PROSTATE CANCER IN ALASKA NATIVE MEN, 1969-2003

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ABSTRACT

Objectives. The incidence of prostate cancer differs significantly between US race groups. In prior reviews of cancer in Alaska Natives, the incidence of prostate cancer has been observed to occur at a low rate compared to US Whites and Blacks. However, a detailed report of prostate cancer in this population has not been previously published.

Study Design. Incidence of prostate cancer in Alaska Native men was determined for the time period 1969-2003 using data from the Alaska Native Tumor Registry. The registry is a population-based registry which participates in the National Cancer Institute Surveillance, Epidemiology and End Results Program, and has collected cancer information on Alaska Natives since 1969.

Methods. Incidence rates were calculated for all Alaska Natives and for each of the three major ethnic groups (Aleut, Eskimo, Indian). Comparisons of incidence rates between Alaska Natives and US Whites were performed using odds ratios. Temporal changes were identified by a Chi square analysis for trend.

Results. During the 35-year period of review, 332 Alaska Native men were diagnosed with prostate cancer. The age-adjusted incidence rate of 69.5 per 100,000 in Alaska Native men during 1994-2003 was significantly higher than the rate of 45.5 per 100,000 for the earlier period 1969-1983. The US White rate for 1994-2002 of 169.5 per 100,000 was significantly higher than the rate for Alaska Native men for 1994-2003. Results of comparisons between Alaska Native ethnic groups for 1969-2003 showed that prostate cancer was highest in Indians and Aleuts and lowest among Eskimos.

Conclusions. Compared to the US White population, the incidence of prostate cancer in Alaska Native men is significantly lower. Prostate cancer rates among Alaska Native ethnic groups differ. The reason for these differences remains undetermined.

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Keywords: prostate cancer, Alaska Native, American Indian/Alaska Native
INTRODUCTION

Within the general US population, prostate cancer continues to be the most common cancer in men, accounting for 30 percent of all new cancers (1). The incidence of prostate cancer in the US doubled between 1973 and 1994. While the incidence of prostate cancer has increased for all age groups, men under 70 years of age have experienced the greatest increase. Much of this increase occurred in the early 1990’s and appears to be associated with the increased use of PSA screening (2). This may have led to a “lead-time” bias in the incidence data and, indeed, there has been a short, but marked, decline in the incidence of prostate cancer in the most recent data from the Surveillance, Epidemiology and End Results (SEER) Program (3). The incidence of prostate cancer among US men now appears to be stable.

Rates for all cancers combined among Alaska Native (AN) men are similar to those of US White men (4). However, rates for specific cancer sites differ from US White rates. In Alaska Natives, cancer rates for the oral cavity, digestive tract, lung, cervix and kidney are higher compared to US Whites, while the cancer rates for larynx, corpus uterus, urinary bladder, brain, melanoma, leukemia, lymphoma and prostate are lower.

US data reported for the time period 1988-92 showed that the incidence rates of prostate cancer varied by race (Figure 1). The highest incidence of prostate cancer was seen in Blacks, with 180.6 per 100 000, and Whites, with 134.7 per 100 000, but substantially lower rates in men of Asian descent, with Korean men having the lowest incidence, at 24.2 per 100 000 (5). Prostate cancer in American Indian/Alaska Native men occurred at a rate similar to that seen in Asian men.

However, there are significant variations in cancer rates among the various US American Indian tribes and Alaska Native groups. The incidence of prostate cancer in American Indian and Alaska Native (AI/AN) men, by Indian Health Service Areas within the United States for the time period 1980-87, ranged from 14 to 43 per 100 000, compared to 88

Figure 1. Incidence of prostate cancer within different US ethnic groups, 1988-1992.

Source: Miller et al. (5).

1 All rates age-adjusted to the US 1970 standard population.
per 100 000 for US white men (6). Prostate cancer incidence in American Indians of New Mexico for the period 1969-1994 was reported as low (42.2 per 100 000) compared to non-Hispanic White men living in New Mexico, but rates have increased to 64.6 per 100 000 during the 25-year period (7). A low incidence rate of prostate cancer has been observed in other indigenous groups of the arctic region, including Inuit men from Greenland and Canada (8, 9) (Figure 2). Ontario First Nations Indians report a prostate cancer incidence rate of 25.4 per 100 000 (adjusted to the world standard population (wsp)) for 1968-91, which is higher than the rate for Canadian Inuit (15.8 per 100 000 wsp 1984-1988) (10) and Greenland Inuit (2 per 100 000 wsp 1988-1997), but lower than for Alaska Natives (46.2 per 100 000 wsp). Prostate cancer among the Sami in northern Finland during 1979-1998 was one-third the rate of the non-Sami population in the North and one-fourth of the national rate in the Finnish Population (11). The International Agency for Research on Cancer (IARC) estimates worldwide prostate cancer incidence for the more developed countries at 46.7 per 100,000 (wsp) for 1993-2001, and at 7.7 per 100 000 for less-developed countries (12).

Prostate cancer mortality rates for Alaska Natives did not change significantly during the 1979-1998 time period, when five-year mortality rates ranged from 7.4 to 13.5 per 100 000. The US White mortality rate of 21.7 per 100 000 for years 1994-1998 was twice that of AN men, which was 12.0 per 100 000 (13). Disparity between US American Indian and Alaska Native populations is also seen in prostate cancer mortality rates. For AI/ANs from five US geographic regions, representing 60% of the AI/AN population at the last census, prostate cancer mortality rates for 1994-1998 ranged from a low of 14.4 in Alaska Natives to 49.7 per 100 000 in Northern Plains American Indians (14). The

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Figure 2. Prostate cancer incidence rates among US and World ethnic groups.

1 All rates age-adjusted to the world std pop.

Sources: AK Native, New Mexico, US White, US Black, US Asian/Pacific Islander; data from SEER Stat for years 1992-01; Canadian Inuit: 1968-88, Prener et al. (8); Greenland Inuit: 1988-97, Friberg et al. (9); Ontario First Nations Indians: 1968-91, Marrett et al. (10); More and less developed countries: 3-5 years prior to 2002, GLOBOCAN, IARC (12).
five-region combined rate of 23.8 per 100,000 was significantly lower than the rate for the US, all races combined (mortality rate ratio 0.07 (95% CI: 0.1, 0.8)). Four of the regions had statistically significant low prostate cancer mortality rates: Alaska, East, Pacific Coast and Southwest; however, the Northern Plains region had a higher mortality rate than the US “all races” (mortality rate ratio 1.48: 95% CI 1.16, 1.89).

The incidence rate of prostate cancer in Alaska Native men has been reported to be approximately half of that seen in the US “all races” population (4). However, the comparison of incidence rates for the period 1969-1973 (30.1/100,000) with those of 1989-1993 (69.8/100,000) showed a significant increase in prostate cancer in Alaska Native men (15). This report provides a detailed review of prostate cancer in Alaska Native men for the 35-year time period 1969-2003.

MATERIAL AND METHODS

Study population
American Indians/Alaska Natives represent a diverse group of people indigenous to North America. The US Bureau of the Census estimates that, in the year 2000, there were 2,402,000 American Indians/Alaska Natives from over 500 tribes, with 119,241 living in Alaska. Approximately one-third of Alaska Natives reside in Anchorage (16). The Alaska Native population includes three major ethnic groups: Eskimos, Aleuts and Alaska Indians. Eskimos, comprising 52 percent of the Native population, can be further subdivided into the Yupik Eskimos of southwestern Alaska and the Inupiaq (Inuit) of northern Alaska. The Inupiaq share the same language with the Inuit of Canada and Greenland. Alaska Indians, comprising 36 percent of the Native population, include the Athabaskan tribes residing in the interior portion of Alaska and Tlingit, Haida, and Tsimshian tribes of southeastern Alaska. The Aleuts comprise 12 percent of the population and have traditionally resided on the Aleutian Islands and the Alaska Peninsula.

Source of data
The Alaska Native Tumor Registry (ANTR), a state-wide population-based registry, was used to identify all cases of prostate cancer occurring during the 35-year time period 1969-2003 in the Alaska Native population. Classification of ethnicity is based on self-reporting by the patients at the time of their hospital/clinic registration. Cases included in the registry are identified through a variety of sources, including: 1) hospital discharge diagnoses for all tribal hospitals in the state; 2) tumor registry and pathology files of the Alaska Native Medical Cancer; 3) other in-state hospital tumor registry, pathology and autopsy reports; 4) the Seattle Area Cancer Surveillance System; and 5) death certificates for Alaska Natives. Prior to 1984, the registry collected data on patient demographics, primary cancer site, histology, and the basis for confirmation of the diagnosis. Since 1984, more detailed information has been collected, including cancer staging, treatment and follow-up. Procedures for data collection and coding follow standards of the SEER Program of which ANTR is a participant.
Statistical analyses
Population statistics were interpolated from 1970, 1980, 1990 and 2000 (National Center for Health Statistics bridged estimate for multiple race categories) US census data. All rate calculations were average annual age-adjusted, based on the US 2000 standard population (all races). Rates were calculated for three time periods: 1969-1983, 1984-1993 and 1994-2003. US prostate cancer incidence rates for race groups are based on SEER data for years 1973-2002. Comparisons of rates were performed using odds ratios (OR) with corresponding 95% confidence intervals (CI). Rates for which the OR did not contain one were considered significantly different. A Chi-square test for linear trend was used to determine temporal changes in rates for three time periods.

The stage at diagnosis of prostate cancer (local, regional, distant) is reported for two time periods 1984-1993 and 1994-2003. Staging is unavailable for ANTR cancer diagnoses prior to 1984.

RESULTS
During the 35-year time period, 1969-2003, 332 Alaska Native (AN) men were diagnosed with prostate cancer. Ninety-four percent were microscopically confirmed diagnoses. Nearly half (48%) of the cases were diagnosed during the last 10 years of the review period. Ethnic characteristics and age-specific prostate cancer incidence rates of the 332 men are shown in Table I. Rates are higher for Indian men than for Eskimo or Aleut men of all age groups. Staging information for Alaska Natives is shown for years 1984-2003 and 1988-2002 for US Whites (Table II). Approximately three-fourths of AN men (72%), diagnosed during the most recent 10-year period, had localized disease, 11% had regional disease, and 9% had distant spread of disease. Staging was unavailable on the remaining 8% of men, with 11% of those aged 70 years and older being unstaged, compared to only 1.9% for those less than 70 years of age. Staging for the earlier

| Table I. Characteristics of Alaska Native (AN) compared to US White (USW) men diagnosed with prostate cancer during the time period 1969-2003. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | All AN | Eskimo | Indian | Aleut | US White* |
| Number          | 332    | 78     | 208    | 46    |            |
| Median age (range) | 68 (40-98) | 70 (46-91) | 68 (40-98) | 70 (53-96) |         |
| Age specific incidence rates |
| Age group       | 6.3    | 4.5    | 11.6   | n/a   | 9.6 |
| 60-69           | 219.8  | 102.2  | 413.3  | 193.9 | 491.3 |
| 70+             | 442.1  | 219.4  | 752.0  | 543.3 | 1015.1 |

*US data for 1973-2002 from SEER Stat, National Cancer Institute Surveillance, Epidemiology and End Results Program.

**All rates age-adjusted to the US 2000 standard population.

n/a: too few cases to calculate a rate
period 1984-1993 shows a lower proportion in the local stage and a higher proportion in the regional stage than for the more recent time period; however, because of the proportion of unknown stage category, testing for a shift in staging was not possible.

The overall age-adjusted incidence rate of prostate cancer in AN men during the most recent time period, 1994-2003 is 69.5 per 100 000. Comparisons of rates for three time periods, 1969-1983, 1984-1993 and 1994-2003, indicate an upward trend (p < 0.001) among all Alaska Natives diagnosed with prostate cancer, as well as among Indian and Aleut ethnic groups (Table III). Rates of prostate cancer in AN men are significantly lower than those seen in US White men for the three time periods.

The incidence of prostate cancer in Alaska differs significantly by ethnic group. Based on 1994-2003 data, Alaska Indian men have significantly higher rates than Eskimo men (OR 3.6: CI 2.4, 5.2), but are not significantly different from Aleuts (OR 1.3: CI 0.8, 2.0). Aleut rates are higher than Eskimo rates (OR 2.7: CI 1.7, 4.8). Within the two major groups of Alaska Indians, the highest rate of prostate cancer is seen among southeast Alaska Indians (190.2 per 100 000), compared to Alaska Indians from the interior of Alaska (101.9 per 100 000; OR 1.8: CI 1.1, 3.0). In comparison to US Whites for 1994-2003, the incidence rate of prostate cancer is significantly lower

| Ethnic group         | 1969-83 | 1984-93 | 1994-03 |
|----------------------|---------|---------|---------|
|                       | No.     | Rate    | No.     | Rate    | No.     | Rate    | p      |
| Alaska Native        | 66      | 45.5*   | 107     | 67.5*   | 159     | 69.5*   | 0.0002 |
| Eskimo               | 18      | 23.8*   | 23      | 27.7*   | 37      | 33.6*   | 0.09   |
| Aleut                | 7       | 34.5*   | 15      | 74.0*   | 24      | 104.0*  | 0.02   |
| Indian               | 41      | 87.4    | 69      | 124.2   | 98      | 107.2*  | 0.06   |
| Southeast Indian     |         |         |         |         |         |         |        |
| Interior Indian      | 20      | 101.9   |         |         |         |         |        |
| US White             | 99.8    | 160.8   | 169.5   |         |         |         |        |

* Significantly different from US rate; odds ratio confidence interval did not include 1.

a probability value for Chi square test for trend.

1 US data for years 1973-2002.

All rates are age-adjusted to the US 2000 standard population.

All US data from SEER Stat, National Cancer Institute Surveillance, Epidemiology and End Results Program.
for Eskimos and Aleuts (Eskimo OR 0.2; CI 0.1, 0.3; Aleut OR 0.5; CI 0.4, 0.8). The incidence for Alaska Indians as a group is also significantly lower (OR 0.7; CI 0.5, 0.8), but the incidence rate for Alaska Indians of southeast Alaska is not different from the US White rate (OR 1.2; CI 0.9, 1.5).

**DISCUSSION**

The occurrence of prostate cancer in indigenous groups in North America has not been well described. Data exists primarily for American Indians from New Mexico, Ontario, Canada, Circumpolar Inuit, Finland Sami and Alaska Natives (4, 7-11). Among all Alaska Natives combined the incidence of prostate cancer occurs at a low rate compared to the general US white population and at a much lower rate than the US Black population. These differences have been maintained throughout the 35-year period, 1969-2003, reviewed in this study.

With the advent of the prostate-specific antigen test for monitoring the disease in 1986, and its subsequent approval as a screening tool for prostate cancer detection in 1992, a notable rise in prostate cancer incidence was recorded in the United States (from 84.4 per 100,000 in 1984, to 163 per 100,000 in 1991). Prostate cancer mortality rates increased in the US, peaking in 1991 at 29.4 deaths per 100,000. Mortality rates in the US have decreased since that time, and significantly so during the years 1994-1999. The US Preventative Services Task Force reported that there is not enough evidence to date to fully attribute the declines in mortality entirely to early detection through PSA testing. Changes in disease management, misclassification of cause of death, and changes in risk or other factors, may have contributed to the reported decline in prostate cancer mortality (17). Analysis of stage-specific prostate cancer incidence among US Whites showed decreases in the incidence of distant stage disease in 1991, a year before decreases in local and regional stage disease.
were observed, and provided evidence for a role of PSA testing in decreasing mortality (18). As PSA testing has not been proven to reduce morbidity or mortality, and because the rate of disease among Alaska Natives is relatively low, the Indian Health Service in Alaska has never recommended PSA testing for prostate cancer screening in asymptomatic AI/AN men. Medical records for 100 (83%) Alaska Native men diagnosed with prostate cancer between 1990 and 1997 were reviewed and only 8 men had a screening PSA test prior to symptoms leading to a prostate cancer diagnosis (personal communication, K. Koller). It is conceivable that the low rate of prostate cancer is due to lack of detection. However, as shown in Figure 3, the proportion of patients diagnosed with local disease is similar to that in the general US population. This finding would suggest that there is not a large number of clinically asymptomatic patients that remain undetected. It is also unlikely that patients with advanced disease are undiagnosed, or unreported. A recent review of cancer-related mortality in American Indians and Alaska Natives showed that all but the Northern Plains Indians had rates significantly below the US “all races” rate, and Alaska Natives had the lowest rate among the Native groups reviewed (14).

Although the overall rate of prostate cancer in Alaska Natives is low, significant variations in incidence occur within the subgroups that comprise the AN population. Alaska Indians, particularly those from southeast Alaska, have an incidence of prostate cancer similar to that of US white men. Eskimos, however, have a significantly lower incidence than that seen in Alaska Indians and US White men. The reasons for these differences are unknown.

For Eskimos in Alaska, the incidence of prostate cancer is below that of other ethnic groups in the US and analogous to that seen in men from Asia. Similar low rates have been noted for Eskimos (Inuit) in Canada and Greenland (8-10). Various explanations for the low rate of prostate cancer in Asian men have been postulated. Studies of descendants of Asian immigrants to the US indicate that they have a higher rate of prostate cancer compared to men in Asia (19), suggesting that environmental and lifestyle factors are of importance. Potential factors of interest have included dietary differences and differences in body mass. A recent study assessing dietary variations between ethnic groups suggested that saturated fat intake may be important, postulating that an increased intake of fat may adversely influence prostaglandins or hormones (20).

Dietary habits of Alaska Natives represent one area of potential importance for understanding the incidence of prostate cancer in this population. Eskimos have traditionally obtained a larger part of their diet from marine mammals, salmon and other fish. Marine mammals and fish, such as salmon, contain a high level of unsaturated fats, particularly omega-3 fatty acids. A diet high in fish has been associated with a lower risk of developing prostate cancer (21). Alaska Indians from the Interior of Alaska have less access to marine mammals. Diets include caribou, moose and waterfowl, and groups living along rivers also consume fish including salmon. However, Alaska Indians from southeast Alaska have traditionally consumed a diet of marine fish and mammals, although to a lesser extent than the Eskimos.

Over time, a shift has occurred from a traditional Native diet to one that incorporates
many non-traditional food items. Even as early as the 1960s, a substantial portion of the caloric intake by Alaska Natives came from imported food items (22). Scott and Heller estimated that canned foods and milk, lard, butter, cereals, flour, sugar and candy accounted for at least 50 percent of the calories consumed. Local game meat and fish, however, constituted a large portion of the meat consumed by Alaska Natives.

In a more recent study, detailed dietary histories of 351 Alaska Natives who resided throughout the state were collected over a 1-year period (1987-88) (23). This study found that traditional subsistence food items still constituted an important portion of the daily diet. Compared with the prior study, the percentage of energy derived from fat remained unchanged at 35-39 percent. However, the source of fat could not be directly compared between the two studies. While dietary changes have occurred for the population as a whole, Alaska Natives, and especially those aged 30 years and younger, consume a significantly larger amount of non-traditional protein, saturated fat and carbohydrates than those who are 60 years old or more (24). With a change in lifestyle marked by a decrease in use of traditional Native foods and an accompanying decrease in energy expenditure, the incidence of obesity and diabetes also increased significantly (25). The role of these changes in the increased incidence of prostate cancer in Alaska Natives remains undetermined.

The prevalence of clinically silent prostate cancer in Alaska Natives is unknown. Autopsy studies of men from Japan and the US have shown that the age-specific prevalences of occult prostate cancer are similar in the two groups (26-28). Such findings would suggest that premalignant lesions, such as prostate intraepithelial neoplasia (PIN), or early stage cancers, may occur at similar rates across populations and ethnic groups. However, the development of clinically apparent cancers differs between groups for as yet undetermined reasons. A large autopsy series of AN men does not exist. The prevalence of PIN in this population has also not been reported.

Specific molecular or genetic factors influencing the development of prostate cancer are not well understood. It has been postulated that variations in the prevalence of certain alleles of genes affecting serum levels of androgens, or of their metabolites, may contribute to ethnic differences in prostate cancer (28). These molecular and genetic factors have been reviewed in detail in several recent reports. Such studies have not been conducted among Alaska Natives. Reports of positive family history among some AI/AN men diagnosed with prostate cancer may warrant a broader review of family relationships and cancer.

In summary, the incidence of prostate cancer has increased in Alaska Natives over 35 years; however, the rate for all AI/AN combined is significantly lower than that seen in the US White population. Significant differences in incidence exist between Native groups within Alaska. The reasons for these differences remain unexplained. Further studies are needed.

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