How did the PSA system arise?

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DECLARATIONS

Competing interests
None

Funding
None

Ethical approval
None

Guarantor
SJ

Contributorship
SJ is the sole contributor

Acknowledgements
None

'A health-conscious 62-year-old man vacationing in the United States … heard about a new test for prostate cancer and wonders if he should have one. … His wife, who undergoes mammography regularly, is encouraging him to have the test.'[1]

A few years ago, a notable paper criticized prostate-cancer screening as a defective system lacking negative feedback. A PSA test yields either an unsuspicious or a suspicious result. If the former, the patient is relieved; if the latter, he is biopsied and cancer is either confirmed, in which case he is dismayed but presumably relieved that it was discovered early, or not confirmed, in which case he is again relieved. PSA testing seems to generate no outcome that does not reinforce the testing regime itself, even though it is well-known, at least to medicine, that it leads to over-detection on a large scale, that diagnosis leads to treatment, and that treatment entails the possibility of such side-effects as impotence. As for the benefits of PSA testing other than feelings of relief regardless of the outcome, they are difficult to establish. 'There seems to be a "disconnection" between the degree of enthusiasm for screening and the quality of the evidence supporting it'.[2] At the time the PSA regime took shape in the USA in the late 1980s and early 1990s, significant mortality benefits were expected but had not yet been confirmed; with two randomized clinical trials of PSA reported in 2009, one showing no mortality benefit and the other a modest benefit at the cost of much over-treatment,[3,4] the hoped-for dividends of PSA testing have still not materialized. For two decades, therefore, men by the thousand have been diagnosed with and treated for prostate cancer in the belief that PSA saves lives, despite a paucity of evidence that it actually does so.

In the early years of the PSA era, some concluded that the use of a screening test as flawed as PSA could only be explained by the undue influence of the healthcare industry on the making of cancer policy.[5,6] The flaws of PSA testing – in particular, its speculative benefits but probable harms – were sharply criticized in the medical literature itself.[7] Yet the test very soon acquired a popularity that enabled it to shrug off the skepticism of critics and the caveats of the US Preventive Services Task Force, which in 1996 declined to recommend either in favour of or against PSA testing owing to the uncertainty of the evidence. How is it that a test of such disputed value was so warmly embraced by American men? The answer lies not only in the endorsement of PSA testing by such bodies as the American Cancer Society and the American Urological Association, but especially in the use of public-relations methods to drive home the powerful but too-simple message that PSA saves lives – methods that had already proven themselves in the case of the sister disease, breast cancer.

The PSA system as we know it could conceivably have been built from the ground up by urologists convinced that they did not have time to wait for the results of RCTs of PSA, given that deaths from prostate cancer stood at 40,000 per year in the USA when screening for the disease began. However, urologists did not invent every element of the system. Key components, including the rhetoric of early detection that drives men to get tested in the first place and vindicates the test no matter the result, were imported from breast-cancer medicine. Historically speaking, mammography has led and PSA testing has followed even though PSA lacks to this day the sort of validating evidence that mammography possessed before the PSA revolution began. One answer to the question 'Why Is

Prostate Cancer Screening So Common When the Evidence Is So Uncertain?'[2] is that those who launched PSA testing copied the successes of a screening mode for which evidence is less uncertain.

Isolated in 1979, PSA was at first used to monitor the progress of prostate cancer, not to identify the disease at an incipient stage. Prostate-cancer screening was introduced in the United States in 1987 – when the use of mammography was already rising rapidly – to be followed in short order by a dramatic increase in detected cancer. By some estimates, from 1990 to 1991 alone the incidence of prostate cancer in the USA rose 25%, and from 1990 to 1993, 60%. That numbers like these did not deter men from getting screened but simply marked the beginning of the PSA revolution suggests a system lacking the braking effect of negative feedback. And the drive to get men tested was patterned closely on the breast-cancer model of community-based screening and the breast-cancer theme of 'awareness'. The promoters of PSA testing in the early 1990s did not start from zero but tapped into an existing model of proven efficacy. In order to ascertain why PSA testing is so common, we should bear in mind when and how it became common.

Between 1986 and 1989 the American Cancer Society conducted a Breast Cancer Detection Awareness Program (BCDAP), the goal of which, according to a proponent, was 'to make women and health professionals aware of the benefits of breast cancer detection'.[8] Awareness, it seems, excluded knowledge of mammography's possible harms. A programme to disseminate information about mammography's benefits and only the benefits (though the public receives a poor idea of their magnitude) is bound to produce a disconnection between enthusiasm for screening and the evidentiary record of the procedure itself. As it happens, the harms of such screening – not only false-positives, but the detection of questionably significant lesions that are nonetheless treated with surgery or radiation – approximate those of PSA testing. Just as Breast Cancer Awareness supplied the precedent and template for Prostate Cancer Awareness, just as the selective understanding of awareness itself passed from the former to the latter, so the treatment of indolent forms of breast cancer under the banner of saving lives found a parallel in the PSA regime, which has somehow been reinforced, not called into question, by over-diagnosis and over-treatment.

In addition to an outpouring of mutually reinforcing articles in the medical literature, the Breast Cancer Detection Awareness Program generated an organized blizzard of pamphlets, television spots, news features, and newspaper inserts, all encouraging women to be screened. The principles of the programme appear to have been to depict mass screening as a procedure without harms but with great benefits, to speak in the name of something impossible to oppose (such as 'education'), to reach people where they live, and to offer mammography at low cost. In Massachusetts, for example:

> *'A … campaign entitled "Mammography: The Breast Test" was conducted to educate people about early detection of breast cancer. The program was held in late April when more than one million Massachusetts households received information on breast cancer during the residential crusade. The following week a toll-free number was available for information on low-cost mammograms ($50 or less) at more than 100 hospitals throughout the state.'*[8]

Well before General Norman Schwarzkopf, the popular war hero, served as spokesman for Prostate Cancer Awareness, it seemed natural to use military metaphors like 'campaign' and 'crusade' in connection with breast cancer. The promotional 'campaign' became the blueprint for Prostate Cancer Awareness. Indeed, Prostate Cancer Awareness Week (PCAW) began in the year the BCDAP ended – 1989 – and drew on the help of mammography advocates to get off the ground. 'Several members of the [Prostate Cancer] Educational Council who had been associated with Breast Cancer Awareness Month contributed significantly' to the initiation of PCAW in 1989.[9] Defining itself as educational and delivering services in a community setting, PCAW was informed by the same principles as its predecessor. If human beings respond not only to evidence but to evocative associations, prostate-cancer awareness was associated with its breast-cancer counterpart by temporal proximity, rhetorical parallels, a similar orchestrated optimism, and analogous tactics of mobilization. And like Breast Cancer Awareness, PCAW caught on. By 1992, when the American Cancer Society endorsed PSA, free tests were being offered at 1800 clinics. Testing over three million

men in the first decade of its existence, PCAW became the largest cancer screening programme in the USA.[10]

Whereas the first trial of mammography – the Health Insurance Plan of Greater New York (HIP) trial, considered the first RCT in cancer screening – dates to 1963, randomized trials of PSA were initiated only in the 1990s. When PSA testing began there was, therefore, no body of evidence showing that it reduced mortality, which made it a sort of experiment on the male population, albeit without the constraint of informed consent that would operate in an actual experiment. But in getting around informed consent too PSA has followed mammography. Despite its professed educational mission, mammography introduced the use of public-relations methods to get the target population to the screening centre. Success was measured by numbers screened, not by improvement of public understanding – a model that would govern Prostate Cancer Awareness as well. So it is that 'the mammography controversy is a foreshadowing of … controversies about prostate cancer', as a critic of uninformed consent to mammography wrote in 1995 in the *Journal of the National Cancer Institute*.[11] The family resemblance between the uninformed woman and the uninformed man persists to this day. Where men getting PSAs tend to overestimate the risk of death from prostate cancer and presume that PSA reduces it, women often overestimate the risk of breast-cancer death and, while correctly assuming that mammography reduces it, greatly misjudge its effect.[12] In both cases many of the screened are unaware that screening also picks up what medicine knows as pseudo-disease – a term inconsistent with the lay understanding of cancer as either a lethal or potentially lethal, but certainly not an innocuous condition – and that such findings set off a cascade of consequences.

Although the evidence in favor of PSA testing falls short of that for mammography, the PSA regime was built on the mammography model and continues to resemble it. (Thus the paradox that while PSA has given rise to the harms of mammography without the demonstrated mortality benefit, it is defended in the language of risks and benefits.) But even the difference in supporting evidence becomes less salient in the light of the common tendency among those screened to overrate benefits, often vastly, and to underestimate harms – indeed, to ground the decision for screening on something other than evidence. So too, neither men nor women treated for screen-detected disease without clinical significance know this to be so (nor does medicine itself know in any given case, or else the patient would not be treated); all they know is that their cancer has been treated, thus marking a win for the system that detected it. Because few would knowingly commit their body to a flawed system, such a system presupposes some sacrifice of informed consent; but because the system could not keep going without willing entrants and public enthusiasm, the lack of informed consent must be masked as something honorific. The celebration of 'awareness' meets this requirement. Today if you search Amazon.com for 'cancer awareness', you will find knee socks, pens, lanyards and stickers, but no books.

In 1997 the ACS qualified its recommendation of PSA testing for men aged over 50 years, now advising that candidates for the test be informed of its liabilities as well as benefits. Recognizing that the evidence for PSA testing was questionable, other bodies too, including the American College of Physicians and the American Academy of Family Physicians, explicitly called for informed consent in the 1990s. However, PSA testing proceeded as if no such requirement were in place.[13,14] In the same way, the test continues to attract takers regardless of its evidentiary deficiencies and the agnostic recommendations of the USPSTF. Only because of the much-advertised belief that early detection saves lives – as is true in the case of mammography, but may or may not be true in that of PSA – has the PSA system flourished despite the doubts that shadowed it from the beginning.

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