Colorectal cancer -

Issues and Visions

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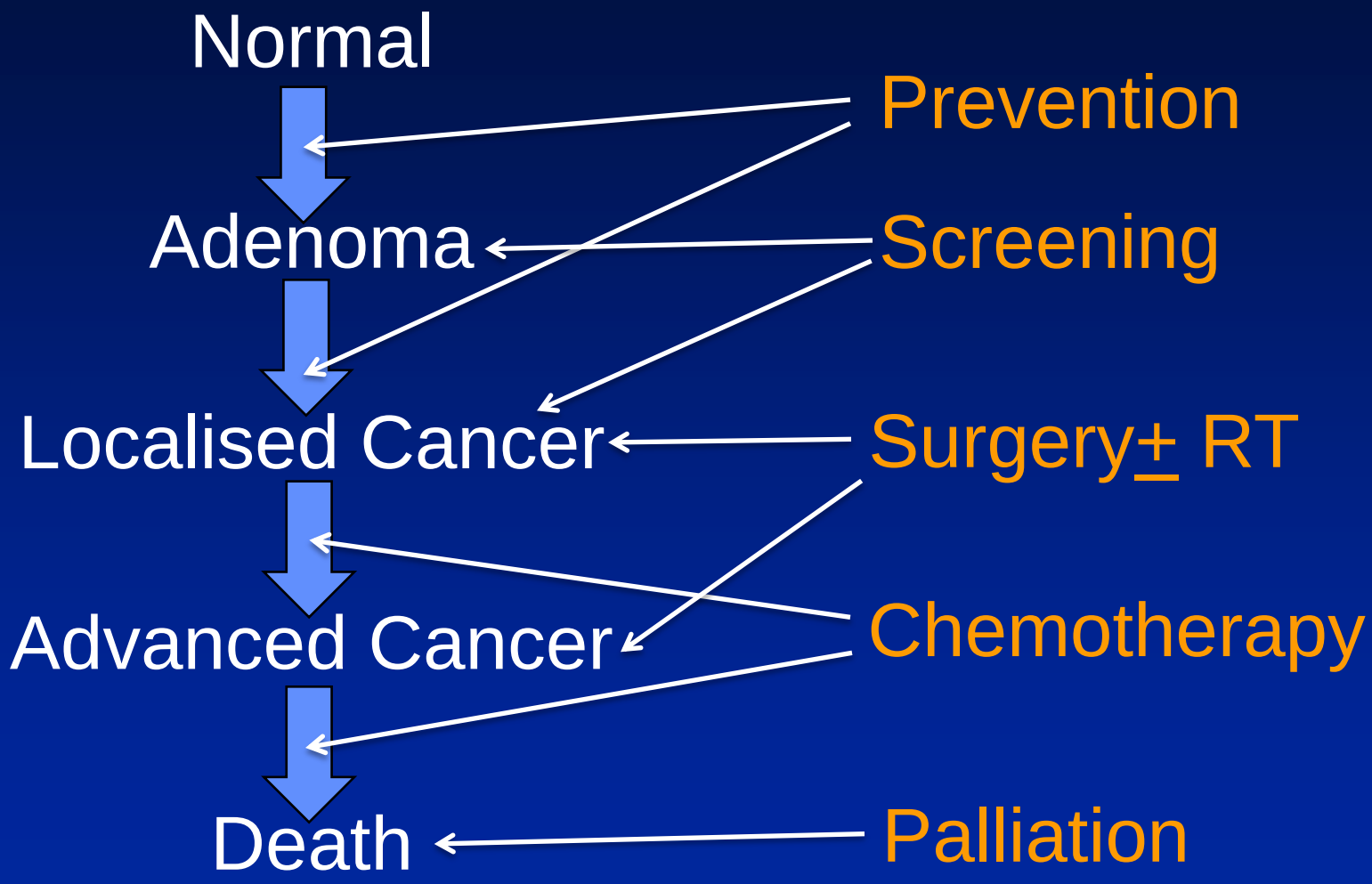
The Person / Patient Pathway



Prevention


Kellogg's
ALL-BRAN
PLUS
NATURALLY LOW IN FAT
cancer
research
campaign
fuelling the fight
with a £1m pledge
LARGE SIZE
750g
TESCO
PURE
Orange
Juice
SMOOTH
200ml

Food, Nutrition, Physical Activity, and Colorectal Cancer (WCRF, 2011)

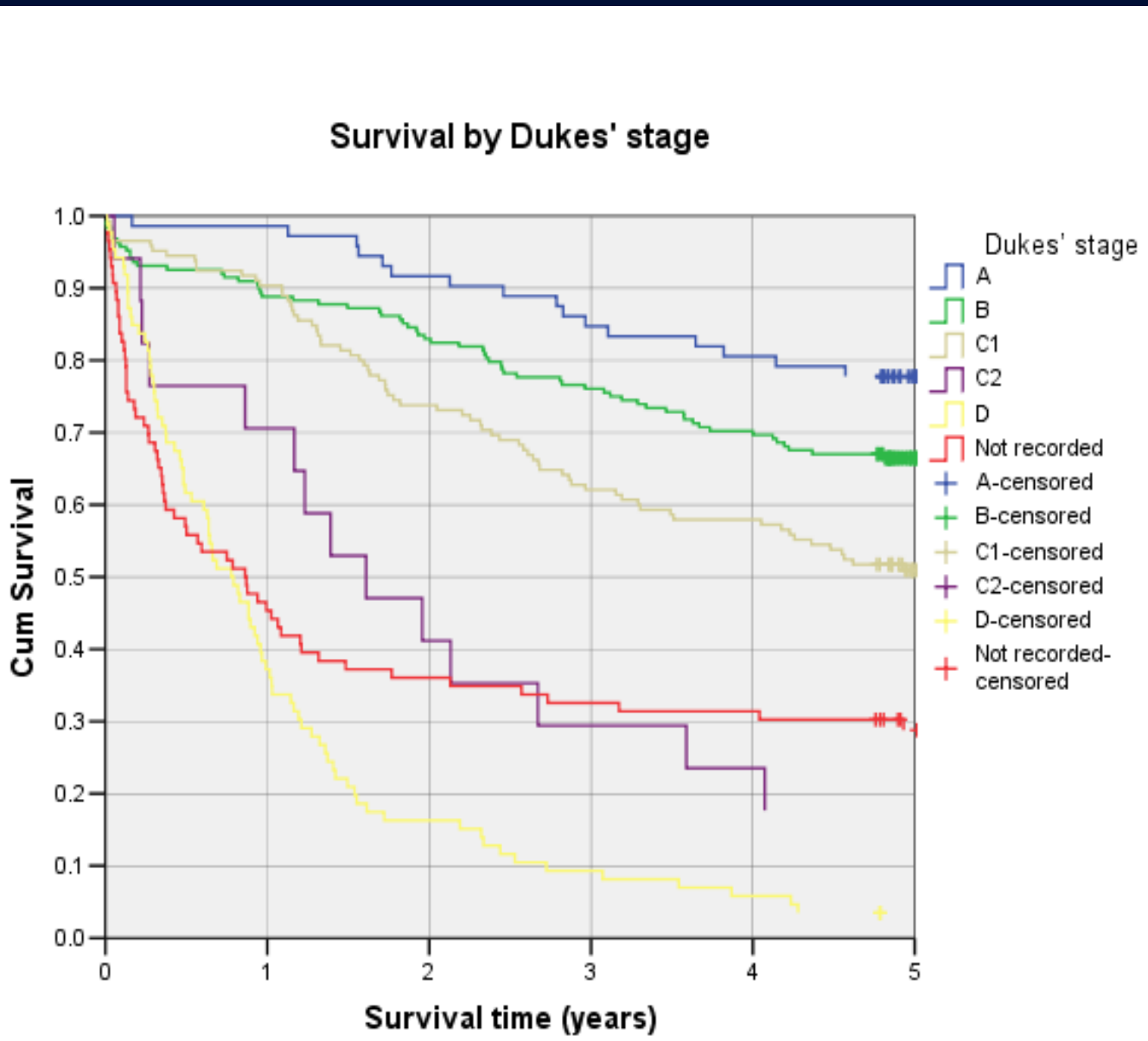
	Decreases risk	Increases risk
Convincing	Physical activity Foods containing dietary fibre	Red meat Processed meat Alcoholic drinks (men) Body fatness Abdominal fatness Adult attained height
Probable	Garlic Milk Calcium	Alcoholic drinks (women)

How to get the message across?

Who to get the message across to?

- General public?
- High risk groups?
- Patients?
- Health care professionals?
- Politicians?
- Industry?

Early Detection


Survival by Dukes' stage
Cum Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
1
2
3
4
5
Survival time (years)
Dukes' stage
A
B
C1
C2
D
Not recorded
A-censored
B-censored
C1-censored
C2-censored
D-censored
Not recorded-censored

Symptoms or Screening?

- Symptom complexes have poor sensitivity for colorectal cancer

Jellema et al
BMJ 2010;340:1269

- Symptoms in a FOBT screen-positive population do not predict neoplastic disease

Ahmed et al
Bjs 2005;92:478

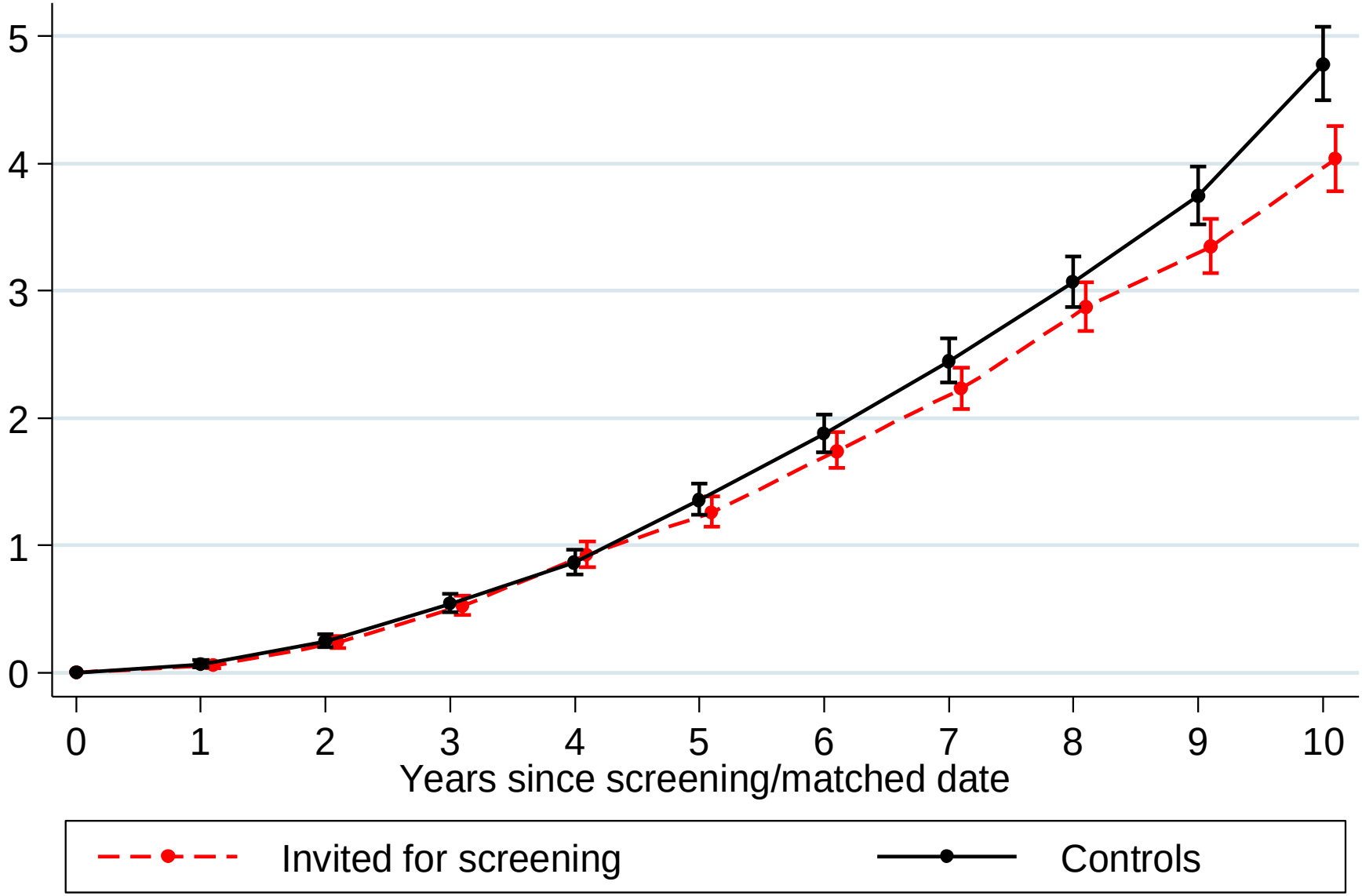
Disease-Specific Mortality in gFOBT Randomised Trials
(Relative Risks)

- Minnesota
  - Annual 0.67 (CI 0.51-0.83)
  - Biennial 0.79 (CI 0.62 - 0.97)
- Nottingham
  - Biennial 0.85 (CI 0.74 - 0.98)
- Funen
  - Biennial 0.82 (CI 0.68 - 0.99)
- Göteborg
  - Biennial 0.84 (CI 0.71-0.99)

Pilot Programme

Cumulative Mortality from Colorectal Cancer

Rate and 95% CI (Nelson-Aalen estimates)



Rate ratio of Colorectal Cancer invited vs controls

Overall

0.90 (0.830 – 0.989)

Relative reduction in CRC mortality 10%

Participants only

0.73 (0.653 – 0.824)

Relative reduction in CRC mortality 27%

Can we combine screening with prevention?

Hypothesis – screening contact is a teachable moment

BeWEL

- Multi-centre randomised controlled trial
- Hospital setting:
  - NHS Tayside, NHS Forth Valley, NHS Ayrshire & Arran
- 12 month BeWEL intervention vs. usual care
- Participants:
  - Patients who have undergone screening colonoscopy for benign adenomas attending follow-up clinic
  - 50-74yrs, BMI >25kg/$m^{2,}$ no carcinoma, able to undertake exercise requirements, able to provide informed consent
  - n=316 (158 intervention + 158 usual care)

⇦ **6 months** ⇨	⇦ **12 months** ⇨	⇦ **6 months** ⇨
Pre-trial development	Recruitment & intervention implementation	Data collection, analysis & interpretation

Intervention vs. usual care

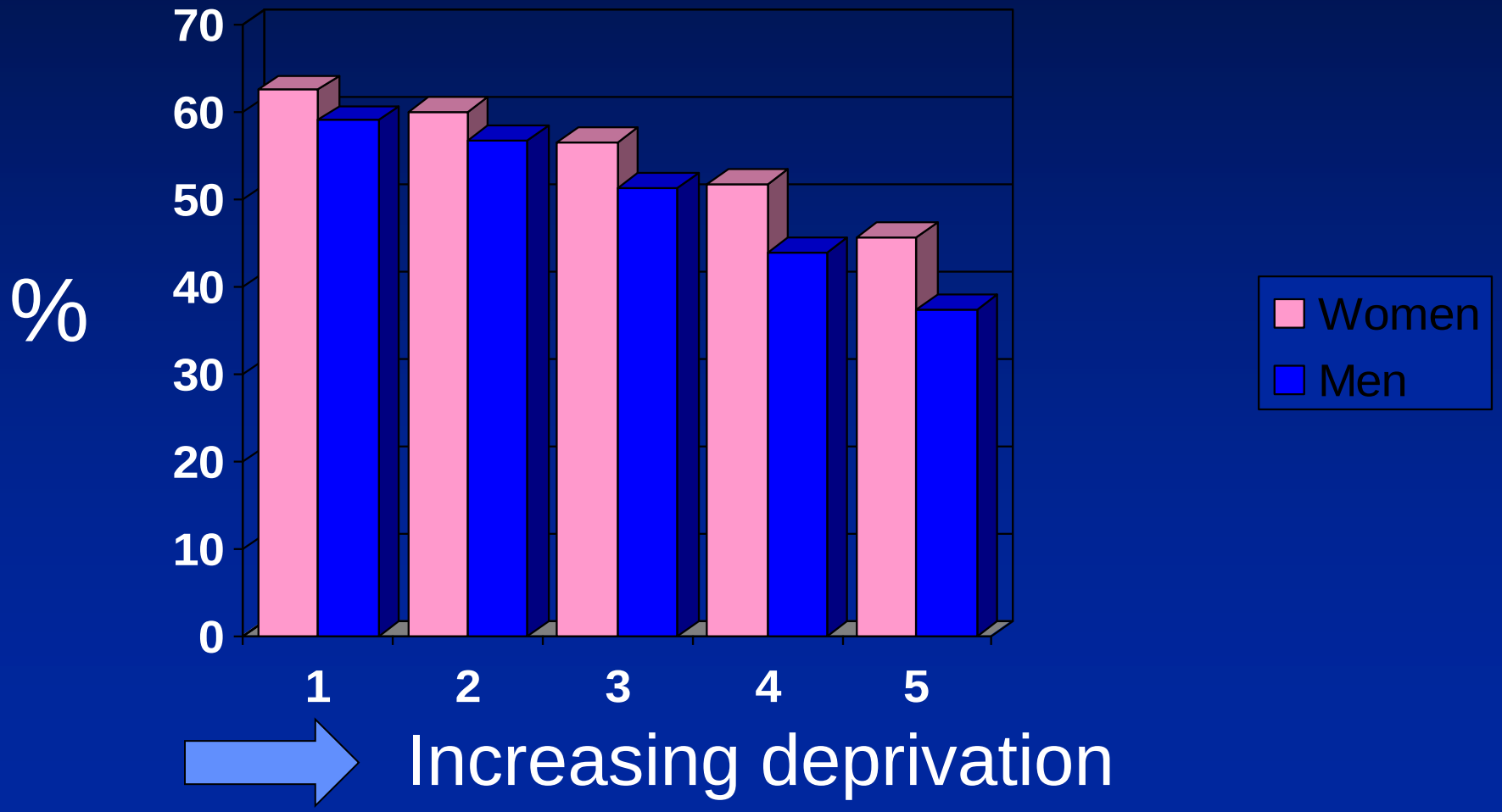
- Usual care: leaflet on healthy lifestyle
- BeWEL intervention (12 months)
  - Modification of the US diabetes prevention programme enhanced with provision of scales for self-monitoring of body weight
  - 3 face-to-face consultations with a lifestyle counsellor at 0, 1 and 2 months
  - Bi-monthly telephone consultations thereafter
- Outcome measures
  - Change in body weight, BMI and waist circumference

Results to Date

- 997 approached
- 492 (49%) expressed interest
- 42 (9%) declined
- 121 (25%) ineligible
- 329 (33%) randomised
- 173 have reached 12 month follow-up

Problems with screening

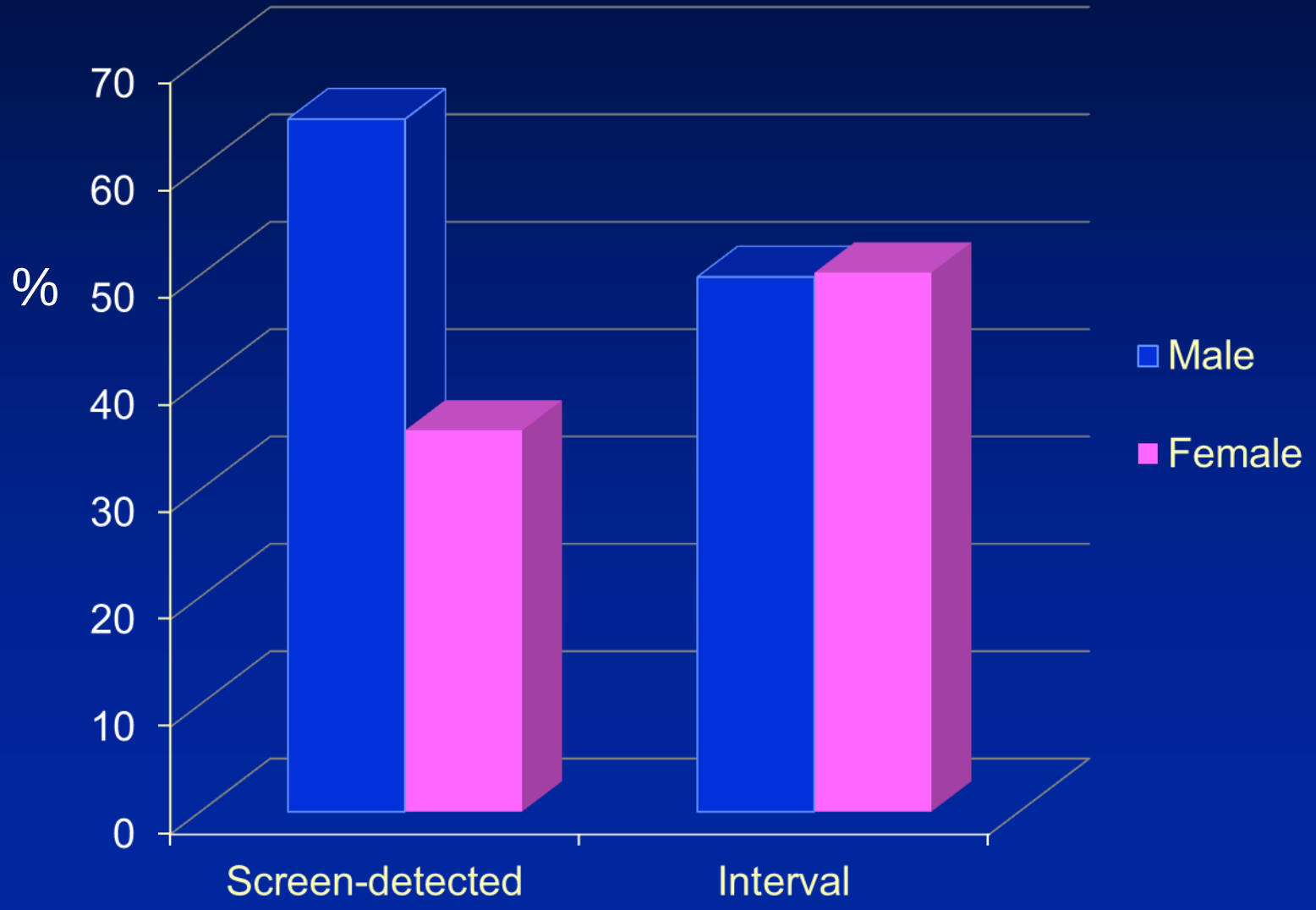
Uptake
- Gender and Deprivation



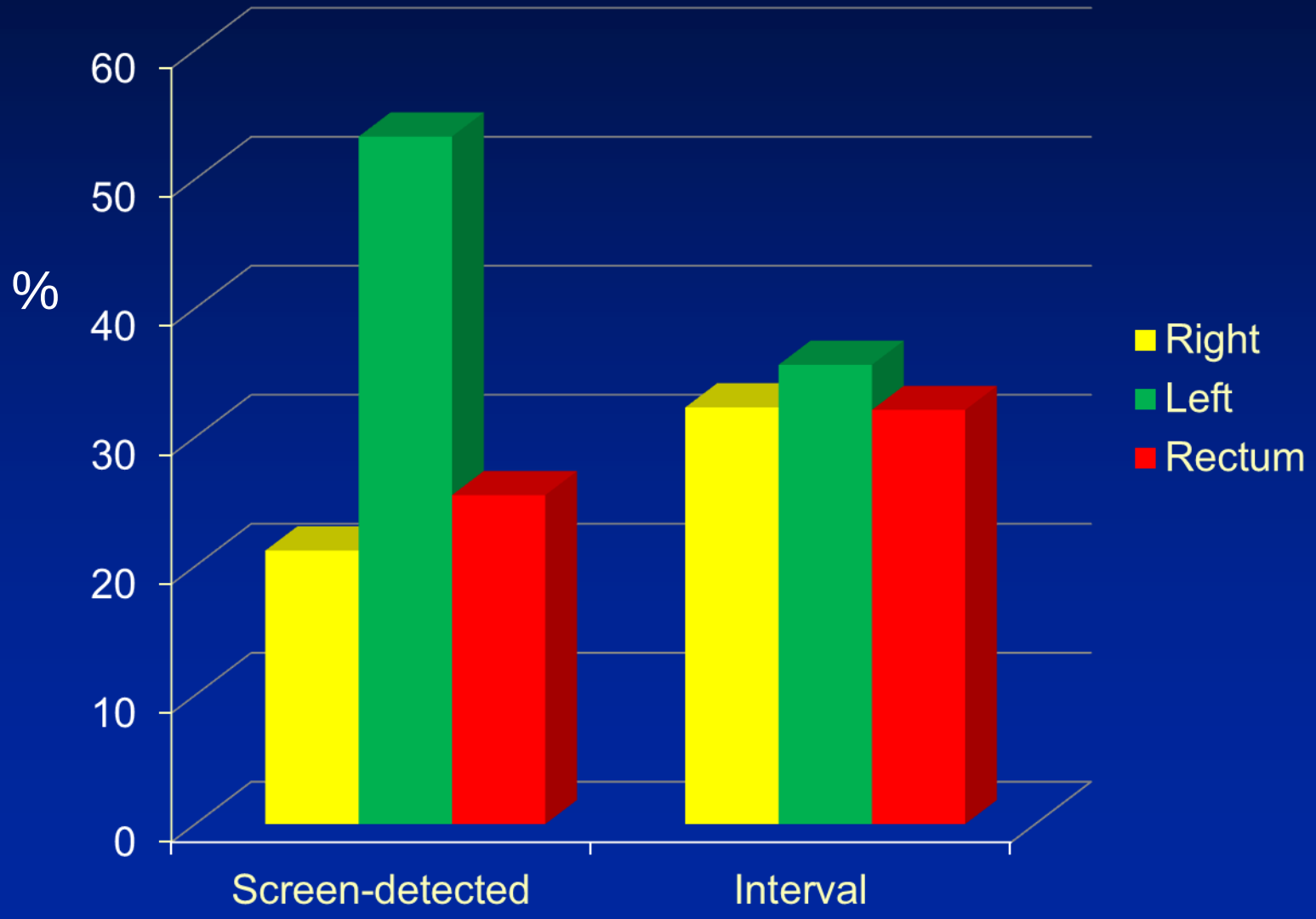
Cancers Diagnosed in the Screened Population

	Round 1	Round 2	Round 3
Screen -detected	351 (56.6%)	208 (46.5%)	139 (35.7%)
True interval	193 (31.2%)	213 (47.7%)	229 (58.9%)
Missed	2 (0.3%)	4 (0.9%)	2 (0.5%)
Miscellaneous	66 (10.7%)	22 (4.9%)	19 (4.9%)
Not on Socrates	6 (1%)	0	0

Gender distribution - all rounds



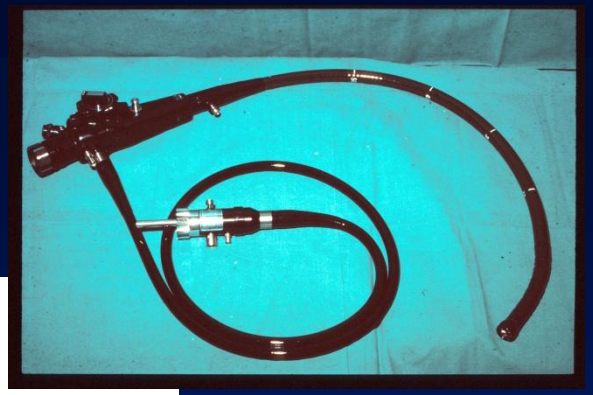
Site distribution - all rounds

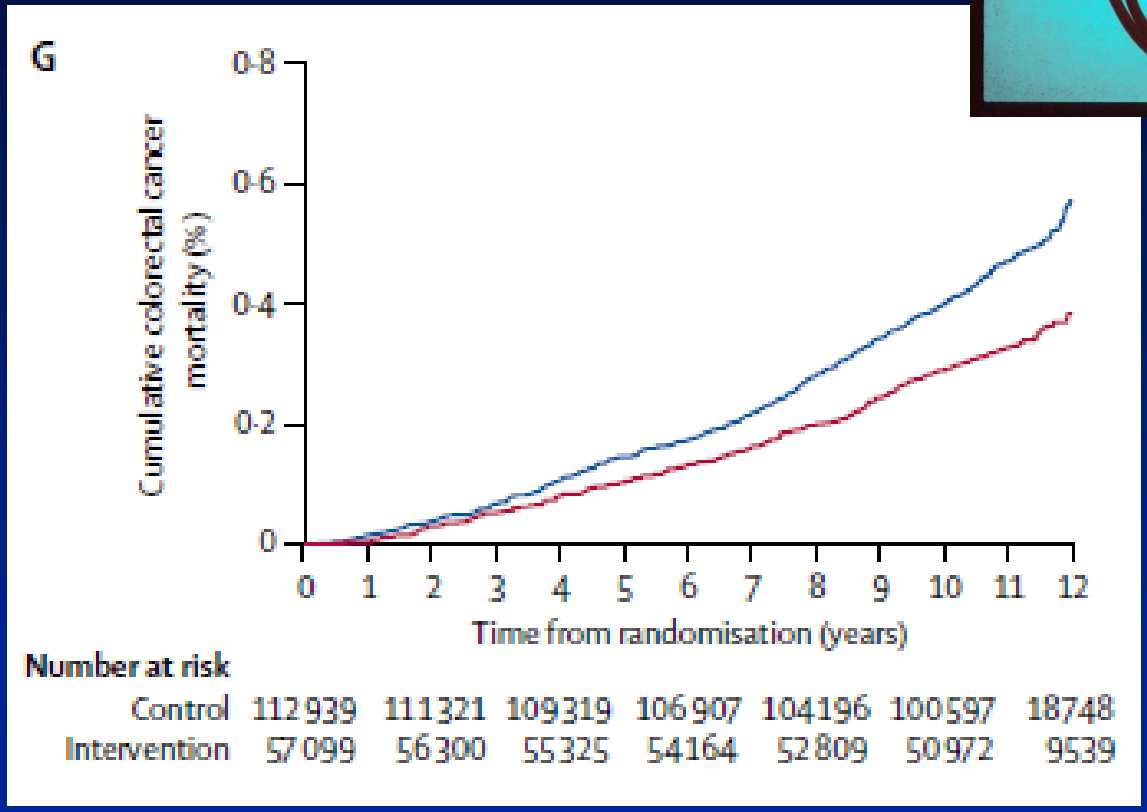


Issues to address

- Uptake
- Interval Cancers
- Gender inequality
- Rectal and right-sided cancers

Mortality from CRC



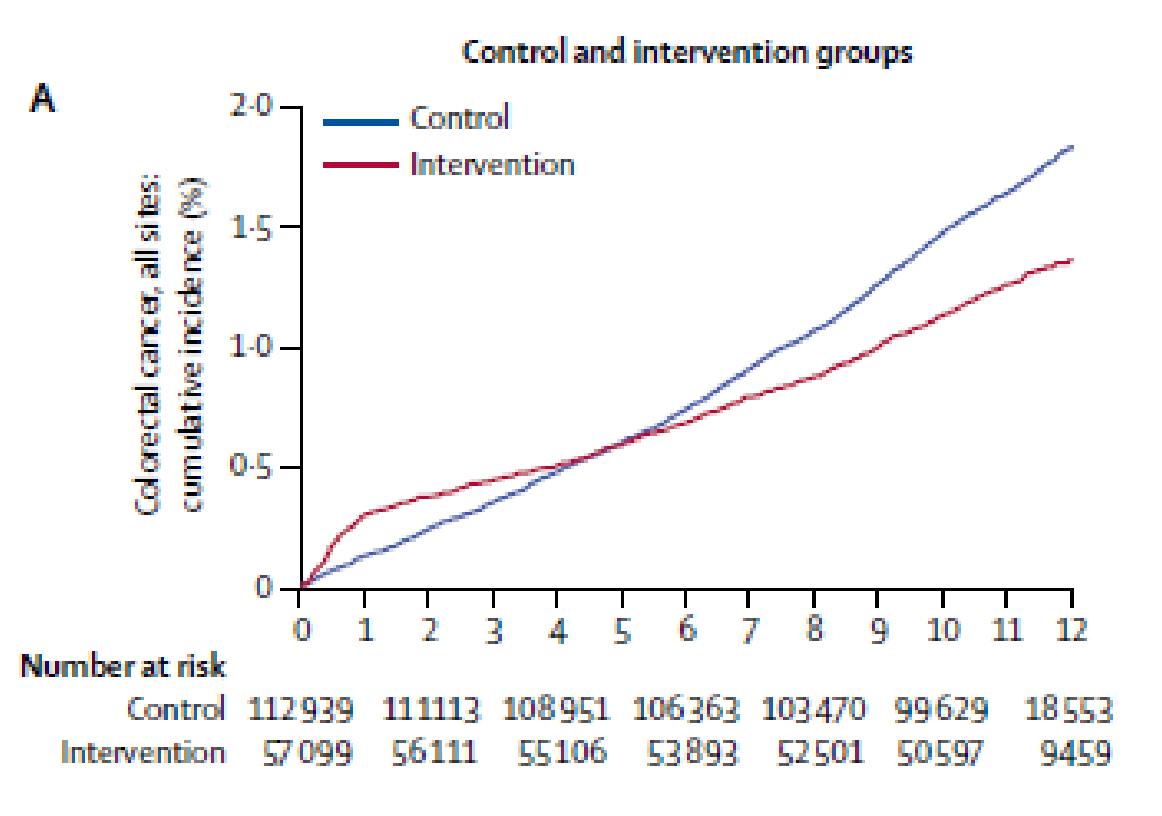


Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

Published Online April 28, 2010
DOI:10.1016/S0140-6736(10)60551-X

Incidence of CRC



Potential Advantages of FS

- Disease prevention
  - Enhanced detection of left-sided adenomas
- Detection of rectal cancer
- Unlikely to be a gender difference

Potential Problems with FS

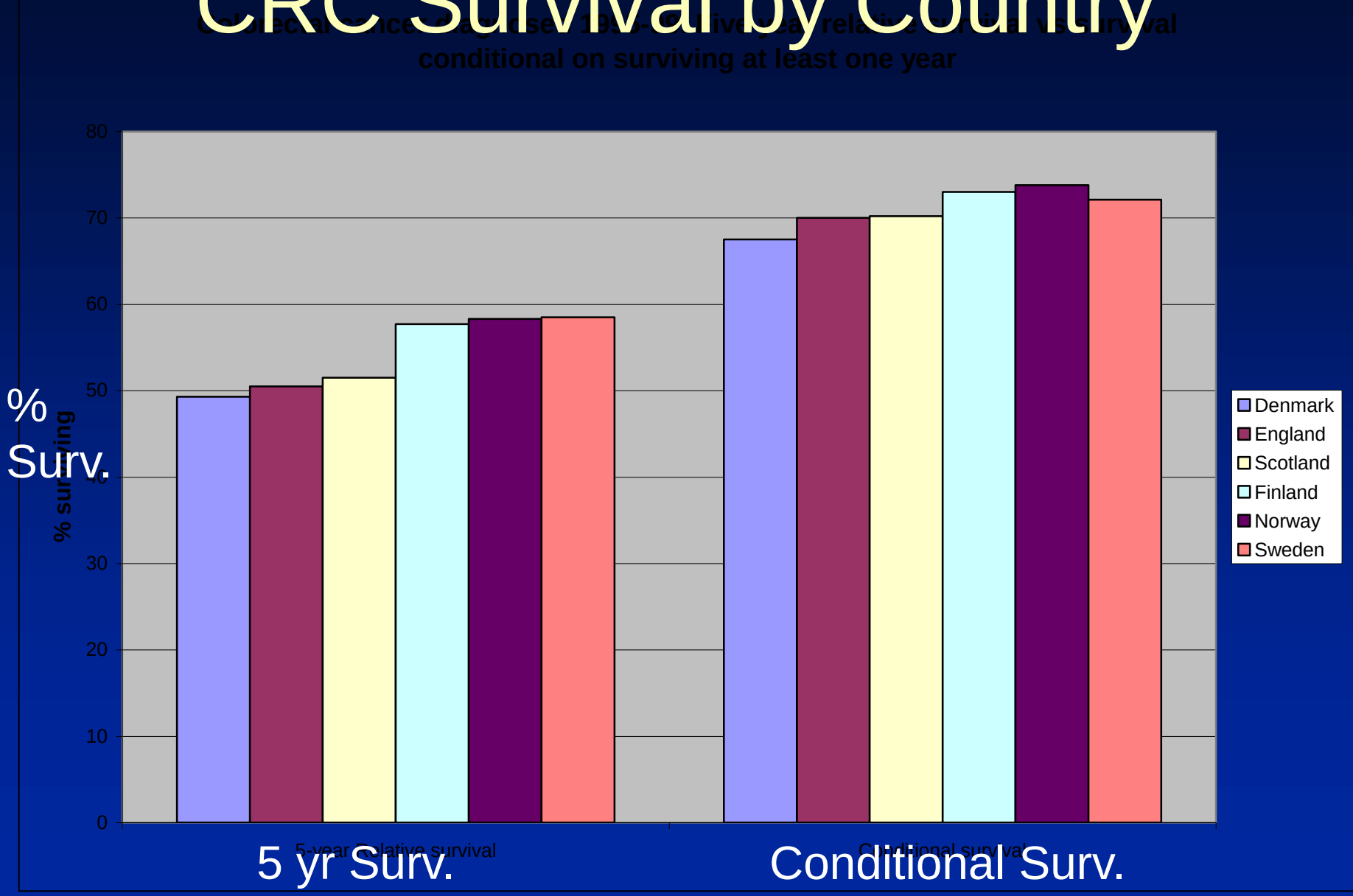
- Uptake
  - Unlikely to be >30%
  - Possibility of exaggerated deprivation gradient
- Effect on right-sided cancers

Future of FS

- Commitment to role out in England
  - At age 55 before FOBT screening starts
- Position in Scotland
  - FOBT screening starts at age 50
  - What is added value of FS in a population that has been offered FOBT?
  - Pilot planned at ~ age 60

How can we improve outcomes of treatment?

CRC Survival by Country

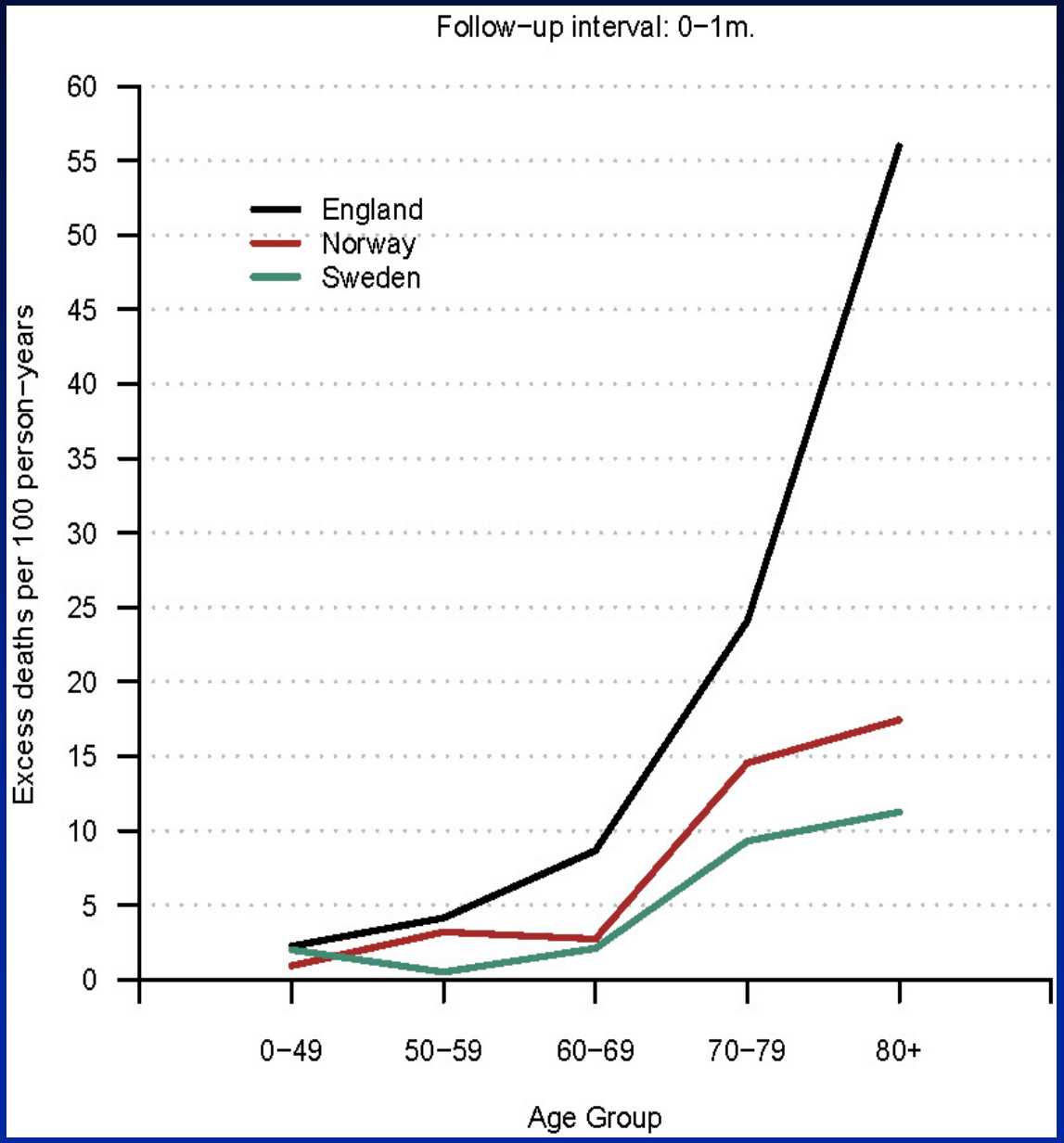


% Surv.

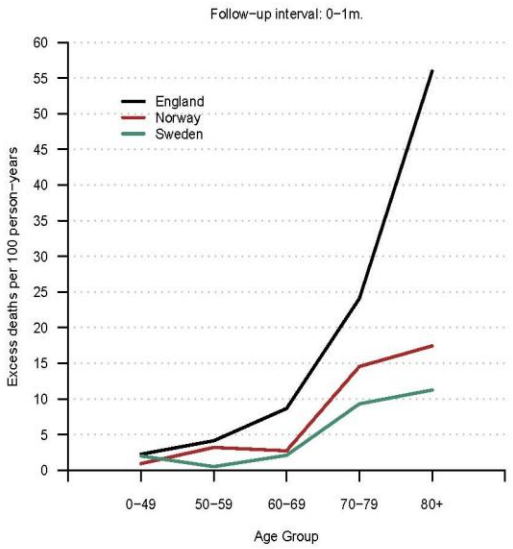
5 yr Surv.

Conditional Surv.

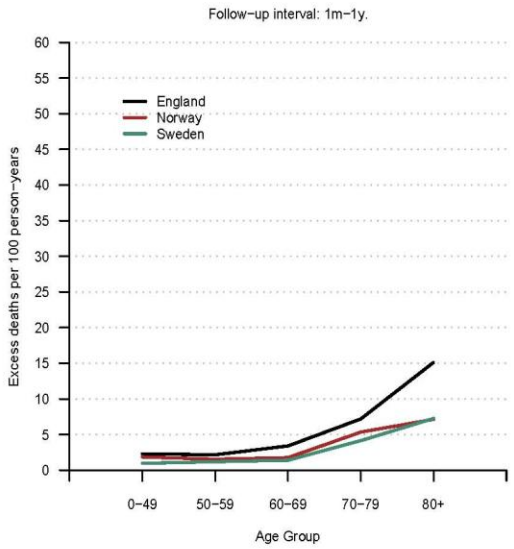
Absolute excess death rates from CRC



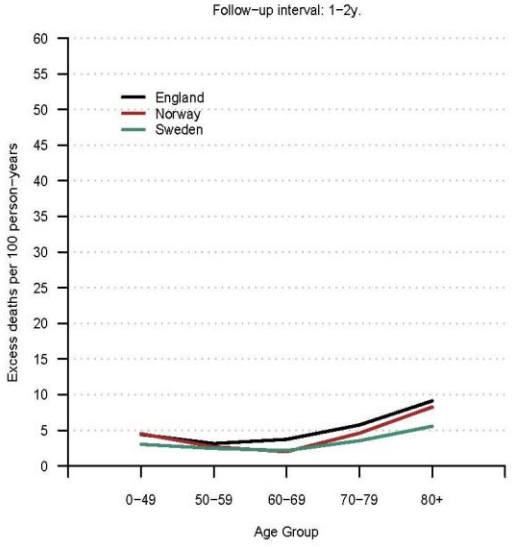
0-1m



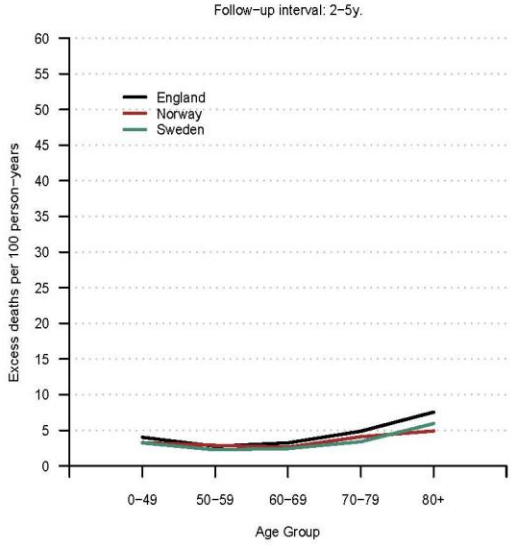
1m-1y



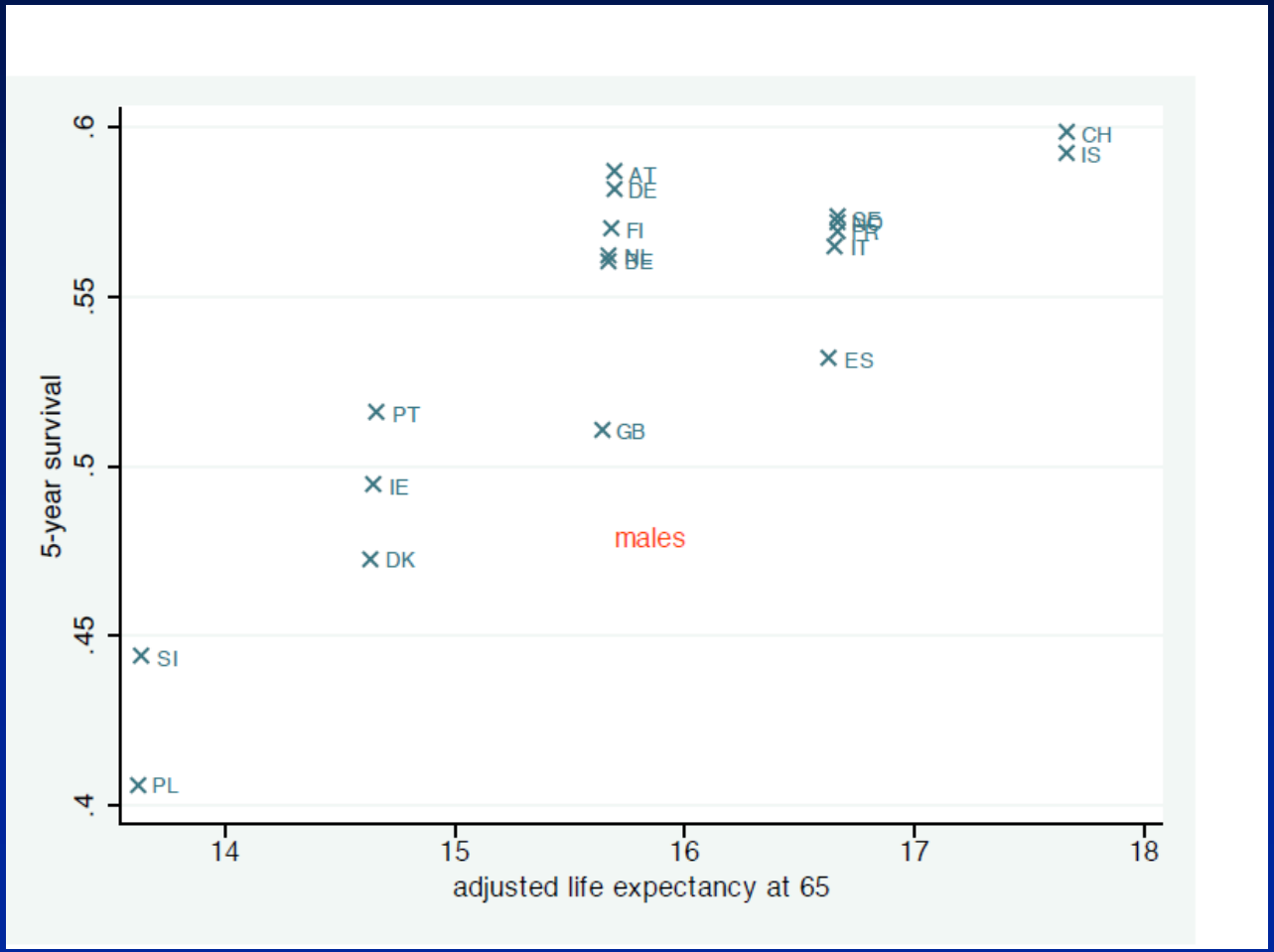
1y-2y



2y-5y



CRC Survival vs Av. National Life Expectancy



P<0.001

Fitness is a Factor

- Deprivation ass. with decreased CRC survival (1st month)
- Deprivation ass. with increased operative mortality
- Deprivation ass. with poor cardiovascular fitness
- Poor cardiovascular fitness ass. with poor short term outcomes

Pre-operative optimization combined with postoperative lifestyle modification ?

StartWELL

- Randomised feasibility study of a lifestyle intervention programme initiated *before* surgery for CRC and continued for 10 weeks after the end of treatment
- Intervention – smoking, physical activity and dietary change
- Outcome measures
  - 1°: treatment related side effects
  - 2°: long term cancer and CV outcomes

Summary

- Effective prevention interventions
- More effective screening
- Role of aspirin
- Optimizing surgical treatment at a population level