Cardiovascular Disease Among Alaska Native Peoples

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Abstract

Although Alaska Native peoples were thought to be protected from cardiovascular disease (CVD), data now show that this is not the case, despite traditional lifestyles and high omega-3 fatty acid intake. In this article, the current understanding of CVD and its risk factors among Alaska Native peoples, particularly among the Yupik and Inupiat populations, will be discussed, using data from three major studies funded by the National Institutes of Health: Genetics of Coronary Artery Disease among Alaska Natives (GOCADAN), Center for Native Health Research (CANHR), and Education and Research Towards Health (EARTH). Data from these epidemiologic studies have focused concern on CVD and its risk factors among Alaska Native peoples. This review will summarize the findings of these three principal studies and will suggest future directions for research and clinical practice.

Keywords

Cardiovascular disease; Epidemiology; Coronary heart disease; Stroke; Alaska natives; Eskimos; Review

Introduction

Data from major epidemiologic studies have focused concern on CVD and its risk factors among Alaska Native peoples. Alaska is composed of diverse groups of Alaska Native people that are often subdivided within geographic regions, and villages are within these regions. Inupiat (Inupiaq) inhabit the northern and northwestern coastal regions; Yupik live in the southwestern regions (Central Yupik) and on St Lawrence Island (Siberian Yupik), which is in the Bering Strait between the coasts of Alaska and Siberia. Athabaskan Indians reside in the interior of the state, and the coastal Indians (Tlingit, Haida, and Tsimshian) inhabit southeastern coastal Alaska. Aleuts include residents of the Aleutian Islands, the Pribilof Islands, the western tip of the Alaska Peninsula, the Kodiak area, and the coastal regions of south-central Alaska. In the 2010 Census, about 15% of Alaska's state population

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(104,871 people) self-identified as American Indian or Alaska Native.[2] Of these, approximately 95% (99,561 people) also self-identified as being from one of the following Alaska Native groups: Inupiat, Yupik Alaskan Athabaskan, Tlingit, Haida, Tsimshian, or Aleut.[3]

Also in 2001, the National Center Research Resources established the Center for Alaska Native Health Research (CANHR), which focused on risk factors as well as protective factors for obesity and chronic diseases, including CVD.[11, 12] Between 2003 and 2006, CANHR obtained biological, genetic, nutritional, and psychosocial data from examinations of nearly 1000 Alaska Native people, >age 14 years, from ten communities in the YK Delta.[11, 12]

Cardiovascular Disease

Subclinical atherosclerosis, coronary heart disease, and stroke data obtained from the three systematic epidemiologic studies described above plus reliable registry or mortality data where applicable will be discussed in this article. High rates of rheumatic heart disease and infective endocarditis have been described among Alaska Native people but will not be covered in this review.[6, 13] Furthermore, data on heart failure are limited and will not be discussed.[14]

Subclinical Atherosclerosis

Subclinical atherosclerosis, detected by carotid artery ultrasound and assessed as either intima-media thickness (IMT) or plaque burden, correlates with CVD risk factors and with both prevalent and incident CVD in large population-based studies, and improves CVD prediction in asymptomatic individuals at intermediate cardiovascular risk.[15–1920] In the SHS of American Indians, plaque score was a better predictor of CVD events than IMT in individuals without preexisting CVD, regardless of diabetes and hypertension status.[21]

GOCADAN is the only study among Alaska Native people that includes measures of subclinical atherosclerosis. Among GOCADAN participants, the age-adjusted prevalence of carotid atherosclerosis exceeded that of U.S. black and white population-based samples.[22] Over 90% of GOCADAN participants (n=1,131) had plaque score assessments, and plaque (in one or more of the eight carotid segments studied) was found in 34% (n=384) of participants.[23] Because over two-thirds of GOCADAN participants reported being current or former smokers, the high rate of smoking likely contributes to the CVD rate, as use of tobacco is independently associated with plaque in participants >45 years of age.[23] Similarly, carotid plaque was associated with higher LDL cholesterol (LDL-C), smaller LDL particles and smaller very low-density lipoprotein (VLDL) particles, and a smaller VLDL particle size.[24] IMT was significantly associated with higher LDL-C and total LDL particle concentration, independently of other traditional cardiovascular risk factors, including current smoking status.[24] However, neither IMT nor plaque score was associated with HDL cholesterol (HDL-C) or with HDL subfraction concentrations.[24] Contrary to expectations, there was no (protective) association of omega-3 fatty acid consumption with plaque prevalence, although there was a negative association with IMT.[25] A positive association between plaque and intake of saturated fats was observed.[25]

Coronary Heart Disease

Until recently, the only population-based data on cardiovascular events were derived from self-report or administrative databases. In contrast, GOCADAN included electrocardiograms and standardized review and adjudication of all cardiovascular events and deaths.[14] Among the 500 GOCADAN participants > age 45, definite coronary heart disease (CHD), defined by either an acute myocardial infarction or a coronary revascularization procedure, was found in 4% (n=20).[14] CHD prevalence was higher in men compared with women (prevalence ratio of 2.47 [1.00–6.09]); however, definite myocardial infarction prevalence was low in both sexes, with less than ten participants meeting criteria.[14]

Prior to GOCADAN, the ASP had begun to re-address the hypothesis that diets rich in omega-3 fatty acid were associated with less CHD. In the ASP, 450 Alaska Native people were screened for CHD using a standardized protocol, and only 6% of the cohort <age 55 years, and 26% of those > age 55 years, had CHD, and no associations were observed between omega-3 fatty acid consumption or plasma concentrations and prevalent CHD.[26]

Recently, an examination of national mortality rates using the NCI's Surveillance Epidemiology and End Results (SEER) program, found that heart disease (as defined by International Classification of Diseases [ICD-10] codes) was the second leading cause of death among Alaska Native people, after cancer.[27] The heart disease mortality rates for Alaska Native people were lower than those for U.S. Whites (270.6 vs. 304.6, 169.5 vs. 197.1, and 210.4 vs. 243.6 per 100,000; for men, women, and overall, respectively), although these differences only reached significance ($p<0.05$) for Alaska Native women.[27] Heart disease mortality for Alaska Native people declined 25% between 1979 and 2003, compared with a 39% decline for U.S. Whites; most of the decline was observed between 1999–2003.[27] Some of this decline may be due to improved survival and treatment of CHD among the general population.[28]

Stroke

Stroke, or cerebrovascular disease, is the fourth leading cause of death in the U.S., with Indian Health Service data suggesting higher than expected stroke rates among Alaska Native people, similar to observations among other Inuit populations.[29–32]

Stroke prevalence, based on adjudicated events a4444444444409, the on aay beatio,bservtho 0 -12 Td(omega-f Cre

increasing quartiles of omega-3 fatty acid intake, even after adjustment (p for linear trend <0.01).[37]

In EARTH, oscillometric BP was measured in a standardized manner. In an EARTH study examining risk factors for chronic disease, hypertension was defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg and overall was found to be less prevalent than the other studies, occurring in only 13% (n=195) of men and 11% (n=255) of women.[38] However, this rate may be an underestimation because it included all participants, even those with self-reported hypertension. Furthermore, the EARTH study did not assess use of hypertension medication, which may have influenced BP values. As expected, hypertension prevalence increased with participant age, although with an apparent sex disparity in this EARTH study, in which hypertension was found in 29% (n=81) of women and only 22% of men (n=30) aged ≥ 60 years.[38]

In CAHNR, BP measurement methods were similar to those in EARTH, although hypertension prevalence was not reported. Abnormally elevated values were defined as SBP ≥ 130 mm Hg and/or DBP ≥ 85 mm Hg. Of the 710 CANHR participants, 23% had an abnormal SBP reading and 10% had an abnormal DBP reading.[39] When stratified by sex, men had a higher prevalence of abnormal SBP (26% vs 20%) compared with women, who had a somewhat higher prevalence of abnormal DBP (11% vs 9%) compared with men.[39]

Lipids

In GOCADAN, fasting lipid profiles were obtained from participants via venipuncture and were analyzed in a central laboratory with standardized assays.[9] Of 1026 participants, 48% had high total cholesterol (≥ 200 mg/dL), 32% had high LDL-C (≥ 130 mg/dL), 26% had high triglycerides (≥ 150 mg/dL), and 11% had low HDL-C (≤ 40 mg/dL).[40] Among GOCADAN participants ≥ ages 45 years (n=499), 34% (n=71) of men and 40% (n=115) of women had hyperlipidemia, defined as LDL-C > 160 mg/dL, non-HDL-C >190 mg/dL, Apo-B>120 mg/dL, or taking lipid lowering medications.[14]

In the CAHNR study, fasting lipid panels also were obtained via venipuncture and analyzed in a central laboratory.[39] Compared with the U.S. general population, mean total cholesterol was higher among CANHR participants (220 vs 203 mg/dL).[39] Fewer than 10% of the participants had elevated triglycerides (≥ 150 mg/dL) and 13% had low HDL (≤ 40 mg/dL for men and ≤50 mg/dL for women).[39]

In the EARTH study, fasting lipid measures were determined from finger-stick whole blood specimens obtained from point-of-care testing.[10] Of the 3822 participants with fasting lipid data, 40% had high total cholesterol (≥ 200 mg/dL), 26% had high LDL-C (≥ 130 mg/dL), 28% had high triglycerides (≥ 150 mg/dL), and 19% had low HDL-C (≤ 40 mg/dL).[38] More lipid abnormalities were found among men compared with women and among those who were older.[38]

Obesity

Age-adjusted prevalence of obesity in the United States during 2007–2008 was 33.8% overall, 32.2% among men, and 35.5% among women.[41] Earlier, the ASP study of Inupiat and Yupik participants from four villages in the Bering Straits Region of northwestern Alaska had found that 33% of the women were obese, body mass index (BMI) ≥ 30 kg/m^2, compared with 16% of the men.[42]

More recently, the GOCADAN study found that almost a third, or 30% of the 1026 participants were obese and another 31% were overweight (BMI 25–29 kg/m^2).[40] Similar to the gender differences found in the ASP, 37% (n=602) of the women in the GOCADAN

study were obese, compared with 20% (n=456) of the men.[37] Likewise, in CANHR, nearly a third or 32% of the 753 participants were obese and another 33% were overweight.[12]

In the EARTH study, the prevalence of obesity, also defined as BMI ≥ 30 kg/m^2, was even higher at 51%. These data were from 3822 Alaska Native people, representing many Alaska Native groups.[38] More women (60%) than men (38%) met the criteria for obesity.[38] Taken together, the data suggest that obesity rates for Inupiat and Yupik are lower than among other Alaska Native people and, for men, are lower than those of U.S. whites.

Diabetes/Metabolic Syndrome

In the GOCADAN study, among the 1189 who underwent standardized oral glucose tolerance testing, overall diabetes prevalence was low, (5.0%, 2.2%, and 3.8%, respectively, in women, men, and overall.[43] Diabetes prevalence was similarly low, 3.3% overall among 753 adult participants in the CANHR study, where diabetes was defined by self-report, use of hypoglycemic medication, or based on American Diabetes Association fasting glucose criteria.[12] However, diabetes prevalence was slightly higher (5.4% overall) in the EARTH

glomerular filtration rate <60 mL min 1.73 m^2), was likewise low (7%), perhaps because of the lower burden of diabetes thus far.[64] Consistent with the GOCADAN data, the Alaska Native Diabetes Registry reports low rates of end-stage renal disease, again, differing from observations in several American Indian populations.[54]

Inflammation

It is thought that pathogen-triggered (particularly from H.pylori infection) autoimmunity may play a role in early atherosclerosis.[65] In GOCADAN, a high level of and lifelong

References

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance

15. Sharrett AR, Sorlie PD, Chambless LE, et al. Relative importance of various risk factors for asymptomatic carotid atherosclerosis versus coronary heart disease incidence: the Atherosclerosis Risk in Communities Study. Am J Epidemiol. May; 1999 149(9):843–852. [PubMed: 10221321]

16. Arnett DK, Tyroler HA, Burke G, et al. Hypertension and subclinical carotid artery atherosclerosis in blacks and whites. The Atherosclerosis Risk in Communities Study. ARIC Investigators. Arch Intern Med. Sep; 1996 156(17):1983–1989. [PubMed: 8823151]

17. Cao JJ, Arnold AM, Manolio TA, et al. Association of carotid artery intima-media thickness, plaques, and C-reactive protein with future cardiovascular disease and all-cause mortality: the Cardiovascular Health Study. Circulation. Jul; 2007 116(1):32–38. [PubMed: 17576871]

18. Nambi V, Chambless L, Folsom AR, et al. Carotid intima-media thickness and presence or absence of plaque improves prediction of coronary heart disease risk: the ARIC (Atherosclerosis Risk In Communities) study. J Am Coll Cardiol. Apr; 2010 55(15):1600–1607. [PubMed: 20378078]

19. Anderson TJ, Charbonneau F, Title LM, et al. Microvascular function predicts cardiovascular events in primary prevention: long-term results from the Firefighters and Their Endothelium (FATE) study. Circulation. Jan; 2011 123(2):163–169. [PubMed: 21200002]

20. Peters SA, Ruijter HM, Bots ML, Moons KG. Improvements in risk stratification for the occurrence of cardiovascular disease by imaging subclinical atherosclerosis: a systematic review. Heart. 2012 Feb; 98(3):177–84. Epub 2011 Nov 17. [PubMed: 22095617]

21. Roman MJ, Kizer JR, Best LG, et al. Vascular biomarkers in the prediction of clinical cardiovascular disease: the strong heart study. Hypertension. Jan; 2012 59(1):29–35. [PubMed: 22068872]

22. Cutchins A, Roman MJ, Devereux RB, et al. Prevalence and correlates of subclinical atherosclerosis in Alaska Eskimos: the GOCADAN study. Stroke. 2008 Nov; 39(11):3079–82. Epub 2008 Jul 10. [PubMed: 18617652]

23. Kaufman DJ, Roman MJ, Devereux RB, et al. Prevalence of smoking and its relationship with carotid atherosclerosis in Alaskan Eskimos of the Norton Sound region: The GOCADAN Study. Nicotine Tob Res. Mar; 2008 10(3):483–491. [PubMed: 18324567]

24. Masulli M, Patti L, Riccardi G, et al. Relation among lipoprotein subfractions and carotid atherosclerosis in Alaskan Eskimos (from the GOCADAN Study). Am J Cardiol. Dec; 2009 104(11):1516–1521. [PubMed: 19932785]

25. Ebbesson SO, Roman MJ, Devereux RB, et al. Consumption of omega-3 fatty acids is not associated with a reduction in carotid atherosclerosis: the Genetics of Coronary Artery Disease in Alaska Natives study. Atherosclerosis. Aug; 2008 199(2):346–353. [PubMed: 18054937]

26. Ebbesson SO, Risica PM, Ebbesson LO, Kennish JM. Eskimos have CHD despite high consumption of omega-3 fatty acids: the Alaska Siberia project. Int J Circumpolar Health. Sep; 2005 64(4):387–395. [PubMed: 16277122]

27. Day GE, Provost E, Lanier AP. Alaska native mortality rates and trends. Public Health Rep. 2009 JalMe, n3aPtae.)[Pu1b7M9ked Ow, aHPelbaltiyer ra2t2e(Al thickness,.PubM3.)Tj 0 Publiy AtigO, ivisTd(cons0.99999 ydiovasculervis. cardiovascuerosca C1nad inesti: a on study. CiAmh Rep. 2009

34. Appel LJ, Brands MW, Daniels SR, et al. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension. Feb; 2006 47(2):296–308. [PubMed: 16434724]
35. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. May; 2003 289(19):2560–2572. [PubMed: 12748199]
36. Fabsitz, RR.; Best, L.; Devereux, RB., et al. Hypertension prevalence, awareness, treatment and control among American Indians and Alaskan Eskimos: results from the Strong Heart and GOCADAN studies. in press
37. Jolly SE, Eilat-Adar S, Wang H, et al. Sex-specific associations of nutrition with hypertension and systolic blood pressure in Alaska Natives findings from the GOCADAN study. Int J Circumpolar Health. Jun; 2011 70(3):254–265. [PubMed: 21631966]
38. Redwood DG, Lanier AP, Johnston JM, et al. Chronic disease risk factors among Alaska Native and American Indian people, Alaska, 2004–2006. Prev Chronic Dis. 2010 Jul.7(4):A85. Epub 2010 Jun 15. [PubMed: 20550843]
39. Boyer BB, Mohatt GV, Plaetke R, et al. Metabolic syndrome in Yup'ik Eskimos: the Center for Alaska Native Health Research (CANHR) Study. Obesity (Silver Spring). 2007 Nov; 15(11): 2535–40. [PubMed: 18070741]
40. Jolly SE, Noonan CJ, Roubideaux YD, et al. Albuminuria among Alaska Natives--findings from the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study. Nephron Clin Pract. 2010; 115(2):c107–113. [PubMed: 20407273]
41. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. JAMA. Jan; 2010 303(3):235–241. [PubMed: 20071471]
42. Risica PM, Schraer C, Ebbesson SO, et al. Overweight and obesity among Alaskan Eskimos of the Bering Straits Region: the Alaska Siberia project. Int J Obes Relat Metab Disord. 2000 Aug; 24(8):939–44. [PubMed: 10951530]
43. Carter EA, MacCluer JW, Dyke B, et al. Diabetes mellitus and impaired fasting glucose in Alaska Eskimos: the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study. Diabetologia. 2006 Jan; 49(1):29–35. Epub 2005 Dec 21. [PubMed: 16369773]
44. Lee ET, Howard BV, Savage PJ, et al. Diabetes and impaired glucose tolerance in three American Indian populations aged 45–74 years, The Strong Heart Study. Diabetes Care. May; 1995 18(5): 599–610. [PubMed: 8585996]
45. National Cholesterol Education Program. Detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) executive summary. National Institutes of Health. U.S. Department of Health and Human Services; Bethesda MD: 2001. NIH Publication no-3670
46. Mozumdar A, Liguori G. Persistent increase of prevalence of metabolic syndrome among U. adults: NHANES III to NHANES 1999–2006. Diabetes Care. Jan; 2010 34(1):216–219. [PubMed: 20889854]
47. Howard BV, Best L, Comuzzie A, et al. C-Reactive protein, insulin resistance, and metabolic syndrome in a population with a high burden of subclinical infection: insights from the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study. Diabetes Care. Dec; 2008 31(12): 2312–2314. [PubMed: 18796618]
48. Rivellese AA, Patti L, Kaufman D, et al. Lipoprotein particle distribution and size, insulin resistance, and metabolic syndrome in Alaska Eskimos: the GOCADAN study. Atherosclerosis. Oct; 2008 200(2):350–358. [PubMed: 18378240]
49. Adler AI, Boyko EJ, Schraer CD, Murphy NJ. Lower prevalence of impaired glucose tolerance and diabetes associated with daily seal oil or salmon consumption among Alaska Natives. Diabetes Care. Dec; 1994 17(12):1498–1501. [PubMed: 7882827]
50. Murphy NJ, Schraer CD, Thiele MC, et al. Dietary change and obesity associated with glucose intolerance in Alaska Natives. J Am Diet Assoc. Jun; 1995 95(6):676–682. [PubMed: 7759744]
51. Adler AI, Boyko EJ, Schraer CD, Murphy NJ. The negative association between traditional physical activities and the prevalence of glucose intolerance in Alaska Natives. Diabet Med. 1996 Jun; 13(6):555–60. [PubMed: 8799660]

52. Eilat-Adar S, Mete M, Nobmann ED, et al. Dietary patterns are linked to cardiovascular risk factors but not to inflammatory markers in Alaska Eskimos. J Nutr. Dec; 2009 139(12):2322–2328. [PubMed: 19828690]
53. Bersamin A, Luick BR, King IB, et al. Westernizing diets influence fat intake, red blood cell fatty acid composition, and health in remote Alaskan Native communities in the center for Alaska Native health study. J Am Diet Assoc. Feb; 2008 108(2):266–273. [PubMed: 18237575]
54•. Narayanan ML, Schraer CD, Bulkow LR, et al. Diabetes prevalence, incidence, complications and mortality among Alaska Native people 1985–2006. Int J Circumpolar Health. Jun; 2010 69(3): 236–252. This analysis of a diabetes registry of Alaska Native people who are cared for by the tribal health systems shows the growing trend of increased diabetes. [PubMed: 20501061]
55. Fortuine R. Historical notes on the introduction of tobacco into Alaska. Alaska Med. Jan-Mar;1996 38(1):3–7. [PubMed: 8936092]
56. Owen P, Ingle DE, Schumacher C. The prevalence of tobacco use among Alaska adults. Alaska Med. Jan-Mar;1996 38(1):21–23. 51. [PubMed: 8936097]
57. Smith JJ, Ferucci ED, Dillard DA, Lanier AP. Tobacco use among Alaska Native people in the EARTH study. Nicotine Tob Res. Aug; 12(8):839–844. [PubMed: 20547558]
58. Wolsko C, Mohatt GV, Lardon C, Burket R. Smoking, chewing, and cultural identity: prevalence and correlates of tobacco use among the Yup'ik-The Center for Alaska Native Health Research (CANHR) study. Cultur Divers Ethnic Minor Psychol. 2009 Apr; 15(2):165–72. [PubMed: 19364203]
59. Makhoul Z, Kristal AR, Gulati R, et al. Associations of obesity with triglycerides and C-reactive protein are attenuated in adults with high red blood cell eicosapentaenoic and docosahexaenoic acids. Eur J Clin Nutr. Jul; 2011 65(7):808–817. [PubMed: 21427737]
60. Ebbesson SO, Devereux RB, Cole S, et al. Heart rate is associated with red blood cell fatty acid concentration: the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) study. Am Heart J. Jun; 2010 159(6):1020–1025. [PubMed: 20569715]
61. Ebbesson SO, Tejero ME, Lopez-Alvarenga JC, et al. Individual saturated fatty acids are associated with different components of insulin resistance and glucose metabolism: the GOCADAN study. Int J Circumpolar Health. Sep; 2010 69(4):344–351. [PubMed: 20719107]
62. Gerstein HC, Mann JF, Yi Q, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA. Jul 25; 2001 286(4):421–426. [PubMed: 11466120]
63. Weiner DE, Tighiouart H, Amin MG, et al. Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. J Am Soc Nephrol. May; 2004 15(5):1307–1315. [PubMed: 15100371]
64. Jolly SE, Mete M, Wang H, et al. Uric Acid, Hypertension, and CKD among Alaska Eskimos-the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) Study. J Clin Hypertens (Greenwich). Jan 4.2012 Article first published online. 10.1111/j.1751-7176.2011.00574.x
65. Zhu J, Katz RJ, Quyyumi AA, et al. Association of serum antibodies to heat-shock protein 65 with coronary calcification levels: suggestion of pathogen-triggered autoimmunity in early atherosclerosis. Circulation. Jan; 2004 109(1):36–41. [PubMed: 14662717]
66. Zhu J, Davidson M, Leinonen M, et al. Prevalence and persistence of antibodies to herpes viruses, Chlamydia pneumoniae and Helicobacter pylori in Alaskan Eskimos: the GOCADAN Study. Clin Microbiol Infect. Feb; 2006 12(2):118–122. [PubMed: 16441448]
67. Demma LJ, Holman RC, Sobel J, et al. Epidemiology of hospitalizations associated with ulcers, gastric cancers, and Helicobacter pylori infection among American Indian and Alaska Native persons. Am J Trop Med Hyg. May; 2008 78(5):811–818. [PubMed: 18458318]
68. Voruganti VS, Cai G, Cole SA, et al. Common set of genes regulates low-density lipoprotein size and obesity-related factors in Alaskan Eskimos: results from the GOCADAN study. Am J Hum Biol. Jul-Aug;2006 18(4):525–531. [PubMed: 16788905]
69. Lemas DJ, Wiener HW, O'Brien DM, et al. Genetic polymorphisms in carnitine palmitoyltransferase 1A gene are associated with variation in body composition and fasting lipid traits in Yup'ik Eskimos. J Lipid Res. Jan; 2012 53(1):175–184. [PubMed: 22045927]

70. Chung WK, Patki A, Matsuoka N, et al. Analysis of 30 genes (355 SNPS) related to energy homeostasis for association with adiposity in European-American and Yup'ik Eskimo populations. Hum Hered. 2009; 67(3):193–205. [PubMed: 19077438]

71. Tejero ME, Voruganti VS, Cai G, et al. Pleiotropic effects on subclasses of HDL, adiposity, and glucose metabolism in adult Alaskan Eskimos. Am J Hum Biol. Jul-Aug;2010 22(4):444–448. [PubMed: 19950191]

72. Voruganti VS, Cole SA, Ebbesson SO, et al. Genetic variation in APOJ, LPL, and TNFRSF10B affects plasma fatty acid distribution in Alaskan Eskimos. Am J Clin Nutr. Jun; 2010 91(6):1574–1583. [PubMed: 20410100]