INTERNATIONAL TRENDS AND PATTERNS OF PROSTATE CANCER INCIDENCE AND MORTALITY

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Prostate cancer is the most commonly diagnosed cancer in western men, and incidence is rising rapidly in most countries, including low-risk populations. Age-adjusted incidence and mortality rates from 15 and 13 countries between 1973–77 and 1988–92, respectively, were compared to provide leads for future analytic studies. Large increases in both incidence and mortality rates of prostate cancer were seen for all countries. For incidence, increases were more pronounced in the United States, Canada, Australia, France and the Asian countries, while the increases in medium-risk countries were moderate. Increases in incidence ranged from 25%–114%, 24%–55% and 15%–104% in high-, medium- and low-risk countries, respectively. Mortality rates rose more rapidly in Asian countries than in high-risk countries. Substantial differences in incidence and mortality across countries were evident, with U.S. blacks having rates that were 50–60 times higher than the rates in Shanghai, China. Increasing incidence rates in the United States and Canada are likely to be due in part to the widespread use of transurethral resection of the prostate and prostate-specific antigen testing, while increases in the Asian countries are probably related to westernization in these low-risk populations. The large disparities in incidence between high- and low-risk countries may be due to a combination of genetic and environmental factors. Future studies are needed to examine gene-gene and gene-environment interactions in various countries concurrently to shed light on the etiology of prostate cancer and to help elucidate reasons for the large differences in risk between populations. *Int. J. Cancer 85:60–67, 2000.*
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Prostate cancer is the most commonly diagnosed cancer among men in most western countries (Parkin *et al.,* 1997). With the aging of the population and increased prostate cancer screening, especially the use of prostate-specific antigen (PSA), the incidence of prostate cancer in the United States and certain western countries has risen sharply during the last decade (Potosky *et al.,* 1995; Mercer *et al.,* 1997; Majeed and Burgess, 1994; Weller *et al.,* 1998). In the United States, the rapid increase in incidence since the introduction of PSA in 1986 has resulted in a lower median age at diagnosis (decreased by 1 year in both blacks and whites) and an earlier stage of cancer at diagnosis, although the benefit of screening on prostate cancer mortality rates remains undetermined (Prorok *et al.,* 1996). Prostate cancer rates in Asian countries, such as China and Japan, are much lower than those reported in western populations (U.S. rates are 50–60 times higher), but they appear to be increasing rapidly as well (Nakata *et al.,* 1995; Hsing *et al.,* 1998). In this report, we examine trends and patterns of incidence and mortality during a 20-year period (from 1973–77 to 1988–92) in more than a dozen countries to provide clues for future studies.

MATERIAL AND METHODS

Incidence data

We retrieved age-specific and standardized incidence rates per 100,000 man-years, age-adjusted to the world standard, for prostate cancer during the 20-year period (1973–77 to 1988–92) in 15 countries from 4 volumes (IV–VII) of publications from the International Agency for Research on Cancer (IARC), Cancer Incidence in 5 Continents, covering the time periods 1973–77, 1978–82, 1983–87 and 1988–92 (Waterhouse *et al.,* 1982; Muir *et al.,* 1987; Parkin *et al.,* 1992, 1997). Data from these 4 volumes were used because the starting year in volume IV coincides with the inception of the Surveillance, Epidemiology and End Results (SEER) program, a population-based cancer registry system now covering 14% of the U.S. population. Long-term data were available from 9 U.S. registries that include about 10% of the U.S. population.

The criteria used to select countries for analysis were the availability of population-based data from all 4 volumes of IARC publications and the quality of the reported data, as reflected by the percent of cases with histologic verification and the number of years of data reported in each volume. Most countries included in this analysis have 5 years of reported data in each time period, a high percentage of histologic verification and an upward trend of histologic verification over time. Using these criteria, we selected 15 from more than 50 countries reporting incidence data to IARC. The number of reported prostate cancer cases in these countries ranged from 219–24,192 during 1973–77 and from 415–66,227 in 1988–92. The percent of cases with histologic verification for the 15 countries ranged from 47%–99%, with high-risk countries having a much higher percent of confirmation (usually >90%). China had the lowest percent confirmed, but other low-risk countries had confirmation rates well over 70%. When data for more than 1 region from a specific country were available, we used the same criteria to select the region that had the highest-quality data and the largest number of cases for analysis.

Because rates for all SEER areas combined were not included before volume VI, we used SEER*Stat, a statistical package issued in April 1998 by the SEER program of the National Cancer Institute, to calculate the rates for U.S. blacks and whites, age-adjusted to the world standard population.

Mortality data

Mortality rates for prostate cancer during the same 20-year period for 13 of the 15 selected countries were retrieved from the World Health Organization (WHO) mortality data bank, available at their website. Mortality rates for prostate cancer in China and India were not available. Standardized mortality rates were also age-adjusted to the world standard population and presented as per 100,000 person-years. Unlike the incidence rates, which were

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mostly region-specific within a particular country, mortality rates were based on data from the entire country.

Data analysis

Based on reported incidence rates during 1988–92, we categorized these 15 countries into high (>40 per 100,000 person-years), medium (between 15 and 40) and low risk (<15). Incidence and mortality ratios, using the country with the lowest rates as the baseline category, were calculated separately to compare the relative difference in rates between high- and low-risk countries. Percentage changes in incidence and mortality rates between 1973–77 and 1988–92 were calculated to show the relative difference in these 2 time periods in each country. These 2 time periods were presented to show the rates and patterns before and after PSA screening. In addition, age-specific incidence ratios were computed by dividing the age-specific rates in 1988–92 by those in 1972–77 in each country to assess the increase in rates in various age groups across countries. Mortality-incidence ratios were calculated for each country to assess the degree of prostate cancer case-fatality in these countries. Figures were prepared using a semi-log scale to facilitate the comparison of temporal trends as well as magnitude; the scale used was such that a slope of 10° indicates a change of 1% per year (Devesa *et al.,* 1995).

RESULTS

Table I shows the age-adjusted incidence rates in 2 time periods (1973–77 and 1988–92) for 15 countries, listed in order of descending rates during 1988–92. Ranks were assigned separately for each of the 2 periods based on the rates. Compared with rankings in 1973–77, 10 countries changed their rankings (usually by 1 or 2 levels) in 1988–92, and with the exception of Denmark and France, all remained in the same risk category (high-, medium- or low-risk countries). Substantial differences in rates across countries are evident, with the United States, Canada, Sweden, Australia and France having relatively high rates (ranging from 48.1–137.0), most other European countries having medium rates (ranging from 23.9–31.0) and Asian countries having very low rates (ranging from 2.3–9.8). In both time periods, U.S. blacks had the highest rates of all, which were 50–60 times higher than the

rates in Shanghai, China, where rates were the lowest in both time periods.

During this 20-year period, there were marked increases in the prostate cancer incidence in all 15 countries, with rates doubling in the U.S. whites, Canada, France and Singapore. With the exception of India, relatively large increases were also seen for Asian countries. Increases in rates ranged from 25%–113%, 24%–55% and 16%–104% in high-, medium- and low-risk countries, respectively. The gaps between high-risk countries and China remained substantially large and were further widened, while the gaps between China and medium- and other low-risk countries remained relatively constant.

Figure 1 shows the age-adjusted incidence trends during the 20-year period in 15 countries. During all 4 time periods, U.S. blacks and whites had the highest rates, while China had the lowest. Rates increased fairly consistently over time in all 15 countries, although there was a slight dip during 1983–87 in 3 countries (Israel, India and China). After 1987, there was a more rapid rise in rates in U.S., Canada, Australia, France, Israel and China. During all 4 time periods, there was substantial geographic (or ethnic) variation, and these differences have become more pronounced with time.

Age-specific incidence curves during 1988–92 in 8 selected countries are shown in Figure 2. In all countries, incidence of prostate cancer was extremely low for men younger than the age of 50, rose exponentially with advancing age and reached a maximum after age 80. In most countries, incidence in men over the age of 75 was 20–83 times higher than that for men ages 50–54. The shapes of age-specific curves were similar across populations, except that the rate of increase started to plateau around ages 65–69 for U.S. men but continued to rise for another 10 years for other countries. For every age-group, U.S. blacks had the highest rates, while Chinese men had the lowest rates.

Table II shows the age-specific incidence ratios of rates in 1988–92 compared with those in 1973–77, representing the relative increases between these 2 time periods within each country; the data are listed in the same order as in Table I. The temporal changes were not uniform across age groups in these populations. For most countries, ratios were generally higher for those younger than age 75, indicating more rapid increases in younger men. In high-risk

TABLE I – AGE-ADJUSTED[1] INCIDENCE RATES OF PROSTATE CANCER IN 15 COUNTRIES, 1973–77 AND 1988–92

Countries	1973–77				1988–92				% change[4]
	Number[2]	Incidence[1]	Rank	Incidence ratio[3]	Number[2]	Incidence[1]	Rank	Incidence ratio[3]	
High risk									
U.S. blacks, SEER[5]	2,664	79.9	1	49.9	7,129	137.0	1	59.6	71.5
U.S. whites, SEER	24,192	47.9	2	29.9	66,227	100.8	2	43.8	110.4
Canada, BC[6]	3,126	39.8	4	24.9	10,473	84.9	3	36.9	113.3
Sweden	16,556	44.4	3	27.8	25,253	55.3	4	24.0	24.5
Australia, NSW[7]	3,661	28.4	5	17.8	10,870	53.5	5	23.3	88.4
France, Bas-Rhin	430	23.0	7	14.4	1,502	48.1	6	20.9	109.1
Medium risk									
Denmark	3,932	23.6	6	14.8	7,392	31.0	7	13.5	31.4
England, S. Thames[8]	5,461	20.1	9	12.6	9,529	29.3	8	12.7	45.8
Italy, Varese	219	22.8	8	14.3	884	28.2	9	12.3	23.7
Spain, Navarra	291	17.6	10	11.0	641	27.2	10	10.4	54.5
Israel, all Jews	1,238	15.5	11	9.7	3,147	23.9	11	11.8	54.2
Low risk									
Singapore, Chinese	100	4.8	15	3.0	415	9.8	12	4.3	104.2
Japan, Miyagi	222	4.9	14	3.1	737	9.0	13	3.9	83.7
Hong Kong	268	5.1	13	3.2	1,185	7.9	14	3.4	54.9
India, Bombay	193	6.8	12	4.3	764	7.9	15	3.4	16.2
China, Shanghai	219	1.6	16	1.0[9]	539	2.3	16	1.0[9]	43.8

[1]Per 100,000 person-years, age-adjusted using the world standard.–[2]Number of cases.–[3]Relative to the incidence in Shanghai, China.–[4]Percent change from 1973–77 to 1988–92.–[5]Surveillanace, Epidemiology and End Results program.–[6]Canada, British Columbia.–[7]Australia, New South Wales.–[8]United Kingdom, England, South Thames.–[9]Reference group.
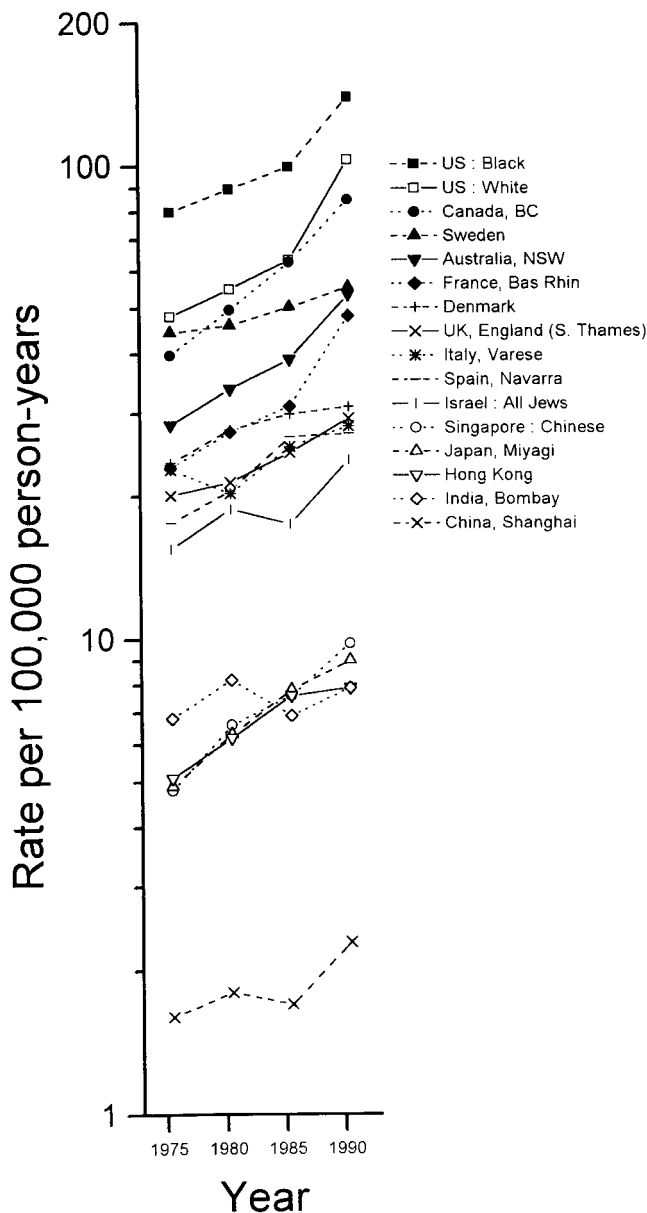
FIGURE 1 – Age-adjusted incidence trends of prostate cancer in 15 countries, 1973–77 to 1988–92.

FIGURE 2 – Age-specific incidence curves of prostate cancer in 8 countries, 1988–92.

countries, especially North America, Australia and France, increases were much higher for those younger than age 70 and declined thereafter. For medium- and low-risk countries, larger increases generally were found for younger men, although the patterns were less consistent.

Age-adjusted mortality rates in these countries (except China and India) in 1973–77 and 1988–92 are shown in Table III, also listed in the same order as in Table 1. In all countries, mortality was much lower than incidence. Most countries were classified in the same risk category as with the incidence data, except for U.S. whites, and the ranking of mortality rates changed only slightly between these 2 time periods. U.S. blacks had the highest mortality rates, which were 12 times higher than the lowest rates reported for Chinese men living in Hong Kong (mortality rates for Shanghai, China were not available). Although incidence in U.S. white men
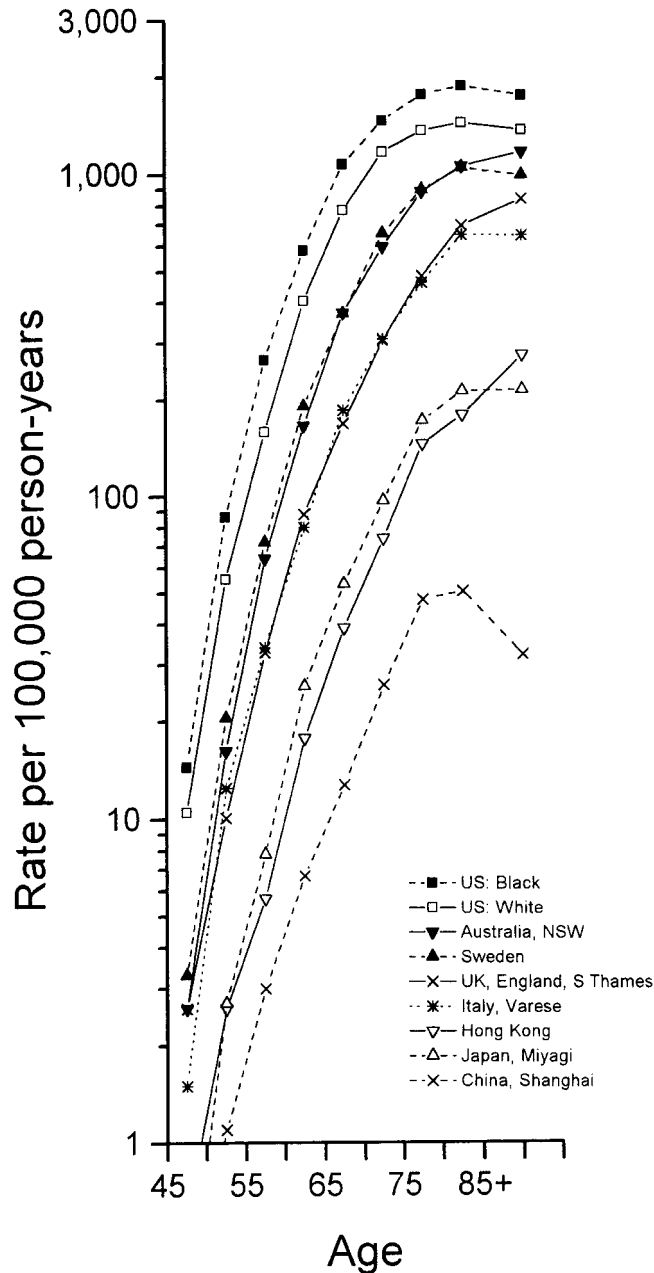
was the second highest in the world, mortality rates ranked only 8th and were much lower than those for other high-risk and even 2 medium-risk countries. Denmark ranked 3rd in mortality rates during 1988–92, while its incidence ranked 7th. With the exception of Sweden, mortality rates increased in all countries during the 20-year period, although the rises were less rapid for mortality than for incidence. The mortality increases ranged from 5.6%–94.7%, with much larger relative increases in Denmark (38%), England (39%) and all Asian countries (33%–95%)

Figure 3 shows the mortality trends in these 13 countries during the 20-year period. With the exception of Sweden, rates generally increased over time across populations, with rates rising faster in

TABLE II – RATIOS[1] OF AGE-SPECIFIC INCIDENCE RATES OF PROSTATE CANCER IN 15 COUNTRIES, 1988–92 RELATIVE TO 1973–77

Countries	Age (years)								
	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
High risk									
U.S. blacks, SEER[2]	0.9	1.7	1.8	1.8	1.9	1.7	1.7	1.5	1.4
U.S. whites, SEER	2.3	2.6	2.4	2.5	2.5	2.3	1.9	1.5	1.3
Canada, BC[3]	1.8	2.5	2.4	2.6	2.7	2.1	1.9	1.7	1.3
Sweden	0.8	1.4	1.3	1.5	1.4	1.3	1.2	1.1	0.9
Australia, NSW[4]	1.3	1.9	2.3	2.0	2.3	1.9	1.8	1.6	1.5
France, Bas-Rhin		5.4	2.7	2.4	1.7	2.0	1.9	2.7	1.8
Medium risk									
Denmark	0.7	1.5	1.3	1.6	1.4	1.3	1.3	1.2	1.3
England, S. Thames[5]	2.0	1.3	1.6	1.7	1.4	1.5	1.4	1.4	1.3
Italy, Varses	0.8	2.8	3.5	1.1	1.5	1.4	0.9	—	—
Spain, Navarra	0.9	1.4	2.3	1.9	2.0	1.8	1.6	1.0	1.0
Israel, all Jews	2.1	2.5	1.2	1.4	1.8	1.6	1.5	—	—
Low risk									
Singapore, Chinese		1.3	2.6	2.2	2.4	2.3	1.4	2.2	—
Japan, Miyagi	0.3	2.3	4.9	3.0	2.8	1.6	1.7	1.4	1.5
Hong Kong	1.3	0.6	1.0	1.2	1.6	1.2	1.8	—	—
India, Bombay	0.9	1.2	1.7	1.9	1.2	2.1	1.2	—	—
China, Shanghai	3.0	1.8	1.0	1.4	1.3	1.4	2.0	1.7	0.8

[1]For each country, the ratio of the corresponding age-specific incidence rates in 1988–92 to those in 1973–77.–[2]Surveillanace, Epidemiology and End Results program.–[3]Canada, British Columbia. –[4]Australia, New South Wales.–[5]United Kingdom, England, South Thames.

TABLE III – AGE-ADJUSTED MORTALITY RATES[1] OF PROSTATE CANCER IN 13 COUNTRIES, 1973–77 AND 1988–92

Countries	1973–77				1988–92				% change[4]
	Number[2]	Mortality[1]	Rank	Mortality ratio[3]	Number	Mortality[1]	Rank	Mortality ratio[3]	
High risk									
U.S. blacks	968	27.6	1	13.1	1,881	34.3	1	12.3	24.3
U.S. whites	7,711	13.4	7	6.4	11,710	15.7	8	5.6	17.2
Canada	9,023	14.3	5	6.8	16,217	17.0	6	6.1	18.9
Sweden	8,516	21.6	2	10.3	10,333	20.8	2	7.4	−3.7
Australia	5,466	15.6	3	7.4	10,465	17.9	4	6.4	14.7
France	30,104	15.0	4	7.1	45,475	17.1	5	6.1	14.0
Medium risk									
Denmark	2,867	13.5	6	6.4	4,703	18.6	3	6.6	37.8
England and Wales	22,186	12.1	9	5.8	40,722	16.8	7	6.0	38.8
Italy	20,625	10.5	10	5.0	30,040	11.5	10	4.1	9.5
Spain	3,072	12.4	8	5.9	21,448	13.1	9	4.7	5.6
Israel	391[5]	7.5	11	3.6	1,374	9.0	11	3.2	20.0
Low risk									
Singapore	47	1.9	14	0.9	63[6]	3.7	13	1.3	94.7
Japan	6,297	2.4	13	1.1	17,824	3.8	12	1.4	58.3
Hong Kong	115	2.1	12	1.0[7]	405	2.8	14	1.0[7]	33.3

[1]Per 100,000 person-years, age-adjusted to the world standard.–[2]Number of deaths.–[3]Relative to the mortality in Hong Kong.–[4]Percent change from 1973–77 to 1988–92.–[5]Reported deaths were for 1975–77 only.–[6]Reported deaths were for 1988–89 only.–[7]Reference group.

Japan, Singapore and Hong Kong (low-risk countries), although there was a decrease in Singapore during the last time period.

Country-specific mortality-incidence rate ratios in the 4 time periods are presented in Table IV. In each time period, U.S. white men had the lowest mortality-incidence rate ratios (0.16 in 1988–92), while France, Denmark and England and Wales had high ratios. Due to the more rapid increases in incidence than mortality for most countries, the ratios decreased over time, with larger reductions in high-risk countries but much smaller decreases in low-risk populations.

DISCUSSION

In this descriptive study, we showed that regardless of the level of absolute risk, there were large increases in both incidence and mortality rates of prostate cancer in all 15 countries. For incidence, much larger and more rapid increases were seen for both high- (United States, Canada, Australia and France) and low-risk (Asian) countries, while the increases in medium-risk countries were moderate. For mortality, larger relative increases were found for Asian countries, while high-risk countries had much smaller increases.

Several factors, including screening, diagnosis and completeness of reporting, can affect the reported incidence of cancer. Prostate cancer incidence is more affected by screening than that of other cancers because it is a slow-growing cancer with a long latency and because the prevalence of latent tumors has been shown to be quite high in the elderly population (about 50% in men over the age of 70) (Villers *et al.,* 1997). Screening and early detection thus can identify many of the silent tumors (stage A1, usually asymptom-
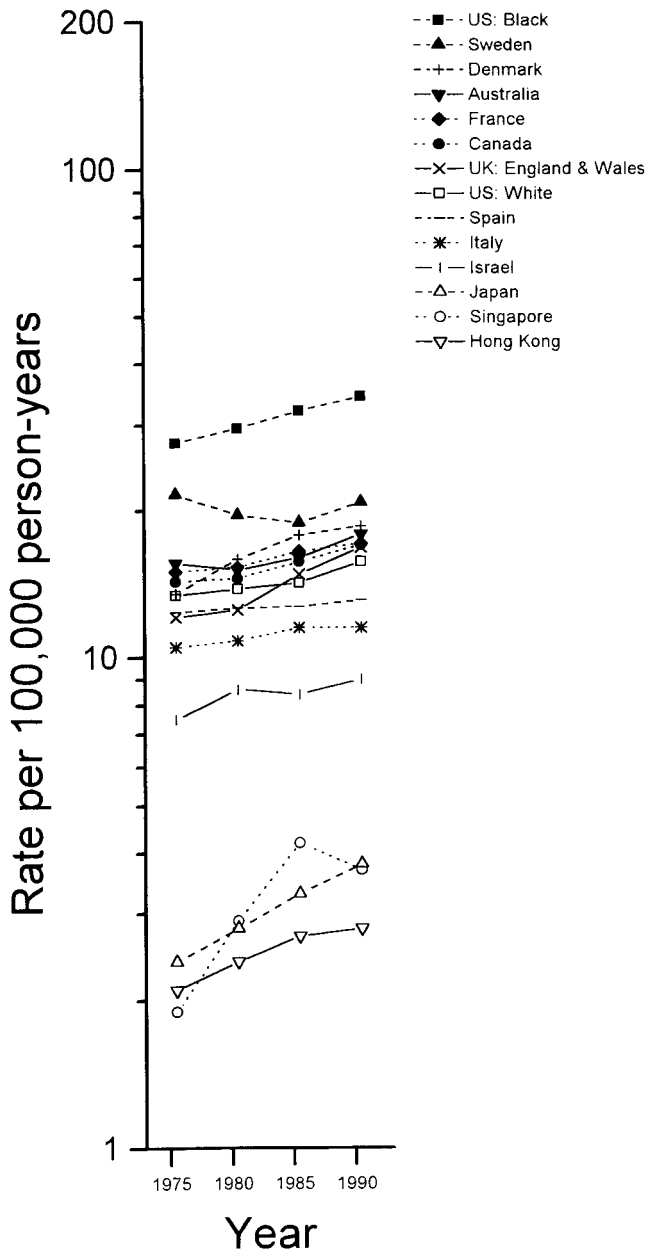
FIGURE 3 – Age-adjusted mortality trends of prostate cancer in 13 countries, 1973–77 to 1988–92.

TABLE IV – MORTALITY-INCIDENCE RATE RATIOS[1] IN 13 COUNTRIES DURING 1973–77 TO 1988–92

Countries	1973–77[1]	1978–82	1983–87	1988–92
High risk				
U.S. blacks	0.35	0.33	0.39	0.25
U.S. whites	0.28	0.25	0.23	0.16
Canada	0.36	0.29	0.25	0.20
Sweden	0.49	0.43	0.38	0.38
Australia	0.55	0.45	0.41	0.33
France	0.65	0.56	0.53	0.36
Medium risk				
Denmark	0.57	0.57	0.59	0.60
England and Wales	0.60	0.58	0.60	0.57
Italy	0.46	0.53	0.45	0.41
Spain	0.70	0.61	0.47	0.48
Israel	0.48	0.46	0.48	0.38
Low risk				
Singapore	0.40	0.44	0.55	0.38
Japan	0.49	0.44	0.42	0.42
Hong Kong	0.41	0.39	0.36	0.35

[1]The ratio of mortality to incidence in each country, by time period.

ment around the periurethral area. Histologic evaluation of the tissue removed sometimes reveals silent malignancies. The steep increase in U.S. incidence since 1986 was largely explained by the widespread use of PSA testing (Potosky *et al.,* 1995). After the introduction of PSA testing in 1986, the incidence of prostate cancer rose steeply (incidence rates increased 108% for U.S. white men from 1986–92), peaked in 1992 and subsequently declined each year from 1993–95 (Stanford *et al.,* 1998). The increase between 1986–92 occurred in all age groups, in both localized and regional stages of prostate cancer, and mostly in moderately differentiated tumors (Stanford *et al.* 1998). The sharp rise in incidence (especially in localized and moderately-differentiated tumors) and the subsequent decline reflect the impact of PSA testing on prostate cancer incidence. In Japan and China, where screening is less common, prostate cancers are diagnosed at more advanced stages (60%–70% of the prostate cancers diagnosed in Japan had extended beyond the prostate and 67% of the Chinese cancers were diagnosed at a remote or distant stage *vs.* 11% of the cases among U.S. whites) with much lower survival (5-year relative survival in China is 33% *vs.* 90% in the U.S.) (Prorok *et al.,* 1996; Hsing *et al.,* 1998; Kumamoto *et al.,* 1990; Harada *et al.,* 1993). An earlier study estimated that, after correction for screening and underreporting, the actual rates in Japan would have been 3–4 times higher than the observed rates (Shimizu *et al.,* 1991*a*; Shibata *et al.,* 1997), which were closer to the rates reported for Japanese-Americans in the United States (43.1 per 100,000 person-years).

The large increases in the incidence in Canada, Australia and France also are due in part to the increasingly widespread use of PSA screening (Majeed and Burgess, 1994; McCaul *et al.,* 1995; Grosclaude *et al.,* 1997; Mercer *et al.,* 1997; Ward *et al.,* 1998; Weller *et al.,* 1998). Differences in screening practices probably also account for some of the variation in age-specific patterns across countries. PSA testing and screening are usually administered to men younger than 75 but not to the very old, thereby picking up small, localized, malignant prostate tumors in younger men and shifting the age distribution of cases to a younger age. Among U.S. black and white men, the rate of increase in incidence slowed after age 70, while the increase continued beyond age 80 in other countries, perhaps suggesting higher screening rates at earlier ages in the United States compared with other countries.

The large increases in incidence in low-risk countries, less affected by screening, are alarming. Such increases are concurrent

atic) in the population. Incidence data reported to IARC does not include information on clinical stage or histologic grade, and early localized malignancies detected through screening are combined with clinically advanced cancer. Thus, incidence in many high-risk countries is likely to be affected by the aggressive screening in their populations, while the lack of screening, the lower quality of cancer diagnosis and the incompleteness of cancer registration may have contributed to a certain degree of underreporting in some low-risk populations.

For example, in the United States, the rise in incidence during the 1970s and early 1980s was attributed partly to the increasing use of transurethral resection of the prostate (TURP) (Potosky *et al.,* 1990), a surgical procedure used to remedy prostate enlarge-

with westernization in these populations and with increases in the incidence of diabetes and cancers of the colorectum and breast (Devesa *et al.,* 1993; Jin *et al.,* 1993; Koyama and Kotake, 1997; Pan *et al.,* 1997; Kitagawa *et al.,* 1998), suggesting that changes in the prevalence of certain common potential risk factors, such as dietary fat, obesity and physical activity, may have contributed partly to the progression and rising rates of prostate cancer (Popkin, 1994; Hsing *et al.,* 1998). Indeed, intake of animal fat and protein in Japan and China has greatly increased during the past 2 decades (Kato *et al.,* 1987; Side *et al.,* 1991; Paeratakul *et al.,* 1998), while the levels of physical activity have decreased substantially (Kono *et al.,* 1991; Hong *et al.,* 1994; Hsing *et al.,* 1994). The combination of these factors may affect hormone metabolism and thereby exacerbate prostate cancer risk.

Because screening has such a large influence on prostate cancer diagnosis, mortality attributed to this cancer is a good index of risk across populations. Mortality, however, can be affected by the accuracy of prostate cancer diagnosis and certification of this cancer as the underlying cause of death on death certificates, particularly for elderly men. With the exception of Sweden, over the 20-year study period, there were increases in mortality across all countries, suggesting real increases in prostate cancer risk.

In the United States, overall age-adjusted mortality rates peaked in 1991, and a 6.7% decline was observed by 1995 (Stanford *et al,* 1998). The benefit of screening in prostate cancer has not been determined, and whether such a decline in mortality is due to aggressive screening in this country is not clear. We do not yet have international data beyond 1992, when a decline in U.S. rates was first seen.

Because most prostate cancers are slow-growing and can be detected early, the 5-year relative survival rates for U.S. patients diagnosed in 1990 was 93% (Stanford *et al.,* 1998). In fact, among all cancers, prostate cancer has one of the largest differences between incidence and mortality. This ratio is affected by the reporting of incidence and mortality, the degree of screening, treatment and survival. Although men in the United States and Canada had the highest incidence and mortality rates in the world, their mortality-incidence ratios were among the lowest in developed countries. Sweden, Australia and France, on the other hand, had mortality-incidence ratios that were as high as those for low-risk countries. Aggressive screening in North America probably contributed largely to the increase in incidence, thereby decreasing mortality-incidence ratios. In most countries, mortality-incidence ratios have decreased over time. Improved treatment and increased survival may also have contributed to the decrease of this ratio over time.

Reasons for the 60- and 15-fold difference in incidence between U.S. men and men from China and Japan, respectively, are currently unknown. This disparity in incidence is one of the largest among cancers and offers unique leads to prostate cancer etiology. Previous autopsy studies have shown that there is little variation in the prevalence of latent prostate tumors across countries (Breslow *et al.,* 1977), so the large difference in clinical (or reported) prostate cancer rates across populations suggests a role for environmental or genetic factors in the progression from latent to clinically significant tumors. The observation that Chinese- and Japanese-Americans have rates that are much higher than their counterparts in China and Japan (26.0 and 43.1, respectively) supports a role for environmental rather than genetic factors (Parkin *et al.,* 1997). Age at migration did not affect the risk of prostate cancer in a migrant study conducted in Los Angeles, suggesting that later life events (presumably environmental factors) can substantially impact the likelihood of developing clinical prostate cancer (Shimizu *et al.,* 1991b).

Additional support for the role of environmental factors is the relatively low rates of prostate cancer in Africa, despite the extremely high rates found in African-Americans. Although population-based incidence rates in Africa are scarce, the reported incidence rates during 1988–92 in Africans living in Harare, Zimbabwe and in Kyadonodo, Uganda were 29.2 and 27.7 per 100,000 man-years, respectively, which are much lower than the rates reported for African-Americans (137.0 per 100,000 man-years) (Parkin *et al.,* 1997). In addition, Europeans living in Harare, Zimbabwe have much higher rates (56.7 per 100,000 man-years). The low reported incidence in Africa may be real or may result, in part, from underreporting of incidence, misclassification of disease and the lack of screening in this population. Future studies are needed to investigate whether the low risk of prostate cancer in Africa can be explained by environmental or other factors.

Despite the substantial morbidity from prostate cancer worldwide, age, ethnicity and a family history of prostate cancer are the only established risk factors (Nomura and Kolonel, 1991). Evidence on diet, especially animal fat intake, is promising but inconclusive (Kolonel *et al.,* 1999). Data on other risk factors, such as circulating levels of hormones, physical activity, body size, smoking, drinking, sexual behavior and occupational exposures, are conflicting (Nomura and Kolonel, 1991). A careful evaluation of the prevalence or distribution of potential risk factors in high- and low-risk populations should provide clues into the role of putative risk or protective factors. For example, certain dietary factors that are common in Asians but uncommon in western men, such as intake of soy, seaweed, rice, shiitake mushrooms, fish and green tea, may have a role in inhibiting the progression of prostate tumors and warrant further investigation.

Environmental factors alone, however, cannot explain fully the large ethnic differences in risk. Variation in genetic susceptibility or metabolism in high- and low-risk populations may have contributed to the large disparity in incidence rates (Shibata *et al.*, 1997). It has been suggested that the substantial ethnic differences in prostate cancer risk are due to differences in androgen levels and in the activity of 5 α-reductase (the enzyme that converts testosterone to dihydrotestosterone, the principal nuclear androgen in the prostate) between western and Asian men (Ross *et al.,* 1992, 1995). To this end, studies have investigated the polymorphisms of certain genes, including *SRD5A2* (the gene encoding 5α-reductase), androgen receptors (ARs) and vitamin D receptors (Coetzee and Ross, 1994; Reichardt *et al.,* 1995; Giovannucci *et al.,* 1997; Stanford *et al.,* 1997). Data from these studies suggest that men with shorter CAG repeats of the AR gene have a higher risk of prostate cancer and that there is ethnic variation in polymorphisms of CAG and GGC trinucleotide repeats and of TA dinucleotide repeats in the *SRD5A2* gene. The list of genetic markers related to prostate cancer is expanding quickly (Ross *et al.,* 1998). Whether these polymorphisms are functional and whether they can explain the substantial ethnic differences in prostate cancer risk need to be investigated further. More data are needed on the prevalence of these common polymorphisms in various populations and on their correlations with circulating and/or tissue levels of hormones to clarify further the role of hormones and genetics in prostate cancer etiology. This is an exciting time to take advantage of these leads to pinpoint factors that might explain the differences and the mechanisms involved.

In summary, incidence and mortality rates for prostate cancer increased substantially over the 20-year study period virtually worldwide. Much larger relative increases were seen in Asian countries, where the absolute risk is low. Studies in low-risk countries may shed light on the role of certain protective factors,

while well-designed and well-executed population-based interdisciplinary studies conducted in several ethnic populations concurrently should help elucidate the independent and combined effects of environmental and genetic factors in prostate cancer etiology and the reasons for the large ethnic differences in risk. Because a decrease in both incidence and mortality has occurred in the United States since 1993, continued monitoring of incidence and mortality trends across countries is warranted.

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