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This house believes that the UK Government should introduce a screening programme for prostate cancer

INTRODUCTION

The UK currently screens for breast, cervical and bowel cancer but does not screen for prostate cancer.[1] Prostate cancer was the most common cancer in men in England in 2011[2] and the second most common cause of cancer death in men in England and Wales in 2012.[3] Incidence rates have increased since the 1990s, and between 2002 and 2011 the rate increased by 10%.[2]

Men's health campaigns, such as Movember[4] and Men United[5], have helped to increase awareness of prostate cancer and there are discussions as to whether a screening programme should be introduced.[6] I do not agree that a screening programme should be introduced for the reasons set out below.

BACKGROUND

Most prostate cancers are adenocarcinomas originating in the peripheral zone of the prostate (figure 1). The cause of prostate cancer remains unknown, but hormonal, genetic and environmental factors are all thought to play a role in its pathogenesis.[7]

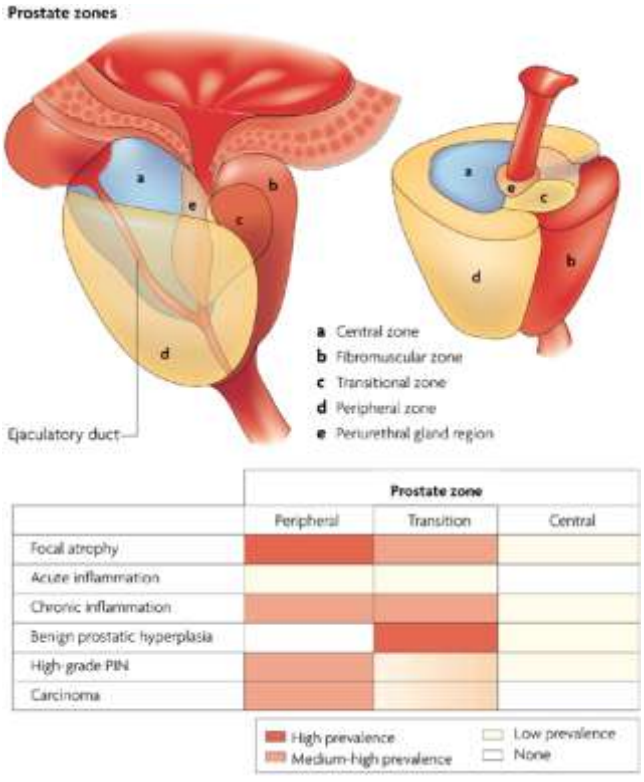

Figure 1: Zonal predisposition to prostate disease[9]

High risk prostate cancer is associated with germline mutations in BRCA2, but this only accounts for 2% of disease onset. There is evidence to suggest that prostate cancer inheritance is complex with many low penetrance genes associated with its development but other genetic defects occurring over time also contribute.[7]

There is an increased risk of prostate cancer with ageing as the physiology of the prostate changes[7] and 89% of all new cases in 2011 in England were in those aged 60 and over.[2] Chronic inflammation of the prostate is associated with atypical hyperplasia of the prostate epithelium with dysplastic changes.[7]

The strongest risk factor is age but family history, black ethnicity, smoking and a lack of exercise may also increase the risk of developing prostate cancer.[7,8]

Diagnosis

Prostate cancer is usually asymptomatic in the early stages but can present with lower urinary tract symptoms (LUTS). Patient with symptoms suspicious for prostate cancer should have a digital rectal examination (DRE), as the tumours in the peripheral zone of the prostate may be palpable, and their prostate specific antigen (PSA) level should be measured.[7]

PSA is produced by the epithelial cells of the prostate and is organ specific but not cancer specific. Levels increase with age and those above the normal for that age group may indicate prostate

cancer. The higher the PSA level the higher the risk of prostate cancer, but levels may be raised due to other causes such as prostatitis.[10]

Abnormalities on DRE or an elevated PSA level for age are indications for prostate biopsies. Diagnosis is based on histological examination of specimens from the gland, obtained by transrectal core biopsies under transrectal ultrasound guidance.[11]

Treatment

The objective of treatment for cancers detected early is to cure the patient. For patients with distant metastases the objective of treatment is palliative. The treatment recommendations from the National Institute for Health and Care Excellence (NICE) depend upon the stage of disease and prostate cancer risk classifications have been developed to help direct treatment (table 1).[11]

Table 1: Risk stratification for men with localised prostate cancer[11]

Level of risk	PSA		Gleason score		Clinical stage
Low risk	<10 ng/ml	And	≤ 6	And	T1-T2a
Intermediate risk	10-20 ng/ml	Or	7	Or	T2b
High risk	> 20 ng/ml	Or	8-10	Or	≥ T2c

Prostate cancer is curable, but this depends upon the stage of disease when diagnosed. Patients with a high tumour burden will do poorly, whilst patients with a low tumour burden will do better. Prognosis is poor if there are distant metastases, with an average survival of 24 to 48 months.[8]

CURRENT SCREENING APPROACHES

In the UK there is no organised screening programme for prostate cancer, but instead an "informed choice programme". Men who are concerned about prostate cancer should receive clear information about the advantages and disadvantages of the PSA test, biopsy and treatments for prostate cancer. [6] The screening body did not feel that there was clear evidence that a screening programme would reduce mortality in the UK without significant numbers of men being overtreated.[12]

The major societies differ in their recommendations (table 2)[13]; with the US Preventative Services Taskforce recommending no screening[14] and the European Association of Urologists recommending a baseline PSA for men aged 40 to 45 and a risk-adapted follow up approach.[15]

Table 2: Screening recommendations of major societies (Adapted from Hayes JH, Barry MJ. JAMA 2014 Mar 19;311(11):1143-1149.)

Organisation	Who should be screened	Screening interval
US Preventive Services Task Force, 2012	Screening should not be offered	
American Urological Association, 2013	Men aged 55-69 y or ≥70 y with >10- to 15-y life expectancy: use shared decision-making approach Men at higher risk <55 y: individualise approach	Consider 2-y interval over annual screening; may individualize intervals based on initial PSA
American Society of Clinical Oncology, 2012	Men with life expectancy >10 y: use shared decision-making approach	
American Cancer Society, updated 2010	Men aged >50 y at average risk with >10-y life expectancy: use shared decision-making approach Men at higher risk (black, first-degree relative diagnosed before 65 y) at 45 y Men at appreciably higher risk (multiple family members diagnosed before 65 y) at 40 y	Base interval on initial PSA: annual if ≥2.5 ng/mL; biannual if <2.5 ng/mL Biopsy recommended for all men with PSA>4 ng/mL Biopsy for PSA levels between 2.5 and 4 ng/mL should be individualized
American College of Physicians, 2013	Men aged 50-69 y with life expectancy >10-15 y: use shared decision-making approach Men at higher risk (black, first-degree relative diagnosed before 65 y) at 45 y Men at appreciably higher risk (multiple family members diagnosed before 65 y) at 40 y	Consider longer intervals than 1 y between screening PSAs
Canadian Urologic Society, 2011	Men ≥50 y with a 10-y life expectancy: use shared decision-making approach Men ≥40 y at high risk Consider baseline PSA in men 40-49 y	Consider intervals up to every 4 y
European Association of Urology, 2013	Baseline PSA≥40-45 y	Risk-adapted strategy based on initial PSA in men with life expectancy >10 y Screening intervals every 2-4 y for men with serum PSA>1.0 µg/L at 45-59 y and up to 8 y in men with serum PSA <1 µg/L

DISCUSSION

The WHO has developed criteria to guide the selection of conditions that would be suitable for screening (table 3).[16] Considering these criteria, then prostate cancer is an important health problem and can be cured if treated early but not if it has metastasised.[8] However, the reliability of early detection is debatable, the natural course of the condition is not fully understood and in the early stages it may be best treated by active surveillance.[11] The criteria will be discussed in greater detail below.

Table 3: WHO screening criteria[15]

1	The condition is an important health problem
2	Its natural history is well understood
3	It is recognisable at an early stage
4	Treatment is better at an early stage
5	A suitable test exists
6	An acceptable test exists
7	Adequate facilities exist to cope with abnormalities detected
8	Screening is done at repeated intervals when the onset is insidious
9	The chance of harm is less than the chance of benefit
10	The cost is balanced against benefit

Screening test
PSA levels and a DRE are commonly used to screen for prostate cancer.[11] However, questions remain whether these tests are reliable, sensitive and specific enough.

The PSA test has poor sensitivity and specificity. One randomised, prospective study using cut-off values of 3.1 and 4.1ng/ml estimated the sensitivity as 32.2% and 20.5% and specificity as 86.7% and 93.8% respectively. As the cut-off value increases, the test becomes more specific but less sensitive, so more patients with prostate cancer may be missed. The sensitivity and specificity of the test improved with an increase in the grade of the cancer.[17]

Screening by DRE alone showed a sensitivity of 57.9% and a specificity of 96.3%.[18]

Cost
A 1997 review by the Health Technology Assessment found the introduction of population screening to be prohibitively expensive. Extrapolating from estimates of cost for the first year of a national screening programme for prostate cancer in the USA, a UK screening programme would cost between £500 million and £1.5 billion.[19]

Prostate cancer screening studies
The debate around prostate cancer screening is dominated by two randomised controlled trials, the European Randomised study of Screening for Prostate Cancer (ERSPC)[20] and The Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial.[21]

The ERSPC randomised men to screening by PSA every four years or to a control group. The most recent data in 2012 showed that a man will have a relative risk reduction of 21% (rate ratio, 0.79; 95% confidence interval [CI], 0.68 to 0.91; P = 0.001) of dying from prostate cancer following screening.[20] In the Netherlands data subset, screening reduced prostate cancer mortality by 32% in the 55 to 69 age range.[22] Overall, 37 additional men needed to receive a diagnosis through screening for every 1 fewer prostate cancer deaths after 11 years of follow-up among men aged 55 to 69 years. However, though there was a reduction in the rate of death from prostate cancer, there was no reduction in the all-cause mortality.[20]

In the 13 year follow up of the PLCO trial, which looked at the difference in death rate between annually screened and opportunistically screened men, there was no statistically significant difference in mortality due to prostate cancer between the two groups. However, the diagnosis of prostate cancer was increased in the control group due to opportunistic screening.[21]

A Cochrane review of 5 randomised controlled trials, including ERSPC and PLCO, concluded that prostate cancer screening did not significantly reduce prostate cancer specific mortality and that overdiagnosis and overtreatment are common and associated with harm. They concluded that any reduction in mortality may take over 10 years to accrue, and so PSA screening is unlikely to be beneficial for men with a life expectancy of less than 10 to 15 years.[23]

Other screening programmes

Breast cancer is the most common cancer in women[2] and since 1988 women aged 50 to 70 in the UK are screened for breast cancer every 3 years.[24] The mammography screening test has much better sensitivity than PSA and DRE, with estimates ranging from 71% to 96% for sensitivity and from 94% to 97% for specificity.[25]

It has been estimated that between 2 and 2.5 lives are saved for every overdiagnosed case.[26] This would indicate screening in terms of lives saved is greater than the harm in terms of overdiagnosis, which is better than the figures for prostate cancer. However, a Cochrane meta-analysis of 13 trials estimates the relative risk reduction in breast cancer mortality as 10-15% after 13 years of follow up and overdiagnosis and overtreatment as 30%. The trials which provided the most reliable evidence showed that screening did not reduce breast cancer mortality.[27]

Whilst breast cancer may be a more appropriate condition to screen for than prostate cancer, due to the conflicting evidence there is now discussion as to whether breast screening should be recommended for any age group. Overdiagnosis has human costs and increases mastectomies and deaths, and reduction in breast cancer mortality is mainly due to improved treatments and better breast cancer awareness.[27]

CONCLUSION

Prostate cancer represents a significant health burden.[2] However, at present, prostate cancer screening does not fulfil the WHO screening criteria – PSA and DRE are unsuitable tests, there is no clear evidence that prostate cancer mortality is reduced, it is prohibitively expensive, and overdiagnosis and overtreatment are common and associated with harm. The benefits of prostate cancer screening do not outweigh the harms and it should not be introduced in the UK.

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