International Perspectives on Screening

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KEYWORDS

• Prostate cancer • PSA • Screening • Incidence • Mortality • Global

KEY POINTS

- Because cancer, especially prostate cancer (PC), is predominantly a disease of the elderly, increases in the number of older people will inevitably lead to more cases of cancer.
- The worldwide variable relation between prostate cancer mortality and life expectancy points toward racial and dietary influences on the occurrence and characteristics of prostate cancer.
- Contradictory study results are the basis of a still-ongoing debate on whether or not prostate-specific antigen (PSA)–based screening should be offered, which has led to many different guidelines worldwide.
- The PSA test has remarkable features as a screening test (easy to implement, reliable, cheap, capable of risk stratifying men at very low risk), but it is unable to identify men at moderate or high risk of having PC and having a potentially indolent and aggressive PC.
- Worldwide, further research on refining PSA-based algorithms, dealing with overdiagnosis, developing and validating more specific biomarkers, and exploring the role of imaging are ongoing; it is hoped that it will lead to an acceptable prostate cancer screening algorithm.

INTRODUCTION

The estimated population of the world in 2008 was 6.75 billion people, increasing by around 79 million people each year.[1] The world population is aging. In 1970, the world median age was 22 years; and it is projected to reach 38 years by 2050. The number of people in the world aged 60 years and older is expected to almost triple to 2 billion by 2050. Because cancer, especially prostate cancer, is predominantly a disease of the elderly, increases in the number of older people will inevitably lead to more cases of cancer, even if current incidence rates remain the same.[2]

PROSTATE CANCER AND LIFE EXPECTANCY

As early as in 1898, Alberran and Hallé[3] noted the presence of a substantial number of prostate cancers in asymptomatic men. In 1954, Franks[4] described that, in a UK population of men older than 50 years, about 38% harbored a "latent" prostate cancer; already at that time it was mentioned that the observed increase in incidence was caused by lengthening of longevity from 46.6 years in 1911 to 67 years in 1947.

Incidence data of prostate cancer per age group for Europe (United Kingdom) and the United States are shown in **Fig. 1** and confirm these early figures; prostate cancer is a disease of the elderly and, hence, will form a potential health problem for those countries where the life expectancy is relatively high (ie, >70 years).[5]

Similar data are available for prostate cancer mortality (**Fig. 2**). These observations are confirmed when looking at the worldwide distribution of deaths caused by prostate cancer. In 2008, approximately 258,000 men died of prostate cancer, with more than half of these deaths occurring in the developed world.

The relation between life expectancy and age-standardized prostate cancer mortality rates is

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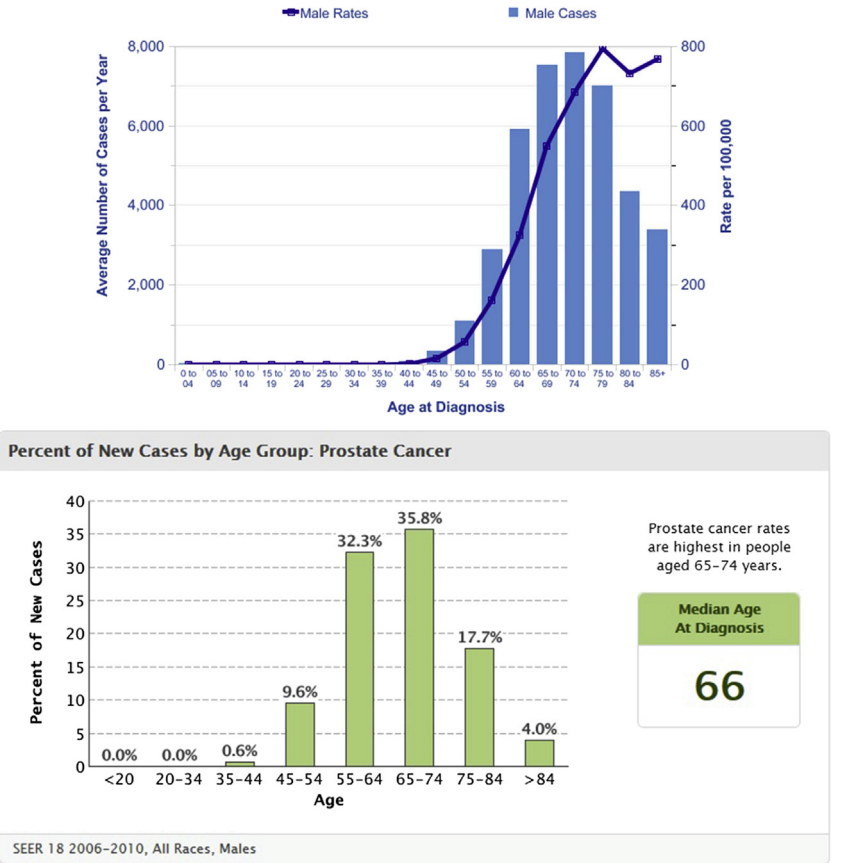

Fig. 1. Prostate cancer incidence per age group (data from the United Kingdom and United States). (*From* CancerStats: cancer statistics for the UK. Available at: http://www.cancerresearchuk.org/cancer-info/cancerstats/ and http://seer.cancer.gov/statfacts/html/prost.html. Accessed January 23, 2014.)

displayed in Fig. 3. Remarkable are the Asian and African continent where, in the Asian countries, despite a high life expectancy, the prostate cancer mortality rates are relatively low. It must be noted, however, that the most recent data show an increase.[6] In the African continent, the opposite is true; life expectancy is relatively low, whereas prostate cancer mortality is one of the highest in the world. These observations point toward racial and dietary influences on the occurrence and characteristics of prostate cancer.[6–9] In addition, the availability of structured health care may also play a role.[10]

RANDOMIZED PROSTATE CANCER SCREENING TRIALS

When looking at Fig. 3, it is not surprising that studies with the goal to investigate whether population-based screening could reduce prostate cancer–specific mortality were initiated in the United States and Europe.[11,12] Both trials, the European Randomized Study of Screening for Prostate Cancer (ERSPC) in Europe and the prostate arm of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) in the United States, reported their results on mortality outcomes in 2009 and 2012.[13,14] Remarkably, the results were contradictory. Although the European trial showed a statistically significant relative reduction of 20% in favor of screening, the US trial showed no effect on disease-specific mortality. It is currently generally accepted that the outcome of both trials, being very different in design and conduct, cannot be compared directly. The ERSPC shows an effect of systematic, strictly protocol, prostate-specific antigen (PSA)–based screening versus no screening, whereas the PLCO shows PSA-based screening according to a protocol but with the possibility of including clinical judgment versus a control arm where opportunistic screening was very common.[15,16] Despite these fundamental differences in design both trials, and with the inclusion of smaller (randomized) trials studying the effect of (PSA-based) prostate cancer screening on prostate cancer (PC)