MRC | Epidemiology Unit

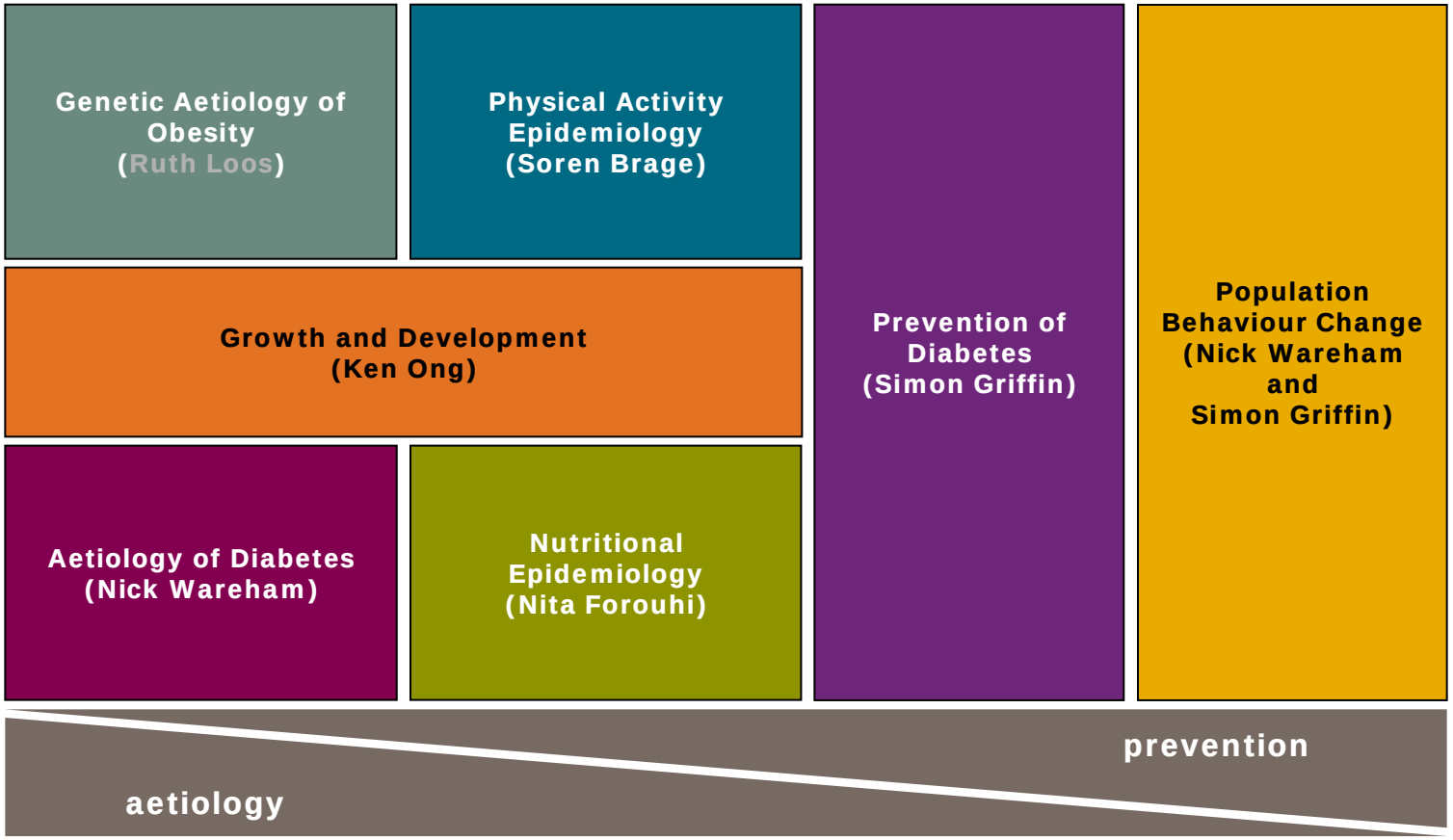
investigating the causes and prevention of diabetes and obesity

From aetiology to prevention: the work of the MRC Epidemiology Unit

Goal

to understand the genetic, developmental and environmental determinants of obesity, diabetes and related metabolic disorders and to translate this understanding into preventive action

Scientific Programmes



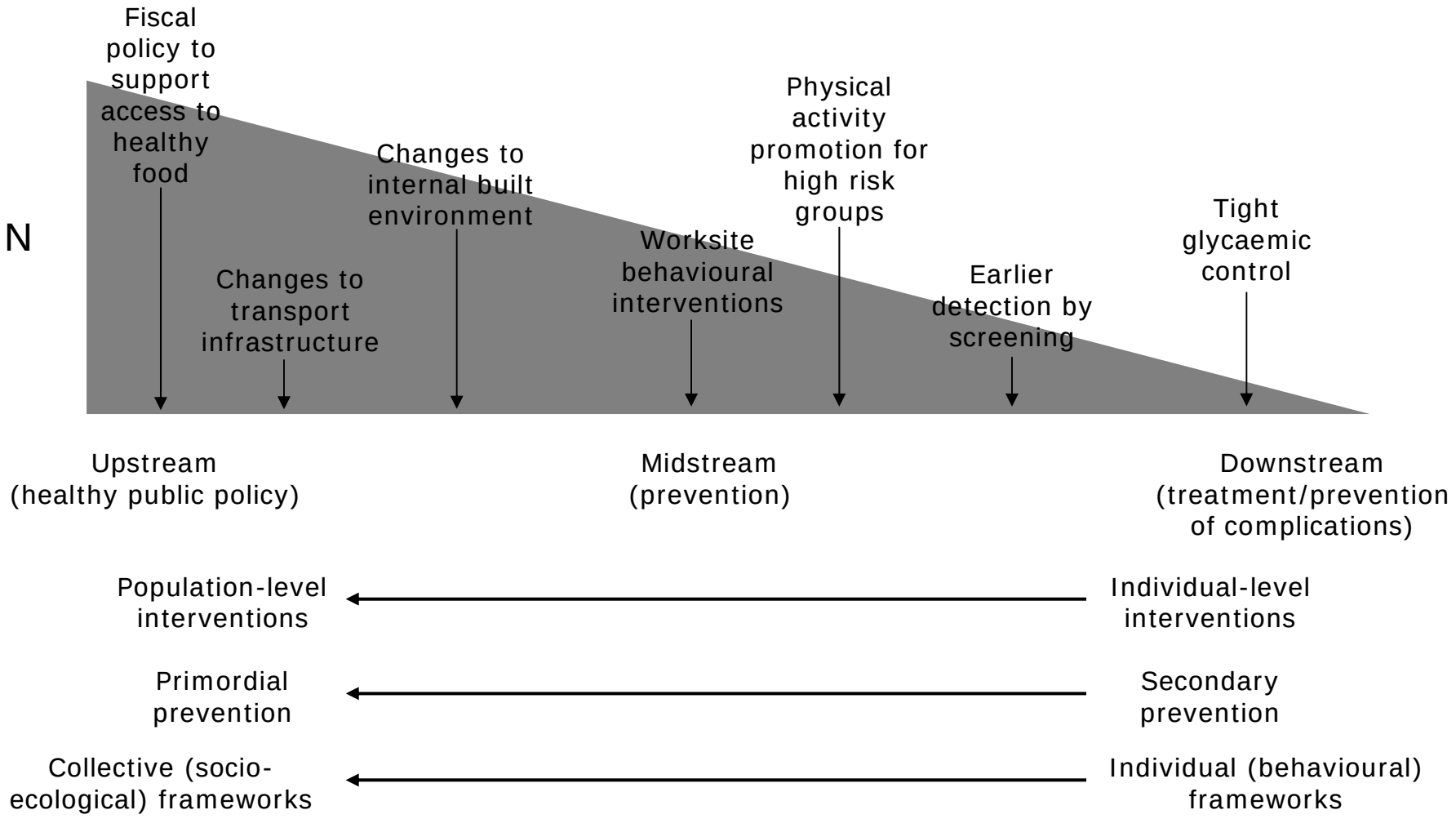
MRC | Epidemiology Unit

The prevention programme

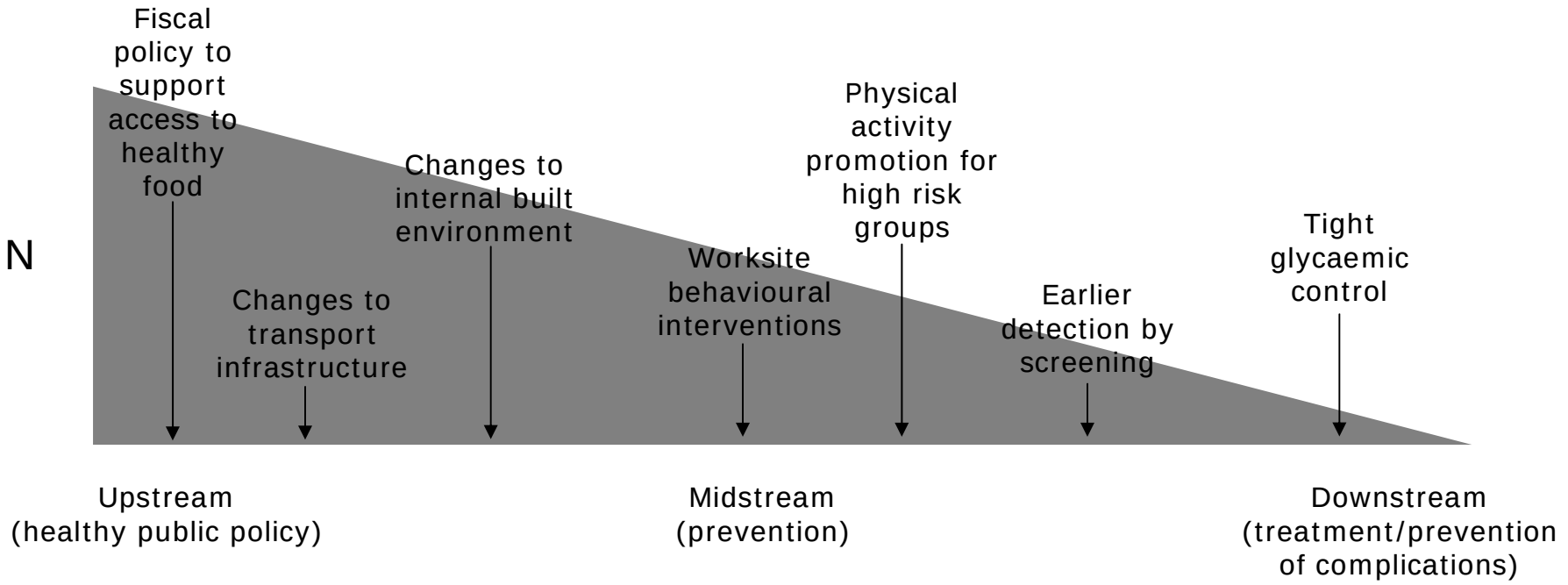
Translates knowledge gained from epidemiological studies into action to prevent diabetes, obesity and related metabolic disorders, including action to influence population dietary and physical activity behaviour.

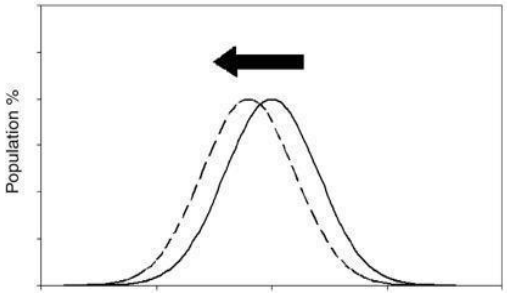
Assesses the effectiveness and impacts of different approaches to behaviour change and disease prevention.

Prevention of diabetes and its complications

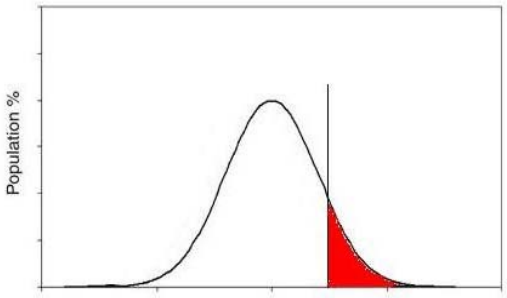


Prevention of diabetes and its complications





Population-based approach



High risk approach

MRC | Epidemiology Unit

Should we screen the population for type 2 diabetes?

Simon Griffin

26th November 2012

The Cambridge Statistics Discussion Group
Centre for Mathematical Sciences

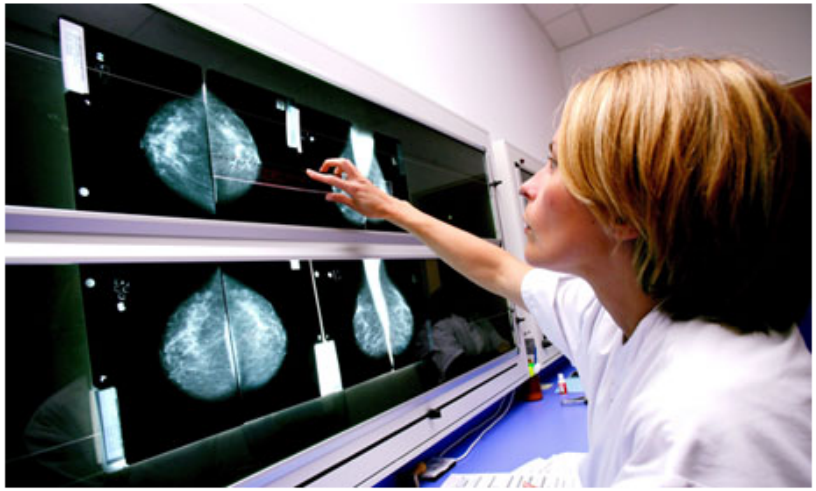
MRC | Medical Research Council

SHORTCUTS
BLOG
A SIDEWAYS LOOK AT THE NEWS

Previous Blog home Next

Breast cancer screening: should you, shouldn't you?

It's a matter of what makes you feel most comfortable, in this doctor's opinion



Posted by
Ann Robinson
Tuesday 30 October
2012 18.01 GMT
The Guardian

Jump to comments (80)

Article history

Society

17 October 2012 Last updated at 01:02

General health check-ups 'offer no benefit'

Visiting a doctor for a general check-up is unlikely to lead to a condition needing treatment being identified, but may cause undue stress, say experts.

Health MoTs check things like blood pressure and cholesterol

The Danish researchers that carried out the latest review, which involved more than 180,000 patients, say doctors should stop offering such check-ups.

Health MoTs did not reduce deaths overall or deaths from cancer and heart disease, according to their review.

In England, people aged 40-74 are offered a free health check.

The initiative, launched in 2009, is designed to spot conditions such as heart disease, stroke and diabetes by looking for silent risk factors such as high blood pressure and cholesterol.

Related Stories

Universal over-40s health checks

Over 40s 'missing heart checks'

Will health screening work?

Top Stories


Obama and Romney in spiky debate

Charities voice benefits concerns

Mantel sequel scoops Man Booker

RBS leaves toxic assets scheme

Ugly scenes mar England U21 win

Features & Analysis


Innit, loo, skint...
And 27 more of your Britishisms being used by Americans


Leap of faith
The youths trained to jump off buildings by the Russian Church

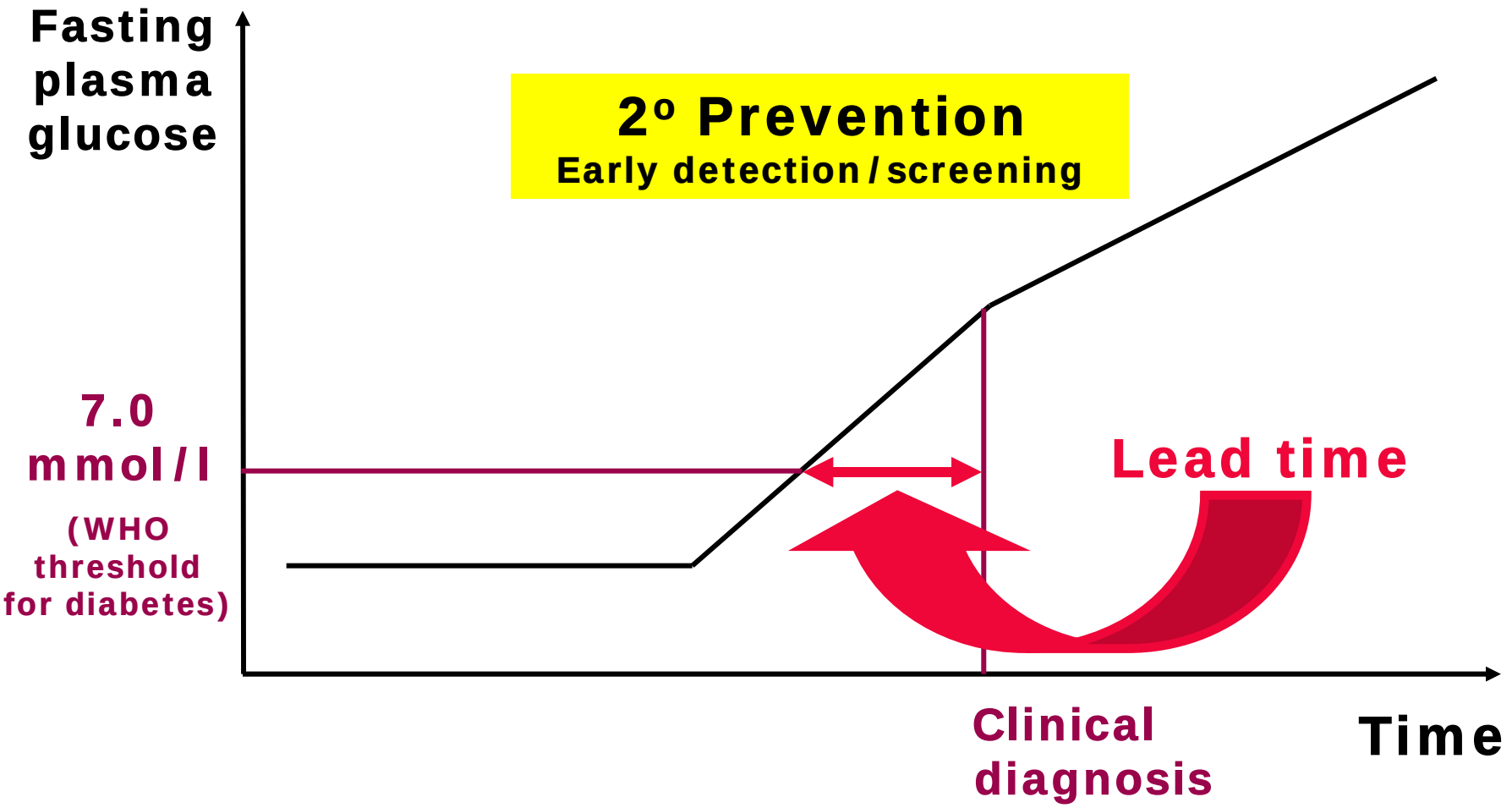

Executive meltdown
Are the rewards worth the excessive stress?

Definition of Screening

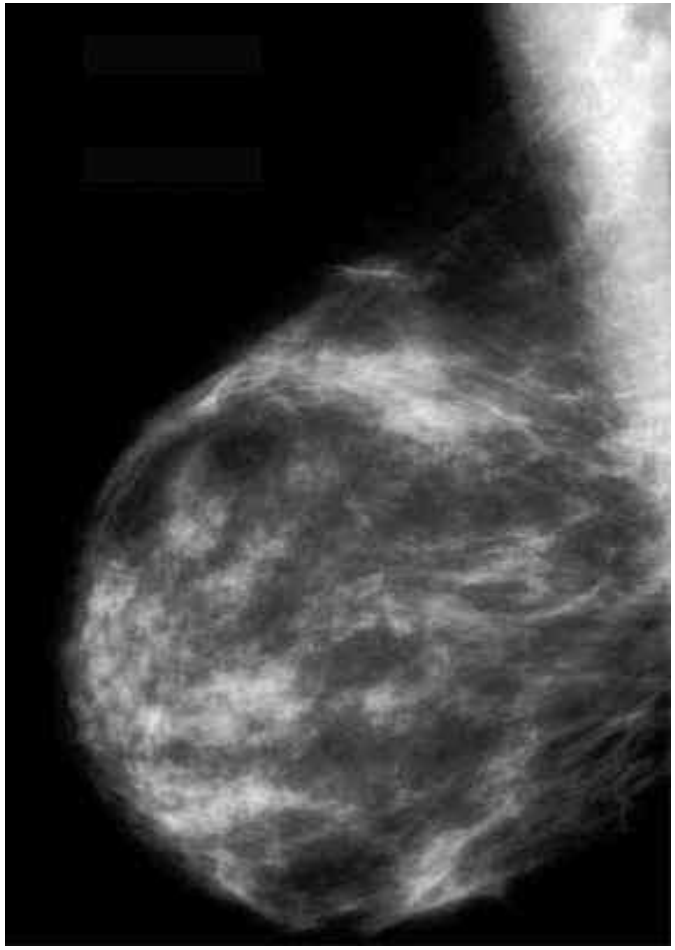
'The systematic application of a test or inquiry, to identify individuals at sufficient risk of a specific disorder to warrant further investigation or direct preventive action, amongst persons who have not sought medical attention on account of symptoms of that disorder'

National Screening Committee, Department of Health, 1998

Screening


Fasting plasma glucose
2º Prevention
Early detection / screening
7.0 mmol/l
(WHO threshold for diabetes)
Lead time
Clinical diagnosis
Time

The screening paradox



Screening is only worthwhile if the effectiveness of treatment for people diagnosed without screening is limited

Ethical Difference Between Medical Practice and Screening

"If a patient asks a medical practitioner for help, the doctor does the best he can. He is not responsible for defects in medical knowledge.

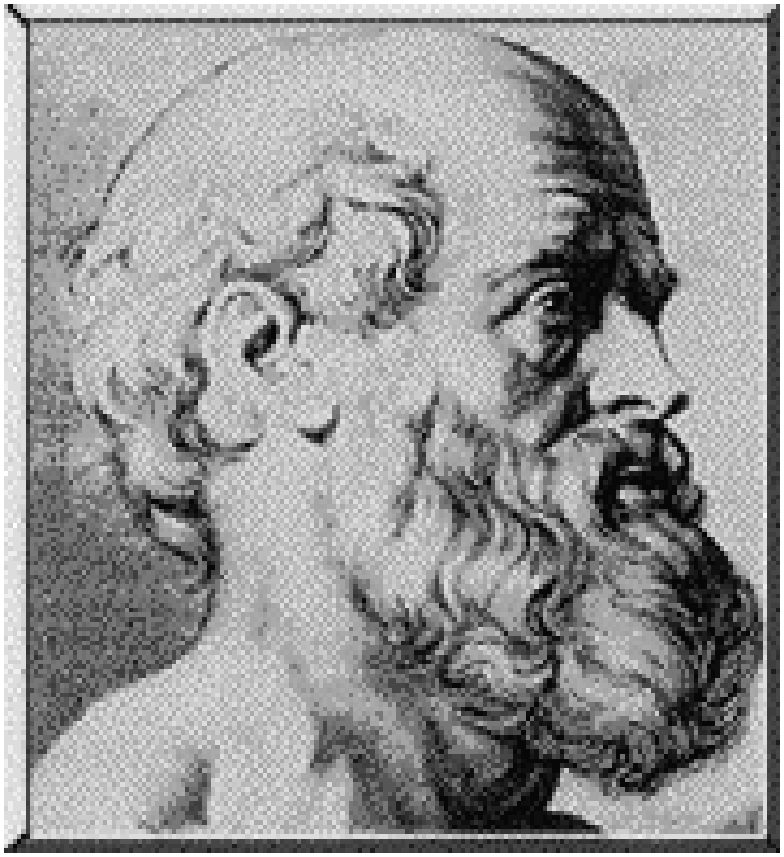
If screening is initiated, he should have conclusive evidence that screening can alter the natural history of the disease in a significant proportion of those screened."

Cochrane and Holland 1971

Screening is always associated with harm, sometimes it is also associated with benefit

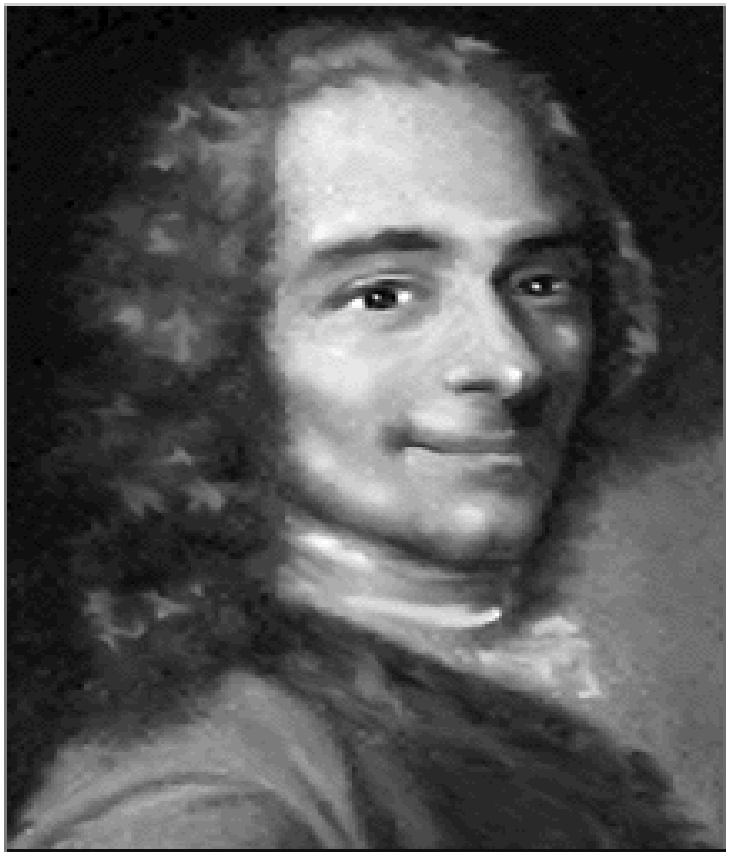
- Screening tests may be harmful
- Screening tests are imprecise leading to false positives and false negatives
- Diagnostic tests may be harmful
- Diagnostic tests are imprecise leading to false positives and false negatives
- Treatment may have adverse effects

Hippocrates



First do no harm

Voltaire



The efficient physician is the man who successfully amuses his patients while nature effects a cure

Downsides of diagnostic labels for asymptomatic CVD risk factors

- **Denial: ~25% did not accept the label hypercholesterolaemia and had negative attitudes to dietary change**

Irvine MJ, Logan AG. Is knowing your cholesterol number harmful? J Clin Epidemiol 1994;47:131-45

- **Negative feelings after a positive result**

Alderman MH. Labelling of hypertensives: a review of the data. *J Clin Epidemiol* 1990;43:195-200

- **Annoyance**

Meland E. Life style intervention in general practice: effects on psychological wellbeing and patient satisfaction. *Qual Life Res* 1996;5:348-54

Screening for Hypertension

- **Screening and diagnosing hypertension in Canadian steel workers:**
  - significantly increased subsequent absenteeism from work (5.2 days, $p<0.025$)

    Haynes et al NEJM 1978:741-44
  - significantly decreased subsequent annual income ($1093)

    Johnston ME et al J Chron Dis 1984;37:417-23

False Reassurance
or “The certificate of good health” effect

MRC | Epidemiology Unit

- Only about 50% of women understand that the term “normal smear result” means there is a residual risk of having or developing cervical cancer in the next five years.

  Marteau T et al. *BMJ* 2001;322:526-8.

- Following screening for risk of cardiovascular disease, 44% (n=45) of those with low risk results felt that this acted as proof that there was no need to make any changes to their lifestyles.

  Tymstra T. *Fam Pract* 1987;4:287-90.

- Individuals at high risk are less inclined to change lifestyles after normal cholesterol blood test results.

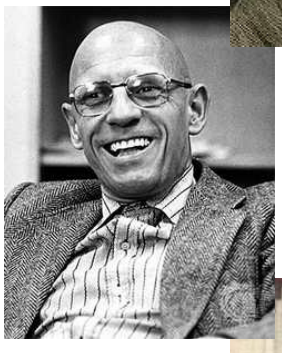
  Kinlay S. *BMJ* 1990;300:1545-7.

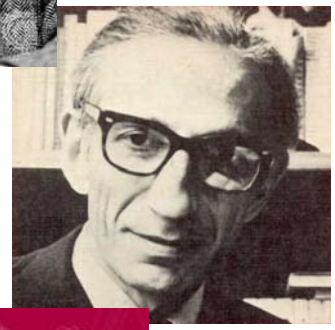
“I consider any emblem or label a prejudice”

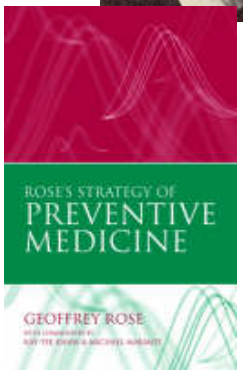
Anton Chekhov (1860–1904)

What is a disease?

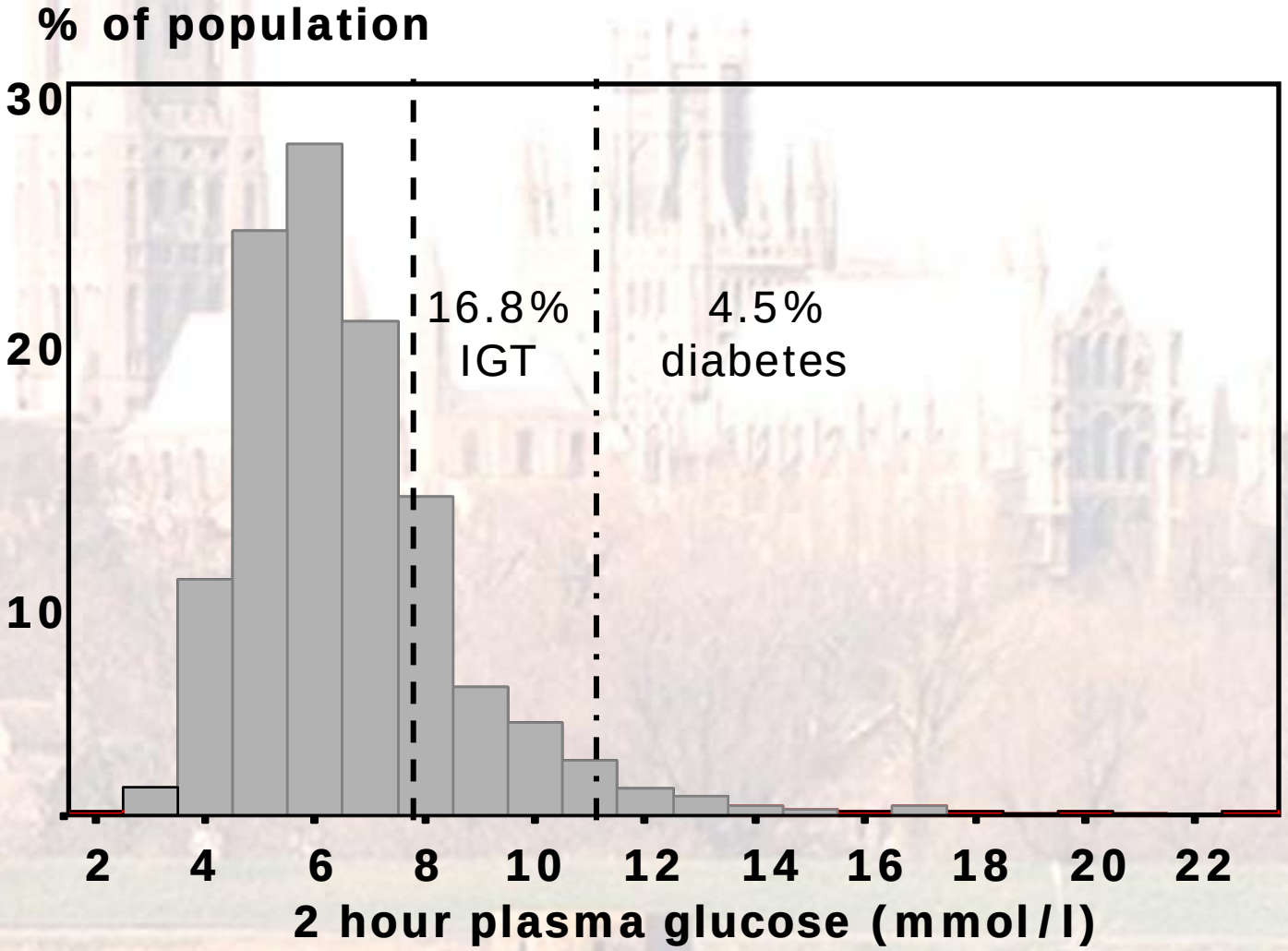
- **Thomas Sydenham** (1624-1689) thought that diseases like plant and animal species exist in nature, ready to be “discovered.”
- **Foucault** views the notion of disease as essentially a means of social control.
- “Each civilisation defines its own diseases. What is sickness in one might be chromosomal abnormality, crime, holiness, or sin in another.” **Ivan Illich**
- “There is no disease that you either have or don't have—except perhaps sudden death and rabies. All other diseases you either have a little or a lot of.” **Geoffrey Rose**







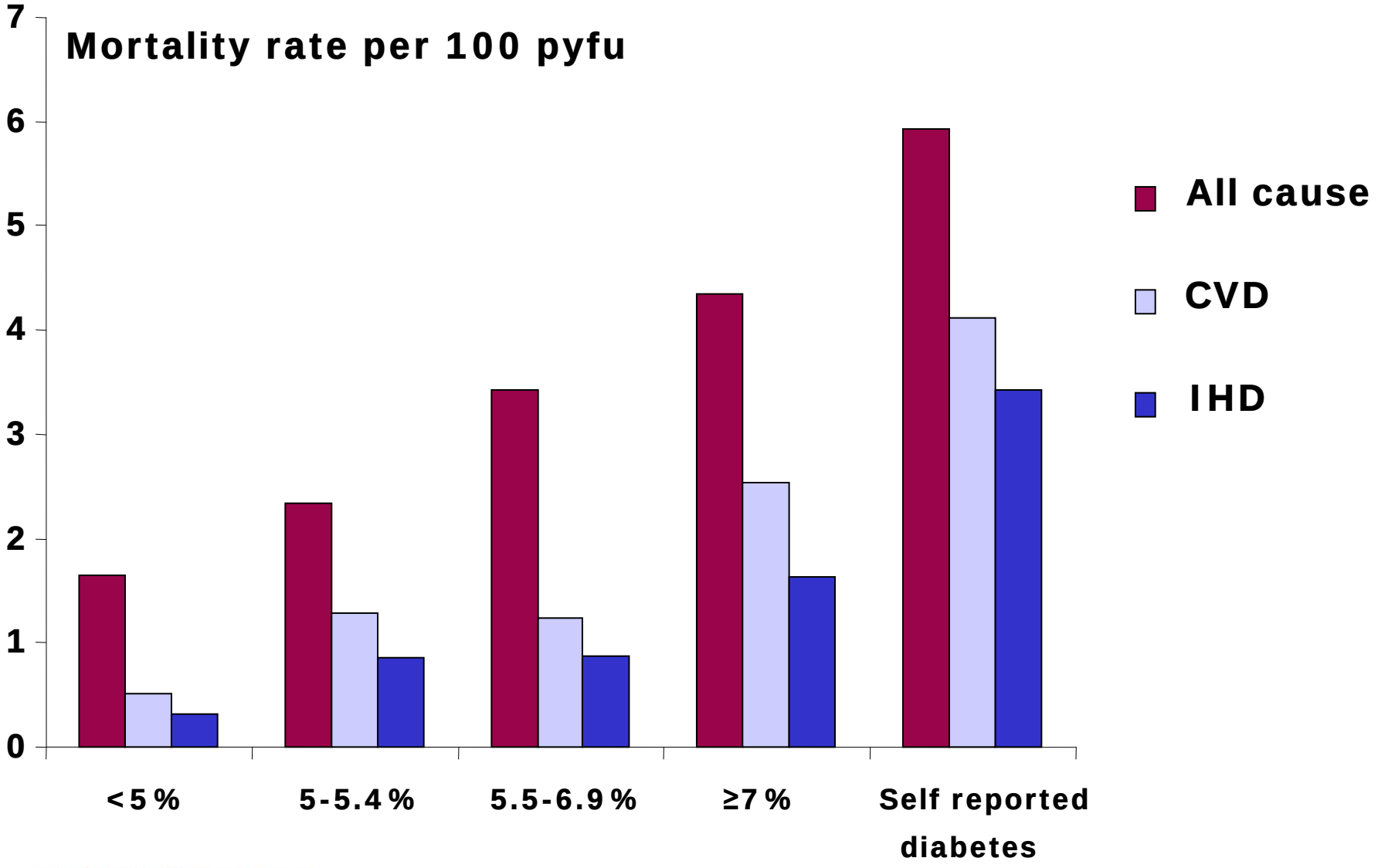
Population Distribution of 2-Hour Glucose in a Previously Unscreened Population: Ely Study



MRC | Medical Research Council

Williams DRR, Wareham NJ et al. *Diabetic Med* 1995;**12**:30-5

The Association Between HbA_{1c} Diabetes and Mortality



MRC | Medical Research Council

Khaw KT, Wareham NJ et al. *BMJ* 2001;322:15-18.

The prevention paradox

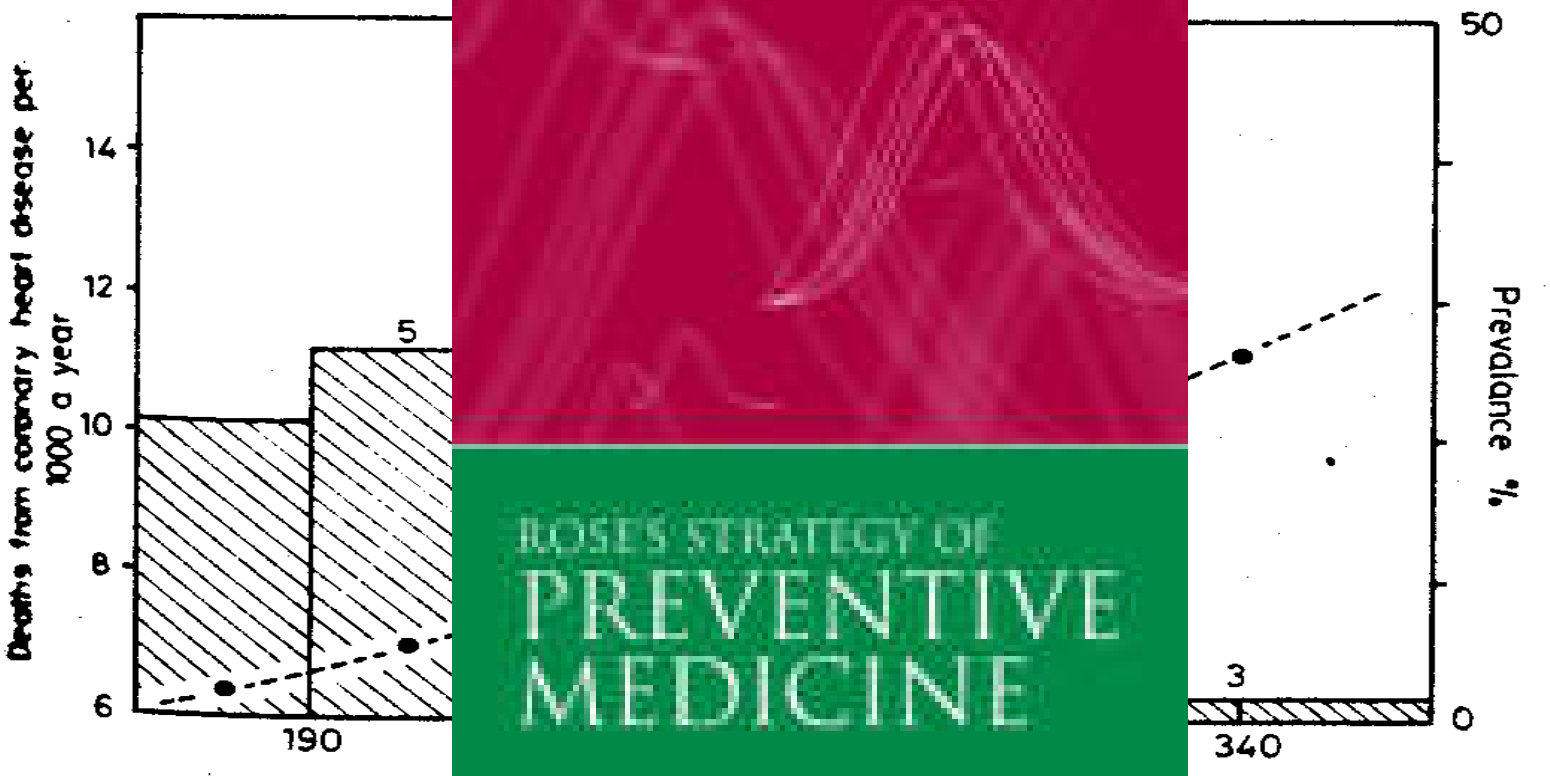
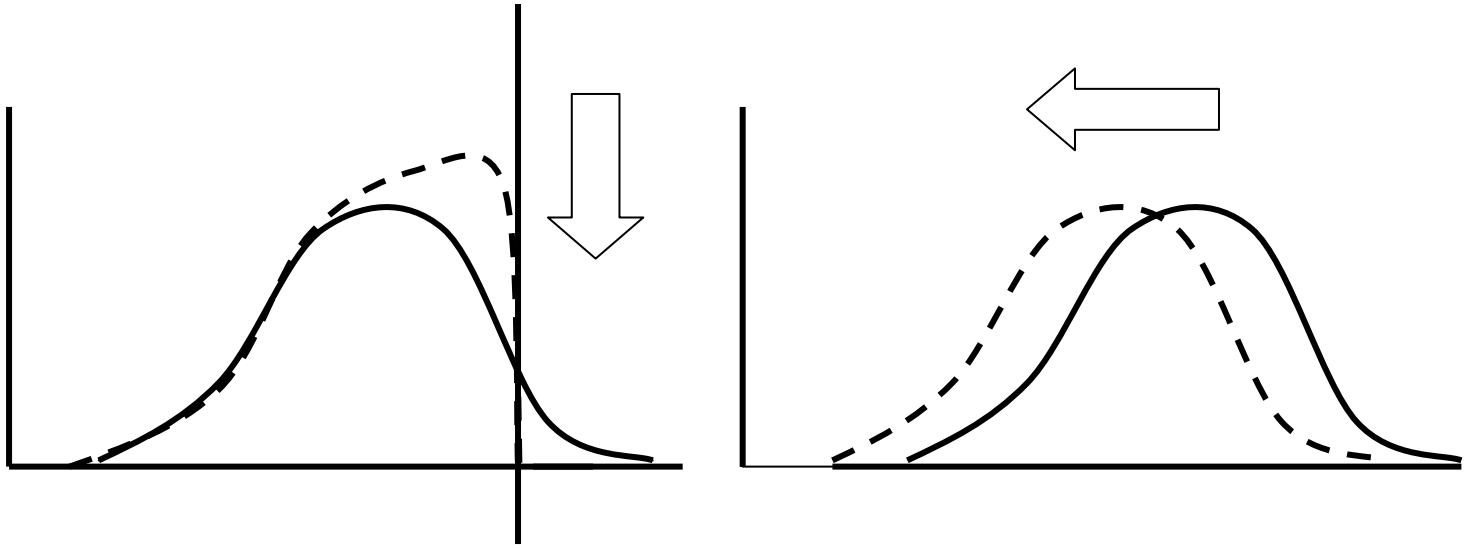


FIG 3—Prevalence distr tration related to coronary heart disease 4. Number above each bar represents est 0 population per 10 years. (Based on Fra
Conversion: SI to tra 1/l ≈ 38·6 mg/100 ml.

Rose G. *BMJ* 1981;282:1847-1851

Population and High Risk Approach



Identify and treat those beyond a threshold for risk factor

Shift the whole population distribution of risk factor

Screening Criteria

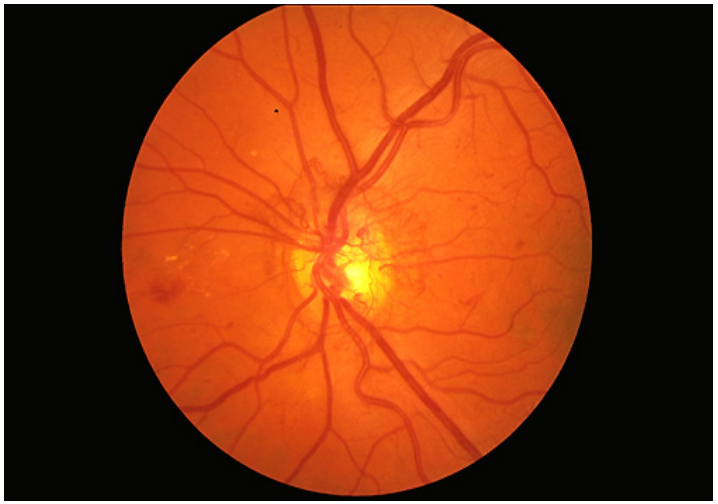
- A well defined disorder with a known prevalence
- A burdensome disease with a long detectable pre-clinical phase
- A simple, safe, accessible, feasible, sensitive / specific screening test / programme
- Absence of significant harm associated with screening
- An efficient intervention that is more effective earlier in the disease process
- Trial evidence of cost-effectiveness of screening
- All primary prevention interventions should be in place
- Clinical management of the condition should be optimised prior to screening

Wilson JGM, Jungner G. Geneva: WHO, 1968

Type 2 Diabetes Meets Many of the Screening Criteria

4.5 % of 40-65 yr olds in Ely have previously undiagnosed diabetes

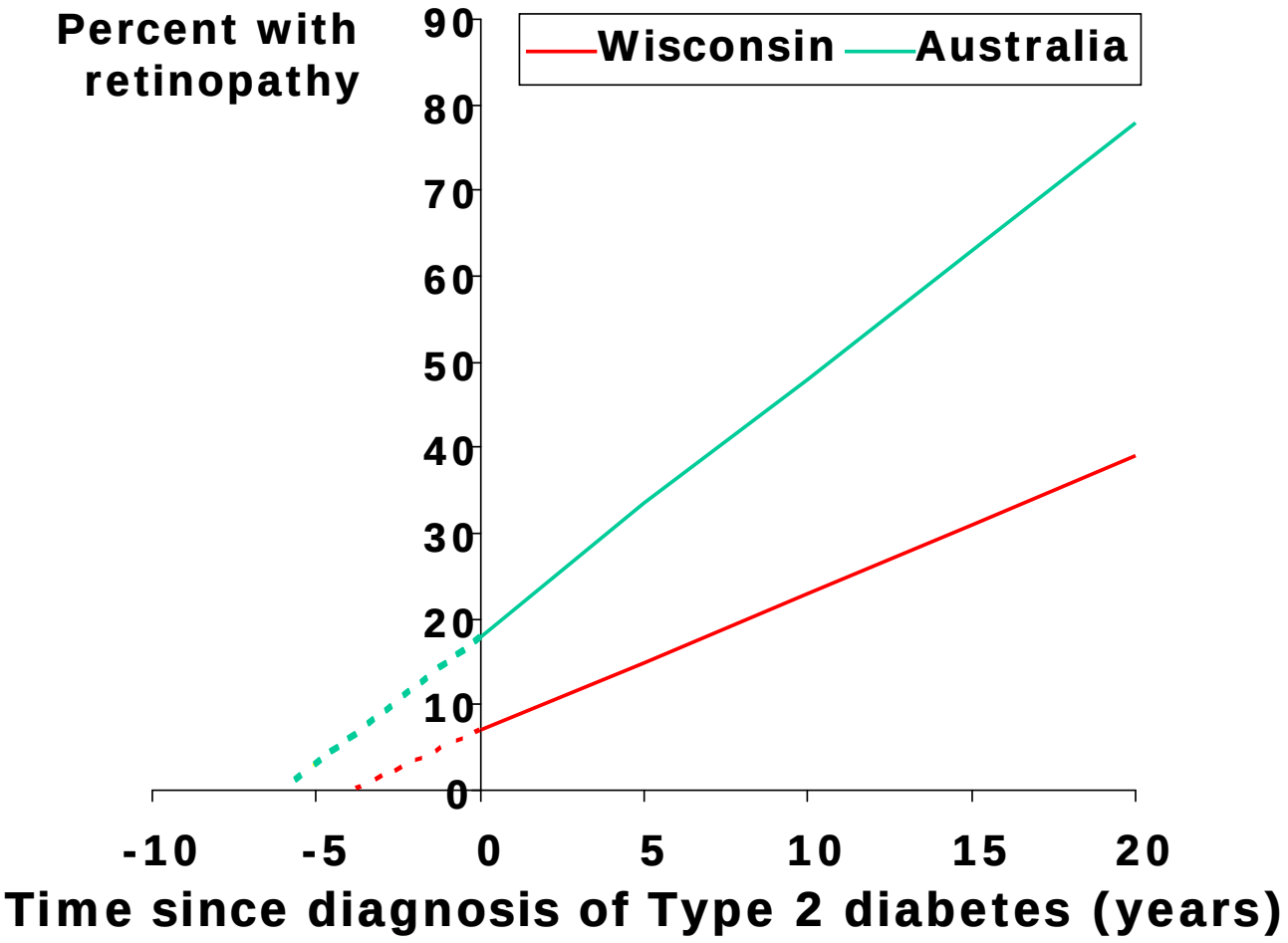
(Williams DRR et al. Diabetic Med 1995;12:30-5)



Up to 50% of newly diagnosed patients have evidence of diabetic tissue damage

(UKPDS. *Diabetologia* 1991;34:877-90)

The Delay Between Disease Onset and Diagnosis May Be up to 10 Years



Harris et al. *Diabetes Care* 1992;15:815-8.

…which cannot be reduced by increased awareness about symptoms

- **Public awareness campaigns have not generated many new cases**
  (Singh et al. *BMJ* 1994;308:632-6)

"Professional alertness" is not an efficient strategy

- **78% of US adults have at least one risk factor for diabetes**
  (Cowie C et al. Diabetes Care 1994;10:1158-63)

Screening Criteria

- ✓ A well defined disorder with a known prevalence
- ✓ A burdensome disease with a long detectable pre-clinical phase
- **A simple, safe, accessible, feasible, sensitive / specific screening test / programme**
- Absence of significant harm associated with screening
- An efficient intervention that is more effective earlier in the disease process
- Trial evidence of cost-effectiveness of screening
- All primary prevention interventions should be in place
- Clinical management of the condition should be optimised prior to screening

Wilson JGM, Jungner G. Geneva: WHO, 1968

Screening questionnaires and scores

TYYPIN 2 DIABE
SAIRASTU

Rengasta oikea vaihtoeh

1. Ikä
   0 p. Alle 45 v.
   2 p. 45 – 54 v.
   3 p. 55 – 64 v.
   4 p. Yli 64 v.

2. Painoindeksi
   (katso taulukosta kääntöp
   0 p. Alle 25 kg/m²
   1 p. 25 – 30 kg/m²
   3 p. Yli 30 kg/m²

3. Vyötärönympärys m
   alapuolelta (yleensä

   MIEHET

   0 p. Alle 94 cm
   3 p. 94 – 102 cm
   4 p. Yli 102 cm

4. Sisältyykö jokaiseen p
   puoli tuntia liikuntaa
   ns. arkiliikunta muka

   0 p. Kyllä
   2 p. Ei

5. Kuinka usein syöt kas
   tai marjoja?

   0 p. Päivittäin
   1 p. Harvemmin kuin jo

Testin suunnitelu: Professori Jaakko Tuo

MRC | Medical

Diabetes Risk Test

Complete the questionnaire below to find out if you are at risk of developing type 2 diabetes.

	Answer	Tick appropriate box	Score
1. How old are you?	44 & under	☐	0
	45-49	☐	7
	50-54	☐	13
	55+	☐	18
2. What sex are you?	Male	☐	4
	Female	☐	0
3. What is your Body Mass Index (BMI)?	24 & under	☐	0
	25-29	☐	7
	30+	☐	15

Use your height and weight to work out your Body Mass Index (BMI) using the graph below: e.g. 4 ft10 ins 11 stone = obese class 1, i.e. BMI is over 30 therefore score 15.

	Answer	Tick appropriate box	Score
4. Have you been diagnosed with high blood pressure?			
	Yes	☐	10
	No	☐	0
5. Are you physically active in your leisure life? *e.g. 30 minutes of moderate physical activity, such as brisk walking, at least 5 days a week*			
	Yes	☐	0
	No	☐	6
6. Are either of your parents diabetic?			
	Yes	☐	7
	No	☐	0
		TOTAL (max 60)	

SCORE RANGES
If you have a total score of 31 or more you may be at increased risk of having undiagnosed diabetes. Please consider following the advice below and overleaf to arrange a simple blood sugar test at a local pharmacy, or discuss the result with your practice nurse.

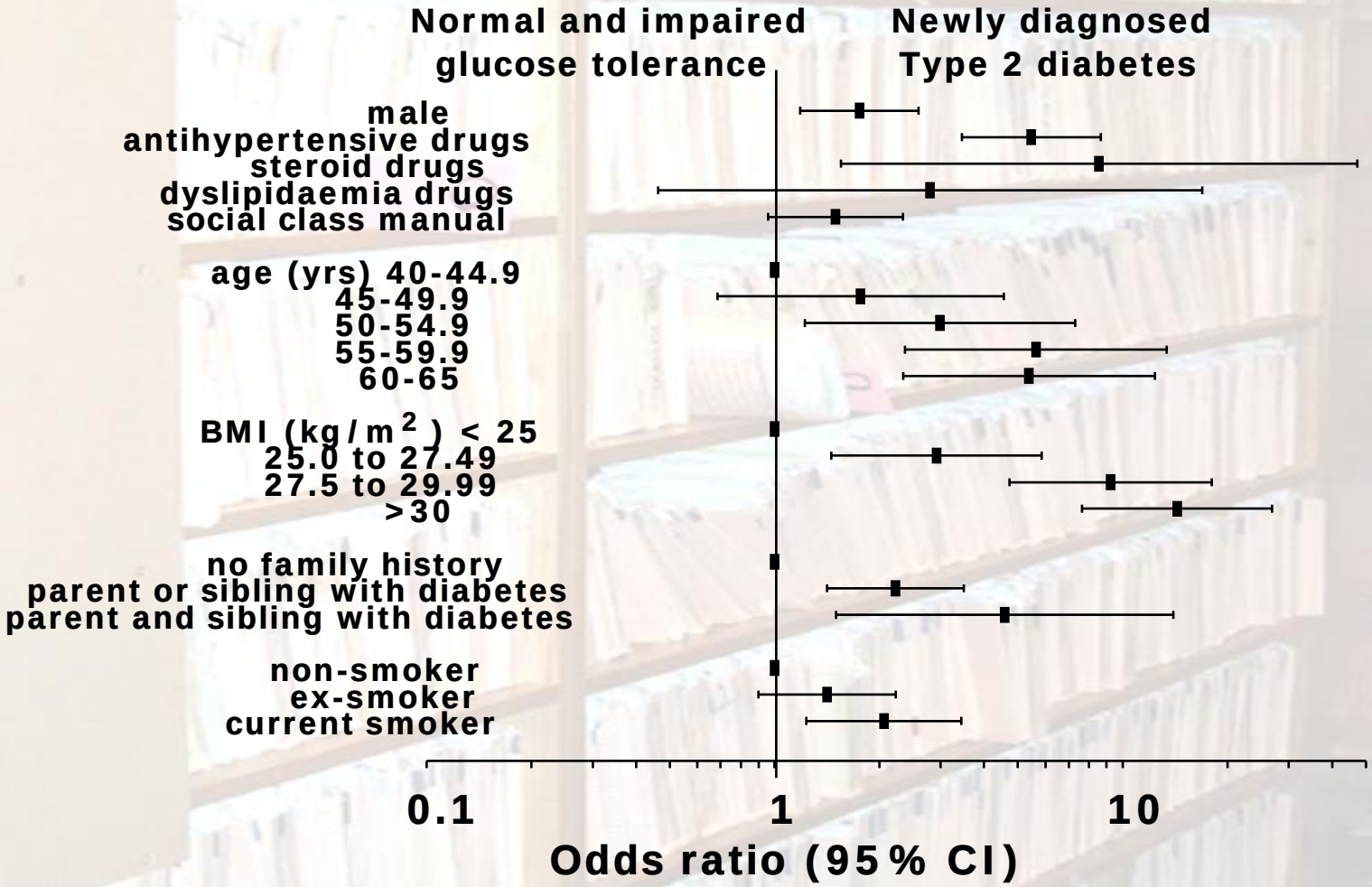
Identify diabetes early

Diabetes causes elevated levels of sugar in the blood and may run in families. Untreated diabetes may cause damage to the heart, eyes, kidneys and feet. Early diagnosis and treatment can reduce the risk of complications.

Some of the signs of diabetes include always feeling tired, being irritable, being thirsty, passing urine excessively and getting infections and numbness in the feet.

See overleaf

Univariate Associations Between Patient Variables and Glucose Tolerance



Diabetes/Metab Res Rev 2000;16:164-171.
Diabetic Med 2007;24:830-835.
J Med Screen 2002;9:187-190.

Screening Criteria

- ✓ A well defined disorder with a known prevalence
- ✓ A burdensome disease with a long detectable pre-clinical phase
- ✓ A simple, safe, accessible, feasible, sensitive / specific screening test / programme
- • Absence of significant harm associated with screening
- • An efficient intervention that is more effective earlier in the disease process
- • Trial evidence of cost-effectiveness of screening
- • **All primary prevention interventions should be in place**
- • **Clinical management of the condition should be optimised prior to screening**

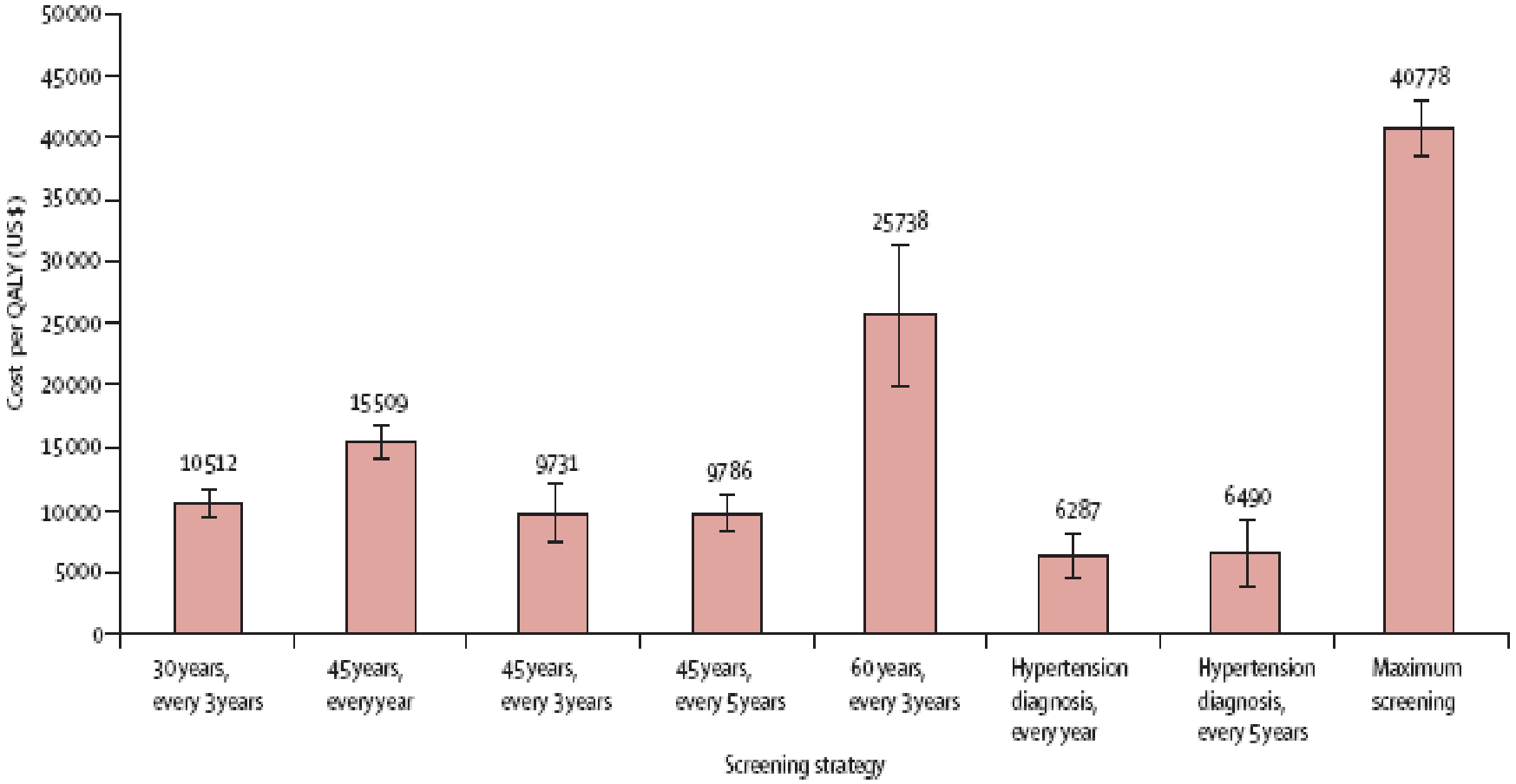
Wilson JGM, Jungner G. Geneva: WHO, 1968

Screening Criteria

- ✓ A well defined disorder with a known prevalence
- ✓ A burdensome disease with a long detectable pre-clinical phase
- ✓ A simple, safe, accessible, feasible, sensitive/specific screening test/programme
- • **Absence of significant harm associated with screening**
- • **An efficient intervention that is more effective earlier in the disease process**
- • **Trial evidence of cost-effectiveness of screening**
- ✗ All primary prevention interventions should be in place
- ✗ Clinical management of the condition should be optimised prior to screening

Wilson JGM, Jungner G. Geneva: WHO, 1968

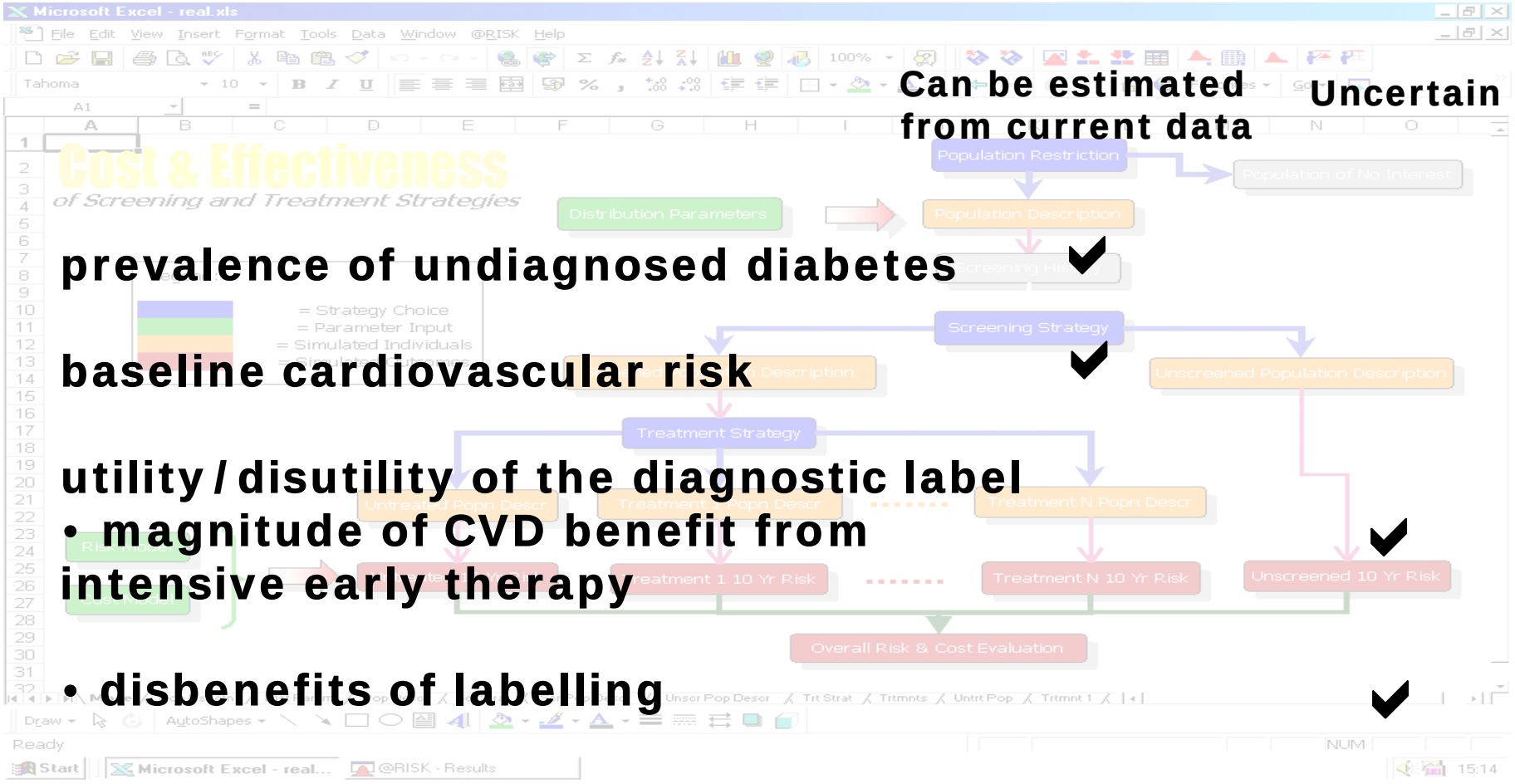
Modelling of cost-effectiveness



Expected cost per quality-adjusted life year (QALY) of screening compared with control after 50 years of follow-up

Lancet 2010;375:1365-74.

What Determines the Cost-effectiveness of Diabetes Screening?



Can be estimated from current data

Uncertain

prevalence of undiagnosed diabetes ✔

baseline cardiovascular risk ✔

utility / disutility of the diagnostic label

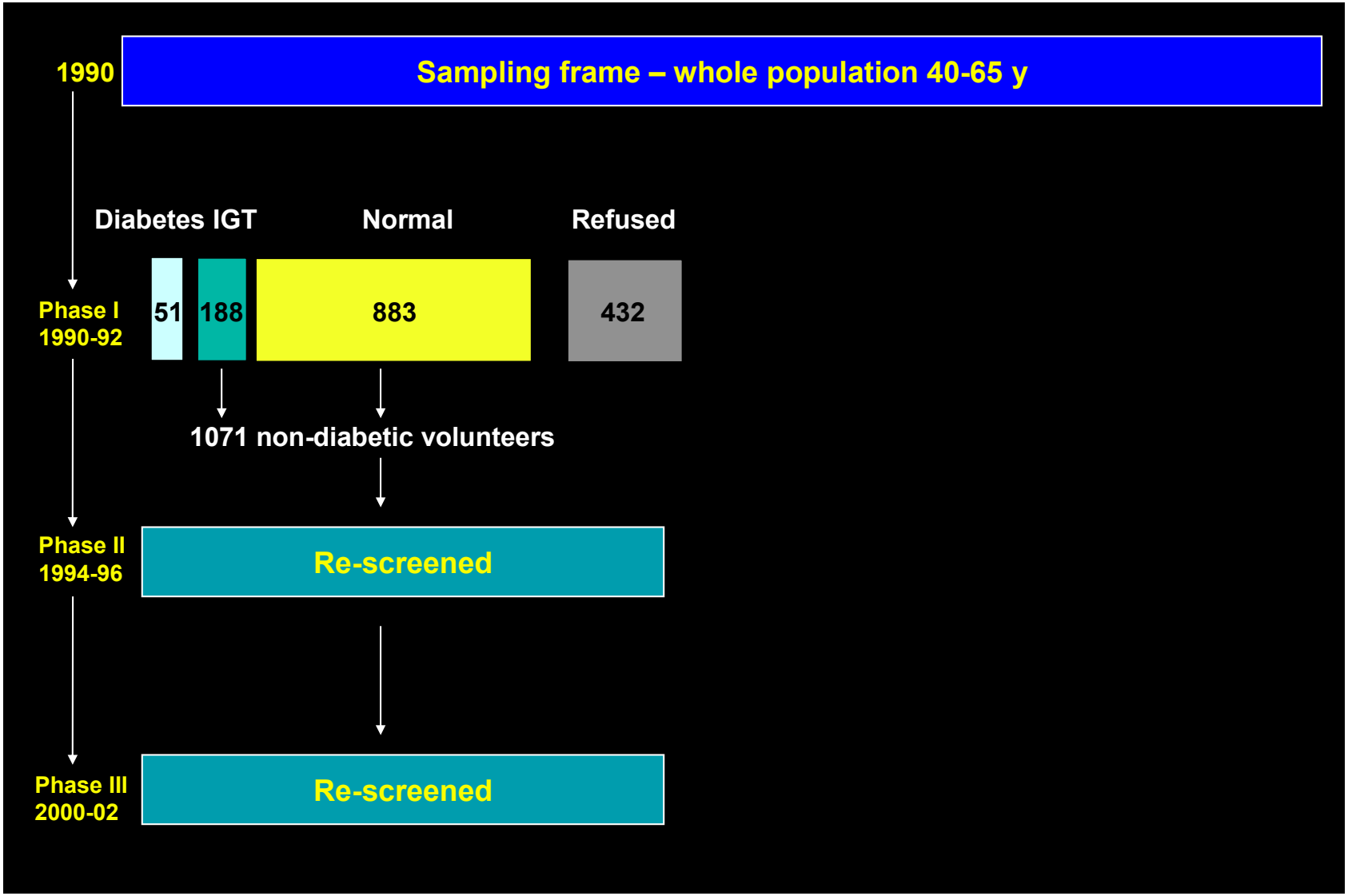
- **magnitude of CVD benefit from intensive early therapy** ✔
- **disbenefits of labelling** ✔

Diabetologia 2006;49:1536-1544
BMJ 2001;322:986-988

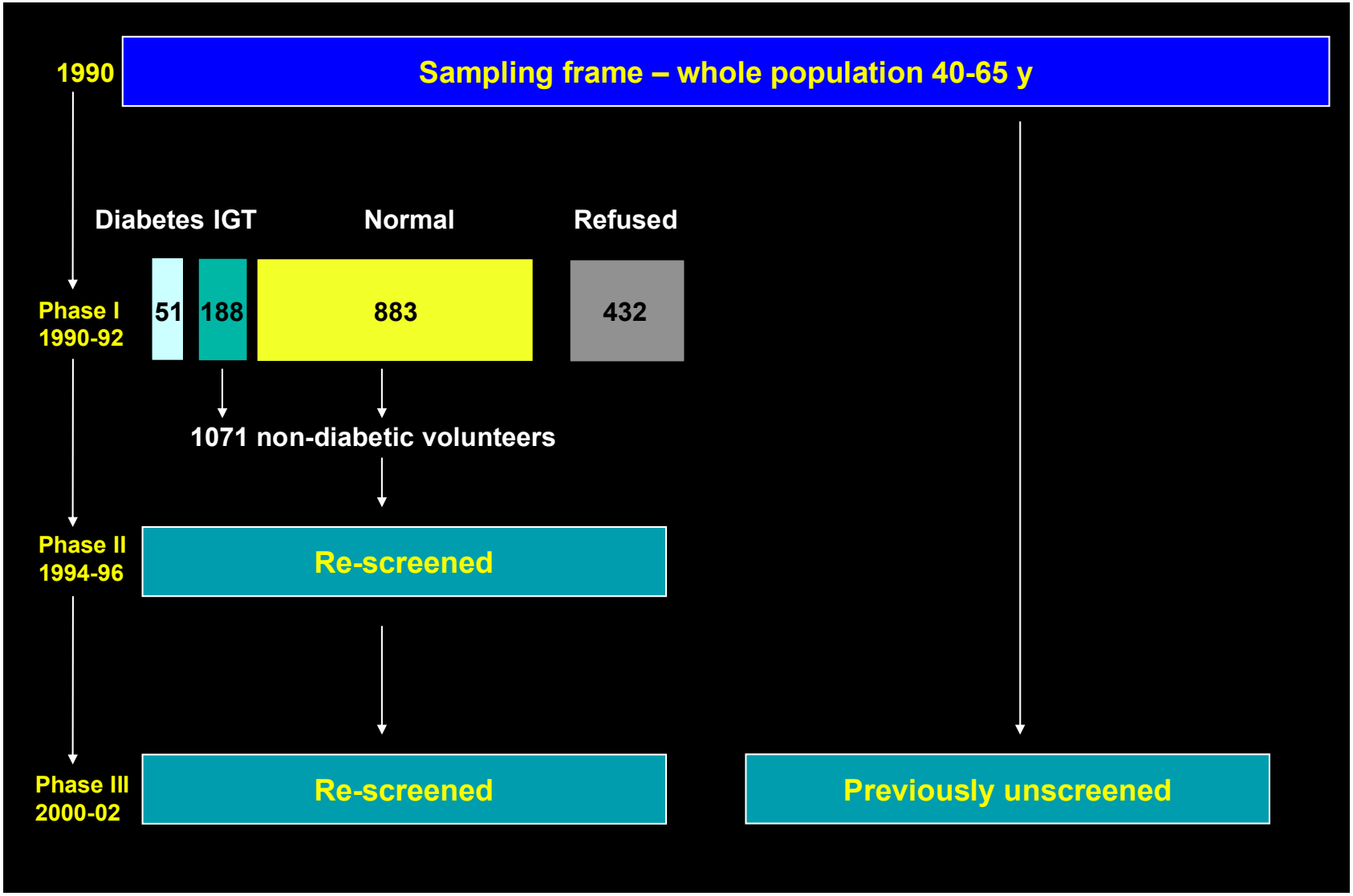
Ely Retrospective Study

Ely Retrospective Study Design

MRC | Epidemiology Unit



Ely Retrospective Study Design

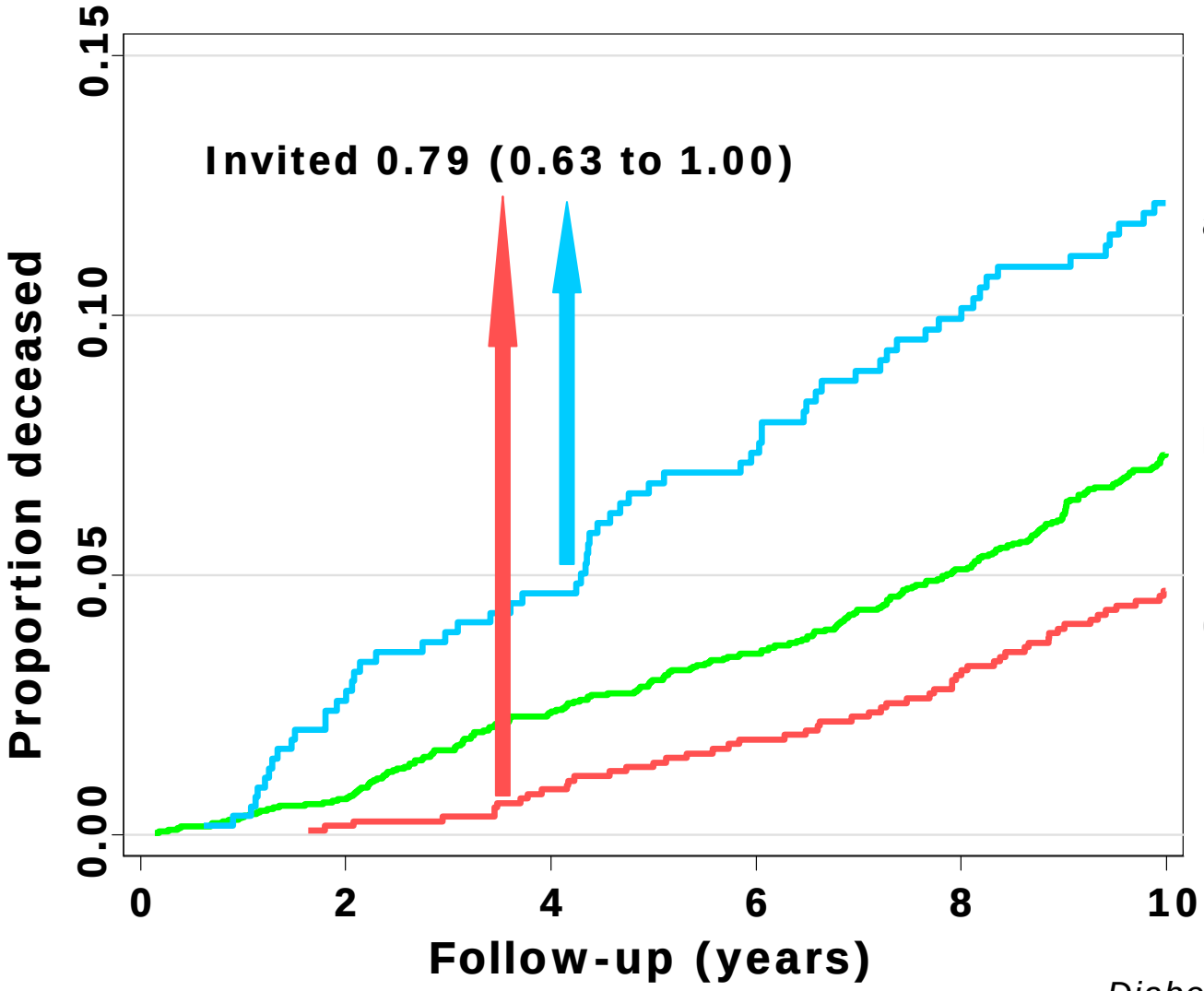


Results

- 68% initial attendance
- Non-attenders were more likely to be male ($p<0.001$) and more deprived ($p=0.005$)
- 345 deaths over a median of 10 years

Kaplan-Meier Curves for the Ely cohort 1990-1999 by Attendance at Screening (adjusted for age, gender and social class)

MRC | Epidemiology Unit



Invited but did not attend
1.36 (1.01 to 1.82)

Not invited

Invited and attended
0.54 (0.40 to 0.74)

MRC | Medical Research Council

Diabetologia 2011;54:312–319.

A Randomised Trial of Screening for Diabetes: Effects on Anxiety

1200 people aged 40-69 yrs without known diabetes

354 in the top 30 % of risk for having undiagnosed diabetes

116 Invited

238 Not Invited

After 6 weeks postal questionnaires:
SF-Spielberger Anxiety, Self Perceived Health

70% response rate

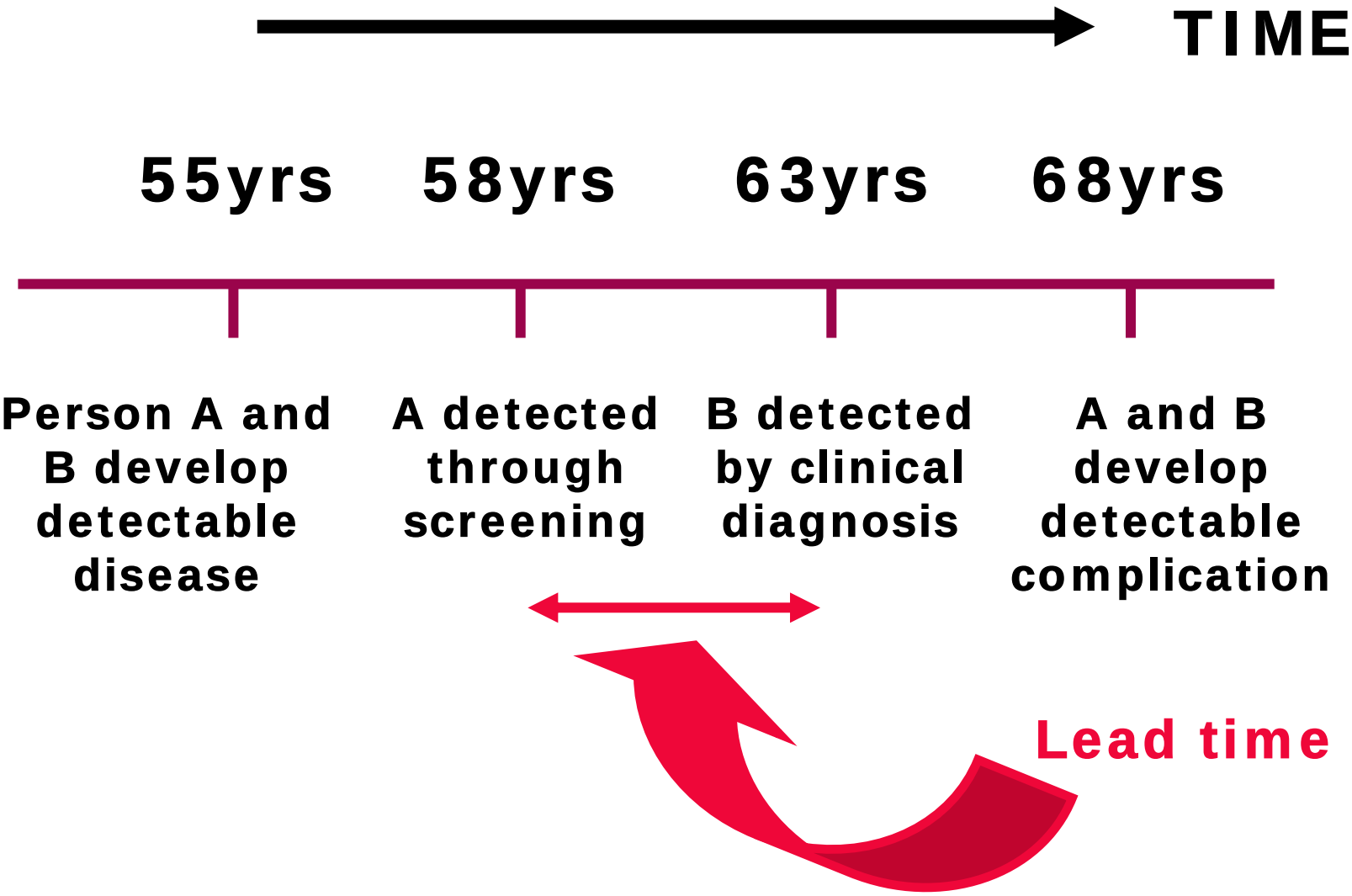
BMC Public Health 2008;8:350.

Results

	Invited Mean (SD)	Not Invited Mean (SD)	p-value (MWU test)
Anxiety	37.6 (12.2)	34.1 (12.1)	0.015
Self perceived health	3.03 (0.86)	3.05 (0.87)	0.998

- **Mean anxiety score in the 6 new patients was 46.7**
- **ICD-10 threshold for 'clinical anxiety' is 42**
- **Mean anxiety score in pregnant women who have just received an abnormal test result for Down's syndrome / Spina Bifida screening is 46.4**

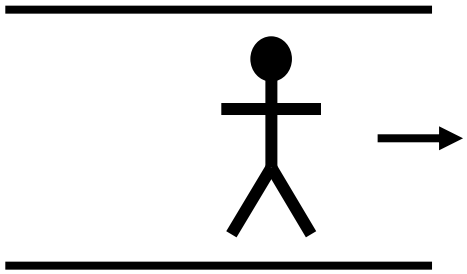
BMC Public Health 2008;8:350.

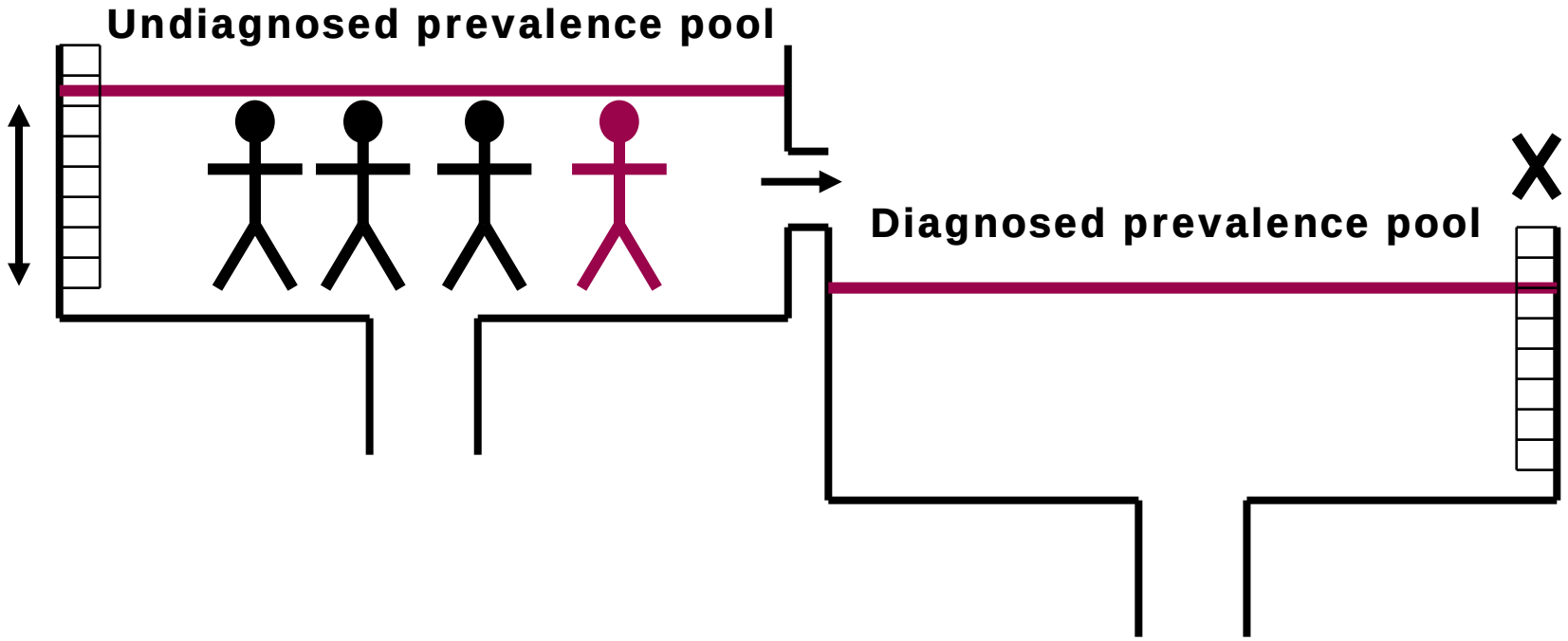

TIME
55yrs
58yrs
63yrs
68yrs
Person A and B develop detectable disease
A detected through screening
B detected by clinical diagnosis
A and B develop detectable complication
Lead time

Lead time bias

… could occur if early detection increased complication-free interval or survival only because detection is earlier not because treatment is effective in delaying or preventing morbidity or death

Incidence

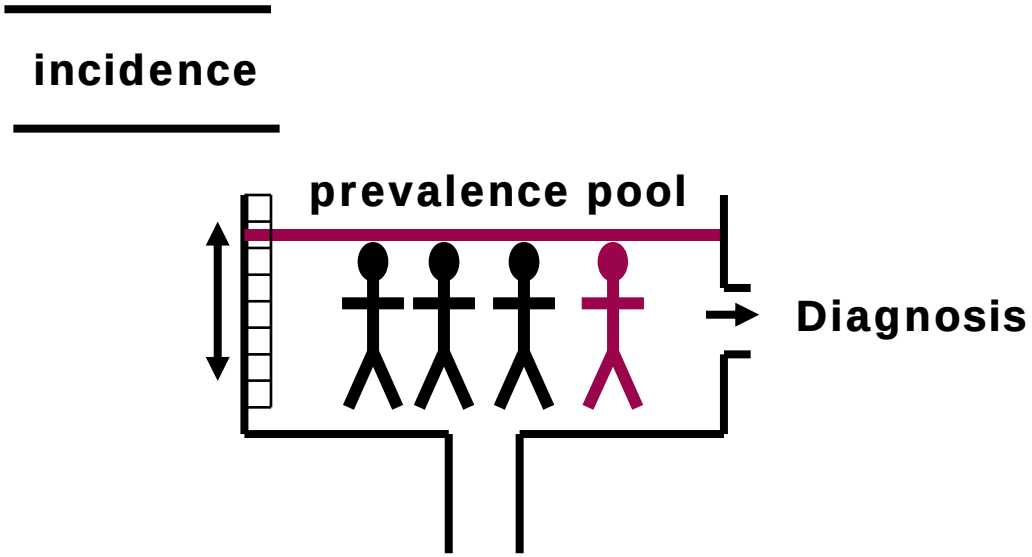




Length-time bias

MRC | Epidemiology Unit

… could occur if individuals identified through screening have a longer pre-clinical phase, milder disease or lower morbidity and mortality regardless of when the disease is detected



ADDITION-Cambridge Study Design

BMC Public Health 2009;9:136.

MRC | Epidemiology Unit

60 practices in the Eastern Region

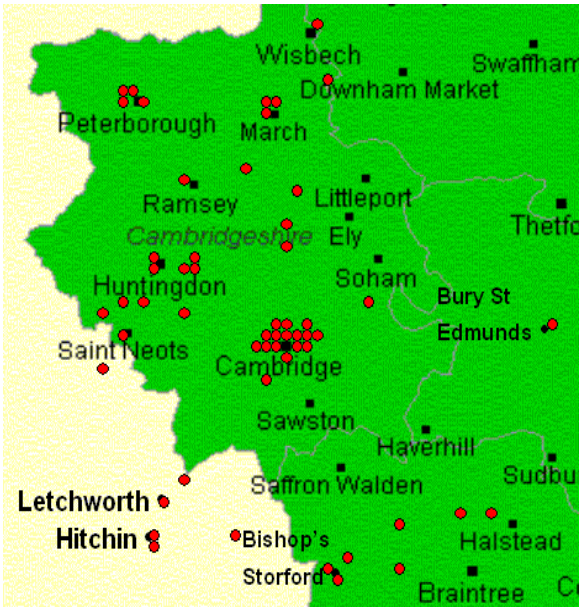
28 practices screening and intensive target driven management of risk factors

27 practices screening and routine care

5 control practices

1 year — **Assessment of CVD risk among screen-detected diabetic patients**

5 years — **Assessment of CVD events and mortality among screen-detected diabetic patients**



MRC | Medical Research Council

DH Department of Health

MRC Medical Research Council

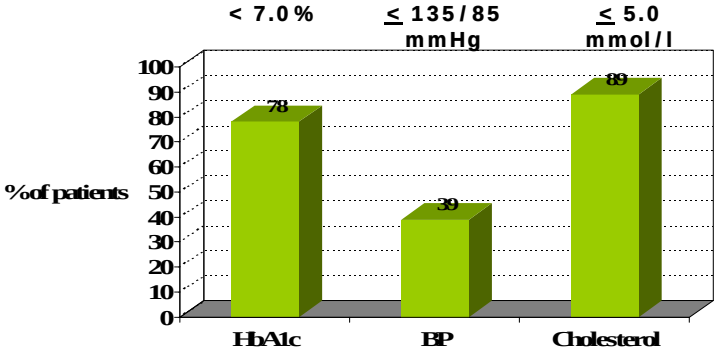
RCGP Royal College of General Practitioners

wellcome trust

Principles of intervention delivery

- Targets GP/practice nurse
  - Practice-based education
  - Academic detailing
  - Opinion leaders
  - Guidelines
  - Target setting
  - Audit and feedback

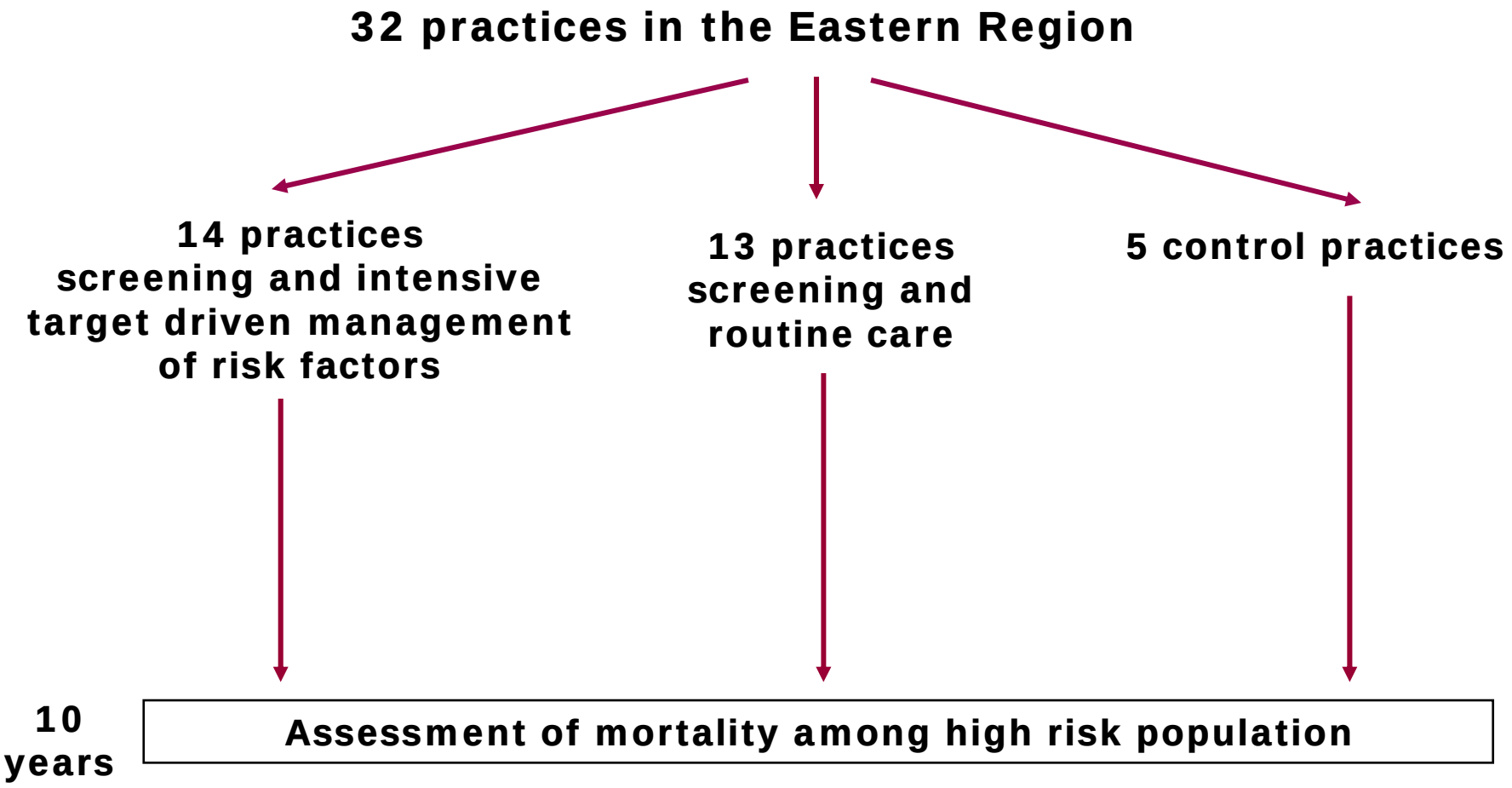
HbA_{1c} < 7.0% (start Rx at 6.5%)
Blood pressure ≤ 135/85 mmHg
Cholesterol < 5.0 mmol/l (IHD-)
< 4.5 mmol/l (IHD+)



- Targets patient
  - Theory-based educational material

ADDITION-Cambridge Study Design

MRC | Epidemiology Unit



MRC | Medical Research Council

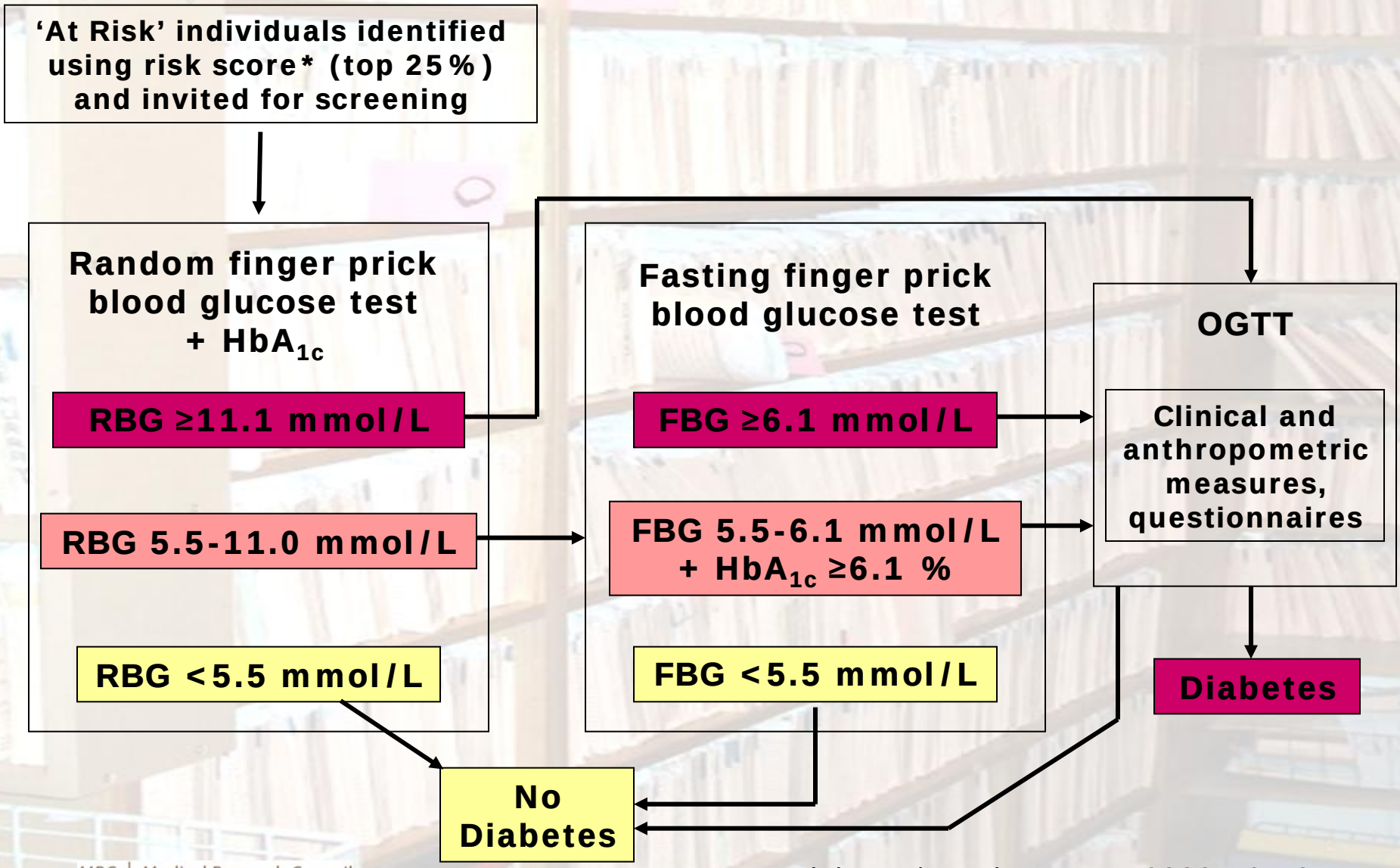
DH Department of Health

MRC Medical Research Council

RC GP Royal College of General Practitioners

wellcome trust

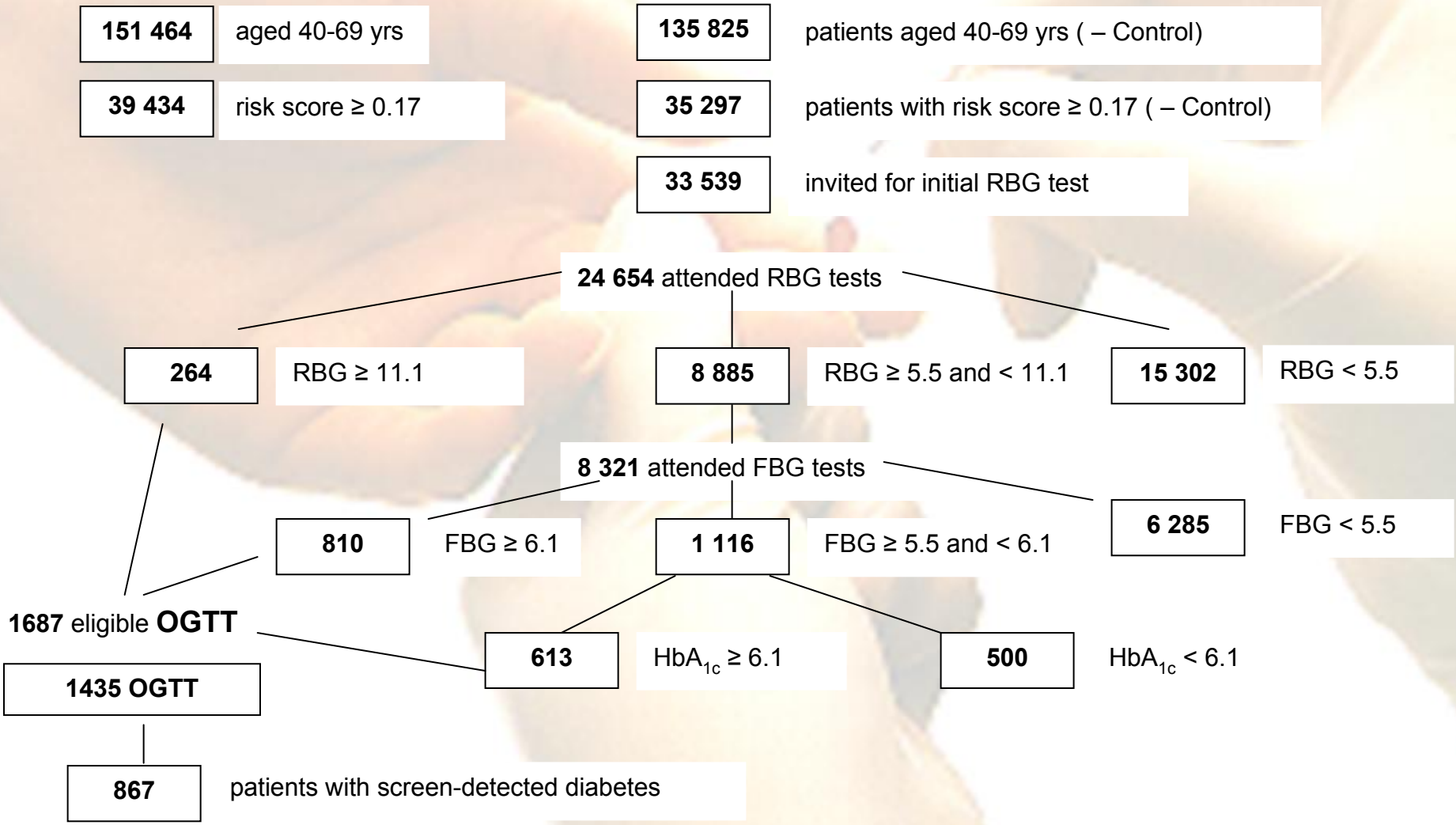
Screening and Diagnostic Procedure



Diabetes/Metab Res Rev 2000;16:164-171.

Outcome of Screening Programme

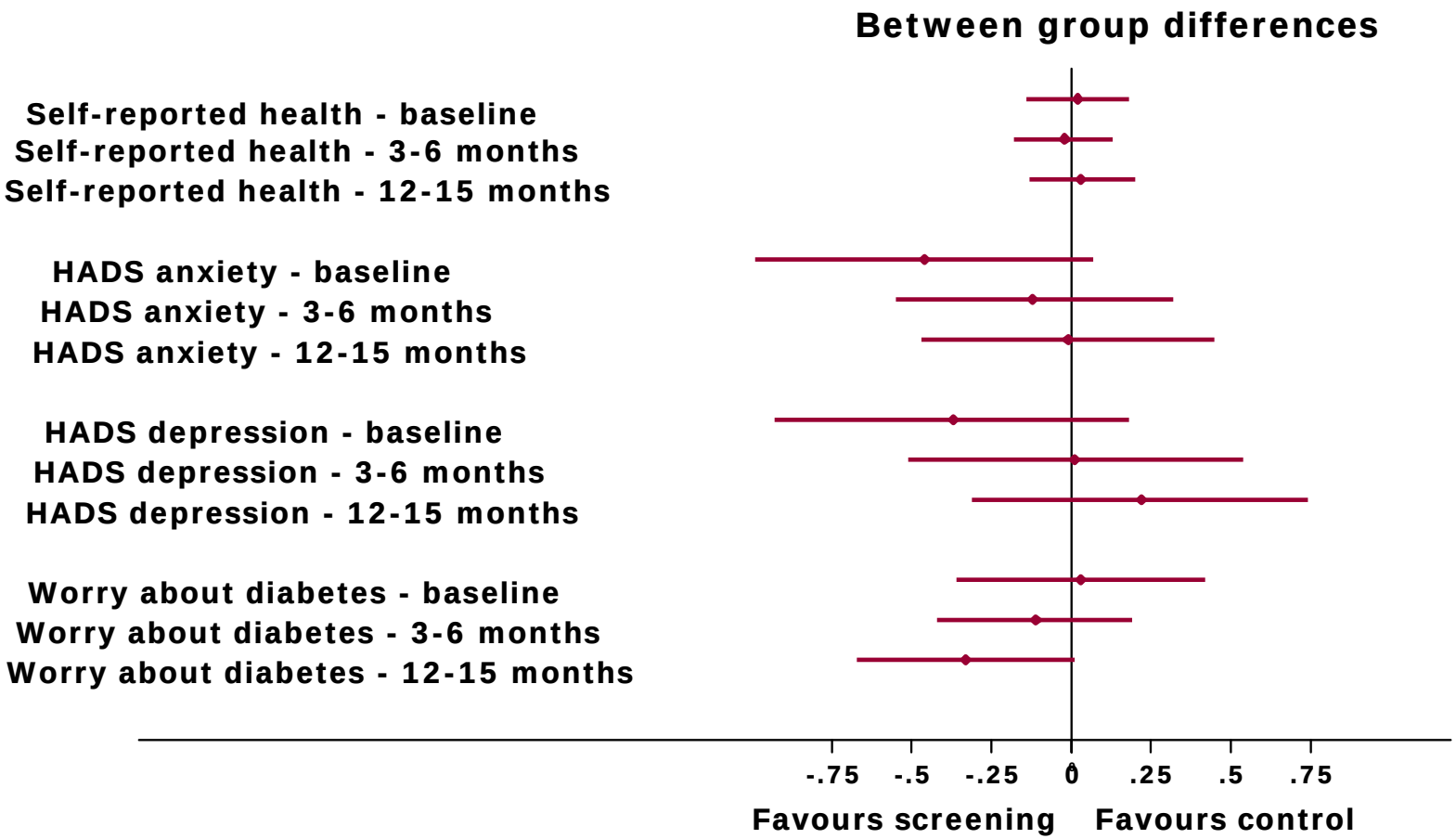
MRC | Epidemiology Unit



No Evidence of Harmful Effects of Screening For Type 2 Diabetes

MRC | Epidemiology Unit

- Parallel group cohort study in 10 screening and five control practices
- Questionnaires sent to 6416 invited for screening and 964 controls



BMJ 2007;335:486-489.
BMJ 2007;335:490-493.

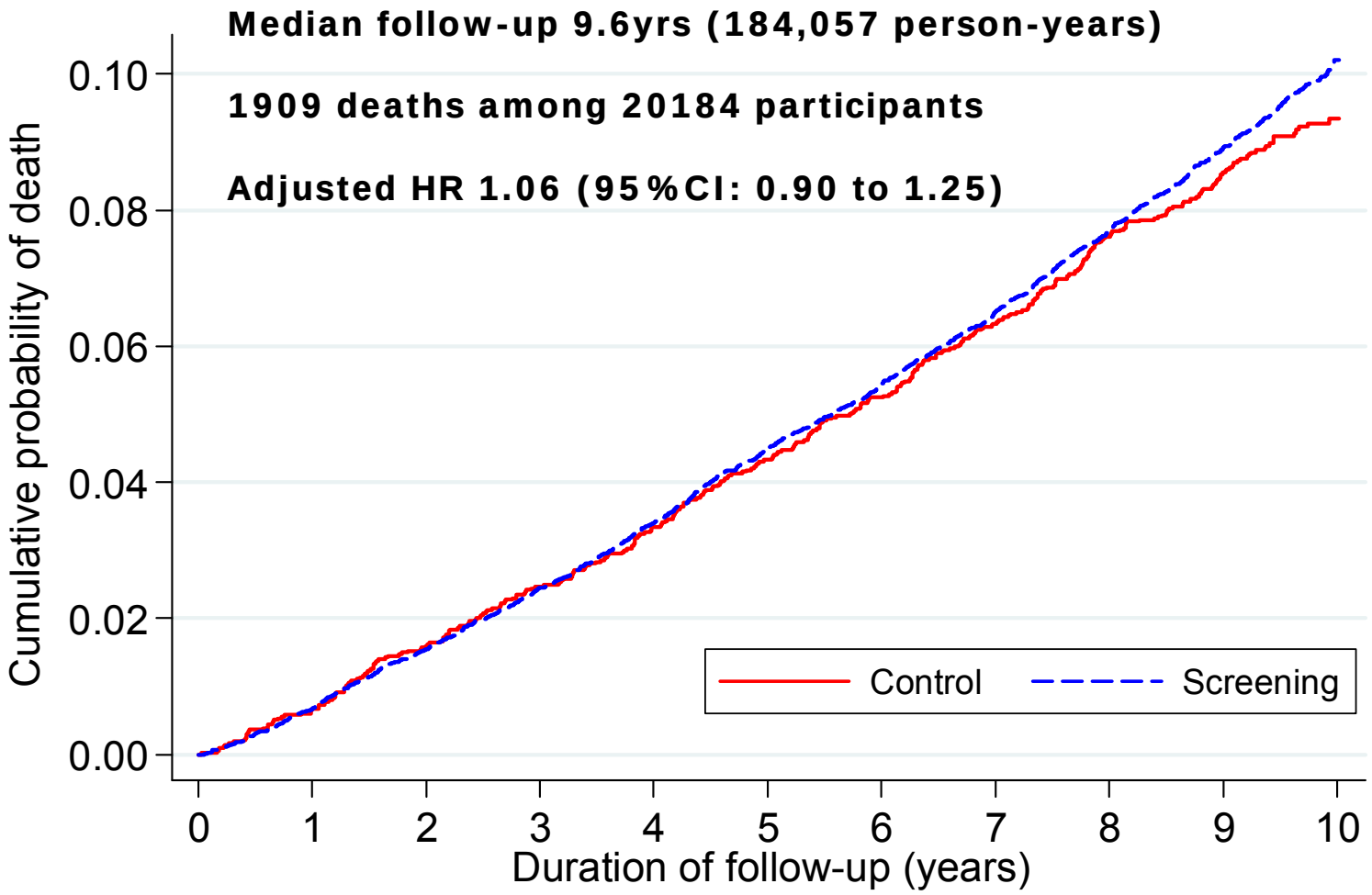
No Evidence of False Reassurance

- Parallel group cohort study in 10 screening and five control practices
- 964 controls and 4370 screening attenders were sent questionnaires
- No significant differences between controls and screen negatives for perceived personal risk, behavioural intentions, or self-rated health after first appointment, at 3-6 months or 12-15 months later

BMJ 2009;339:b4535.

MRC | Epidemiology Unit

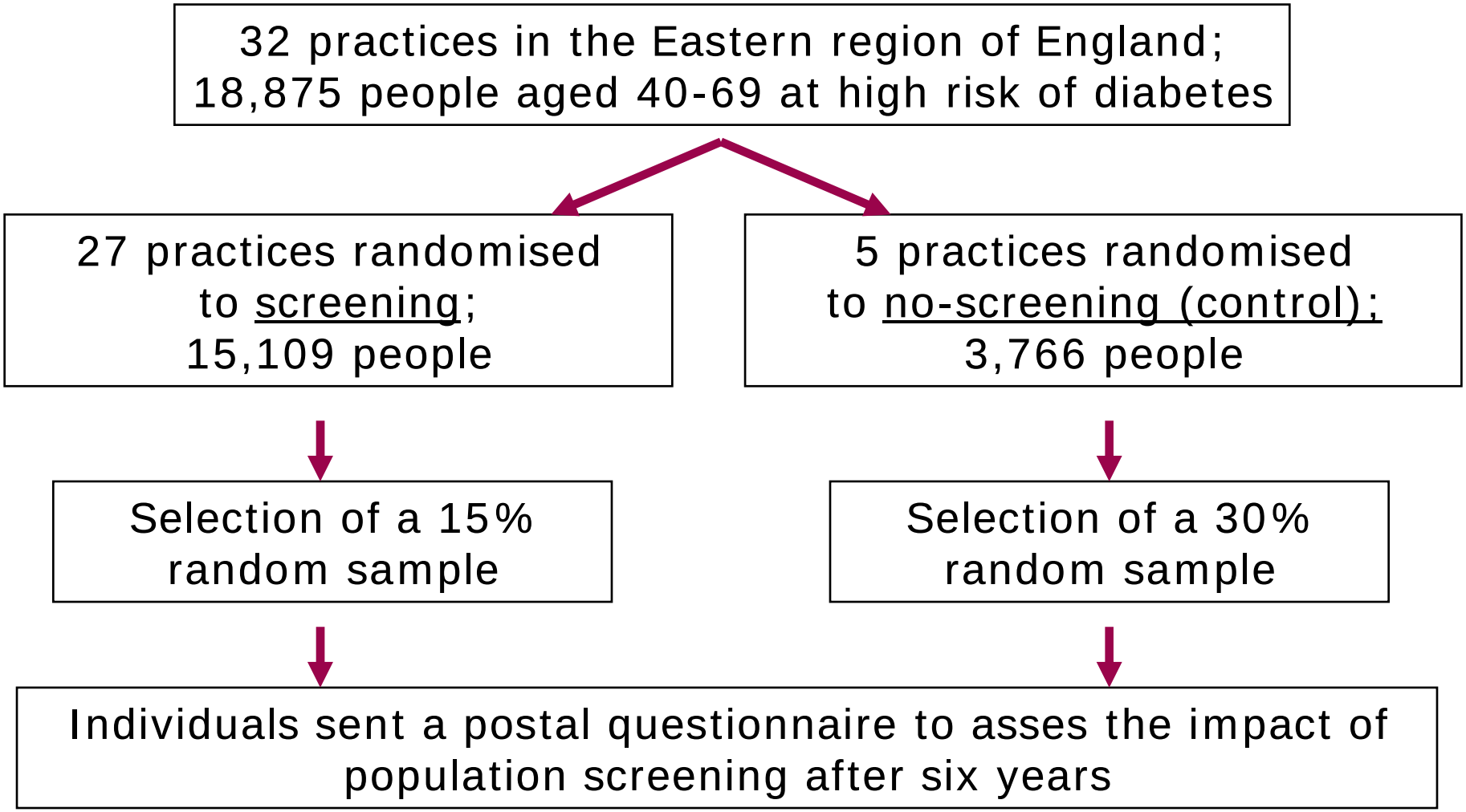
Cumulative incidence of death in the screening and no-screening control groups (ADDITION-Cambridge trial)



MRC | Medical Research Council

Lancet 2012;380:1741-1748

Screening and morbidity



Effect of screening on self-reported cardiovascular morbidity

MRC | Epidemiology Unit

Endpoint	Screening group (n= 1,372)	No-screening group (n=573)	Effect estimate (95% CI)
Angina	11.5%	13.2%	-1.8% (-5.6 to 2.1)
Cardiovascular disease	21.9%	24.7%	- 2.8% (-7.1 to 1.6)
Cardiovascular events	12.5%	13.5%	-1.0% (-5.0 to 3.0)

Effect of screening on self-rated health

Endpoint (mean, SD)	Screening group (n= 1,372)	No-screening group (n=573)	Effect estimate (95% CI)
SF-8 physical summary score	47.4 (9.8)	47.8 (10.3)	-0.23 (-1.69 to 1.22)
SF-8 mental summary score	51.8 (5.6)	52.2 (8.1)	-0.37 (-1.25 to 0.51)
EuroQol-5D rating	0.81 (0.23)	0.80 (0.24)	0.00 (-0.03 to 0.04)
EuroQol visual analogue score	74.5 (16.5)	73.7 (17.2)	0.89 (-1.42 to 3.19)

Screen-detected patients have high but potentially modifiable CVD risk

- 18.5% had pre-existing CVD
- 85.8% had hypertension (BP≥135/85)
  - 35% not prescribed drugs
  - 42.0 % were sub-optimally treated
- 72.5% had dyslipidemia (tot chol>5.0mmol/l)
  - 67.9% not prescribed medication
- 20.0% had microalbumiuria
- 18.1% were smokers
- Median 10-year CVD risk
  - UKPDS: 34.0% in men and 21.5% in women
  - Framingham: 38.6% in men and 24.6% in women
- Absolute risk reduction* achievable through multifactorial therapy ranged from 4.9-9.5 % (UKPDS) and 5.4-10.5% (Framingham)
- Numbers needed to treat* were 11-20 and 10-19

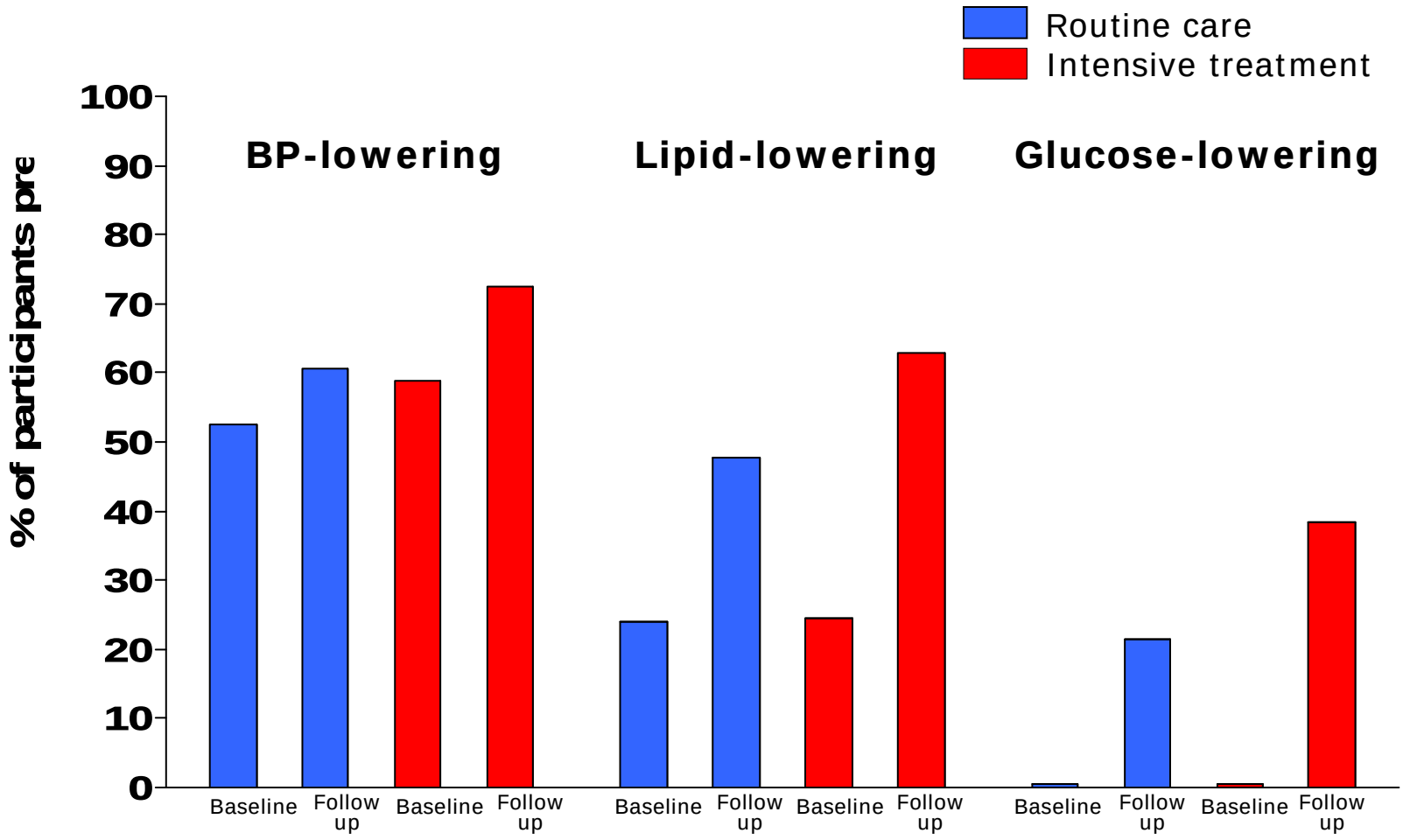
* Conservative scenario (no additive effect of therapies)

Diabet Med 2008;25:1433–1439.

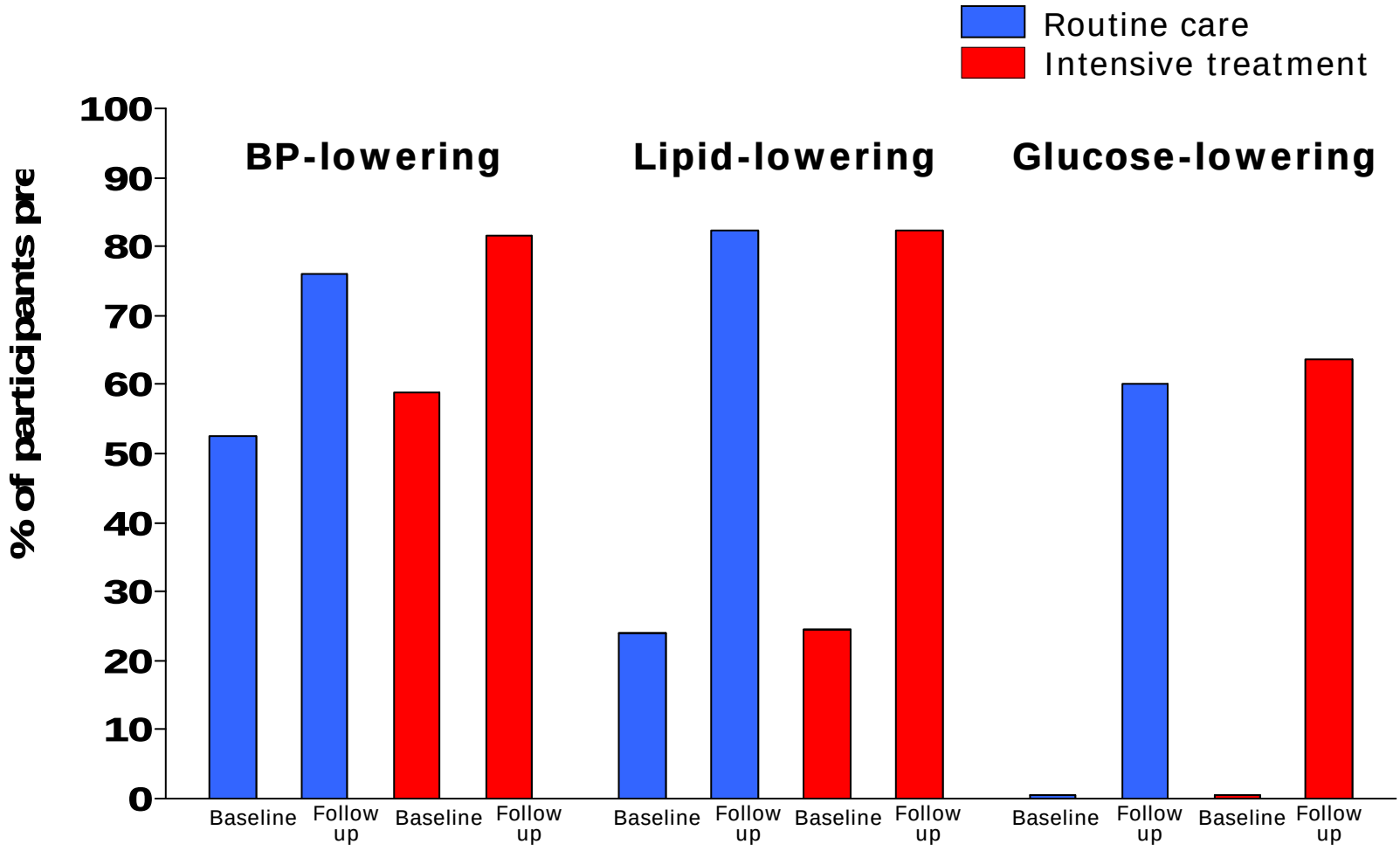
Change in Outcomes Over 1 Year Among Routine Care Participants

	Baseline Mean (SD)	One Year Mean (SD)
HbA1c (%)	**7.33 (1.65)**	**6.62 (0.95)**
BMI kg/m^2	**33.6 (5.9)**	**32.6 (6.0)**
Systolic BP (mmHg)	**142.1 (20.0)**	**138.0 (18.6)**
Diastolic BP (mmHg)	**81.4 (10.3)**	**79.6 (9.9)**
Cholesterol (mmol/l)	**5.42 (1.18)**	**4.74 (0.96)**

Prescribed treatment at baseline and 1yr follow-up

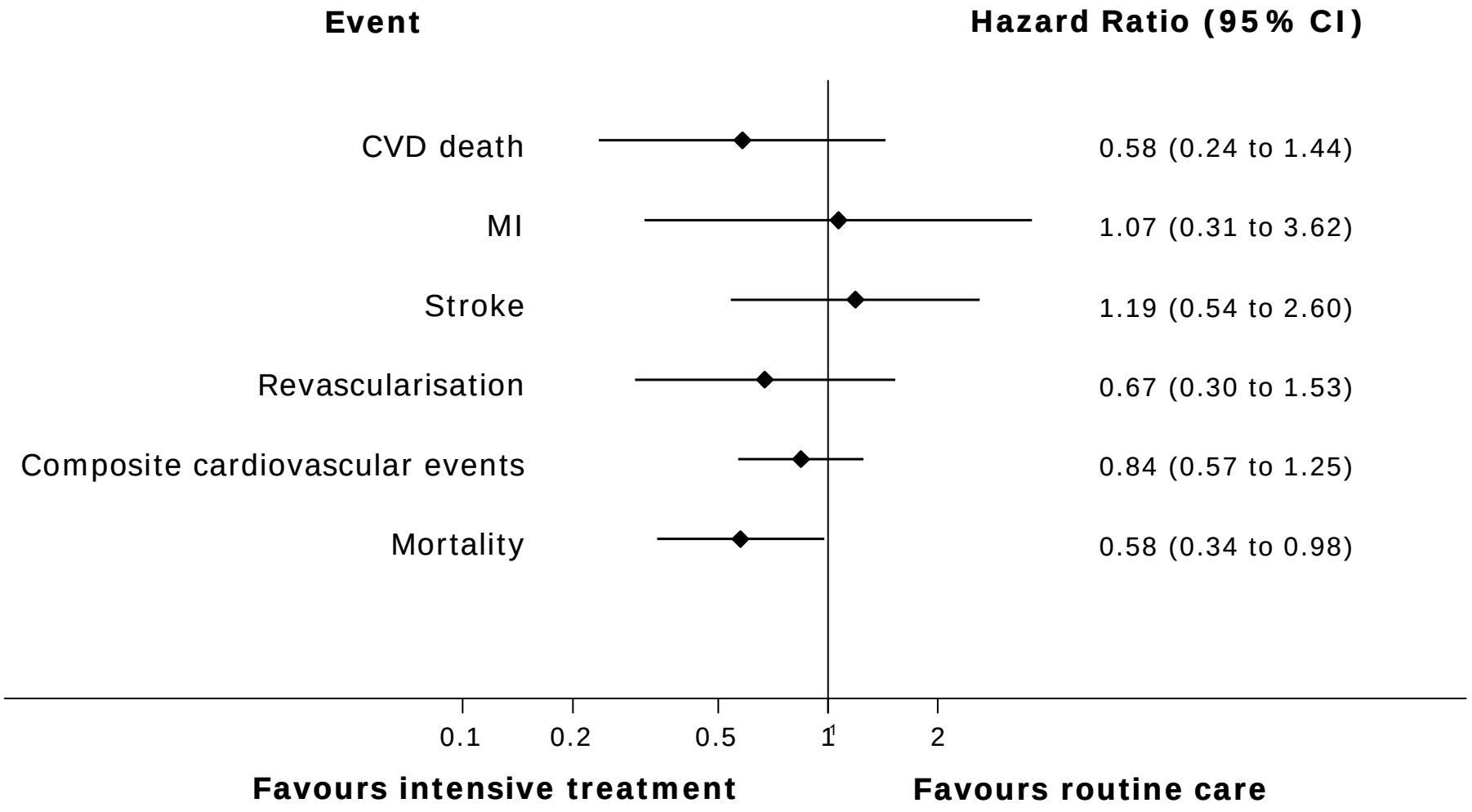


Prescribed treatment at baseline and 5yr follow-up



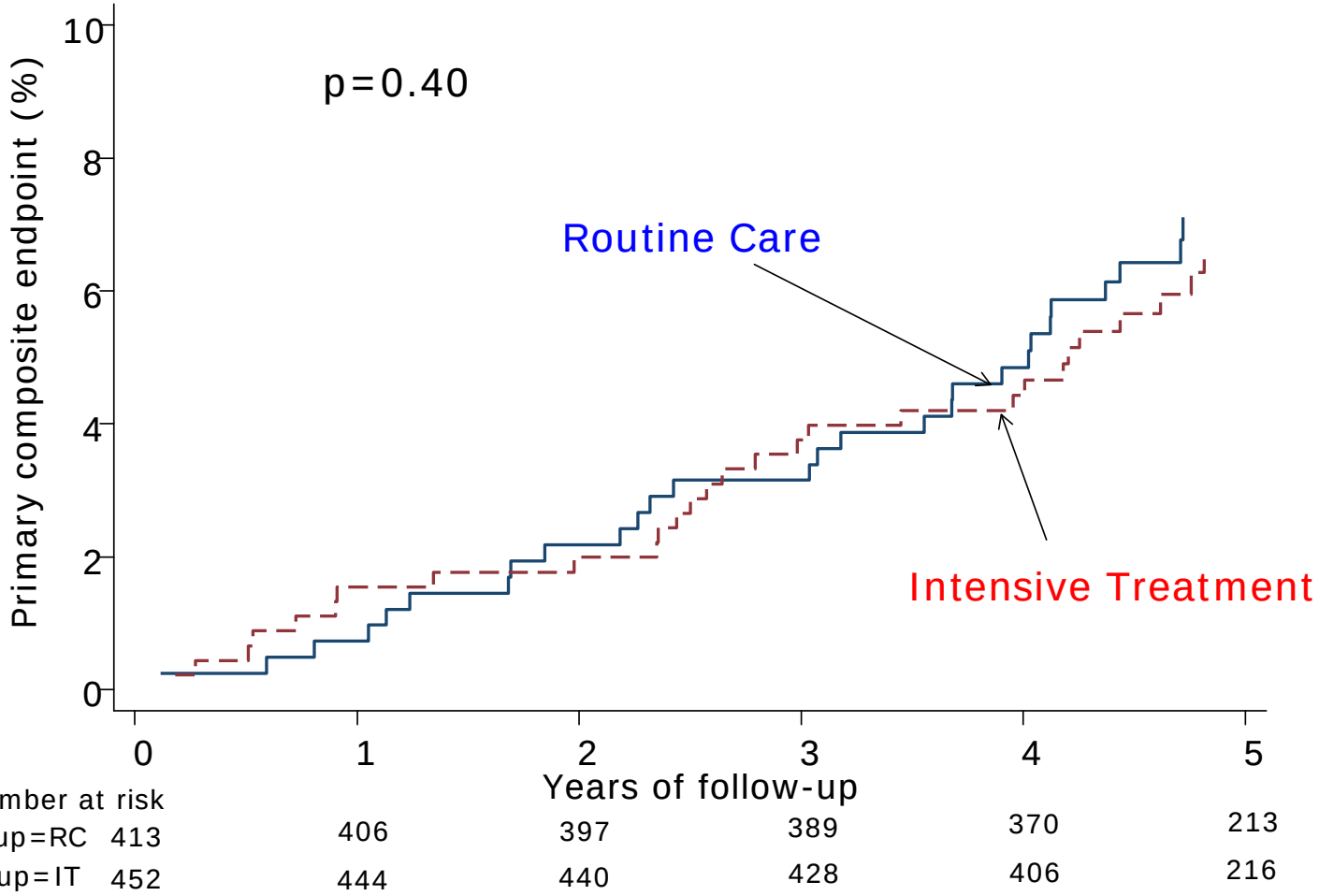
MRC | Epidemiology Unit

Relative risk of CVD endpoints as a first event and total mortality



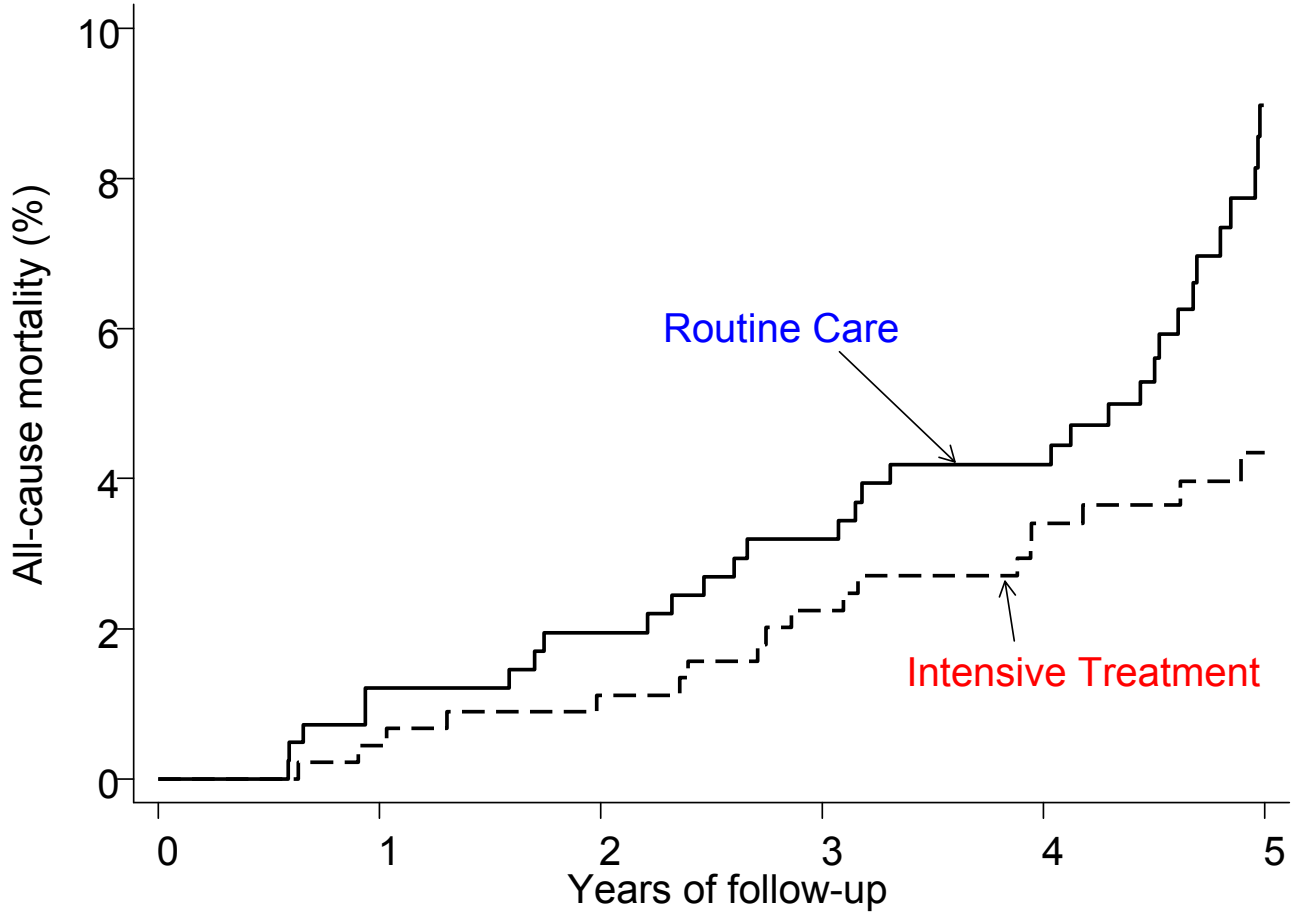
Lancet 2011;378:156-167.

Cumulative probability of composite CVD endpoint



Lancet 2011;378:156-167.

Kaplan-Meier plot of all-cause mortality



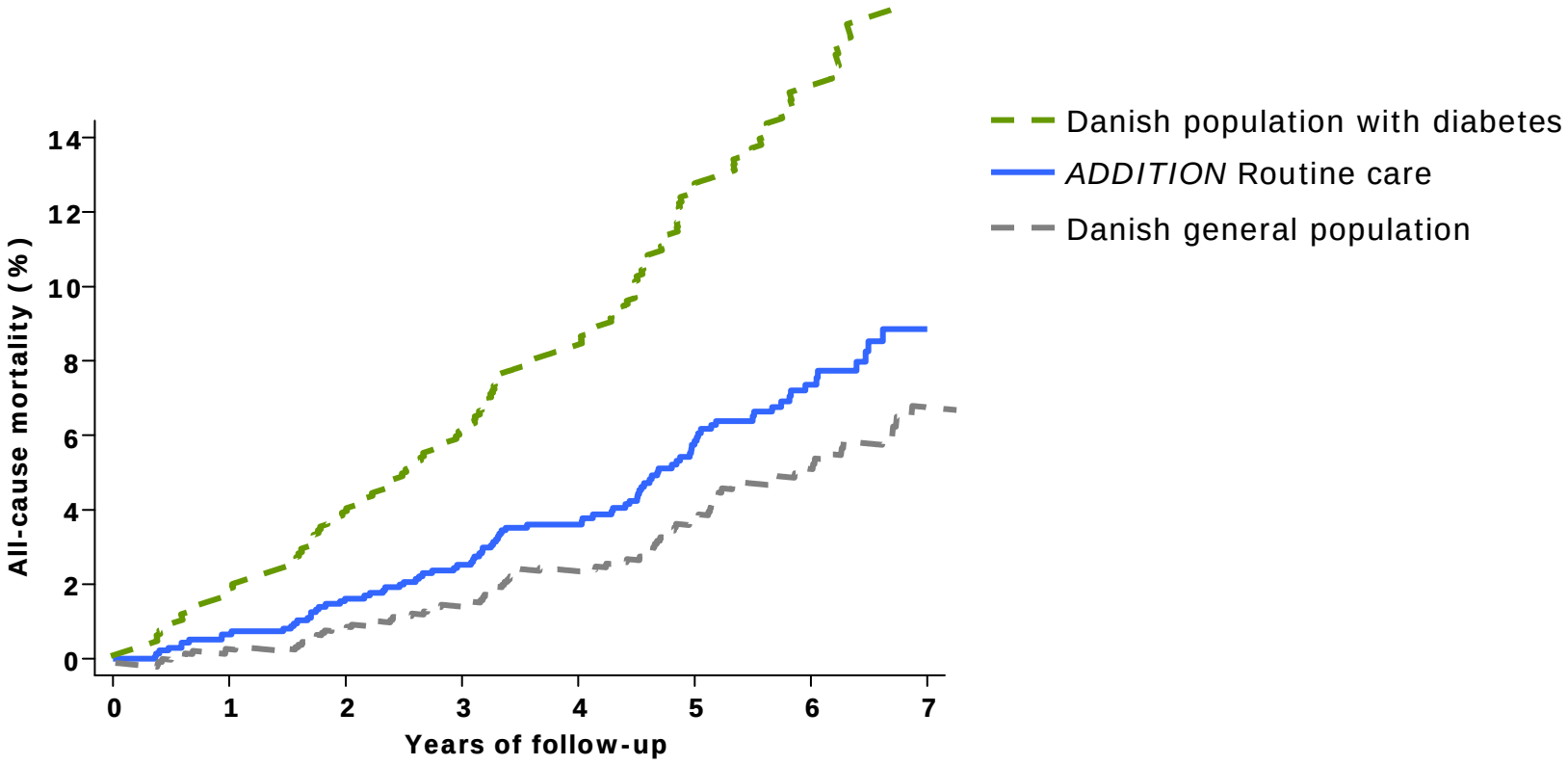
Number at risk

Group = RC	413	406	397	390	371	214
Group = IT	452	445	441	430	408	216

Lancet 2011;378:156-167.

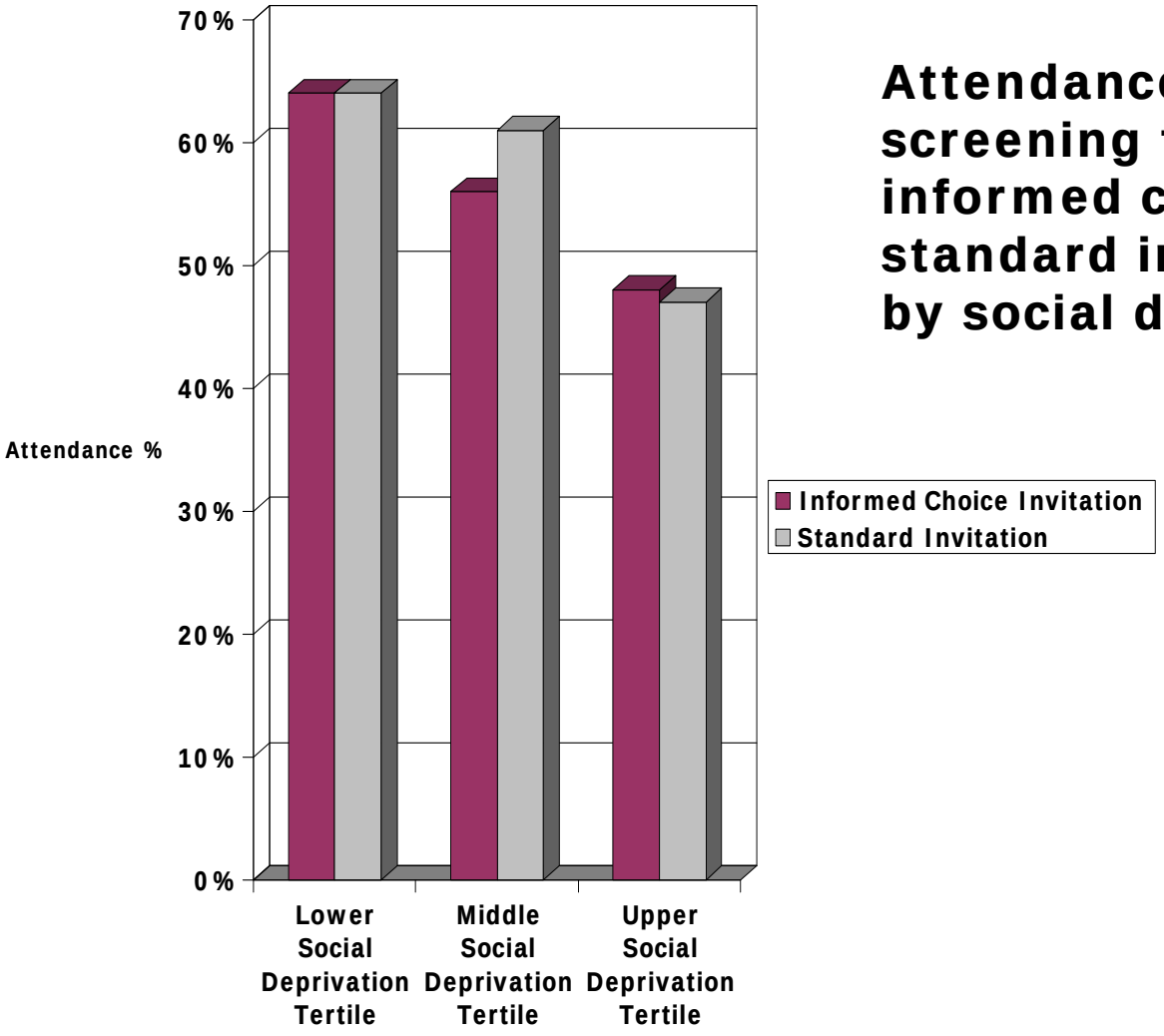
Results in context

- **Mortality in both groups was low**



Danish general registry: Carstensen et al. Diabetologia 2008;51:2187-2196

Attendance for Screening: Social Patterning and Informed Choice



Attendance (%) at diabetes screening following receipt of an informed choice invitation or a standard invitation, grouped by social deprivation tertiles

***BMJ* 2010;340:c2138**

Conclusions

- **Population-based screening for type 2 diabetes is probably feasible…..just**
- **Screening identifies individuals with high but modifiable cardiovascular risk which is reduced following diagnosis, particularly by early intensive treatment**
- **The harmful effects of screening appear to be minimal**
- **The benefits of detection and treatment earlier in the disease trajectory appear to outweigh the harms**

However….

- Uncertainties remain, particularly concerning the cost-effectiveness of
  - treatment in the lead time before clinical diagnosis
  - stepwise screening programmes
- Screening does not reduce overall population mortality
- Given the uncertainties screening should be targeted at those at increased risk
- If screening for diabetes is undertaken it should be combined with screening for other CVD risk factors and preventive interventions among those at risk of diabetes/CVD


MRC | Epidemiology Unit
Thank you for your attention
MRC | Medical Research Council