Identifying the utility and disutility associated with the overtreatment of early breast cancers for use in the economic evaluation of breast screening programmes

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Background information: Health Economics

- Economic Evaluation: Comparison of alternative courses of action in terms of costs and outcomes
  - Cost-effectiveness analysis/cost utility analysis
    - Meaningful to decision makers (NICE) when
      - outcome in quality adjusted life years (QALYs))
      - Cost per QALY (acceptable threshold)
      - QALY captures utility

- **Utility** is an economic term referring to the total satisfaction received from consuming a good or service.
Incremental Cost-Effectiveness Ratio (ICER)

- A = screening; B = no screening

- ICER = \( \frac{C_A - C_B}{E_A - E_B} \)

Costs (screening) – Costs (no screening)
QALY (screening) - QALY (no screening)

= £cost per QALY
Aims of research

1. To systematically and critically review the evidence used to derive the outcome measures used in economic evaluations of breast cancer screening programmes.

2. To explore the hypothesis that the explicit inclusion of potential disutility associated with the treatment of over-diagnosed early breast cancers will change the relative cost-effectiveness of current breast screening strategies.
Background: Breast Cancer

- One of the leading causes of morbidity and mortality worldwide (CRUK 2012)

- Second commonest cause of cancer related death in women in US, UK and Australia (Ferlay et al. 2013)

- 1 in 8 women will be diagnosed with breast cancer during their lifetime (Saseni et al. 2011)

- Huge demand on healthcare and financial resources (Seiel et al. 2013)
Benefits

- Evidence suggests screening saves lives
- Reduction in breast cancer related mortality (Gotzsche and Jorgensen 2011)
- Cancers identified at an earlier stage
  - Lower treatment related morbidity (Marmot et al. 2011)
- Psychological gain from attending screening (Welch et al. 2011)
- Reassurance from a ‘true negative’ mammogram (Johnston et al. 1998)
Harms

- Overdiagnosis and overtreatment
- Pain and stress from screening process
- Screening induced anxiety/depression
- Unnecessary procedures due to abnormal screens ("false positive")
- Unrealistic risk perception
- False reassurance (false negative)
- Radiation exposure

(Partridge et al. 2008, Gotzsche and Jorgensen 2011, Marmot et al. 2011, Bond et al. 2013, Fuller et al. 2015, Morris et al. 2015)
“False positive” vs. Overdiagnosis

“A false positive is an abnormal mammogram (one requiring further assessment) in a woman ultimately found to have no cancer…”

…Overdiagnosis refers to the diagnosis and treatment of cancer that would never have caused symptoms.”

(IARC, 2002 p. 135)
Overdiagnosis

Use of mammography and effect on US breast cancer incidence from Bleyer and Welch (2012)
Ductal carcinoma in situ (DCIS)

- Heterogeneous condition where abnormal cells accumulate within the milk ducts
- Not technically a “cancer”
- Few if any clinical symptoms – rarely diagnosed before breast screening
- Now accounts for 20% of all breast screening related cancers
- Natural history unknown but low grade may never progress into invasive cancer

(Sagara et al. 2015)
Loris Trial – UK funded trial (NIHR-HTA)

- A Phase III Trial of Surgery versus Active Monitoring for Low Risk Ductal Carcinoma *in Situ* (DCIS)
- PI is Professor Adele Francis, UoB
- Economic Evaluation alongside the trial led by Tracy Roberts, Health Economics Unit
- Main concern is that we capture all the outcomes – good and bad for the evaluation
- Women treated as a result of screening are likely to assume that treatment was necessary
Economic evaluations of breast screening

- Forrest et al. report (1986)
  - deemed breast screening a “cost-effective” method of reducing breast cancer mortality
  - Cost per QALY approach but did not include impact of false positive or overdiagnosis screens on QoL

- Raftery and Chorozoglou (2011)
  - Updated Forrest report to include harms of false positive screens and surgery on QoL
  - showed explicit inclusion changed relative cost-effectiveness of the UK breast screening programme for initial 8 years
  - Lack of data on overdiagnosis on QoL
Methods

- Systematic review of 11 databases
- Any economic evaluation or model based economic evaluation of a breast screening mammography
- MeSH and keyword search related to economic evaluations and mammography
- Search limited to English language
- Year 2000 to May 2016
- Reference list chasing for earlier articles
- Main outcomes to see methodology used and parameters included in the cost-effectiveness analysis
- Sources and methods for screening related HSUVs
Results (PRISMA)

Records identified through database searching (n = 4,146)

Additional records identified through other sources (n = 29)

Records after duplicates removed (n = 2,170)

Duplicates excluded (n = 2,005)

Full-text articles assessed for eligibility (n = 127)

Excluded from title/abstract (n = 2,043)

Studies included in qualitative assessment (n = 64)

Full-text articles excluded with reasons (n = 63)

Studies included in final review (n = 64)
Results (1)

- 4,175 studies identified
- **64 economic evaluations included in final review**
- **Utilities included in studies:**
  - gain from attending screening, true positive and true negative results, less invasive treatment, more favorable stage disease (costs and QoL)
- **Disutilities included in studies:**
  - screening related anxiety, diagnostic work up, false positives, DCIS, cancer diagnosis, treatment, recurrence, lost wages/productivity
- Overdiagnosis- only in most recent studies and still typically included as an extra costs but not its impact on QoL
Results (2)

- All largely stated Breast Screening Programmes were cost-effective
- Huge heterogeneity in the literature
- Most economic evaluations did not include all relevant parameters in their model – few included overdiagnosis
- Where overdiagnosis was included usually only loss in costs measured rather than utility
- Few reliable values of utility/disutility associated with breast screening states
Results (3)

- Pharoah et al. (2013)
  - Included overdiagnosis in analysis
  - Assumed relative rate of overdiagnosis of breast cancer related to screening of 1.19
  - Absolute costs of treating one overdiagnosis of breast cancer was £1800
  - General reduction in QoL associated with a cancer label of 0.9 but no difference in utility whether treatment was deemed to be necessary or not
  - Overdiagnosis expressed in costs only
Mandelblatt et al. (2016)

“The effect of overdiagnosis on QALYs was captured by the disutility of being treated for cancer but dying of other causes without a change in life expectancy.”

Based on loss in utility relating to treatment of:
- DCIS/local cancer (-0.1) or regional cancer (-0.25) for 2 years or distant cancer (-0.6) for life
- -0.006 for 1 week for attending cancer screening and -0.105 for 5 weeks if screen abnormal
- No difference in QoL regardless of whether treatment was required or not (overdiagnosis)
“None of the surveys of quality of life included overtreatment, implicitly assuming all surgery was necessary. To answer this question surveys would have to ask each woman whether her quality of life would be affected if it could be shown that her surgery had been unnecessary.”
Incremental Cost-Effectiveness Ratio (ICER)

- $A =$ screening; $B =$ no screening

- ICER = $\frac{C_A - C_B}{E_A - E_B}$

Costs (screening) (+ve) – Costs (no screening)
QALY (screening) - QALY (no screening)
Incremental Cost-Effectiveness Ratio (ICER)

- A = screening; B = no screening

- ICER = \( \frac{C_A - C_B}{E_A - E_B} \)

Costs (screening) – Costs (no screening)
QALY(screening)(-ve) - QALY (no screening)
Conclusion (2)

- Where HSUVs for breast screening states were used:
  - Based heavily on assumptions
  - Numbers and methods varied between papers
- Most papers used same referenced: de Haes et al. (1991)
  - measured 15 health states of which only 2 were screening/diagnostic related
  - Significant advancements in breast screening technology and treatment in last 2 decades
Plans for further research

- Explore appropriate methods to get appropriate data on overdiagnosis and overtreatment of DCIS to inform quality of life values.
- Plans to undertake primary data collection to ascertain values for breast screening related states by interviewing women (vignettes describing health states – to get valuations).
- Such values can be used in a model based economic evaluation of the breast screening programme to determine how this affects the cost-effectiveness of current international strategies.
Summary

- Breast screening saves lives
- Overdiagnosis does exist and is a key harm resulting from breast screening programmes
- Current economic evaluations of screening mammography do not include all relevant utility and disutility parameters in their cost/QALY estimates.
- No clear consensus on how best to calculate the cost-effectiveness of current breast screening programmes
- Need for further research on validated health state utility values of breast screening states, particularly those relating to overdiagnosis and overtreatment.
- Inclusion of such harms may change relative cost-effectiveness of current screening strategies.
References


