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Breast screening using 2D-mammography or integrating digital breast tomosynthesis (3D-mammography) for single-reading or double-reading – Evidence to guide future screening strategies

Nehmat Houssami [a,*], Petra Macaskill [a], Daniela Bernardi [b], Francesca Caumo [c], Marco Pellegrini [b], Silvia Brunelli [c], Paola Tuttobene [b], Paola Bricolo [c], Carmine Fantò [b], Marvi Valentini [b], Stefano Ciatto [b,c,†]

[a] *Screening and Test Evaluation Program (STEP), School of Public Health, Sydney Medical School, University of Sydney, Sydney, Australia*
[b] *U.O. Senologia Clinica e Screening Mammografico, Department of Diagnostics, Azienda Provinciale Servizi Sanitari (APSS), Trento, Italy*
[c] *Centro di Prevenzione Senologica, Marzana, Verona, Italy*

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Abstract ***Purpose:*** We compared detection measures for breast screening strategies comprising single-reading or double-reading using standard 2D-mammography or 2D/3D-mammography, based on the '*s*creening with *t*omosynthesis *or* standard *m*ammography' (STORM) trial.

Methods: STORM prospectively examined screen-reading in two *sequential* phases, 2D-mammography alone and integrated 2D/3D-mammography, in asymptomatic women participating in Trento and Verona (Northern Italy) population-based screening services. Outcomes were ascertained from assessment and/or excision histology or follow-up. For each screen-reading strategy we calculated the number of detected and non-detected (including interval) cancers, cancer detection rates (CDRs), false positive recall (FPR) measures and *incremental* CDR relative to a comparator strategy. We estimated the false:true positive (FP:TP) ratio and sensitivity of each mammography screening strategy. Paired binary data were compared using McNemar's test.

Results: Amongst 7292 screening participants, there were 65 (including six interval) breast cancers; estimated *first-year* interval cancer rate was 0.82/1000 screens (95% confidence interval (CI): 0.30–1.79/1000). For single-reading, 35 cancers were detected at both 2D and

* *Corresponding author:* Address: School of Public Health (A27), Sydney Medical School, University of Sydney, Sydney 2006, Australia. Tel.: +61 0419 273510; fax: +61 2 9351 5047.
E-mail address: nehmath@med.usyd.edu.au (N. Houssami).
† Post-humous (deceased May 2012).

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2D/3D-mammography, 20 cancers were detected only with 2D/3D-mammography compared with none at 2D-mammography alone ($p < 0.001$) and 10 cancers were *not* detected. For double-reading, 39 cancers were detected at 2D-mammography and 2D/3D-mammography, 20 were detected only with 2D/3D-mammography compared with none detected at 2D-mammography alone ($p < 0.001$) and six cancers were *not* detected. The incremental CDR attributable to 2D/3D-mammography (versus 2D-mammography) of 2.7/1000 screens (95% CI: 1.6–4.2) was evident for single and for double-reading. Incremental CDR attributable to double-reading (versus single-reading) of 0.55/1000 screens (95% CI: −0.02–1.4) was evident for 2D-mammography and for 2D/3D-mammography. Estimated FP:TP ratios showed that 2D/3D-mammography screening strategies had more favourable FP to TP trade-off and higher sensitivity, applying single-reading or double-reading, relative to 2D-mammography screening.

Conclusion: The evidence we report warrants rethinking of breast screening strategies and should be used to inform future evaluations of 2D/3D-mammography that assess whether or not the estimated incremental detection translates into improved screening outcomes such as a reduction in interval cancer rates.

1. Introduction

Mammography screening has been shown to reduce breast cancer mortality in overviews of the randomised trials, and both its benefits and harms have been evaluated and debated [1–3]. Recently, two prospective population-based screening trials [4,5] have shown that adding digital breast tomosynthesis or 3D-mammography, a derivative mammographic technology [6–9], to conventional 2D-mammography significantly increases breast cancer detection. Both of these landmark studies have also shown that the addition of 3D-mammography can also reduce false recalls [4,5], although the extent that it could reduce false recalls varies according to the screen-reading and recall strategy, and may be more evident in screening settings where false recalls are relatively more frequent [10–12]. Given that international variations exist with regard to screen-reading strategies, specifically whether single-reading or double-reading is used, and the emerging data on 3D-mammography for population screening, evidence on the comparative contribution of various screening strategies to detection measures will be critical in guiding future breast screening research, practice and policy.

In this study, we examine the effect of various screen-reading strategies on cancer detection and false recall measures, based on the '*s*creening with *t*omosynthesis *or* standard *m*ammography' (STORM) trial [4]. We compare mammography screening strategies comprising single-reading or double-reading using standard 2D-mammography or using integrated 2D/3D-mammography for population screening, in terms of cancer detection and false recalls.

2. Methods

2.1. Screening setting and participants

This study is based on the prospective population-based STORM [4] screening study which compared two sequential mammography screen-readings, 2D-mammography alone and *integrated* 2D/3D-mammography whereby 3D-mammography is reported with the availability of 2D-mammography. The STORM study methods and population, and initial results, have been reported by Ciatto and colleagues [4], and are described briefly in the present paper. STORM recruited asymptomatic women aged $\geqslant$48 years through two North Italian services that provide biennial population breast screening in Trento and Verona, August 2011 to June 2012 [4]. Screening participants were invited to have integrated 2D/3D mammography screening, and those opting not to participate in the study had (standard) 2D-mammography [4]. The study was granted institutional ethics approval, and informed consent was obtained from participants [4].

Screening participants in STORM had digital mammography using a Selenia Dimensions Unit with integrated 2D/3D mammography performed as the COMBO© procedure (Hologic, Inc., Bedford, MA, United States of America (USA)): 2D and 3D images were acquired with a single breast positioning and compression, with each of the 2D and 3D acquisitions comprising bilateral two-view (cranio-caudal and mediolateral oblique) mammography.

2.2. Screen-reading

Screening mammograms were interpreted *sequentially* by radiologists initially using standard 2D-mammography alone, and were then re-interpreted by the same

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