Screening for breast cancer

To the Editor: Professor Dent and Dr Panieri[1] wrote an excellent summary of many of the issues surrounding breast screening and highlighted many of the problems in trying to identify a commonsense approach. One can find a trial to support almost any viewpoint.

For a disease to be amenable to screening, it should fulfil certain criteria which include: (*i*) it should be a common disease in the population to be screened; (*ii*) there should be benefit from earlier diagnosis; and (*iii*) there should be a period in which the disease can be detected before it is detected in the normal course of events.

Clearly breast cancer in women aged over 50 fulfils the first two criteria, but it is the third point that is inconsistent with the 3-yearly programme proposed in the UK. The 'sojourn' time is the duration of time that an occult tumour can be detected before the onset of symptoms. Applying this to breast cancer (for the average non-screening-detected breast cancer of 1 - 2 cm) it has been estimated as 3.3 years in women aged 50 - 59 years. It is therefore illogical to propose 3-yearly screening in this age group, and 2-yearly mammograms and yearly clinical examination would be more suitable.

The reason the UK selected 3 years was based on costing as screening is funded by government and the cost of a missed cancer was less than the cost of 2-yearly screening of the population in general. As 'breast screening' in South Africa is individually funded, 2-yearly mammograms for the over-50-year-old would be a more appropriate recommendation.

In an excellent overview entitled 'Limitations in the interpretation of the mammography trials' (San Antonio Breast Cancer Symposium, December 2002), Professor I Craig Henderson stated that all the studies used mammography techniques that would be considered inferior today. He went on to say that it is assumed that an inverse linear relationship exists between tumour size and reduction of mortality. At present, we do not know whether this is correct, therefore we need to continue with the public health recommendations in place. Recommendations from the USA are yearly mammography, those from the UK 3-yearly mammography. Until newer techniques that take into consideration increasing knowledge of tumour biology are proven, it would seem prudent that we should settle on 2-yearly mammograms which fit into the natural history of the disease.

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1. Dent DM, Panieri E. Screening for breast cancer — finding a place between common sense and the evidence base. (Editorial). *S Afr Med J* 2004; **94:** 354-355.

To the Editor: The editorial in the May *SAMJ*[1] by Dent and Panieri was not only prominently placed in the journal, but also earned a banner headline on the cover. Much of what was written is highly controversial, misleading and unusual for a publication in a peer-reviewed journal of such eminence as the *SAMJ*.

Firstly, the work of Olsen and Gotzsche[2] and their publications including the Cochrane group[3] in the *Lancet* in 2000 and 2001 have been widely discussed and analysed and most responsible scientists have denigrated their conclusions, so much so that not one country or major medical school/institution/learned society has changed its attitude or practice with regard to breast screening. Their work is seriously flawed and provides no grounds for the scientific community to alter its conclusions that breast screening results in a substantial reduction in breast cancer mortality. I refer you particularly to the 4th Milan Breast Cancer Meeting, and also to an excellent review on mass breast screening by Peter Boyle as published in *The Breast* in December 2003[4] and presented at the St Gallen Conference on the Primary Therapy of Early Breast Cancer.

There is no longer any controversy concerning mass screening as there is incontrovertible proof that screening is beneficial and significantly reduces the death rate from breast cancer.[5-8] There is also no statistical or clinical evidence that clinical breast examinations and breast self-examination influence the detection of breast cancer or affect its death rate as these cannot detect early cancers as well as mammography does.

Yes, mammography can be criticised and the necessity for high quality needs no further discussion. In the USA and Sweden, for example, mammographers have to be additionally qualified and certified as do their departments, equipment and quality control measures by legislation. The quality issue was well brought out in the Canadian Trial where this factor considerably altered their conclusions.

Dent and Panieri complain of the high costs of false-positive mammograms. How is the value of a human life measured? Is $1 200 000 expensive in saving a human being? Ask a relative of that individual. Mammograms, FNAs and other percutaneous diagnostic procedures are cheap and do not remove a breadwinner from her job. Why don't they rather teach surgeons to avoid unnecessary breast surgery requiring hospital admission? Far too many diagnostic surgical biopsies are being done on women who have no disease at all, a large number of whom have not had a mammogram before surgery. What of mature women who are subjected to plastic surgical breast procedures without prior mammography being done?

Investigation and treatment of breast diseases is now a multidisciplinary endeavour requiring surgeons, radiologists

and pathologists/cytologists to work in unison as a team. This gives the patient the best deal and minimises the possibility of the dreaded delayed cancer diagnosis — a serious error and one that leads to the highest volume of litigation.

It has been clearly shown and agreed upon by the scientific community in numerous large demographic trials that screening mammography conclusively reduces the death rate from breast cancer significantly, most trials showing this to be in the order of 20 - 25%.

I resent strongly the implication that mammography screeners are members of the 'screening industry'. I would like to see Dent and Panieri spend some time in a busy radiology or mammography department to see the costs involved and the level of sophistication of the equipment and staff, and to realise the level of anxiety in the patients who all fear breast cancer, so often unnecessarily. I would have hoped that their experience of mammography and radiologists and other breast experts would have given them a better insight into the scourge of breast cancer, its rising incidence and the true value of early diagnosis.

I end with a quote from Boyle (which could be modified for underprivileged South Africans): 'Every women has the right to participate in an organized breast screening programme with high quality standards and audit built in. To discourage an early detection procedure which has been shown in trial after trial to reduce breast cancer mortality, on the basis of an error prone review in a field in which one is not an expert, seems to be questionable in the extreme.'

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1. Dent DM, Panieri E. Screening for breast cancer — finding a place between common sense and the evidence base (Editorial). *S Afr Med J* 2004; **94:** 354-355.
2. Gotzsche PC, Olsen O. Is screening for breast cancer with mammography justifiable? *Lancet* 2000; **355:** 129-134.
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To the Editor: I refer to the recent editorial by Dent and Panieri[1] on screening for breast cancer.

Screening for disease differs from the diagnostic testing of symptomatic individuals in ways that have scientific, economic and ethical consequences. It is perfectly just and necessary that screening mammography be constantly re-evaluated for its scientific and economic validity.

Your introduction of the topic to the *Journal* with a front cover banner, editorial and Editor's Choice insert makes obvious your concern for the subject. This is laudable. As is the statement by Dent and Panieri: 'Nonetheless, it must also be regarded as incontrovertibly evident that mammographic screening saved women's lives. All but one trial show reduction in breast cancer death, and the meta-analyses robustly support this.'

However, readers must be asking themselves, as I did, why the authors of the editorial have chosen to describe proponents of breast cancer screening with the pejorative phrase 'members of the screening industry'?

To describe the article by Gotzsche and Olsen[2] with the words 'The Cochrane Group has also recently questioned the validity . . .' is erroneous.[3] The article was published in the *Lancet* in 2000, the two are on the staff of the Cochrane Library, but the Cochrane Group Editors in fact refused to support their conclusions without modifications. And the trials they referred to were conducted in the 1970s and 1980s.

To do it twice — 'The most recent criticism has been in the form of an analysis of the Swedish trials by the Cochrane group . . . ' — must be seen as deliberately misleading.

It is not my intention to respond by pointing out all the other obviously biased opinions expressed in the editorial. Let me rather place before your readers some other considerations that may influence their decision whether or not to recommend mammographic screening to their patients.

No sensible discussion of screening mammography in South Africa can be conducted without entering this caveat: All the references to screening mammography in the literature are to mass screening mammography programmes, usually state-sponsored or third party-paid. The shortcomings of mammography — the perceived harms and costs per life saved — are the shortcomings of mass screening mammography.

There is no such programme here, nor is any proposed. In South Africa mammography is individualised. The benefits of this individualisation are considerable.

The addition of a physical examination by the radiologist reading the films and whole breast ultrasound (US)[4] gives increased sensitivity and a high negative predictive value. Under these circumstances a normal examination and mammogram presents the ideal opportunity to teach the patient breast self-examination.

The accent is placed firmly on the positive aspects; the patient is encouraged not to make a monthly search for disease but rather a monthly affirmation of normalcy.

Patients frequently seek information regarding risk factors and breast cancer. This provides an opportunity to point out the benefits of a proper diet and exercise programme and the risks associated with obesity.

This 'hands on' approach enables the radiologist to perform percutaneous image-guided diagnostic biopsies when cancer is suspected or when the patient's anxiety is such that reassurance alone will not allay her fears.

It may also be curative as in the case of cysts.

The maligned Swedish trials have in fact added a great deal to our understanding of the biology of the group of diseases referred to by the term breast cancer.[5] The co-operative efforts of their radiologists, pathologists and surgeons have demonstrated a spectrum of disease with differing properties and propensities to become invasive. The majority of breast cancers are progressive but some are systemic from the outset, thus explaining some of the deficiencies of past trials and their analyses.

With regard to screening intervals, keep the following considerations in mind:

- Risk for breast cancer varies with age, ethnicity, family and obstetric history.
- The majority of screen-detected cancers are found in individuals with no risk factors.
- While incidence rises with age, mortality decreases over the age of 55 years.
- Younger women frequently have more aggressive tumour biology.
- Breast cancers are progressive; cancers undetected in the younger woman are more likely to become invasive.
- Younger women are more likely to have dense breast tissue and will especially benefit from the addition of US screening.

The recommended screening intervals are therefore:

- Baseline mammogram and breast self examination instruction between 35 and 40 years.
- 40 - 55 years: mammograms every 12 - 18 months depending on risk profile.
- 55 years and over: mammograms every 18 - 24 months.
- It is also recommended that all patients have physical examinations by their medical advisors between mammograms.

A reduction in mortality has long been considered the most valid endpoint in breast cancer screening. It is not the only benefit, however.[6]

- The 10-year fatality rate is reduced by 50% in screen-detected cancers.

- Early, preclinical detection has enabled less extensive surgery, and less need for cytotoxic chemotherapy.
- There has been a consistent downsizing of breast cancers detected in screening programmes.
- Fewer screen-detected cancers are node positive.
- Ductal carcinoma *in situ* (DCIS) is found more frequently in screened populations.

While not all DCIS becomes invasive, all invasive cancers begin *in situ*. Prevention of invasive cancers by local excision mimics carcinoma prevention by procedures such as removal of colonic polyps, cervix cancer prevention by eradicating dysplasia and carcinoma *in situ*, excision of dysplastic naevi or removal of mucosal *in situ* lesions in the head and neck.

Pre-operative information gained from image-guided biopsy staging and receptor status determination replaces the uncertainty previously experienced by the patient sent for excision biopsy. Treatment strategies can be discussed and tailored to the patient's circumstances, before surgery.

Mammography is not an exact science, however. Factors that will improve sensitivity and specificity include training of radiologists and quality control; the needs of women remote from mammography facilities must be addressed. A collaborative approach by those of us involved in breast cancer detection and treatment will ultimately benefit all the women of South Africa.

The authors of your editorial appear to be barking up the wrong tree and at the same time complaining about the noise.

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1. Dent DM, Panieri E. Screening for breast cancer — finding a place between common sense and the evidence base (Editorial). *S Afr Med J* 2004; **94:** 354-355.
2. Gotzsche PC, Olsen O. Is screening for breast cancer with mammography justified? *Lancet* 2000; **355:** 129-133.
3. Smith R. Ongoing analyses of breast cancer: Two steps forward, one step backward. *Breast Disease* 2000; **11:** 252-253.
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5. Tabar L, Duffy SW, Virak B, *et al*. The natural history of carcinoma: What have we learned from screening? *Cancer* 1999; **86:** 449-462.
6. Cady B. Breast cancer in the third millennium. *The Breast Journal* 2000; **6:** 280-287.

To the Editor: Dent and Panieri[1] review current knowledge about screening for breast cancer, pointing out that self-examination appears to be ineffective, while clinical examination is unproven.

They wade through the treacherous marsh of literature on screening mammography and emerge with the opinion that mammography reduces mortality from breast cancer, although at a considerable cost — both financial and (for the victims of mammography's high false-positive rate) traumatic.

Had they been content to remind those of us in the 'screening industry' of our duty to correctly inform our patients of both the strengths and weaknesses of our examinations, I would have considered the editorial to be a useful contribution to the literature.

However, they propose an alternative regimen for breast cancer screening that I find hard to fathom. The discredited self-examination is to give way to . . . self-examination, but this time with an injection of mystical 'breast awareness' to boost its effectiveness.

Mammography is to be done every third year. Simple arithmetic suggests that when a screening examination is done at intervals longer than the average lead time (2 years in the case of mammography), its effectiveness will be markedly reduced. To address mammography's weak points (expense and false positives) in this manner is like negotiating a special deal with an armed response company to monitor your house every third night, thus reducing costs and ensuring that you are not disturbed by false alarms on the other two nights.

Women must be given enough information to make an informed decision about screening mammography. Some will opt out; that is their prerogative. For those who choose to have screening mammograms, we should do them properly: until further research defines subgroups, possibly based on age or genetic profile, who can expect to get tumours of a more indolent nature than average, properly means annually.

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1. Dent DM, Panieri E. Screening for breast cancer — finding a place between common sense and the evidence base (Editorial). *S Afr Med J* 2004; **94:** 354-355.

Professor Dent and Dr Panieri reply: Many years ago this journal ran a regular provocative column entitled 'Klip in die bos', analogous to the expression 'shake the tree'. In the case of our editorial, much emerged from the foliage. We are pleased to respond.

At the outset we must state that we never denied the scientific evidence that mammographic screening saves lives, writing unequivocally and strongly that '. . . it must be regarded as incontrovertibly evident that mammographic screening saves women's lives'. We also concluded that 'mammography was probably a good thing to do'. The issues we raised — which provoked the ire of the correspondence above — were the frequency, cost and harms of the procedure. The final red flag to the correspondent bulls was no doubt our citing Richard Smith, Editor of the *British Medical Journal*, who made an editorial stab at 'the screening industry'. This perhaps struck a chord somewhere.