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EDITORIAL

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Recently, we saw the publication of two landmark studies for prostate cancer screening. Unfortunately, the studies arrived at different conclusions, so that, instead of settling the debate, they have only served to fuel the controversy that already surrounds this issue. The European Randomized Study of Prostate Cancer Screening (ERSPCS) showed a 20% reduction in mortality in the screened arm of their study (Schroder *et al. NEJM* 2009; **360**: 1320–8), while, by contrast, the US-based PLC screening study reported no difference between the two arms at 9 years (Andriole *et al. NEJM* 2009; **360**:1310–9). However, there are several important differences between the two studies that may account for the discrepancy. The ERSPCS, studied 182 000 men and was based on a cut-point of 3.0 ng ml^{-1} rather than the 4.0 ng ml^{-1} value selected for the US-based PLC screening study as a trigger for further investigations. This may have allowed the Europeans to identify more cancers at a stage when they were still curable. Another problem with the US-based PLC study of 76 693 men is the pre-existent widespread use of prostate-specific antigen screening within the population. This has led to the contamination of the non-screened arm by men who went and had their prostate-specific antigen tested outside the study. Clearly, this will have significantly reduced the power of the trial to detect a difference between the two arms, especially as the US study recruited less than half the number than the European group. Thus, the jury remains out on this issue; but urologists and oncologists whose aim is to reduce the death toll from prostate cancer will be encouraged that in the United Kingdom alone, on the basis of the ERSPCS data, 2000 lives per annum potentially could be saved. With longer follow-up, there is certainly the potential for an even greater reduction in mortality in the men screened for prostate cancer, but also a concomitant risk of over-diagnosis.

Another highly controversial issue in prostate cancer management is the role of chemoprevention. Three large-scale chemoprevention trials including SELECT (testing selenium and vitamin E), the Prostate Cancer Prevention Trial (PCPT)—testing the 5-α-reductase inhibitor (5-ARI) finasteride and REDUCE (testing dutasteride) are completed or nearing completion. The initial results of SELECT have now been reported and find no benefit from either selenium or vitamin E on risk of prostate cancer (Lippmann *et al. JAMA* 2008; **147**: 217–23). The results of the REDUCE trial investigating dutasteride as a chemopreventative agent should be available shortly. The results of the PCPT showed a significant (measured relative risk reduction of 24.8%) reduction of risk of prostate cancer (Thompson *et al. NEJM* 2003; **349**: 215–24). The initial observation of an excess risk of high-grade disease appears to be related to improved detection of cancer and high-grade cancer related to improved sensitivity of prostate-specific antigen, digital rectal examination and prostate biopsy. Modelling studies suggest that with finasteride the risk of high-grade cancer is either unchanged or reduced. Sexual dysfunction and gynaecomastia were observed but the rates were low and probably would not in themselves militate against the widespread use of a 5-ARI to prevent prostate cancer.

All these newly reported studies not only add significantly to the evidence base regarding the prevention and early detection of prostate cancer, but also throw into relief many of the excellent reviews and original papers published in this issue of *Prostate Cancer and Prostatic Diseases.* In Van Poppel's review, for example, the unequivocal value of serial PSA measurement in the follow-up of men who have undergone radical prostatectomy is emphasized as a highly sensitive and specific means of detecting disease recurrence and identifying those patients in whom further treatment is required. Two articles analyze the value of transrectal ultrasound guided biopsies in the detection of prostate cancer; in particular, Parker *et al.* assess the value of Ki-67 as a progression marker in a cohort of men with localized tumours managed by active surveillance.

If chemoprevention were to be widely used we will certainly need to identify a high-risk cohort, to avoid treating everybody. Genetic testing will almost certainly be the way forward, and Collin *et al.* and Ostrander *et al.* report two candidates: namely multiple endocrine neoplasia type 1 gene and *FGFR4* genetic polymorphisms, for the evaluation of prostate cancer risk and prognosis. Many other genetic markers are becoming available, but all will need to be carefully evaluated before they can be used clinically.

Some of the more difficult management decisions in patients with prostate cancer arise when the disease recurs in spite of surgery or radiotherapy. Kane and colleagues interrogated the SEARCH database to evaluate the impact of nerve sparing at the time of radical prostatectomy, whereas Chalasani *et al.* review the use of high-intensity focussed ultrasound in the management of post-radiation recurrence.

In trying to live up to the name of our journal, we always include some articles on the extremely prevalent, but sometimes over-looked, benign diseases of the prostate, namely BPH and prostatitis, rather than focus exclusively on cancer. This issue is no exception: Hammarsten *et al.* evaluate insulin and oestradiol levels as risk factors for the development of BPH. Dorsam *et al.* review 5-ARI therapy and Chung reports new data relating to the use of combination therapy with the 5-ARI inhibitor dutasteride and the α-blocker tamsulosin. In addition, Shoskes *et al.* report a potentially important clinical management strategy for patients suffering from chronic pelvic pain, which may assist both patients suffering from and clinicians dealing with this difficult disorder.

Finally, an article on exercise and muscle strength serve to remind us to exhort our patients, as well as ourselves, to undertake regular vigorous exercise to avoid, not only obesity, metabolic syndrome and cardiovascular disease, but also to maintain prostate and bone health.

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