

## Has PSA testing truly been a “public health disaster”?

Anthony J Costello and Declan G Murphy

*PSA testing may lead to overtreatment, but this should not rule out its judicious use as an early predictor of prostate cancer*

Two recent articles, an opinion piece from Richard Ablin, the discoverer of prostate-specific antigen (PSA) and a self-proclaimed “authority in the field”, published in the *New York Times*,<sup>1</sup> and a subsequent interview with Ablin published in the *BMJ*,<sup>2</sup> contend to inform the public of the “hugely expensive public health disaster” of PSA testing. Yes, PSA testing is not without its flaws, but to malign it in this manner is truly lamentable.

Before 1980, there was no diagnostic test for prostate cancer; there was no effective radiation therapy; there was no safe surgery, and the only option for most men with prostate cancer was to have their testes removed — surgical castration. Most men, of course, feel quite attached to their testes, and castration carries myriad physical and psychological side effects. A common emergency department presentation at that time was acute paraplegia due to prostate cancer metastatic lumbar spine cord compression.<sup>3</sup> This is a rare presentation in 2010. Since the introduction of PSA testing in the 1980s, we have seen a 25% reduction in mortality from prostate cancer; stage migration means 80% of men now present with localised, either small-volume or advanced, prostate cancer.<sup>4</sup> Because the PSA test facilitates early diagnosis, most men with prostate cancer are diagnosed with a lead time of about 9 years before the onset of metastatic disease.<sup>5</sup>

The contention, however, is that the PSA test is a poor screening tool; and this is reasonable, because we ask far too much of a single blood test. The PSA test will not differentiate between aggressive and indolent prostate cancer. Furthermore, after the onset of benign prostatic hyperplasia (BPH) in men from about 45 years of age, background noise due to BPH reduces the sensitivity of the PSA test at PSA levels below 10 ng/mL, although a PSA level above 10 ng/mL is still very indicative of the presence of prostate cancer.

The key problem facing health professionals dealing with prostate cancer can be readily articulated: it is the inability to discriminate between aggressive and indolent prostate cancer. It is acknowledged that, while PSA testing has led to greatly reduced mortality, its widespread use has also led to greatly increased detection of prostate cancers, many of which will not prove to be life-threatening.<sup>6</sup> This has led to considerable overtreatment of indolent prostate cancer by surgery and radiation therapy, although increased use of active surveillance has demonstrated that clinicians are being more considered when counselling men about their management options.<sup>7</sup>

What if we were to use PSA testing in a more judicious and targeted manner so that men could have a single test before the onset of BPH? Swedish researchers have elegantly shown that the effect of benign transition zone-related PSA levels can be eliminated by testing all men at baseline before the development of BPH. In a study of a large cohort of men in Malmö, Sweden, PSA levels in men below the age of 45 years reliably predicted the development of significant prostate cancer up to 25 years later.<sup>8</sup> Between 1974 and 1986, 21 000 Swedish men aged under 45 years provided blood samples as part of a cardiovascular study. At the end of 1999, participants who had developed prostate cancer were identified using Swedish Cancer Registry data. PSA level at 45 years of age was found to be a very strong predictor of prostate cancer being diagnosed up to 25 years later, with an area under the receiver operating characteristic curve of 0.76 (signifying high discriminatory ability). PSA levels between 2 and 3 ng/mL (which are often cited as being within the normal range) were associated with a more than 19-fold increased risk of subsequent prostate cancer development. The researchers went on to show that 80% of

advanced cancers (stages T3, T4 and metastatic at diagnosis) occurred in men who had had PSA levels above the median when tested at age 44–50 years.<sup>9</sup>

This study suggests that we could use a single PSA level as a predictor for the long-term risk of prostate cancer in younger men around the age of 45 years. This supports the advice from the Urological Society of Australia and New Zealand and the American Urological Association that men aged 40 years should have the merits of a PSA test discussed with them. Those with a PSA level well below the median for men in their 40s of about 0.6 ng/mL<sup>5</sup> (the vast majority at this stage) could be reassured that they are at very low risk of developing prostate cancer and advised to have another test 5 or 10 years later.

The nihilistic musings of Ablin do nothing to help inform a rational policy towards the early detection of prostate cancer. Rather than dispense with a test that has contributed significantly to the reduction in mortality from prostate cancer over the past 30 years, and while we wait for better biomarkers in the future, we should instead advocate a more discriminating use of PSA testing.<sup>10</sup>

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