# Possibilities of New Cancer Screening Programmes

Prof. Bob Steele

University of Dundee and UK NSC

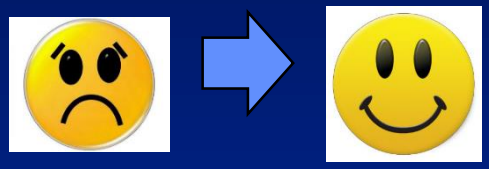
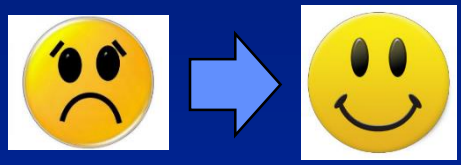
# UK National Screening Committee (NSC)

- Advises ministers and NHS
- Keeps abreast of new evidence
- Is accountable to the 4 CMOs

# Advising on Screening Policy (UK NSC)

- Starting screening
- Modifying screening
- Stopping screening
- *Stopping screening starting*

# Screening is Popular

- *Most* people have a negative test 
- A *few* people have screen-detected disease and are cured 
- A *few* people have a false +ve test 
- A *few* people are harmed by false reassurance, investigations or treatment 

# Screening RCTs

Population

No screening offered

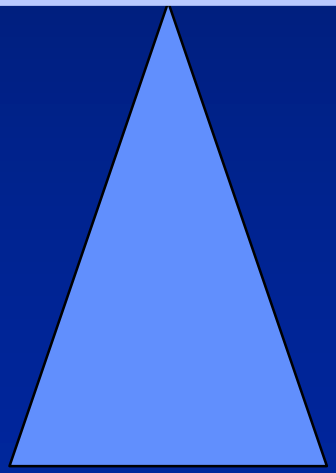
Screening Offered

(including those who choose not to participate and those developing interval disease)

Compare numbers of deaths or adverse outcomes from disease

Benefit to people with disease

Harm to people with disease *and* HARM TO THE HEALTHY POPULATION



# Possible Future Population Cancer Screening Programmes

- Prostate
- Ovary
- Lung

# Prostate Cancer Screening

# RCTs of PSA Screening

21% reduction in prostate cancer deaths

*but…*

28 patients needed to treat to prevent 1 cancer death

1 cancer death avoided for 1000 men screened over 10 years

# Harm

- Biopsy induced sepsis
  - 1/1000 screened
- Side effects of Surgery
  - Incontinence - 3/1000 screened
  - Impotence – 25/1000 screened

# ProtecT Study

- PSA-detected early prostate cancer
- Three-way randomisation
  - Active monitoring
  - Conformal RT + NA androgen suppression
  - Radical Prostatectomy

# ProtecT Study Results

- No difference in prostate cancer deaths at 10 years
- *But* – higher rates of metastatic disease in the active monitoring group.

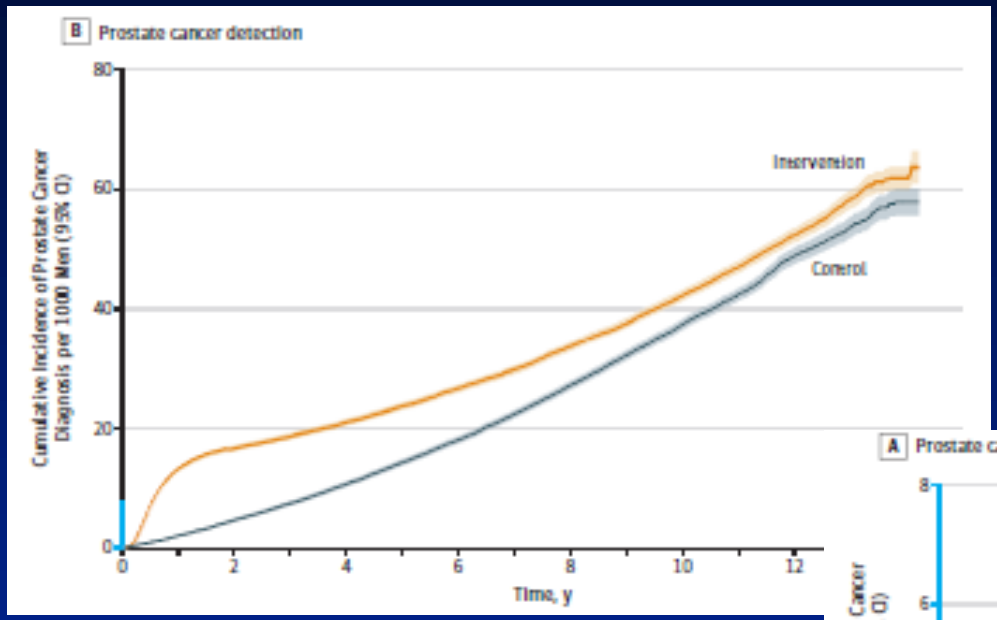
# ProtecT Study @ 10 years

| | Surgery n=533 | Radiotherapy n=545 | Monitoring n=545 |
|---|---|---|---|
| Deaths | 5 | 4 | 8 |
| Recurrence | 13 | 16 | 33 |

# CAP Trial
## 2001-2009 (FU until 2016)

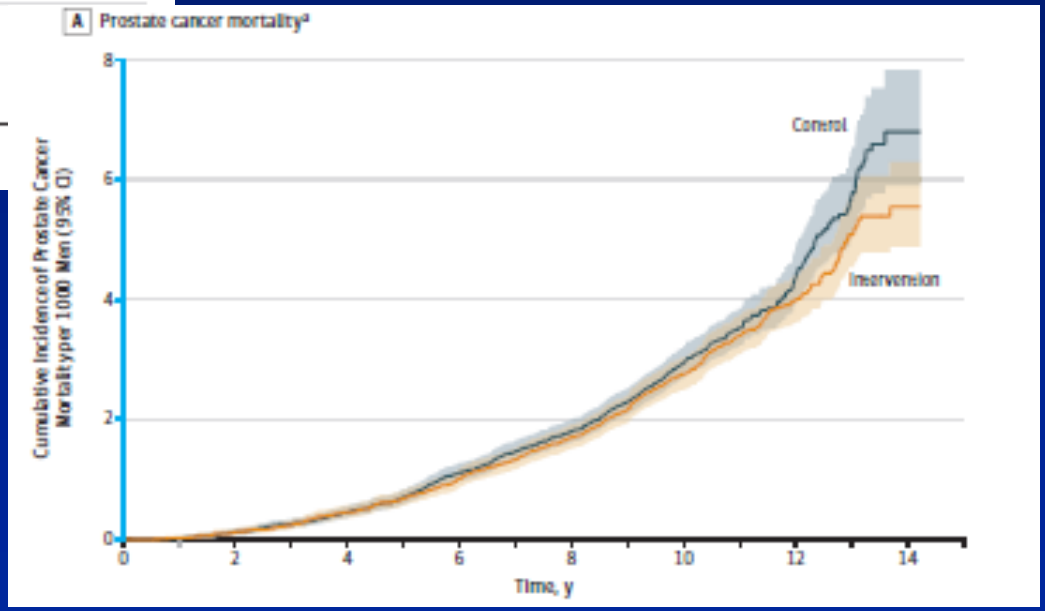
- Cluster RCT of PSA Testing
- Random assignment of primary care centres
  - Standard Care (no routine PSA testing)
  - ProtecT (written invitation to PSA testing to 228,966 men in 337 practices)

# CAP Trial




Martin et al
JAMA
2018

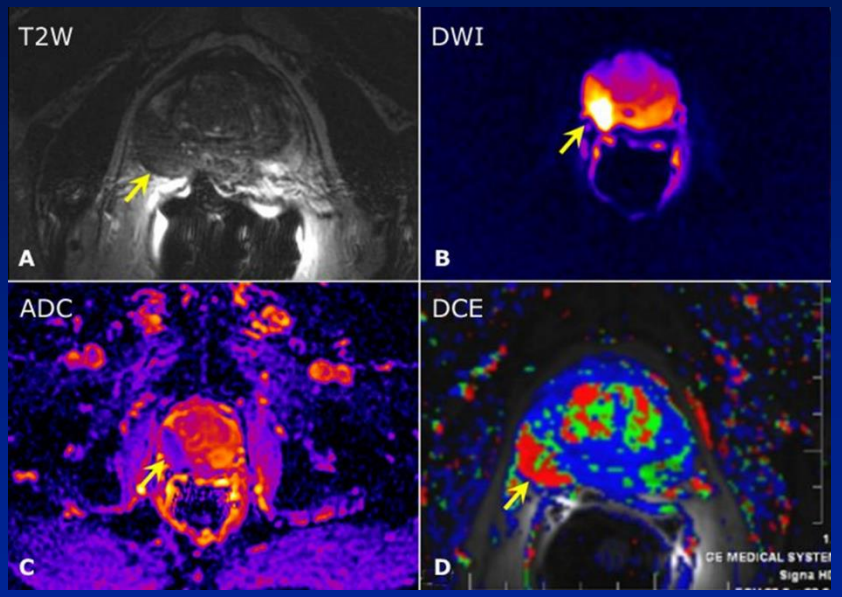
Incidence




Mortality

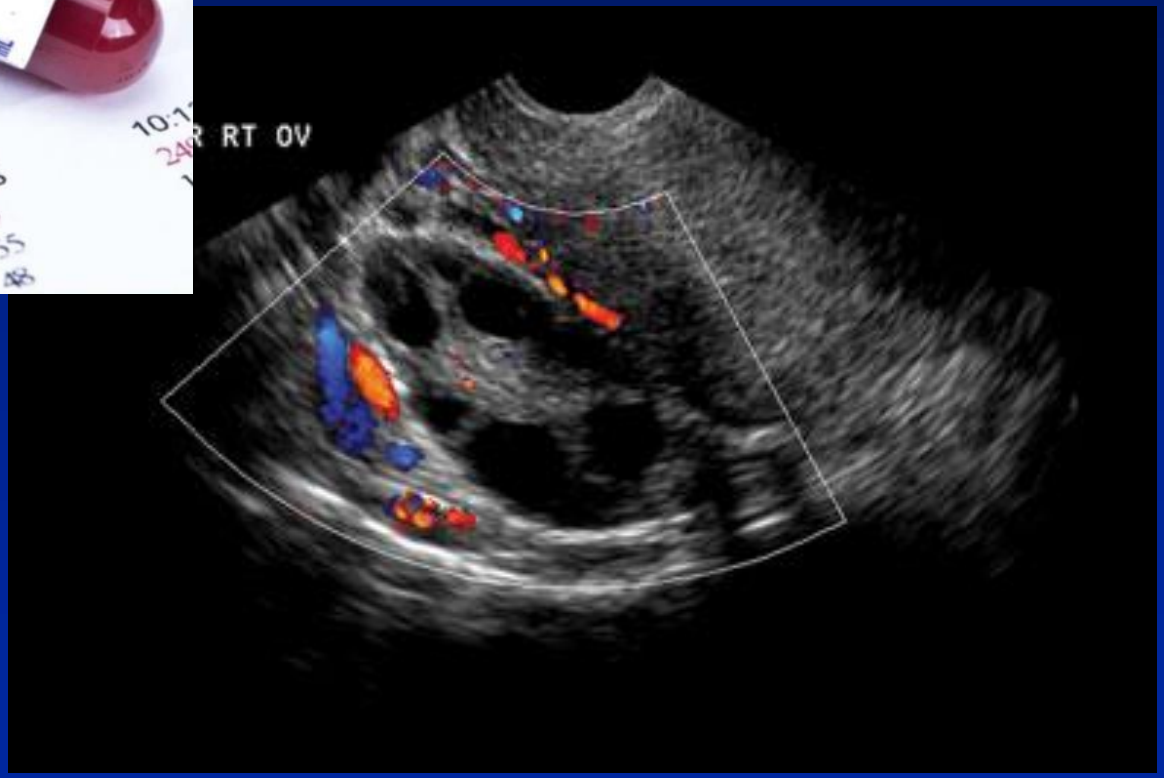
# Where now?

- More discriminatory biomarkers?
- PSA trajectory?
- Multiparametric MRI?
- PET/CT/MRI?



# Ovarian Cancer


CA 125


RT OV

# UKCTOCS RCT

- 202638 women aged 50-74 randomised between 2001-2005
- No screening
- Annual transvaginal ultrasound (TVU)
- Annual CA125 with TVU if indicated by ROCA (MMS)

# UKCTOCS – 14 yr FU

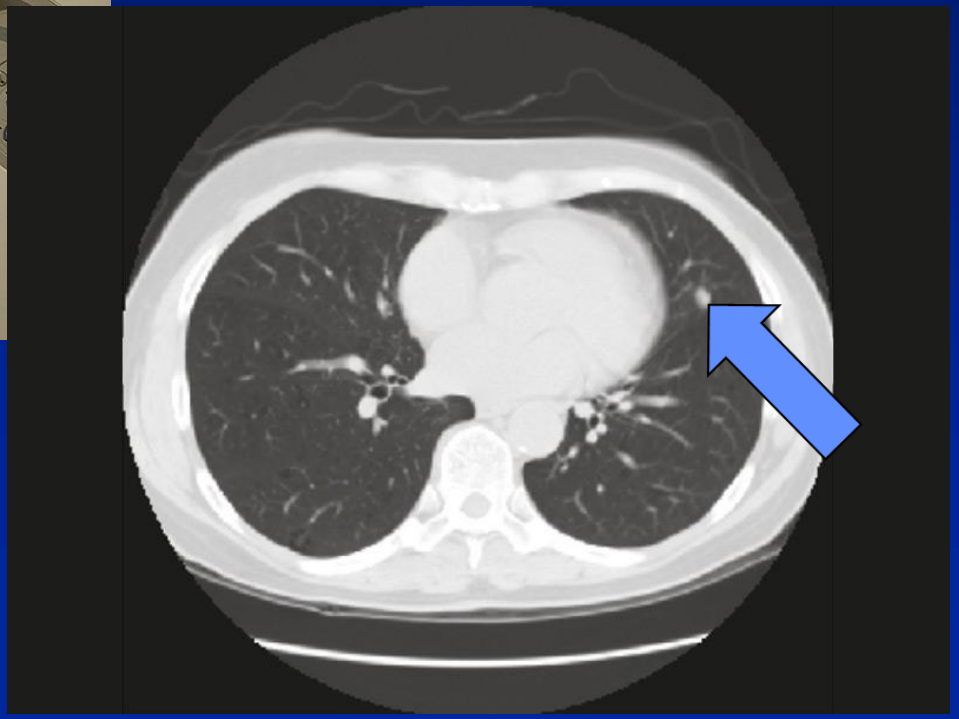
| Arm | Sensitivity % | Specificity % | PPV % |
|---|---|---|---|
| MSS | 89.4 | 99.8 | 43.3 |
| TVU | 84.9 | 98.2 | 5.3 |

Disease specific mortality reduction over 14 years:

MMS – 15%
TVU – 11%

*Not significant* – Longer term follow up needed

# Lung Cancer Screening



# NELSON
## 2003-2015

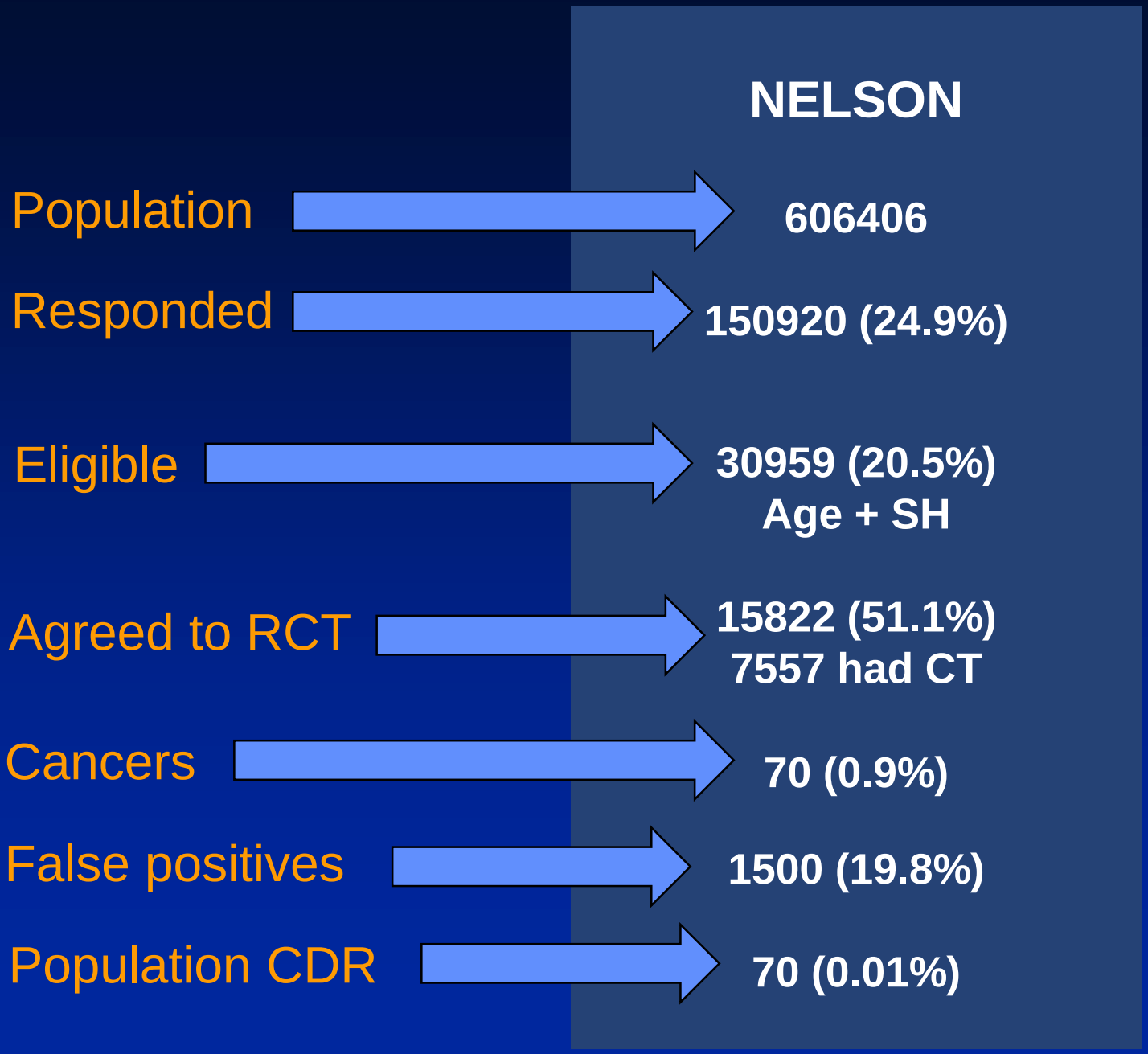
- High risk group identified by questionnaire to 50-75 age range
- Current or former smokers aged 50-75 (n=15600) recruited into trial
- CT vs. No screening
- 26% reduction in LC death

# What does the evidence tell us?

- LDCT in engaged, high-risk people prevents lung cancer death
- Therefore, those at risk should have the opportunity to request LDCT screening

# What does this *not* tell us?

That *population* screening for lung cancer is necessarily a good thing.


NELSON
Population
606406
Responded
150920 (24.9%)
Eligible
30959 (20.5%)
Age + SH
Agreed to RCT
15822 (51.1%)
7557 had CT
Cancers
70 (0.9%)
False positives
1500 (19.8%)
Population CDR
70 (0.01%)

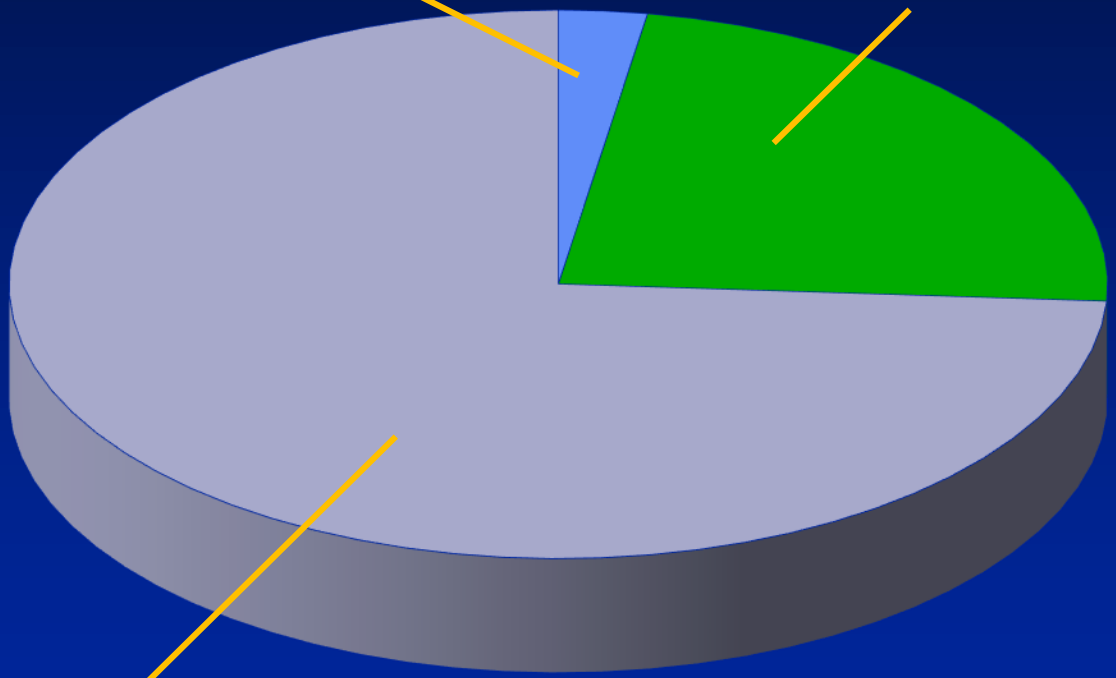
# So…

- 2.6% of whole population entered trial
- But ~ 26% of adults in Belgium and the Netherlands were smoking daily in 2015
- 10% of the target population entered the trial

# Why does this matter?

A - high risk in trial

B - high risk not in trial



C – not high risk

A is *not* the same as B

# Can B be identified?

- Questionnaires don’t work
- GP records
  - How complete?
  - How feasible?
- May introduce inequalities

# If B is identified and invited:

- They may not attend
  - More likely in those of lower SES
- They are likely to be heavier smokers with more co-morbidity
- Therefore *may*
  - Be less able to withstand treatment
  - Have more false positives
  - Have more aggressive disease

# Harm to the “Healthy” Population ?

- False positives leading to invasive investigation
- False positives leading to early repeat LDCT
  - psychological morbidity
- Use of radiology resource
- Effect on quit rates?

# Where now?

- Can we recommend screening for lung cancer?
  - Yes, for those that are engaged
- Can we recommend *population* screening for lung cancer?
  - Not yet

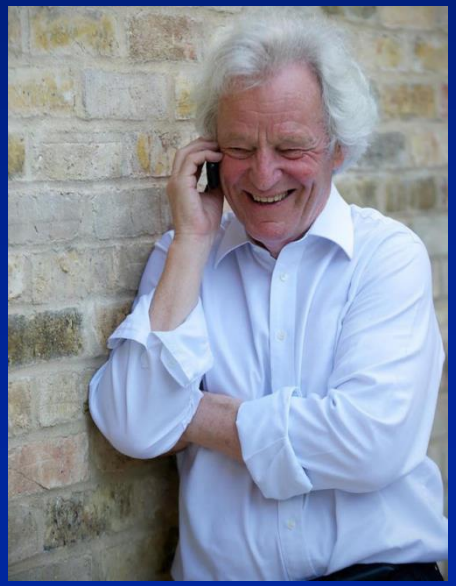
# Way forward for targeted Lung Cancer Screening

- Information aimed at the general population and general practice
  - Current and past smokers should be considered for LDCT screening *and* smoking cessation
- Clear process for a targeted screening programme with managed and efficient recall (surveillance) and strict quality assurance

# What is needed for a population screening programme?

- Reliable method of identifying *the whole* at-risk population
- Evidence from randomisation at the point of invitation

“All screening programmes do harm. Some do good as well and, of these, some do more good than harm at reasonable cost. It is the responsibility of policy-makers, public health practitioners, managers and clinicians to ensure that only programmes that do more good than harm at reasonable cost are implemented and, when they are implemented, that they are managed in such a way as to achieve a level of quality which will ensure that the balance of good and harm demonstrated in research is reproduced in real life.”



Muir Gray, 2007