Breast screening with ultrasound in women with mammography-negative dense breasts: evidence on incremental cancer detection and false positives, and associated cost

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study objective was to evaluate the impact of breast screening with ultrasound (US) in self-referring women with dense breasts and a negative report on mammography. US detected early-stage cancers in women with mammography-negative dense breasts, especially in women younger than 50 years, but with substantial financial implications. Overall, the reporting of the clinical data was satisfactory. However, there was little information on the cost analysis and the issue of uncertainty was not addressed, so caution is required when interpreting the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to evaluate the clinical and economic impact of breast screening with ultrasound (US) in self-referring women with dense breasts and a negative report on mammography, in comparison with mammography alone.

Interventions
The study examined the use of bilateral US in women with negative Breast Imaging Reporting and Data System (BI-RADS) D3 and D4 mammography. US findings classified as indeterminate, suspicious or malignant were further assessed with detailed mammography views, percutaneous needle biopsy (needle cytology or core biopsy), and surgical biopsy where indicated. US was compared with mammography-based diagnosis.

Location/setting
Italy/outpatient.

Methods
Analytical approach:
This economic evaluation was based on a single study. The time horizon of the analysis was not reported, but it is likely that it reflected the whole diagnostic period. The authors did not explicitly report the study perspective.

Effectiveness data:
The clinical data were derived from a diagnostic study that involved 26,047 consecutive mammograms in self-referring women attending one study centre (a charity-funded multidisciplinary breast service) between January 2000 and February 2007. The mean age of the participants was 52 years. Women were followed up until the diagnosis was ascertained. No statistical analysis was undertaken to take potential confounding into account. The key clinical outcomes were the rate of cancer detection with US with respect to mammography alone and the percentage of false positives with US.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The summary benefit measure was the incremental cancer detection rate (ICDR). This was derived directly from the effectiveness analysis. Other outcome measures, such as percentage of false positives and distributions of cancers detected with US versus mammography, were considered but were not combined with the costs.
Cost data:
The health services included in the cost analysis were US, US-guided needle biopsy, surgical biopsy as inpatient or outpatient, and histopathology. The resource use data were derived from the sample of women considered in the effectiveness study. The costs were derived from national tariffs. The price year was not reported. The costs were in euros (EUR).

Analysis of uncertainty:
Not performed.

Results
The rate of cancers detected with mammography was 0.82% (216 of 26,047 examinations).

Cancer was suspected on the basis of mammography findings in 475 women who underwent further assessment, and 166 cancers were diagnosed (positive predictive value for recall to assessment: 36.3%).

Of the 25,572 negative mammography reports, 9,157 (35.8%) were classified as dense breasts and underwent US examination. US identified 37 asymptomatic cancers. Thus, the ICDR was 0.40% (95% confidence interval, CI: 0.39 to 0.41) for the total group, 0.33% in women aged younger than 50 years and 0.51% in those aged 50 years or older.

US detected 41.3% of the cancers in women aged younger than 50 years and 13.5% in those aged 50 years or older. An audit of mammography examinations led to an additional recall in about 10% of normal mammography screens.

In addition, US-only detected cancers had a more favourable stage than cancers detected on mammography (early stages: 64.8% versus 35.5%, p=0.001; more advanced stages: 13.5% versus 31.3%, p=0.047).

The estimated incremental cost of including US in screening per woman examined with mammography alone was EUR 59.06 using outpatient surgical biopsy (local anaesthesia) and EUR 61.55 using inpatient surgical biopsy (general anaesthesia).

The estimated cost per US-only detected cancer was EUR 14,618.20 using outpatient surgical biopsy (local anaesthesia) and EUR 15,234.93 using inpatient surgical biopsy (general anaesthesia).

The rate of false positives attributable to US (benign on surgical biopsy) was 0.9% (83 cases out of 9,157).

Authors' conclusions
The authors concluded that US detected early-stage cancers in women with mammography-negative dense breasts, especially in women younger than 50 years, but with substantial financial implications. The cost ranged from EUR 59 to EUR 62 per US-screened woman and from EUR 14,618 to EUR 15,234 per US-detected cancer.

CRD commentary
Interventions:
The two strategies under examination appear to have been appropriately selected to reflect the relevant comparators (usual care versus additional diagnostic examinations) in the authors' setting.

Effectiveness/benefits:
The clinical data were derived from a longitudinal study, which followed a large sample of women. The duration of follow-up was not clear, but it appears to have been that of the diagnostic findings. The whole sample selection process and the clinical outcomes were described clearly. It should be noted that self-referring women were included in the analysis and, even if symptomatic women were not considered in the analysis, caution will be required if extrapolating these findings to other patient populations. The benefit measures considered are typical of diagnostic studies and were appropriate given the objective of the analysis.

Costs:
The authors did not explicitly state the perspective of the study. The costs were presented as macro-categories, the unit...
costs being presented separately from the resource quantities. Little information on the sources of the costs and other
details, such as price year, was provided. (Note: since this abstract was published, we have been informed by the authors
that, although the price year as not reported, 2007 tariffs were used. The authors acknowledge that national tariffs are
not fully representative of real costs, however they point that that they are the only existing official national reference
available, and that single centre assessment of real costs depends heavily on local efficiency and cannot therefore be
reliably generalised)

Analysis and results:
The synthesis of the costs and benefits was appropriate. The results of the clinical study were extensively presented. The
issue of uncertainty was not addressed as no sensitivity analyses were carried out. The authors presented a detailed
discussion of their findings and the reasons for differences in the detection rates and false-positive rates obtained in
other studies (mainly due to different patient populations).

Concluding remarks:
Overall, the reporting of the clinical data was satisfactory. However, little information was given on the cost analysis
and the issue of uncertainty was not addressed, so the authors’ conclusions should be considered with a degree of
cautions.

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Bibliographic details
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Ciatto S. Breast screening with ultrasound in women with mammography-negative dense breasts: evidence on
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Other publications of related interest
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