**ADDRESS LETTERS TO**

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## Another incentive to lose weight

**Dear Editor**

Obesity can be an independent risk factor for biochemical failure following prostatectomy.

Prostate cancer is the second most common cancer among men in the western world. Although there are algorithms to predict risk of progression following surgery, most nomograms in clinical use include only traditional tumour specific criteria (such as grade, stage, and PSA) to predict recurrence.[1] Post-therapy, a rising serum PSA can indicate 'biochemical failure' and thus serve as a surrogate of meaningful recurrence.

Previous animal and well controlled cohort studies have shown some association between obesity and more aggressive prostate cancer. But we would like to bring the attention of our colleagues to a paper on 'Obesity, weight gain, and risk of biochemical failure among prostate cancer patients following prostatectomy'.[2] This paper is probably the first to demonstrate that obesity as an independent risk factor for biochemical failure following prostatectomy. Although it indicates that further studies at multicentre settings (which are currently being undertaken at several Queensland hospitals) are required to validate the nomogram, we believe that is only a matter of time for the validation.

The link between obesity and aggressive prostate cancer is likely to be complex and involve multiple mechanisms. More studies will need to be conducted, and it is anticipated that this better understanding will lead to new diagnostic measures, prognostic tools, and therapeutic manoeuvres to reduce prostate cancer burden in the future.

In the meantime, the best advice we can give to patients is to exercise regularly, eat a balanced diet, and to achieve and maintain a healthy weight. We all know that this advice will help to reduce the risk of heart disease and other cardiovascular related conditions that are the leading causes of mortality and morbidity in the modernised world. There is now another reason that we should be strongly advising our male patients to lose weight to reduce the risk of aggressive prostate cancer.

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## Ductal carcinoma in situ

**Dear Editor**

As pointed out by Stuart et al,[1] (*AFP* November 2005) the routine use of tamoxifen for DCIS is contentious, but it deserves more consideration. While NSABP B-24 trial on 1804 patients showed benefit for the use of tamoxifen, the UKCCCR trial with 1711 patients (partly done in Australia) did not show significant benefit; the difference is explained on the basis of different exclusion criteria (exclusion of patients with positive margins or the older age of patients in the UK trial) and the different study design.

DCIS has such a good prognosis that it is difficult to show improvement in survival. Indeed, the benefit of radiotherapy after breast conservation surgery is restricted to reduction in local recurrence; there is no demonstrable difference in overall survival. For instance, updated 12 year results from NSABP B-17 show no difference in survival (86 vs. 87%, $p$=0.80).[2]

The risk of a second tumour (either invasive or in situ) in the contralateral breast of patients with DCIS is similar to that among women with primary invasive breast cancer – approximately 0.5–1.0% per year.[3] Unlike radiotherapy, tamoxifen is useful in reducing contralateral breast disease.[2]

This is especially so in DCIS that is ER positive. At the 2002 San Antonio Breast Cancer Symposium, Allred et al presented data from the same trial assessing the tamoxifen benefit according to the ER status of the primary DCIS tumour.[4] Oestrogen receptor status was available in 628 patients (327 placebo, 301 tamoxifen). Seventy-seven percent of patients were ER positive. In these patients, the effectiveness of tamoxifen was significant (RR for all breast cancer events: 0.41, $p$=0.0002). Significant reductions in breast cancer events were seen in both the ipsilateral and the contralateral breast. In patients with ER negative tumours, little benefit was observed (RR for all breast cancer events: 0.80, $p$=0.51) but number of events was too small to rule out a benefit.

Tumour recurrence is related to age of the patient and tamoxifen should have a greater impact in premenopausal women.

Current data would thus seem to support the use of tamoxifen at least in premenopausal women with ER positive DCIS. This would decrease the development of a contralateral, second primary breast cancer (risk reduction therapy) and, in those who received breast conserving therapy, to reduce the risk of an ipsilateral recurrence (adjuvant therapy).

Based on the results of the ATAC trial, which showed benefit of aromatase inhibitors over tamoxifen in adjuvant therapy of postmenopausal women, the NSABP is currently accruing patients in the B-35 trial, which will test the efficacy of anastrozole in adjuvant therapy of DCIS.

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## Reply

### Dear Editor

We thank Dr Venniyoor for his letter, which focused on some of the controversial areas about the use of tamoxifen in patients with DCIS. Our article[1] was directed at GPs as an overview rather than an in depth analysis of the data from the NSW Breast Cancer Institute.[2–4] Only two randomised controlled trials have explored the use of tamoxifen for patients with DCIS and their findings, in our opinion, do not support the routine use of tamoxifen.

The NSABP B-24 trial found a small, statistically significant benefit in reducing ipsilateral breast recurrence ($p$=0.04) for 5 years of adjuvant tamoxifen compared with a placebo after a lumpectomy and radiotherapy (RT), particularly for women aged under 50 years or having tumours with positive margins.[5] It remains unclear however, if tamoxifen was of significant benefit for tumours excised with negative margins. The analysis was hampered in that 295 of 899 patients who were randomised to tamoxifen discontinued treatment, and it remains unclear as to how many of these patients had RT and/or negative margins.

The UKCCCR trial found that ipsilateral breast tumour recurrences were not reduced by tamoxifen.[6] All tumours had negative margins on excision.

It is well known that tamoxifen can be used to decrease a woman's risk of a contralateral breast cancer but this needs to be balanced against side effects, some of which may be life threatening. These complications may not be worth the small benefit gained from the tamoxifen, and need to be weighed carefully in every patient's situation. The side effects may include early menopause, possible weight gain, blood clots and, rarely, endometrial cancer.[7] There are situations when tamoxifen may be worthwhile: when a patient has a family history of breast cancer, when there is lobular carcinoma in situ or when there is extensive, low grade, ER positive DCIS with close or dubious margins.

It is easy to give everything to every patient. It is harder when responsible clinical judgment requires experience of the natural history of DCIS and a clear understanding of the magnitude of the benefits and risks of treatment, particularly when the disease is not invasive.

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## Research in general practice

### Dear Editor

Research is not a welcome distraction for practitioners firmly focused on seeing patients. This is also true in the UK despite differences in health care systems compared with Australia.[1] Given the demand from patients it seems to make little difference whether fees are earned on a capitation basis or per item of service. Therefore research capacity builders have to ponder hard how to do business with general practitioners and their colleagues in primary care. Certainly offering research training may help.

Experience in the UK suggests that a critical aspect of research skills workshops is clinical back fill. A daunting prospect if only because GPs are scarce and make expensive locums. The University of Sheffield facilitated a more radical solution by employing a researcher to serve in a series of practices running journal clubs and teaching skills on small pilot projects. A vital element was the allied offer to consult patients at no cost to the practice. The scheme was popular and to a limited extent, successful.[2] However, one cannot underestimate the role of academic departments of general practice in conducting well designed clinically relevant studies with minimal work load implications which will enthuse practitioners and deliver important outcomes for their patients.

A growing danger in the world of the now fashionable cluster randomised clinical trials is to replicate the experience of others where practices harbour an ambivalence to research but sign up to projects which then fail.[3] Research capacity building is important for the reasons articulated by Brett[1] most especially given that most patients are seen in primary care. As funding bodies have acknowledged the very future of health care depends on relevant research in our field. This requires a top down as well as bottom up approach. The challenge for those charged with realising the vision is to deliver a research savvy, questioning workforce.

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