



Screening: Past and Future perfect?

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- Screening past
- Where are we now?
- Questions for the future:
 - Whether to screen?
 - How to screen?
 - Who to screen?
 - What to tell them?
- The future



No
No
No

The NHS BSP a brief history

1988

- 1988- established : Fully funded
- Training centres developed
- Quality Assured
- Trials of known questions
 - Age
 - 2 view
 - Frequency

The NHSBSP : A brief history 1988-2016

- Changes with emerging technology and evidence:
 - Skill mix
 - Core biopsy
 - 2 views
 - Extend age to 70
 - Assessment of axilla
 - Double reading
 - High risk screening
 - Vacuum biopsy
 - B3 management

The NHSBSP : A brief history 1988-2016

Errors and challenges:

- Faulty administrative systems
- Poor understanding of data: intervals too high
- Public anger about interval cancers
- Public confusion about screening harms and benefit
- Assessment failures

Learning from them:

- Quality management systems
- Reset targets for UK incidence of cancer
- Frank communication about imperfections of screening
- Independent review of level of benefit and harm
- Review

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Where are we now?

- NHSBSP screens women age 50-70
- 2 view digital mammography
- 76 / 80 units offer extended age 47-73 in trial
- High risk women are screened by the NHSBSP
- Medium risk women : screening a/c NICE may be commissioned by local CCGs

Where are we now?

- 2014/15 : screened 2.11 million women
- 18,015 cancers (8.6/1000 screens)
- SDR 1.49
- Population coverage 75.4%
- Performed in 80 units at cost of £100 million

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Whether to screen?

Benefits : Mortality reduction

- ‘Breast screening extends lives. The panel’s review of the evidence on benefit – the older RCTs and those more recent observational studies – points to a 20% reduction in mortality in those invited for screening.
- This corresponds to...one death averted for every 180 women who attend screening’

Whether to screen?

Benefits : Cancer prevention

- ‘for every three screen detected cases of DCIS there was one fewer invasive interval cancer in the next 3 years’

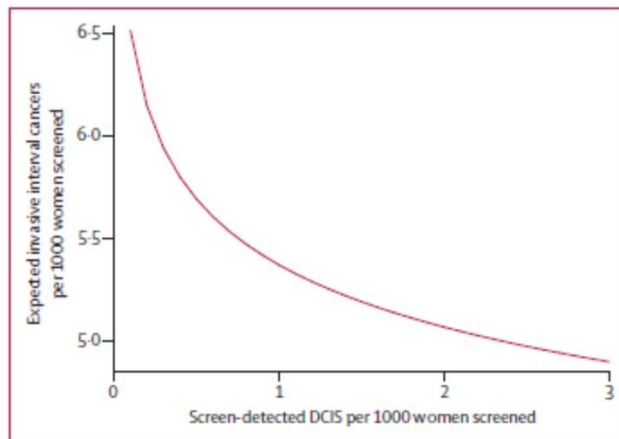
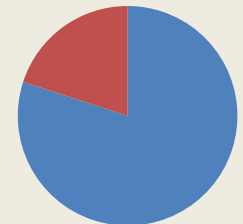


Figure: Fitted invasive interval cancer incidence from Poisson regression as a function of DCIS detection frequency at the previous screen
DCIS=ductal carcinoma in situ.

Whether to screen?

Harms : Accuracy

- False positives:
 - Recall rate 4.3% (43 /1000)
 - Cancer detection rate 0.86% (8.6 /1000)
- False negatives:
 - Cancer detection rate 8.6/1000
 - Interval cancer rate about 3/1000 in next 3 years
 - 2.4 = 80 % true negatives
 - 0.6 = 20 % false negatives



■ TN ■ FN

Whether to screen?

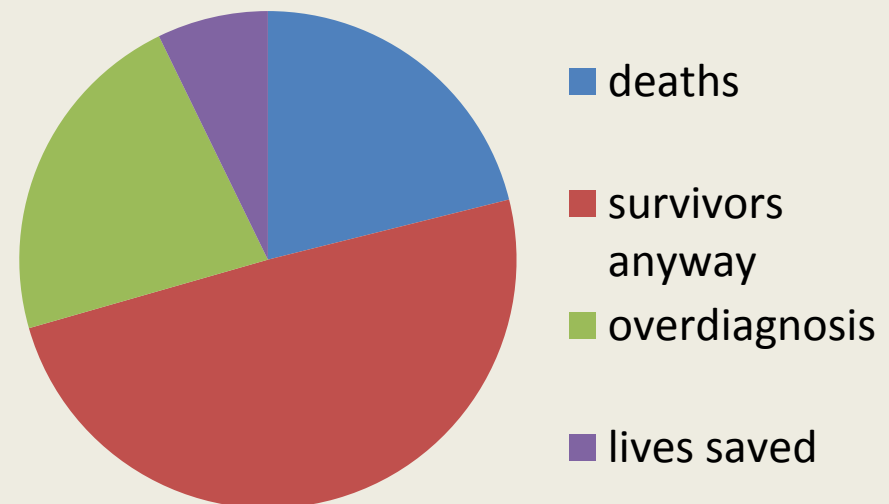
- Harms:
 - Over diagnosis and overtreatment : harms of treatment reducing : LORIS, VACE for B3, targeted DXT, SNB
 - Costs : £20,000 per QALY
 - Radiation : 3-6 cancers induced per 10,000 women regularly screened

Whether to screen?

- 18,000 breast cancers diagnosed annually through screening
 - 3800 die despite screening
 - 8900 treated and would survive without screening
 - 4000 over diagnosed (and treated)
 - 1300 lives saved

- Cost £100 million
- No plans to withdraw screening

Screen detected cancers



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How to screen?



- The perfect test:
 - Accurate : Low false positives and false negatives
 - Effective : Reduction in mortality, detects killer cancers but less over diagnosis
 - Also: Simple, safe, acceptable and cheap

How to screen?

- Available tests
 - Digital mammography
 - DBT
 - MRI
 - US
- Possible others
 - CESM
 - Breath tests, scinti mammography, thermography electrical impedance scanning , breast CT
- Use as single test or as an adjunct

How to Screen? Mammography (DM)

| | Age 50-70 NHSBSP |
|-------------------------------|---|
| Sensitivity/ cancer detection | 8.6/1000 Sensitivity 74% Intervals 3/1000 |
| Specificity/ recalls | Recalls 4.3 % |
| Mortality reduction | 20% from RCTs |
| Over diagnosis | 3 per life saved |
| Safe, acceptable , cheap | Tariff £ 50-90 per screen NHSBSP Radiation |

How to Screen? DBT

| | Prospective studies addition DBT to DM |
|-------------------------------|--|
| Sensitivity/ cancer detection | Increase 2.4 / 1000 |
| Specificity/ recalls | Recalls decrease 1.6- 4.5 (retrospective) |
| Mortality reduction | Unknown |
| Over diagnosis | Unknown |
| Safe, acceptable , cheap | Cost Radiation Questions over protocols : with DM or synthetic |

How to Screen? MRI

| | Studied in high risk young women with DM |
|----------------------------------|---|
| Sensitivity/ cancer detection | Cancer detection 17.9/1000 NHSBSP |
| Specificity /recalls | 13.5 % recall rate NHSBSP |
| Mortality reduction | Unknown Modelled 25% |
| Over diagnosis | Unknown |
| Safe, acceptable , cheap | No Ionising radiation \$135,000 per LYG vs DM \$55,000 in <age 50 IV injection contrast |

NICE FH screening guidance 2013
HSCIC data NHSBSP 2015
Saardatmand et al JCNi 2013

Supplemental screening dense breasts

Dense breasts : 43 % women, categories 3 & 4

Mammography less sensitive and less specific (63 % age 40-49)

Increased risk : By 1.2-2.1 fold in dense cf with average density

>30 US states legislation requiring women to be informed re density

No current clinical guidelines re what to do about it

| | Cancers detected DM | Additional cancers | Recall rate DM | Additional recalls/ biopsies |
|------|---------------------|--------------------|------------------|------------------------------|
| HHUS | | 4.4/1000 | | Recalls 13.9 % |
| ABUS | | 1.9-4.6/1000 | | Recalls 8.7-15 % |
| MRI | | 3.5-28.6/1000 | | Recalls 11.5-23.5 % |
| DBT | 4-4.1/1000 | 1.3-2.6/1000 | Recalls 7.2-16.6 | Recalls 6.6-10.8 % |

Supplemental screening for breast cancer in women with dense breasts...Melnikow et al 2016 Annals Int Medicine

How to screen : Future

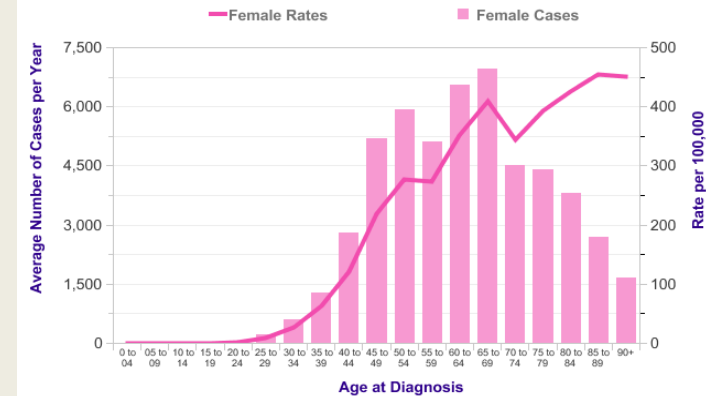
- Mammography: Known outcomes
- DBT : Shows promise as raises cancer detection AND reduces recalls, outcomes unknown : DBT trial of outcomes needed
- MRI : Accepted for High risk screens, high sensitivity and high recalls (FAST MRI may enable wider access)
- No current plans to offer supplemental screening because of density on NHSBSP

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Who to screen

- Population screening : what age range?
- Risk screening : who?
- Personalised screening?
- Does everybody need screening?

Who to screen : Age ?



- Under 50: Variable evidence....
 - RCT 40-49 subgroups NS
 - Meta analysis RCT subgroups significant (18%)
 - RCT age trial NS (17%) for invitees, sig 24% for attenders
- Over 70: Weak evidence...
 - RCT subgroups no mortality benefit
 - No RCT focussed on this age group
 - Over diagnosis increased problem

Hendrick et al JNCI 1997
Moss et al Lancet 2006
Nystrom et al Lancet 2002

Who to screen : Age ?

- NHS BSP extending age to 47-73
- Not capacity to extend both immediately
- Randomise phased extension in batches of 47-49 and 71-73, follow up outcomes including mortality.
- Started in 2009, will report in 2020's
- Will be largest RCT of screening ever.

Who to screen: Risk

What is high risk? Familial

- Risk :NICE: Lifetime risk Familial and genetic-
 - High >30%
 - Moderate 17-30
 - Population < 17
- There are no RCTS of screening high risk women with mortality as an end point
- Evidence for high risk screening is very weak

Who to screen: Risk?

Which Risks?

- There are many risk factors
- Easier to identify women at risk from:
 - Family and genetic
 - Personal history cancer
 - Post DXT
- Combinations of risk factors more difficult to identify but can add up to moderate risk:
 - Atypia
 - Density
 - Epidemiological : parity, obesity, alcohol, hormone use

Who to screen: Risk?

Which Risks?

- Working party proposals:
 - Population risk $<3\times$ average risk : Routine
 - Relative risk $3-8\times$ average : Mammography age 40-73 every 18/12
 - Relative risk $\geq 8\times$ average : High risk surveillance



Public Health
England

Protecting and improving the nation's health

**Report of the Working Party for
Higher Risk Breast Screening**

Holmberg et al Report of the working party into higher risk screening PHE 2015

Who to screen? Low risk?

- Are there some women whose risk is so low they don't need screening? Can we identify them?
- 'The majority of breast cancers will still be diagnosed in those with an average or low risk'

Who to screen: Risk?

| Risk | Ages | Surveillance protocol | frequenc |
|-----------------------------|-------------------------|------------------------|------------------|
| BRCA1 BRCA2 Or = risk | 20-29 30-39 40-49 | n/a MRI MRI+ mam | annual annual |
| TP53 | 20-39 40-49 | MRI MRI +mam | annual annual |
| A-T homozygous | 25+ | MRI | annual |
| A-T heterozygous | 40-49 | mam | 18/12 |
| SD DXT < 30 | 30-39 40-49 | MRI MRI +/- mam | annual annual |

- Who gets screened?
 - High risk: NHSBSP
 - Personal history cancer : NICE 5 years
 - Moderate : NICE from age 40
 - Population: NHSBSP

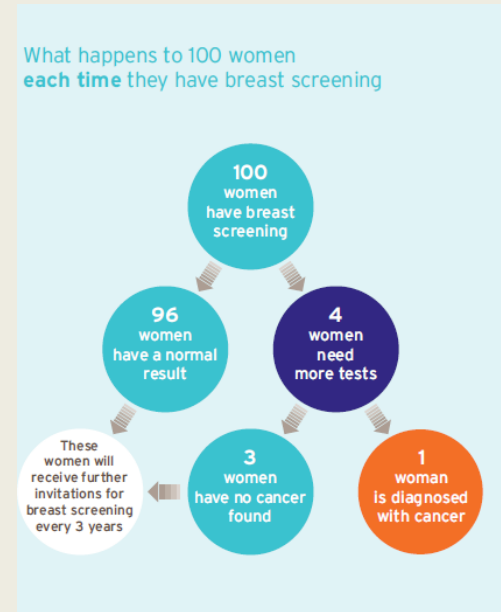
Who to screen – The future

- Population screening : what age range?
 - Results age extension trial needed
- Risk screening : who
 - Should have consistent NHSBSP screening for all those deemed to have similar risk
- Personalised screening?
 - Not foreseeable in NHSBSP for whole population
- Does everybody need screening?
 - No risk group low enough to abandon screening

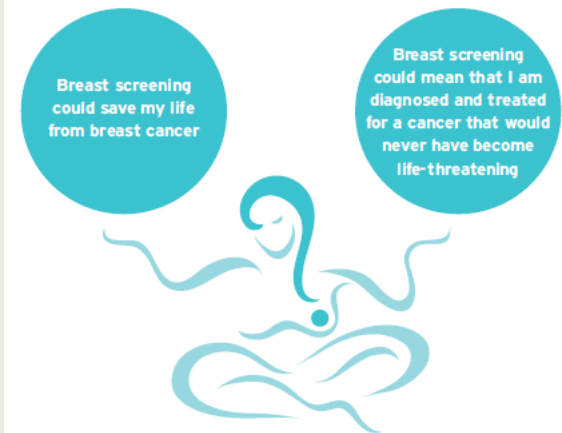
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What to tell them ?

- Informed consent : open and transparent
- Comprehensible language
- New leaflets : infographics
- Decision tools



Weighing up the possible benefits
and risks of breast screening



Communication, Duty of Candour and intervals

CQC regulation 20 April 2015 in
response to Francis report

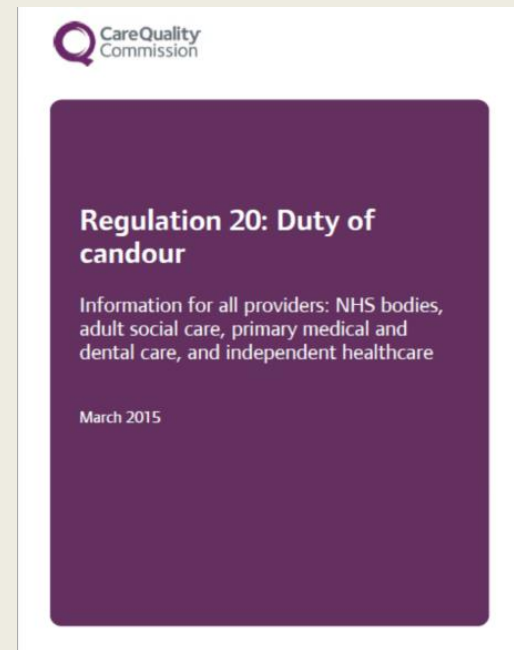
Must act in open and transparent way

Must tell users about notifiable safety incidents and
apologise

Interval cancers:

NHSBSP will publish guidance about handling
intervals and which ones are incidents

eg inadequate assessment, system failures



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Future perfect

- An accurate , effective, cheap and acceptable test
- Offered to the right people at the right time and frequency
- Open communication and understanding of the harms and benefits of screening



Known unknowns

- Foreseeable/ possible changes
 - Continued debate on harms vs benefits
 - Moderate risk screening in NHSBSP
 - Age extension: answer to age limits
 - DBT : increasing evidence on screening outcomes
 - Personalised screening based on
 - risk combinations
 - screening test combinations

The killing
that shocked
the world

TALKING POINTS P22



LOST AMONG
THE POLAR
BEARS

LAST WORD P52



Roald Dahl's
letters to his
mother

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Unknown unknowns

- A brand new test that replaces current tests?
- A government with increased/ decreased will and money to undertake screening programmes?
- Treatment advances that make screening unnecessary?

