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Advising men on prostate cancer screening – is the cart before the horse in terms of evidence?

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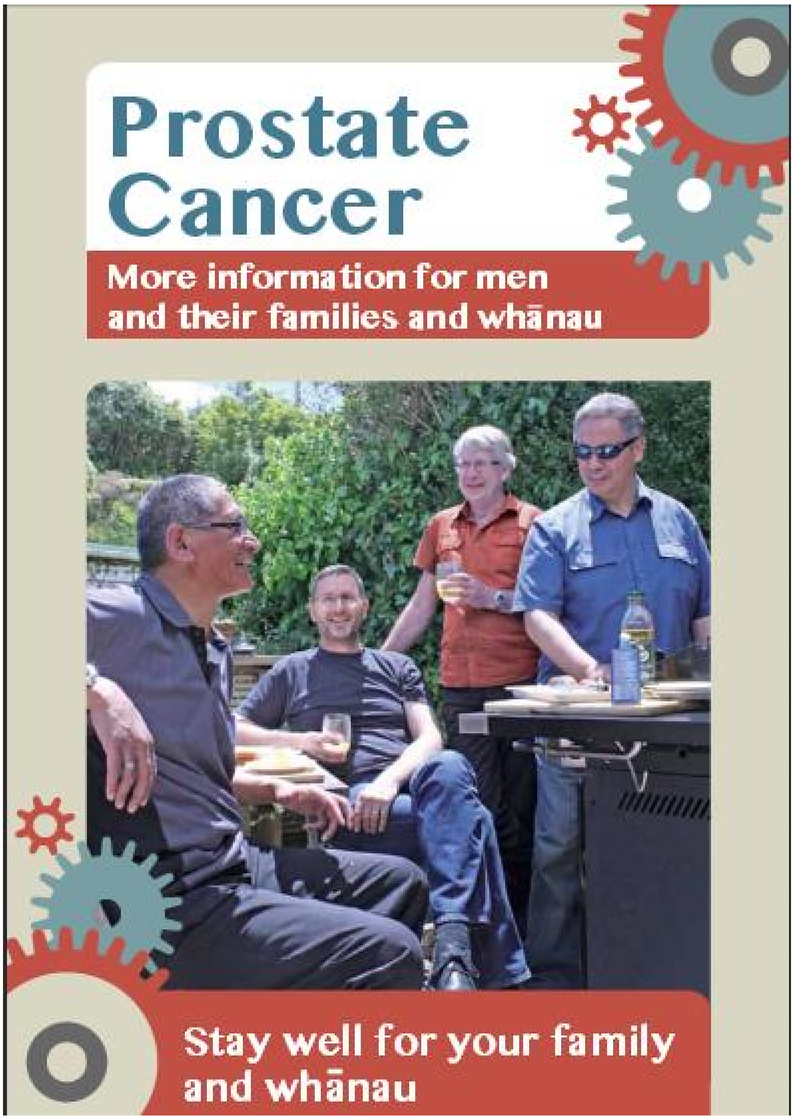

Prostate Cancer

More information for men and their families and whānau

Stay well for your family and whānau

Another review of the evidence for prostate cancer screening with prostate specific antigen (PSA) was published in the last week in the journal *JAMA*.[1] This blog considers the key recent evidence relating to prostate cancer screening. There remain many problematic issues with this type of screening – including the cloudy nature of the overall evidence on benefits vs harms. It is not reasonable to ask individual men and clinicians to make decisions regarding PSA-based screening. The Ministry should withdraw the recent pamphlets from circulation, and advice GPs and the public that there is insufficient evidence to recommend screening.

Recent developments

The authors of the new *JAMA* article advocate PSA ‘testing’ to occur only among men who express a definite preference for screening after discussion with their clinician. This is similar to the current recommendations of the NZ Ministry of Health appointed “Prostate Cancer Taskforce” that men should decide about whether prostate cancer screening is appropriate for them after being given information and discussing the issues with their general practitioner. To support this process, the Ministry of Health released a pamphlet for men and their families. This sparked considerable controversy about whether the information provided was adequate and balanced (see this NZ media story).

Why is there controversy about screening for prostate cancer?

The big issue is whether the benefits in terms of reducing deaths from prostate cancer clearly outweigh the harms of over-diagnosis and over-treatment. Prostate cancer is common among older men, and often so slow growing that it will not cause any problems in the lifetime of the man. Testing for prostate cancer in this context results in over-diagnosis of cancer that would never have been diagnosed in the lifetime of the man, causing unnecessary anxiety for these men and their families, and risks of substantial side effects from treatment (e.g. a recent RCT found 11% higher incontinence and 43% higher impotence in men offered PSA testing compared to controls [2]). This all comes at a considerable cost to the health system too – and questions of cost-effectiveness are also unresolved.

Despite the fact that all the men who fall into this category have been harmed from screening, and none have benefited, it results a ‘popularity paradox’; “*the greater the harm through overdiagnosis and overtreatment from screening, the more people there are who believe they owe their health, or even their life, to the [screening] programme*”.[3]

What is the evidence about the benefits and harms of prostate cancer screening?

The evidence is cloudy at best. There have been two recent major randomised controlled trials (RCTs), with contradictory results. The US-based Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer screening trial found no mortality benefit among those randomised to the screening arm after 13 years of follow up.[4,5] But there was substantial contamination of the ‘unscreened’ arm of the study, with over half of this group being screened for prostate cancer by the sixth year of the trial. This means that this trial evolved to become a comparison of more screened men with less screened, a difference that it was not powered to detect.

The other major RCT was the European Randomized Study of Screening for Prostate Cancer (ERSPC) trial.[6,7] After 11 years of follow-up, they found that men in the screening arm were 63% more likely to be diagnosed with prostate cancer, but also 21% less likely to die from it (with a plausible range of 9% to 32% risk reduction). However there has been criticism of the ERSPC trial due to differences in screening and treatment approaches used in different centres.

Furthermore, there is concern that the follow up time of (both) the above RCTs was insufficient to detect the full scale of health impacts.

To try and overcome the limitations of the RCTs, there have been a number of studies based on modelling benefits and harms of screening over longer periods.[8-10] They tend to find that the benefit to harm ratio improves with longer follow-up – a potentially promising result for screening. But these studies require many assumptions. On the other hand, a key advantage is that these studies provide multiple comparisons for different screening strategies. For example, screening different age ranges, with different frequencies (e.g. yearly vs two-yearly) and with different positivity thresholds of the PSA result. The results of this work tend to indicate that the majority of the benefits of prostate cancer screening can be achieved with lower intensity (less frequent) screening, whereas the harms are maximised in high intensity screening – which if true could be useful.

So who should decide?

This brings us back to the NZ brochures provided to men and their families by the Ministry of Health. They are very one-sided in the information provided. Men are told that “[w]hile the PSA blood test and the DRE [digital rectal examination] may be uncomfortable, there is no risk from having them. They do not harm you in any way.” There is no mention of the fact that if men undergo screening they are substantially increasing their risk of incontinence and impotence, nor that the benefits for screening remain controversial.

They state that “You can reduce the risk of dying from prostate cancer by finding the cancer early” and that “Having a PSA blood test… is the first step”. This would appear to be a fairly unequivocal plug for screening.

However, in some respects the debate about whether or not this information was balanced misses the point; even if perfectly balanced information was provided, asking men and their families to make the decision regarding prostate cancer screening remains problematic for several reasons:

- It assumes that general practitioners are up to date with all the evidence relating to both the benefits and harms of prostate cancer screening, and have both the time and inclination to communicate that complex evidence to men in a way that allows men to make an informed choice.
- It assumes men are able to ignore the very strong intuitive appeal of screening (‘catching cancer early’) and to weigh up the complex information relating to prostate cancer screening.
- It ignores the fact that the benefits and harms cited for prostate cancer screening occurred in well-organised randomised controlled trials. The history of screening repeatedly suggests to us that any benefits are likely to be far smaller and the harms greater in the context of opportunistic screening or screening in the absence of adequate quality control.[3]
- It is not enough to decide whether or not to screen. The benefits and harms will vary greatly depending on the intensity of screening. The harms are likely to be less with less frequent screening, a high PSA threshold for biopsy and a conservative approach to treatment.
- Finally, and very importantly, it ignores the upfront and downstream effects on the health system. The impact of PSA screening is not just on the man and his family but the entire tax-payer funded health system. PSA testing comes at a substantial cost and opportunity cost due to the increased need for treatment for cancers identified by

screening. There may be many other ways to improve men's health that are better value-for-money (see this previous PHE Blog).

It is irresponsible and arguably unethical to encourage screening without consideration of the broader issues; it certainly is not good policy to do so in the absence of balanced information to citizens and their health providers. Focusing attention and public resources on screening programmes for which there is actually good evidence of a positive benefit to harm ratio (such as bowel cancer screening) would seem a considerably better use of the country's scarce health dollars.

Because the evidence on prostate cancer screening is so cloudy, it should not be promoted. The Ministry should withdraw the recent pamphlets from circulation, and advice GPs and the public that there is insufficient evidence to recommend screening.

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