tackle prostate cancer

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PROSTATE CANCER SCREENING

PSA Testing: A More Informed Approach

Despite continuing controversy, at the moment the PSA (Prostate Specific Antigen) blood test remains the only initial, simple, cheap option available to screen for Prostate Cancer (PCa) in asymptomatic men to detect PCa at an early, curable stage.

Since PSA came into general use in the 1990s, controversy over its benefits and harms have led to widely varying rates of use across different countries, and to differences of opinion between professionals and patients. This has happened largely because, although many PCas are not aggressive or lethal, PSA-based screening has led to invasive investigation and 'over-diagnosis', followed by 'over-treatment' through radical surgery or radiotherapy and their associated complications of impotence, incontinence and bowel disturbance. It is equally true, however, that many thousands of men have avoided a slow and painful death through the early treatment of PCa that was detected by PSA screening.

There have been many PCa screening trials in many countries over many years, trying to clarify the 'benefits versus harm' controversy, with varying results.[1,2,3] This has led to medical policy-makers making decisions on national policies for PSA screening on inadequate data.[4] For instance, in 2012 the United States National Preventive Services Task Force advised against PSA testing for any asymptomatic men[5] but, since then, the death rate from metastatic PCa has started to rise, and we understand this guidance is now being reconsidered..

PCa is the commonest major cancer in UK men and second commonest cause of cancer deaths with over 47,000 new registrations and over 11,000 deaths each year.[6] This is one of the highest death rates in the world even though we have one of the world's richest economies. However, the UK National Screening Committee (NSC) argues that PSA-based screening is too imprecise and that the dangers of 'over-diagnosis' and 'over-treatment' outweigh the benefit of cure for a minority of men with early, aggressive disease.[4]

Nearly all current major national and international urological guidelines recommend PSA-based screening for appropriately selected, counselled men who can then make an informed decision.[7,8,9] In summary, the majority of international expert panels recommend or propose:

- Screening from age 45 for men with a family history of an immediate male relative with PCa and black African or African Caribbean men (risk 1 in 4).
- Obtaining a baseline PSA in a man's forties to predict future risk.
- Linking PSA to a "risk calculator" to assess need and frequency of future PSA testing.
- Not screening men below 40 or with less than 10 years' life expectancy.

UK Clinical Practice

UK PCa mortality is higher than in most European countries, possibly because fewer than 10% of UK men seek screening.[10] The UK relies upon GPs to deliver PSA testing, both for symptomatic and asymptomatic men, in line with the recommendations of the Prostate Cancer Risk Management Programme[11] but in 2012 only a quarter of GPs were familiar with the programme[12] and, despite a legitimate right to a PSA test[11], many men were denied PSA tests without adequate counselling. This is of particular concern for black African and African Caribbean men who carry a 1 in 4 risk of developing PCa, and for men with a family history of the disease. Neither is it wise to advise withholding PSA until the symptoms develop. Consistent publications since 2002 have shown that men referred due to symptoms have a higher risk of PCa mortality, disease progression and metastases compared with asymptomatic, PSA-screen detected men[13].

Finally, despite awareness campaigns raising the profile of PCa, the low rate of PSA testing has led to few opportunities to use the tools we already have for early detection and discrimination between aggressive and non-aggressive cancer; and the cheaper option of early, curative treatment compared with late, expensive, palliative and often unsuccessful treatment of advanced cancer leading to 11,000 deaths each year.

Against this background it is not surprising that UK statistics are so poor in comparison with the best trial results of screening that are being reported from Europe, where they have achieved 40-50% reductions in PCa mortality.[14,15]

To this more optimistic outlook we can now add the recently published evidence from two hugely significant UK trials: the PROMIS Trial[16] and the ProtecT Trial.[17] These provide important UK data on the diagnosis and treatment of non-aggressive PCa and pose two main questions:

- How does the latest information on PSA screening alter the benefit versus harm debate?
- How does this relate to best practice in screening, early diagnosis and treatment of organ-confined PCa?

The PROMIS Trial

The results of the PROMIS trial of multiparametric MRI (mpMRI) scans offer the hope of early recognition of significant cancer likely to progress, whilst saving those with insignificant, non-aggressive cancers even the need for invasive biopsies; this would mean a major reduction in 'over-diagnosis'. However, the offer of a mpMRI scan itself relies on PSA screening to detect a potential problem in the first place.

Due to the PROMIS trial, NICE suggests guideline CG175 will in future recommend that mpMRI should be performed before TRUS biopsy.[18]

The ProtecT Trial

This UK trial reports the 10-year clinical outcome of 1,643 UK men with non-aggressive, PSA screen-detected PCa randomised to receive radical treatment or active surveillance. After 10 years' follow-up, the death rate was only 1%, whichever group men were in, although in those undergoing surveillance, over half developed progression and changed to active treatment. Presumably, without screening in the first place, these men would have presented with late stage, incurable disease and most likely added to our PCa death toll. This progression rate is not surprising given the limitations on the accuracy of standard TRUS biopsies during the trial period 1999-2009.

Conclusion

In conclusion, we now have emerging evidence that appears to support PSA-based testing for appropriately informed men, backed up by further evidence that shows how we can now avoid the pitfalls of over-diagnosis and over-treatment. It is therefore essential that this positive information is disseminated as widely as possible and especially to those countries where men are discouraged from PSA-based screening and PCa death rates are higher than the best results that are achieved in Europe.

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