'Should I get a PSA test?' – the question is not that simple

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PSA screening for prostate cancer is a controversial issue around the world. In this article the authors describe the situation in North America where screening is not being advised. They argue that patients should be tested and that men will adapt and learn to live with the results as active surveillance becomes more acceptable.

As more men are screened for prostate cancer, active surveillance will become a more accepted approach to management of low-risk disease (© Life in View/Science Photo Library)

In 2012, the US Preventive Services Task Force (USPSTF), a panel of doctors and epidemiologists appointed by the US Department of Health and Human Services, recommended against prostate-specific antigen (PSA) screening for prostate cancer.[1] Its advice arose from randomised clinical trial data suggesting that many biopsies resulted in men being diagnosed and treated for low-grade prostate cancer that did not warrant treatment. Given their advanced age and comorbidity, the men were much more likely to die of causes other than prostate cancer. Furthermore, aggressive treatment led to substantial adverse effects that negatively impacted the patients' quality of life. So, to avoid unnecessary biopsies and treatment, the USPSTF recommended abandoning PSA screening. In the last year, an advisory body in Canada, the Canadian Task Force on Preventative Health Care, has made a similar recommendation following a similar line of reasoning.[2]

WHAT DO PATIENTS THINK?

The thought of harbouring a treatable disease is intolerably stressful for some men. Destroying the offending organ and the cancer it contains is consistent with the 'take action' American psyche. There is no getting around the fact that living well with cancer, inconsequential or otherwise, does not compute as logical or reasonable for many men.

We believe, however, that the USPSTF did not consider the nuances of a situation where patients' beliefs are not so rigid. How patients view prostate cancer can change and we believe will change, but not by following the position espoused by the USPSTF.

Admittedly there has been some decrease in the number of biopsies performed in the

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USA since the USPSTF released its report.[3] Predictably though, that is associated with proportionately more men being diagnosed with intermediate- or high-risk cancer.[4]

It is not surprising then that the USPSTF position has led to a major outcry from many urologists in the USA and elsewhere,[5] who found it too rigid and absolute. Indeed many patients, who had been treated for prostate cancer, joined the protest arguing that they might have died of prostate cancer had it not been detected in time via the PSA test.[6] This highly polarised debate has left many men wondering and worrying whether they should or should not get a PSA test.

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WHAT TO SAY IF ASKED

So what should we in the prostate cancer community say when asked, 'Should I get a PSA test?' We would say, 'Yes, you should get tested', but a simple 'yes' or 'no' answer does not solve the difficult problem many of the men will face should they be diagnosed with low-grade disease following confirmatory biopsy. What has not been resolved is how to best protect the men from a lethal cancer, while concurrently minimising their distress from a positive cancer diagnosis when their cancer is indolent and does not require prompt treatment.

If that is our goal, and we believe it should be, then we should proffer some counter-questions: 'Can you live comfortably knowing that you have a low-grade cancer, but are very likely better off not receiving therapy? And, if aggressive cancer is found, would you pursue treatment options?' These are the relevant questions that get at the psychological core of the 'test' or 'not test' PSA controversy. Such questions have led to extensive discussion about the challenges in educating patients so they have the necessary information to make an informed decision about PSA screening.[7]

In some ways, these questions have already been answered. And they bring to the surface a psychological issue not addressed in the epidemiology-driven recommendations from the USPSTF. Simply stated, the USPSTF did not consider the adaptability of men diagnosed with prostate cancer. The issues we should consider are discussed below.

Life expectancy

Because of improving healthcare — vaccines, antibiotics, good public sanitation — male life expectancy has increased greatly since prostate cancer was first identified some 160 years ago. According to the SEER Stat Fact Sheet (http://seer.cancer.gov/statfacts/html/prost.html), the median age of prostate cancer diagnosis in the USA now is 66 years, and for prostate cancer death, 80 years. Furthermore, there has been a striking decrease in prostate-cancer-specific mortality in recent decades.[8] If not 'cured', prostate cancer can now be controlled in many cases along the lines of other chronic diseases, such as diabetes or high blood pressure.

Living with untreated cancer is not easy

This is evidenced by the fact that many men on active surveillance (AS) withdraw within three years.[9] Disease progression is one driving factor for abandoning AS, but anxiety is clearly another factor for why some men elect for treatment. However, there is every reason to believe that this mindset can change. As noted in Davison and Goldenberg,[10] physician recommendation is the strongest factor for men to elect AS. The case for AS when presented to patients can be bolstered by informing patients about discussion among academic pathologists as to whether a Gleason ≤6 diagnosis should even be called 'cancer'.[11] As more men understand that Gleason ≤6 prostate cancer has little, if any, metastatic capability, more men should be willing to elect for and comply with AS.

The USPSTF understood, of course, the indolent nature of Gleason ≤6 prostate cancer. However, they did not explore the fact that the public's understanding of the benign nature of low-risk prostate cancer can also change.

In response to the USPSTF, many organisations have called for doctors and patients to discuss the pros and cons of screening. Vickers *et al*[7] provides a decision-making tool, acknowledging the need to balance evidence-based data against the risk of overloading the patient with too much information. One thing they do not consider, however, is the relative experience that the patients have had with other patients on AS protocols. This, we believe, is an important and under-appreciated variable.

Identifying the inherently anxious

The raw fact is that some men, who are on AS, experience substantial anxiety, especially younger patients or those who have been diagnosed for a long time.[12] Clearly, there are those who abandon AS because of anxiety and seek potentially curative treatments.[13] They do this, not because the disease has necessarily changed to a more aggressive form, but because they simply can't dispel the intrusive thought that they have cancer.

The men who find AS psychologically intolerable, however, appear to be an inherently anxious minority.[14] According to Anderson *et al*,[15] a small percentage of patients on AS had clinically significant anxiety that could be related to prostate cancer itself (12.8%), fear of recurrence (8.1%) or PSA testing (1.2%). In another study,[10] 19% of patients reported moderate

to severe anxiety while on AS. These relatively low numbers appear to reflect a subset of men, whose innate anxiety level is probably too high to make them good candidates for AS, regardless of their Gleason score. Indeed, one study indicates that patients with neurotic personality have unfavourable anxiety and distress scores while on AS.[16] As such, we need good, simple assessment instruments that can help identify such individuals upfront in the clinical setting. Potentially, such instruments may also help avoid overdiagnosis and overtreatment in men who have anxiety issues. Knowing their propensity to catastrophise might save physicians from spending protracted amounts of time convincing such patients to go on AS, only to have them debilitated by anxiety and prematurely abandon the protocol.

Excluding that minority of men, we predict that as AS becomes a more common 'standard of care', more men diagnosed with low-risk prostate cancer will elect to stay on AS for a longer time. The anxiety associated with being diagnosed with cancer, and not having it treated, should progressively decrease as each new patient becomes aware of the number of other patients who are already on an AS protocol.

Individualising the approach

Right now the American Cancer Society estimates some 220 000 new prostate cancer cases in 2015 with around 27 500 deaths due to prostate cancer. As USPSTF noted, PSA screening will lead to more men being diagnosed with indolent cancer. But as more men become aware that in most cases prostate cancer – diagnosed in the modern PSA era – is slow-growing and non-life-threatening, AS itself will increasingly be acceptable and tolerated.

Although currently available nomograms to distinguish insignificant from significant prostate cancer are not ideal,[17] they are improving. With better imaging (*ie* state of the art MRI) and new biomarkers, uro-oncologists are increasingly in a position to advise men with increasing confidence about whether they should or should not remain on an AS protocol. Using 'smart' PSA screening, doctors can establish individualised schedules for PSA testing, *ie* this recognises that not every man needs an annual PSA test, not every rise in PSA needs to lead to a biopsy (reducing the risk of septic complications for multiple biopsies), and not every patient with a positive biopsy needs prompt treatment. There is no question, though, that with more patients accepting AS protocols, potentially lethal cancer will be captured along the way and treated when still curable.

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Coping confidence

A recent paper identified that what mattered most when it came to living comfortably with AS is patients' 'coping confidence'.[18] Other psychological factors that one might suspect would be relevant, such as the ability to relax, were not nearly as important. Although the psychological adjustment to AS was beyond the purview of the USPSTF, from a public health perspective what is critical is the fact that 'coping confidence' is not a fixed trait, but a variable state. One's coping confidence in dealing with any potentially stressful situation, such as living with prostate cancer, is likely to be low if one's most dominant experience with the disease is the death of close friends or relatives. Conversely, as the number of men dying of prostate cancer goes down and the number on AS goes up, more men will be confident that they can cope with a prostate cancer diagnosis. There is already a hint that this is going on in some cancer centres. For example, at one site in Michigan some 50% of patients with low Gleason scores are now going on AS.[19]

Coping with AS, and living with cancer in general, typically involves not just a challenge for patients but also other family members.[20] It is noteworthy that interventions to enhance coping not just for patients, but also their partners, are now being designed and evaluated.[21]

CONCLUSION

When it comes to health risks, humans are Bayesian organisms[22] and our anxiety levels are always adjusted by changes in the frequency of associations that can raise or lower anxiety. The USPSTF did not consider the fact that tolerance for AS should increase in a feedback fashion as more men embark on AS protocols.

So, when we are asked 'Should I get a PSA test?', our answer should acknowledge the fluid nature of cancer fear. 'Yes', we should say — 'You should get tested'. But also tell them that they may get diagnosed with low-risk disease that may not warrant any treatment for years, if at all. Ask them how many men they know right now, who are on AS? Do they know that the numbers of men on AS is rising while the number of men dying of prostate cancer is falling? Tell them, though, that because some men still die of this disease, it is best to know where they stand and have a PSA test.

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REFERENCES

1. Moyer VA. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2012;157:120–34.
2. Bell N, Gorber SC, Shane A, *et al.* Recommendations on screening for prostate cancer with the prostate-specific antigen test. *CMAJ* 2014;186:1225–34.
3. Perez TY, Danzig MR, Ghandour RA, *et al.* Impact of the 2012 United States Preventive Services Task Force Statement on prostate-specific antigen screening: analysis of urologic and primary care practices. *Urology* 2015;85:85–9.
4. Hall MD, Schultheiss TE, Farino G, Wong JYC. Increase in higher risk prostate cancer cases following new screening recommendation by the US Preventive Services Task Force (USPSTF). *J Clin Oncol* 2015;33(Suppl 7):abstr 143.
5. Murphy DG, Ahlering T, Catalona WJ, *et al.* The Melbourne Consensus Statement on the early detection of prostate cancer. *BJU Int* 2014;113:186–8.
6. Orom H, Underwood W, Homish DL, *et al.* Prostate cancer survivors' beliefs about screening and treatment decision-making experiences in an era of controversy. *Psychooncology* 2015;24:1073–9.
7. Vickers AJ, Edwards K, Cooperberg MR, Mushlin AI. A simple schema for informed decision making about prostate cancer screening. *Ann Intern Med* 2014;161:441–2.
8. Allemani C, Weir HK, Carreira H, *et al.* Global surveillance of cancer survival 1995-2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2). *Lancet* 2014;385:977–1010.
9. Dall'Era MA, Albertsen PC, Bangma C, *et al.* Active surveillance for prostate cancer: a systematic review of the literature. *Eur Urol* 2012;62:976–83.
10. Davison BJ, Goldenberg SL. Patient acceptance of active surveillance as a treatment option for low-risk prostate cancer. *BJU Int* 2011;108:1787–93.
11. Lepor H, Donin NM. Gleason 6 prostate cancer: serious malignancy or toothless lion? *Oncology* 2014;28:16–22.
12. Burnet KL, Parker C, Dearnaley D, *et al.* Does active surveillance for men with localized prostate cancer carry psychological morbidity? *BJU Int* 2007;100:540–3.
13. Bul M, Zhu X, Valdagni R, *et al.* Active surveillance for low-risk prostate cancer worldwide: the PRIAS study. *Eur Urol* 2013;63:597–603.
14. van den Bergh RC, Bangma CH. Active Surveillance: Protocol Makes Perfect. *Eur Urol* 2014;67:239–40.
15. Anderson J, Burney S, Brooker JE, *et al.* Anxiety in the management of localised prostate cancer by active surveillance. *BJU Int* 2014;114(Suppl 1):55–61.
16. van den Bergh RC, Essink-Bot ML, Roobol MJ, *et al.* Anxiety and distress during active surveillance for early prostate cancer. *Cancer* 2009;115:3868–78.
17. Wong LM, Neal DE, Finelli A, *et al.* Evaluation of models predicting insignificant prostate cancer to select men for active surveillance of prostate cancer. *Prostate Cancer Prostatic Dis* 2015;18:137–43.
18. Yanez B, Bustillo NE, Antoni MH, *et al.* The importance of perceived stress management skills for patients with prostate cancer in active surveillance. *J Behav Med* 2014;38:214-23.
19. Womble PR, Montie JE, Ye Z, *et al.* Contemporary Use of Initial Active Surveillance Among Men in Michigan with Low-risk Prostate Cancer. *Eur Urol* 2015;67:44–50.
20. Gorin MA, Soloway CT, Eldefrawy A, Soloway MS. Factors that influence patient enrollment in active surveillance for low-risk prostate cancer. *Urology* 2011;77:588–91.
21. Lambert SD, Girgis A, Turner J, *et al.* "You need something like this to give you guidelines on what to do": patients' and partners' use and perceptions of a self-directed coping skills training resource. *Support Care Cancer* 2013;21:3451–60.
22. Fisher LD. Comments on Bayesian and frequentist analysis and interpretation of clinical trials. *Control Clin Trials* 1996;17:423–34.