CURRENT ONCOLOGY

EDITORIAL

The mammography debate, round two: science, smoke and mirrors

C. Kaniklidis, Research Director, No Surrender Breast Cancer Foundation*[a]

Regrettably, some aspects of the breast cancer screening debate display their own uniquely obfuscating argumentation, more smoke and mirrors than scientific clarity. I begin here by providing some brief examples, and warnings, of those arguments to help guide through the fog. Following this, the journal also provides, as it did in the June issue[1–4], the best antidote: namely, contributions from several content experts offering true science that scythes through the obscurities—the point, after all, of science in the interest of illumination.

SOME SMOKE AND MIRRORS

Although it must be admitted that some overdiagnosis occurs in mammographic screening, the psychosocial impact of false positives, and especially those triggering a subsequent biopsy, might not be as large or as clinically adverse as often suggested. In this connection, it could be useful to distinguish two subclasses of false positives: simple false positives and complex false positives[5,6]. The incidence of complex false positives involving a biopsy (5%—and 6.3% under annual screening for the 40+ age group) was dramatically lower than cumulative total recall risk (19.9%), showing that not all false positives are created equal. Furthermore, a subgroup analysis of another study[7] found that the adverse psychosocial impact was in fact comparable for women managed invasively (biopsy) and for women managed noninvasively, contradicting the common claim that degree of distress after false-positive mammography depends on the invasiveness of any subsequent follow-up required. In any equitable discussion, we must clear the smoke clouding much of the claims of significant harms secondary to false positives and be honest in communicating the realities to affected screening-eligible women.

Similarly, in a recent paper, Saquib *et al.*[8] comprehensively reviewed the randomized controlled trial and meta-analytic evidence of disease-specific and all-cause mortality benefits from screening for various diseases, concluding that "reductions in disease-specific mortality are uncommon and reductions in all-cause mortality are very rare or non-existent." But two issues significantly muted those conclusions. First, as I expressed in my Perspectives review in *Current Oncology*[3] in agreement with others[9], it is arguable whether all screening tests should be assessed with mortality as the main outcome. Second, however, a close critical reading of study finds that the "uncommon" disease-specific mortality benefit referenced—and heralded in dozens of uncritical online media reports, even with headlines such as "Mortality benefit rarely achieved"—actually translates to 30% (10%–25% for mammography specifically), which, to the minds of most is not a trivial or "uncommon" reduction at all[10]. More mirrors.

To help women make more informed decisions about mammography screening, another randomized study used a decision aid that included information on overdetection. The authors concluded that "information on overdetection of breast cancer provided within a decision aid increased the number of women making an informed choice about breast screening. Becoming better informed might mean women are less likely to choose screening"[11]. However, although the decision aid was hailed as making a significant positive contribution, 75% of the participants actually found that the included information on overdetection was *not* helpful in making a decision. Worse still, more than twice as many women in the intervention group than in the control group reported being unsure about their intention to screen (16% vs. 7%). It is arguable whether any decision aid that—after providing information about overdetection (overdiagnosis) to screening-eligible women—*increases* uncertainty can be deemed a clinically relevant success in terms of helping women to make more informed decisions about screening. Similarly, it is unclear whether, with mammography-screening decision-aid studies in general, the claimed increase in the proportion of women counted as "informed" after exposure to the decision aid isn't really a conflation of the ability to repeat the cautionary content presented, with an in-fact unproven gain in true comprehension of the content. Comprehension is not just "playback."

THE SCIENCE: A GUIDED TOUR

The foregoing three examples, out of many, should serve to illustrate that, to progress in the debate, participants have to move past claims that soar beyond the evidence or obscure it. To that end, the contributors in the present issue of *Current Oncology* provide the science.

[a] 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.

Correspondence to: Constantine Kaniklidis, No Surrender Breast Cancer Foundation, PO Box 84, Locust Valley, New York 11560 U.S.A.
E-mail: edge@evidencewatch.com ■ **DOI:** http://dx.doi.org/10.3747/co.22.2890

Misleading "Authorities"

The Perspectives article by Dr. Daniel Kopans ("Breast cancer screening panels continue to confuse the facts and inject their own biases"[12]) continues a decades-long quest toward the systematic exposure of what Kopans regards as the methodologically corroded edifice long supporting an anti-screening posture. The warrants of each layer of the anti-screening foundation—the recalls and false positives that are posited to be fundamental and overriding harms of screening, together with associated psychological distress and overtreatment; the artificiality of age 50 as a motivated lower screening initiation boundary; the biennial schedule; the ethically compromised calculus of benefits-rationing through "high-value screening"; and the compromising limitations of methodology, internal incoherencies, and external contradictions of "authoritative" guidelines—are subjected to intensive critical scrutiny. Although the Kopans article is formally an examination of the recent International Agency for Research on Cancer recommendation, the author more broadly provides a unified distillation and guided tour of the issues under one "cover," a challenge to advocates against screening.

How to Think About Mammography

What's a poor working oncologist to do? In trying to step nervously over and between the many conceptual landmines of the mammography debate, with its arcana of lead-time bias, length bias, overdetection, projected background breast cancer incidence rates, prevalent and incident screens, simulation models, and some truly numbing statistical gymnastics (a complex, near-Byzantine battlefield), the answer would appear to be "not much." No welcome here. No basket of clinical "pearls" to come away with.

In her contribution ("Has screening mammography become obsolete?"[13]), Dr. Mary Costanza provides overdue clarity and penetration through the fog, without compromising the sophistication of the underlying issues, and in the process upends the usual discussion of harm–benefit ratios with a masterful account of the harms of *not* screening. In her contribution, Costanza has managed to provide that "missing manual," the working oncologist's survival guide to the mammography debate.

Screening by Magnetic Resonance Imaging

In the arcana of the mammography controversy, it is easy to lose sight of the fact that the true topic of conversation is *breast cancer screening* in the service of early cancer detection, of which mammography is only one of many modalities, the "screening spectrum" including ultrasonography, magnetic resonance imaging (MRI), and the emerging technologies of abbreviated breast MRI and digital breast tomosynthesis. The important and closely-reasoned paper ("Utilization of magnetic resonance imaging in breast cancer screening"[14]), from a team of New York University oncology experts serves as an invaluable reminder that different evidence-based recommendations are needed to assess the precise role and value of screening MRI for early breast cancer detection in elevated-risk populations, and that little in the way of "received wisdom" can be taken for granted here. If you thought you knew what is important to know about screening MRI, think again; this paper is the corrective.

The Limits of Modelling Mammography

Simulation models have played a relatively large role in the assessment of the benefit–harm associated with mammographic screening and of screening guidelines. Such modelling can provide a formal means to evaluate, for outcomes at the population level, the comparative effects of various alternative screening strategies (while holding any arbitrary condition or conditions constant) and can often detect otherwise below-the-radar differences over time in cohorts and groups.

An insight-rich paper, "To screen or not to screen for breast cancer? How do modelling studies answer the question?"[15], from an eminent Dutch team of modelling experts uses a consistent framework for the qualitative assessment of such simulation models, but ultimately—and with rare and uncompromising honesty—finds a high risk of bias in outcomes after a review of the central issues and limitations of modelling when deployed for the valuation of screening mammography's benefits and harms.

Critical Issues in Mammography Screening

Last, not least—and don't let the title, "Response to: 'Beyond the mammography debate: a moderate perspective'," fool you—Dr. Martin Yaffe's contribution is far more than a response to and commentary on my invited editorial and Perspectives in Oncology review in the May–June issue of *Current Oncology*[3,4], because he adds his own uniquely perceptive observations and reflections to the central questions and themes of the mammography debate, namely randomization, overdetection, different forms and degrees of bias in the trials, and bias in the popular media reporting on mammography, among others. My response takes nothing away from the value of those shrewd and inestimable insights, and indeed only serves to underline the importance of paying meticulous attention to his rich commentary. Collectively, his contributions significantly advance the conversation on the state of the art of breast cancer screening today.

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.

AUTHOR AFFILIATIONS

*No Surrender Breast Cancer Foundation, Locust Valley, NY, U.S.A.

REFERENCES

1. Yaffe MJ. Point: mammography screening—sticking to the science. *Curr Oncol* 2015;22:174–6.
2. Narod SA. Counterpoint re: "Mammography screening-sticking to the science". *Curr Oncol* 2015;22:177.
3. Kaniklidis C on behalf of the No Surrender Breast Cancer Foundation. Beyond the mammography debate: a moderate perspective. *Curr Oncol* 2015;22:220–9.
4. Kaniklidis C on behalf of the No Surrender Breast Cancer Foundation. Through a glass darkly: the mammography debate. *Curr Oncol* 2015;22:171–3.
5. Winch CJ, Sherman KA, Boyages J. Toward the breast screening balance sheet: cumulative risk of false positives for annual versus biennial mammograms commencing at age 40 or 50. *Breast Cancer Res Treat* 2015;149:211–21.
6. Heleno B, Sierma V, Brodersen J. Author Reply to Dr. Arleo and to Dr Newell [Web commentary]. *Ann Fam Med* 2015;:.

[Available at: http://annfammed.org/content/13/3/242/reply; cited 7 August 2015]
7. Heleno B, Siersma VD, Brodersen J. Diagnostic invasiveness and psychosocial consequences of false-positive mammography. *Ann Fam Med* 2015;13:242–9.
8. Saquib N, Saquib J, Ioannidis JP. Does screening for disease save lives in asymptomatic adults? Systematic review of meta-analyses and randomized trials. *Int J Epidemiol* 2015;44:264–77.
9. Shekelle PG. Commentary on N Saquib *et al.* Does screening for disease save lives in asymptomatic adults? Systematic review of 5 meta-analyses and randomized trials. *Int J Epidemiol* 2015;44:277–8.
10. Taylor P. Commentary: tempering expectations of screening: what is the most authoritative advice we can give, given the data that we have? *Int J Epidemiol* 2015;44:280–2.
11. Hersch J, Barratt A, Jansen J, *et al.* Use of a decision aid including information on overdetection to support informed choice about breast cancer screening: a randomised controlled trial. *Lancet* 2015;385:1642–52.
12. Kopans DB. Breast cancer screening panels continue to confuse the facts and inject their own biases. *Curr Oncol* 2015;22:e376-79.
13. Costanza ME. Has screening mammography become obsolete? *Curr Oncol* 2015;22:e328-31.
14. Lin D, Moy L, Axelrod D, Smith J. Utilization of magnetic resonance imaging in breast cancer screening. *Curr Oncol* 2015;22:e332-35.
15. Koleva-Kolarova RG, Zhan Z, Greuter MJW, Feenstra TL, De Bock GH. To screen or not to screen for breast cancer? How do modelling studies answer the question? *Curr Oncol* 2015;22:e380-82.