ABSTRACT

Objectives. Alaska Native (AN) women have exhibited some of the highest incidence rates of cancer overall, and different patterns of site-specific incidence compared to other U.S. populations. This study compares incidence rates between AN and U.S. white women (USW) for cancers of the breast, uterus, ovary and cervix, and examines effects of time period and birth cohort as determinants of incidence trends among AN women.

Study design. Observational, population-based study.

Methods. Cancer incidence data from the Alaska Native Tumor Registry and SEERStat, 1974–2003. Age-adjusted World Standard Population rates were calculated for a current 5-year period and over time (30 years), and compared to other populations using rate ratios with 95% confidence intervals. Log-linear regression models used to assess impact on trend of age, time period and birth cohort.

Results. Compared to U.S. white women, current cancer rates among AN women are not significantly different for cancer of the breast and cervix, and significantly lower for cancers of the ovary and uterus. Trends over time over a 30-year time period also differ for these cancer sites. There were significant increases in breast and uterine cancer, and in contrast, a marked decline in cervical cancer. There was no significant change for cancer of the ovary. Changes appear to be due largely to period, not birth cohort effects.

Conclusions. Increases in breast cancer may be due to a combination of modifiable behaviours; increased BMI and a shift to a non-traditional diet. Increases in uterine cancer could be associated with increased BMI and diabetes. Cervical cancer rates have declined to USW levels. The marked decline is likely due to enhanced screening and control efforts within the Alaska Native
INTRODUCTION

Cancers of the breast, cervix, uterus and ovaries account for approximately 40% of neoplasms in women worldwide (1). In general, high rates for cancers of the breast, uterus and ovary are seen in Western, industrialized nations, particularly northern Europe and North America, whereas lower rates are observed in less industrialized and Asian nations (1,2). Conversely, rates are much higher for cervical cancer in underdeveloped countries, where 80% of all cases occur (3).

Incidence rates of breast cancer have increased in most areas of the world until recently. By and large, regions with historically low rates have been experiencing the largest percentage increases (1). Breast cancer in the U.S. increased approximately 26% for all races during the 1980s, and less rapidly through the 1990s (4). Rates decreased by 3.5% per year from 2001 to 2004. This decline is probably due to declines in hormone replacement therapy use (5). In contrast, uterine cancer incidence rates in northern Europe and North America have declined overall during the last 50 years (6). Ovarian cancer rates in northern Europe and North America have remained almost constant over the last 2 to 3 decades. An increase in ovarian cancer rates, however, has been reported in Japan and developing countries (3). Cervical cancer incidence has declined dramatically in industrialized countries, but declines are also evident in some developing countries. This trend could be partially attributed to the widespread practice of screening and treatment of preneoplastic cervical lesions (1).

In the United States, Alaska Native (AN) women have exhibited different patterns of incidence for cancers of the breast, uterus, ovary and cervix from all other U.S. races. A 1998 report of U.S. cancer rates by race and ethnicity showed that compared to U.S. white women, AN women had moderate rates of breast cancer, very low rates of uterine cancer, similar rates of ovarian cancer and the highest cervical cancer rates of all racial and ethnic groups in the U.S. (7).

Before 1950, cancer among Alaska Natives was thought to be a rare occurrence. Now, the overall cancer incidence rates for all cancers combined among AN women equals that of USW women, while rates in AN men are nearly as high as those of USW men (8). Additionally, cancer among Alaska Natives is
the leading cause of death. A report of cancer mortality among Alaska Natives, 1994–1998, showed that Alaska Native rates exceeded U.S. white rates by 30% for both women (AN women 261.8 vs. USW women 201.8 per 100,000) and men (AN men 187.2 vs. USW men 141.6 per 100,000) (9). Comparisons of cancer mortality between Indian Health Service (IHS) areas suggest marked differences in cancer patterns between American Indians/Alaska Natives residing in different geographic areas of the U.S. (10,11).

During the 30 years of our study period, Alaska Natives experienced many changes in their lifestyle and diet, as well as the management and delivery of health care services. These changes may have impacted reproductive problems and other factors known to be significant risks for specific cancers in women. We studied trends in the incidence of cancers of the breast, uterus, ovary and cervix in AN women for the period 1974–2003 specifically to examine the effects of time period and birth cohort on incidence. We conducted an exploratory search without any a priori assumptions. Additionally, we provided updated comparisons of incidence rates between AN and USW women for the most recent 5-year period, 1999–2003.

METHODS

Study population
The U.S. Bureau of the Census estimates that in the year 2000, there were 119,499 Alaska Natives residing in Alaska, 97,012 of whom checked only the American Indian/Alaska Native (AI/AN) category for race among multiple options. Annual population estimates for Alaska Natives were based on the Indian Health Service (IHS) population estimates for 1974 to 2003, which used U.S. Census data provided by National Center for Health Statistics (NCHS), and IHS Alaska Area user population information.

Source of incidence data
Incidence data for AN women in this report are from the Alaska Native Tumor Registry (ANTR). Beginning with data from 1969, this registry includes all AN patients statewide who were eligible for Indian Health Service benefits and who were diagnosed with invasive cancer while a resident of Alaska. Data for the 30-year period, 1974–2003, were examined for this study. The ANTR has been one of the National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) program registries since 2001. Data, however, have been collected in accordance with SEER guidelines since the registry’s inception (11). Case ascertainment is thought to be nearly complete for the entire study period. The majority of cases were confirmed by pathology (90%). Data for U.S. white women for the years 1974 to 2003 are from the SEER public-use datafile (12).

Rate calculations
All incidence rates were adjusted to the World Standard Population. We created rate ratios for comparison between AN women and USW women, and calculated confidence intervals around these ratios (13). We considered AN women’s rates significantly different if the 95% confidence interval around the ratio did not contain one. We used StatsDirect software to calculate these confidence intervals. Age-stratified Mantel-Haenszel Chi Square Tests for Trend were calculated to determine significant changes for AN cancer rates over time (14).
Percent change over the 30-year period was calculated using the difference in rates between the most recent 5-year period (1999–2003) and the earliest 5-year period (1974–1978) divided by the earliest 5-year period.

Age-specific rates
Age-specific rates for each 10-year age group for AN women were compared with USW women for each cancer site for the entire 30-year study period. Since there were small numbers of cases for all but breast cancer, age was stratified into 2 groups (age under 50 vs. 50 years and over). These age groupings were selected as a proxy for menopausal status. Rates were age-adjusted within these 2 groups, and the analysis performed for 3 10-year time periods, 1974–1983, 1984–1993, and 1994–2003. For consistency, breast cancer was also examined using the 2 age groups, as well as 10-year time periods Log scale transformations of the rates were performed to more clearly demonstrate relative differences on the graphs. However, percent changes in pre- and postmenopausal rates over time reported in the narrative were calculated using the non-transformed rates.

Age-period-cohort analysis
Log-linear regression models were used to assess the relative impact of age, time period and birth cohort on cancer rates. The observed numbers of cases were assumed to follow a Poisson distribution. Models assessed included the full model with age, time period and birth cohort effects, and reduced models with age and birth cohort, age and time period or age alone. In addition, age was also examined as a continuous variable with possible linear, quadratic and cubic effects, and time period was assessed as a continuous variable (referred to as age-drift). Goodness-of-fit was examined for all models and the significance of effects was assessed by changes in the scaled deviance. Models were fit both including and excluding single cohorts at the ends of the birth cohort spectrum (15).

Because of small numbers of cases, rates were calculated for 10-year age and period categories for cervical, uterine and ovarian cancer, and for both 10-year and 5-year groups for breast cancer. For 10-year groups, cases aged 20 to 79 years were analysed. This age range was selected because of the small numbers of cases in 10-year age groups that were older or younger. Analysis of breast cancer cases by 5-year groups covered the entire 30 year period and included cases aged 25 to 79 years. Birth cohort was calculated as the interaction of age group and time period. In order to fit the full model, constraints were placed on the birth cohort effect. Differing constraints result in different parameter estimates, but relative changes can be interpreted.

RESULTS

During the 30-year period, 1974 to 2003, AN women experienced 2,977 invasive cancers. Among these, 1,092 (37%) were at the 4 sites reported in this study: 773 breast, 66 uterus, 97 ovary and 156 cervix.

Breast cancer
Breast cancer was the most frequently diagnosed cancer among AN women for the first 10 years of the study period, 1974–1983, and the most frequent during the current 5-year period, 1999–2003. It was also the most frequently occurring cancer among USW women during both these time periods (Table I). During the
### Table I. Ranking of cancer incidence for Alaska Native and U.S. white women for the earliest period and the most recent time period.

| Time Period       | Alaska Native Women | U.S. White Women | Alaska Native Women | U.S. White Women |
|-------------------|---------------------|------------------|---------------------|------------------|
| 1974–1983         |                     |                  |                     |                  |
| Breast            | 1 Breast            | 1 Breast         | 1 Breast            | 1 Breast         |
| 2 Colon and Rectum| 2 Colon and Rectum  | 2 Colon and Rectum| 2 Colon and Rectum  | Lung and Bronchus |
| 3 Cervix Uteri    | Uterus              | 3 Lung and Bronchus| Uterus              | Lung and Rectum  |
| 4 Lung and Bronchus| Lung and Bronchus   | 4 Stomach        | Uterus              |                  |
| 5 Ovary           | Ovary               | 5 Thyroid        | Melanoma            |                  |
| 6 Kidney and      | Non-Hodgkins        | 6 Uterus         | Non-Hodgkins        | Lymphoma         |
| Renal Pelvis      | Lymphoma            |                  |                    |                  |
| 7 Gallbladder     | Cervix Uteri        | 7 Pancreas       | Ovary               |                  |
| 8 Pancreas        | Leukemia            | 8 Kidney and     | Thyroid             | Renal Pelvis     |
| 9 Thyroid         | Melanoma            | 9 Cervix Uteri   | Urinary Bladder     |                  |
| 10 Nasopharynx    | Pancreas            | 10 Ovary         | Leukemia            |                  |
| 11 Stomach        | Urinary Bladder     | 11 Non-Hodgkins  | Pancreas            | Lymphoma         |
| 12 Uterus         | Stomach             | 12 Leukemia      | Kidney and          | Renal Pelvis     |
| 13 Non-Hodgkins   | Thyroid             | 13 Multiple Myeloma| Cervix Uteri        |                  |

### Table II. Comparison of age-adjusted incidence rates for cancers of the breast, uterus, ovary and cervix by 5-year period among Alaska Native women and U.S. white women 1974–2003.

| Year Diagnosis | Alaska Natives | USW | RR 95%CI | Alaska Natives | USW | RR 95%CI |
|----------------|---------------|-----|----------|---------------|-----|----------|
| 1974–78        | 47.0(43)      | 77.0| 0.61*    | 1.6(3)        | 26.3| 0.06*    |
| 1979–83        | 45.5(53)      | 78.1| 0.58*    | 3.4(5)        | 20.8| 0.16*    |
| 1984–88        | 69.8(95)      | 93.6| 0.75*    | 4.9(6)        | 18.6| 0.26*    |
| 1989–93        | 79.3(135)     | 96.2| 0.83*    | 8.5(15)       | 18.2| 0.47*    |
| 1994–98        | 99.7(211)     | 100.2| 0.99 | 7.4(15)       | 18.6| 0.40*    |
| 1999–03        | 96.3(236)     | 100.7| 0.96  | 9.6(22)       | 18.5| 0.52*    |

% Change 105↑ 31↑ 500↑ 30↑

| Year Diagnosis | Alaska Natives | USW | RR 95%CI | Alaska Natives | USW | RR 95%CI |
|----------------|---------------|-----|----------|---------------|-----|----------|
| 1974–78        | 9.9(9)        | 12.5| 0.79     | 30.5(27)      | 9.8 | 3.11*    |
| 1979–83        | 8.8(10)       | 11.9| 0.74     | 31.1(41)      | 7.9 | 3.95*    |
| 1984–88        | 9.6(14)       | 12.2| 0.79     | 17.7(29)      | 7.5 | 2.38*    |
| 1989–93        | 13.9(25)      | 11.6| 1.21     | 14.7(29)      | 7.6 | 1.92*    |
| 1994–98        | 13.0(26)      | 10.9| 1.19     | 5.0(12)       | 6.8 | 0.74     |
| 1999–03        | 5.2(13)       | 10.5*| 0.53   | 6.4(18)       | 5.8 | 1.12     |

% Change 47 (NS) 16↑ 79↑ 41↑

( ) Numbers of Alaska Native cancer cases in Alaska.
* 95% Confidence intervals do not overlap for Alaska Native versus U.S. white rates.
† Adjusted by the direct method to the World Standard Population.
↓↑ Direction of statistically significant trend
most recent 5-year period, 1999–2003, AN women experienced 236 new cases of invasive breast cancer. As shown in Table II, the age-adjusted invasive breast cancer rate for AN women for this period appears to be lower, although not significantly lower, than that for USW women (96.3 vs. 100.7 per 100,000). Over the period 1974–2003, age-adjusted rates for invasive breast cancer increased 105% for AN women, compared to a 31% increase for USW women in the same period, 1974–2003 (Table II).

Figure 1 shows age-specific breast cancer rates by 10-year age groups for the period 1974–2003 among AN and USW women. Breast cancer first appears in the 10–19 age group for both AN and USW women. Rates were similar through the 50–59 age group. Age-specific rates for ages 60 and over were significantly lower for AN versus USW women. Among AN women there was little increase in rates from 50 years onward. However, rates continued to rise with age for USW.

Supplementary Figure 1 (http://www.ijch.fi/issues/691/SupplementaryDay.pdf) shows
trends for 2 age groups (<50 years and ≥50) over the study period for AN and USW women. There were significant increases in breast cancer rates among both age groups for AN women. Incidence rates for women <50 increased 44% compared to increased incidence of 154% for women ≥50 years. Among USW women, rates also increased significantly, but to a lesser extent for both age groups (7% and 43%, respectively).

An analysis of age-period-cohort effects showed that changes in breast cancer incidence by birth cohort were not significant after controlling for changes by period of diagnosis (Fig. 2). There was a statistically significant linear increase in invasive breast cancer rate by year of diagnosis for the period 1974 to 2003. The final model included age (linear, quadratic and cubic effects) and a period effect.

_Uterine cancer_

Uterine cancer ranked twelfth in cancer incidence among AN women during the first 10 years of the study, 1974–1983, and now ranks sixth. It ranked third among USW women’s cancers among Alaska Natives.

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**Figure 3.** Age-specific incidence rates for uterine cancers among Alaska Native women and U.S. white women 1974–2003.

**Figure 4.** Uterine cancer among Alaska Native women by birth cohort, 1974–2003.
women during the 1974–1983 period, and currently ranks fourth (Table I). During the most recent 5-year period, 1999–2003, AN women experienced 22 new cases of uterine cancer. Shown in Table II, the age-adjusted uterine cancer rate for AN women for the most recent period was less than half that for USW women (9.6 vs. 18.5 per 100,000). AN women’s rates have been significantly lower than USW women’s rates throughout the entire 30-year study period. Over the study period, age-adjusted rates for uterine cancer for AN women increased 500%. In contrast, rates declined 30% among USW women (Table II).

Figure 3 shows uterine cancer among both AN and USW women occurs early (10–19 age group) and peaks in the 60–69 year age group. Rates were significantly lower among AN women as compared to USW women for all age groups 40 years and older.

Examining trends by 2 age groups (<50 and ≥50) as shown in Supplementary Figure 2 (http://www.ijch.fi/issues/691/SupplementaryDay.pdf), there was no significant change in rates for women <50, whereas rates for AN women ≥50 increased significantly by 454% over the 30-year study period. Among USW women, rates declined significantly for both age groups (16% and 17%, respectively).

An analysis of age-period-cohort effects resulted in a final model containing age (linear and quadratic terms), as well as a birth cohort effect. Cohorts that correspond primarily to women born from 1929 through 1943 were significantly different from the other cohorts (Fig. 4). Changes in uterine cancer incidence by period of diagnosis were not significant after controlling for changes by birth cohort.

**Ovarian cancer**

Ovarian cancer ranked fifth in cancer incidence among AN women for all cancers diagnosed during the first 10 years of the study period, 1974–1983. Ovarian cancer now ranks tenth. Among USW women, ovarian cancer ranked fifth for the period 1974–1983, and is currently seventh (Table I). During the most recent 5-year period, 1999–2003, AN women experienced 13 new cases of ovarian cancer. There was no significant trend in age-adjusted rates for ovarian cancer among AN women across the 30-year period, 1974–2003. Rates for USW women declined 16% from 1974–2003. As shown in Table II, the age-adjusted ovarian cancer rate for AN women for the period 1999–2003 was less than half that of USW women (5.2 vs. 10.5 per 100,000), however, this was the only 5-year period in which AN rates were significantly lower than USW.

Figure 5 shows that ovarian cancer rates for both AN and USW women began in the 0–9 age group and were similar for age groups less than 60. AN women experienced significantly lower rates among the 60 and over age groups. Rates for both AN and USW women peaked in the 70+ age group.

As shown in Supplementary Figure 3 (http://www.ijch.fi/issues/691/SupplementaryDay.pdf), there were no significant trends in rates over time for either pre- or postmenopausal groups among AN women. Among USW women, rates declined significantly among women <50 (26%), and 3% for USW women ≥50.

An age-period-cohort analysis of ovarian cancer rates demonstrated that neither period of diagnosis, nor birth cohort better explained the model than age at diagnosis.
**Cervical cancer**

Invasive cervical cancer ranked third in cancer incidence among AN women for the period 1974–1983. However, incidence rates have declined dramatically since the peak in the 1974–1978 time period, and currently ranks ninth for the most recent 5-year period (1999 to 2003). Cervical cancer ranked seventh for USW women for the period 1974–1983, and currently ranks thirteenth (Table I). During the most recent 5-year period, 1999–2003, AN women experienced 18 new cases of invasive cervical cancer. The age-adjusted cervical cancer rate for AN women for the most recent 5-year study period, 1999–2003, was not significantly different from that for USW women (6.4 vs. 5.8 per 100,000) (Table II). Rates over time for invasive cervical cancer among AN have varied from those of other cancers. Based on data from the Alaska Native Tumor Registry, cervical cancer incidence rates were high during the first time period (1974–1978), rose slightly, and then declined. Over the 30-year period, 1974–2003, age-adjusted rates for cervical cancer

![Figure 5. Age-specific incidence rates for ovarian cancers among Alaska Native women in Alaska and U.S. white women 1974–2003.](image)

![Figure 6. Age-specific incidence rates for cervical cancers among Alaska Native women and U.S. white women 1974–2003.](image)
decreased 79% among AN women. Among USW women, the 1999–2003 rate represents a decline of 41% from the 1974–1978 time period (see Table II).

Figure 6 shows that cervical cancer was diagnosed as early as the second decade of life (ages 10–19) among both AN and USW women. Among USW women, rates rose steeply until the 30–39 age group. A slow rise in rates follows, with the highest rate in the 60–69 age group. Among AN women, rates rose steadily to peak in the 50–59 age group. AN women rates were higher than USW women rates for all age groups except the earliest (ages 10–19), and significantly higher for age groups 20 to 59.

Examining cervical cancer rates over time by 2 age groups (<50 and ≥50) revealed significant decreases in rates among both age groups (Supplementary Figure 4, http://www.ijch.fi/issues/691/SupplementaryDay.pdf). Among USW women, rates also declined over time for both age groups. Rates for AN women ≥50 were higher than those <50 for all age groups, but only significantly higher for the 1974–1978 time period. Rates for USW women ≥50 were significantly higher at every time point compared to rates for USW women <50.

An analysis of age-period-cohort effects showed a significant linear decrease in cervical cancer rates by period of diagnosis. The final model contained terms for age (linear and quadratic), and an age-drift term (period of diagnosis: 1974–1983; 1984–1993; 1994–2003) treated as a continuous variable. Changes in cervical cancer incidence by birth cohort were not significant after controlling for changes by period of diagnosis.

**DISCUSSION**

In this study we reviewed age specific rates and trends over time for breast, uterus, ovary and cervix cancers among AN women to examine the effects of age, time period and birth cohort as determinants of incidence trends. Prior studies of cancer in AN women have demonstrated different patterns for these cancers compared to other racial groups within the U.S. (7). Therefore, we conducted an analysis of these cancers in AN women to better understand factors responsible for these cancer patterns.

This study has limitations which are the result of a small number of cases, especially for select cancers. However, it has strength in that it uses population-based incidence data that are available and complete for a 30-year time period. Data collection has followed SEER standards, and over 90% of cases were confirmed by pathology. Risk factor data have not been collected as completely for the entire population, and only since 1991. Nonetheless, the marked changes in rates over a relatively short period of time (30 years) that appear to be due largely to period effects rather than birth cohort effects should be useful to future research on cancer in this and other populations.

The incidence of invasive breast cancer in AN women had previously been half of USW women’s rates, but is now nearly as high, representing a 105% increase in 30 years. This dramatic rise in breast cancer incidence occurred in both pre- and postmenopausal AN women (44% and 154%, respectively). USW women have also experienced increases for both pre- and postmenopausal breast cancer during this time period, although of a
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lesser magnitude (7% and 43%, respectively). A recent study of cancer rates among Inuit populations worldwide also shows a pattern of lower breast cancer rates compared to USW, with large increases in the last 2 decades. Rates among Alaska Native women, however, are more than twice those for Canadian and Greenland Inuit (16).

An age-period-cohort analysis of breast cancer found that changes in rates among AN women were not due to changes among birth cohorts, but were best explained by a linear period effect, suggesting that the change is due to an exposure which effects all age groups during a given time period. Some of the most noticeable changes in the AN population over the last half century are an increasing prevalence of obesity and diabetes, and a change in diet (17). Alaska BRFSS data show an increase in the prevalence of overweight and obesity (BMI≥25) from 54% in 1991–1993 to 66% in 1999–2001. Prevalence of overweight and obesity during the 1991–1993 and 1999–2001 time periods for U.S. women were 40% and 49%, respectively (18). Obesity is considered a risk factor for breast, uterine and ovarian cancer. Several prospective cohort studies have shown that high BMI is related to a reduced risk of breast cancer among premenopausal women and an increased risk among postmenopausal women (19). Since both pre- and postmenopausal rates increased among AN women, increases in obesity levels alone do not appear to explain rate changes.

An increase in the prevalence of diabetes mellitus is associated with an increase in BMI, while diabetes is also considered an independent risk factor for breast and uterine cancer (20). Alaska Natives have a low prevalence rate of diabetes (31 per 100,000 in 2000) as compared to all U.S. race estimates (42 per 100,000 in 1999), although rates for Alaska Natives increased 80% between 1985 and 1998 and continue to rise (17). However, New Mexican AI women, who have much higher rates of diabetes (88 per 1000 in 1999) (21) than AN women, have significantly lower rates of breast cancer (48.4 per 100,000 in 1999–2002) (11).

The traditional diet of Alaskan Natives has differed from that of non-Natives in the U.S. However, changes in Native diet have occurred over the last 3 decades, with increasing consumption of store-bought food (22). Younger age groups in particular appear to be eating less traditional diets than older age groups. In a recent study in northern Alaska, store-bought foods were the main sources of energy, carbohydrates, fat, saturated fat and fiber for AN adults (22). Consumption of foods high in carbohydrates has increased, while consumption of foods rich in omega-3 fatty acids has declined. Omega-3 fatty acids have been shown to inhibit tumor formation in animal models (23,24). It is possible that the traditional AN diet was protective from breast and other cancers, and that this protection is being lost with dietary change.

Fertility rates among AN women, a protective factor, have declined significantly during the study period, although the percentage of nulliparity has not changed significantly (25). Other important risk factor data such as age at first birth and prevalence of hormonal therapy are not readily available for this population. These data are important to collect for this population.

Uterine cancer rates among AN women have been low since data collection began in 1969, as they have been for other AI groups (16,21). During the study period, incidence rates for AN
women appeared to increase 500%, while rates for USW women declined 30%. However, the numbers of deaths among AN women are so small that even a missed case in the earliest time period would greatly change the magnitude of these trends. Still, although uterine cancer rates for AN women have clearly increased over the study period, they are now only about half those of USW women. Examination of uterine cancer rates for pre- and postmenopausal AN women revealed that increases were significant only among post-menopausal (≥50 years) women. An age-period-cohort analysis suggested that changes in uterine cancer rates may be best explained by birth cohort effects. Women born in birth cohorts between 1929 and 1943 appeared to be driving the increase in uterine cancer rates. However, given that uterine cancer typically occurs at an older age, it is possible that the rate will increase for the more recent birth cohorts as they age. If this were to occur, it would more strongly suggest a period effect rather than increased risk within a particular birth cohort.

Another important consideration is that the prevalence of hysterectomies among AN women, an obvious protective factor, has increased during the study period. Age-adjusted rates of annual hysterectomies based on Alaska Native hospital data show that only 18.9 per 100,000 AN women received hysterectomies annually in the first 5-year time period of our study as compared to 1019.2 per 100,000 during the 1999–2003 time period (personal communication Neil Murphy, June 2004). The increase in hysterectomies may be masking a potentially greater increase in uterine cancer, as well as a period effect.

The strongest risk factors for uterine cancer are exposure to exogenous or endogenous estrogens and obesity (26). Birth cohort effects for uterine cancer, therefore, might be due to increased exposure to endogenous estrogens caused by a decrease in age at menarche, or an increase in nulliparity. Prevalence of nulliparity in the population (9.7%) has not changed significantly by birth cohort (25). There are currently no published studies demonstrating a decline in age at menarche to support this.

While BMI levels have increased among all age groups of AN women over the past 30 years, it is puzzling that uterine cancer rates have only increased among postmenopausal AN women. Uterine cancer is strongly and positively associated with BMI regardless of menopausal status (27). Diabetes incidence, while related to BMI, is also an independent risk factor for uterine cancer (28). Although AN women have a lower prevalence of diabetes than all other U.S. races, the prevalence over the last decade has been steadily increasing (17). It is possible that the increasingly high prevalence of obesity and “rapidly increasing” prevalence of diabetes are associated with the increases in uterine cancer rates.

AN women had similar rates of ovarian cancer as USW women for the first 25 years of the study period, while rates for AN women for the 5-year period 1999–2003, were lower than rates for USW women. Little is known of the etiology of ovarian cancer, except that advanced age, nulliparity and a family history of ovarian cancer have been consistently associated with an increased risk, whereas a number of full-term pregnancies, history of hysterectomy or tubal ligation and oral contraceptive use have been consistently associated with decreased risk (15).

AN women had higher rates of ovarian cancer with advancing years similar to USW.
Prevalence of nulliparity has not changed, and so would not explain the lower rates in the most recent 5-year period. Fertility rates among AN women, a protective factor, have declined significantly during the study period (25). The prevalence of hysterectomies among AN women, another protective factor, has increased during the study period. Oral contraceptives, also a protective factor for ovarian cancer, have been increasingly available to AN women for several decades. A 1992 study of AN women found that 92% of women 20–29 had used or were using oral contraceptives, and over half of all AN women who had reached maturity in the 1960s or later had used oral contraceptives at some time (29). Declines in ovarian cancer rates are expected within 1 decade of introduction of oral contraceptives (30). It seems unlikely that oral contraceptive use would account for the recent decline in rates, since such a large percentage of the population has used it over the last 3 decades. However, there is the possibility that the very low rate of ovarian cancer among AN women for the 1999–2003 period may be a consequence of small numbers. An informal examination of rates for the 2004–2008 time period is inconclusive (the rate is halfway between the 1994–1998 and 1999–2003 rates for AN women).

AN women had invasive cervical cancer incidence rates more than 3 times higher than USW women during the first 10 years of our study (1974–1983). Rates declined steadily from this high point through the end of our study period. Examining the data by 2 age groups (proxy for menopausal status) showed that there were excess cases among women 50 years and over as well as women under 50 years, and that the decline occurred in both groups. An analysis of age-period-cohort effects found a linear decrease in rates with period of diagnosis.

Human papillomavirus (HPV) infection is a known cause of cervical cancer (30). Oral contraceptives and smoking have been implicated as risk factors (31,32). Smoking rates remain high, but may have declined among AN women during the study period. Oral contraceptive use also appears to have been high throughout the study period (29). It seems unlikely that changes in these factors played a major role in the decline in AN women's cervical cancer rates.

It is most likely that the decline in invasive cervical cancer rates among AN women is due to screening and control efforts on the part of health care providers. The Pap test has been effective in detecting early cervical changes, which can then be treated before invasive disease occurs (29). Based on the number of total Pap tests performed in the Alaska Native health care system, it is estimated that only 45 to 65% of eligible women could have been screened in a given year before 1990. Prevalence of screening for all races in the U.S. was estimated to be 75% in 1987 (34). In 1992, the Women's Health Project (WHP) reported the frequency of cervical cancer screening among AN women in Anchorage to be approximately 75% for the years 1989–1991 (28). It is likely that women in Anchorage had higher screening rates than AN women in the rest of the state, mainly due to greater access to health care facilities.
The WHP and subsequently the CDC’s Breast and Cervical Cancer Early Detection Program (BCCEDP) made increased resources available to enhance cervical screening through education, increased pap testing and follow-up of abnormal tests. Since 1995, the CDC has supported 4 tribal BCCDPs, and a State of Alaska program. These programs appear to have been successful. Alaska BRFSS data records a steady increase in Pap screening prevalence throughout the 1990s. In 2004, 90% of AN women throughout the state reported having had a Pap test in the previous 3 years (35). This prevalence was slightly higher than the 86% reported in 2004 by BRFSS for all races in the U.S. (36). It is likely that these increases in screening are responsible for the lower rates of invasive cervical cancer.

Conclusions

In summary, this study documents continued differences in cancer rates and trends over time of AN women compared to USW women. Cancers of the breast and uterus have increased, while cancer of the cervix has decreased and cancer of the ovary has been stable for all except possibly the last 5 years of the 30-year study period. The significant rise in breast cancer incidence may be best explained by a period effect (i.e., changes in environmental factors), and the increase in uterine cancer could be explained this way as well. If a period effect exists for breast and uterine cancer, the greatest changes in known risk factors have been in increased obesity and a progressive change to a non-Native diet. The decrease in cervical cancer is most likely due to improved screening programs. Continuing surveillance of cancer and studies of risk factors are needed to better understand the observed patterns and trends in breast, uterine, ovarian and cervical cancer among Alaska Native women.

REFERENCES

1. Parkin DM, Pisani P, Ferlay J. Global cancer statistics. CA Cancer J Clin 1999;49:33–64.
2. Mettlin C. Global breast cancer mortality statistics. CA Cancer J Clin 1999;49:138–144.
3. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. Int J Cancer 1999;80:827–841.
4. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics 2002. CA Cancer J Clin 2002;52:23–47.
5. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics 2008. Cancer J Clin 2008;58:71–96.
6. Grady D, Erstner VL. Endometrial cancer. In: Schottenfeld D, Fraumeni JF Jr, editors. Cancer epidemiology and prevention. 2nd ed. New York: Oxford University Press; 1996. p. 1058–1089.
7. Parker SL, Johnston Davis K, Wingo PA, Ries LAG, Heath CW Jr. Cancer statistics by race and ethnicity. CA Cancer J Clin 1998;48:31–48.
8. Lanier AP, Kelly JJ, Holck P, Smith B, McEvoy T, Sandidge J. Cancer incidence in Alaska Natives – thirty year report, 1969–1998. Alaska Med 2001;43:87–115.
9. Ehrsam G, Lanier AP, Holck P, Sandidge J. Cancer mortality among Alaska Natives, 1994–1998. Alaska Med 2001;43(3):50–69.
10. Cobb N, Paises RO. Cancer mortality among American Indians and Alaska Natives in the United States: regional differences within the Indian Health Service, 1989–1993. Rockville, MD: Department of Health and Human Services, Indian Health Services, IHS Pub. No. 97-615-23;1997. 83 p.
11. Davis SM, Cunningham-Sabo L, Lambert LC. Native outreach, a report to American Indian, Alaska Native and Native Hawaiian communities. Executive summary, Appendix C. SEER incidence and mortality rates, 1988–1992. National Institutes of Health 98–4341s, 1999. 25 p.
12. SEER®Stat Database: Incidence - SEER 9 Regs Public-Use, Nov 2003 Sub (1973–2001), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch. [cited 2004 Apr 14]. Available from: http://www.seer.cancer.gov/ 
13. Matthews JNS. Statistical methods in medical research. 4th ed. Oxford: Blackwell Science; 2002. 832 p.
14. Schlesselman JJ, Stolley PD. Case-Control Studies. New York: Oxford University Press; 1982. p. 203-206.
15. Zhang J, Ugnat A-M, Clarke K, Mao Y. Ovarian cancer histology-specific incidence trends in Canada 1969–1993: age-period-cohort analyses. Br J Cancer 1999; 81(1):152–158.
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16. Kelly J, Lanier A, Santos M, Healy S, Louchini R, Friiberg J, et al. Cancer among the circumpolar Inuit, 1989–2003 II. patterns and trends. Int J Circumpolar Health 2008;67(4):408–420.

17. Naylor JL, Schraer CD, Mayer AM, Lanier AP, Treat CA, Murphy NJ. Diabetes among Alaska Natives: a review. Int J Circumpolar Health 2003;62(4):363–387.

18. The burden of overweight and obesity in Alaska. Anchorage (AK): Alaska Department of Health and Social Services, Division of Public Health, Section of Epidemiology, Health Promotion Unit; 2003. 28 p.

19. Hunter DJ, Willet WC. Diet, body size, and breast cancer. Epidemiol Rev 1993;15:110–132.

20. Collaborative group on hormonal factors in breast cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. Lancet 1996;347:1713–1727.

21. Gilliland FD, Mahler R, Hunt WC, Davis SM. Preventive healthcare among rural American Indians in New Mexico. Prev Med 1999;28:194–202.

22. Nobmann ED, Ponce R, Mattil C, Devereux R, Dyke B, Ebbesson SOE, et al. Dietary intakes vary with age among Eskimo adults of northwest Alaska in the GO-CADAN study, 2000–2003. J Nutr 2005;135:856–862.

23. Rose DP, Connolly JM. Omega-3 fatty acids as cancer chemopreventive agents. Pharmacol Ther 1999;83:217–244.

24. Ip C. Review of the effects of trans fatty acids, oleic acid, n-3 polyunsaturated fatty acids, and conjugated linoleic acid on the mammary carcinogenesis in animals. Am J Clin Nutr 1997;66:1523S–1529S.

25. Status of Alaska Natives report 2004, chapter 2, May 2004. [cited 2009 Dec 18]. Available from: http://www.iser.uaa.alaska.edu/Home/ResearchAreas/statusaknatives.htm.

26. Parazzini F, La Vecchia C, Negri E, Fedele L, Balotta F. Reproductive factors and risk of endometrial cancer. Am J Obstet Gynecol 1991;164:522–527.

27. Weiderpass E, Persson I, Adami HO, Magnusson C, Lindgren A, Baron JA. Body size in different periods of life, diabetes mellitus, hypertension, and the risk of postmenopausal endometrial cancer. Cancer Causes Control 2000;11:185–192.

28. Ma J, Pollak MN, Giovannucci E, Chan JM, Tao Y, Hennekens C, et al. Prospective study of colorectal cancer risk in men and plasma levels of insulin-like growth factor (IGF)-1 and IGF-binding protein-3. J Natl Cancer Inst 1999;91:620–625.

29. Lanier AP, Kelly JJ, Berner J. The Alaska Native women’s health project to reduce cervical cancer. In: Glover CS, Hodge FS, editors. Native outreach: a report to American Indian, Alaska Native and Native Hawaiian communities. NIH, NCI; 1992. 138 p.

30. McKeen-Cowdin R, Feigels HS, Ross RK, Pike MC, Henderson BE. Declining cancer rates in the 1990s. J Clin Oncology 2000;18(11):2258–2268.

31. Moreno V, Bosch FX, Muñoz N, Meijer CJ, Shah KV, Walboomers JM, et al. Effect of oral contraceptives on risk of cervical cancer in women with human papillomavirus infection: the IARC multicentric case-control study. Lancet 2002;359(9312):1085-1092.

32. Ylitalo N, Sørensen P, Josefsson A, Frisch M, Sparén P, Pontén J, et al. Smoking and oral contraceptives as risk factors for cervical carcinomas in situ. Int J Cancer 1999;81(3):357–365.

33. McNagnhten AD, Neal JJ, Li J, Fleming PL. Epidemiologic profile of HIV and AIDS among American Indian and Alaska Natives in the USA through 2000. Ethnicity and Health 2005;10(1):57–71.

34. Hiatt RA, Klabunde C, Breen N, Swan J, Ballard-Barbash R. Cancer screening practices from national health interview surveys: past, present, and future. JNCI 2002;94(24):1837–1846.

35. Health Risks in Alaska Among Adults - State of Alaska BFRSS [Internet]. Juneau: Alaska Department of Health & Social Services; 2005 [cited 2009 Dec 18]. Available from: http://www.hss.state.ak.us/dph/chronic/hsl/bfrss/pubs/BFRSS0405.pdf

36. National Center for Chronic Disease Prevention & Health Promotion Behavioral Risk Factor Surveillance System. Prevalence and trends data [Internet]. Nationwide (States and DC) ’2004 women’s health [cited 2009 Jul 6]. Available from: http://apps.nccd.cdc.gov/BRFSS/display.asp?cat=WH&yr=2004&qkey=4426&state=UB

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