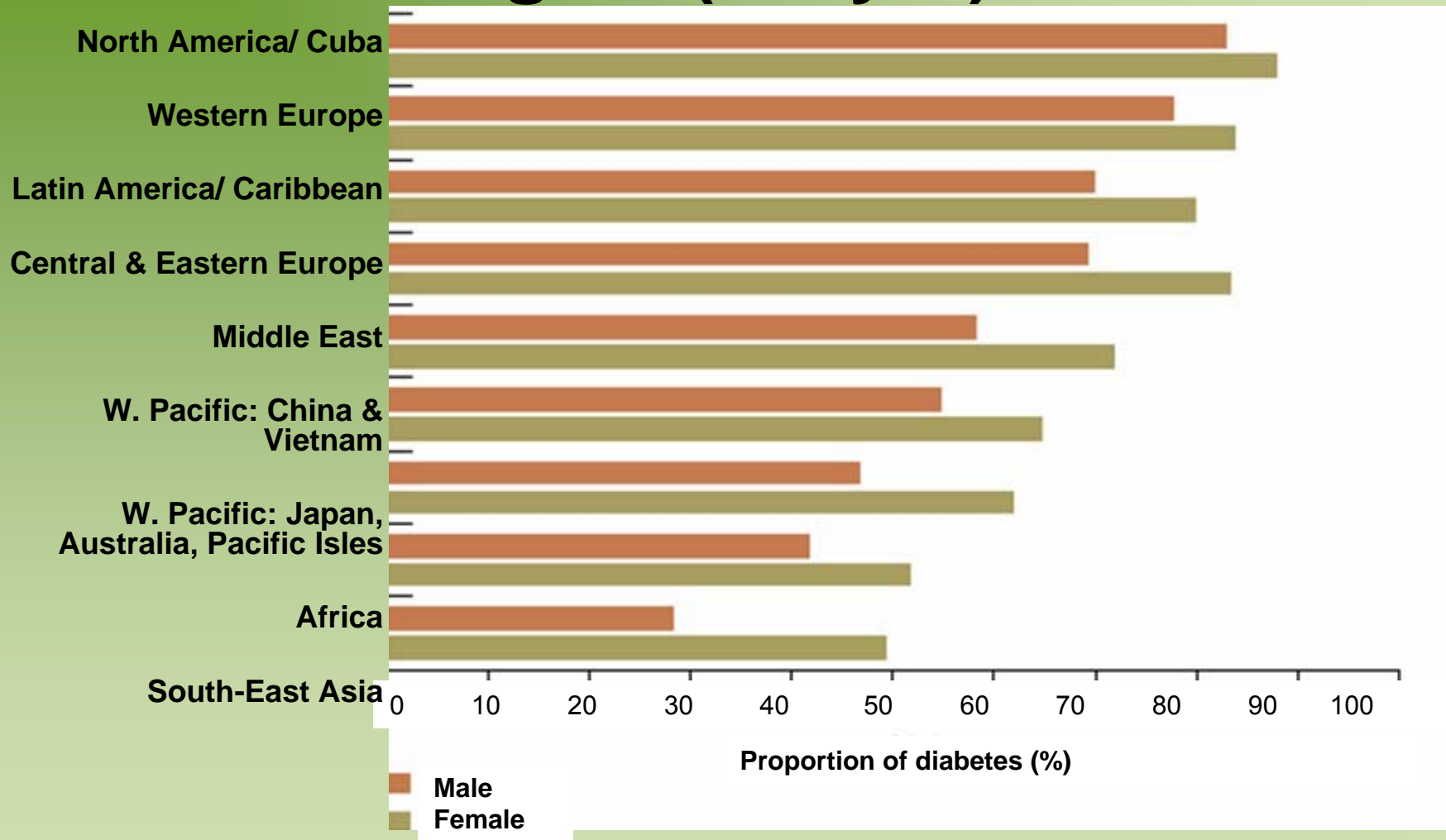
**Pre diabetes- The Hidden
Health time bomb
HbA1C as a diagnostic tool**

Dr Mark Edwards
Clinical Lead, Diabeticare
The Hillingdon Hospital

Diabetes NSF Standards to be Reached by 2013

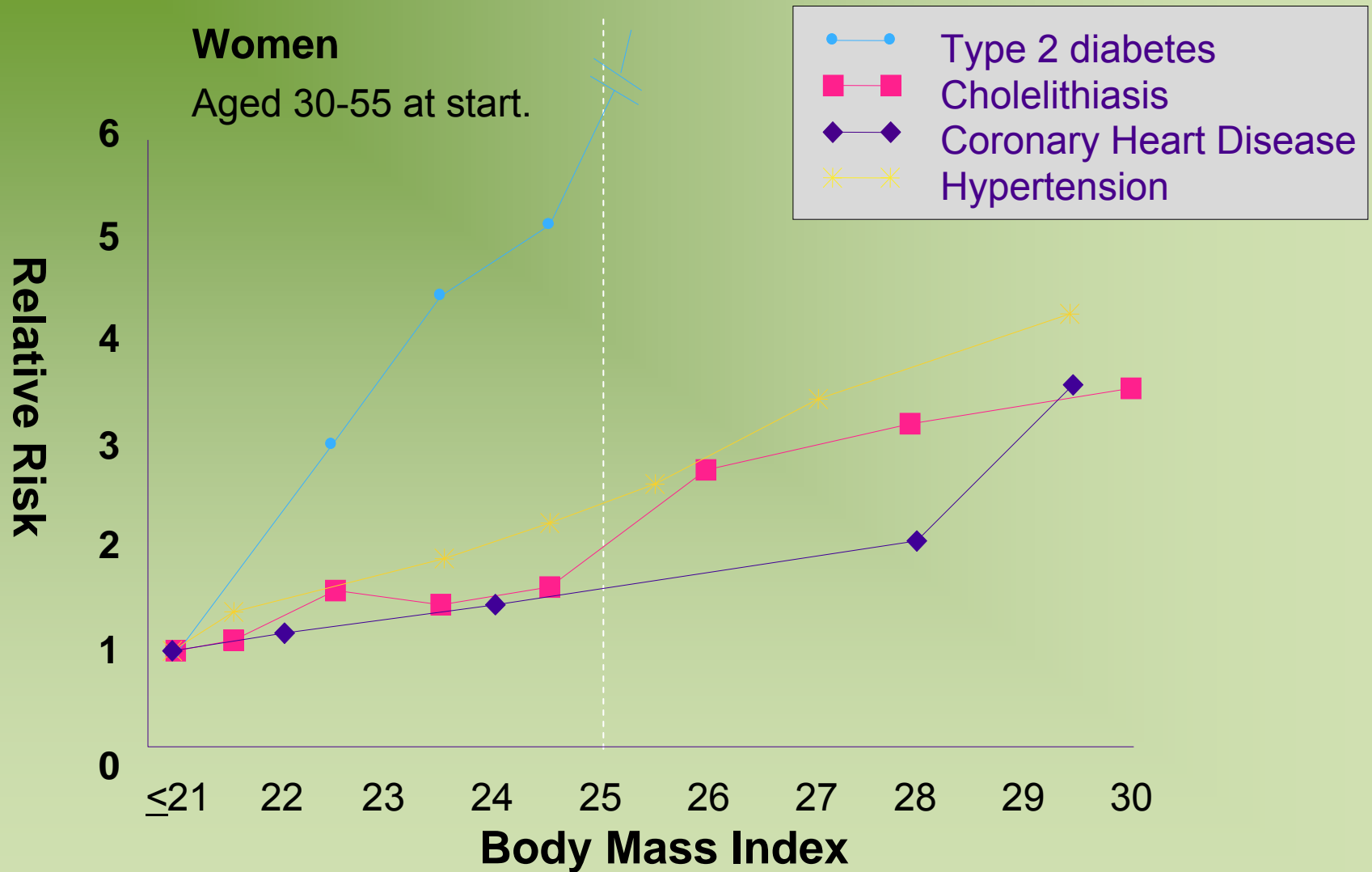
- **Prevent risk of developing T2D**
- **Identify those with diabetes**
- Patient partnership in decision-making
- High quality clinical care of adults & children
- Effective treatment of diabetic emergencies
- Effective treatment of diabetes during hospital admission
- Support pregnant women with diabetes
- Detection and effective tx of complications

% of DM attributable to weight gain (30+yrs)

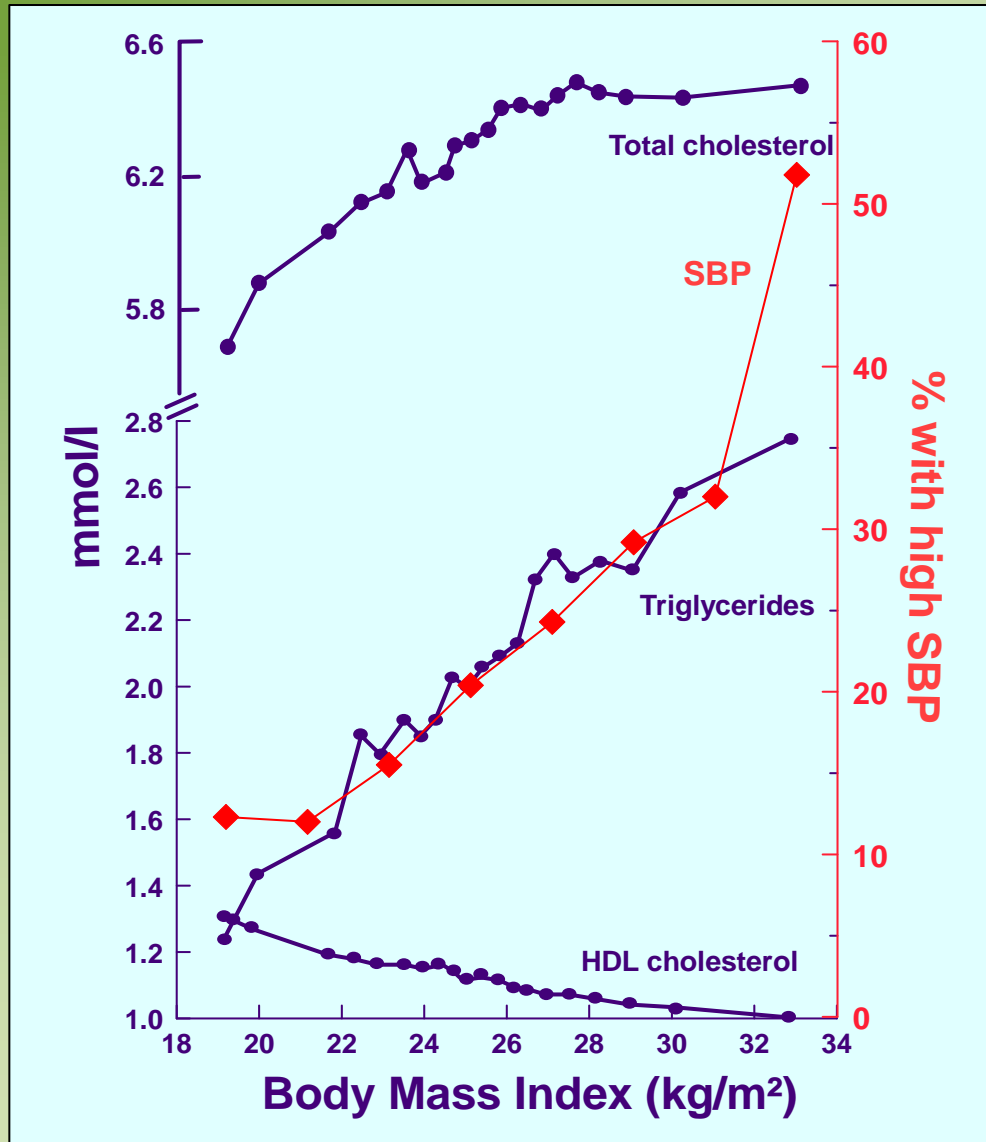


*International Diabetes Federation 2003;
International Obesity Task Force, 2003*

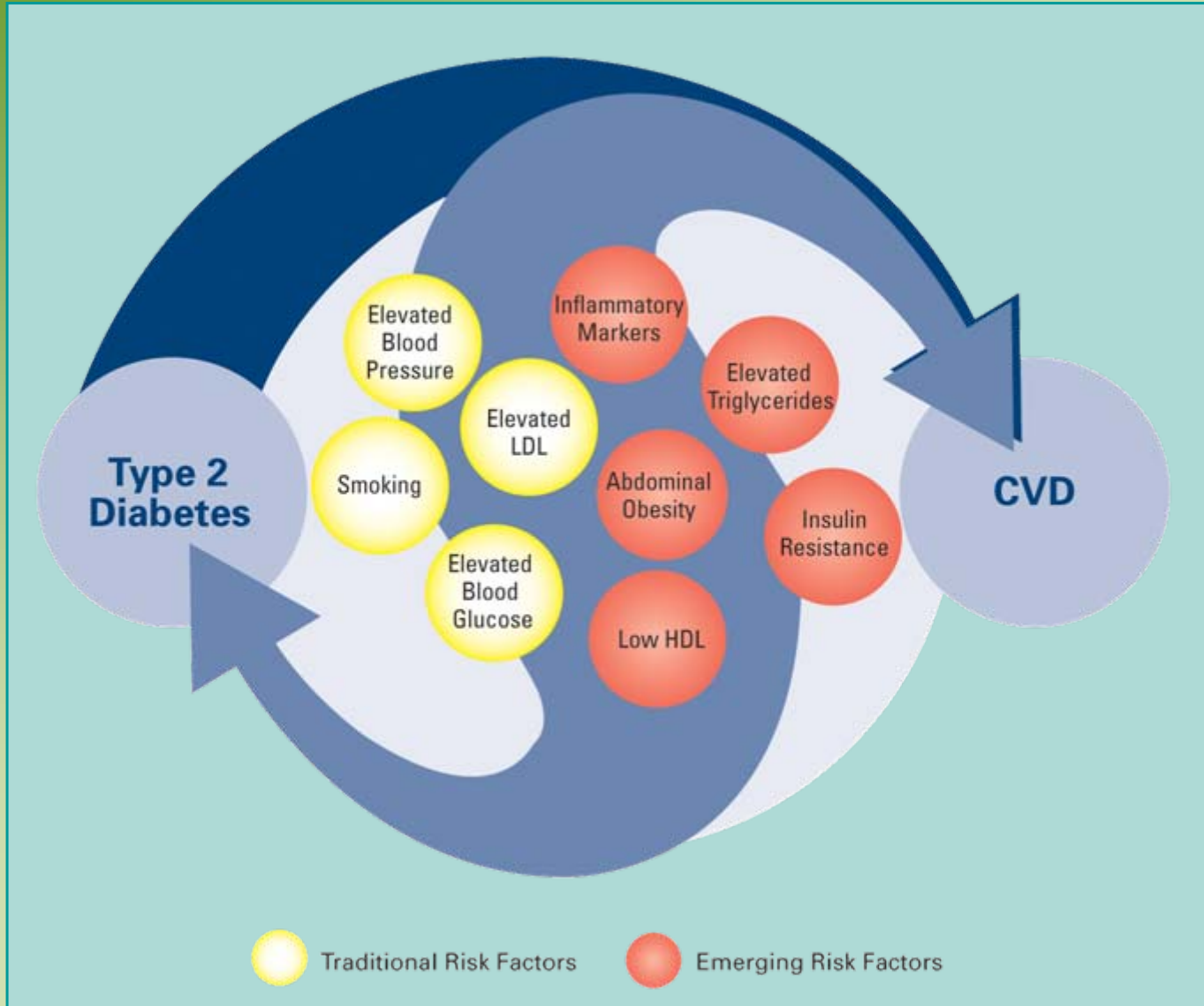
BMI in relation to morbidity over 18 years



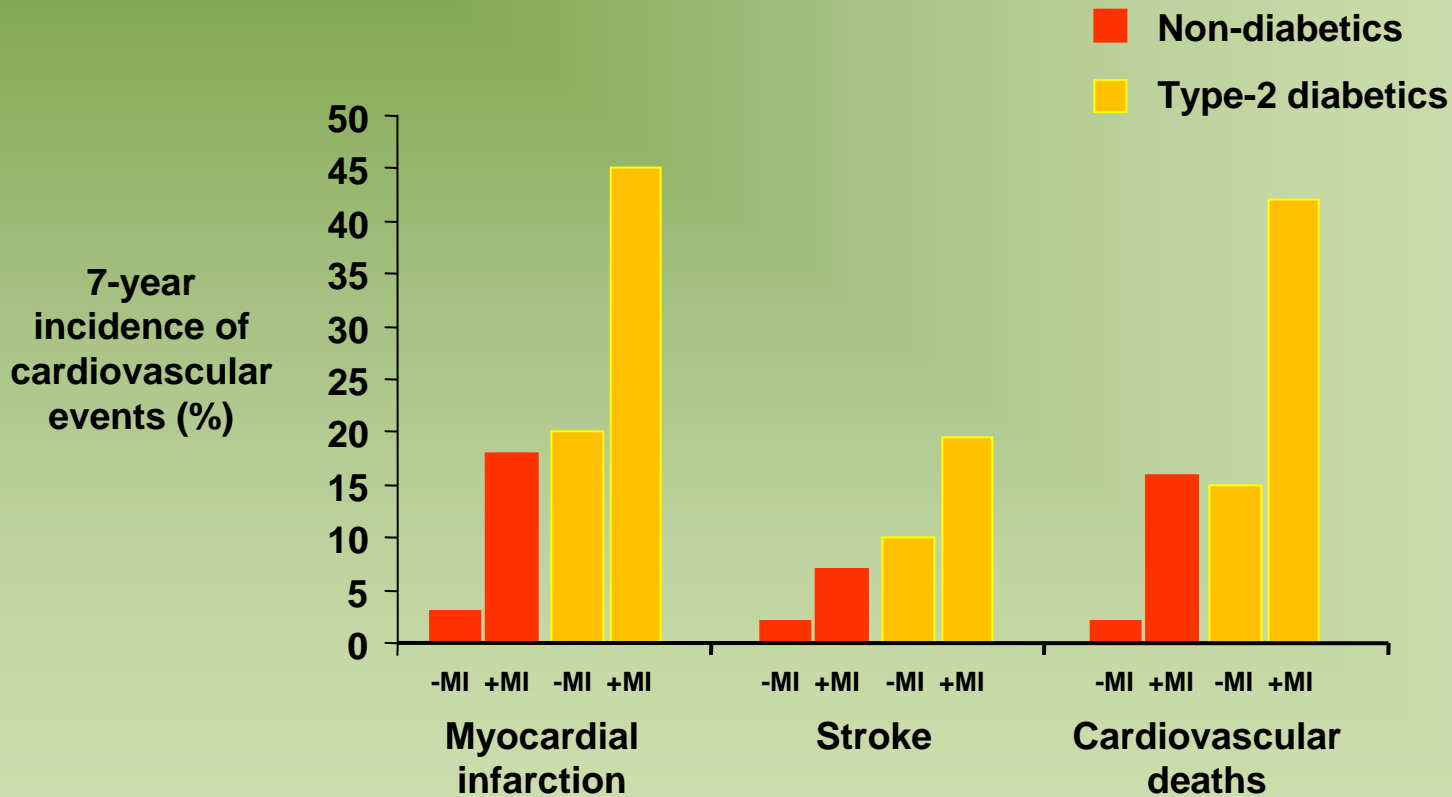
British Regional Heart Study.



Clustering of Cardiometabolic Risk Factors creates a high risk of suffering a cardiovascular event

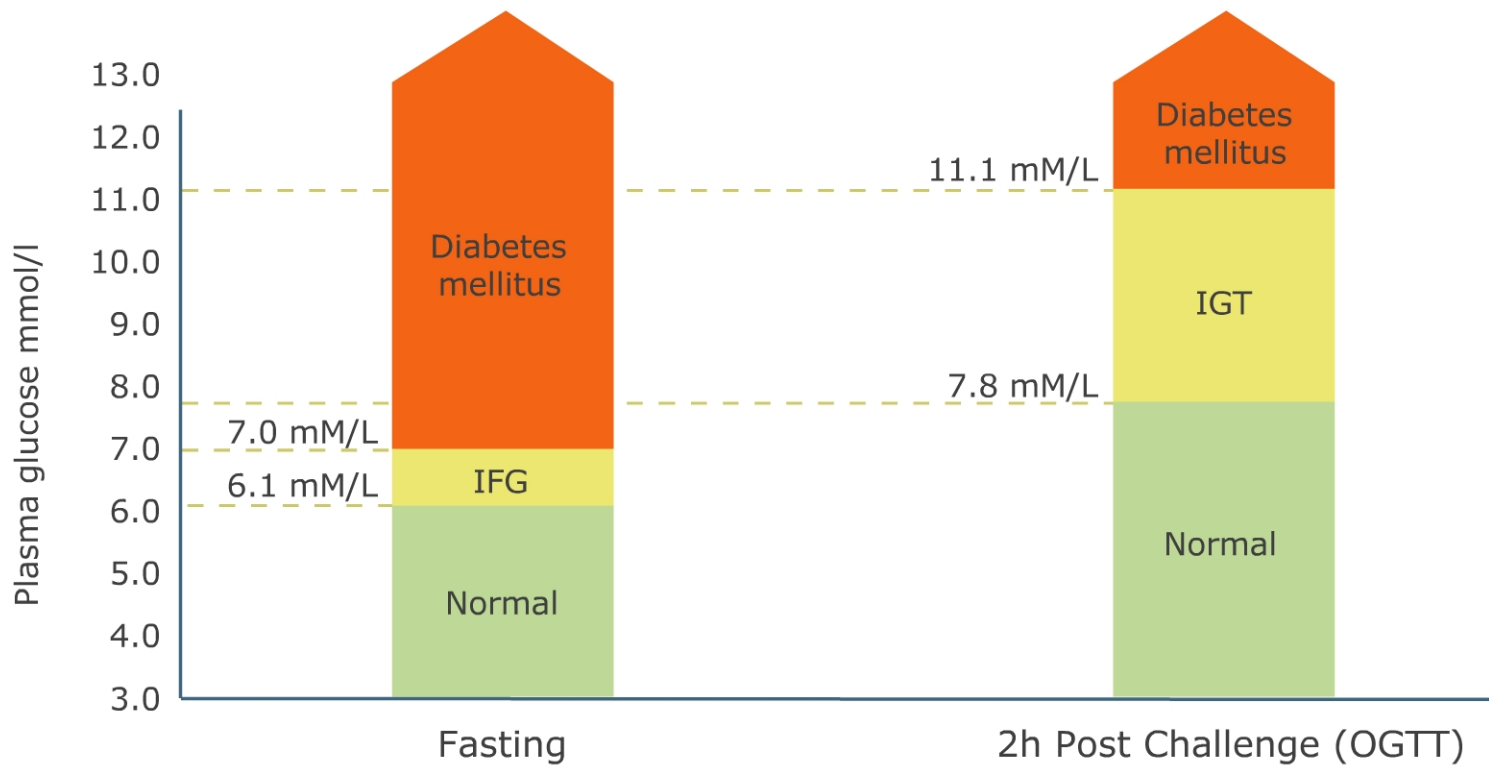


High risk of cardiovascular events in type-2 diabetes

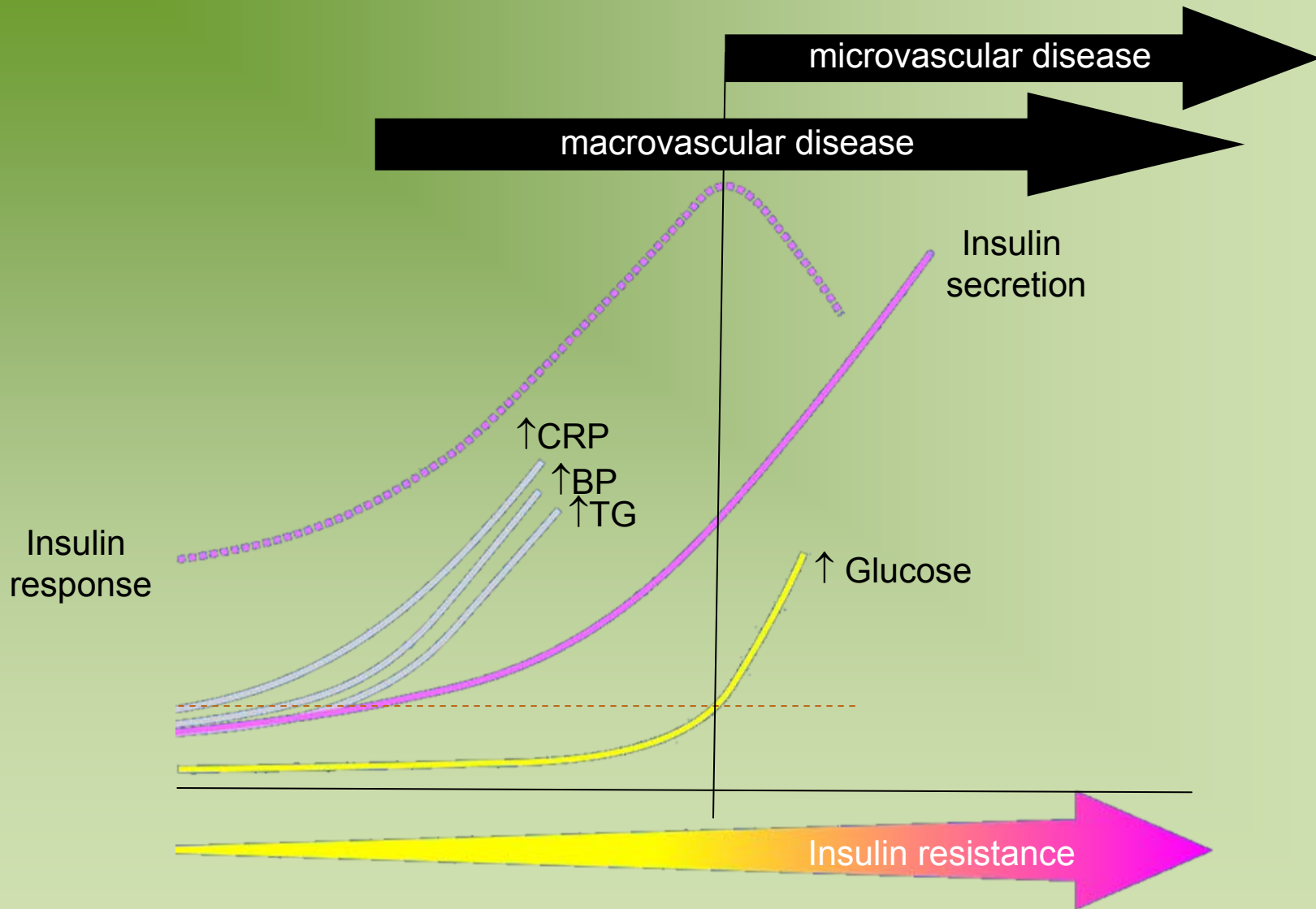


Prevalence - IGT and IFG

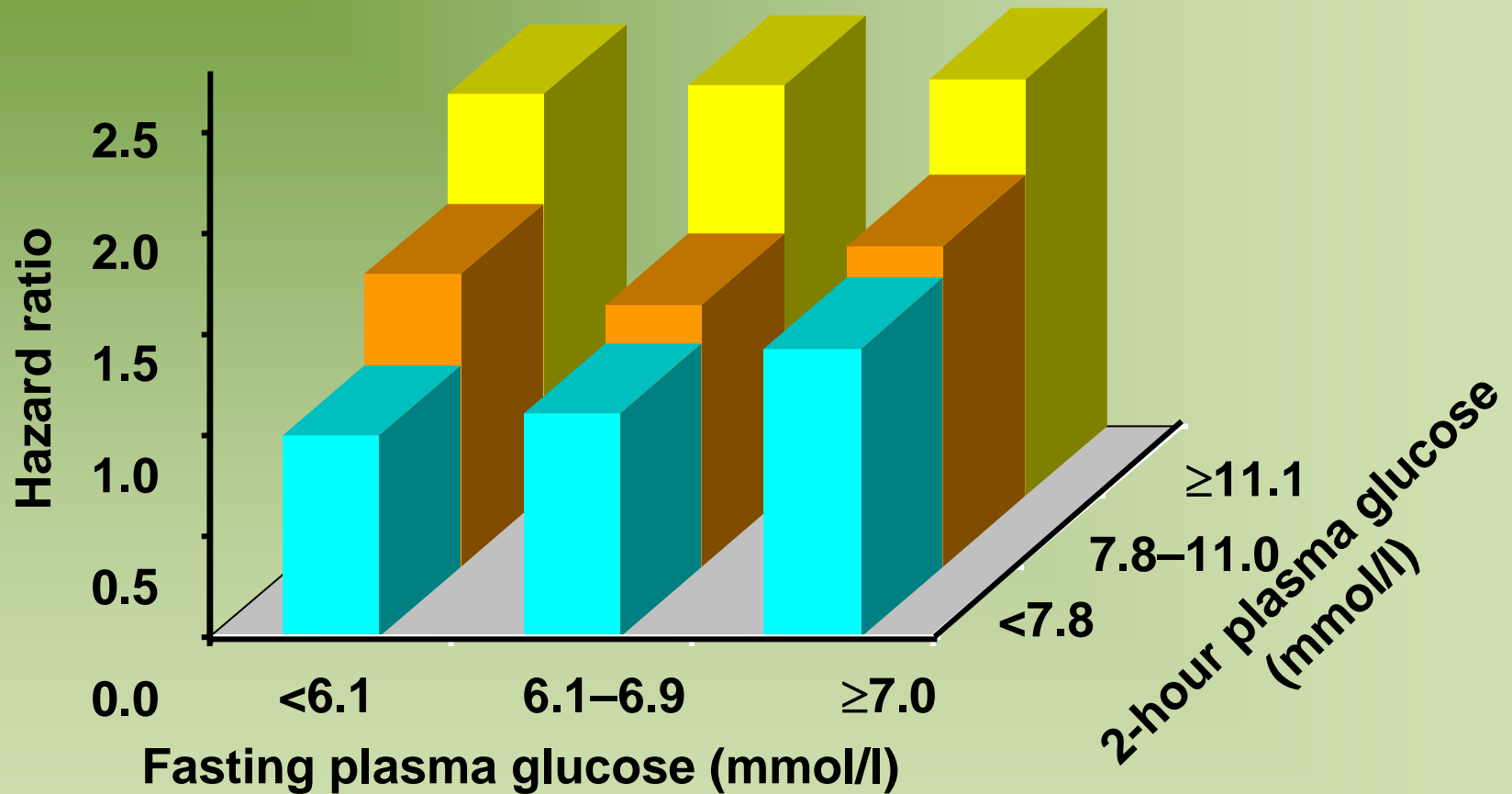
Overall prevalence rates: IGT 10% and IFG 5%



Development of Type 2 diabetes



DECODE: Relative risk for 'all-cause' mortality in subjects not known to have diabetes



Adjusted for age, centre, sex, cholesterol, BMI, SBP and smoking

Prevention/ Delay of Type 2 Diabetes

- 5 well-designed randomized-controlled trials:
 1. Finnish Study, 2001
 2. Diabetes Prevention Program (DPP), 2002
 3. Da Qing Study, 1997
 4. STOP-NIDDM trial, 2002
 5. XENical in the prevention of Diabetes in Obese Subjects (XENDOS) Study, 2004

The Da Qing Study

- Men & women from Da Qing city screened with OGTT
- Those with IGT randomized to:
 - Control
 - Intervention 1: diet only [bi-annual review]
 - Intervention 2: exercise only [bi-annual review]
 - Intervention 3: diet plus exercise [bi-annual review]
- Result: after average of 6 yrs follow-up:
 - Diet alone 31% rel reduction in developing diabetes
 - Exercise alone 46% rel reduction in developing diabetes
 - Diet + exercise 42% rel reduction in developing diabetes

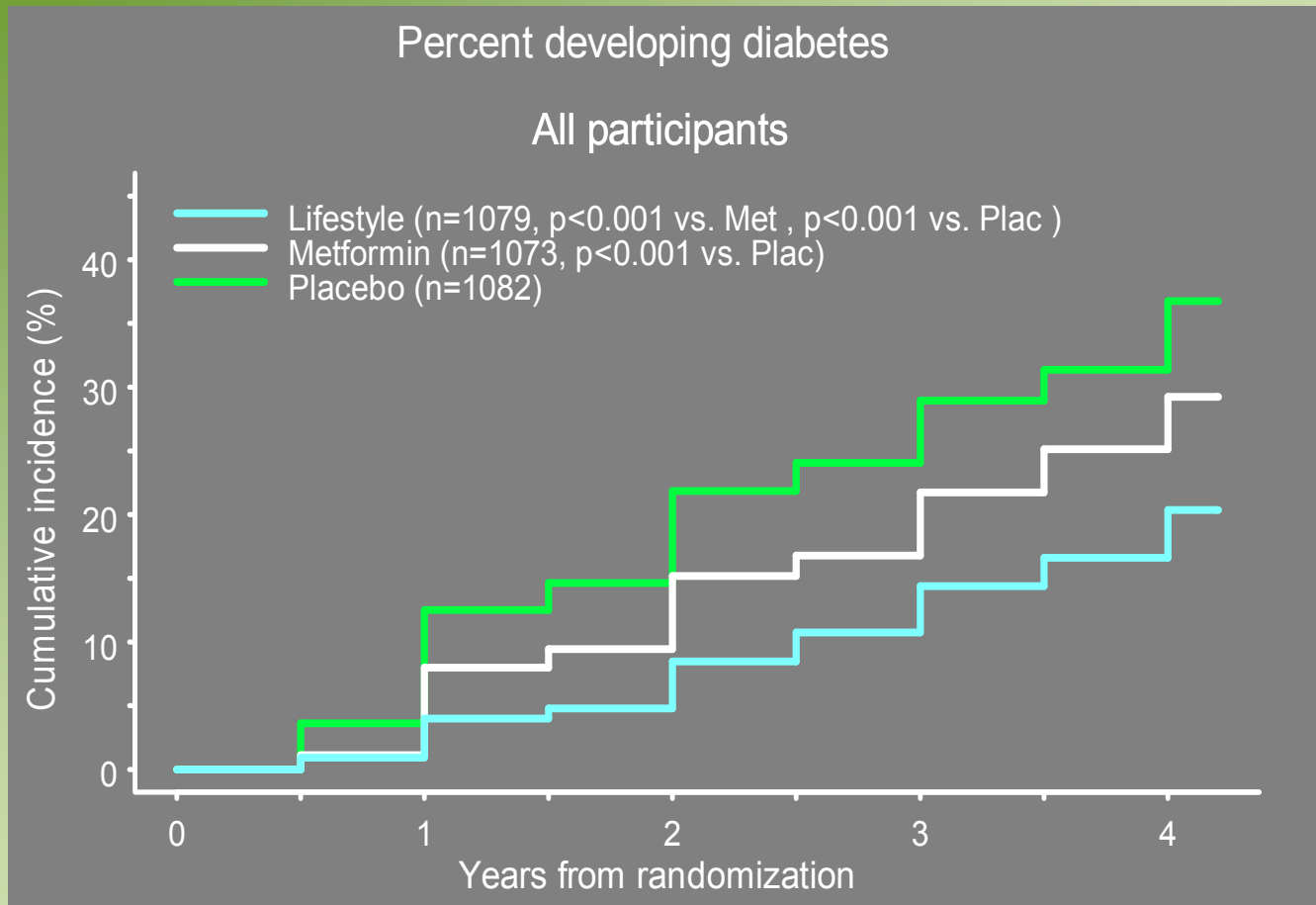
The Finnish Study (3.2 years)

- Middle-aged obese subjects with IGT
 - ❑ Control = brief diet + exercise counselling
 - ❑ Intervention = intensive individual instruction on
 - Diet/physical activity 30 minutes walking daily
 - ❑ 58% relative reduction in incidence of diabetes
 - ❑ Weight loss averaged 9.2, 7.7 and 4.6 lb at yrs 1,2&5
 - ❑ Direct relationship between adherence to lifestyle intervention and reduced incidence of diabetes

The Diabetes Prevention Program (DPP)

- Slightly younger subjects enrolled, and mostly obese
- 45% of subjects from minority groups
- 20% over 60 yrs
 - ❑ Intervention gp 1 – “Lifestyle group” (exercise + low-fat ± low cal diet)
 - ❑ Intervention gp 2 – metformin + standard diet & exercise
 - ❑ Intervention gp 3 – placebo + standard diet & exercise
- Result: after average of 2.8 yrs follow-up
 - ❑ 58% relative reduction in incidence of diabetes in Lifestyle group
 - ❑ 31% relative reduction in metformin group compared to control
 - ❑ 50% of lifestyle group achieved $\geq 7\%$ weight loss and
 - ❑ 74% maintained at least 150 min/week of moderately intense activity

DPP: incidence of diabetes per treatment group



- Placebo (n=1082)
- Metformin (n=1073, $p < 0.001$ vs. Placebo)
- Lifestyle (n=1079, $p < 0.001$ vs. Metformin, $p < 0.001$ vs. Placebo)

Risk reduction
31% by metformin
58% by lifestyle

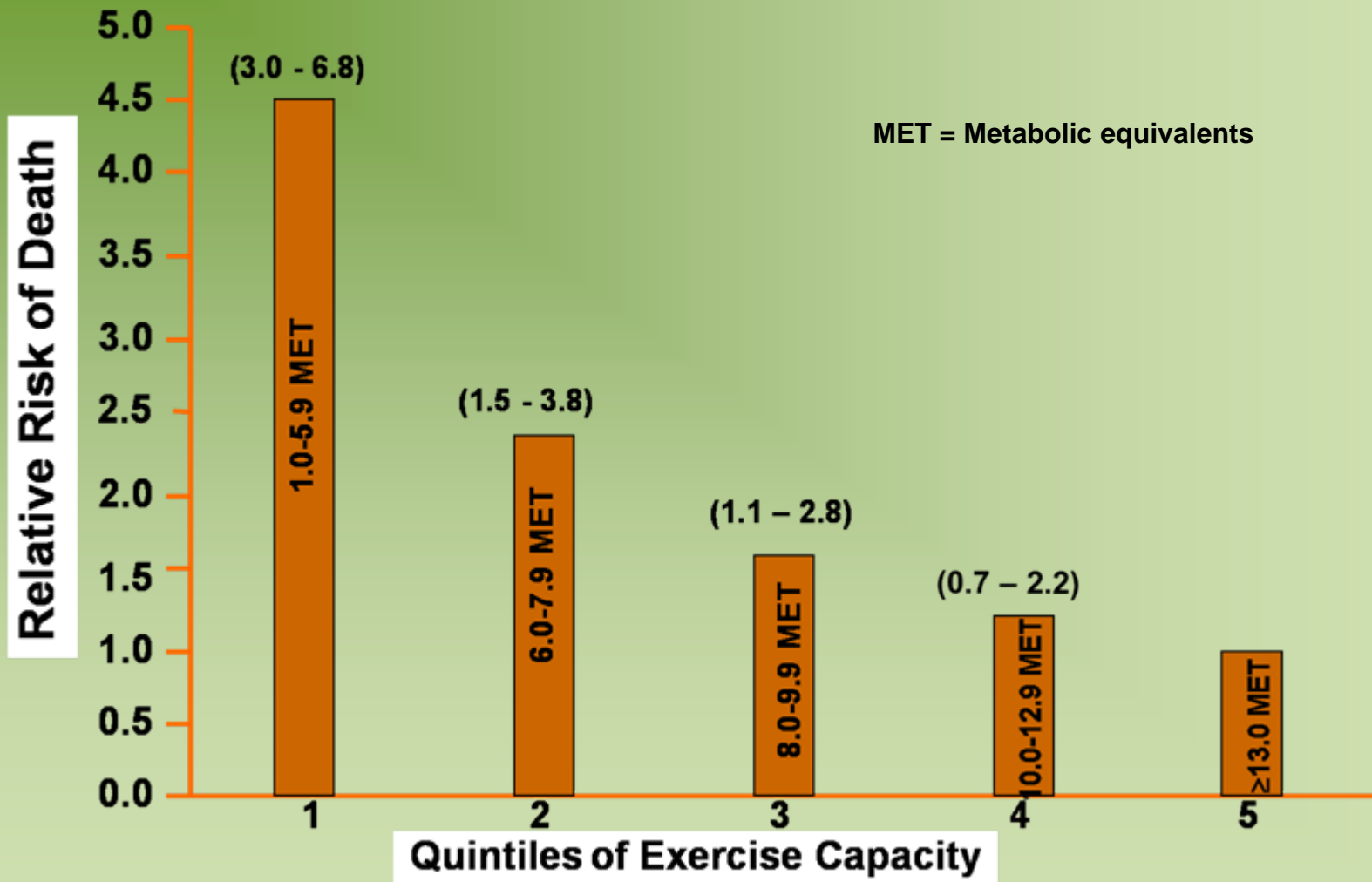
Is diet more important than exercise

- Weight loss potentially identical (calories)
- Diet may deliver calorie reduction more readily than exercise (therefore seen as better/easier) but real questions are:
- Which is easier to deliver/sustain in the real world?
- Are there additional benefits of either intervention over and above weight loss?

Diet

- Undoubtedly effective (if you do it !!!)
- Very difficult with pressures and temptations of our modern world
- Unsustainable for most
- Is seen as a negative/excluding/pejorative activity
- Outside a structured/supportive programme will have real difficulties in delivering sustained health care benefit
- Change in food landscape requires political will to take on big business, which seems unlikely !!!
- Diet comes with many mixed healthcare messages

Benefit of physical activity on all cause mortality: age-adjusted relative risk reductions



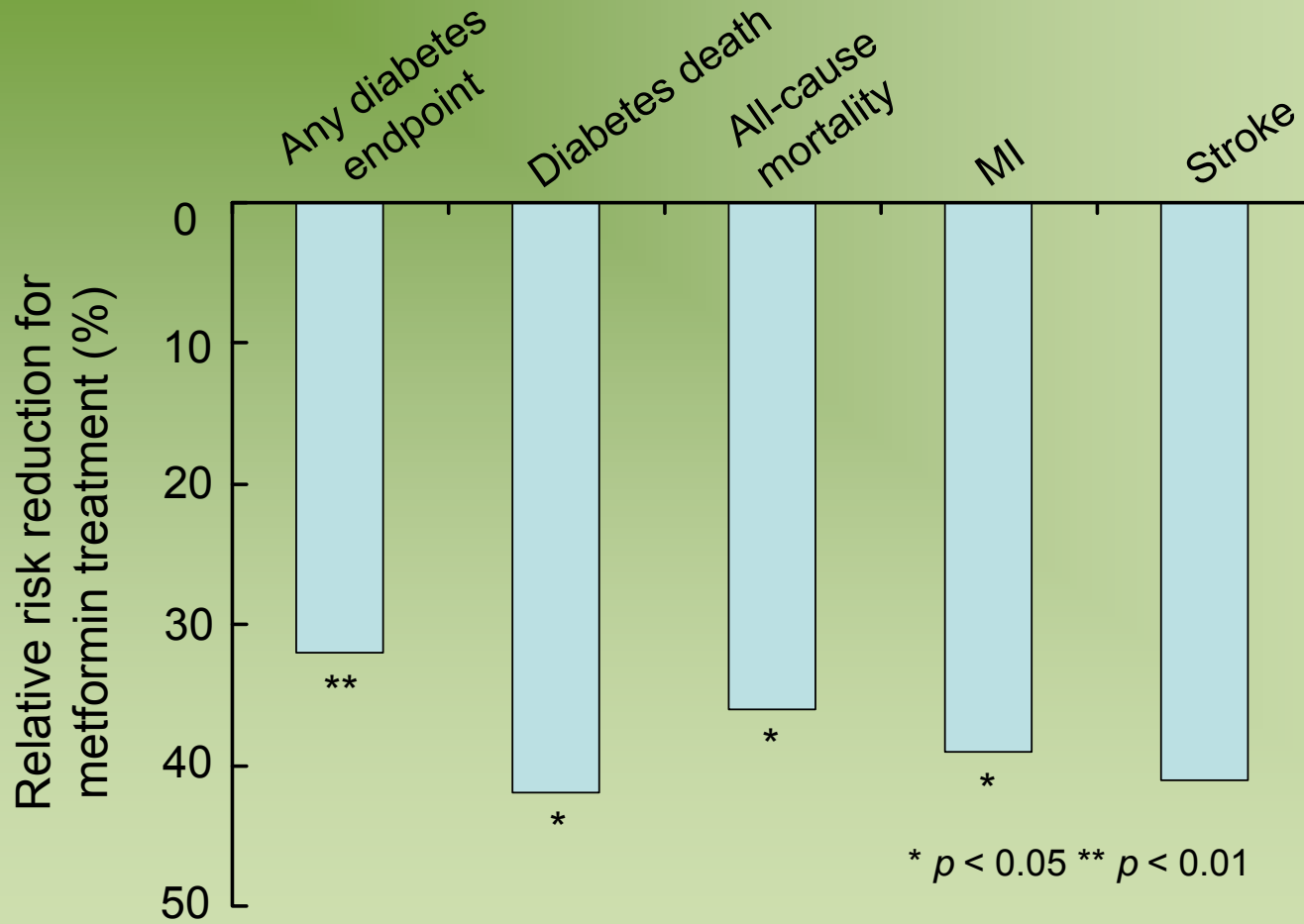
In the attribution of importance: diet vs exercise

- Diet is a negative/pejorative process of exclusion and is for most unsustainable
- Physical exercise is a positive affirming action
- Can and should be an extension of daily activity : fits in
- Additional health benefits clear
- Message is consistent and accepted
- Delivers on multiple political drivers
- Only tenable population solution

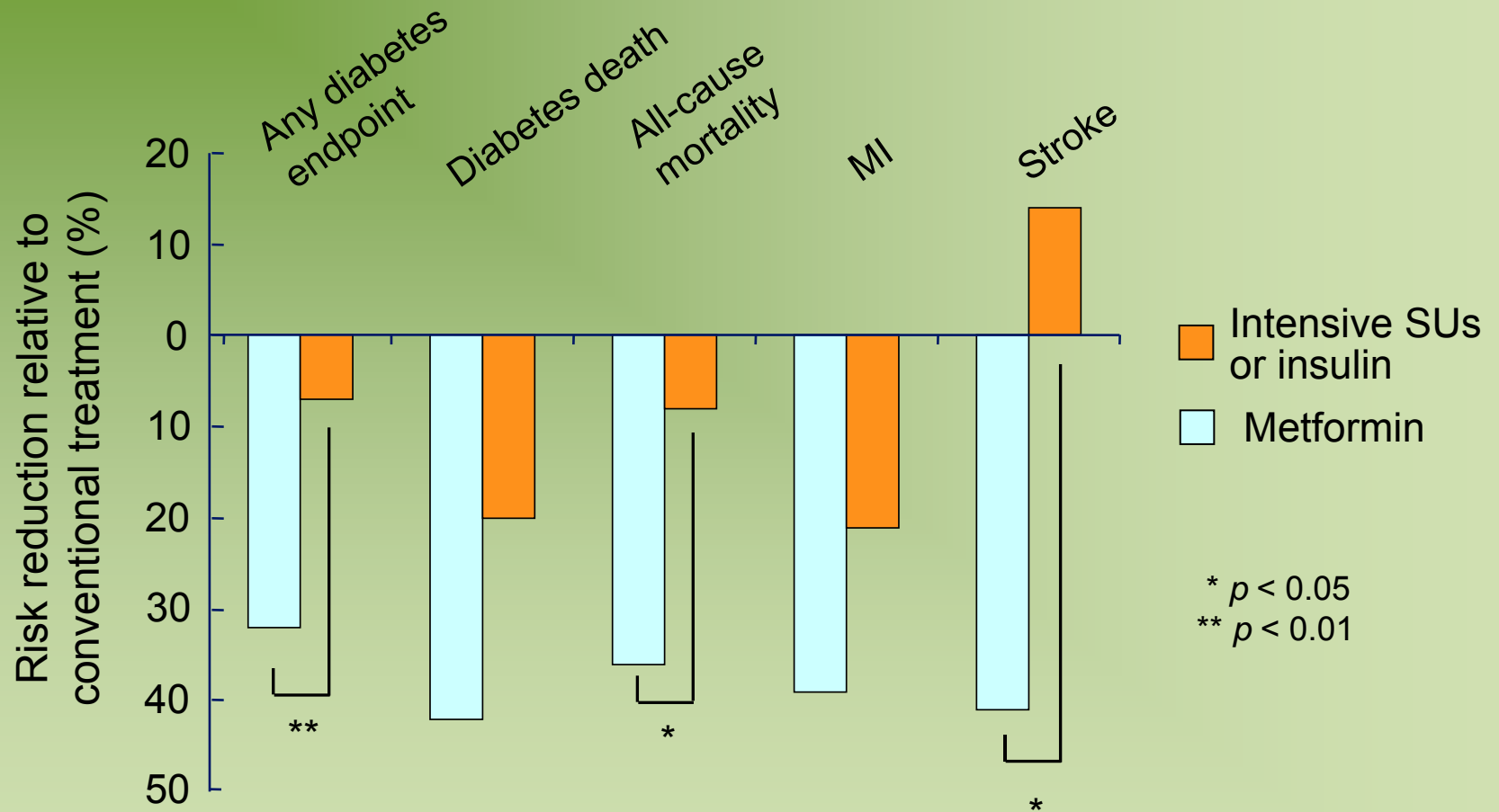
Significance of weight loss

- 10 % reduction body weight
 - 60% reduction in intra-abdominal fat
 - 10 mmHg reduction systolic BP
 - 1% reduction in HbA1c
- 7% weight reduction in DPP reduced incidence of diabetes by 58%
- Metabolically significant

UKPDS 34: relative risk reduction with metformin vs conventional treatment

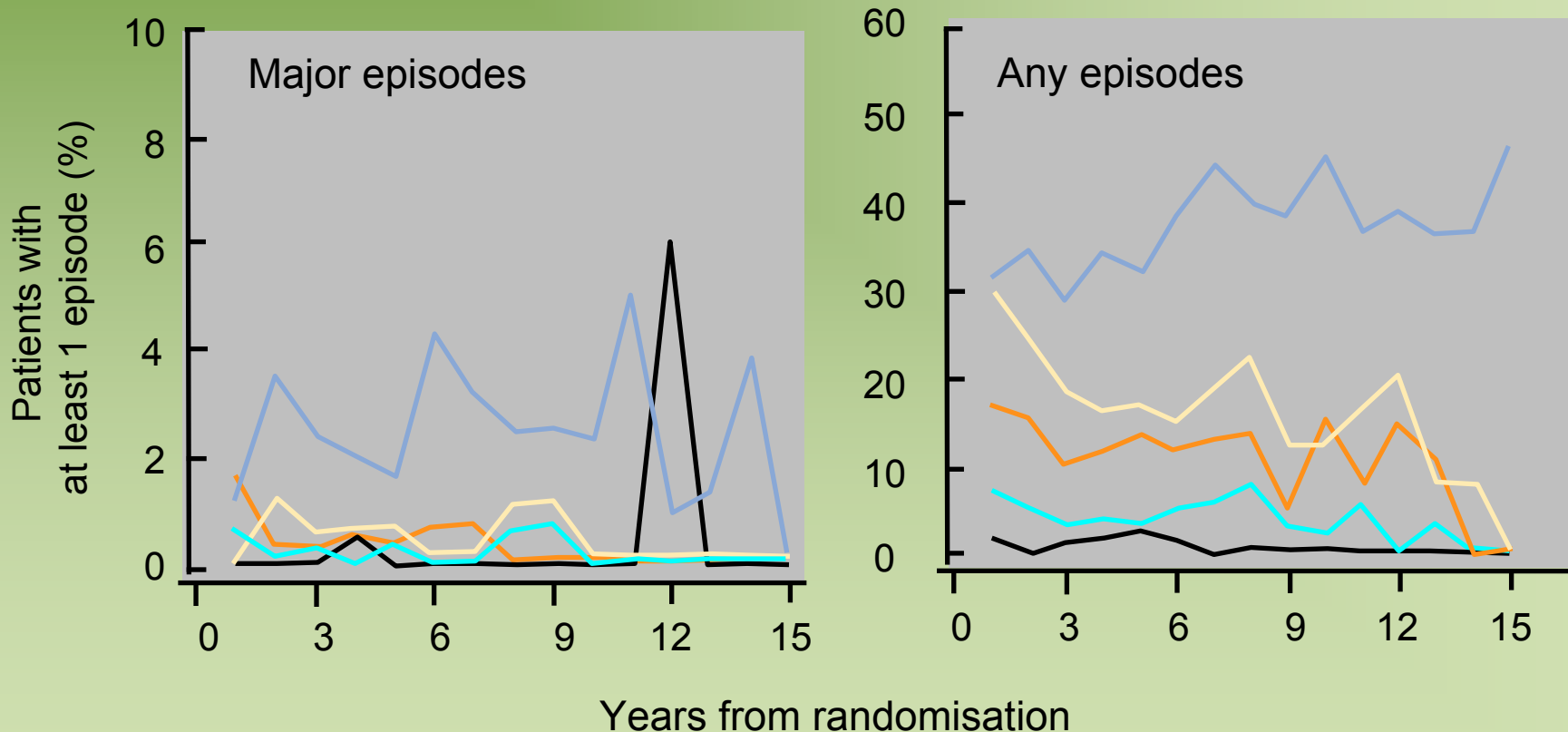


UKPDS 34: relative risk reduction with metformin or SUs/insulin



UKPDS 34: metformin was associated with less hypoglycaemia than insulin or SUs

- Insulin
- Chlorpropamide
- Glibenclamide
- Metformin
- Conventional



Side effects of metformin

- Gastrointestinal:
 - diarrhoea
 - nausea
 - vomiting
 - bloating
- Anorexia
- Contraindicated in patients with:
 - cardiovascular impairments
 - renal dysfunction
 - hepatic dysfunction

Metformin: treat early, save lives

- Reduces risk of Diabetes
- Reduces progression of diabetes (with early treatment)
- Reduces the risk of CVD, 40%
- Has a legacy effect
- Reduces the risk of cancer by circa 50%
- No hypos
- No weight gain

HbA1c

Hyperglycaemia and cardiovascular disease: epidemiology

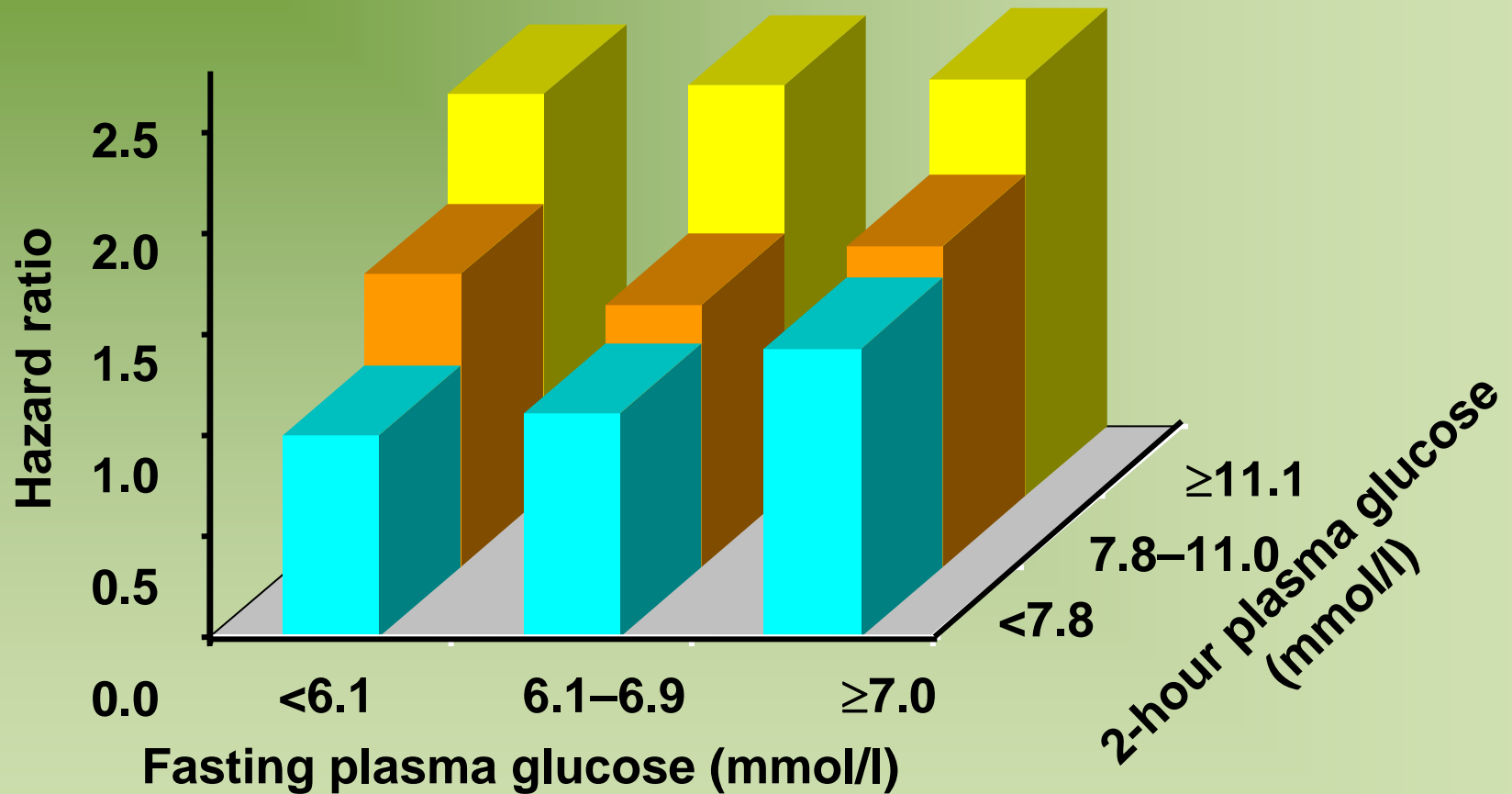
Study	n	~yrs	Outcome
1987 Honolulu Heart Study	8006	20	Risk of fatal/non-fatal CHD increased with 1h PPG
1991 Diabetes Interven Study	1139	11	1h PPG associated with increased risk of death
1998 Rancho Bernado Study	1858	7	IPH double risk of CVD related death
1999 DECODE Study	25364	10	2h PPG associated with increased risk of death
1999 Funagata Diabetes Study	2651	7	IGT double risk of CVD related death
1998 Whitehall Study	10025	20	CV mortality, men in upper 2.5% of the 2h glucose at higher risk
Paris Prospective Study	6629	20	
Helsinki Policeman Study	631	20	
1999 Mauritius, Fiji, Nauru	9179	5-12	PPH doubles mortality rate
2000 Hoorn study	2363	8	2h PPG associated with increased CVD death

DECODE Study: Glucose tolerance and cardiovascular disease

Mortality	Hazard Ratios	
	Fasting BG	2h BG*
All cause	1.21	1.73
Cerebrovascular	1.20	1.40
Coronary artery disease	1.09	1.56
Stroke mortality	1.64	1.29

2-hour PG not FPG an independent risk factor of CVD mortality

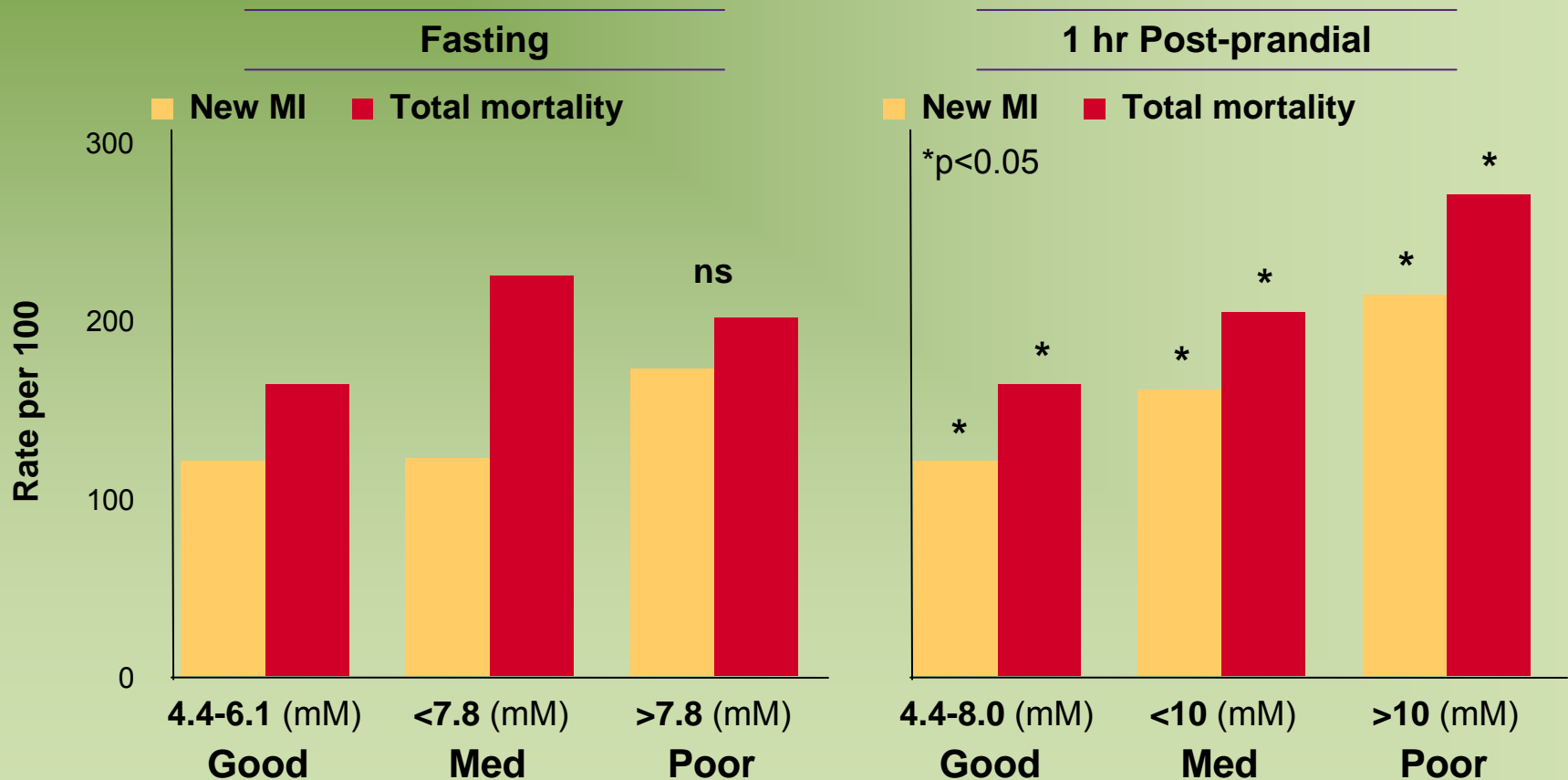
DECODE: Relative risk for 'all-cause' mortality in subjects not known to have diabetes



Adjusted for age, centre, sex, cholesterol, BMI, SBP and smoking

Diabetes Intervention Study (DIS): 11-year follow-up

Incidence of myocardial infarction, total mortality in newly diagnosed Type-2 diabetic subjects (984)



International Expert Committee report on the role of the A1c assay in the diagnosis of diabetes

- International Expert Committee appointed by ADA, EASD, and IDF to consider current and future means of diagnosis of diabetes
- Committee convened in 2008 and reported in 2009
- Committee recommended use of HbA_{1c} for diagnosis, based on
 - Close correlation between HbA_{1c} and diabetic retinopathy
 - Improved instrumentation and standardization of HbA_{1c} assay
 - Less biologic variability, greater preanalytic stability of HbA_{1c} versus glucose tests (FPG, OGTT)
 - No requirement for pretest fasting
 - Broad familiarity with HbA_{1c} in diabetes management
- Committee recommended HbA_{1c} diagnostic threshold of ≥ 6.5 % and preventive intervention when HbA_{1c} is < 6.5 % but ≥ 6.0 %

ADA=American Diabetes Association; EASD=European Association for the Study of Diabetes;
FPG=fasting plasma glucose; IDF=International Diabetes Federation; OGTT=oral glucose
tolerance test

Case Presentation

Case Presentation

Geoff - a 66 year old retired bus driver is reviewed in clinic. He suffers with occasional, infrequent episodes of angina, but has never suffered a myocardial infarction. He exercises little, smokes, is married and has three children. On examination his body weight is 91 kg, his BMI is 34 Kg /m² and his blood pressure is 148 / 78 mm Hg. Fasting glucose is 6.7 on one occasion. T Chol 4.1 mmol/l, LDL 2.2 mmol/l, HDL 0.8 mmol/l, TG 2.1 mmol/l. He is taking Aspirin 75mg, Perindopril 2mg, Atenolol 50 mg

What would you do??

What would you do??

- **OGTT or Repeat FPG?**

What would you do??

- **OGTT or Repeat FPG?**
- **2hr glucose 9.3 mmol/l**

What would you do??

- **OGTT or Repeat FPG?**
- **2hr glucose 9.3 mmol/l**
- **IFG and IGT – higher risk**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**
- **Check compliance**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**
- **Check compliance**
 - **Discuss with patient and wife??**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**
- **Check compliance**
 - **Discuss with patient and wife??**
- **Increase Perindopril/Add Amlod/BF**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**
- **Check compliance**
 - **Discuss with patient and wife??**
- **Increase Perindopril/Add Amlod/BF**
- **Rx – Metformin/Orlistat**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**
- **Check compliance**
 - **Discuss with patient and wife??**
- **Increase Perindopril/Add Amlod/BF**
- **Rx – Metformin/Orlistat**
- **Surgery???**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**
- **Check compliance**
 - **Discuss with patient and wife??**
- **Increase Perindopril/Add Amlod/BF**
- **Rx – Metformin/Orlistat**
- **Surgery???**
- **Refer??**

What would you do??

- **OGTT or Repeat FPG?**
- **Stop smoking**
- **Simva 40**
- **Exercise and diet advice**
- **Check compliance**
 - **Discuss with patient and wife??**
- **Increase Perindopril/Add Amlod/BF**
- **Rx – Metformin/Orlistat**
- **Surgery???**
- **Refer for ETT??**