EDITORIAL

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Recognising the benefits and harms of breast cancer screening: an opportunity to target improvement

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This very important report from the United Kingdom assessing breast cancer screening clearly states that we must balance the potential benefits and harms of screening (Marmot *et al*, 2013). If we are not honest about the contributing causes of the adverse consequences in population screening, we have no chance to improve what we do. Importantly, understanding the magnitude of harms and benefits is a starting point for developing a comprehensive strategy to significantly improve the field (Esserman and Thompson, 2010).

This report concludes that the benefits of screening still outweigh the harms, but the UK Panel elevates this tension so that we can put screening into perspective. The panel outlines the opportunities to reduce harm, and therefore improve the net benefit of screening. Importantly, this report describes the likelihood of women participating in screening being diagnosed and also overdiagnosed with breast cancer. Of the approximately 307 000 women aged 50–52 years who are invited to screening each year, just over 1% would have an overdiagnosed cancer during the next 20 years. The table below summarises the reported results of women invited to screen and provides the appropriate perspective.

Screen-related events	Number of women	Percent
Invited to screening 50–52 years	307 000	100.0
Diagnosed with breast cancer	20 907	6.8
Overdiagnosed	3960	1.3
Lives saved due to screening (mortality benefit)	1320	0.4

There are several points that can be made from this assessment of screening. First is that the panel definitively acknowledges overdiagnosis (Esserman *et al*, 2009; Welch and Black, 2010). Second, women participating in a screening programme are more likely to be overdiagnosed than to have their life saved by screening. However, saving a life has much higher priority to most women than going through additional treatments that they many not need. We have this discussion regularly about all treatments and the majority of women opt for more aggressive therapy even when they recognise that it may not improve their health.

The third point is that the chance of a woman having her life saved because she had a screen-detected cancer is not 100%, which is what most people assume. In fact, this report indicates it is 1320/20 907, or 6.3% of women have a mortality benefit from screening. This is consistent with what others have reported (Welch and Frankel, 2011). In fact, the 6.3% figure is likely to be an overestimate given that the original trials were conducted prior to the use of modern adjuvant/neoadjuvant therapy and we know that the contribution of adjuvant therapy to further reducing mortality is in the range of 50–67% (Berry *et al*, 2005; Kalager *et al*, 2010), indicating that the current chance of a woman having her life saved from screening is closer to 2–3%. That is not to say that there is no benefit of screening, but simply to say that it is small and not as great as we would have hoped. The needed effort to improve screening is surely worth the significant amount of time and energy.

We do not have to accept the current situation as immutable. The final point to be made is that there are significant opportunities to make big changes that would alter the benefit risk ratio. Overdiagnosis, for example, would not be a problem if recognised and overtreatment was therefore averted. There are several promising signatures that are in the process of development to identify cancers that have an extremely low risk of ever progressing even in the absence of any systemic therapy (Buyse *et al*, 2006; Esserman *et al*, 2011a, b; Naoi *et al*, 2011). The validation of such signatures should be made a priority.

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Concomitant development of more appropriate thresholds for intervention based on mammographic findings would also reduce the burden of overdiagnosis, overtreatment and the harms due to false positives. European and Scandanavian countries already have significantly lower recall thresholds than are routinely used in the United States. In the United States, the mammography score BIRADS 4 is the standard for recommending a biopsy, though it encompasses a huge risk range that spans 3–95% of risk for either DCIS or invasive cancer. Further, the translation of BIRADS scores to English language terms that are 'loaded' with meaning, such as the term 'suspicious',engenders fear (of missing a cancer, or of being sued for malpractice if the lesion is not worked up) and has resulted in cancer-to-biopsy rates that are much lower in the United States than in Europe. Interestingly, the United Kingdom have developed a different lexicon (the UK 5-point Breast Imaging Scoring System), in which the threshold for invasive cancer must be higher prior to recommending a biopsy (Taylor *et al*, 2011).

As a community, we must make a concerted effort to think about what disease is worth identifying. The problem of surfacing 20–30% of precancerous lesions in the course of screening for cancer is not even mentioned in this report. DCIS, for example, was never intended as the target for screening. We have yet to demonstrate that early intervention for DCIS has made an impact on mortality, and the majority of these lesions are not destined to develop into invasive cancer (Ozanne *et al*, 2011). At the very least, the low and intermediate grade DCIS lesions should not have the term cancer in the diagnostic lexicon. DCIS should be reclassified as high-risk lesions, those that confer increased risk for development of invasive cancer over 5–10 years, and perhaps trigger prevention interventions and more frequent screening. Introducing the notion of disease dynamics to determine when to intervene for conditions that have a slow growth trajectory may allow us to learn what should and should not constitute a meaningful trigger for diagnostic intervention. Surely if screening every 3 years is considered safe or optimal in the United Kingdom, then following a potentially concerning lesion at 6 - to 12-month intervals would also be safe.

We need less religious fervour around the topic of mammography. If a case is found through screening, we need to recognise that there is a small chance that we will have impacted mortality for that individual, and a higher chance that they will undergo treatments that they do not need. Having a less inflated sense of the benefits of screening will lead us to embark on the necessary changes for significant improvements in screening performance. The promise of precision medicine is perhaps most ripe for fuelling such changes. We must embrace the challenge of learning how to redirect our screen detection features to finding consequential cancers, to using disease dynamics to enable us to ignore inconsequential cancers or precancers, and to develop and apply robust molecular diagnostics at the point of diagnosis to determine how we can safely test doing less to reduce the harms and promote the benefits of screening.

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