tackle prostate cancer
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PROSTATE CANCER SCREENING

Campaigning for the early diagnosis and cure of men with prostate cancer

Submission to the UK National Screening Committee

JANUARY 2020

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Executive Summary

Prostate Cancer (PCa) screening with the simple blood test PSA aims to detect PCa at an early, curable stage. Although fully entitled, most UK men do not avail themselves of the test and many doctors decline to provide the test on the grounds that the "harms" of screening outweigh the benefits of cure for a small number of men with aggressive PCa. However, 12,000 UK men die from PCa every year, our mortality rate languishes below most of our western neighbours and the UK has not experienced the fall in PCa mortality seen in countries extensively using PSA; indeed, our death rate is rising.

That the "harms" of screening outweighed the benefits was arguably true in many countries during the first 20 years of PSA use. This stems from PSA not being a specific marker for PCa and unable to differentiate between aggressive, lethal PCa and non-aggressive, insignificant PCa. Neither did we have an accurate, non-invasive, second line test to provide the answers. Consequently, thousands of men diagnosed with cancers we now know to be harmless, underwent radical treatment with its significant risk of serious complications – impotence, incontinence and bowel damage.

During the last 10 years research evidence and clinical practice in the UK have entirely changed this picture. The key advances have been:

- The risk factors for PCa have been clearly identified.
- mp-MRI has been confirmed as an accurate, non-invasive, second line test capable of differentiating between aggressive and non-aggressive PCa.
- International screening guidelines have achieved a high degree of consensus, and there is comprehensive UK guidance available for the optimum use of PSA.
- Over-treatment of non-aggressive PCa in the UK has been virtually eliminated with active surveillance proven as a safe "treatment" option.
- Screening studies running up to 20 years are demonstrating up to 50% falls in PCa mortality.
- Screening and early intervention is a superior clinical option and cheaper than long term treatment and eventual death from advanced PCa.

In summary, this evidence supports radical re-appraisal of PSA-based screening and a fundamental change in its delivery. Anything less would be highly discriminatory.

Introduction

The objective of screening is to identify cancer at an early, curable stage to prevent death from late stage cancer. Prostate Cancer (PCa) remains the UK's commonest male cancer and second commonest male cancer killer causing over 47,000 new cases and nearly 12,000 deaths every year, a figure now exceeding deaths from breast cancer[1]. Half of UK men still present with late stage PCa with no sign that this ratio is decreasing[2].

UK Background

In 2016 the UK National Screening Committee recommended against the introduction of a PSA-based national screening programme because PSA was not specific for PCa and could not discriminate between aggressive and non-aggressive PCa[3]. The former results in "false positives" leading to unnecessary, invasive prostate biopsies whilst the latter leads to detection of non-aggressive PCa for which many men have received unnecessary radical "over-treatment". The resultant harms of "over-diagnosis" and "over-treatment" thus outweighed the benefit of cure for a minority of men detected with early, aggressive PCa.

Although the UK has no national screening programme, the Prostate Cancer Risk Management Programme (PCRMP)[4] permits men over age 50 to have a PSA test, once counselled by a professional.

Alongside this somewhat paradoxical position, UK clinical practice has made substantial advances. The 6th National Prostate Cancer Audit (NPCA) for the latest clinical year, 2017/2018, shows that mp-MRI scanning is replacing prostatic biopsy as the optimum second line test for men with a persistently raised PSA[2] and NICE guidance now recommends mp-MRI before biopsy[5]. The likelihood of an underlying aggressive PCa existing when an MRI is normal is extremely low[6] leading to biopsy rates falling by 30%[7]. If an MRI is abnormal, more accurate, targeted biopsies can take place with the trans-perineal route being increasingly used to lessen the infection rate associated with the trans-rectal route[2].

The 6th NPCA shows that the UK over-treatment rate has now dropped to only 4%[2] with Active Surveillance proven as a safe treatment option for men diagnosed with non-aggressive PCa[8].

Unfortunately, UK men still remain largely unaware of the potential risk their prostates pose and UK PSA test rates remain low[9]. GPs are advised not to "pro-actively raise the question of PSA testing"[10]. Two surveys have shown that insufficient GPs are familiar with PCRMP or have sufficient knowledge to offer balanced counselling[11,12]. Substantial anecdotal evidence confirms that numerous men, even men at high risk, are refused a PSA test or told to report back "only when symptoms arise"; PCa that has grown sufficient to cause symptoms is usually advanced and incurable.

The overall consequence of this situation is that the UK death rate from PCa continues to rise and our mortality rate continues to languish below most of our western neighbours.

International Background

In all countries extensively using PSA for screening after its introduction in the 1990s, the PCa mortality rate fell, but at the cost of substantial over-treatment. Whilst urologists then sought to bring order and consensus into PCa screening [13], some early screening trials failed to show that screening reduced PCa mortality[14]. Thus in 2012 the influential United States Preventive Services Task Force (USPSTF)counselled unequivocally against screening[15]. Since then the percentage of US men presenting with metastatic disease has risen[16] and the death rate has started to rise for the first time [17] forcing a change in the USPSTF recommendation to individual informed decision making for PSA tests[18].

During the last decade well conducted screening studies running up to 20 years are reporting reductions in mortality reaching 50%[19] or more[20].

Consequently, 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[13,21,22]. In summary, the majority of international expert panels recommend:

- 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).
- Screening from age 45 with a family history of breast cancer on the maternal side[23].
- Obtain a baseline PSA in a man's 40s to predict future risk:
    - For men aged 40-60 a "normal" initial PSA of 1-2ng/ml carries a 26% risk of later PCa; an initial PSA of 2-3ng/ml carries a 40% risk of later PCa[24].
    - Do not screen men below 40 or with less than 10 years' life expectancy.
- Link PSA to a "risk calculator" to assess need and frequency of future PSA testing.

Summary of Research, Trial & Practice-based Evidence

- There are **no** new markers available to replace PSA as the initial screening test for PCa.
- There are comprehensive UK consensus guidelines available on the optimum use of PSA[25].
- Men confirm PSA is an acceptable test[26].
- PSA is a useful marker for identifying BPH[27].
- Risk prediction models can double the sensitivity of PSA for PCa detection .
- Men in PSA screening programmes running for up to 20 years are benefiting from c.50% reductions in PCa mortality with numbers needed to screen and to diagnose falling to 139 and 13 respectively to prevent 1 PCa death – numbers lower than current colon and breast screening[28].
- A persistently raised PSA must be followed by second line tests **before** a prostate biopsy. In the UK mp-MRI is the NICE recommended test[5], but numerous blood and urine tests are competing for recognition.
- A normal mp-MRI indicates that a significant, aggressive PCa is unlikely to be present.
- mp-MRI has reduced the number of biopsies by approximately one-third and greatly reduced over-diagnosis.
- The UK treatment options are determined by multidisciplinary teams and together with informed choice have reduced the over-treatment rate over the last 4 years from 12% to 4%[2].
- Active surveillance is a safe treatment option for non-aggressive PCa[8].
- Minimally invasive treatments for localised PCa report reduced side effects and good cancer control.
- There is an economic case for increased PSA screening. PCa develops slowly in its early stages when detectable and curable but when diagnosed at a late state, treatment is rarely successful and very costly. A robotic radical prostatectomy costs £15,000 compared with a typical cost of £300,000 for late stage palliation[29].

A risk-based screening model based on age, race and polygenic risk assessment can reduce over-diagnosis and provide a cost-effective screening programme for large populations[30].

Conclusion

The UK's current annual death rate of 12,000 men – that's one death every 45 minutes – is unacceptable and the argument that the harms of screening outweigh the benefits is no longer valid.

Despite awareness campaigns raising the profile of PCa, the low rate of PSA testing in the UK has resulted in little opportunity to use the tools we already have for early detection, discrimination between aggressive and non-aggressive cancer and the cheaper option of early, curative treatment compared with late, expensive, palliation of advanced PCa. Adoption now of proven, best practice use of PSA on a national scale could halve the UK death rate. However, Primary Care does not have the capability to manage such a programme.

In the light of this evidence, the status quo discriminates against men, is financially unsound and medically unsustainable. We therefore recommend a fundamental change in the utilisation and delivery of PSA screening commencing with men at high risk as the first steps in establishing an adequate, national approach to reducing the UK's unacceptable death rate from this most pernicious cancer.

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This submission is dedicated to Roger Wotton (1949-2019), Chairman, National Federation of Prostate Cancer Support Groups.

Tackle Prostate Cancer is the campaign name of The National Federation of Prostate Cancer Support Groups

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