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Screening – benefits or harms?

Screening asymptomatic patients is now an established part of medical practice. We routinely measure blood pressure, test urine, and carry out a chest X-ray pre-operatively. Screening is also offered to those who haven't asked for medical intervention. Many medical aids advise women over 50 to have an annual mammogram and to have their bone mineral density (BMD) measured at various intervals. Some even reward these women in the form of 'points' in various schemes linked to medical cover. People are advised to have an annual health check that includes cholesterol measurement. Screening has become routine – but few stop and ask whether it is beneficial, and even fewer stop to look at potential harms.

I'm going to concentrate on two well-established screening programmes: screening mammography for breast cancer and screening for BMD. In the past 12 months alone, the *British Medical Journal*, the *Lancet* and the *New England Journal of Medicine* have published 24 articles or communications debating the value of breast cancer screening. Let's ask the question that every screening intervention attempts to answer – does earlier treatment improve the prognosis? It has become an undisputed assumption that the earlier a cancer is diagnosed, the better the prognosis. But there is little evidence that this is in fact the case – and not just in breast cancer. In the CRC1 trial,[1] Haybittle *et al.* reported on a cohort of 2 800 women who were randomised to mastectomy with or without radiotherapy. The cohort was recruited at the same time as those in the old randomised trials of screening by mammography. The 10-year survival rate was about 55%. After around 8 years of follow-up, the curves for deaths other than breast cancer began to separate, favouring those women who avoided radiotherapy. Nearly 20 years later, in 2008, Baum was co-author of a paper in the *Lancet* that compared adjuvent tamoxifen with adjuvent anastrozole for postmenopausal women with early breast cancer.[2] The 10-year survival in that cohort was 80%, with 5-year survival around 90%. Baum argues that as systemic therapy improves, the window for the impact of screening narrows and, as overdiagnosis rates increase, the importance of the relatively rare lethal toxicities of treatment increase. This brings me to the importance of overdiagnosis. Bleyer and Welch[3] estimate that about 30% of all breast cancers, or about 50% of those detected by screening, are overdiagnosed each year in the USA. This rate of overdiagnosis is similar to that reported by the Nordic Cochrane Centre,[4] and translates to 70 000 women a year told that they have breast cancer who have pathology that will not become life threatening.[5] The harms of overdiagnosis are substantial. Anxiety associated with the 'cancer' label lasts a lifetime. Then there are the risks associated with surgery and anaesthetics. Women who go onto adjuvant therapy face a series of side-effects – alopecia, neutropenic sepsis, hot flushes, vaginal dryness and increased risk of fracture from endocrine treatment. Long-term consequences, which particularly concern Baum, are those associated with radiotherapy – cardiovascular and respiratory complications, reduced quality of life,[6] and treatment-induced secondary cancers. Baum, an outspoken critic of screening mammography for breast cancer, estimates from UK figures that over the 25 years of the National Health screening mammography programme, 3 - 4 deaths from breast cancer are avoided for every 10 000 women screened. However, he points out that among these 10 000 women, 120 to 140 cases will be overdiagnosed. Four-fifths of these women will receive radiotherapy and, as a consequence, be at increased risk of dying of ischaemic heart disease and lung cancer. He estimates that an additional 1 - 3 deaths might be expected from other causes for every breast cancer death avoided.[5]

Now to BMD. Just how well does a measurement of BMD predict fragility fractures? Norton Hadler, in his excellent book *Rethinking Aging*,[7] points out that we know that BMD is only one of many risk factors for fragility fractures. Age is one such risk factor – a 55-year-old woman with a particular T score has a lower chance of a fragility fracture than a 70-year-old woman with the same T score, for example. That is true even for a low T score (-2.5 or less). The occurrence of one fragility fracture, whatever the T score, means an increased risk of another fracture. We have known for decades that older women (and men) have an increased risk of fragility fractures. The point of screening is to identify people 'at risk' and treat them early. But does screening by BMD for the risk of fragility fractures achieve this aim? A diagnosis of osteopenia – which will show up as a low T score – is known to be a poor predictor of future fragility fractures. This is because bone strength itself is not the only factor in a fragility fracture – neuromuscular health, for example, is at least as important, hence the greater risk of a fragility fracture in a 70-year-old than in a 55-year-old. To counter that – and to encourage continued screening – the World Health Organization Metabolic Bone Disease Group introduced the FRAX model. This model is based on multiple, easily measured risk factors such as age, gender, fracture history, use of oral steroids, presence of rheumatoid arthritis or other conditions associated with secondary osteoporosis, smoking status, family history, early menopause, low body mass index and excessive alcohol consumption. As a result of the FRAX model the International Osteoporosis Foundation and the National Osteoporosis Foundation in the USA recommend treating adults over 50 if their BMD score shows osteopenia and they are predicted to have a 10-year probability of hip fracture of 3% or more and of any osteopenic fracture of 20% or more, based on FRAX. The problem is that the epidemiological data show no greater accuracy of fracture prediction using FRAX than simply BMD.[8] The other question that Hadler asks – one that I find particularly compelling – is, 'Is osteopenia a disease?'. Are we not simply screening for a natural process of old age – or as Hadler puts it, 'Screening by BMD for the risk of fragility fracture ... is basically an expensive way to ask a thin white or Asian woman her age'. This begs the question of intervention once osteopenia has been 'diagnosed', unfortunately beyond the scope of this editorial. Suffice it to say that the increasingly popular bisphosphonates do indeed treat the BMD score. Whether they actually prevent fragility fractures is more contentious, however.

Screening has become accepted medical practice over the past couple of decades – often with little or no epidemiological

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evidence that it is fulfilling the requirements of a screening programme: that the screening modality shows what it is designed to show, the disease is important, and, having found the disease, we can do something about it. There is a growing movement[9] against 'overdiagnosis' – a negative feature of modern medicine. A more rational and scientific approach to screening would be a good way to start addressing this problem.

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