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Cardiovascular Disease in American Indian and Alaska Native Youth: Unique Risk Factors and Areas of Scholarly Need

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In August 2016, the National Heart, Lung, and Blood Institute convened a scientific forum with 18 investigators active in the field of population health disparities. The purpose was to discuss heart, lung, and sleep disorders in children and adolescents of American Indian/Alaska Native (AI/AN) heritage. All participants acknowledged the paucity of age- and population-specific data on these disorders and called for new research to remedy the gap.

As participants in that forum and seasoned investigators in the field, we summarize the current state of research on cardiovascular disease (CVD) in AI/AN youth from our unique perspective. We review the available evidence on environmental exposures, diet, physical activity, and early-onset obesity in AI/ANs, with a focus on data from individuals younger than 21 years as available, against the background of a rapidly increasing prevalence of CVD and its risk factors. It should be mentioned that the available evidence is sparse,

with much of what is known about CVD in Native communities coming from the SHS (Strong Heart Study), a longitudinal, population-based study of the epidemiology of CVD and its risk factors in adult AIs from communities in Oklahoma, Arizona, North Dakota, and South Dakota. From 1989 to 1991, SHS recruited a cohort of adults aged 45 to 75 years and followed them for several waves of data collection.[1] An ancillary project, the SHFS (Strong Heart Family Study), recruited participants aged 14 years and older who belonged to the families of SHS cohort members.[2] Both SHS and SHFS collected detailed information on cardiovascular events, risk factors for CVD (including genetic and environmental factors), and markers of preclinical CVD. Our review is intended to elucidate viable avenues for future research in this neglected area.

CVD Risk Factors and Subclinical CVD in AI Youth

CVD was once considered rare in AIs, but lifestyle and dietary changes have contributed to a substantial increase in recent decades.[3,4] As would be expected, the population prevalence of established CVD risk factors, including obesity and diabetes mellitus, has also increased relative to the US general population.[5] Despite advances in raising community awareness of CVD risk factors among AIs, the prevalence of dyslipidemia, smoking, and high blood pressure is also rising.[6,7] CVD is more likely to be fatal in AIs relative to other races, with mortality rates 20% higher than in the general population,[3] while age at death because of CVD is significantly lower among Native people. Fully 36% of AIs with CVD die before age 65, versus 15% of non-Hispanic whites.[8] This premature morbidity and mortality among AI/AN adults likely reflects the high prevalence of CVD risk factors in Native youth.

Compared with other races, AI youth are disproportionally affected by obesity, which tends to begin earlier in life, as shown by data on weight from birth to preschool age.[9] One

longitudinal cohort study in Arizona that followed 4857 AI children (median age 11.3 years on enrollment) found that childhood obesity was associated with subsequent hypertension and insulin resistance. In addition, obesity and glucose intolerance were strongly associated with premature death from endogenous causes.[10] Furthermore, a large national study found that the incidence rate of type 2 diabetes mellitus in AI/AN youth (≥19 years) rose from 22.6/100 000 in 2003 to 46.5/100 000 in 2012.[11]

In the SHFS cohort, 24.9% of AI adolescents met criteria for the metabolic syndrome (defined as obesity with associated hypertension, dyslipidemia, and insulin resistance).[12] Metabolic syndrome is therefore substantially more prevalent in this sample than in populations of other races and ethnicities, with the National Health and Nutrition Examination Survey offering the following prevalence estimates: Mexican Americans (12.9%), non-Hispanic whites (10.9%), and non-Hispanic blacks (2.5%).[13] Among SHFS youth with metabolic syndrome, the most prevalent risk factors were larger waist circumference, a surrogate of obesity (54.3%); low levels of high-density lipoprotein (46.4%); hypertension (30.3%); high levels of triglycerides (27.8%); and high fasting glucose (2.5%).

SHFS results also demonstrated an association between CVD risk factors and subclinical CVD in AI youth. Similar findings have been reported for youth in the general US population.[14] Obese SHFS participants displayed prevalent left ventricular hypertrophy with abnormalities in left ventricular function.[15] Despite the youth of participants with hypertension, they demonstrated premature left ventricular hypertrophy with diastolic abnormalities, as well as increased arterial stiffness and elevated peripheral vascular resistance.[16] Compared with participants who did not meet criteria for metabolic syndrome, those who did had a higher prevalence of cardiac abnormalities on echocardiogram, including left ventricular hypertrophy, left atrial dilation, and reduced left ventricular systolic and diastolic function.[12] In the same subset of participants, prediabetes mellitus and diabetes mellitus in adolescence were associated with an untoward cardiac phenotype with left ventricular hypertrophy and left ventricular systolic and diastolic abnormalities.[17] All these subclinical CVD markers are independent risk factors for adult CVD and CVD-related mortality.[18–20]

Environmental Risk Factors for CVD in AI Youth

Although modifiable behavioral risk factors account for a large proportion of incident CVD, increasing evidence suggests that environmental factors are also pertinent for populations around the world.[21–24] Such factors include the built environment, local opportunities for physical activity, access to retail outlets for healthy foods, and sociodemographic factors; however, these elements are difficult to study in rural populations. For example, quantifying the built environment relies on accurate geocoding, which is not available for AI reservations. Future study might be useful focused on neighborhood socioeconomic status in these communities.

Evidence indicates that factors such as air pollution and metal exposures also contribute to CVD, and may disproportionally affect rural populations.[21,22] For example, arsenic and cadmium lead to endothelial dysfunction, apoptosis, and vascular injury which may, in turn, exacerbate atherosclerosis.[25,26] Compared with the US all-races population, AI communities are disproportionately exposed to several metals, including arsenic, cadmium, uranium, and tungsten.[27–30] For instance, SHS and SHFS participants had higher urinary concentrations of these metals, including a 30% higher concentration of cadmium and 2.4 times the amount of urinary arsenic, than did similar-age participants in other large studies, including MESA (Multi-Ethnic Study of Atherosclerosis), a prospective cohort study of whites, blacks, Hispanics, and Chinese Americans from 6 urban areas,[28] and National Health and Nutrition Examination Survey. Other studies with AIs have also shown relatively high levels of arsenic and uranium exposure.[29,30]

With regard to arsenic, uranium, and tungsten, elevated exposure might reflect groundwater contamination, which is more common in rural than in urban areas. Contamination is more likely in small community water systems in the Midwest and the Southwest and in private wells, which are currently unregulated. With regard to cadmium, both cigarette smoking and diet have been implicated as sources of exposure in the general population.[31] However, elevated cadmium concentrations were found even among never-smokers in the SHS cohort, suggesting that factors other than smoking are involved. Diet seems a more likely source of risk, as a recent study with SHFS participants found that higher urinary concentrations of cadmium were associated with higher intake of processed meats and lower intake of dairy products, fruits, and fruit juice.[32]

In the SHS cohort, after adjustment for sociodemographic and traditional cardiovascular risk factors, exposure to arsenic and cadmium was associated with higher incidence of cardiovascular events (including coronary heart disease and stroke) over almost 20 years of follow-up.[25,26] For arsenic alone, the associations with CVD incidence and mortality were stronger in the subgroup of participants younger than 55 years. In the overall SHS cohort, both arsenic and cadmium were also related to higher incidence of peripheral arterial disease, while for arsenic alone, the same condition was associated with an ankle–brachial index higher than 1.4.[33,34] Similar analyses are lacking for cadmium, for which associations with carotid atherosclerosis have been reported

in other populations.[35,36] Overall, the available evidence suggests that arsenic and cadmium heighten the risk of CVD in AI communities. They might also contribute to a disproportionate burden of CVD compared with other populations, including an excess of subclinical CVD in childhood and adolescence. Unfortunately, no research to date has addressed metals exposure among AI adolescents and young adults.

The evidence for disproportionate exposure to metals highlights the need for effective prevention strategies and supports ongoing efforts to install new water systems in affected AI communities. For instance, the Mni Wiconi Project has brought safe water from the Missouri River to the Oglala Sioux community in Pine Ridge.[37] However, many AIs live in remote areas with limited access to community water systems and rely on unregulated private wells for drinking water. To evaluate prevention strategies for families served by such wells, an ongoing multilevel participatory intervention is testing the efficacy of a point-of-use drinking water filter in conjunction with an educational intervention in SHS communities in North and South Dakota. Known as the Strong Heart Water Study for Private Wells, its goal is to reduce arsenic exposure. Other strategies will also be needed, given the ubiquity of environmental exposures and the difficulty of mitigating them. One potential avenue is dietary interventions, given the evidence for associations between environmental exposures and food intake.[32]

In addition to metals, air pollution is an environmental exposure of major interest in AI communities. Although atmospheric pollution from vehicular traffic and industrial sources is typically lower in rural communities than in cities and suburbs, pollution from other sources might still have deleterious effects. Agriculture, livestock production, forest fires, domestic heating with coal or wood, and wind-blown dust can all be important pollutants in rural environments. Moreover, levels of indoor air pollution can be higher than outdoor levels because of contributions from heating, cooking, and smoking tobacco.[38] Solid fuel is the principal heating source for at least 2.5 million households in the United States, primarily in rural and low-income areas, leading to high levels of indoor air pollution.[39] In addition, in many "shale play" regions, unconventional gas development (often called fracking) is a booming industry with poorly quantified effects on local air quality.[40] Little research to date has explored the contribution of air pollution to CVD in AIs, highlighting another important avenue for future studies.

Dietary Quality Among AI Youth

In AI communities, diet has changed substantially over the past several decades. The malnutrition and undernutrition common among AI youth in the 1960s and 1970s have been replaced by high rates of obesity and CVD.[41] Yet despite this growing burden, large gaps persist in nutrition research with AI youth.[41] The small number of extant studies suggests that AI youth consume diets high in fats and added sugars and low in fruits and vegetables.[41–46] However, it is challenging to make generalizations from this body of work, because most studies were conducted in single communities[43,45,46] with small sample sizes,[42,46] using dietary measures of either unknown or poor validity and reliability in youth.[43–45] In addition, collection of dietary data from children and adolescents can face challenges of limited literacy, memory, attention span, and food knowledge.[47] For example, some youth might be unable to accurately identify or recall ingredients in multi-ingredient meals and might therefore under- or over-report intake of particular foods. Among adults, three 24-hour recalls are considered necessary to obtain a valid measure of "usual diet," while as many as nine 24-hour recalls might be needed for adequate assessment in youth.[48] Although some studies with youth have tried to compensate for the use of self-reported dietary measures by recruiting parents or caregivers as proxies, the proxies themselves often do not know what school-age youth eat throughout the day.[47] This limitation is particularly concerning in research with low-income populations, including many AI communities, where youth may eat 2 or 3 meals per day at school or during after-school activities.

SHFS participants completed the Block Food Frequency Questionnaire and a supplemental AI foods questionnaire from 2001 to 2003 to ascertain usual dietary intake over the previous year.[49] The Block instrument is one of the most widely used food questionnaires, with demonstrated reliability and validity.[50–53] Overall, as shown in Figure, the diet of SHFS participants was poor relative to that of the US general population.[54,55] In National Health and Nutrition Examination Survey data collected from 1988 to 2008, 25% of all-races respondents who were free of CVD achieved at least 2 of the 5 dietary goals set by the American Heart Association: at least 4.5 cups of fruits and vegetables per day, at least two 3.5-ounce servings of fish per week, at least 3 servings of whole grains per day, <1500 mg sodium per day, and <36 ounces of sugar-sweetened beverages per week.[56] Only 6% of the SHFS cohort achieved 2 of these 5 goals, while none achieved more than 2 goals, and 65% achieved none at all.[54] Results were consistent across both sexes, all ages, and all study sites.

Despite a large body of evidence demonstrating that poor diet elevates CVD risk, programs that provide dietary education and promote better nutrition for AI youth have not led to long-term improvements in diet or cardiovascular health. Moreover, efforts to increase the availability of healthy foods at grocery stores and schools in underserved communities have had mixed results,[42,57,58] as access to healthier foods does not always translate into healthier food choices.[59]
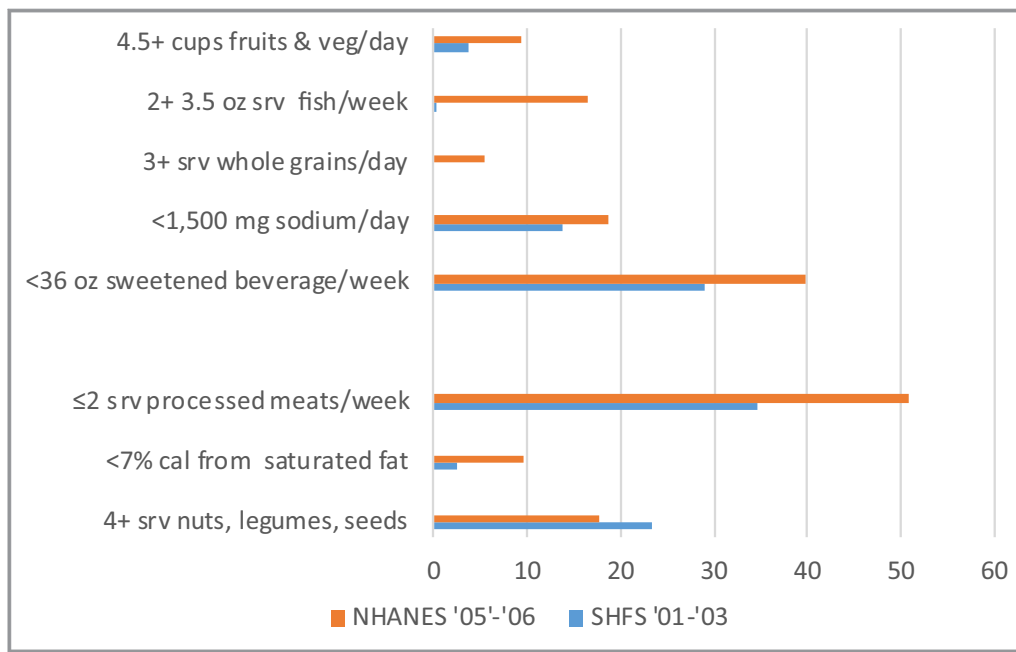
Figure. Achievement of American Heart Association Dietary Goals.[54,55]NHANES indicates National Health and Nutrition Examination Survey; SHFS, Strong Heart Family Study.

A lack of familiarity with healthy foods, especially their flavors, can deter children from eating them. Children are also particularly vulnerable to marketing campaigns for unhealthy processed foods.[60] Such factors must be considered and addressed in developing and implementing interventions to improve diet among AI youth.

Physical Activity in AI/AN Children

Studies of the determinants and correlates of physical activity among AI/AN adults and children, as well as intervention studies to promote physical activity in Native communities, are just as rare as research in the other areas discussed in this review. A number of studies have addressed overweight and obesity in Native people, with physical activity assessed as a covariate.[61–65] Other studies of the correlates of physical activity in AI/ANs have recruited either children or adults, but not both.[66–70] Only 20% to 27% of AI/AN adults are estimated to engage in regular physical activity.[71,72] Data on AI children in Oklahoma show similar trends, with only 30% meeting the 2008 Physical Activity Guidelines for Americans.[73]

A systematic literature review of physical activity levels among AI/AN and First Nations people found that 26.5% of children met World Health Organization or Canadian physical activity guidelines according to studies using self-reported data, while 45.7% of children met guidelines according to studies based on accelerometry or pedometry, although self-reporting in children may be less reliable.[74] Other research

shows that AI/AN children who do not participate in team sports, rarely engage in physical activity, and perform poorly on fitness tests have a higher risk of obesity.[61,63] In a study of AI children ages 3 to 8 years in Wisconsin, number of hours of outdoor play significantly predicted percentage of body fat after controlling for age, sex, and maternal body mass index (BMI).[75] In the Pathways study with AI children, accelerometry data revealed an association between higher levels of physical activity and smaller percentages of body fat in normal-weight but not overweight second graders.[65]

One systematic review identified 33 physical activity interventions in US tribal communities published between 1970 and 2015. Twenty were research-based interventions and 13 were community-wide initiatives.[76] None reported statistically significant improvements in weight-related outcomes, and only 4 reported improvements in knowledge or attitudes regarding physical activity.[76] The community-wide studies did not share systematic information or analysis on the local environment, policy, or system-based approaches.

This body of research highlights the importance of objective measures of physical activity in AI/AN children, especially accelerometry.[65,75,77] It also emphasizes the need for studies, not only to understand the individual determinants of physical activity in AI/AN youth, but also to develop effective, multilevel strategies to promote physical activity in families and communities through interventions in behavior, policy, health systems, and natural as well as built environments.

Early Obesity in AI/AN Children

Obesity rates in AI/AN children are among the highest of all races and ethnicities.[78–80] The Centers for Disease Control and Prevention estimate that AI/ANs ages 2 to 5 years have a higher combined prevalence of overweight and obesity (58.8%) than children of any other race or ethnicity (30%).[78,81] AI/AN children are also the only group of children for which an increase in obesity prevalence has been reported since 2003.[82] Once established, obesity persists into later life and greatly increases the risk of chronic disease.[83,84] In AI communities in Wisconsin, 46% of children aged 3 to 8 years were overweight or obese, with obesity defined as sex-specific BMI for age >95th percentile.[57,85] AI preschoolers had more than double the prevalence of obesity when compared with the general population and are the only group to experience an increase since 2003.[57,86] Furthermore, 38% of obese children in this study had significantly abnormal blood lipids, higher blood glucose, and higher abdominal adiposity relative to normal-weight children (*P*<0.01). Unfortunately, AI parents and primary caregivers rarely recognize overweight in their children and rarely realize that excess weight has adverse health consequences later in life.[85] Given evidence that disparities in obesity prevalence emerge in early childhood,[87] tailored intervention strategies at a range of intensities are needed for young AI/AN children.

Research is also needed to understand the effects of prenatal and early postnatal factors on adiposity, cardiovascular risk markers, and the trajectory of BMI in AI/ANs. In WINGS (Wisconsin Indian Nutrition and Growth Study), 471 AI children aged 5 to 8 years from 3 Wisconsin tribes were assessed with anthropometric measures, body fat measures, and nonfasting lipids and glucose by fingerstick blood samples.[88] Tribal records from Women, Infants, and Children programs and clinic charts provided longitudinal data on the trajectory of children's BMI, maternal prenatal factors, and the early postnatal feeding environment. Forty-seven percent of children were overweight or obese. Analysis of growth trajectories showed that children's BMI category was largely determined within the first year of life. Significant predictors of BMI at age 1 year included macrosomia (odds ratio [OR]: 4.38), excess gestational weight gain (OR: 1.64), and early termination of breastfeeding (OR: 1.66). Children who were overweight or obese at age 1 year had greater odds of being overweight (OR: 3.42) or obese (OR: 3.36) and having unhealthy levels of body fat (OR: 2.95) and low-density lipoprotein (OR: 1.64) at ages 5 to 8 years.

Despite this evidence for the importance of the first years of life in individual CVD risk, few primary prevention studies have targeted young children.[89] Yet early childhood is a critical window for the development of health-related behaviors, such as food preferences and physical activity, with guidance from parents and caregivers.[90] Family-level interventions are therefore urgently needed to encourage healthy eating and physical activity among AI/AN children.

Cardiovascular Disease Among AN Peoples

While there are no systematic data on cardiovascular disease among the AN pediatric population, data in younger adults show prevalent CVD risk factors such as obesity and impaired glucose metabolism that provide background information to use in planning studies and interventions. Older literature generally assumed that ANs were protected against CVD by lifestyle factors, although a comprehensive review in 2003 found little evidence to support this hypothesis. The authors reported that incident CVD has been increasing among ANs at least since the 1980s, and that current incidence rates for hypertension and CVD are similar to those in the all-races population of Alaska and the United States overall.[91] They related the increase in CVD to a high community prevalence of cigarette smoking, obesity, and diabetes mellitus; ongoing lifestyle changes that favored physical inactivity; and consumption of nonmarine fatty acids.[91] Further, CVD mortality in ANs appears to be comparable to that of the general population.[92]

Members of our author group recently published a review of the literature on CVD in ANs that has appeared since 2013.[93] We draw on that review in the following paragraphs.

The Alaska Siberia Project, a cross-sectional survey conducted in 1994, was one of the earliest epidemiologic studies to use thorough and validated methods to assess prevalent CVD and its risk factors in ANs.[94] This project was modeled closely on SHS.[95] Investigators recruited more than 50% of residents aged 25 years or older of 4 villages in the Bering Straits region of Northwestern Alaska. A subsequent study funded by the National Heart, Lung, and Blood Institute, the GOCADAN (Genetics of Coronary Artery Disease in Alaska Natives), investigated genetic and nongenetic determinants of CVD and its risk factors in a sample of 1214 predominantly Inupiat participants from the Norton Sound region of Northwestern Alaska. Baseline data collection was conducted from 2000 to 2004, with follow-up in 2006 to 2010.[96] The EARTH (Education and Research towards Health) study, funded by the National Cancer Institute, recruited AN participants from several regions, including more than 1000 from the Yukon-Kuskokwim Delta, for a study of chronic diseases (including cancer) and their risk factors.[97] The CANHR (Center for Alaska Native Health Research), funded by the National Center for Research Resources, started in the early 2000s and focused on risk and protective factors for obesity and chronic diseases, including CVD.[98,99] CANHR obtained biological, genetic, nutritional, and psychosocial data from examination

of nearly 1000 ANs aged 14 years or older from 10 communities in the Yukon-Kuskokwim Delta.[98,99] However, they report the cardiometabolic baseline profile of those aged 18 years or older (n=753) and found that CANHR participants with normal glycemia were younger and had a healthier cardiometabolic profile compared with those with impaired fasting glucose or with diabetes mellitus.[99]

The WATCH study (Western Alaska Tribal Collaborative for Health) is a unique collaboration among investigators with CANHR, GOCADAN, and EARTH. Its purpose is to harmonize data and methods in order to improve surveillance of CVD and diabetes mellitus and to facilitate studies of their risk factors and outcomes in ANs.[100] The WATCH cohort comprises 4569 western AN people (2116 men, 2453 women). WATCH investigators collect prospective surveillance data with an average 6.7-year follow-up on a subset of the cohort comprising 2754 participants (1218 men, 1536 women) who consented to continued surveillance. They have established that total mortality rates among western AN peoples are higher than those of US whites.[101] CVD was the leading cause of death, with mortality rates only slightly higher in men than in women. Although mortality rates attributable to coronary heart disease tended to be lower among WATCH participants than among US whites, rates of fatal stroke appeared to exceed those in US whites. Among WATCH women, mortality rates because of stroke were almost as high as those for coronary heart disease. Among both sexes, the prevalence of hypertension and prehypertension was slightly lower than in the US general population, while the prevalence of diabetes mellitus was lower not only than in the general population but also than in AI/ANs residing in the contiguous 48 states.[102]

Discussion

Measures of subclinical disease confirm that the high prevalence of CVD risk factors among AI/ANs leads to significant adverse changes in cardiac structure and function. Combined with other findings in the literature, this conclusion indicates a high probability that the incidence of CVD events in Native adults will continue to rise. Notably, AI/AN youth with multiple risk factors exhibit more extensive subclinical CVD than those without.[89,91] Thus it seems obvious that atherosclerosis starts in childhood and is associated with the same risk factors as CVD in adults. Accordingly, more data on CVD risk factors unique to AI/AN youth are sorely needed. In addition, a glaring omission in the medical literature is an understanding of adverse childhood experiences and other psychosocial factors and their relation to CVD in AI/ANs. There is a fair body of literature associating adverse childhood experiences with CVD in the general population, though our knowledge of adverse childhood experiences in indigenous

populations is limited to their prevalence in AI/ANs.[103] The prevalence of a significant adverse childhood experience score (3 or more) is more than double that of the general population, which highlights the need to explore the long-term effects of this disparity.[104] Furthermore, we identify exposure to environmental contaminants, diet, and physical activity as areas in particular need of future research.

Few studies have assessed the role of exposure to metals and environmental pollutants in the development of CVD in AI/ANs. Major population disparities are known to exist in exposure to environmental toxicants, and AI communities in particular experience heightened risk. Unfortunately, environmental exposures are involuntary and often beyond the control of exposed individuals. Moreover, they are likely to have adverse health effects not only in childhood but even before birth, potentially before other pathophysiological risk factors for CVD become significant. For these reasons, cohort studies are needed to understand the contribution of environmental exposures to incident CVD.

The challenges of collecting dietary data from youth and the paucity of longitudinal studies among AI/ANs are well known. Nevertheless, it is clear that the diets of Native youth, like those of most Americans, are lacking in fresh fruits, vegetables, meats, and grains, with disproportionate contributions from processed foods and sugar-sweetened beverages. Early dietary interventions are critical, as life-shaping habits develop early in life, while the risk of obesity and other cardiometabolic disease increases with age. Although some intervention research has promoted healthy eating among AI/AN youth, most programs are brief, and they have shown little efficacy in achieving long-term dietary improvement. Negative outcomes might be attributable in part to an overly narrow scope of implementation (eg, school-based programs with little effect outside the classroom). Thus, multilevel interventions that encompass children, families, and communities are essential, as are sustainable programs that can be implemented in resource-limited settings with inadequate access to healthy foods.

Our understanding of the role of physical activity in preventing CVD among AI/AN youth is restricted by the paucity of randomized trials designed to increase physical activity in community settings. With regard to obesity, few interventions have prioritized adolescents, and fewer still have targeted prenatal or early-life influences. With regard to emerging CVD risk factors, such as stress, sleep, nutritional factors, seasonal change, climate change, and changes in the gut microbiome, the state of research is even more rudimentary. Investigators urgently need to understand which improvements in policies, systems, or physical environments can promote and sustain healthy behaviors. Studies of community-level policies and systems are ill-suited to

randomized trials, given the small size of many AI/AN communities and the expense of community-based programs, yet such trials are essential.

With regard to ANs, further pediatric research and engagement is needed on novel as well as traditional CVD risk factors, particularly among young children. Continued surveillance is indispensable to elucidate emerging sources of risk, including genetic and environmental factors. Studies must also examine lifestyle factors (eg, traditional patterns of diet and physical activity) that might explain community-level differences in diabetes mellitus incidence. Also needed are educational interventions that use community resources and highlight resiliency in reducing CVD risk.

Thankfully, our knowledge of CVD risk factors in AI/AN youth is expanding. Noninvasive imaging has established that children and adolescents with multiple CVD risk factors also have subclinical CVD. Thus, given the notable risk of early CVD mortality among AI/ANs, primary prevention and treatment must begin early in life. Interventions that wait until adulthood have clearly failed to stem the tide of CVD in Native communities. Of course, identifying pediatric predictors of incident CVD will require focused longitudinal study, but we believe that cardiovascular screening during pediatric care is one of the most promising avenues for reducing the harsh disparities in CVD mortality experienced by Native people. This strategy might ultimately diminish the burden of CVD in a highly vulnerable US population.

Acknowledgments

Disclosures

None.

References

1. Lee ET, Welty TK, Fabsitz R, Cowan LD, Le NA, Oopik AJ, Cucchiara AJ, Savage PJ, Howard BV. The Strong Heart Study. A study of cardiovascular disease in American Indians: design and methods. *Am J Epidemiol*. 1990;132:1141–1155.

2. North KE, Howard BV, Welty TK, Best LG, Lee ET, Yeh JL, Fabsitz RR, Roman MJ, MacCluer JW. Genetic and environmental contributions to cardiovascular disease risk in American Indians: the Strong Heart Family Study. *Am J Epidemiol*. 2003;157:303–314.

3. Veazie M, Ayala C, Schieb L, Dai S, Henderson JA, Cho P. Trends and disparities in heart disease mortality among American Indians/Alaska Natives, 1990–2009. *Am J Public Health*. 2014;104(suppl 3):S359–S367.

4. Howard BV, Lee ET, Cowan LD, Devereux RB, Galloway JM, Go OT, Howard WJ, Rhoades ER, Robbins DC, Sievers ML, Welty TK. Rising tide of cardiovascular disease in American Indians. The Strong Heart Study. *Circulation*. 1999;99:2389–2395.

5. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER III, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB; American Heart Association Statistics C and Stroke Statistics S. Executive summary: heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation*. 2014;129:399–410.

6. Schweigman K, Eichner J, Welty TK, Zhang Y. Cardiovascular disease risk factor awareness in American Indian communities: the Strong Heart Study. *Ethn Dis*. 2006;16:647–652.

7. Welty TK, Rhoades DA, Yeh F, Lee ET, Cowan LD, Fabsitz RR, Robbins DC, Devereux RB, Henderson JA, Howard BV. Changes in cardiovascular disease risk factors among American Indians. The Strong Heart Study. *Ann Epidemiol*. 2002;12:97–106.

8. Centers for Disease C and Prevention. Disparities in premature deaths from heart disease—50 States and the District of Columbia, 2001. *MMWR Morb Mortal Wkly Rep*. 2004;53:121–125.

9. Schell LM, Gallo MV. Overweight and obesity among North American Indian infants, children, and youth. *Am J Hum Biol*. 2012;24:302–313.

10. Franks PW, Hanson RL, Knowler WC, Sievers ML, Bennett PH, Looker HC. Childhood obesity, other cardiovascular risk factors, and premature death. *N Engl J Med*. 2010;362:485–493.

11. Mayer-Davis EJ, Lawrence JM, Dabelea D, Divers J, Isom S, Dolan L, Imperatore G, Linder B, Marcovina S, Pettitt DJ, Pihoker C, Saydah S, Wagenknecht L; Study SfDiY. Incidence trends of type 1 and type 2 diabetes among youths, 2002–2012. *N Engl J Med*. 2017;376:1419–1429.

12. Chinali M, de Simone G, Roman MJ, Best LG, Lee ET, Russell M, Howard BV, Devereux RB. Cardiac markers of pre-clinical disease in adolescents with the metabolic syndrome: the Strong Heart Study. *J Am Coll Cardiol*. 2008;52:932–938.

13. de Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the Third National Health and Nutrition Examination Survey. *Circulation*. 2004;110:2494–2497.

14. Berenson GS, Srinivasan SR, Bao W, Newman WP III, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. *N Engl J Med*. 1998;338:1650–1656.

15. Chinali M, de Simone G, Roman MJ, Lee ET, Best LG, Howard BV, Devereux RB. Impact of obesity on cardiac geometry and function in a population of adolescents: the Strong Heart Study. *J Am Coll Cardiol*. 2006;47:2267–2273.

16. Drukteinis JS, Roman MJ, Fabsitz RR, Lee ET, Best LG, Russell M, Devereux RB. Cardiac and systemic hemodynamic characteristics of hypertension and prehypertension in adolescents and young adults: the Strong Heart Study. *Circulation*. 2007;115:221–227.

17. De Marco M, de Simone G, Roman MJ, Chinali M, Lee ET, Calhoun D, Howard BV, Devereux RB. Cardiac geometry and function in diabetic or prediabetic adolescents and young adults: the Strong Heart Study. *Diabetes Care*. 2011;34:2300–2305.

18. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med*. 1999;340:14–22.

19. Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death. The Framingham Heart Study. *Circulation*. 1995;92:835–841.

20. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med*. 1990;322:1561–1566.

21. Cosselman KE, Navas-Acien A, Kaufman JD. Environmental factors in cardiovascular disease. *Nat Rev Cardiol*. 2015;12:627–642.

22. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364:937–952.

23. Sallis JF, Floyd MF, Rodriguez DA, Saelens BE. Role of built environments in physical activity, obesity, and cardiovascular disease. *Circulation*. 2012;125:729–737.

24. Franco M, Diez-Roux AV, Nettleton JA, Lazo M, Brancati F, Caballero B, Glass T, Moore LV. Availability of healthy foods and dietary patterns: the Multi-Ethnic Study of Atherosclerosis. *Am J Clin Nutr*. 2009;89:897–904.

25. Tellez-Plaza M, Guallar E, Howard BV, Umans JG, Francesconi KA, Goessler W, Silbergeld EK, Devereux RB, Navas-Acien A. Cadmium exposure and incident cardiovascular disease. *Epidemiology*. 2013;24:421–429.

26. Moon KA, Guallar E, Umans JG, Devereux RB, Best LG, Francesconi KA, Goessler W, Pollak J, Silbergeld EK, Howard BV, Navas-Acien A. Association between exposure to low to moderate arsenic levels and incident cardiovascular disease. A prospective cohort study. *Ann Intern Med*. 2013; 159:649–659.

27. Navas-Acien A, Umans JG, Howard BV, Goessler W, Francesconi KA, Crainiceanu CM, Silbergeld EK, Guallar E. Urine arsenic concentrations and species excretion patterns in American Indian communities over a 10-year period: the Strong Heart Study. *Environ Health Perspect*. 2009;117:1428–1433.

28. Pang Y, Peng RD, Jones MR, Francesconi KA, Goessler W, Howard BV, Umans JG, Best LG, Guallar E, Post WS, Kaufman JD, Vaidya D, Navas-Acien A. Metal mixtures in urban and rural populations in the US: the Multi-Ethnic Study of Atherosclerosis and the Strong Heart Study. *Environ Res*. 2016;147:356–364.

29. Blake JM, Avasarala S, Artyushkova K, Ali AM, Brearley AJ, Shuey C, Robinson WP, Nez C, Bill S, Lewis J, Hirani C, Pacheco JS, Cerrato JM. Elevated concentrations of U and co-occurring metals in abandoned mine wastes in a northeastern Arizona Native American community. *Environ Sci Technol*. 2015;49:8506–8514.

30. Lewis J, Gonzales M, Burnette C, Benally M, Seanez P, Shuey C, Nez H, Nez C, Nez S. Environmental exposures to metals in Native communities and implications for child development: basis for the Navajo birth cohort study. *J Soc Work Disabil Rehabil*. 2015;14:245–269.

31. Satarug S, Moore MR. Adverse health effects of chronic exposure to low-level cadmium in foodstuffs and cigarette smoke. *Environ Health Perspect*. 2004;112:1099–1103.

32. Olmedo P, Grau-Perez M, Fretts A, Tellez-Plaza M, Gil F, Yeh F, Umans JG, Francesconi KA, Goessler W, Franceschini N, Lee ET, Best LG, Cole SA, Howard BV, Navas-Acien A. Dietary determinants of cadmium exposure in the Strong Heart Family Study. *Food Chem Toxicol*. 2017;100:239–246.

33. Newman JD, Navas-Acien A, Kuo CC, Guallar E, Howard BV, Fabsitz RR, Devereux RB, Umans JG, Francesconi KA, Goessler W, Best LT, Tellez-Plaza M. Peripheral arterial disease and its association with arsenic exposure and metabolism in the Strong Heart Study. *Am J Epidemiol*. 2016;184:806–817.

34. Tellez-Plaza M, Guallar E, Fabsitz RR, Howard BV, Umans JG, Francesconi KA, Goessler W, Devereux RB, Navas-Acien A. Cadmium exposure and incident peripheral arterial disease. *Circ Cardiovasc Qual Outcomes*. 2013;6:626–633.

35. Messner B, Knoflach M, Seubert A, Ritsch A, Pfaller K, Henderson B, Shen YH, Zeller I, Willeit J, Laufer G, Wick G, Kiechl S, Bernhard D. Cadmium is a novel and independent risk factor for early atherosclerosis mechanisms and in vivo relevance. *Arterioscler Thromb Vasc Biol*. 2009;29:1392–1398.

36. Tellez-Plaza M, Jones MR, Dominguez-Lucas A, Guallar E, Navas-Acien A. Cadmium exposure and clinical cardiovascular disease: a systematic review. *Curr Atheroscler Rep*. 2013;15:356.

37. Interior BoRDot. Mni Wiconi Rural Water Supply Project. 2015.

38. Samet JM, Marbury MC, Spengler JD. Health effects and sources of indoor air pollution. Part I. *Am Rev Respir Dis*. 1987;136:1486–1508.

39. Rogalsky DK, Mendola P, Metts TA, Martin WJ II. Estimating the number of low-income Americans exposed to household air pollution from burning solid fuels. *Environ Health Perspect*. 2014;122:806–810.

40. Adgate JL, Goldstein BD, McKenzie LM. Potential public health hazards, exposures and health effects from unconventional natural gas development. *Environ Sci Technol*. 2014;48:8307–8320.

41. Story M, Strauss KF, Zephier E, Broussard BA. Nutritional concerns in American Indian and Alaska Native children: transitions and future directions. *J Am Diet Assoc*. 1998;98:170–176.

42. LaRowe TL, Adams AK, Jobe JB, Cronin KA, Vannatter SM, Prince RJ. Dietary intakes and physical activity among preschool-aged children living in rural American Indian communities before a family-based healthy lifestyle intervention. *J Am Diet Assoc*. 2010;110:1049–1057.

43. Cunningham-Sabo LD, Davis SM, Koehler KM, Fugate ML, DiTucci JA, Skipper BJ. Food preferences, practices, and cancer-related food and nutrition knowledge of southwestern American Indian youth. *Cancer*. 1996;78:1617–1622.

44. Nelson DE, Moon RW, Holtzman D, Smith P, Siegel PZ. Patterns of health risk behaviors for chronic disease: a comparison between adolescent and adult American Indians living on or near reservations in Montana. *J Adolesc Health*. 1997;21:25–32.

45. Ballew C, White LL, Strauss KF, Benson LJ, Mendlein JM, Mokdad AH. Intake of nutrients and food sources of nutrients among the Navajo: findings from the Navajo Health and Nutrition Survey. *J Nutr*. 1997;127:2085s–2093s.

46. Hoffhines H, Whaley KD, Blackett PR, Palumbo K, Campbell-Sternloff D, Glore S, Lee ET. Early childhood nutrition in an American Indian community: educational strategy for obesity prevention. *J Okla State Med Assoc*. 2014;107:55–59.

47. Collins CE, Watson J, Burrows T. Measuring dietary intake in children and adolescents in the context of overweight and obesity. *Int J Obes (Lond)*. 2010;34:1103–1115.

48. St George SM, Van Horn ML, Lawman HG, Wilson DK. Reliability of 24-hour dietary recalls as a measure of diet in African-American youth. *J Acad Nutr Diet*. 2016;116:1551–1559.

49. Fretts AM, Howard BV, McKnight B, Duncan GE, Beresford SA, Mete M, Eilat-Adar S, Zhang Y, Siscovick DS. Associations of processed meat and unprocessed red meat intake with incident diabetes: the Strong Heart Family Study. *Am J Clin Nutr*. 2012;95:752–758.

50. Block G, Thompson F, Hartman A, Larkin F, Guire K. Comparison of two dietary questionnaires validated against multiple dietary records collected during a 1-year period. *J Am Diet Assoc*. 1992;92:686–693.

51. Boucher B, Cotterchio M, Kreiger N, Nadalin V, Block T, Block G. Validity and reliability of the Block98 food frequency questionnaire in a sample of Canadian women. *Public Health Nutr*. 2006;9:84–93.

52. Caan B, Slattery M, Potter J, Quesenberry C, Coates A, Schaffer D. Comparison of the Block and Willett self-administered semiquantitative food frequency questionnaires with an interview-administered dietary food history. *Am J Epidemiol*. 1998;148:1137–1147.

53. Subar A, Thompson F, Kipnis V, Midthune D, Hurwitz P, McNutt S, McIntosh A, Rosenfeld S. Comparative validation of the Block, Willett, and National Cancer Institute food frequency questionnaires. *Am J Epidemiol*. 2001;154:1089–1099.

54. Fretts AM, Howard BV, McKnight B, Duncan GE, Beresford SA, Mete M, Zhang Y, Siscovick DS. Life's Simple 7 and incidence of diabetes among American Indians: the Strong Heart Family Study. *Diabetes Care*. 2014;37:2240–2245.

55. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Greenlund KJ, Hailpern SM, Heit JA, Ho PM, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, McDermott MM, Meigs JB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Rosamond WD, Sorlie PD, Stafford RS, Turan TN, Turner MB, Wong ND, Wylie-Rosett J; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2011 update: a report from the American Heart Association. *Circulation*. 2011;123:e18–e209.

56. Huffman MD, Capewell S, Ning HY, Shay CM, Ford ES, Lloyd-Jones DM. Cardiovascular health behavior and health factor changes (1988–2008) and projections to 2020 results from the National Health and Nutrition Examination Surveys. *Circulation*. 2012;125:2595–2602.

57. Tomayko EJ, Prince RJ, Cronin KA, Adams AK. The Healthy Children, Strong Families intervention promotes improvements in nutrition, activity, and body weight in American Indian families with young children. *Public Health Nutr*. 2016;19:2850–2859.

58. Gittelsohn J, Davis SM, Steckler A, Ethelbah B, Clay T, Metcalfe L, Rock BH. Pathways: lessons learned and future directions for school-based interventions among American Indians. *Prev Med*. 2003;37:S107–S112.

59. Mozaffarian D, Afshin A, Benowitz NL, Bittner V, Daniels SR, Franch HA, Jacobs DR Jr, Kraus WE, Kris-Etherton PM, Krummel DA, Popkin BM, Whitsel LP, Zakai NA. Population approaches to improve diet, physical activity, and smoking habits: a scientific statement from the American Heart Association. *Circulation*. 2012;126:1514–1563.

60. Kumanyika S, Grier S. Targeting interventions for ethnic minority and low-income populations. *Future Child*. 2006;16:187–207.

61. Ness M, Barradas DT, Irving J, Manning SE. Correlates of overweight and obesity among American Indian/Alaska Native and non-Hispanic White children and adolescents: National Survey of Children's Health, 2007. *Matern Child Health J*. 2012;16(suppl 2):268–277.

62. Adams A. Understanding community and family barriers and supports to physical activity in American Indian children. *J Public Health Manag Pract*. 2010;16:401–403.

63. Horn OK, Paradis G, Potvin L, Macaulay AC, Desrosiers S. Correlates and predictors of adiposity among Mohawk children. *Prev Med*. 2001;33:274–281.

64. Jollie-Trottier T, Holm JE, McDonald JD. Correlates of overweight and obesity in American Indian children. *J Pediatr Psychol*. 2009;34:245–253.

65. Stevens J, Suchindran C, Ring K, Baggett CD, Jobe JB, Story M, Thompson J, Going SB, Caballero B. Physical activity as a predictor of body composition in American Indian children. *Obes Res*. 2004;12:1974–1980.

66. Duncan GE, Goldberg J, Buchwald D, Wen Y, Henderson JA. Epidemiology of physical activity in American Indians in the Education and Research Towards Health cohort. *Am J Prev Med*. 2009;37:488–494.

67. Holm JE, Lilienthal KR, Poltavski DV, Vogelanz-Holm N. Relationships between health behaviors and weight status in American Indian and white rural children. *J Rural Health*. 2013;29:349–359.

68. Berg CJ, Daley CM, Nazir N, Kinlacheeny JB, Ashley A, Ahluwalia JS, Greiner KA, Choi WS. Physical activity and fruit and vegetable intake among American Indians. *J Community Health*. 2012;37:65–71.

69. Polley DC, Spicer MT, Knight AP, Hartley BL. Intrafamilial correlates of overweight and obesity in African-American and Native-American grandparents, parents, and children in rural Oklahoma. *J Am Diet Assoc*. 2005;105:262–265.

70. Storti KL, Arena VC, Barmada MM, Bunker CH, Hanson RL, Laston SL, Yeh JL, Zmuda JM, Howard BV, Kriska AM. Physical activity levels in American-Indian adults: the Strong Heart Family Study. *Am J Prev Med*. 2009;37:481–487.

71. Barnes PM, Adams PF, Powell-Griner E. Health characteristics of the American Indian or Alaska Native adult population: United States, 2004–2008. *Natl Health Stat Report*. 2010:1–22.

72. Johnson NB, Hayes LD, Brown K, Hoo EC, Ethier KA; Centers for Disease C and Prevention. CDC National Health Report: leading causes of morbidity and mortality and associated behavioral risk and protective factors—United States, 2005–2013. *MMWR Suppl*. 2014;63:3–27.

73. Dennison ME, Sisson SB, Lora K, Stephens LD, Copeland KC, Caudillo C. Assessment of body mass index, sugar sweetened beverage intake and time spent in physical activity of American Indian children in Oklahoma. *J Community Health*. 2015;40:808–814.

74. Foulds HJ, Warburton DE, Bredin SS. A systematic review of physical activity levels in Native American populations in Canada and the United States in the last 50 years. *Obes Rev*. 2013;14:593–603.

75. Adams A, Prince R. Correlates of physical activity in young American Indian children: lessons learned from the Wisconsin Nutrition and Growth Study. *J Public Health Manag Pract*. 2010;16:394–400.

76. Fleischhacker S, Roberts E, Camplain R, Evenson KR, Gittelsohn J. Promoting physical activity among Native American youth: a systematic review of the methodology and current evidence of physical activity interventions and community-wide initiatives. *J Racial Ethn Health Disparities*. 2016;3:608–624.

77. Brown B, Noonan C, Harris KJ, Parker M, Gaskill S, Ricci C, Cobbs G, Gress S. Developing and piloting the Journey to Native Youth Health program in Northern Plains Indian communities. *Diabetes Educ*. 2013;39:109–118.

78. Obesity and American Indians/Alaska Natives. 2007. Available at: https://aspe.hhs.gov/pdf-report/obesity-and-american-indiansalaska-natives. Accessed 12/2/2016.

79. Lindsay RS, Cook V, Hanson RL, Salbe AD, Tataranni A, Knowler WC. Early excess weight gain of children in the Pima Indian population. *Pediatrics*. 2002;109:E33.

80. Salbe AD, Weyer C, Lindsay RS, Ravussin E, Tataranni PA. Assessing risk factors for obesity between childhood and adolescence: I. Birth weight, childhood adiposity, parental obesity, insulin, and leptin. *Pediatrics*. 2002;110:299–306.

81. Dalenius K, Borland E, Smith B, Polhamus B, Grummer-Strawn L. *Pediatric Nutrition Surveillance 2010 Report*. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2012.

82. Centers for Disease C and Prevention. Obesity prevalence among low-income, preschool-aged children—United States, 1998–2008. *MMWR Morb Mortal Wkly Rep*. 2009;58:769–773.

83. IoM. *Early Childhood Obesity Prevention Policies*. Washington, DC: The National Academies Press; 2011.

84. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med*. 1997;337:869–873.

85. Adams AK, Quinn RA, Prince RJ. Low recognition of childhood overweight and disease risk among Native-American caregivers. *Obes Res*. 2005;13:146–152.

86. Ogden CL, Carroll MD, Fryar CD, Flegal KM. Prevalence of obesity among adults and youth: United States, 2011–2014. *NCHS Data Brief*. 2015:1–8.

87. Pan L, May AL, Wethington H, Dalenius K, Grummer-Strawn LM. Incidence of obesity among young U.S. children living in low-income families, 2008–2011. *Pediatrics*. 2013;132:1006–1013.

88. Lindberg SM, Adams AK, Prince RJ. Early predictors of obesity and cardiovascular risk among American Indian children. *Matern Child Health J*. 2012;16:1879–1886.

89. Hoelscher DM, Kirk S, Ritchie L, Cunningham-Sabo L; Academy Positions Committee. Position of the Academy of Nutrition and Dietetics: interventions for the prevention and treatment of pediatric overweight and obesity. *J Acad Nutr Diet*. 2013;113:1375–1394.

90. Bruss MB, Morris J, Dannison L. Prevention of childhood obesity: sociocultural and familial factors. *J Am Diet Assoc*. 2003;103:1042–1045.

91. Schumacher C, Davidson M, Ehrsam G. Cardiovascular disease among Alaska Natives: a review of the literature. *Int J Circumpolar Health*. 2003;62:343–362.

92. Bjerregaard P, Young TK, Hegele RA. Low incidence of cardiovascular disease among the Inuit—what is the evidence? *Atherosclerosis*. 2003;166:351–357.

93. Jolly SE, Howard BV, Umans JG. Cardiovascular disease among Alaska Native peoples. *Curr Cardiovasc Risk Rep*. 2013;7:438–445.

94. Ebbesson SO, Schraer CD, Risica PM, Adler AI, Ebbesson L, Mayer AM, Shubnikof EV, Yeh J, Go OT, Robbins DC. Diabetes and impaired glucose tolerance in three Alaskan Eskimo populations. The Alaska-Siberia Project. *Diabetes Care*. 1998;21:563–569.

95. Welty TK, Lee ET, Yeh J, Cowan LD, Go O, Fabsitz RR, Le NA, Oopik AJ, Robbins DC, Howard BV. Cardiovascular disease risk factors among American Indians. The Strong Heart Study. *Am J Epidemiol*. 1995;142:269–287.

96. Howard BV, Devereux RB, Cole SA, Davidson M, Dyke B, Ebbesson SO, Epstein SE, Robinson DR, Jarvis B, Kaufman DJ, Laston S, MacCluer JW, Okin PM, Roman MJ, Romenesko T, Ruotolo G, Swenson M, Wenger CR, Williams-Blangero S, Zhu J, Saccheus C, Fabsitz RR, Robbins DC. A genetic and epidemiologic study of cardiovascular disease in Alaska Natives (GOCADAN): design and methods. *Int J Circumpolar Health*. 2005;64:206–221.

97. Slattery ML, Schumacher MC, Lanier AP, Edwards S, Edwards R, Murtaugh MA, Sandidge J, Day GE, Kaufman D, Kanekar S, Tom-Orme L, Henderson JA. A prospective cohort of American Indian and Alaska Native people: study design, methods, and implementation. *Am J Epidemiol*. 2007;166:606–615.

98. Boyer BB, Mohatt GV, Lardon C, Plaetke R, Luick BR, Hutchison SH, de Mayolo GA, Ruppert E, Bersamin A. Building a community-based participatory research center to investigate obesity and diabetes in Alaska Natives. *Int J Circumpolar Health*. 2005;64:281–290.

99. Mohatt GV, Plaetke R, Klejka J, Luick B, Lardon C, Bersamin A, Hopkins S, Dondanville M, Herron J, Boyer B; Center for Alaska Native Health Research. The Center for Alaska Native Health Research Study: a community-based participatory research study of obesity and chronic disease-related protective and risk factors. *Int J Circumpolar Health*. 2007;66:8–18.

100. Koller KR, Wolfe AW, Metzger JS, Austin MA, Hopkins SE, Kaufmann C, Jolly SE, Ebbesson SO, Umans JG, Howard BV, Boyer BB. Utilizing harmonization and common surveillance methods to consolidate 4 cohorts: the Western Alaska Tribal Collaborative for Health (WATCH) study. *Int J Circumpolar Health*. 2013;72:20572.

101. Howard BV, Metzger JS, Koller KR, Jolly SE, Asay ED, Wang H, Wolfe AW, Hopkins SE, Kaufmann C, Raymer TW, Trimble B, Provost EM, Ebbesson SO, Austin MA, Howard WJ, Umans JG, Boyer BB. All-cause, cardiovascular, and cancer mortality in western Alaska Native people: western Alaska Tribal Collaborative for Health (WATCH). *Am J Public Health*. 2014;104:1334–1340.

102. Koller KR, Metzger JS, Jolly SE, Umans JG, Hopkins SE, Kaufmann C, Wilson AS, Ebbesson SO, Raymer TW, Austin MA, Howard BV, Boyer BB. Cardiometabolic correlates of low type 2 diabetes incidence in western Alaska Native people—the WATCH study. *Diabetes Res Clin Pract*. 2015;108:423–431.

103. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. *Am J Prev Med*. 1998;14:245–258.

104. Kenney MK, Singh GK. Adverse childhood experiences among American Indian/Alaska Native Children: the 2011–2012 National Survey of Children's Health. *Scientifica (Cairo)*. 2016;2016:7424239.

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