Review

International epidemiology of prostate cancer: Geographical distribution and secular trends

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This review outlines current international patterns in prostate cancer incidence and mortality rates and survival, including recent trends and a discussion of the possible impact of prostate-specific antigen (PSA) testing on the observed data. Internationally, prostate cancer is the second most common cancer diagnosed among men (behind lung cancer), and is the sixth most common cause of cancer death among men. Prostate cancer is particularly prevalent in developed countries such as the United States and the Scandinavian countries, with about a six-fold difference between high-incidence and low-incidence countries. Interpretation of trends in incidence and survival are complicated by the increasing impact of PSA testing, particularly in more developed countries. As Western influences become more pronounced in less developed countries, prostate cancer incidence rates in those countries are tending to increase, even though the prevalence of PSA testing is relatively low. Larger proportions of younger men are being diagnosed with prostate cancer and living longer following diagnosis of prostate cancer, which has many implications for health systems. Decreasing mortality rates are becoming widespread among more developed countries, although it is not clear whether this is due to earlier diagnosis (PSA testing), improved treatment, or some combination of these or other factors.

Keywords: Epidemiology / Incidence / Mortality / Prostate cancer / Survival

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1 Introduction

With uncertainty about the natural history of prostate cancer [1, 2], the lack of definitive treatment for prostate cancer [3] and the impact of ‚prostate-specific antigen' (PSA) testing [4, 5], prostate cancer is associated with much controversy among the oncology profession [1, 2], and confusion among the general community about the risks that it poses [6]. This review describes the most recent international geographical patterns and trends for prostate cancer incidence, survival and mortality, with a particular emphasis on the possible impact of PSA testing on the observed patterns and trends for these outcomes.

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2 PSA testing

2.1 General

PSA is the protein secreted almost exclusively by a normal prostate gland to help nourish sperm. The theory is that elevated levels of PSA detected by a blood test suggest something is wrong with the prostate. This includes prostate cancer, but elevated PSA can also be caused by benign disease such as benign prostatic hyperplasia and prostatitis [2, 7].

The PSA test was first introduced into clinical practice in the United States in the mid-late 1980s [8, 9], into Canada in 1989 [10] and the UK [11] and Australia [12] around 1990. PSA testing has been shown to increase prostate cancer detection by 81% compared to digital rectal examination alone [13]; however its use remains debated due to the lack of sensitivity and specificity for the presence of the lethal variety of prostate cancer at an early stage [14].

Many prostate cancers either remain undiagnosed, or behave in an indolent manner after diagnosis, with little impact on a man's health even in the absence of treatment [4]. Autopsy studies have suggested that substantial propor-

tions of men have histological prostate cancer, even though it may not cause symptoms or death [15, 16]. With the advent of PSA testing, more of these indolent or latent prostate cancers are now being diagnosed [5], which has important implications for the interpretation of prostate cancer incidence and survival data [4].

2.2 Prevalence of PSA testing

Prevalence estimates for PSA testing are not available for all countries, and are often not directly comparable due to differences in reported age groups and time periods. However there are clear international differences in the uptake of PSA testing. Estimates of the prevalence of PSA testing were highest in the USA, where 75% of men over 50 years of age in 2001 reported ever having a PSA test [17]. In Canada, 48% of men who were 50 or older in 2000/2001 had ever had a PSA test [18], while 36% of men aged over 50 in part of the UK had at least one PSA test between 1990 and 1999 [19]. Just over half (52%) of men in Queensland, Australia aged over 50 in 2004 reported having ever had a PSA test, with 80% of these men saying their most recent test was performed for screening purposes [20].

The annual prevalence of PSA testing among men aged over 50 was 57% in the USA during 2001 [17] and 34% in Canada for 2000/2001 [18]. In contrast, the annual prevalence of PSA testing in the UK among men aged 45–84 years in 2002 was only 6% [21], but this is increasing [21–24]. Approximately 11% of Australian men aged 55 years and over had a PSA test for screening purposes in 2001, and this increased to 21% in 2006 (Medicare Australia, 2007). In South Korea 15% of men aged over 50 in 2004 reported having been screened during the previous 2 years [25].

Prevalence estimates for PSA testing in other countries are limited. Although the actual prevalence has not been quantified, there is strong, indirect evidence that the opportunistic use of PSA testing is increasing in Sweden after being introduced during the early 1990s [26, 27] and PSA testing has also been on the rise in Japan since 1998, when it became available on an outpatient referral basis [28].

3 Methodology

GLOBOCAN 2002 is a database constructed by the World Health Organisation (WHO) which contains estimates of incidence, mortality and prevalence data for different types of cancer for every country [29]. In order to clearly identify differences in prostate cancer incidence and mortality throughout the world and to give comparisons between countries greater parity, data from GLOBOCAN was reported in terms of more developed and less developed countries. More developed countries included those in Europe and North America along with Australia, New Zealand and Japan, while less developed countries were defined as those in Africa, Central and South America, Asia (excluding Japan), and all other island nations (*i.e.* those in the Caribbean, Melanesia, Micronesia and Polynesia) [30].

Trends in prostate cancer incidence and mortality were assessed using a statistical method called Joinpoint analysis [31], which evaluates changing linear trends over successive segments of time. A joinpoint is the point at which the linear trend changes significantly, either in terms of direction or magnitude. The analysis begins with the assumption of constant change over time (*i.e.* no joinpoint). Up to four joinpoints were tested in each model, depending on the number of years of data available and the stability of the yearly estimates. The selected trend line was the one with the fewest joinpoints which provided the best fit to the observed data, based on Monte Carlo permutation tests [31]. To reduce the chance of reporting trends that were just due to random fluctuations, we set the minimum number of data points in the trend line at either end of the year range to five [32].

4 Prostate cancer incidence

In 2002, about 679 000 men worldwide were estimated to have been diagnosed with prostate cancer, an age-standardised rate (using the World standard population) of 25.3 cases/100 000 population [29]. About three-quarters (76%) of these men lived in more developed countries.

Prostate cancer was the second most common cancer diagnosed among men worldwide (12% of all cancers), behind lung cancer [29]. In more developed countries it was the most common type of cancer diagnosed among men, accounting for nearly one in five (19%) of all cancers diagnosed. In less developed countries, prostate cancer was the sixth most common cancer among men, responsible for one in 20 (5%) of all cancer diagnoses [29].

After allowing for differences in the age structure of the populations, there was about a six-fold difference between the prostate cancer incidence in more developed countries (56.2 cases/100 000 population) compared to less developed countries (9.4 cases/100 000 population) [29] (Fig. 1, Table 1). The highest country specific age-standardised incidence rate (*per* 100 000 population) in 2002 was 124.8 in the USA, and the lowest 0.3 in Bangladesh [29].

Much of the observed geographic variation in prostate cancer incidence may be due to differences in PSA testing, and the ability to detect latent prostate cancer [4, 5, 33]. However, differences in the uptake of PSA testing cannot explain all of the international variation, since there was already more than a 50-fold difference in international prostate cancer incidence rates across countries in 1980 before the PSA test was introduced [34, 35]. Furthermore, the general ranking of countries for prostate cancer incidence in

Table 1. Estimated age-standardised incidence and mortality rates (*per* 100 000 population) for prostate cancer in selected countries, 2002

Incidence			Mortality		
Country[a)]	Cases	ASR[b)]	Country[a)]	Deaths	ASR[b)]
World	679 023	25.3	World	221 002	8.2
More developed countries	513 464	56.2	More developed countries	130 382	13.5
Less developed countries	165 347	9.4	Less developed countries	90 514	5.2
More developed countries					
United States of America	239 930	124.8	Norway	1 133	28.4
New Zealand	2 678	100.9	Sweden	2 550	27.7
Sweden	7 848	90.9	New Zealand	560	20.3
Finland	3 556	84.4	The Netherlands	2 529	19.7
Norway	3 071	81.8	Austria	1 282	18.4
Canada	17 900	78.2	France	9 789	18.2
Australia	10 807	76.0	Finland	774	18.0
Austria	4 701	71.4	United Kingdom	9 834	17.9
Germany	44 383	60.5	Australia	2 646	17.7
France	29 434	59.2	Canada	3 989	16.6
The Netherlands	7 112	56.7	United States of America	32 442	15.8
United Kingdom	27 463	52.2	Germany	12 158	15.8
Italy	23 518	40.5	Spain	5 857	14.9
Spain	13 253	35.9	Poland	3 114	12.4
Poland	6 016	24.1	Italy	7 419	12.2
Japan	16 808	12.6	Japan	7 667	5.7
Less developed countries					
Puerto Rico	2 428	100.1	Barbados	77	55.3
Barbados	133	99.7	Bahamas	37	35.6
Bahamas	71	65.3	Cuba	1 979	26.4
Brazil	31 956	53.2	Puerto Rico	576	23.0
Colombia	6 457	48.3	Colombia	2 885	21.6
Mexico	9 635	29.9	Nigeria	5 098	19.2
Cuba	2 105	28.2	Brazil	9 391	15.8
Nigeria	6 236	23.3	Mexico	4 795	14.8
Kenya	1 007	16.6	Kenya	850	14.1
Indonesia	5 074	7.0	Indonesia	3 181	4.4
Pakistan	2 308	5.6	Egypt	741	3.8
India	16 789	4.6	Pakistan	1 436	3.5
Egypt	867	4.4	India	10 867	3.0
China	10 125	1.6	China	5 919	1.0
Bangladesh	115	0.3	Bangladesh	71	0.2

Data source: GLOBOCAN 2002. International Agency for Research on Cancer (IARC).
a) See Section 3 for details of ‚more developed' and ‚less developed' countries.
b) Rates age-standardised to the 1960 World Standard Population in broad age group.

1973 – 1977 [34] and 1978 – 1982 [35] was very similar to the current comparisons. Completeness of cancer registration may also impact comparisons [36], as greater levels of estimation were required for less developed countries [29].

4.1 Age-specific variation

Prostate cancer in men under 50 is rare, after which incidence rates increase with age [29]. Worldwide the estimated age-specific rates (*per* 100 000 population) in 2002 were 0.2 (15 – 44 years), 10.6 (45 – 54 years), 72.9 (55 – 64 years) and 259.6 (65 years and over) [29]. The age-specific incidence rates of prostate cancer among men in more developed countries were generally between five and nine times higher than for men in less developed countries, however the age-specific proportions were almost identical for more developed and less developed countries.

One impact of the introduction of PSA testing has been to reduce the average age at diagnosis [37]. In countries where PSA testing has been more common, the proportion of prostate cancers diagnosed among men aged 65 and over has decreased. For example among African Americans in the USA the proportion decreased from 74% in 1982 – 1986 to 53% in 1999 – 2003 [38]. In Australia the corresponding percentages decreased from 85 to 72% (AIHW, Australian Institute of Health and Welfare 2007). In comparison, the

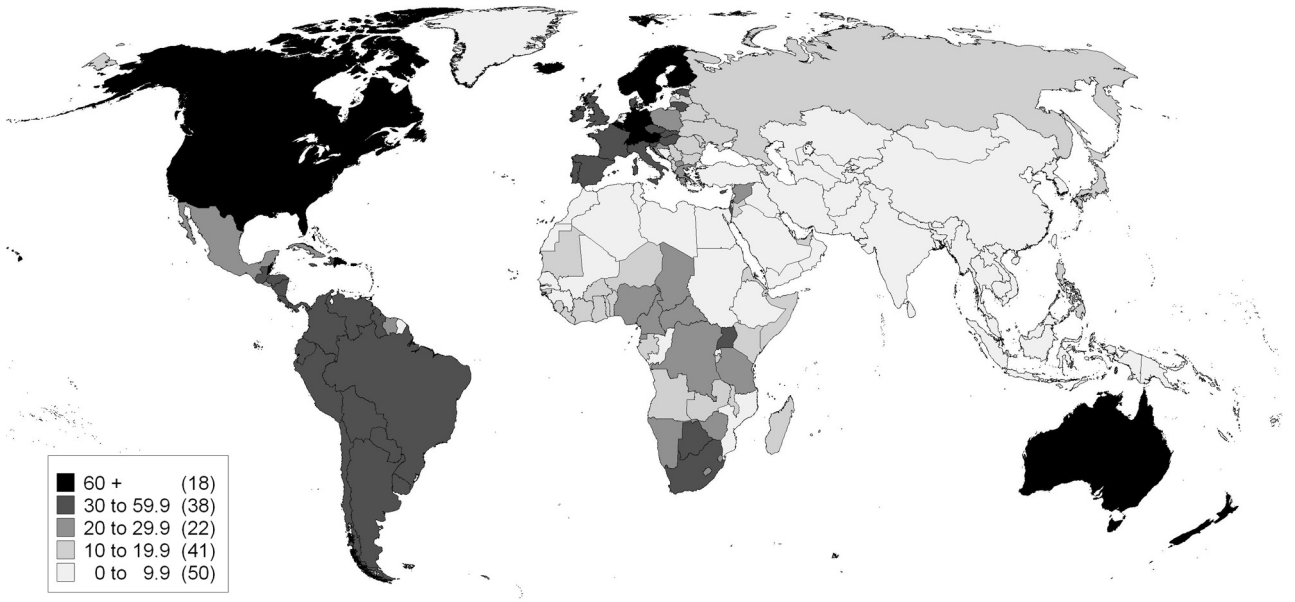

Figure 1. International variations in estimated incidence rates (*per* 100 000 population) of prostate cancer in 2002. (Data source: GLOBOCAN 2002, International Agency for Research on Cancer (IARC)).

percentage of men in Japan (where PSA testing is less prevalent) who were aged 65 and over at diagnosis remained virtually unchanged from 1982 – 1986 (89%) to 1997 – 2001 (88%) (NCC, Cancer Control and Information Services, National Cancer Center, Japan 2007; http://ganjoho.ncc.go.jp/professional/statistics/statistics.html).

4.2 Racial variation

Along with increasing age or a family history of prostate cancer, Sub-Saharan African ancestry has long been recognised as an important risk factor [8, 39]. Within the USA, the age-standardised incidence rate (World population) among African-American men in 2004 was 165.8/100 000 population, substantially higher than for European – Americans (105.5/100 000) [38]. In addition, there is evidence that African-Americans are more likely to be diagnosed at a younger age and have more aggressive forms of prostate cancer than European-American men [39]. High incidence rates have also been reported among men in the French Caribbean archipelago of Guadeloupe, where 90% of the residents are of African descent [40] This contrasts with the lower rates of prostate cancer diagnosed among Asian men [25, 41]. While the exact reasons for these racial differences are unclear [39], they could include genetic susceptibility to prostate cancer, different levels of androgenic activity within the prostate gland [25, 39, 41 – 43], in addition to differences in diet, socioeconomic status, environmental and lifestyle factors [39].

The effect of race on prostate cancer risk also appears to be influenced by country of residence. In 1980, prior to the introduction of PSA testing, prostate cancer incidence rates among men of either Chinese or Japanese origin living in the USA were much higher compared to men living in China or Japan, respectively [35].

4.3 Trends

Incidence trends in countries with a higher uptake of PSA testing, such as the United States, Canada and Australia, followed a generally consistent pattern (Fig. 2), highlighted by the rapid rise in incidence soon after the introduction of PSA testing, followed by a sharp reduction in rates. Steady increases were then observed. More recently, significant decreases in incidence rates have been observed since 2001 in United States and Canada (Fig. 2). The pattern and timing of the trends is consistent with the diagnosis of asymptomatic men following the initial introduction and increasing use of PSA testing in these countries [5].

While the incidence of prostate cancer in the UK (England and Wales) was reported to be steadily increasing during the early-mid 1990s [24, 44], more recent data (Fig. 2) suggests the rate of change became more pronounced during the late 1990s [45 – 47]. At least some of this increase would be consistent with the reported increase in PSA testing in the UK [21, 23], however a peak in rates for the UK has not yet been observed. This difference in the incidence trends between the UK and other countries such as the United States and Canada probably relate to the substantially lower prevalence of PSA screening in the UK (described earlier).

An argument against PSA testing explaining all of the increases in prostate cancer incidence is that the rates were already increasing in countries such as the USA and Aus-

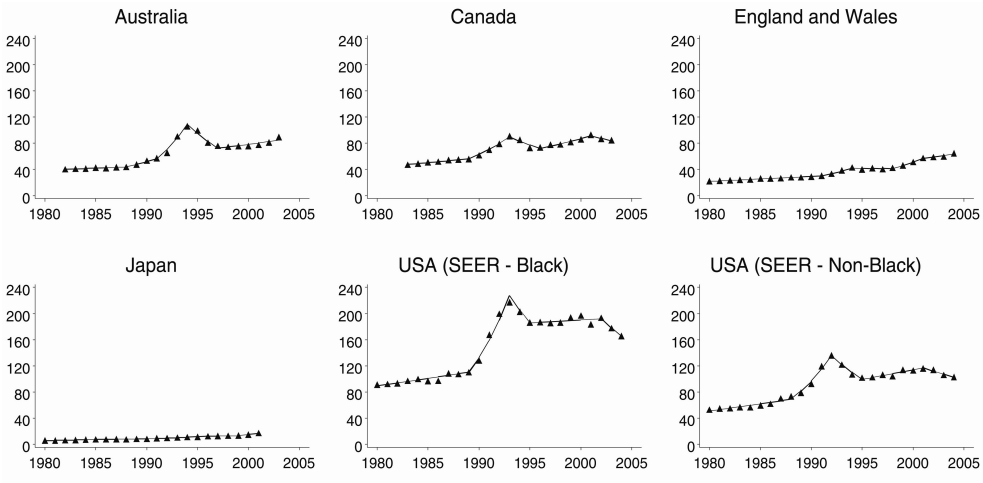

Figure 2. Recent trends in prostate cancer incidence rates among males (all ages) for selected more developed countries, 1980 to 2005 [a,b,c]. (Data sources: Australian Institute of Health and Welfare (Australia); Public Health Agency of Canada and International Agency for Research on Cancer (Canada); Welsh Cancer Intelligence and Surveillance Unit and Office for National Statistics (England and Wales); National Cancer Centre (Japan); National Cancer Institute (USA)). a) Y-axis represents ‚incidence rate *per* 100 000 population *per* year;'; b) X-axis represents ‚year;'; c) Incidence rates have been age-standardised to the 1960 World Standard Population.

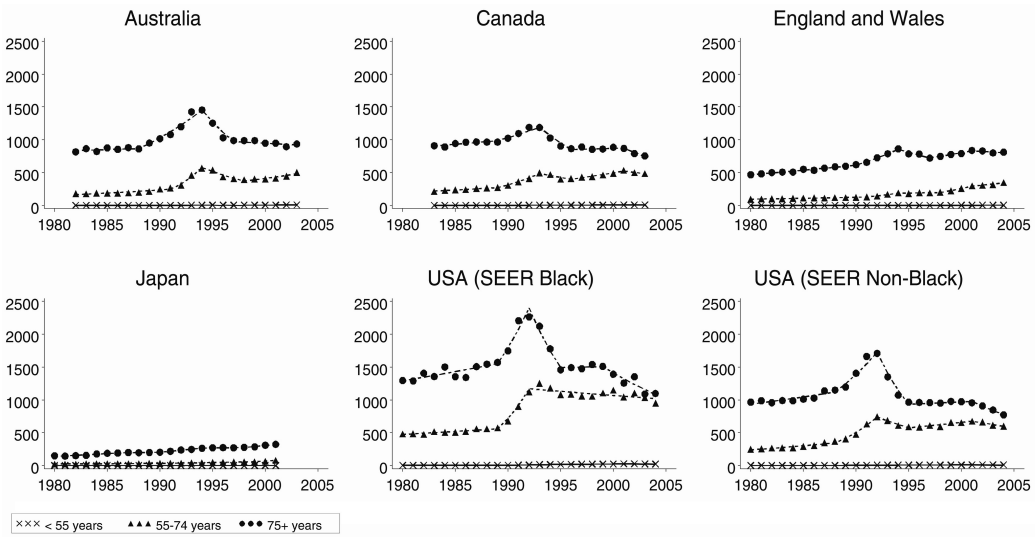

Figure 3. Recent age-specific trends in prostate cancer incidence rates among males for selected more developed countries, 1980 to 2005 [a,b,c]. (Data sources: Australian Institute of Health and Welfare (Australia); Public Health Agency of Canada and International Agency for Research on Cancer (Canada); Welsh Cancer Intelligence and Surveillance Unit and Office for National Statistics (England and Wales); National Cancer Centre (Japan); National Cancer Institute (USA)). a) Y-axis represents ‚Incidence rate *per* 100 000 population *per* year'. b) X-axis represents ‚year'. c) Incidence rates have been age-standardised to the 1960 World Standard Population.

tralia prior to the introduction of PSA testing [48]. Moreover, increases have been observed in countries with a lower prevalence of PSA testing, such as Japan (Fig. 2) and other Asian countries [25, 41, 49, 50]. Asian populations have also experienced increases in the incidence of diabetes and colorectal cancer, prompting suggestions that the escalation of prostate cancer in these countries is consistent with the increasing influences of Western culture, such as rises in the intake of animal fat and protein, and reductions in physical activity [25, 41, 43, 49].

Trends in incidence are not consistent across age groups, nor between countries (Fig. 3). In Australia, Canada and the United States, the peak in incidence soon after the introduction of PSA testing was evidence for men aged 55 – 74 years, and those aged 75 years and over, with the latter group having clearly the higher rates. Since then, the inci-

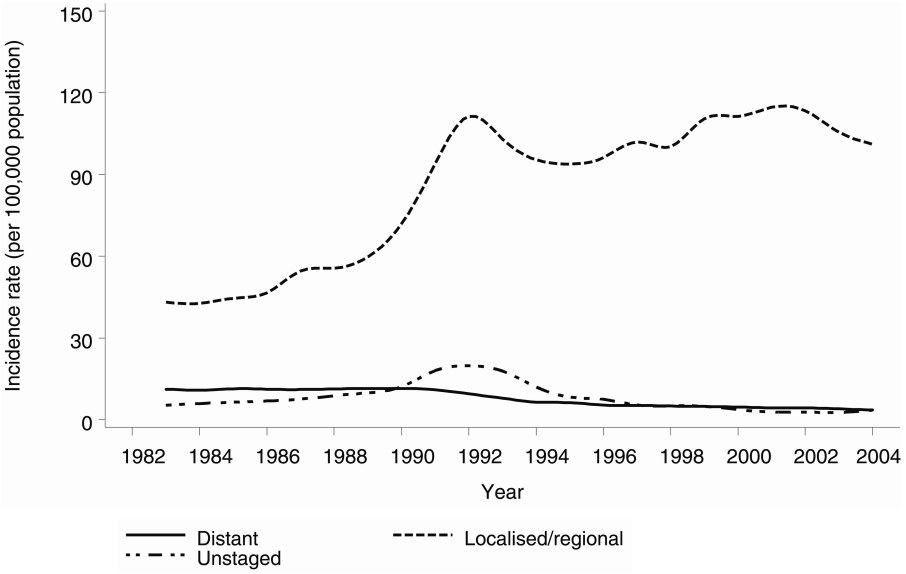

Figure 4. Prostate Cancer Incidence Rates by Stage, 1983 – 2004 (USA, SEER-9 registries) [a,b]. a) Data Source: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) Limited-Use Data (1973 – 2004); b) Incidence rates have been age-standardised to the 1960 World Standard Population.

dence rates among the older group have tended to consistently decrease, while, after an initial decrease, rates among men aged 55 – 74 years have increased, resulting in a converging incidence rates over time. The trend for older men in England and Wales was similar, although less pronounced, to those reported for Australia, Canada and the United States, while no corresponding peak in incidence rate was evident among men aged 55 – 74 in England and Wales. Age-specific trends in Japan have shown consistent increases among older men (75 years and over), without the peak that has been observed in other countries. Published data from Sweden suggest that up to 1995 the increases in incidence were predominately among men over 70 years of age, whereas since the introduction of PSA testing the increase has been predominately among younger men aged 50 – 69 years [27, 51].

4.4 Trends by stage

Although stage-specific data is not available for most countries, data from the SEER registries in the USA (Fig. 4) clearly shows that incidence patterns are dominated by the trends in localised/regional prostate cancer, while the rate of distant cancers has steadily decreased. In particular, the peak in incidence rates in 1992 was almost entirely due to localised cancers. A similar, although less pronounced, trend differential by stage has also been reported for the UK [24]. Much of this stage migration has been attributed to PSA testing [52].

In contrast, the stage distribution of prostate cancer in Asian countries is less favourable than in more developed countries, with a higher proportion of distant stage cancers in Asia. However, this stage distribution appears to be improving [28, 49] with reports that the proportion of locally advanced and metastatic prostate cancers in South Korea decreased gradually, being 82, 77 and 72% in 1990, 1995 and 2000, respectively [49].

5 Prostate cancer survival

Interpretation of prostate cancer survival information is complicated by a number of issues, particularly in areas where PSA testing is common. In Fig. 5, case A gives an example of the detection process for a typical patient. First the cancer initiates, then at some point in its progression it is diagnosed. The survival time is then calculated as the time between diagnosis and death. This survival time can be increased in several ways. First, the cancer can be detected earlier (case B), without actually prolonging the overall survival [53]. This is known as lead time bias, and for prostate cancer has been estimated to be between 5 and 13 years, depending on a man's age [54]. This effect can also be observed because of overdiagnosis, in that screening may detect a prostate cancer that would not otherwise have been detected before a man's death. Second the patient's life can be extended by using effective treatment that prolongs the patient's life (as in case C). Finally, survival can be increased through a combination of earlier diagnosis and effective treatment (case D), particularly if treatments are shown to be more effective on cancers that are diagnosed earlier.

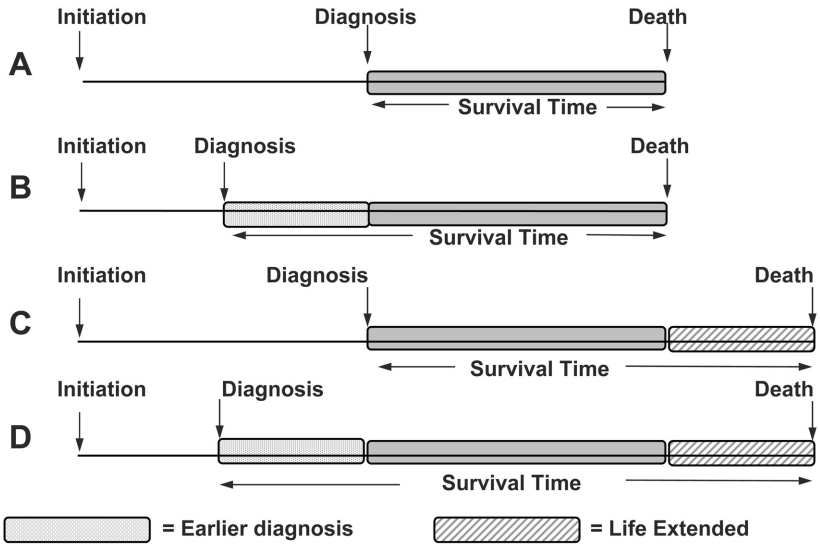

Figure 5. Causes of change in survival estimates.

Global estimates of cancer survival are derived by comparing the age-adjusted mortality and incidence of prostate cancer cases [55]. Globally the 5 year survival for prostate cancer in 2002 (all ages combined) was estimated to be 60% (World Cancer Research Fund, American Institute for Cancer Research, AICR, Washington DC 2007). Survival was higher among men living in more developed nations (76%) compared to less developed nations (45%) [55].

Survival estimates for specific countries are typically reported in terms of relative survival, which compares the proportion of men surviving a given length of time after a diagnosis of prostate cancer to the expected survival of the general (male) population. In Europe the average 5 year relative survival for prostate cancer between 2000 and 2002 has been estimated at 78% (lowest of 58% in the Czech Republic, highest of 89% in Austria) [56]. In one area of Australia between 1996 and 2000 5 year relative survival was 81% [57]. These estimates were substantially lower than the 99% 5 year survival reported in the USA for 2000 – 2002 [56].

Based on analysis of SEER data [38], the 5 year relative survival from all prostate cancers in the USA had increased from 78% for men diagnosed between 1983 – 1988 to 99% for men diagnosed between 1998 – 2004. Although this improvement in survival in part reflects the increasing proportion of prostate cancers diagnosed when localised/regional (Fig. 4), there have also been stage-specific increases in survival. Five-year relative survival in the USA was 103% for localised/regional cancers diagnosed between 1998 and 2004, 31% for distant cancers and 77% for unknown stage. These were all higher than the corresponding relative survival estimates by stage for prostate cancers diagnosed between 1983 and 1988 (90, 29 and 77%, respectively) [38].

For relative survival estimate of 103% for men in the USA diagnosed with localised or regional prostate cancers reflects that the observed survival was actually higher than the general male population [38, 58]. There are at least two possible explanations for this phenomenon. The first is that the relative survival of over 100% reflects a selection bias, in that a higher proportion of men being screened are in socially advantaged population groups, who typically have a lower mortality risk to begin with [59]. Another potential explanation is that men generally have low utilisation of health care services; however a diagnosis of prostate cancer increases the chance they will have increased medical interventions, with a positive impact on their general health and overall survival [60].

5.1 Age differences

Men diagnosed with prostate cancer at a younger age have typically had more aggressive disease and poorer prognosis in the past [61 – 64]. More recently, the widespread use of PSA testing in countries such as the USA has led to a migration towards younger age and less advanced stage of disease at diagnosis [52], to the point where some contemporary studies have found no statistically significant survival differences by age among men with localised prostate cancer receiving similar medical treatment [64].

5.2 Racial differences

For localised/regional disease, survival rates were similar for African-American men compared to Caucasian-American men in the USA [39]. However survival rates have consistently been lower among African-Americans for distant prostate cancers [39].

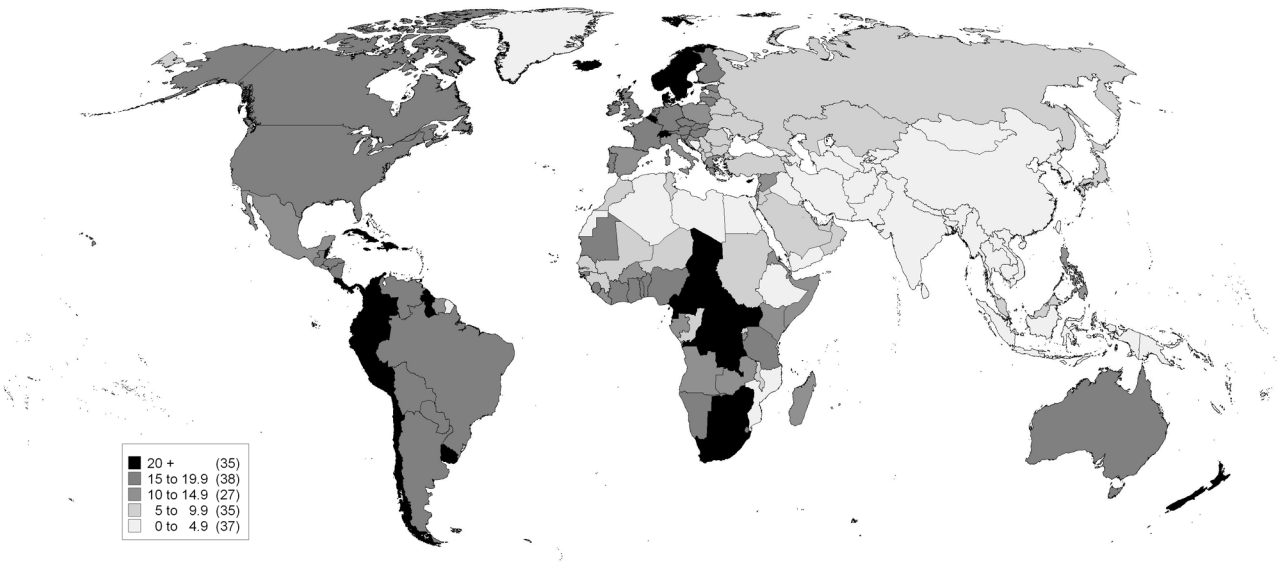

Figure 6. International variations in estimated mortality rates (*per* 100 000 population) due to prostate cancer in 2002. (Data source: GLOBOCAN 2002. International Agency for Research on Cancer (IARC)).

6 Prostate cancer mortality

An estimated 221 000 men died from prostate cancer throughout the world in 2002, an age-standardised rate (World population) of 8.2 deaths/100 000 population [29]. Almost 60% of these men lived in more developed countries (Fig. 6, Table 1). After allowing for age differences, the prostate cancer mortality rate was around two and a half times higher in more developed countries (13.5 deaths/100 000 population) compared to less developed countries (5.2 deaths/100 000 population) [29]. During 2002, mortality rates due to prostate cancer ranged from 0.2 deaths/100 000 population in Bangladesh to 55.3 deaths/100 000 population in Barbados [29]. The estimated ratio of mortality rates to incidence rates (MR/IR) for prostate cancer between 1993 and 2001 ranged from 0.13 in North America to 0.80 in Africa [30]. The ratio in Africa is similar to the MR/IR ratio for lung cancer in North America [29], suggesting that the survival prospects of men in Africa diagnosed with prostate cancer are similar to those of men in North America diagnosed with lung cancer.

Prostate cancer caused just under 1% of all male deaths and about 7% of all cancer-related deaths among males worldwide during 2002 [65]. In high income countries (*i. e.* net income *per* capita in 2001 of US$9206 or more) prostate cancer was estimated to be the seventh most common cause of death in 2005 (4% of all male deaths), but it did not rank in the top 20 causes of death among males in middle or lower income countries (less than 1% of all deaths) [66]. The proportion of cancer-related male deaths due to prostate cancer ranged from 9% in more developed countries to 4% in less developed countries [29]. It is not clear how the reduced accuracy of cause of death coding in less developed countries [29, 67] impacts on these comparisons.

6.1 Age-specific variation

Mortality rates increased with age. Worldwide the estimated age-specific mortality rates (*per* 100 000 population) in 2002 were 0.1 (15 – 44 years), 1.9 (45 – 54 years), 11.8 (55 – 64 years) and 100.4 (men aged 65 years and over) [29]. The age-specific mortality rates (*per* 100 000 population) of prostate cancer in more developed countries were similar to less developed countries for men aged 45 – 54 years (2.0 *vs.* 1.9), nearly twice as high among men aged 55 – 64 (16.9 *vs.* 9.6) and nearly three times as high among men aged 65 years and older (169.9 *vs.* 59.5). [29]. As a result, the proportion of all prostate cancer deaths among men aged 65 years and over was greater in more developed countries (91%) compared to less developed countries (79%) [29].

There was very little variation in this proportion over the period 1999 – 2003 between Australia (93%), Canada (93%), the USA (92%), Japan (93%) or England and Wales (93%) [68]. These percentages represent only a slight increase since 1982 – 1986, when the proportion of prostate cancer mortality among men aged 65 and over ranged from 89 to 91% in each of these countries [68]. Combined with the age-variation in incidence (see earlier), these data are consistent with the idea that PSA screening brings forward the age at diagnosis, while having little impact on the age at death (see Section 3).

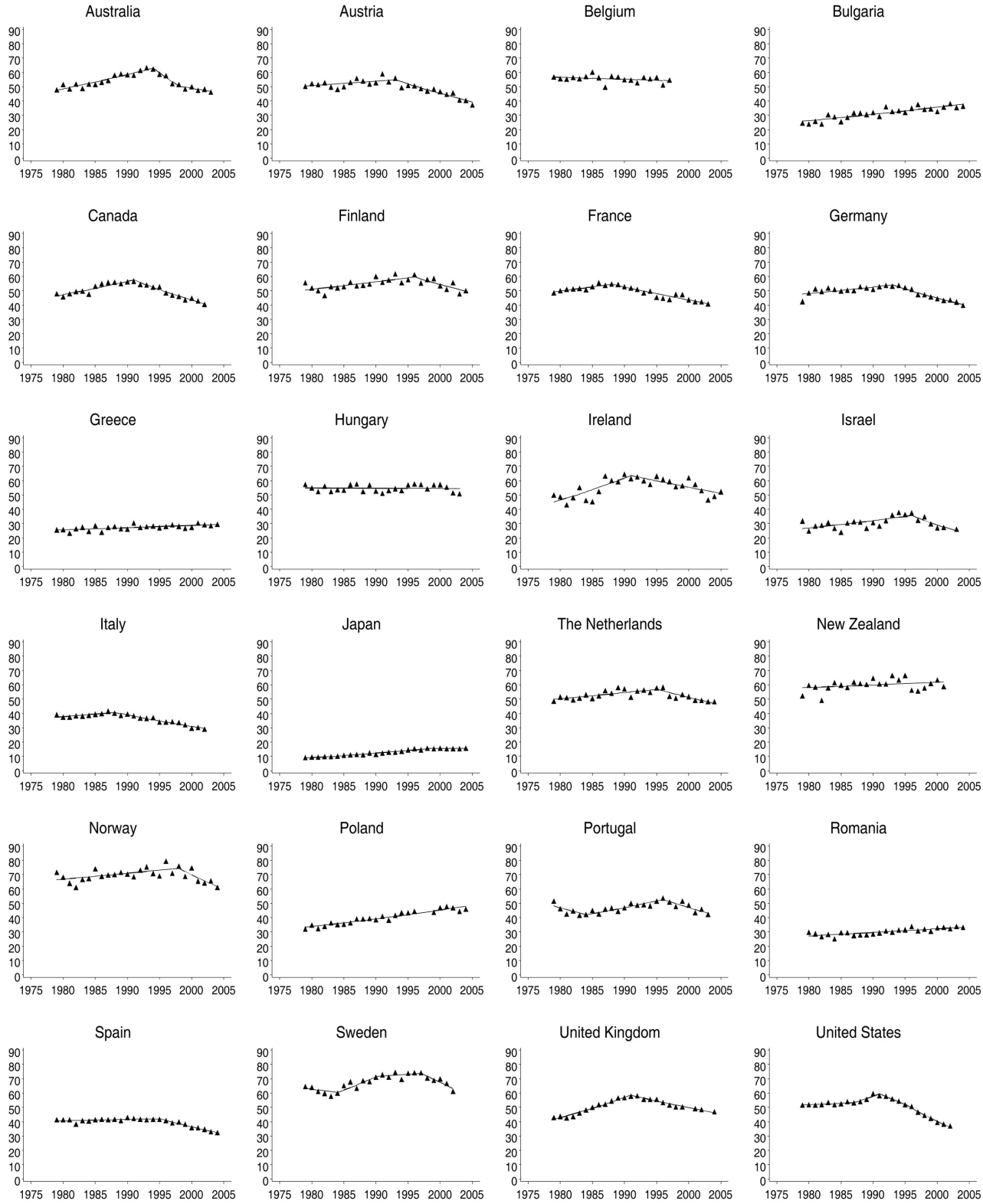

Figure 7. Recent trends in prostate cancer mortality among males aged 50 – 79 years for selected more developed countries, 1979 to 2005 [a,b,c,d]. (Data source: World Health Organisation Mortality Database). a) Y-axis represents 'Mortality rate *per* 100 000 population *per* year'; b) X-axis represents 'year of death'. c) Not all countries had data available for all years; d) Mortality rates have been age-standardised to the 1960 Word Standard Population.

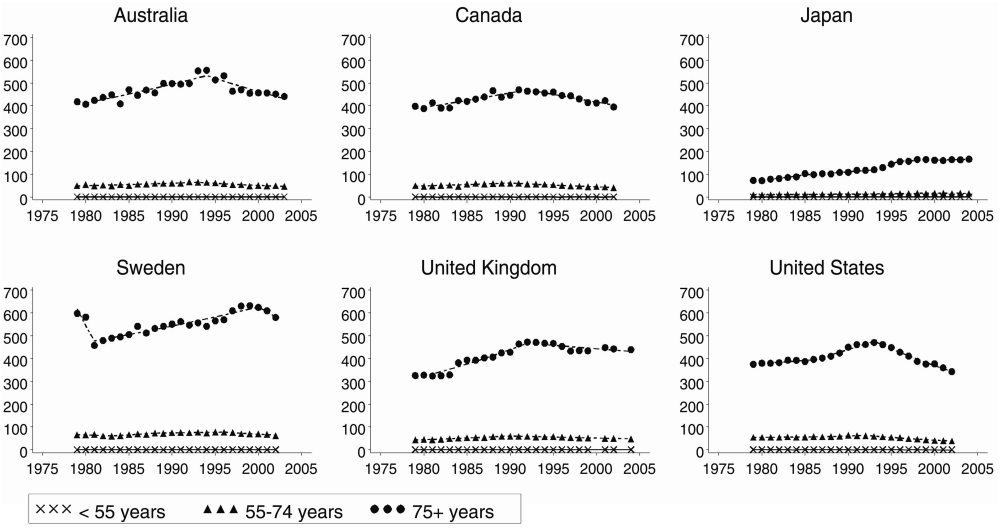

Figure 8. Recent age-specific trends in prostate cancer mortality rates among males for selected more developed countries, 1980 to 2005 [a,b,c]. (Data source: World Health Organisation Mortality Database). a) Y-axis represents 'Mortality rate *per* 100 000 population *per* year'; b) X-axis represents 'year of death'; c) Not all countries had data available for all years; d) Mortality rates have been age-standardised to the 1960 Word Standard Population.

6.2 Racial differences

In the United States, death rates from prostate cancer were more than twice as high in African-American males than for European-American males. Age-standardised (World) mortality rates from 2000 to 2004 were 33.0/100 000 in African-American men and 12.6/100 000 in European-American men [69]. High mortality rates have also been noted in men of Sub-Saharan African descent in Jamaica and Brazil, and among Scandinavian men in Europe [70].

6.3 Trends

The latest trends in prostate cancer mortality among men aged 50 – 79 years in 24 more developed countries from 1979 to 2005 are shown in Fig. 7. This age group and starting year was chosen to facilitate comparisons with two previous reports of international mortality trends [71, 72]. Using this most recent mortality data, statistically significant reductions in mortality were observed in 15 out of the 24 countries. Two previous studies reported statistically significant reductions among men of this same age group in 7 and 9 of these 24 countries up to 1997 [72] and 2001 [32], respectively, suggesting that decreases in prostate cancer mortality rates are continuing to become more widespread among more developed nations. Since the latest report [32], the additional countries with significant reductions in prostate cancer mortality include Israel, Portugal, Ireland, The Netherlands and the Scandinavian countries of Norway, Sweden and Finland. Rates were also continuing to decrease in Australia, although the most recent trend (since 1998) was not statistically significant.

As was the case for incidence trends, trends in mortality were not consistent across age groups nor by country (Fig. 8). In Australia, Canada, the United Kingdom and the United States, mortality rates among men aged 55 – 74 and 75 years and over have been decreasing since the early 1990s. In Japan the mortality rates among men aged 75 years and over continue to increase significantly (although the rate of increase is reducing) while among men aged 55 – 74 the previously significant increasing trend is now a nonsignificant decrease since 2000. In Sweden there is also evidence that the previously increase in mortality rate among men aged 75 years and over started to decrease (nonsignificantly) in 2000, and mortality among men aged 55 – 74 has been decreasing since 1996.

Definitive reasons for these reductions in prostate cancer mortality rates cannot be determined using ecological data such as these. Two randomised controlled trials currently underway [73, 74] may provide definitive conclusions about the effectiveness of screening and subsequent treatment in the near future. However, the consistency of the decreases across an increasing number of more developed countries suggest that they are due to one or more factors (possibly working together), rather than simply random variation. Intuitively these factors could include decreases in the prevalence of some risk factors, changes in how prostate cancer deaths are recorded, better treatment or improved detection [32, 72].

For a change in risk factors to be driving a reduction in mortality, the mortality reduction would need to be preceded by a reduction in incidence. That there is no evidence this has occurred [75], combined with the absence of any

cohort effects [76], suggests against this being an explanation for the reduction in prostate cancer mortality [77].

A change in cause of death coding is also an unlikely explanation due to lack of recent changes in international coding recommendations for prostate cancer mortality [78, 79], and the confidence placed in the accuracy of prostate cancer mortality data based on death certificates [78, 80]. Although one American study suggested that elderly prostate cancer patients treated aggressively were less likely to have prostate cancer listed as an underlying cause of death compared to those receiving conservative treatment [81], this would need to be a consistent pattern across many countries to explain the widespread reduction in mortality rates.

The timing of the reduction in mortality rates in countries such as the USA, Canada and Australia, closely following the introduction of PSA testing, raises the pivotal question of whether prostate cancer screening using PSA has had a positive effect on mortality [82, 83]. There are several arguments suggesting against this possibility. One point of contention is the generally slow growth of prostate cancer [82]. A recent study demonstrated that men can die from prostate cancer more than 20 years after being initially diagnosed with localised prostate cancer [84]. Combined with the very high 5 year relative survival for men diagnosed with early stage prostate cancer [38, 58, 85], the five to six year period between the widespread introduction of PSA testing and the observed reduction in mortality may be insufficient time to make any definitive links [82]. However, some prostate cancers can grow quickly [86], and it may be that a combination of PSA testing and appropriate, timely treatment prevents or at least postpones mortality from these fast-growing cancers [53, 87, 88]. A second argument against a role of PSA testing on the observed reduction in prostate cancer mortality is that the decline has not always been largest in areas with more screening [75, 89 – 91].

Changes in treatment patterns are more likely to have played a role. There were refinements during the 1990s in radical prostatectomy techniques [92, 93] and radiation therapy [92, 94, 95] for early stage localised prostate cancer. The more widespread use of these treatments internationally [96 – 98] could be a result of increased numbers of men presenting with early stage disease [99, 100], and this could be a possible impact of PSA testing [96, 100]. One randomised trial recently demonstrated significantly reduced disease-specific mortality for patients with localised prostate cancer following radical prostatectomy, compared to conservative treatment [101]. This long-term study started before the widespread introduction of PSA screening; therefore it is not clear how broadly these results can be generalised [102]. However there has been a notable increase in the proportion of men in the USA with localised prostate cancer who received radical treatment [103].

Although not curative, developments in hormonal treatments for advanced disease [86] could also be contributing to reduced disease-specific mortality [77, 104]. The availability of LHRH agonists and nonsteriodal antiandrogens increased the acceptability of hormonal therapy compared to bilateral orchidectomy, and there is evidence that earlier application of hormonal therapy can improve survival [77]. This could influence trends in disease-specific mortality, even if only by deferring mortality from prostate cancer long enough for the patient to die from another unrelated condition [77, 104].

7 Conclusions

Prostate cancer is a major health concern among men, particularly within more developed countries. Although the incidence of diagnosed prostate cancer is increasing worldwide, a diagnosis of prostate cancer has unclear implications, particularly for PSA-detected localised cancers which could be indolent tumours with limited potential to cause mortality. The rise in prostate cancer incidence among Asian countries suggests an effect of risk factors stemming from an increasingly westernised lifestyle.

Mostly driven by the impact of PSA testing, larger proportions of younger men are now being diagnosed with prostate cancer, and these men are living for longer following their diagnosis. They are, however, more likely to die from, rather than with, their cancer compared to men diagnosed when older [6]. Apart from the increased demand on cancer treatment services, this has additional implications for health systems including the need to address the psychological effects of younger men living with a cancer diagnosis and reducing the uncertainties about appropriate treatment decisions and associated side effects [3, 105].

While the causes of the widespread reduction in prostate cancer mortality rates within more developed countries are unknown, progressively more effective treatment practices rather than a direct relationship with the introduction of PSA testing appears to be a more defensible explanation.

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