MRC Epidemiology Unit

Investigating the Causes and Prevention of Diabetes and Obesity

NICE Public Health Programme Guidance

Type 2 diabetes: preventing the progression from pre-diabetes

Dr Simon Griffin

Tuesday 5th July

Plan

- Context
- Finding ‘high risk’ individuals
  - ‘high risk’ of what?
  - effects and adverse effects of ‘risk screening’
- What to do with ‘high risk’ individuals

Approaches to Risk Reduction

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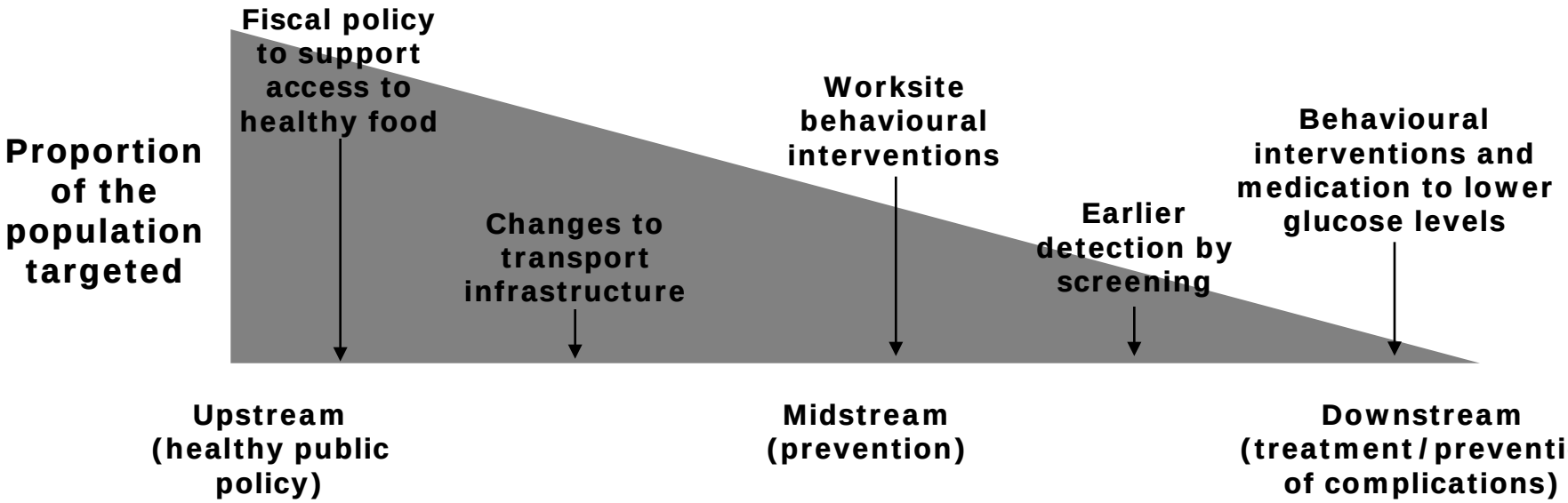
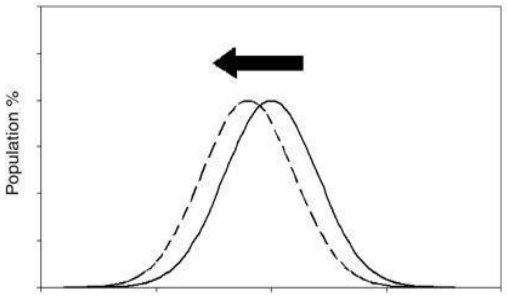
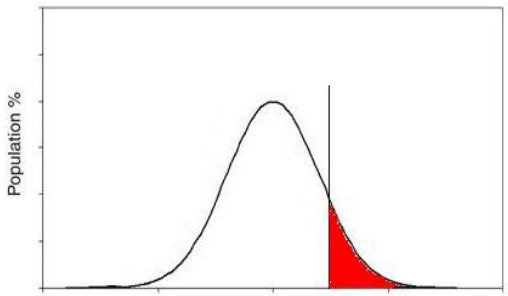




Population-based approach



High risk approach

Long term follow up of the Da Qing study

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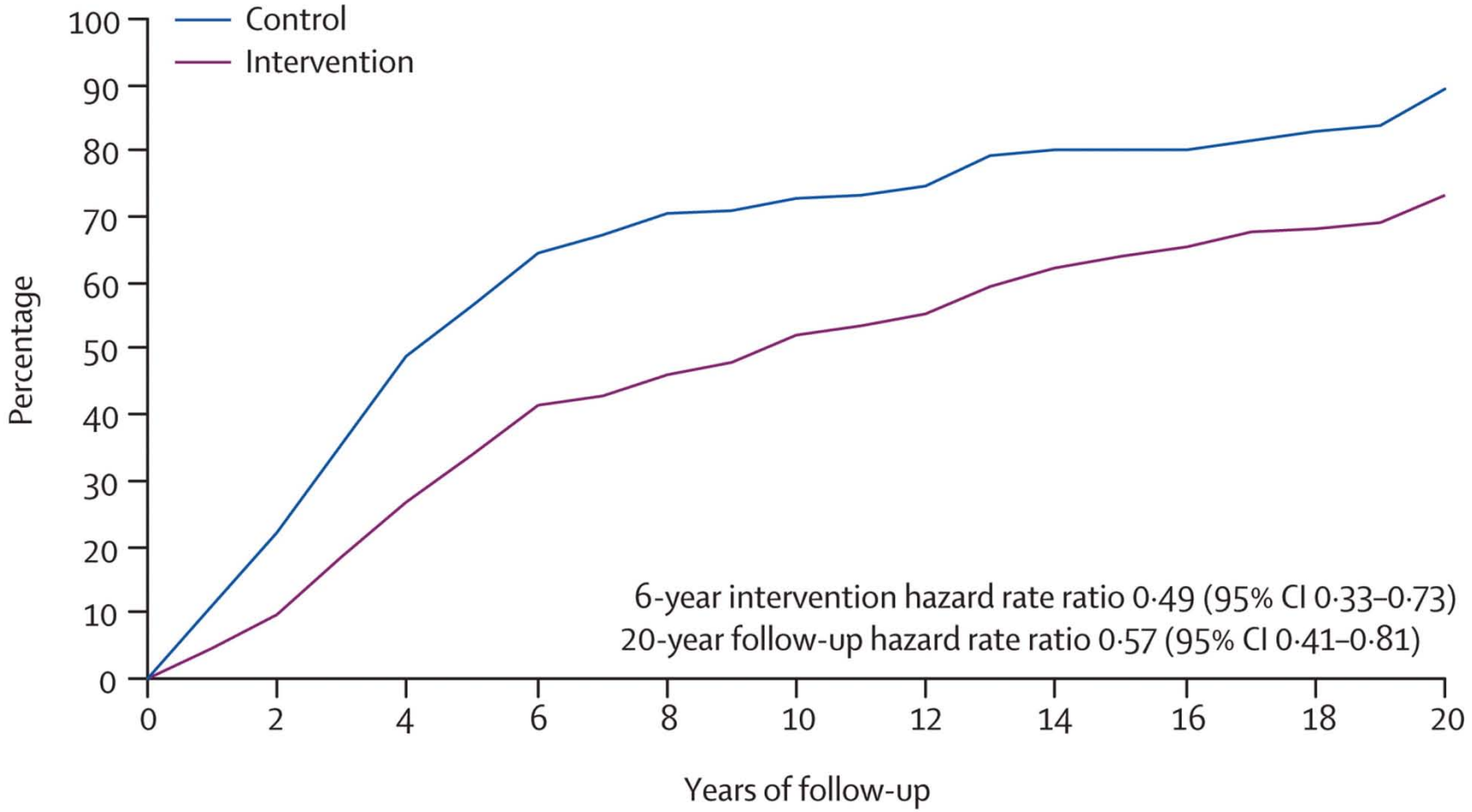

Number at risk

Control	135	105	69	48	40	37	34	27	27	23	14
Intervention	428	387	314	250	230	206	192	161	147	136	114

Li et al, Lancet 2008

Potential Limitations to Translation

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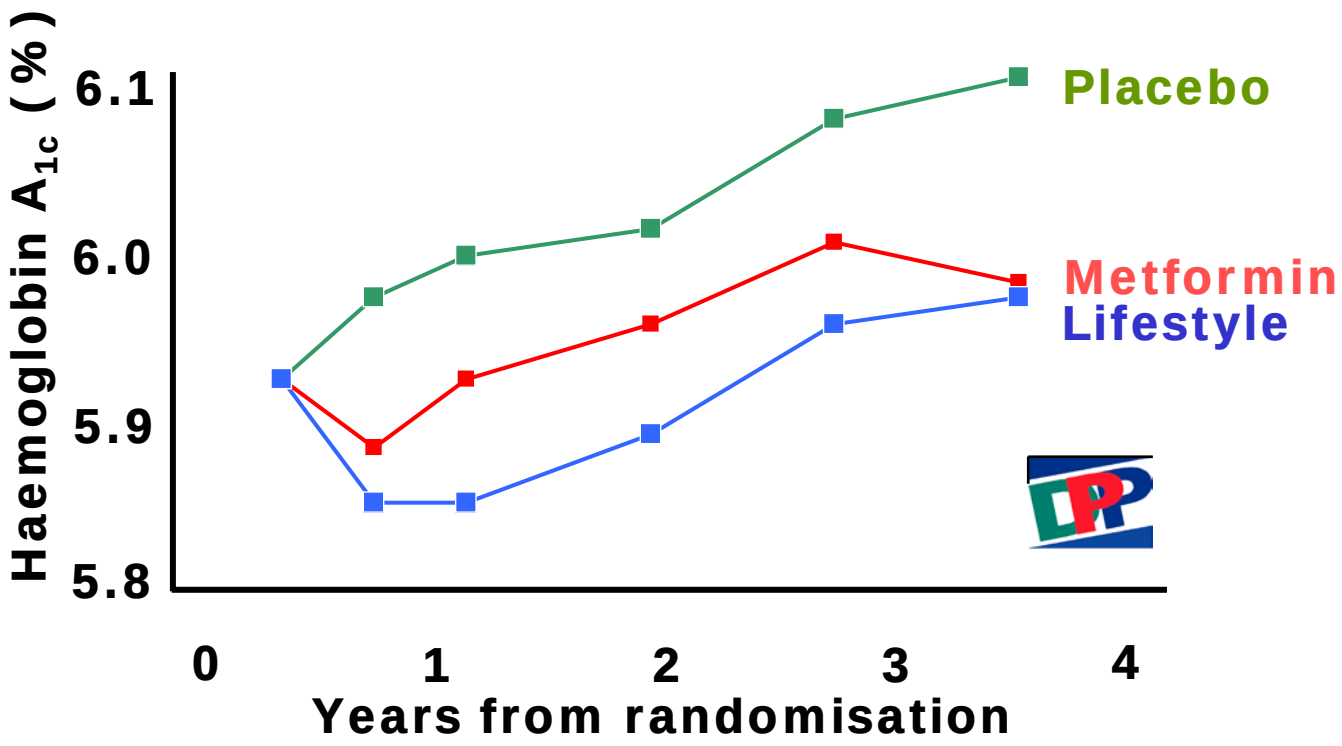
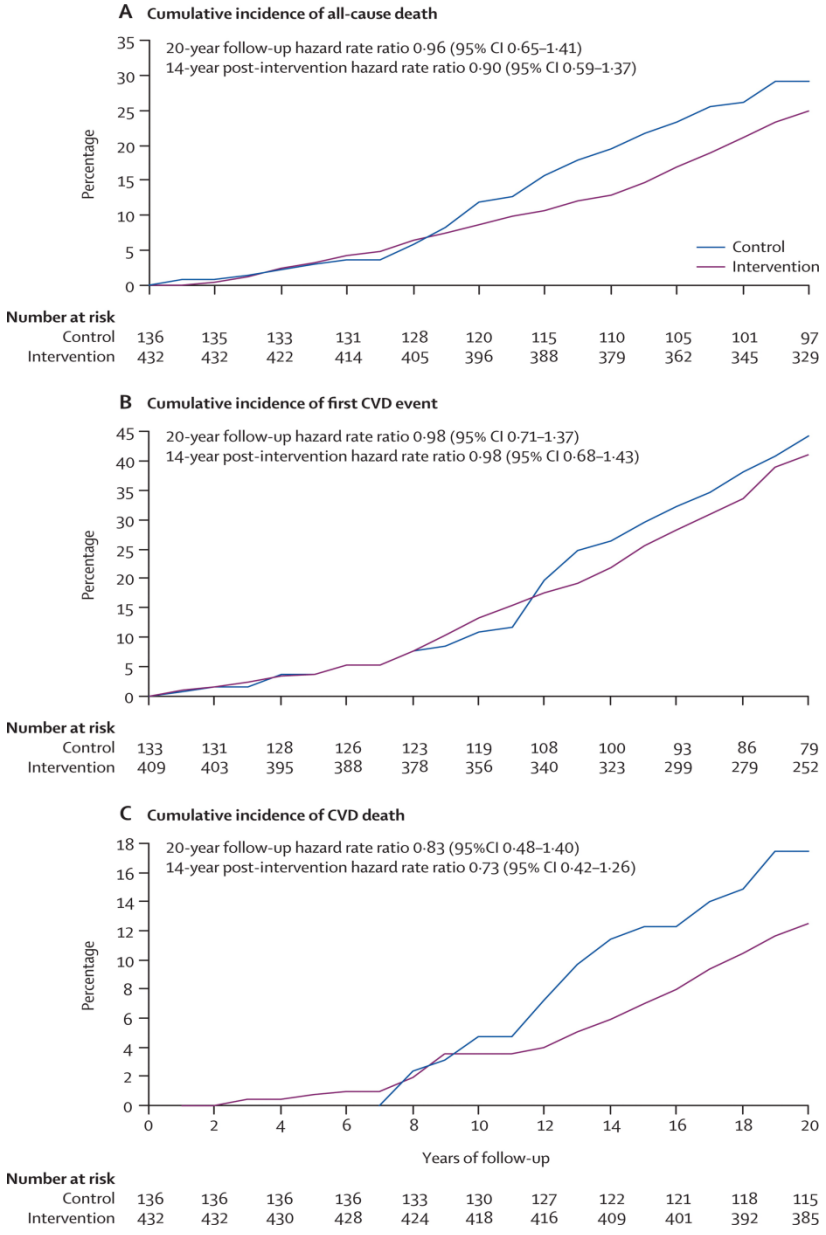
- Feasibility / cost of identification of high risk individuals
- **Feasibility / cost of interventions**
- **Magnitude of effects**

Mean change in HbA_{1c} in the Diabetes Prevention Programme



Long term follow up of the Da Qing study



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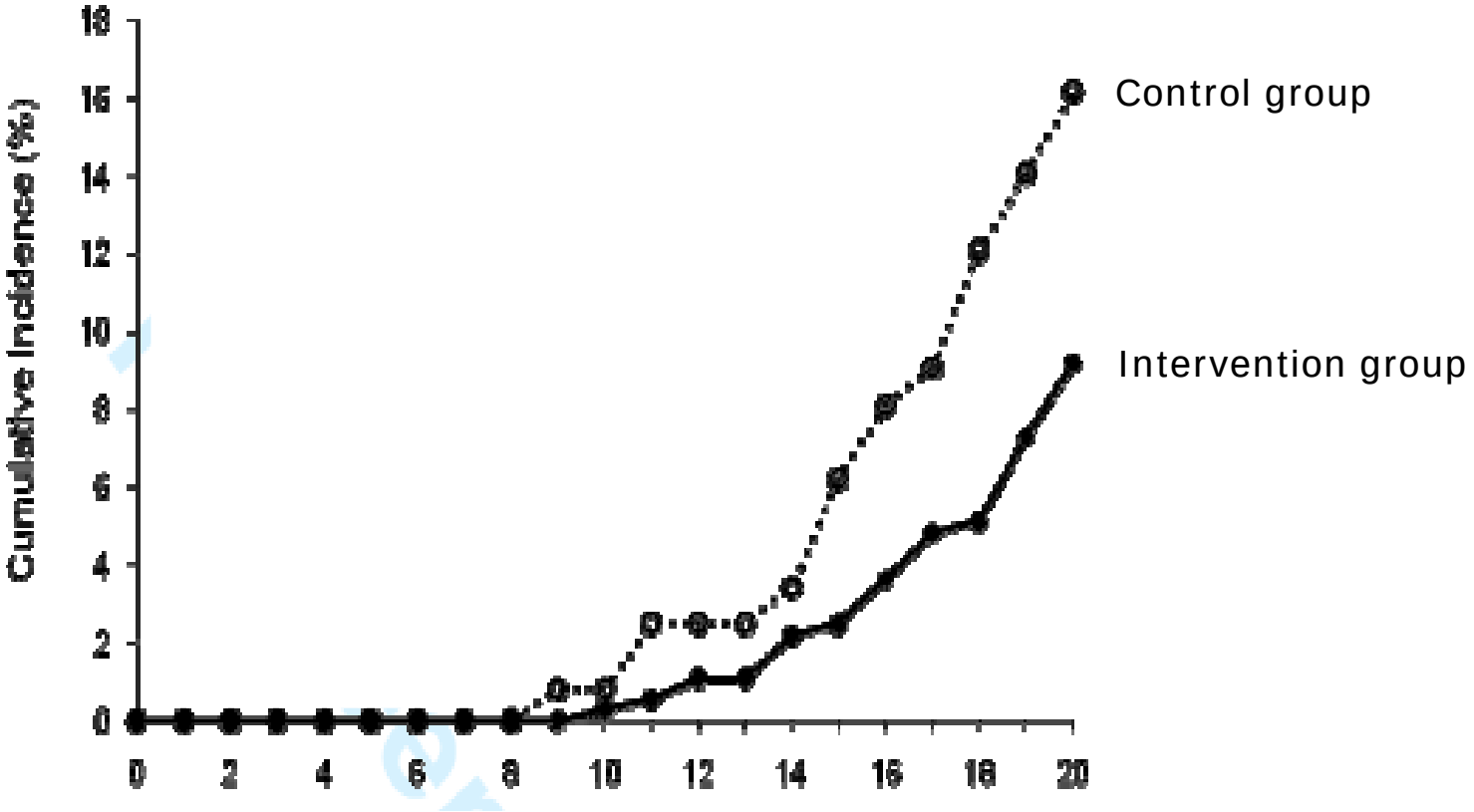
Hazard ratios

All-cause mortality	0.90 (0.59-1.37)
Incidence of first CVD	0.98 (0.68-1.43)
CVD mortality	0.73 (0.42-1.26)

Li et al, Lancet 2008

Long term follow up of the Da Qing study

Cumulative incidence of severe retinopathy
(hazard ratio 0.53 95%CI: 0.29 to 0.99)

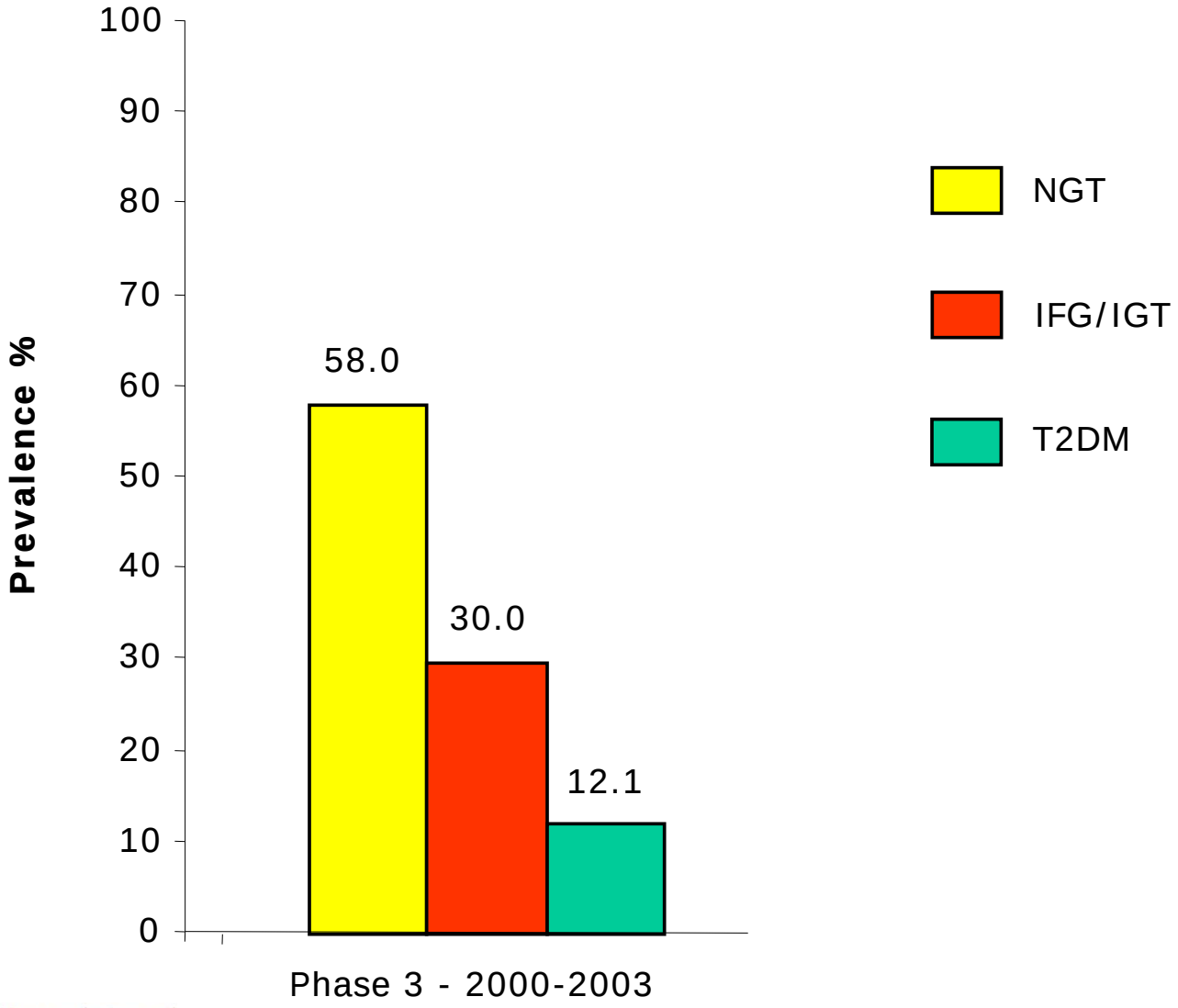


Diabetologia 2011;54:300-307

Plan

- Context
- **Finding 'high risk' individuals**
  - **'high risk' of what**
  - **effects and adverse effects of 'risk screening'**
- **What to do with 'high risk' individuals**

Glucose tolerance category at follow-up among those with IFG/IGT in 1990-92: The Ely Study



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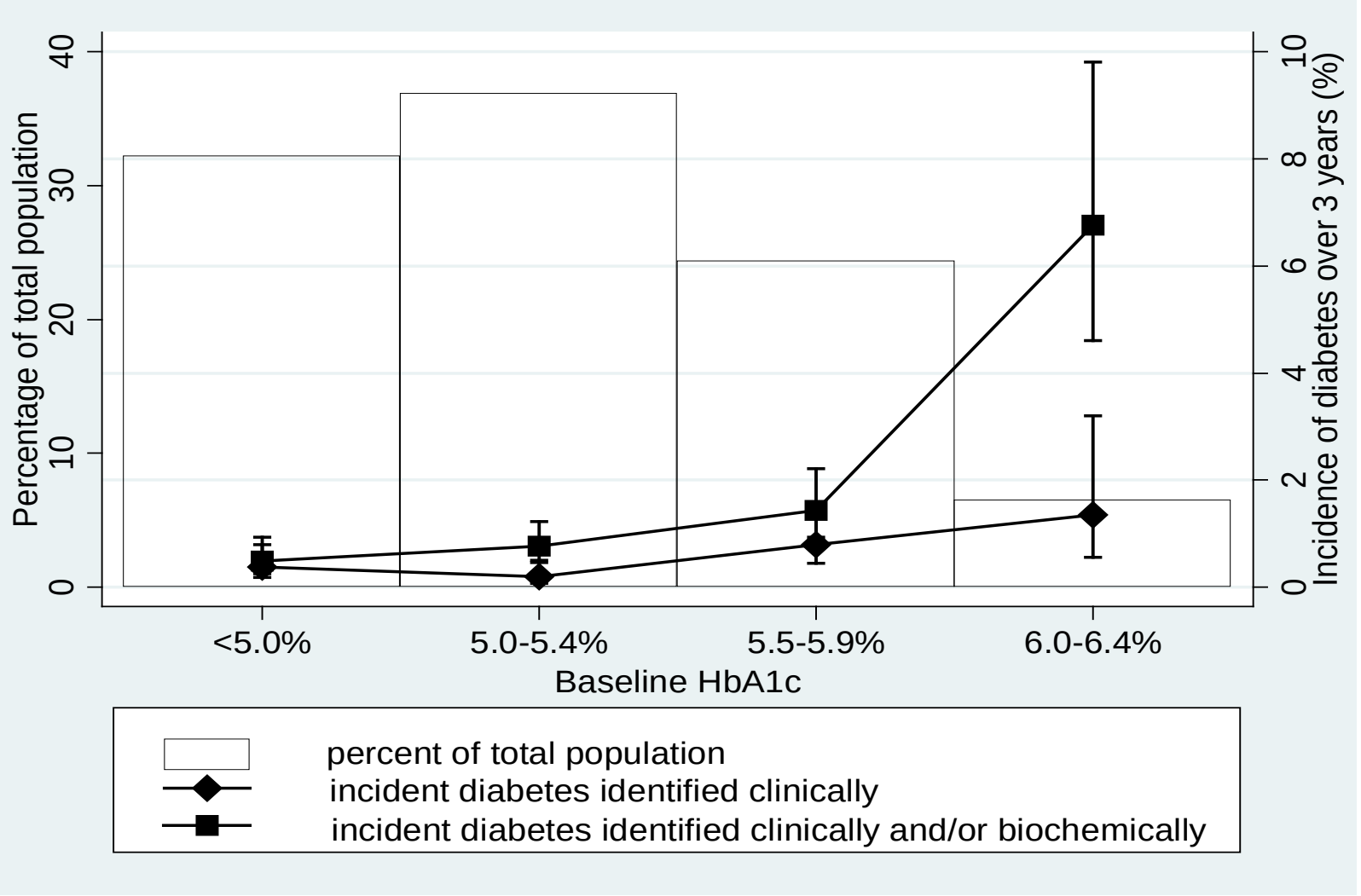
Forouhi et al, *Diabetic Med* 2007;24:200-7.

Incidence of diabetes over 3 years by baseline HbA1c categories in the EPIC-Norfolk cohort (n=5,735)



Diabetes Care 2011;34:950-956

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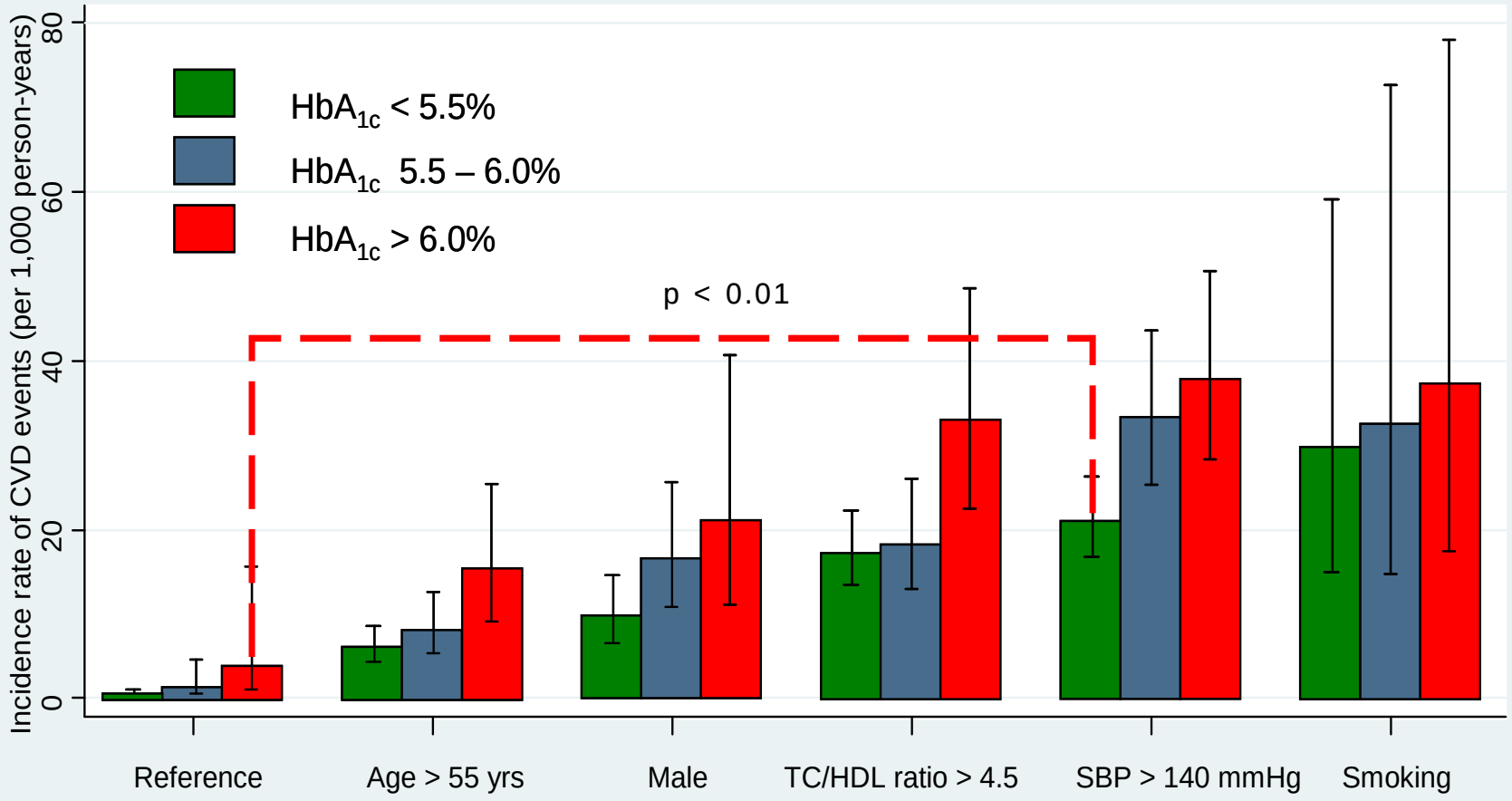
Absolute rates of cardiovascular events over 10 years in individuals with different levels of CVD risk factors in EPIC-Norfolk (n=10,144)



Reference group: non-smoking women aged ≤ 55 years with a SBP of ≤ 140 mm Hg and a TC/HDL ratio of ≤ 4.5, * p < 0.001

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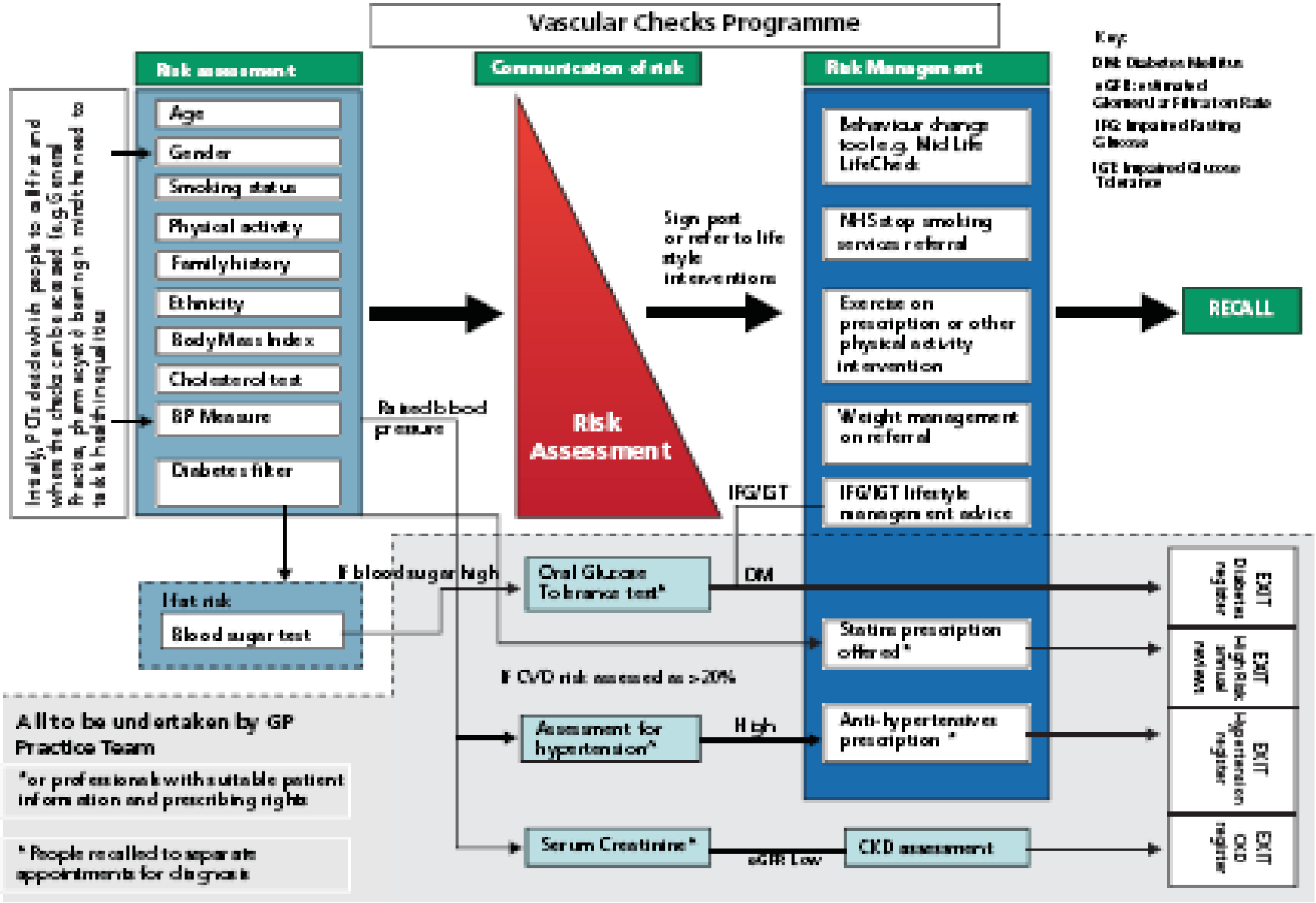
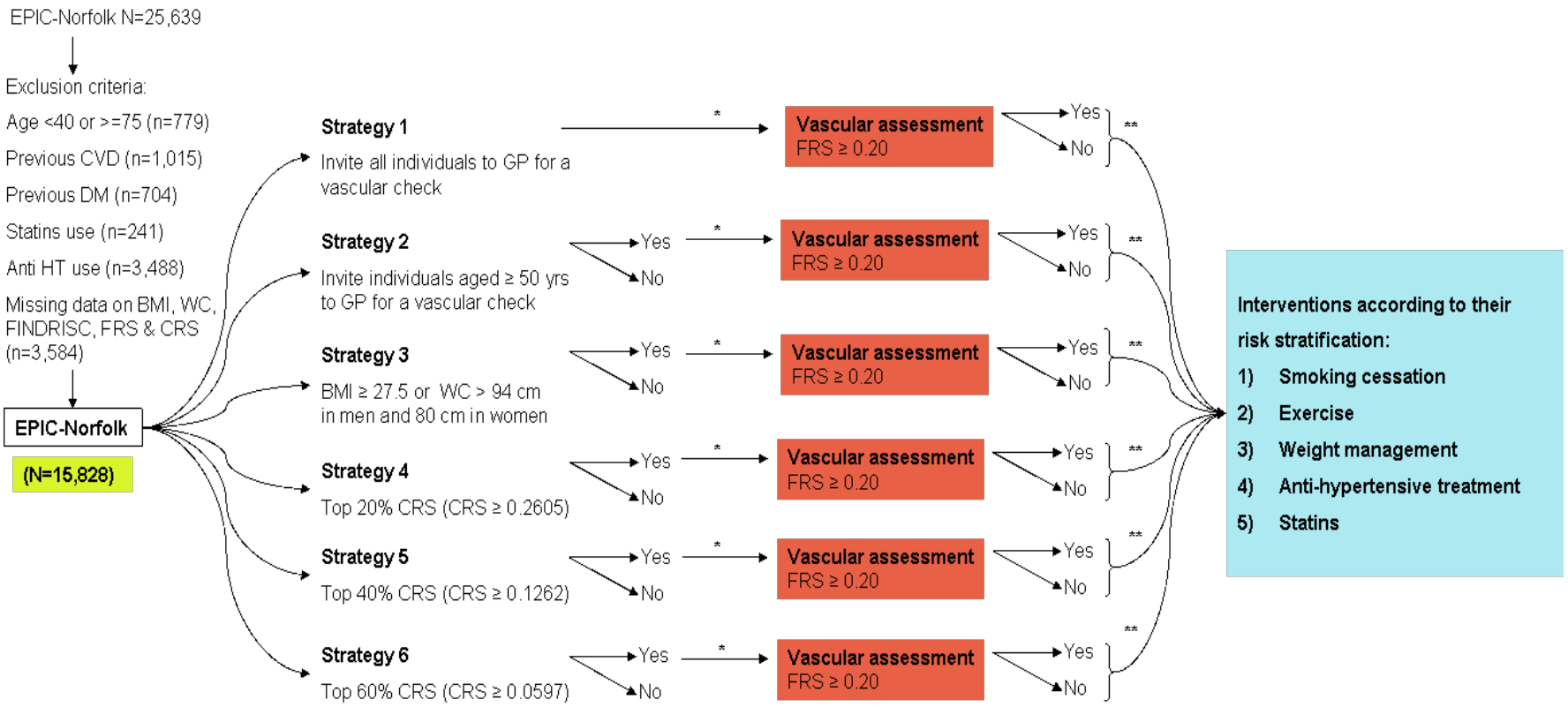
Diabetologia 2010;54:291-299


Vascular Checks Programme
Risk assessment
Communication of risk
Risk Management
Key:
DM: Diabetes Mellitus
eGFR: estimated Glomerular Filtration Rate
IFG: Impaired Fasting Glucose
IGT: Impaired Glucose Tolerance
Initially, PCTs decide which people to call first and when the checks can be assessed (e.g. 5 annual Practice, pharmacy etc) bearing in mind the need to tackle health inequalities
Age
Gender
Smoking status
Physical activity
Family history
Ethnicity
Body Mass Index
Cholesterol test
BP Measure
Diabetes filter
Raised blood pressure
Risk Assessment
Sign post or refer to life style interventions
Behaviour change tool e.g. Mid Life LifeCheck
NHS stop smoking services referral
Exercise on prescription or other physical activity intervention
Weight management on referral
IFG/IGT lifestyle management advice
RECALL
IFG/IGT
At risk
Blood sugar test
If blood sugar high
Oral Glucose Tolerance test*
DM
Statins prescription offered*
If CVD risk assessed as >20%
Assessment for hypertension*
High
Anti-hypertensives prescription *
Serum Creatinine*
eGFR Low
CKD assessment
EXIT
Diabetes register
EXIT
High Risk annual review
EXIT
Hypertension register
EXIT
CKD register
All to be undertaken by GP Practice Team
*or professionals with suitable patient information and prescribing rights
* People recalled to separate appointments for diagnosis

Modelled population-based screening strategies



* 75% turn up for vascular assessment

** stratified by obese, smoking, hypertension with different rates of uptake, adherence, and RRR for each intervention

BMJ 2010;340:c1693

Predictive ability of different strategies

Strategy		Number of individuals invited to vascular risk assessment (%)	Sensitivity (%)	Specificity (%)	aROC
Strategy 1	Total	15,828 (100)	53.6 (50.7-56.4)	81.5 (80.9-82.1)	0.68 (0.66-0.69)
All individuals	Men	7,077 (100)	67.5 (64.1-70.7)	65.8 (64.6-67.0)	0.67 (0.65-0.68)
	Women	8,751 (100)	27.6 (23.5-32.2)	93.3 (92.7-93.9)	0.60 (0.58-0.63)
Strategy 2	Total	11,482 (73)	52.2 (49.4-55.1)	82.0 (81.4-82.6)	0.67 (0.66-0.69)
Age ≥ 50 yrs	Men	5,266 (74)	65.6 (62.1-68.9)	66.9 (65.8-68.1)	0.66 (0.65-0.68)
	Women	6,216 (71)	27.4 (23.3-31.9)	93.4 (92.8-93.9)	0.60 (0.58-0.63)
Strategy 6	Total	9,495 (60)	51.8 (49.0-54.7)	82.3 (81.7-83.0)	0.67 (0.66-0.69)
60% top CRS	Men	5,588 (79)	66.2 (62.8-69.5)	66.6 (65.4-67.7)	0.66 (0.65-0.68)
	Women	3,907 (45)	25.1 (21.1-29.5)	94.3 (93.7-94.7)	0.60 (0.58-0.62)

BMJ 2010;340:c1693

CVD cases that could be prevented

Strategy		Number needed to screen to prevent one new CVD case	Number needed to intervene to prevent one new CVD case	NEPP	NEPP for the UK (26,954,900 people aged 40-74 years)
Strategy 1	Total	794	110	15.0 (11.5 - 20.6)	25,464 (19,537 - 35,090)
All individuals	Men	473	77	11.2 (8.9-14.5)	19,090 (15,240 - 24,679)
	Women	1,754	208	3.7 (2.5 - 6.1)	6,374 (4,297 - 10,411)
Strategy 2	Total	619	97	13.9 (10.8 - 18.9)	23,698 (18,333 - 32,211)
Age ≥ 50 yrs	Men	377	70	10.5 (8.4 -13.3)	17,854 (14,378 - 22,729)
	Women	1,358	181	3.4 (2.3 - 5.6)	5,844 (3,954 - 9,483)
Strategy 6	Total	507	94	14.1 (10.8 - 19.5)	23,940 (18,327 - 33,126)
60% top CRS	Men	385	71	10.9 (8.7 - 14.1)	18,529 (14,772 - 24,002)
	Women	922	172	3.2 (2.1 - 5.4)	5,410 (3,554 - 9,124)

BMJ 2010;340:c1693

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Predictive performance of different screening strategies for risk of type 2 diabetes over 3 years

Strategy	Number of individuals invited to screening (%)	Incident cases of diabetes in risk group (%)	aROC (95%CI) for prediction of incident diabetes
Prestratification followed by HbA_{1c} 6.0-6.4%			
All individuals	5,910 (100)	77 (100)	0.66 (0.60-0.71)
Age ≥ 50 yrs	4,443 (75)	68 (88)	0.65 (0.60-0.71)
Age ≥ 50 yrs and overweight	2,977 (50)	57 (74)	0.64 (0.59-0.70)
CRS ≥0.15	2,361 (40)	49 (64)	0.62 (0.57-0.67)
Prestratification followed by HbA_{1c} 5.0-6.4%			
Age ≥50 yrs AND overweight	2,977 (50)	57 (74)	0.69 (0.64-0.75)
CRS ≥0.15	2,361 (40)	49 (64)	0.68 (0.62-0.73)
Single-step without blood tests			
CRS ≥0.50	N/A	18 (23)	0.57 (0.52-0.62)

In press *Diabet Med* 2011

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Population impact of different screening strategies for risk of type 2 diabetes over 3 years

Strategy	Number of people eligible for lifestyle interventions (% of total population)	Number needed to screen with HbA_{1c} to prevent one new case	Number needed to intervene to prevent one new case	NEPP for an average PCT with 136,900 people aged 40-74 years (lower and upper estimates)
Prestratification followed by HbA_{1c} 6.0-6.4%				
All individuals	289 (5%)	459	23	224 (157-315)
Age ≥ 50 yrs	264 (4%)	358	22	216 (151-306)
Age ≥ 50 yrs and overweight	188 (3%)	268	17	193 (132-277)
CRS ≥0.15	167 (3%)	253	18	162 (107-241)
Prestratification followed by HbA_{1c} 5.0-6.4%				
Age ≥50 yrs AND overweight	818 (14%)	152	43	339 (226-505)
CRS ≥0.15	671 (11%)	136	40	301 (195-459)
Single-step without blood tests				
CRS ≥0.50	599 (10%)	N/A	53	139 (76-202)

In press *Diabet Med* 2011

Screening questionnaires and scores

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

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 kääntö
   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
   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

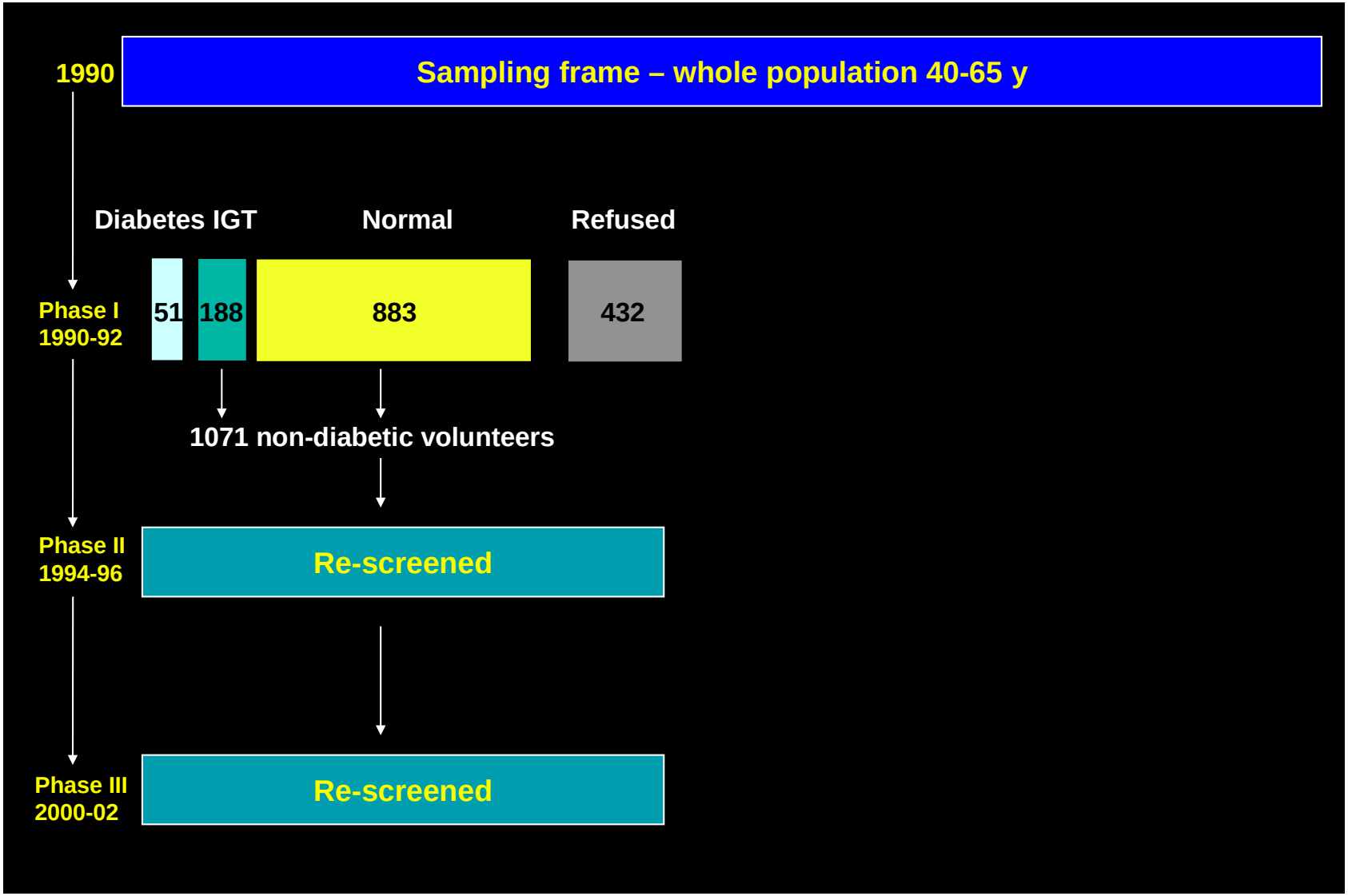
Testin suunnittelu: Professori Jaakko Tu

Diabetes risk scores

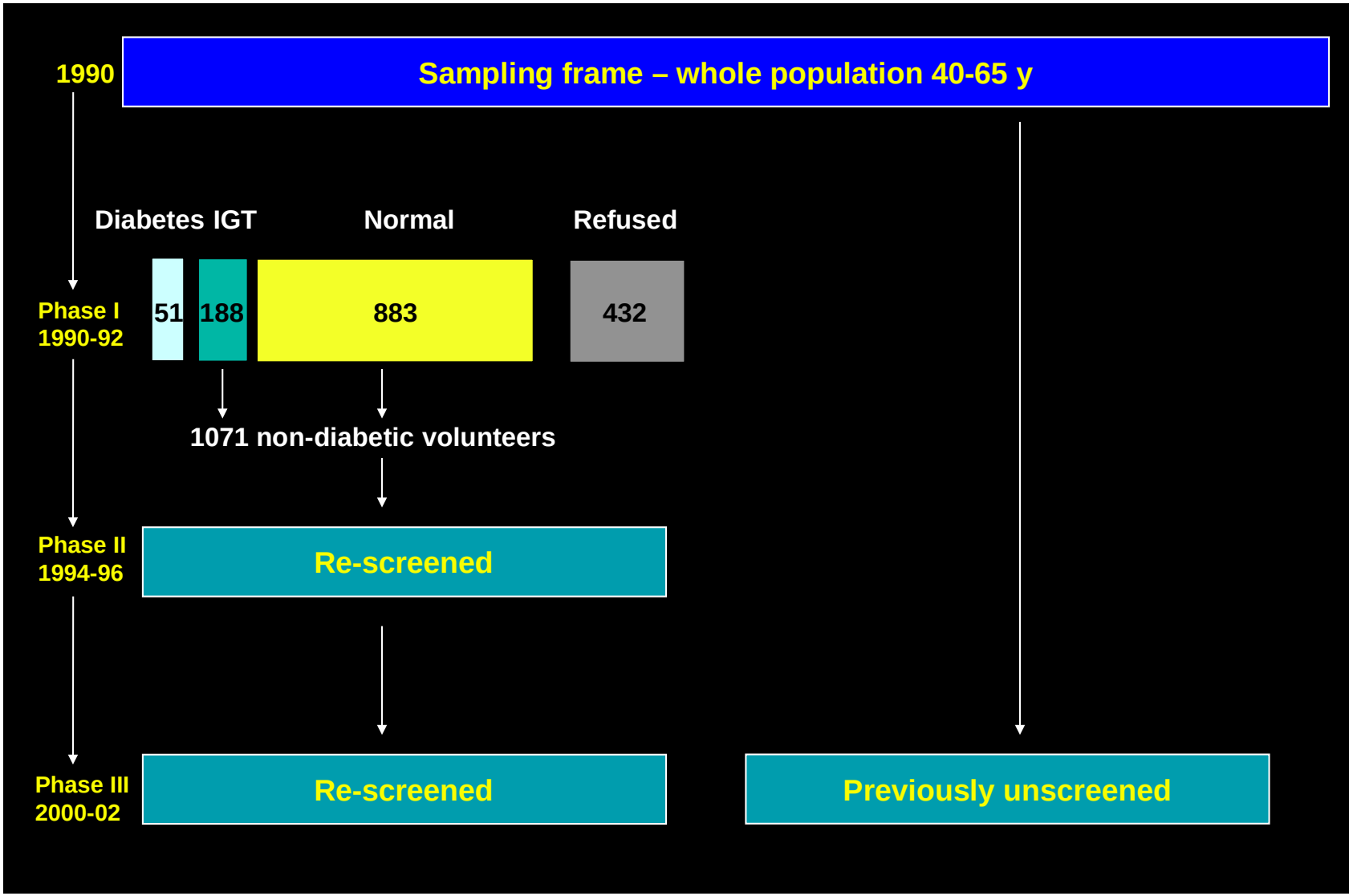
- **Reasonable discriminant ability**
- **Accuracy of risk estimates less clear**
- **Performance over-estimated due to validation against 'clinically diagnosed' diabetes not 'incident' diabetes**

Epidemiol Rev 2011;33:46-62
and EPIC study unpublished data

Ely Retrospective Study Design



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)

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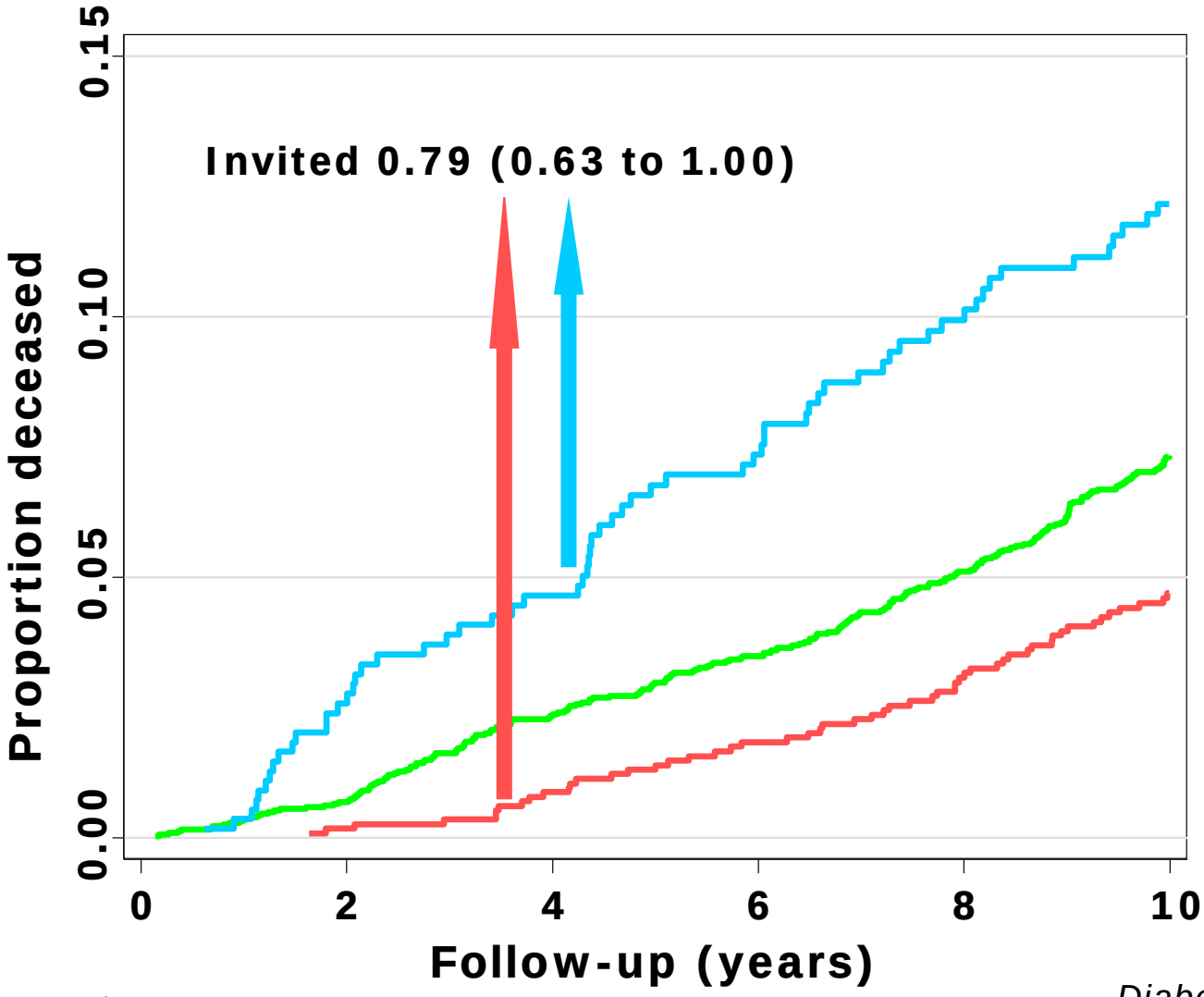

Invited but did not attend
1.36 (1.01 to 1.82)

Not invited

Invited and attended
0.54 (0.40 to 0.74)

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Diabetologia 2010;54:312-319.

Long-term follow-up of the Ely cohort

- **People with diabetes**
  - **Diagnosis of diabetes brought forward (lead time) by 3.3 years**
  - **People with diabetes in the screened population had a lower risk of retinopathy than people with diabetes in the unscreened population**
- **People without diabetes**
  - **Similar health outcomes (including SF-36 and EQ-5D) in the screened and unscreened populations**

Submitted to *Diabetologia* 2011

ADDITION-Cambridge Study Design

BMC Public Health 2009;9:136.

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60 practices in the Eastern Region

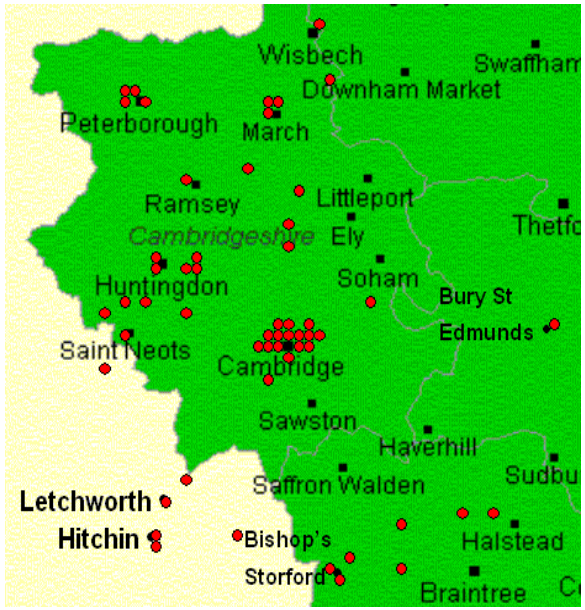
28 practices screening and intensive target driven management of risk factors

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

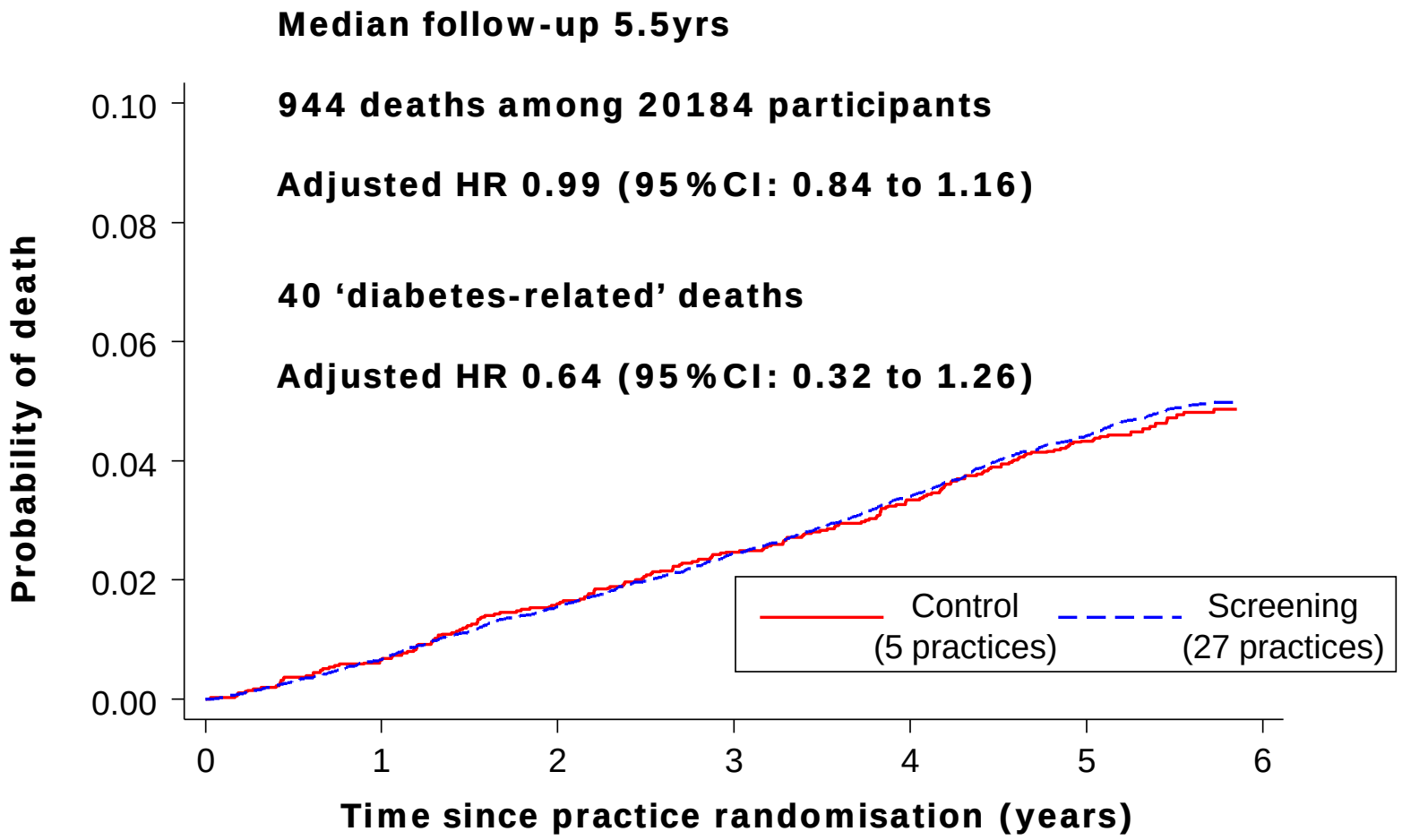
DH Department of Health

MRC Medical Research Council

RCGP Royal College of General Practitioners

wellcome trust

Effects of Screening on Mortality in the High Risk Population



Unpublished data

Effect of screening on cardiovascular morbidity

Endpoint	No screening (N=573) n (%)	Screening (N=1372) n (%)	Effect estimate* (95% CI)
Angina	13.2 (74/563)	11.5 (156 /1,355)	-1.8 % (-5.6 to 2.1)
Self-reported cardiovascular disease	24.7 (123/498)	21.9 (257/1,175)	- 2.8% (-7.1 to 1.6)
Self-reported cardiovascular events	13.5 (67/497)	12.5 (143/1,147)	-1.0 % (-5.0 to 3.0)
*** Accounting for cluster design**			

Unpublished data

Effect of screening on self-rated health

Endpoint	No screening N= 573	Screening N= 1372	Effect estimate* (95% CI)
SF-8 PCS score	47.8 (10.3)	47.4 (9.8)	-0.23 (-1.69 to 1.22)
SF-8 MCS score	52.2 (8.1)	51.8 (5.6)	-0.37 (-1.25 to 0.51)
EuroQol-5D rating (scale -0.3 to 1.0)	0.80 (0.24)	0.81 (0.23)	0.005 (-0.027 to 0.037)
EuroQol Visual Acuity Scale rating (scale 0 to 100)	73.7 (17.2)	74.5 (16.5)	0.89 (-1.42 to 3.19)

***Accounting for cluster design; PCS: Physical Component Summary, MCS: Mental Component Summary, 5D: 5 Dimensions**

Unpublished data

Effect of screening on physical activity

Endpoint	No screening N= 573	Screening N= 1372	Effect estimate* (95% CI)
Total Physical Activity (MET-hours / week)	44.5 (51.2)	44.6 (51.1)	0.14 (-4.88 to 5.16)
Vigorous activity (MET-hours/ week)	14.5 (31.1)	15.2 (31.0)	0.70 (-2.32 to 3.73)
Moderate activity (MET-hours / week)	12.0 (20.3)	11.1(18.4)	-0.87 (-2.71 to 0.99)
Walking (MET-hours/ week)	18.0 (21.1)	18.4 (20.7)	0.31 (-2.01 to 2.62)
Sedentary time (hours /day)	4 .1 (2.1)	4.2 (2.3)	6.01 (-7.10 to 19.13)

* Accounting for cluster design

Unpublished data

Effect of screening on diet, smoking and alcohol consumption

Endpoint	No screening (N=573) % (n)	Screening (N=1372) % (n)	Effect estimate* (95% CI)
Green leafy vegetables (one or more portions/day)	20.7 (117/ 565)	25.2 (339/1,347)	4.4 (0.3 to 8.6)
Fresh fruit (one or more portions/day)	43.8 (249/ 569)	46.5 (627/1,349)	2.7 (-2.2 to 7.6)
Wholemeal / brown bread (one or more portions/day)	29.8 (167/560)	30.8(414/1,345)	1.0 (-3.6 to 5.5)
Current smoking (% prevalence)	10.0 (57 /571)	10.1 (138/1,365)	0.5 (-2.9 to 3.9)
Alcohol (units/week)	8.10 (11.1)	8.3 (12.0)	0.2 (-1.2 to 1.6)

*Accounting for cluster design

Unpublished data

No Evidence of Harmful Effects of Screening For Type 2 Diabetes

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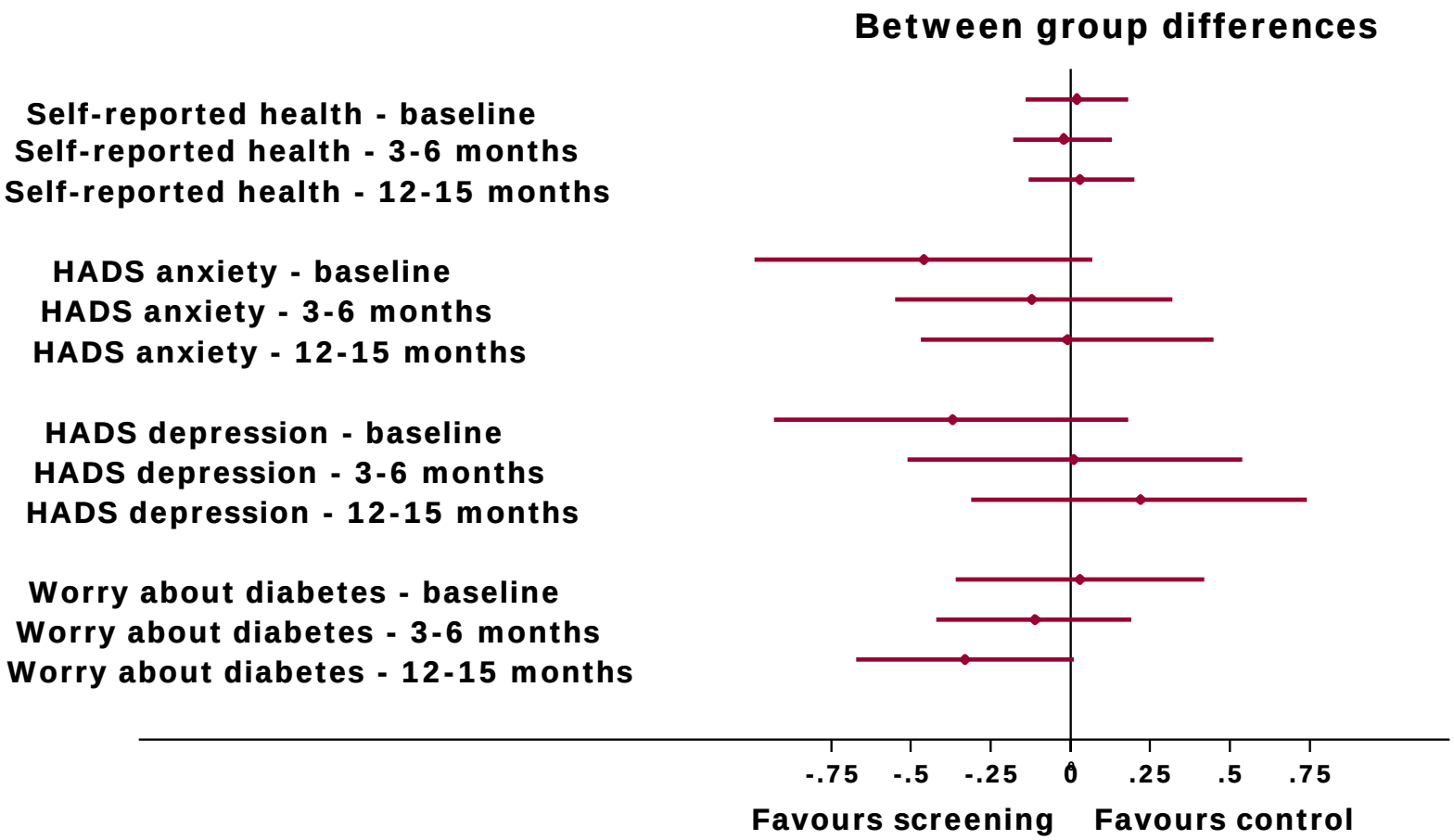
- Parallel group cohort study in 10 screening and five control practices
- Questionnaires sent to 6416 invited for screening and 964 controls



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 on 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.

BanglaDip

- **Uptake of risk assessment by OGTT**

	Letters sent	% (n) replied yes	% (n) replied no	% (n) no response	% (n) recruited from sent	% (n) recruited from yes
Total	7742	5.2 (406)	2.7 (210)	92 (7126)	0.9 (66)	16.3 (66)

Unpublished data

Plan

- Context
- Finding ‘high risk’ individuals
  - ‘high risk’ of what
  - effects and adverse effects of ‘risk screening’
- **What to do with ‘high risk’ individuals**

ProActive trial

BMC Public Health 2004;4:48.

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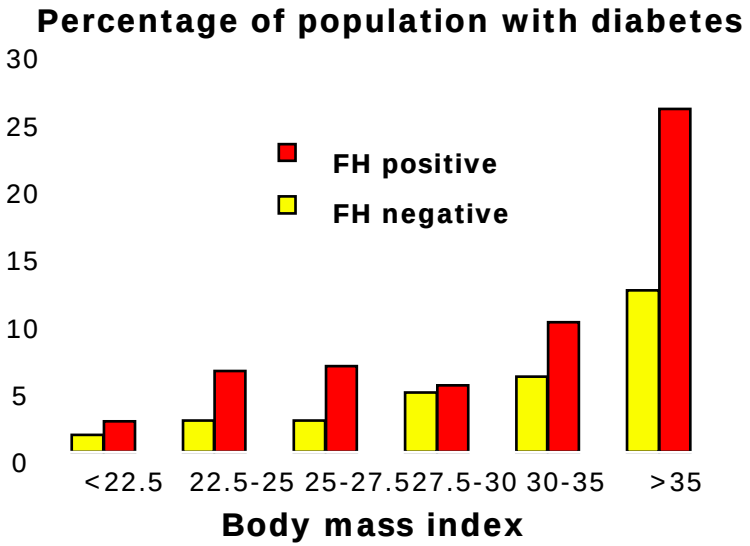

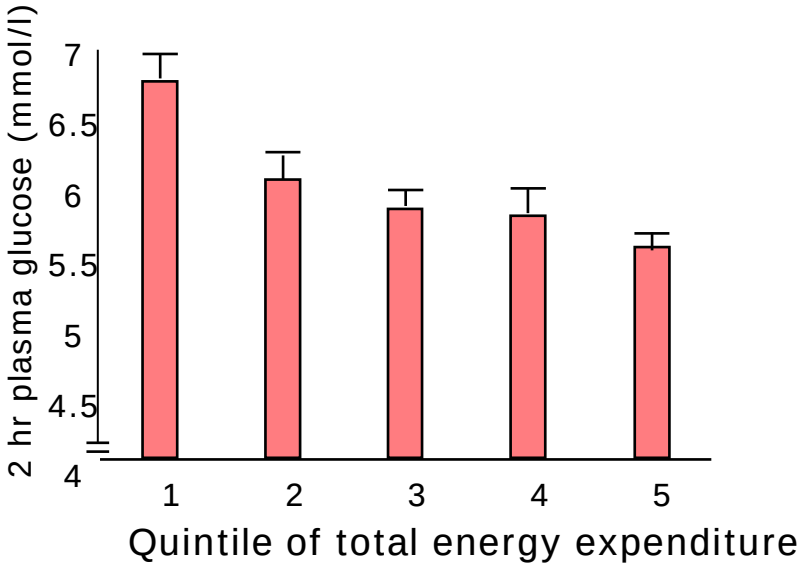

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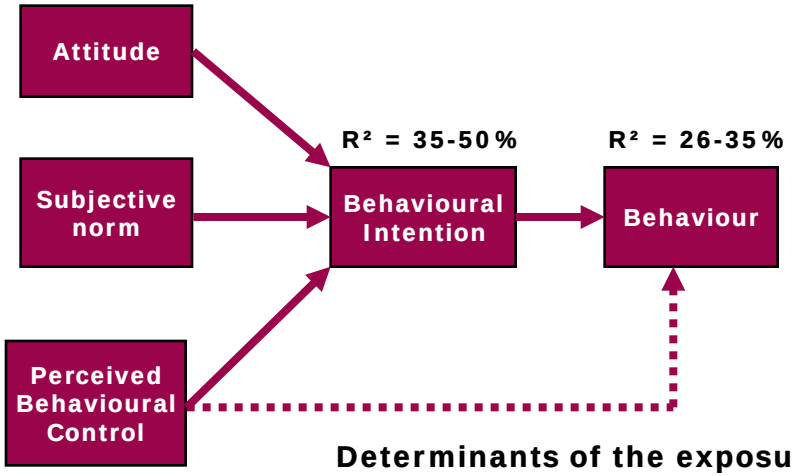
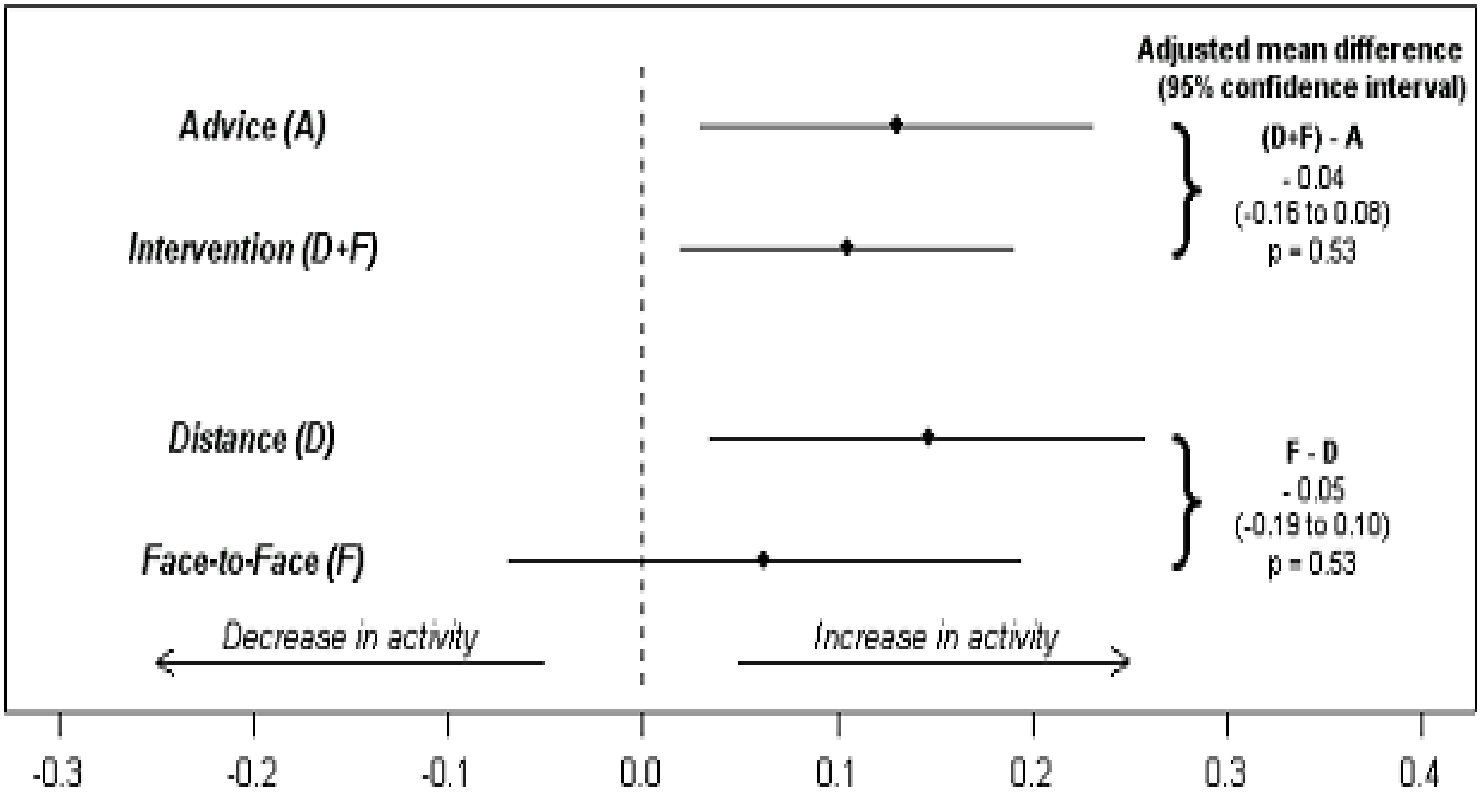


Determinants of the exposure: Theory of Planned Behaviour

Results: Principal outcome



Mean change in physical activity (dayPAR) from baseline to 12 months compared across groups

The Lancet 2008;371:41-48

Take home messages

- Glucose is one of many CVD risk factors, and a relatively weak one. It seems sensible to link assessment of diabetes and CVD risk
- Screening for individuals at high risk of having/developing diabetes appears not to be harmful (direct and indirect via false reassurance)
- Uptake of risk assessment/screening may be disappointing
- Given current uncertainties use of population stratification to focus on those at highest risk may enhance efficiency
- HbA1c of 6.0-6.49% has the potential to define a group at sufficient risk of diabetes but of feasible size to warrant preventive interventions

Take home messages

- Specification of 'high risk' also depends on the cost and effectiveness of the proposed preventive intervention (as per statins and 20% Framingham risk)
- Without specific interventions the benefits of identification of high risk individuals appear to be restricted to those found to have undiagnosed diabetes
- Intensive behavioural interventions can halve progression to T2DM among those at high risk and may reduce risk of CVD and retinopathy in the long term
- However effects of behavioural interventions in routine practice are likely to be smaller than seen in prevention trials
- The potential of brief interventions in those undergoing risk assessment merits further consideration

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Thank you for your attention

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