



Letter to the Editor

Reply to Rune Kvåle, Eivor Hernes and Freddie Bray's Letter to the Editor re: E. David Crawford, Per-Anders Abrahamsson. PSA-based Screening for Prostate Cancer: How Does It Compare with Other Cancer Screening Tests? *Eur Urol* 2008;54:262–73

The primary basis of our article was to remind our colleagues that, with regard to cancer screening, we live in an imperfect world [1]. Although prostate-specific antigen (PSA), in common with other screening tests, has a less-than-perfect sensitivity and specificity profile, it has been depicted by some in negative terms that belie the findings from studies such as the European Randomised Study of Screening for Prostate Cancer (ERSPC) [2,3] and the Prostate Cancer Prevention Trial (PCPT) [4]. Although the ERSPC study remains incomplete, analyses from the Rotterdam section demonstrate statistically significant shifts to more favourable clinical stages and histological grades, as well as a reduction in distant metastases, and lower rates for biochemical progression after surgery, radiotherapy, and endocrine therapy for screened *versus* unscreened men [2,3]. One of the most important findings of the PCPT, which does not suffer from the ascertainment biases seen in screening studies, was that PSA is indeed more effective at detecting high-grade disease than low-grade disease [4]. While we await the mortality outcomes of the ERSPC and the Prostate, Lung, Colorectal, and Ovary (PLCO) studies with great interest, we believe the current evidence base is compelling, if incomplete.

The evidence to date does not suggest that the psychological burden of watchful waiting for early disease, more frequently detected through screening, is a substantive issue. In the Scandinavian Prostatic Cancer Group Study Number 4, which randomised men with localised disease to radical prostatectomy or watchful waiting, the prevalence of anxiety and depression, overall well-being, and

quality of life were similar in the two groups [5]. We do not believe, and have no evidence to suggest, that this concern should interfere with a basic premise: that the morbidity, both physical and psychological, associated with delayed diagnosis is considerable and that earlier detection is therefore desirable. The use of PSA is now widespread in our society. The health inequality created by providing the test *on demand* to men who ask for it but denying it to those who do not is a real concern.

We concur that PSA-based screening needs to be tailored to the individual patient. One of the features of PSA is that, beyond its predictive value for a positive biopsy at the time of screening, it has value as a marker of longitudinal risk [6–9]. An initial PSA value for a middle-aged man can be used to determine future screening frequency, a concept enshrined in the current US National Comprehensive Cancer Network guidelines [10]. In an analysis from the Rotterdam section of the ERSPC, just 0.9% of men with a PSA of ≤ 1.0 ng/ml in first-round screening went on to have a PSA ≥ 3.0 ng/ml at the second round 4 yr later, while around 50% of those with a PSA of 2.0–2.9 ng/ml progressed over this threshold. Almost one in three men with an initial PSA of 2.0–2.9 ng/ml who traversed this threshold 4 yr later and were biopsied had prostate cancer, with 70% having an intermediate or high 2-yr risk of PSA recurrence [11]. These data demonstrate the importance of more frequent screening for some men *versus* others, based on an initial PSA assessment.

Conflicts of interest: E. David Crawford and Per-Anders Abrahamsson are on the GlaxoSmithKline advisory board. E. David Crawford has been a speaker for GlaxoSmithKline, BPH.

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