

# PROSTATE CANCER SCREENING

## *A double-edged sword*

*Prostate cancer screening is not currently recommended for asymptomatic men in New Zealand. But a growing chorus of voices – chiefly urologists, radiation oncologists and patient advocates – is calling for change. Amanda Cameron speaks to supporters and opponents of prostate cancer screening and finds the evidence cuts both ways*

Both arguments are compelling.

Jim Vause, Blenheim GP and member of the New Zealand Guidelines Group prostate cancer screening advisory group, is a staunch opponent of prostate cancer screening. Dr Vause reckons the evidence has changed very little since the advisory group made its 2004 recommendation against prostate cancer screening. There is still, he says, no high quality evidence showing screening prevents either death or illness from prostate cancer.

Dr Vause doesn't usually raise the subject of prostate cancer screening with his patients, but he provides a thorough explanation to men who ask.

"I'm quite happy to go ahead if they understand the issues," he says. But they need to understand what they're letting themselves in for. And, once they know what's involved, most of them don't want a bar of it, Dr Vause says.

The screening pathway goes something like this. First a man has one or more blood tests to check his prostate specific antigen (PSA) levels and a digital rectal examination. If his PSA result or rectal exam raises the suspicion of cancer, tissue samples from the prostate gland are taken by needle biopsy and tested. If cancer is detected, a man has the option of several treatment strategies, ranging from a wait-and-see approach to radical prostatectomy (where the prostate gland is removed entirely).

It sounds fairly straightforward, but the way Dr Vause explains it, the process is fraught with error, uncertainty and potential harm.

For a start, he says, PSA levels can rise as a result of several things – including prostate cancer, benign prostate enlargement, infection, and even recent sex or heavy exercise – and the blood test gives no indication at all of the cause.

Second, the test itself is far from perfect: for every 1000 asymptomatic men (aged 55 to 69) who have the PSA test, 15 will have prostate cancer that goes undetected because their PSA levels are normal, and 95 with suspicious PSA levels will later be found to have no prostate cancer.

Then there's the biopsy, an unpleasant experience involving a needle being inserted into the prostate gland via the rectum. For every 1000 PSA-tested men, 136 will need a biopsy and, of these, eight will have prostate cancer that goes undiagnosed. Only 33 will be diagnosed with prostate cancer, and it is not known how many of these men would have actually suffered any illness or death if it had not been detected early anyway. The biopsy cannot distinguish between an aggressive harmful cancer and a slow-growing one unlikely to cause any harm in a man's lifetime, Dr Vause says.

Further, it is not known which men with prostate cancer will benefit from the "curative" treatments available, and they can all cause unpleasant side effects. Radical prostatectomy is linked with a 1–2 per cent chance of death, a 20–80 per cent chance of erectile dysfunction and a 15–50 per cent chance of urinary incontinence. Radiotherapy is also linked to erectile dysfunction in 20–45 per cent of patients, and can impact urinary and bowel function in 2–25 per cent.

Finally, there's the context of the risks across a lifetime: prostate cancer is uncommon in men under 50, and the risk climbs slowly over the next three decades. Nearly 80 per cent of men who get prostate cancer are over 65.

It's all starting to sound a bit like a game of Russian roulette.

Enter the urologist. Robin Smart was one of three members of the 15-strong New Zealand Guidelines Group prostate cancer screening advisory group who strongly opposed the 2004 recommendation against prostate screening for asymptomatic men. The Auckland urologist argues the group could have used more up to date research in its 2004 report, came to the wrong conclusion based on the information it did use, and that the evidence base has moved on in a way that more strongly supports prostate cancer screening.

"The position of the New Zealand Guidelines Group was wrong

then and it's even more wrong today," Dr Smart says. "It leaves men in the same position as the early 1990s before PSA testing was available."

Personally, Dr Smart would like to see a national screening programme. Publicly, he – along with most urologists, radiation oncologists and men affected by prostate cancer – is calling for opportunistic prostate cancer screening. This group believes asymptomatic men should be offered regular PSA testing once they hit age 50, and the offer should start 10 years earlier for men with a close family member who has had prostate cancer.

Prostate cancer, he says, is the most common cancer for men over 65, and is responsible for 3.8 per cent of all male deaths in New Zealand. Each year, the disease is found in around 2000 men and kills about 600 men. The lifetime risk of prostate cancer (12 per cent) doubles in men who have a family member with the disease and more than quadruples in men with two or more affected family members. Further, the disease is mostly asymptomatic while it's curative. "If you wait until people have got symptoms from this it's nearly always too late," Dr Smart says.

He acknowledges the flaws in the screening process and the potential harms noted by Dr Vause, but argues improvements in recent years have tipped the balance so the benefits "definitely" outweigh the harms.

First, Dr Smart says, biopsy techniques have improved to the point where diagnostic accuracy is better and the harms are fewer. The infection and complication rate from biopsy has fallen to around 1–2 per cent over the last decade, and a grading system of prostate tissue samples called "Gleason scoring" can now identify the third of prostate cancers aggressive enough to require treatment, he says.

Second, a relatively new management strategy called "active surveillance" means a man with a low Gleason score can be monitored until curative treatment is called for, thus reducing the number of unnecessary treatment interventions.

Third, the treatments themselves have improved. For example, radical prostatectomy is less likely to be associated with urinary incontinence and there are better management strategies available for erectile dysfunction.

All in all, he says, the odds of receiving an accurate diagnosis and appropriate treatment with fewer complications are much improved and men should be actively offered screening – with complete information of all the attendant risks and benefits – and left to make up their own minds.

It's a position Prostate Cancer Foundation head and prostate cancer survivor Barry Young entirely agrees with.

Mr Young says he regularly takes calls from men diagnosed with prostate cancer angry they were never offered screening or that they asked for it and were talked out of it by their GP. The horror stories are "blessedly few", he says, but the foundation has started to document them

and is considering taking at least one recent case to the health and disability commissioner.

Within the last year, Mr Young received a call from the wife of an Auckland man who had regular PSA and rectal tests care of his insurance company. His PSA levels began rising steadily but he was talked out of a biopsy by his GP who told him biopsies come with a high risk of infection. The man now has aggressive metastatic disease.

"Here is a man who had done everything right and his GP quite frankly misinformed him," Mr Young says.

He is particularly concerned for the group of men he calls "walking timebombs" who have a family history of prostate cancer but are completely unaware of it for various reasons including adoption.

"You have only got one chance to get this cancer. Once it's out of the prostate it's incurable."

Despite the New Zealand guidelines, and possibly because of increasing media coverage about prostate cancer screening, increasing numbers of asymptomatic men are getting their PSA levels checked.

Southland pathologist Guy Mulligan says the number of PSA tests Medlab South does has grown steadily over the last decade.

The community laboratory provider, which services a population of about 700,000, now does as many PSA tests as HbA1c tests – about 2000 a month. Most of these come as part of a routine wellness check ordered by a patient's GP, so Dr Mulligan suspects they are ordered chiefly for the "worried well".

He also sees the biopsy samples ordered by GPs and urologists, and he is less convinced than Dr Smart about the usefulness of Gleason scoring to estimate the danger a tumour presents. Dr Mulligan says Gleason scores of 9 or 10 are more likely to be aggressive cancer, but most biopsies have a score "in the middle" of 6 or 7.

"At 6 or 7 you're literally at sixes and sevens. Some will and some won't have aggressive cancer and we can't tell which ones."

Personally, Dr Mulligan's not sold on prostate cancer screening. But, in New Zealand, he says: "There's this sense that 'people are trying to stop us having this test so we want one'."

One of the key reasons the National Health Committee recommended against prostate cancer screening in 2004, based on the New Zealand Guidelines Group's report, was that, in their estimation, "there is still no conclusive evidence to demonstrate that screening using the PSA test or digital rectal examination for prostate cancer reduces mortality or morbidity".

In support of that view, Dr Vause quotes a 2006 Cochrane review which concluded "there is insufficient evidence to either support or refute the routine use of mass, selective or opportunistic screening compared to no screening for reducing prostate cancer mortality" (Cochrane Database of Systematic Reviews 2006, Issue 3, Article No. CD004720. DOI: 10.1002/14651858.CD004720pub2). However, Dr Smart says one

of the two trials included in the review showed PSA testing reduced prostate cancer mortality by 62 per cent.

Two ongoing large-scale, multicentre, randomised, controlled trials – the European Randomised Study of Screening for Prostate Cancer (ERSPC) and the US-based Prostate, Lung, Colorectal and Ovarian cancer screening trial (PLCO) – should provide more



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information about the benefits of prostate cancer screening in the next year or two.

But already the experts are disagreeing over early results from these trials.

Early data from ERSPC indicate you'd have to screen 450 men for 10 years to prevent one man having metastatic disease at initial diagnosis, Dr Vause says. "The benefit is there, but it's very small," he says. Further, results from the ongoing "Holmberg trial" (*N Engl J Med* 2005;352[19]:1977-84) indicate it takes five radical prostatectomies to save one life over 10 years in a screened population, Dr Vause says.

Dr Smart questions Dr Vause's "number needed to screen" (NNS) calculation, adding that, besides, the NNS to save one life is 1792 for breast cancer and 8000 for cervical cancer. Furthermore, early ERSPC results actually show screening reduces prostate cancer deaths by 15 per cent and metastatic disease by 50-70 per cent, and the Holmberg trial indicates radical prostatectomy nearly halves prostate cancer mortality and reduces the prevalence of metastatic disease by 40 per cent.

In addition, Dr Smart says, mortality data from several countries – the US, the UK, the EU and Australia included – suggest the introduction of PSA testing has reduced prostate cancer deaths by up to a third.

Meantime, the Ministry of Health is keeping a watching brief on the two international trials to see whether policy changes are needed. It says it is currently working with the New Zealand Guidelines Group on an updated review of the evidence, and on a tool to help GPs support men in their decision to have a PSA test.

As it stands, the advice – backed by the NZ Cancer Society – is men should be fully informed about the risks and benefits of prostate cancer screening. Both Dr Vause and Dr Smart are eager that men should hear the numbers and make up their own minds. But therein lies the rub. How the information is presented depends on who presents it.

"It's possible to select experts on one side of the fence or another," Dr Smart acknowledges. "The experts on the other side of the fence tend to be epidemiologists and a few GPs. On our side are all the specialists and the men involved in prostate cancer treatment."

Dr Vause, on the other hand, has this to say: "The important thing is GPs are the people who do screening and urologists treat people who have already been screened. And I think it's important that we as GPs look at it from a GP perspective and also from a patient perspective."  
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*Postscript: New US guidelines released last week recommend against routine prostate cancer screening for men over 75 years and say more evidence is needed to determine if men under 75 could benefit from screening (Annals of Internal Medicine 2008;149[3]:185-191)*