

# Through a glass darkly: the mammography debate

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All screening programmes do harm; some do good as well, and, of these, some do more good than harm at reasonable cost. The first task of any public health service is to identify beneficial programmes by appraising the evidence. However, evidence of a favourable balance of benefit to harm in a research setting does not guarantee that a similar balance will be reproduced in practice, so screening programmes need to be introduced in a way that allows their quality to be measured and continuously improved.

— Sir Muir Grey, former director of the U.K. National Screening Committee<sup>1</sup>

About the ongoing breast cancer screening mammography debate (less a controversy, because many points of consensus and convergence are present if not always apparent), we can make these points as prelude: that it is complex; that it is naïvely implausible to expect any decisive final resolution to the residual issues that will be convincing to the principle contending parties; and that behind it all, the devil is in the methodology.

Only sufficiently powered randomized trials—if still feasible in this age—with access to discriminatory individual patient data can hope to be more decisive on the central issues of a debate often exhibiting an unintended degree of entertainment, replete with impassioned and sometimes imprudent rhetoric, colorful personalization of charges, and the occasional eccentric position (Dr. Peter Gøtzsche suggesting that the proper way to “reduce the breast cancer incidence in the screened age group” is to not screen<sup>2</sup>, which would be ethically questionable to some).

Through it all, it has to be realized that much of the contention is less about the facts and more about the methodologic integrity of the underlying studies. Far from the madding crowd, the reader is advised to review closely Dr. Steven Narod’s strong defense of the CNBSS (Canadian National Breast Screening Study) trials in this issue of *Current Oncology*<sup>3</sup> and in his Countercurrents series paper<sup>4</sup>, and Dr. Martin Yaffe’s critique, also in this issue<sup>5</sup>. Outside of his defense of the CNBSS trials, Narod is also an important voice on magnetic resonance imaging (MRI); and Yaffe, a screening proponent and critic of the CNBSS trials, is vitally

involved in contributions to digital breast tomosynthesis. Another key player, Dr. Dan Kopans, was instrumental in the development of tomosynthesis<sup>6</sup> and, together with Yaffe, has contributed to its emergence as a potential “über-mammography”—a title for which abbreviated breast MRI technologies are also contending.

## Hidden Convergence

However, there remain many distractive and misleading elements in this debate, allowing for the appearance of greater contention than might be the case after a process of normalization. One such process is suggested by the question “Do the many divergent claims in this debate fundamentally represent true conflicts or just different elected linguistics frameworks, and hence are they more a matter of surface-discordant presentation than of clashing or irreconcilable content?” For the central themes that are identified and discussed more fully in the accompanying review in this issue (especially the mortality benefits derivable from screening mammography, and the countervailing harms, in particular overdetected), the answer appears to be “Not always (or even often).” There is more divergence than genuine competitive content in the rendition of the underlying data, but when properly relativized and weighted to common parameters, far more comparable results are uncovered.

Consider randomized controlled trials at the two extremes: those included in the U.S. Preventive Services Task Force (USPSTF) study and the population-based EUROSREEN systematic review and meta-analyses (discussed more fully in my review in this issue), with USPSTF using the metric of number needed to invite to prevent 1 breast cancer death, finding it to be no less than 1904; and EUROSREEN using the number needed to screen, which is methodologically stronger because it excludes women invited but not actually attendant, and finding it to be between 111 and 143—a seemingly wide stretch for a mortality reduction estimation. However, Stephan Duffy and colleagues<sup>7</sup> have ingeniously “normalized” these disparate findings to the same endpoint (using estimates from the Independent U.K. Panel on Breast Cancer Screening as the commonality), providing the numbers needed (to invite or to screen) to prevent 1 breast cancer death at ages 55–79 among screening U.K. women 50–69

<sup>a</sup> The No Surrender Breast Cancer Foundation is a U.S.-based 501(c)3 not-for-profit organization providing high-quality critically reviewed and appraised information and guidance to the breast cancer community.

years of age for 20 years. For USPSTF, the number (needed to invite) was 193; for EUROSREEN, the number (needed to screen) was 64–96. Thus, although the magnitude of disagreement on mortality reduction between EUROSREEN and USPSTF appeared superficially to be vast as reported in the literature before normalization (roughly a factor of 17 at the upper range and 13 at the lower), the discordance became minimal after normalization, clustering together at only a factor of 2–3. Screening 1904 women to reduce 1 breast cancer death might challenge acceptance, but screening as few as 64–193 women for the same mortality benefit (and 257 at most, if other meta-analytic data are included) is vastly less likely to confound. Despite apparently wide discordance, substantial confluence is observed—with even more convergence if analysis is restricted to number needed to screen.

To some extent, overdetection can also be “normalized” using a well-honed critical razor that includes studies restricted to, for instance, those using (at minimum)

1. individual patient data (these enumerated more fully in my review in this issue).
2. screening-attendant cohorts.
3. high methodologic trial consistency and integrity.
4. sufficiently long follow-up.
5. control for both lead time and background breast cancer incidence during screening (per my review).

Applying that razor, we would again see the emergence of significantly greater concordance about the degree of overdetection (on the order of no more than 10%). Rendition must therefore be discriminated from genuine conflicting content. Not all debates are true controversies. That perspective does not remove all legitimate points of contention, but does show that some of the opacity—and some of the discordance—is far more muted than it appears, disguising the convergence of robust, critically appraised, and normalized interpretation, thus helping to motivate a more constructive look both beyond and underneath (as it were) the narrow borders of the current debate.

My goal here is therefore not to become another disputant, but rather to step back and view mammography in a broader context as it plays out among the front-line stakeholders (screening-eligible women and their health care providers) and, more critically, to suggest how to move beyond the current debate to new screening technologies, themes more fully developed in my review. Along the journey, we will also learn (a bit to our chagrin) that whatever we think of the wide divide between the partisans in the debate, the patients and the frontline providers appear to occupy almost a parallel universe, rarely intersecting with the debate and seemingly rendering it an irrelevancy through a distinct set of their own preferences, little affected by the action on the stage. The debate might seem overlaid to us *in* it, but it appears that, *outside*, few are truly listening.

## Going Beyond

One commentator has recently concluded that we need “a new approach to our long history of in-fighting over screening guidelines. Such in-fighting neither makes best use of

our professional resources nor serves to enhance the trust and confidence that the public holds for medicine and science” and that “The public still lacks basic knowledge about the benefits and harms of screening”<sup>8</sup>. I am not so sanguine: first, I believe—and there are data to suggest—that even when patients are better informed, they will, for complex reasons, continue to favour screening over potentially real harms; second, I do not believe, as noted, that even health professionals themselves have a consistently reliable grasp on the complex issues involved or that they possess the critical appraisal skills that are imperative for objective evaluation of underlying research methodologies. Instead, I argue for a greater focus on

1. moving beyond the current borders of the mammography debate to secure superior screening technologies that will erode the central status currently occupied by conventional mammography.
2. making research advances that will minimize the harms, especially of overdiagnosis or overdetection.
3. furthering research to provide validated markers for the discrimination of low-risk and indolent disease.

## Looking Forward

With updated USPSTF recommendations anticipated by fall of 2015 (indeed, revised draft guidelines from the USPSTF, reaffirming the original 2009 guidelines, were just released 21 April 2015)<sup>9</sup>, likely to be followed by updated Canadian guidelines, further contention and debate are sure to be ignited—especially given that the publication will almost certainly reflect recent U.S. National Cancer Institute recommendations on overdiagnosis: namely, that screening guidelines should be revised to lower the chance of detection of minimal-risk cancers and IDLE (indolent lesions of epithelial origin)<sup>10</sup>. But, hopefully, the community should be better prepared this time for a more measured and more productive response, modulated and informed by the emerging strategies discussed here for the effective reduction of mammographic screening harm.

The foregoing reflections on digital breast tomosynthesis and both traditional breast MRI and abbreviated or ultraFAST breast MRI are intended to stimulate rethinking about population screening programs so as to encourage new trials investigating new breast screening strategies that would avoid the many limitations of current mammographic screening (especially the substantial recall rates) and help to lift us out and above the not-always-productive mammography debates. If the new technologies are not “the way out,” they are at least the hint of the way *forward*, beyond the current cycle of contentions and contentious repartee that often don’t quite intersect, are largely ignored by the women affected, rely on data often corrupted by methodologic limitations, and rarely therefore convincing to other than the faithful.

## CONFLICT OF INTEREST DISCLOSURES

I have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and I declare that I have none.

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## REFERENCES

1. Gray JA, Patnick J, Blanks RG. Maximizing benefit and minimizing harm of screening. *BMJ* 2008;336:480–3.
2. Gøtzsche PC, Jørgensen KJ. Effect of population-based screening on breast cancer mortality. *Lancet* 2012;379:1297.
3. Narod SA. Counterpoint re: “Mammography screening—sticking to the science.” *Curr Oncol* 2015;22:177.
4. Narod SA. Reflections on screening mammography and the early detection of breast cancer: A Countercurrents Series. *Curr Oncol* 2014;21:210–14.
5. Yaffe MJ. Mammography screening—sticking to the science. *Curr Oncol* 2015;22:174–6.
6. Kopans DB. Digital breast tomosynthesis from concept to clinical care. *AJR Am J Roentgenol* 2014;202:299–308.
7. Duffy SW, Chen TH, Smith RA, Yen AM, Tabar L. Real and artificial controversies in breast cancer screening. *Breast Cancer Manage* 2013;2:519–28.
8. Stefanek ME. Uninformed compliance or informed choice? A needed shift in our approach to cancer screening. *J Natl Cancer Inst* 2011;103:1821–6.
9. U.S. Preventive Services Task Force (USPSTF). Draft Recommendation Statement. Breast Cancer: Screening [Web page]. Rockville, MD: USPSTF; 2015. [Available at: <http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementDraft/breast-cancer-screening1> (link will become obsolete when the finalized version is posted)]; cited 28 April 2015]
10. Esserman LJ, Thompson IM, Reid B, *et al.* Addressing overdiagnosis and overtreatment in cancer: a prescription for change. *Lancet Oncol* 2014;15:e234–42.