DIABETES AMONG ALASKA NATIVES: A REVIEW

dedicated to the memory of Dr. Edward Scott and Dr. George Mouratoff,
and to those who participated in their studies – the pioneers

ABSTRACT

This review summarizes the published information on diabetes mellitus and gestational diabetes among Alaska Natives. The most recently published age-adjusted prevalence was 28.3/1000 in 1998. There is evidence of a steadily increasing prevalence, documented both by cross sectional screening studies and patient registry methods. The overall incidence rates in 1986-1998 of lower extremity amputation (6.1/1000) and renal replacement therapy (2.1/1000) appear to be lower than those in other Native American populations in the United States. Incidence of stroke and MI in 1986-1998 varied widely by ethnic group and gender with Eskimo women having the highest rate of stroke (19.6/1000), and Aleut men the highest rate of MI (14/1000).
The overall mortality among diabetic Alaska Native people in 1986-1993 (43.2/1000) was somewhat lower than that in other US diabetic populations, with heart disease being the most common cause of death. A high rate of gestational diabetes (6.7%) was reported in one region in 1987-88, but this appeared to decline following nutritional education intervention. In screening studies, the prevalence of abnormal glucose tolerance has been found to be positively associated with body mass index and negatively associated with daily seal oil or salmon consumption and higher levels of physical activity. Observations on the prevalence and relationships among other factors in the insulin resistance syndrome are summarized. Suggestions for prevention of diabetes and further studies are presented.

Keywords: diabetes, Alaska Natives, Alaskan Indian, Aleut, gestational diabetes, complications
INTRODUCTION

In the 1950s and 1960s diabetes was thought to be a rare condition among Alaska Natives. However, in the 1980s, health care providers suspected that the condition was becoming increasingly common. In 1985, the Indian Health Service Diabetes Program conducted a conference for health care providers in the Alaska Native health care system. At this conference, the high prevalence of diabetes among American Indians and the aspects of care deemed important for optimum treatment were presented. However, it became apparent that information on the prevalence of diabetes among Alaska Natives and the level of care provided were only anecdotal.

In response to those observations, the Indian Health Service and the tribal health care facilities initiated a program to review records and identify those individuals who had evidence of glucose intolerance. This review led to the establishment of a registry of patients with diabetes and other degrees of glucose intolerance. From this registry, the prevalence of diagnosed diabetes was determined and efforts to optimize care for these individuals were undertaken. As interest in the problem grew, several research projects to screen adults in selected regions were carried out. The purposes of this paper are to summarize the published data on diabetes among Alaska Natives, to elucidate the strengths and limitations of the information, and to suggest directions for future endeavors.

METHODS

The authors of this article have been involved in every study of glucose tolerance among Alaska Natives conducted since 1985 and maintain a file of publications resulting from these studies. This file and the reference lists were reviewed. In addition, the published literature on diabetes and Alaska Natives was searched using PubMed.

Early Studies

The earliest survey for diabetes among Alaska Natives was conducted in 1957 (1). This survey among Eskimos from all parts of Alaska tested 869 National Guardsmen and 358 urban residents over the age of 35 years. A variety of screening tests were used, including capillary glucose determinations using different laboratory methods. Selected
individuals received follow-up fasting and/or glucose tolerance testing. A survey of all health care facilities serving the 16,000 Eskimo residents of Alaska was performed, though the details of methodology were not described. Results of this study indicated that three to six cases of diabetes were present in the population; all were over the age of 35 years, for a prevalence of 0.8-1.6/1000 in this age group and an overall crude prevalence of 0.2-0.4/1000, depending on diagnostic criteria. A review of vital statistics revealed no deaths due to diabetes among Eskimos from 1949 to 1954.

Over the next 15 years four more studies among Alaska Natives were conducted, two among Eskimos, one among Athabascan Indians, and one among Aleuts of St. Paul Island (2-5). A survey in 1962 stated that 8 Eskimo individuals were known to have "clinical diabetes mellitus" while a screening study in Yupik residents of 10 villages in the Yukon-Kuskokwim region revealed 8 of 705 people \( \geq 20 \) years of age \((11.3/1000)\) probably had diabetes based on glucose tolerance tests interpreted by World Health Organization (WHO) 1985 criteria (2,6). Among those \( \geq 40 \) years, 5 of 296 (16.9/1000) had type 2 diabetes. A decade later the same researchers studied 320 people from six of the same villages (4). While they did not publish results of individual glucose tolerance tests, they concluded that "4.5% more were intolerant of glucose" and that "about 6% more persons were overweight". They observed that a 10 kg change in weight was associated with an average change in the 2-hour glucose level of 20 mg/dl in men and 16 mg/dl in women. Among those tested in both studies, a 10-year increase in age resulted in an average increase of 4 mg/dl in the fasting and 2 hour glucose values. They made the interesting observations that there were so few obese Eskimos that the relationship of obesity to glucose tolerance could not be assessed, and speculated that the rare occurrence of diabetes was related to "a high degree of physical fitness."

The same researchers carried out a glucose tolerance survey among 306 Alaskan Athabascan Indians \( \geq 20 \) years of age in 1965 (3). They were interested in comparing this group to Alaskan Eskimos because they noted that the diets of both groups were "of similar composition—high in protein, low in carbohydrate, and moderate in fat content. The average daily sugar consumption by Eskimos is 32 grams, and that by Indians 56 grams." Interpreted by 1985 WHO criteria, three people \((9.8/1000)\) had diabetes. All the individuals with diabetes were \( \geq 40 \) years old for a prevalence of 18.4/1000 in this age
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In the 1960s, Mouratoff and Scott (1) surveyed Yupik Eskimos and Athabascans in the Circumpolar North and found higher prevalences of diabetes than did their surveys of health care facilities and limited screening among Eskimos in general a decade earlier. The differences may be due to changes over time, different populations studied, or different laboratory methods. However, it is more likely that it demonstrates a greater sensitivity of screening studies as compared to compilation of clinically recognized cases, especially in the pre-computerized records era. This must be considered when comparing prevalence data derived from screening studies as compared to clinical registries and database searches.

There were several limitations to these early studies. There were no consistent definitions of diabetes or impaired glucose tolerance, screening methods and criteria for follow-up testing varied, and several different laboratory techniques for the determination of glucose were employed. Some of these involved venous whole blood, some involved plasma, and some utilized capillary blood. The earliest study (1) screened many National Guardsmen, who were unlikely to have diabetes, although this probably was not realized at the time. The objectives of the studies do not appear to have been focused on determination of prevalence of diabetes, but rather on the correlation of glucose levels with other factors such as age, weight, gender, and parity of women. There were no computerized medical records systems in place at that time, so surveys for clinically recognized cases depended on local knowledge and extensive reviews of unselected...
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records. Nevertheless, these researchers and the participants in these studies provided us with valuable background information against which future clinicians and researchers would be able to evaluate an evolving picture of this complex condition.

Prior to the mid 1980s, the only other published information on the occurrence of diabetes among Alaska Natives consists of two letters to the editors of JAMA from physicians at the Alaska Native Medical Center and the Public Health Service Hospital in Barrow in 1974 (7,8). These physicians attested to the rarity of diabetes; one pointed out that seven cases, all over 44 years of age, were known among the Native residents of Barrow. The letter claimed that the 1970 census showed 315 residents over 44 years of age; this would indicate that the prevalence was 22/1000 in this age group. The other physician claimed that most diabetic patients had some European or Russian ancestry, often individuals who themselves were diabetic. He noted that he had never seen type 1 diabetes among full-blooded Alaska Natives.

Prevalence information from the mid-1980s until present
The lack of any further studies of diabetes among Alaska Natives in the nearly 20 years following Mouratoff’s and Scott’s work seemed reasonable, given its low prevalence in most of the early studies and its rarity as a recognized clinical problem. However, by the 1980s, evidence clearly showed that diabetes and its complications had become a devastating condition for many tribes of American Indians. In 1979, a computerized patient care information system (PCIS) was begun in the Alaska Native health care systems. It stored International Classification of Disease, Ninth Edition, (ICD-9) coded information on outpatient visits, admissions, and problem list entries for all people using the Native health care system.

An initial search of the PCIS system and case reports from health care providers revealed that 1607 patients’ records contained ICD-9 codes for diabetes and other diagnoses of glucose intolerance (9). The authors reviewed the records of these patients and found that 610 Alaska Natives residing in Alaska at the end of 1985 met WHO 1985 criteria for diabetes (6). Of these, 564 (92.5%) had type 2 diabetes, 15 (2.5%) had type 1 diabetes, and 31 (5.1%) had diabetes secondary to other conditions or inadequate data to determine the type.

The overall crude prevalence of diagnosed diabetes among Alaska Natives in 1985 was determined to be 8.3/1000 (610 cases, 73,798
There was a wide range of age-adjusted prevalences among the three major ethnic groups; 8.8/1000 among Eskimos, 22.0/1000 among Indians, and 27.2/1000 among Aleuts. There was an even wider range by geographic area (which largely corresponds to ethnic sub-divisions of the population) from 5.8/1000 in the Yukon Kuskokwim Delta region (primarily Yupik Eskimo) to 31.1/1000 among the Tsimshian Indians of Annette Island in southeastern Alaska.

It was noted at that time that the population referred to as "Aleut" in the medical records system actually consisted of sub-populations of people indigenous to the Aleutian and Pribiloff Islands, the Kodiak area, parts of the Alaska Peninsula, Cook Inlet, and Prince William Sound regions. The people of the Alaska Peninsula, Kodiak Islands, Cook Inlet, and Prince William Sound have a separate ancestry from those of the Aleutian and Pribiloff Islands and today are referred to as Alutiiq or Suqpiq (10). The age-adjusted prevalence of diabetes in "Aleut" sub-groups ranged from 69.2/1000 on St. Paul Island to 20.0/1000 for the Aleuts of the Aleutian Islands while the "Aleuts" not residing in the Aleutians or Pribilofs (primarily Alutiiq or Suqpiq people) had a prevalence of 24.4/1000. Thus in 1985, the populations with the highest prevalence of diabetes were several ethnicities from the Aleutian Islands through the southeast panhandle. These populations had the earliest contact with Caucasian cultural influence (9).

Following the initial publication of 1985 prevalence, an update described the prevalence in 1987 (11). This updated information was used as the basis for a comparison of prevalences of diagnosed diabetes in several circumpolar populations. The data on those indigenous to the Chukotka Peninsula and Canada were based also on patient care registries (12). All prevalences were age standardized to the hypothetical world population used by the International Agency for Research on Cancer (13). This comparative review demonstrated that the lowest prevalence of diagnosed diabetes occurred among the Chukotka Native people (1.8/1000) and the highest among Alaskan Aleuts (22.7/1000). Young pointed out the east to west gradient of increasing prevalence across the Canadian Arctic and Alaska. He noted that this corresponded to the history of influence by Euro-American culture, a pattern consistent with our observations within Alaska (9).

In most Alaska Native ethnic groups, the prevalence was lower than that in Non-Alaskan American Indians, among whom many have an
exceptionally high occurrence of type 2 diabetes. The Pima Indians of Arizona had a prevalence as high as 341/1000 in 1977 (14). However, Alaska Natives had a lower prevalence than the US general population of 24.7/1000 as recorded in 1985 (15).

Only two studies among Alaska Natives have reported the prevalence of diabetes based on oral glucose tolerance tests (OGTT) given to all participants. These were conducted among the Eskimos of the Bering Straits region. The first survey, a small pilot study done in 1992 among Siberian Yupik people (Yupik people indigenous to St. Lawrence Island), examined participants ≥ 40 years of age. Participants received a fasting determination of lipids, insulin, and glucose, and a 2-hour 75 gm OGTT (16). Among the 65 participants ≥ 40 years of age, 9% met WHO criteria for diabetes and 12% met criteria for impaired glucose tolerance (IGT). This diabetes prevalence was considerably higher than that among all Alaskan Eskimos ages ≥ 45 of 3.3% in 1993 based on the clinical registry (17).

In 1994, this study was expanded to include four villages in the Bering Straits region; two Siberian Yupik Eskimo, one Central Yupik and one Inupiat village. (The term "Central Yupik" refers to Yupik Eskimo populations indigenous to regions of Alaska other than St. Lawrence Island). In this expanded study all residents ≥ 25 years of age were invited to participate (18). Of the 497 eligible men and 402 women, 43% of the men and 60% of the women participated, with a higher proportion of the ≥ 55 age group participating. The prevalence of diabetes among the Siberian Yupik was significantly higher than in either of the other two groups (Siberian Yupik 9.6%, Inupiat, 3.7%, Central Yupik 2.8%). The prevalence of IGT ranged from 6.4% to 14.2% and did not differ significantly vary by ethnic group. Overall, women had a higher prevalence of abnormal glucose tolerance (diabetes and IGT: women 20.4%, men 8.9%) and obesity (women 47.3%, men 25.5%) than men.

Type 1 diabetes is rare in Native Americans (19) and is also rare in Alaska Natives. In 1985, a review of 610 Alaska Natives residing in Alaska showed fifteen (2.5%) had type 1 diabetes. However, only one was an Alaska Native with full blood quantum (9). Data from two of the Eskimo villages studied by Ebbesson in 1994 showed that the presence of type 1 related autoantibodies GAD65Ab and IA-2Ab had no relationship to glucose tolerance status (20). The investigators concluded that these populations were affected by type 2 diabetes and not by latent autoimmune diabetes of adulthood (LADA).
Evidence for an increase in prevalence of diabetes

Prevalence based on cases in the same patient care management registry was reassessed in 1993 and 1998 and showed a steady increase (17,21). Overall, the prevalence increased from 15.7/1000 in 1985 to 28.3/1000 in 1998, an 80% increase. A steady increase was seen in all regions and sub-populations. However, among the major ethnic groups, Eskimos, who consistently had the lowest prevalence, showed the highest rate of increase from 1985 to 1998 (Eskimos 110%, Aleuts 81%, Indian 57%). During a similar time period, 1985 to 1996, the US had an increase in prevalence from 26.7/1000 to 30.1/1000, a 13% increase (22).

Further evidence of this change in prevalence was provided by a study done in the Yukon-Kuskokwim Delta Region in 1987-88 (23). In this study residents ≥ 40 years of age of the same Yupik villages surveyed by Mouratoff and Scott in 1962 were invited to participate in screening for elevated glucose, which consisted of a random glucose determination by fingerstick and venous blood sample. If the random glucose value was ≥ 120 mg/dl (6.72 mM) on the fingerstick or the venous sample, the participant was asked to return on a later day for a 2-hour 75 gram oral glucose tolerance test (OGTT). The results were interpreted according to the 1985 WHO criteria. In addition to the 10 Yupik villages, four Athabascan villages participated (different villages from those screened by Mouratoff). Among Yupik participants ≥40 years of age, the prevalence of diabetes had increased from 1.7% in 1962 to 4.7% over the 25-year time interval. Among the Athabascans >40 years, the prevalence was 10.0%, compared to 1.8% in the earlier study. The 1987 study found that the prevalence of diabetes was higher for women than men in both ethnic groups (Eskimo: women, 6.3%, men 2.8%; Athabascan: women 12.5%, men 7.4%). Overall, the difference between men and women in both ethnic groups was statistically significant. In this study, 2.3% of the Eskimo and 4.5% of the Athabascan participants met criteria for IGT.

A national study based on medical records addressed the increase in prevalence of diabetes among Alaska Natives compared to that among other Native Americans (24). The national Indian Health Service computerized medical record database, which includes the Alaska Native computerized records, was searched for patients with a diagnosis of diabetes based on ICD-9-CM codes. These records were then grouped into geographic areas rather than tribes. Age-adjusted prevalence was calculated for each year from 1990 to 1997. The Alaska Native
prevalence was calculated to be 3% (age adjusted to the 1980 US population), the lowest among Native American geographic groups (highest: Atlantic region 17.4%). However, Alaska Natives had the highest rate of increase at 76% (lowest: Northern Plains region 16%). There are two important differences in methods between this study and the Alaska Native studies based on individual medical record review. The national study included all Native Americans living in Alaska while the Alaska studies reported data only on Alaska Natives. The national study did not review records to determine which patients met diagnostic criteria for diabetes based on laboratory values. In spite of these differences, the overall conclusions are consistent: that Alaska Natives have a lower prevalence of diabetes than other Native Americans but are experiencing a rapid increase.

### Table I. Diabetes prevalence at various points in time, Alaska Natives.

| Ethnicity         | Year of Study | Age | Cases | Population | Prevalence | Study Method | Reference          |
|-------------------|---------------|-----|-------|------------|------------|--------------|--------------------|
| **ESKIMO**        |               |     |       |            |            |              |                    |
| All Eskimo        | 1957          | ≥35 | 3-6   | 3680       | 0.8 to 1.6 | C            | Scott 1957 (1)     |
| All Eskimo        | 1985          | ≥35 | 166   | 10082      | 16.5       | C            | Schraer 1988 (9)   |
| All Eskimo        | 1993          | ≥35 | 297   | 13578      | 21.9       | C            | Schraer 1997 (17)  |
| All Eskimo        | 1985          | ≥45 | 148   | 6481       | 22.8       | C            | Schraer 1988 (9)   |
| All Eskimo        | 1993          | ≥45 | 269   | 8048       | 33.4       | C            | Schraer 1997 (17)  |
| Central Yupik***  | 1962          | ≥40 | 5     | 296        | 16.9       | S            | Mouratoff 1967 (2) |
| Central Yupik     | 1987          | ≥40 | 26    | 556        | 46.8       | S            | Murphy 1992 (23)   |
| Central Yupik     | 1994          | ≥45 | 2     | 47         | 42.6       | S            | Ebbesson 1998 (18) |
| Siberian Yupik****| 1992          | ≥40 | 6     | 65         | 92.3       | S            | Schraer 1998 (16)  |
| Siberian Yupik****| 1994          | ≥45 | 19    | 126        | 150.8      | S            | Ebbesson 1998 (18) |
| Inupiat           | 1974          | ≥45 | 7     | 315        | 22.2       | C            | Fisher 1974 (8)    |
| Inupiat           | 1994          | ≥45 | 4     | 57         | 70.2       | S            | Ebbesson 1998 (18) |
| **INDIAN**        |               |     |       |            |            |              |                    |
| All Indian        | 1985          | ≥45 | 257   | 4273       | 60.1       | C            | Schraer 1988 (9)   |
| All Indian        | 1993          | ≥45 | 413   | 6394       | 64.6       | C            | Schraer 1997 (17)  |
| Athabascan        | 1965          | ≥40 | 3     | 163        | 18.4       | S            | Mouratoff 1969 (3) |
| Athabascan        | 1987          | ≥40 | 11    | 110        | 100.0      | S            | Murphy 1992 (23)   |
| **ALEUT**         |               |     |       |            |            |              |                    |
| Aleut, St. Paul Is| 1973          | ≥35 | 18    | 156        | 115.4      | S            | Dippe 1975 (5)     |
| All Aleut         | 1985          | ≥35 | 129   | 2686       | 48.0       | C            | Schraer 1988 (9)   |
| All Aleut         | 1993          | ≥35 | 211   | 3598       | 58.6       | C            | Schraer 1997 (17)  |
| All Aleut         | 1985          | ≥45 | 110   | 1706       | 64.5       | C            | Schraer 1988 (9)   |
| All Aleut         | 1993          | ≥45 | 183   | 2132       | 85.8       | C            | Schraer 1997 (17)  |

* per 1000
** S=screening study, C=clinically recognized cases
*** Yupik Eskimo populations indigenous to regions of Alaska other than St. Lawrence Island
**** Yupik Eskimo population indigenous to St. Lawrence Island
Table I summarizes the estimates of the prevalence of diabetes among Alaska Natives at different points in time until 1994. The table was devised by looking at published numbers of cases and populations, and computing prevalences based on those data. This summary suggests that prior to 1980 diabetes may not have been as rare among Eskimos as previously thought, compared to our data in 1985 based on clinically recognized cases. For example, the prevalence of diabetes in Eskimos >45 years of age in 1985 was 22.8/1000, almost identical to that reported in Barrow in 1974 (9,8). Mouratoff’s publication of cases among the Central Yupik in 1962 indicated a prevalence of 16.9/1000 in those aged ≥ 40 years (2). The overall Eskimo prevalence in 1985 among those ≥ 35 years was 16.5/1000.

Comparison of these studies over time has some limitations. As noted above, the earlier studies were not designed primarily to determine prevalence. The only studies in which every participant received an OGTT were those in the Bering Straits region in 1992 and 1994. In all the others, some individuals were selected to receive an OGTT based on screening values that were above certain cut-off points. The data based on the clinical registry cannot be directly compared to that in research studies since the registry includes only those people with diabetes diagnosed in the course of routine care. Nevertheless, some comparisons are meaningful. Murphy’s 1987 data compared to that of Mouratoff in the 1960s probably indicates a true increase among Central Yupiks and Athabascans. Comparison over time of clinical registry data can be made because this data was collected by consistent methods over the 13 years of reporting, and no major changes in the routine screening for diabetes were known to have taken place during the years reported. The national study (24) showing a 76% increase over seven years likewise had consistent methods applied over time.

Data based on patient care registries may underestimate prevalence because of undiagnosed cases. Conversely, screening studies may overestimate prevalence, if those at higher risk are more likely to participate. In reviewing available information from three screening projects in separate regions of Alaska (17), we found that the proportion of new cases to previously diagnosed ranged from 1:3 to 1:12. However, our experience in screening activities is that people who believe they are at risk to develop diabetes or cardiovascular disease for reasons such as family history, or prior diagnoses of elevated glucose levels, tend to seek out opportunities to be screened. For example, in
the study in the Bering Straits villages, 80% of the people already known to have diabetes participated, while the overall participation rate was 50.5% (18). This has two potential effects on the study results; one is a falsely high estimate of prevalence, and the other is that the ratio of new to previously diagnosed cases may be falsely low.

The State of Alaska Section of Epidemiology analyzed data from the Alaska Behavioral Risk Factor Surveillance System (BRFSS), which is an ongoing telephone survey of residents age 18 and older (25). Data compiled from 1991-2000 showed that Alaska Natives had a prevalence of 38/1000. This was lower than the prevalence for African-Americans (48/1000) and Hispanics (43/1000) but slightly higher than that for whites (33/1000). The fact that Alaska Natives now have a higher prevalence than whites is of concern.

Incidence
Only one publication has addressed the incidence of diabetes among Alaska Natives (17). Overall, the incidence in the years 1986 to 1993 was 15.0/10,000. Aleuts experienced the highest incidence at 22.2/10,000 while Eskimos had the lowest at 10.0/10,000 and Indians were intermediate at 18.5/10,000 (age-adjusted to the US 1980 population). Among regions, only Annette Island (Tsimshian Indian) had an incidence in excess of that reported for the US (Annette Island: 31.7/10,000, US: 24.2/10,000, (26)).

It may seem paradoxical that the Alaska Native prevalence of diabetes increased rapidly over a period of time when the incidence was relatively low compared to the US rate. However, at baseline, the prevalence was low compared to that of the US, so a relatively small increase in the number of cases could raise the prevalence by a high percentage from the baseline. Furthermore, there is a limitation in this incidence data because it is based on clinically recognized cases rather than systematic repeated screening of the population. Some patients diagnosed in 1986 through 1993 may have had the disease onset prior to 1986 but this was not recognized.

Complications of diabetes
Data on complications of diabetes derives from the Alaska Native diabetes registry and has been published in two articles (17, 21) The first article describes the incidence of myocardial infarction (MI) and stroke for the period 1986-1991, and the incidence of end-stage renal di-
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Amputation

Amputation incidence overall for 1986-1998 was 6.1/1000 (21). This is lower than rates for other Native Americans with diabetes, which have been reported to range from 7.3 to 29/1000 (21,27,28), and within the range reported for the US (3.7 to 8.8/1,000 (29)). For years 1986-93, the rates were calculated for each major ethnic group and gender. Men and Aleuts had the highest rates (all men 7.5/1000, all women 3.4/1000, Aleuts 10.5/1000, Indians 4/1000, Eskimos 3/1000). The differences between Aleuts and each of the other groups were significant, as was the difference between men and women. Of note was the fact that Aleuts also had a higher risk of repeat amputation. The incidence of amputation declined by over 50% following the initiation of a foot care program that involved education of providers, including village health aides, and institution of a specialized foot clinic (17). The lower amputation rate among Alaska Natives compared to other Native Americans may be the result of clinical programs, a shorter duration of diabetes, or as yet unidentified intrinsic factors.

End Stage Renal Disease

The overall dialysis incidence for diabetic ESRD for 1986-1998 was 2.1/1000 (21) which was substantially lower than rates reported for other Native American diabetic populations (30,31). For the period 1986-93, the rates were reported for each major ethnic group and gender (17). Indians had the highest rate (2.6/1000) followed by Aleuts (1.9/1000) and Eskimos (1.0/1000). Indians of southeastern Alaska had the highest rate at 4.4/1000, significantly higher than other Alaska Indians. Overall, including all ethnic groups, women had a slightly higher rate (2.3/1000) than men (1.6/1000). However, the gender difference was not statistically significant. As for amputations, the incidence of renal replacement fell with time during the 1986-93, which may have been a result of improved care practices, including the use of renal- protective agents in blood pressure control. However, the overall lower rate compared to other Native Americans may also be due to a shorter duration of diabetes or other intrinsic factors.
Myocardial infarction and stroke
Between 1986 and 1991, the overall incidence of confirmed MI was 8.1/1000 (confirmed by EKG and/or enzyme criteria, age adjusted to the US diabetic population). Eskimos had the lowest rate of MI (6.2/1000 person-years), Indians were intermediate (8.4/1000) and Aleuts had the highest rate (10.2/1000) (17). Overall, men had a higher rate than women (men, 11.4/1000, women 5.8/1000). For stroke the picture was different. The overall incidence was 10.6/1000; Eskimos had the highest rate at 17.6/1000, Aleuts were intermediate at 11.5/1000, and Indians had the lowest incidence at 5.7/1000. The Eskimo-Indian difference was significant. Women had a higher stroke incidence than men (women, 12.8/1000, men, 7.2/1000). Of all the ethnic and gender groups of diabetic people, Aleut men had the highest rate of MI (14/1000) and Eskimo women had the highest rate of stroke (19.6/1000). Compared to reports of stroke and MI in other diabetic populations, the overall stroke rate was comparable to that reported from the Mayo Clinic in earlier years (10.1/1000 (32)). However, Alaska Native women had a stroke rate much higher than that reported for a group of Caucasian diabetic nurses who were somewhat younger (Native women, 13.1/1000, Caucasians, 1.5/1000, (33)). Incidence of confirmed MI for Alaska Native women (5.7/1000) exceeded rates reported for diabetic women in the Nurses Health Study Cohort of 4.2/1000 (33) and overall for southwestern American Indians in earlier years of 1.7/1000 (34).

In summary, the incidence of stroke and MI varies considerably by ethnicity and gender, with some groups experiencing rates higher than those for other diabetic populations in the United States.

Gestational Diabetes
Routine screening for gestational diabetes among pregnant Alaska Native women was not done prior to 1986 as this condition, as well as type 2 diabetes, was believed to be rare. In 1987 several regions began screening and follow-up testing according to guidelines generally used at the time. A 1-hour 50-gram OGTT was given at 24-28 weeks gestation without regard to time since last meal; a result of ≥ 140 mg/dl (7.8 mM) was followed on a subsequent date by a 3-hour 100 gram OGTT interpreted by O’Sullivan criteria (35). Results of tests were tabulated for Alaska Native women who were residents of the Yukon-Kuskokwim Delta region (predominantly a Yupik Eskimo
population) and delivered during a 12-month period in 1987-88 (36). Among 605 women, 545 (90%) were screened, 35 had a positive OGTT, and two had previously documented diabetes, for a total of 6.1% with diabetes in pregnancy, or a total of 6.7% of those screened. This was noted to be about twice the rate for the US population and to exceed the rate of many other populations, including one American Indian population. In response to these results, an intensive effort at nutrition education, with an emphasis on reduction of sweetened beverage consumption, was initiated among pregnant women in the region. The rate of diabetes in pregnancy was reassessed in two 6-month periods in 1991 and 1993 (37). It declined to 2.3% in 1991 (p=0.03) with no change in the proportion of women tested overall or in the third trimester. In 1993, the rate had declined still further to 1.6% but the proportion of women tested in the third trimester had declined significantly, raising the possibility that detection of late onset cases was less likely.

The data on gestational diabetes in the Yukon Kuskokwim region suggests two points. One is that the high rate may indicate a potential for a further increase in type 2 diabetes, as has occurred among the Navajo Indians (38). It is notable that Yupiks had a higher rate of GDM yet a lower rate of type 2 diabetes. However, Eskimos have shown the highest rate of increase in type 2 diabetes (17). The second is that nutritional education emphasizing a reduction in sweetened beverage intake; a straightforward, discreet change in dietary habits, may hold promise in helping women to avoid this condition. However, this data was based on a limited time period and number of women, and needs further investigation to verify its applicability.

The only other report of GDM among Alaska Native women showed a prevalence of 2.5% in Southeast Alaska, predominantly Tlingit and Haida (39).

**Mortality**

Mortality among Alaska Natives with diabetes follows similar patterns to that of other diabetic populations (17). Heart disease is the most common cause of death. In the time period 1986-1993, the overall mortality rate among Alaska Natives with diabetes was 43.2/1000 person-years of observation, a rate somewhat lower than that observed in studies of diabetic populations in the US (40). The overall mortality rate was similar for the major ethnic groups and both genders.
However, Aleuts were more likely to die from ischemic heart disease than Eskimos, while Eskimos were more likely to die from cerebrovascular disease.

Factors associated with diabetes among Alaska Natives

Insulin resistance

Insulin resistance is believed to be the underlying condition leading to type 2 diabetes. The development of insulin resistance is partly genetically determined but is worsened by centripetal obesity and lack of physical activity. The insulin resistance syndrome (IRS) consists of a number of characteristics associated with a high risk of coronary artery disease (CAD). These include obesity, abnormal cholesterol with elevated triglycerides, low HDL-C, high insulin levels, glucose intolerance, and hypertension (41). Whether or not IRS is present in Alaska Natives and especially among Eskimos has been the subject of debate. However, several studies provide evidence bearing on the presence or absence of these factors associated with insulin resistance.

Obesity and Body Fat Distribution

In other populations, obesity and centripetal body fat distribution as measured by waist: hip ratios (WHR) are well-documented risk factors for type 2 diabetes. Several studies provide information on obesity in the Alaska Native population. The Yupik residents of villages studied in 1962, 1972, and 1987 documented a steady increase in the percentage of the population ≥ 40 years weighing ≥ 13.6 kg above the Caucasian average for the same age, height, and gender (2, 4, 23). The proportion increased from 3.0% to 16.3% among men and 6.1% to 27% among women. Controlling for age, the participants in Murphy’s study who had IGT or diabetes were significantly more likely to be overweight by National Center for Health Statistics criteria at that time (BMI ≥ 27.8 for men and ≥27.3 for women, (42)) than those with normal glucose tolerance. By these criteria, 34% of Eskimo men and 56% of the women were overweight; among Athabascans, 29% of the men and 55% of the women were overweight.

The Murphy study also included participants ≥ 20 years. However, those 20-39 years had a lower participation rate, and were excluded from analyses summarized above. Analyses of data from this study that included the entire sample found that prevalence of overweight significantly increased with age for all groups except Indian men and
confirmed the finding that those with IGT or diabetes were significantly more likely to be overweight (43). As with the older age category, the younger group of Yupiks when compared with Mouratoff’s participants showed a striking increase from 1962 to 1987 in the prevalence of those overweight by the earlier criteria (men, 4% to 14.9%, women, 10.1% to 28.8%) (43).

The fact that obesity correlates with abnormal glucose tolerance in Alaska Natives is especially concerning in view of the data from Eskimo participants in Ebbesson’s 1994 study in the Bering Straits region. In that study, 27.9% of the women and 36.2% of the men had a BMI of ≥25 but <30 (WHO definition of overweight, (44)); while an additional 32.8% of the women and 15.6% of the men had a BMI ≥ 30 (WHO definition of obese) (45).

Waist: hip ratios were also examined in the 1994 study (18). Women in all ethnic groups in this study were found to have mean WHR > .90 and over 90% of the women in each BMI group (normal, overweight, obese) had a WHR ≥ 0.8, which was defined as "high" for purposes of comparison to other populations (46). In contrast, among men high WHR was associated with overweight status. High WHR (≥ 0.9) was found in 42% of normal weight, 85% of overweight, and 100% of male obese participants. Since high WHR and BMI are associated with glucose intolerance, it is of concern that over 60% of women were overweight or obese and a large percentage of women had a high WHR regardless of BMI.

Other Associations
The 1992 pilot study among 65 Siberian Yupiks measured fasting insulin, glycated hemoglobin, percent body fat by bioelectric impedance, and blood pressure in addition to fasting lipids (16). Analysis showed that the participants had lower mean systolic and diastolic blood pressure, lower triglycerides, and higher HDL cholesterol compared to the US all races sample aged 45-74 years in the NHANES II survey. However, a significant positive linear correlation was noted for fasting insulin and BMI, and patients with diabetes had higher mean systolic blood pressure. The authors noted that fasting insulin levels were found to be lower than those of US Caucasians, implying greater insulin sensitivity among the Yupik participants, although several features of the insulin resistance syndrome were present. Fasting insulin was significantly and positively associated with diastolic blood pressure and fas-
ting triglycerides, even after adjustment for age, percent body fat, WHR, gender, and antihypertensive medication. However, it was emphasized that the small sample size was a limitation in the study (16).

Murphy’s 1987 study also shed some light on the components of insulin resistance syndrome among Central Yupiks and Athabascans of the Yukon-Kuskokwim Delta region. Hypertension (systolic blood pressure ≥ 140 and/or diastolic ≥ 90) was significantly associated with glucose intolerance and overweight in both genders (47).

**Genetics and Environment**

Higher fasting insulin levels have been found to be predictive of type 2 diabetes (48). In the 1994 study among the three Eskimo populations in the Bering Straits region (18), the insulin levels were determined in the same laboratory using the same technique as those in the Strong Heart Study (49). The fasting insulin levels were compared after exclusion of all participants in either study who had either IGT or diabetes by WHO criteria, or who had inadequate data to determine glucose tolerance status. Fasting insulin did not differ significantly by age or by ethnicity among the three Eskimo populations (Siberian Yupik, Central Yupik, and Inupiat) but was significantly higher for women than for men and was higher with increasing BMI (50). In a regression model adjusting for age and BMI, Eskimo men and women had significantly lower insulin levels than American Indian men and women. The lower insulin levels in Eskimos could indicate a lesser degree or prevalence of insulin resistance as compared with other Native Americans and would be consistent with the observation that Alaskan Eskimos have a lower prevalence of diabetes compared with other Alaska Natives. However, it is also possible that dietary factors and physical activity are playing a protective role.

In the 1994 Bering Straits study, participants from the three Eskimo populations were asked about a history of diabetes in parents, aunts or uncles, siblings, and children (18). In statistical models containing age, family history and obesity, all three variables were significantly associated with total abnormal glucose tolerance and with diabetes. The authors concluded that as in many populations, genetic and environmental factors play a significant role. In an effort to further examine the relative roles of these factors, a comparison was made of the diabetes prevalence among Siberian Yupik people in Alaska and those living on Russia’s Chukotka Peninsula, just across the Bering
Straits. Before the cold war, these two populations traveled back and forth frequently and some families had members living on both sides of the Straits. While among Siberian Yupik people in Chukotka, ages 25-64, the prevalence of diabetes was 1.5%; it was 6.6% among the Siberian Yupik people in Alaska. Further study among these populations may elucidate the role of diet, physical activity and other factors in the development of diabetes.

A study in Canada raised other questions about the role of insulin resistance in the health of northern people. Among Canadian Inuit, obesity was not found to correlate with glucose or insulin levels (51). Young did find however that one or more of the lipids showed a relationship to BMI. He postulated a type of selective insulin resistance among Inuit whose metabolism may reflect a traditional diet consisting almost entirely of fat and protein.

In summary, there is evidence that in spite of the lower prevalence of diabetes among Alaska Natives as compared with other Native Americans, there is some evidence of the insulin resistance syndrome in the northern indigenous populations studied. However, further observations would be needed to elucidate the role of genetic factors in different groups, and environmental factors such as diet and physical activity.

Dietary Factors
Murphy’s 1987 study in the Yukon-Kuskokwim Delta region has contributed information on the possible relationships between dietary factors and glucose intolerance among Alaska Natives. In this study, participants were given a food frequency questionnaire asking them about the 10 most common indigenous and 15 most common nonindigenous foods consumed in the region. Participants were asked whether they ate each food daily, weekly, monthly, or never, and how many times in the stated time period they ate the food (43). Among participants ≥ 40 years of age, daily consumption of seal oil suggested a protective effect against glucose intolerance with an odds ratio of 0.2 (95% CI 0.1-0.7) (52). This association was not confounded by ethnicity, age, BMI, or gender. Daily salmon consumption was also associated with protection when limited to newly diagnosed cases of glucose intolerance. The authors speculated that the fatty acid content of these indigenous foods, which are high in polyunsaturated fatty acids (PUFAs) and omega-3 fatty acids, may be protective (52).
Further observations on the possible role of fatty acids in the development of glucose intolerance were based on an analysis of fatty acid profiles in the plasma of the participants of Ebbesson’s 1994 survey in the Bering Straits region. It was reported that the 68 people with glucose intolerance had lower concentrations of some omega-3 and omega-6 fatty acids (PUFAs) and higher concentrations of palmitic and oleic acid than those with normal glucose tolerance (53). It has been postulated that omega-3 fatty acids play a role in cell membrane phospholipids and thus affect insulin secretion and action (54). Ebbesson’s data emphasize the importance of understanding the roles of dietary factors in serum fatty acid levels and their relationship to insulin resistance.

Other analyses of Murphy’s data in the Yukon-Kuskokwim Delta region, which included responses of all participants ≥ 20 years, found many associations of frequency of indigenous foods vs. non-indigenous foods with age ethnicity, glucose tolerance status and obesity (43). No clear or consistent pattern emerged with regard to glucose tolerance. For example, with Athabascans and Yupiks included, controlling for age and ethnicity, those with euglycemia had significantly higher frequencies of intake of seal oil. However, among Yupiks only, controlling for age, those with euglycemia had lower frequencies for salmon/fish and seal oil. In general, participants with glucose intolerance reported a significantly more frequent consumption of protein from nonindigenous sources. The findings regarding associations between elements of glucose intolerance and dietary intake appear to be complex, and are strongly influenced by the specific foods, ages, genders and ethnic groups involved in the analyses.

A review of dietary patterns before contact with non-indigenous societies found, in summary, that the pre-contact diet of Arctic and sub-Arctic peoples probably contained very small amounts of carbohydrate and that the major changes with contact were an increase in carbohydrates, and a decrease in total fat and protein (55). A survey of the diets of Alaska Native adults in 11 communities in several different regions of the state was conducted in 1987-88 (56). Alaska Natives in this sample consumed twice the amount of table sugar and slightly more sweetened soft drinks (not artificially sweetened) than a national sample in the NHANES II survey. Similarly, a 1985 survey of dietary intake of teenagers in the Yukon-Kuskokwim region indicated that the participants consumed three to four times the amount of sweetened soft drinks consumed by teens in the U.S. general population (57).
Some evidence suggests a possible association between dietary carbohydrate and the occurrence of diabetes among Alaska Natives. First, comparison of the dietary data gathered from Alaska Native adults in several regions and in Chukotka tundra and coastal residents indicated that Chukotka residents, who have a much lower prevalence of diabetes, ate less carbohydrate (58). Second, as dietary carbohydrate intake has increased over time so has the prevalence of diabetes among Alaska Natives. Thirdly, unpublished data from the 1994 study in the Bering Straits region found that higher carbohydrate in the diet correlated with higher waist: hip ratio (Risica, unpublished data). However, an association between high carbohydrate intake and the development of diabetes is not well supported in the literature. Further study of this issue is important in order to formulate scientifically sound recommendations for diabetes prevention.

**Physical activity**

Murphy’s 1987 study provided some evidence that physical activity may help protect against glucose intolerance (59). In this study, participants were given examples of common tasks in the region and asked whether they usually performed these activities using mechanized means or carried them out without mechanical assistance (for example, cutting wood by chainsaw or handsaw, using a motor versus paddling a boat, etc). Points were assigned to each activity based on frequency and whether or not mechanized methods were used. The points were summed for each participant and the scores were classified by tertiles into low, moderate and high levels of activity. The analysis was applied to those ≥ 40 years of age. A higher level of activity was associated with lower odds ratios for glucose intolerance when controlling for age, ethnicity, BMI, gender, and seal oil consumption. Overall, a greater percentage of Eskimos than Athabascans had high (31.6% vs. 6.7%) and moderate (33.4% vs. 24.8%) levels of activity.

The 1992 pilot study in one Eskimo village in the Bering Straits region also assessed physical activity by asking participants “How often do you exercise vigorously enough to work up a sweat or breathe hard?” Those who reported exertion of this magnitude less often than once a week were designated as sedentary in the analysis (16). Among those with diabetes, IGT and normal glucose tolerance, 50%, 25%, and 10% respectively, were sedentary.
FUTURE DIRECTIONS

There is much to be learned about the occurrence of diabetes and its determinants among northern indigenous people. All research studies to date have been cross-sectional and therefore have major limitations in terms of examining risk factors and effectiveness of possible interventions in the area of primary prevention. There exists a strong need for longitudinal studies using population-based cohorts to establish better prevalence and incidence data, and to examine the roles of lifestyle factors in the genesis of type 2 diabetes. While there is a need to further elucidate the basic physiologic ramifications of insulin resistance, diet, exercise, and body fat distribution among northern indigenous people, the real frontier is the translation of knowledge of basic physiologic processes into healthy lifestyle choices. Therefore, it is especially important that such studies involve partnerships with social scientists, behavioral and mental health specialists, and village leaders, especially the elders.

Studies involving screening in villages face several challenges. One is that village populations are small and geographically distant from each other. More statistical power could be obtained by coordinated efforts by various groups of investigators using consistent methods and case definitions among different groups of participants. Another challenge is that studies in rural circumpolar regions are expensive and logistically difficult. Obtaining blood samples, storing, processing, and shipping them under precise conditions necessary for laboratory analysis is usually quite difficult. A study conducted by Murphy in 1987 demonstrated that a fingerstick method of glucose determination was practical and quite accurate for determination of glucose tolerance status. The Accu-check II performed with a sensitivity of 75%, a specificity of 93%, and a positive predicative value of 63.1% to detect a glucose of >126 mg/dl (6.72 mM) as determined by the hexokinase method on venous plasma (60). Gastrointestinal intolerance of glucose test beverages also presents difficulties with screening efforts in rural settings. However, a study in southeast Alaska showed polymer beverages were better tolerated than monomer beverages (61).

Funding decisions regarding studies in northern populations, especially in village settings, need to take into account the costs of travel and housing of workers, securing adequate exam facilities, difficulties of using computerized systems in settings where a steady electric supp-
ly is not guaranteed, and other such obstacles. Furthermore, studies should be viewed not only as an opportunity to obtain data, but also as a pathway for the involvement of village residents in the research process. Their observations are crucial to meaningful design of studies. Their involvement also offers potential steps into careers in the fields of research, health care delivery, and community development.

CONCLUSIONS

In summary, the evidence indicates that while Alaska Natives have a low prevalence of diabetes compared with other Native Americans, they are experiencing a more rapid rate of increase than other groups. It appears that in the Alaska Native populations studied, three changes have occurred concurrently over the past few decades; an increased proportion of carbohydrate in the diet, increasing prevalence of obesity, and increasing prevalence of diabetes.

On the positive side, traditional lifestyles in Alaska Native communities are still an intrinsic part of every day life and may be providing some protection. There is evidence that elements of the traditional diet, specifically frequent seal oil and salmon intake, correlate with a lesser risk of glucose intolerance. Alaska Natives are consuming fish six times more frequently and in larger amounts when compared to the US general population (56). Thus, promoting the continued consumption of traditional foods through nutrition education may protect against the development of diabetes. There is also evidence that physical activity may be protective among Alaska Natives as it is in other populations. Murphy’s 1987 study showed that 65% of Yupik and 32% of Athabascan participants engaged in high or moderate levels of physical activity (59).

While there is much to be learned about the occurrence of insulin resistance among Alaska Natives and other northern indigenous people, it appears that we know enough to make some recommendations. Native foods are to be promoted over diets high in simple carbohydrates; physical activity and weight management need to be encouraged. Further research is needed on factors involved in insulin resistance, the occurrence and implications of gestational diabetes, and the translation of information into lifestyle practice. Those involved in health care and research among northern peoples should search for ways to form partnerships that will assist populations in their own quest for better health.
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