Published in final edited form as:

Diabetes Res Clin Pract. 2015 June ; 108(3): 423–431. doi:10.1016/j.diabres.2015.03.001.

Cardiometabolic Correlates of Low Type 2 Diabetes Incidence in Western Alaska Native People -- the WATCH Study

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Abstract

Aims—Previously rare among Alaska Native (AN) people, type 2 diabetes (DM2) prevalence as indicated by registry data has increased by as much as 300% in some western Alaska regions. We sought to determine prevalence and incidence of DM2 and analyze associated cardiometabolic risk factors in western AN people.

Methods—DM2 and prediabetes prevalence and incidence were determined by the Western Alaska Tribal Collaborative for Health using consolidated data from cohort studies conducted during 2000–2010. Crude and age-adjusted incidence for DM2 and prediabetes were calculated using 2010 American Diabetes Association criteria. Effects of covariates on DM2 and prediabetes were determined using univariate and multivariate Cox proportional hazards analyses, adjusted for age and sex.

Results—Excluding baseline diabetes (n=124, 4.5%), 53 cases of new DM2 were identified among 2,630 participants. Age- and sex-adjusted DM2 incidence was 4.3/1,000 (95% CI 2.9, 5.0)

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Disclosure statement: The authors have nothing to declare.

Conflicts of interest: none.

person-years over an average 5.9-year follow up. After excluding baseline prediabetes, 387 new cases of prediabetes were identified among 1,841 participants; adjusted prediabetes incidence was 44.5/1,000 (95% CI 39.5, 49.5) person years. Independent predictors for DM2 included age, impaired fasting glucose, and metabolic syndrome; family history of diabetes and obesity were additional independent predictors for prediabetes.

Conclusions—DM2 incidence in western AN people is substantially lower than that for U.S. whites; however, incidence of prediabetes is more than 10-fold higher than western AN DM2 incidence and more closely aligned with U.S. rates. Interventions aimed at achieving healthy lifestyles are needed to minimize risk factors and maximize protective factors for DM2 in this population.

Keywords

Alaska Native (AN); DM2; metabolic syndrome; prediabetes; risk factors; Western Alaska Tribal Collaborative for Health

Introduction

As recently as 60 years ago, type 2 diabetes mellitus (DM2) was rare among Alaska Native (AN) people (1). Since the mid-1980s, the statewide Alaska Native Diabetes Registry (ANDR) has reported that DM2 prevalence has increased by as much as 300% in some regions (2). Prevalence varies by region, and cross-sectional data from the Norton Sound and Yukon Kuskokwim (YK) regions in western Alaska suggest prevalence is much lower among Inupiat and Yup'ik/Cup'ik peoples (2, 3, 4, 5, 6, 7) than among other AN and non-Native Alaskan ethnic groups. Inupiat and Yup'ik/Cup'ik peoples, once referred to as "Eskimo" but now called western Alaska Native people, comprise nearly 50% of the AN population in Alaska (8). Distantly related to Canadian and Greenland Inuit peoples, they are culturally and linguistically distinct from these groups as well as from the Indian and Aleut peoples of Alaska (9,10,11).

Currently available estimates of DM2 in this western AN population, however, are biased. ANDR data are diagnosis-based and do not include undiagnosed diabetes (2). The majority of reported U.S. diabetes cases (95%) are type 2 (12). While we acknowledge that a handful of diabetes cases in western Alaska may be type 1, the vast majority of diabetes in this population is DM2 (13). DM2 risk factors include age, gender, insulin resistance, and family history of diabetes. Because screening by providers is generally focused on individuals at increased risk, DM2 incidence estimates generated by the ANDR reflect rates within a high-risk sector of the population and/or of persons with greater access to health care. Thus, systematic population-based assessments of disease prevalence and incidence (where all are screened, regardless of risk or access to care) and examination of risk factors associated with DM2 incidence in Inupiat and Yup'ik/Cup'ik people living in western Alaska have not been conducted.

While previous small population-based studies suggested low DM2 prevalence in these regions (3,4,5), they were underpowered to determine incidence or prospectively examine risk factors. In this study, prevalence and incidence of DM2 as well as prediabetes were

estimated by sex and region, and associated cardiometabolic risk factors were analyzed in a follow-up cohort, of the Western Alaska Tribal Collaborative for Health (WATCH) study.

Material and Methods

The WATCH study combined four cohort studies conducted in two western Alaska regions since 1994 (14). The four studies were the Alaska-Siberia Project (ASP, enrollment 1994 and 1998), the Center for Alaska Native Health Research (CANHR, 2003–2010), the Alaska Education and Research Toward Health (EARTH, 2004–2006), and the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN, 2000–2004). Three of the four studies, CANHR, EARTH, and GOCADAN, have follow-up data obtained since baseline. Data consolidation of these three prospective studies resulted in a follow-up cohort (2,754 participants) large enough to examine population-based incidence of DM2, prediabetes, and risk factors in western AN people living in the Norton Sound and YK regions of Alaska.

Methods used to consolidate variables and baseline data from the participating cohort studies and overall mortality estimates have been described (14, 15). Briefly, baseline data included self-reported age, sex, ethnicity, and family history of diabetes. All participants were Inupiat or Yup'ik/Cup'ik ethnicity, age 18 years or older. Although each cohort was assembled using convenience sampling, a very large proportion of participants from the participating AN communities were accrued in all studies. Participating AN communities comprised 80%–90% of AN people living in these two regions. Frequency distributions of known population characteristics (e.g., age, sex, ethnicity, income level) compared closely with the regional population (14). All data were de-identified by each original cohort study and then combined in the WATCH data set. Objective measurements of baseline metabolic syndrome (MetS) markers (BMI; abdominal circumference; blood pressure; and fasting plasma high-density lipoprotein cholesterol [HDL-C], triglycerides, and glucose and/or non-fasting HbA1c) were also collected. These measurements were directly consolidated into the WATCH data set as continuous variables.

Assessment of baseline MetS components was based on the Adult Treatment Panel III guidelines (16). Hypertension was defined as blood pressure $\geq 130/85$ mmHg at baseline exam, a history of hypertension documented in the medical record, and/or having been prescribed medication for hypertension control. Central obesity was defined as an abdominal girth >102 cm (>40 inches) in men or >88 cm (>35 inches) in women. Elevated fasting glucose was defined as plasma glucose ≥ 100 mg/dl (≥ 5.6 mmol/l) following an 8-hour fast. Low HDL-C was defined as fasting levels <40 mg/dl (<1.03 mmol/l) in men or <50 mg/dl (<1.29 mmol/l) in women, and a high triglyceride level was defined as having fasting triglycerides ≥ 150 mg/dl (≥ 1.7 mmol/l). All continuous measures were converted to dichotomous variables indicating the presence or absence of any one of the five MetS components. MetS was determined by the presence of three or more MetS components at baseline. Additionally, overweight (BMI 25 – 29.9 kg/m²) and obesity (≥ 30 kg/m²) were defined using National Heart, Lung and Blood Institute (17) criteria.

Diagnosed diabetes prevalence prior to baseline was ascertained from self-report of diabetes medication use confirmed by interviewer inspection of medication labels or by the presence

of at least one diabetes ICD-9 code in the participant's medical record at baseline review. In accord with American Diabetes Association criteria (18), undiagnosed diabetes at baseline was determined by a fasting plasma glucose (FPG) measure ≥ 126 mg/dl (≥ 7.0 mmol/l); a 2-hour OGTT or random measure ≥ 200 mg/dl (≥ 11.1 mmol/l); or an HbA1c $\geq 6.5\%$ (≥ 48 mmol/mol) when no diabetes medication use or prior diabetes diagnosis was indicated in the medical record. Prediabetes was defined as baseline FPG 100–125 mg/dl (5.6–6.9 mmol/l); 2-hr OGTT (or non-fasting glucose) 140–199 mg/dl (7.8–11.0 mmol/l); or HbA1c 5.7–6.4% (39–47 mmol/mol) (18). The term, prediabetes is often used in the literature, with the understanding that not all prediabetes will convert to DM2. All participants with diabetes (previously diagnosed or undiagnosed) at baseline were excluded from the follow-up cohort used to estimate DM2 incidence and analyze associated risk factors in this study. In the subsequent analysis of prediabetes, all participants with baseline values in the prediabetic range were excluded from the subset to estimate prediabetes incidence and analyze risk factors associated with prediabetes incidence.

The same procedures were used prospectively in the WATCH follow-up cohort to identify new cases of DM2 and prediabetes since baseline (14). Incidence of both outcomes was determined by repeat physical examination conducted by study investigators and/or by medical record review of laboratory values obtained by Alaska Tribal Health System healthcare providers between the baseline measurement and the study's end. Incident DM2 and incident prediabetes during the study period were defined in the follow-up cohort using the same criteria noted above.

This study was approved by the institutional review boards of the University of Alaska Fairbanks, the MedStar Health Research Institute, and the Alaska Area Indian Health Service. Tribal approval was granted by the Alaska Native Tribal Health Consortium, the Norton Sound Health Corporation, and the Yukon-Kuskokwim Health Corporation. The authors cannot release any data or results without Tribal authorization. All research must have *a priori* review and approval by all participating Tribal entities.

Statistical Analysis

All statistical analyses were conducted using SAS[®] version 9.3. Person-years (PY) for each participant were calculated from the baseline exam to DM2 onset, date of last medical record review, or date of death. Crude incident rate ratios were calculated comparing rates among those with and without select risk factors within our cohort. Crude rates were then age-adjusted to the 2010 U.S. standard population (19) by the direct method, and Cox proportional hazard regression analyses were conducted to determine hazard ratios for incident DM2 between participants with and without baseline risk factors. Analyses adjusting only for age and sex were followed by multivariate analyses to determine the independent effects of covariates. Univariate and multivariate analyses were conducted similarly for incident prediabetes after the aforementioned baseline exclusions. Significance was determined by $p < 0.05$ and 95% confidence intervals for hazard ratios that did not include 1.0.

Results

The WATCH cohort consists of 4,569 western AN participants, with follow-up data available for 2,754 participants (60%), nearly 10% of the adult population in these regions. Baseline characteristics for participants consenting to follow-up have been reported previously (14); key variables used for the present analysis are presented (Table 1). No significant differences in baseline characteristics were detected between the follow-up cohort and the total WATCH cohort (14). Only 6.5% of the follow-up cohort reported a family history of diabetes, which was more prevalent in the YK region than in Norton Sound and among women compared with men. Smoking prevalence was high (70%).

Central obesity was more prevalent in the YK region and among women. Low HDL-C was more prevalent among women (all $p < 0.001$). Hypertension was more prevalent among men than women ($p = 0.004$) and in the YK region compared with Norton Sound ($p = 0.010$). Overall, prevalence of MetS was low (18.1%) but it was significantly higher among women (21.8% vs. 13.5% in men, $p < 0.001$) and among participants in the YK region ($p = 0.030$). DM2 prevalence also was low, 4.5%; 76 cases were diagnosed (prior to baseline) and 48 additional cases were detected at baseline (undiagnosed). Men (51%) had a higher prevalence of undiagnosed diabetes than women (30%, $p = 0.016$).

Excluding all participants with prevalent diabetes, 2,630 participants remained in the follow-up subset from which DM2 incidence was calculated. During an average follow-up of 5.9 years, 53 cases of new onset DM2 were identified; cumulative DM2 incidence was 2.0%, and crude DM2 incidence was 3.4/1,000 PY. Age- and sex-adjusted DM2 incidence was 4.3/1,000 PY (95% CI 3.1, 5.5) (Figure 1). Age at onset ranged from 22 to 85 years, with the highest incidence noted among participants ages 55 years. DM2 incidence did not differ significantly by sex or region.

Following exclusions for prevalent prediabetes, 1,841 participants with normal baseline values for glucose and HbA1c remained in the follow-up subset. Cumulative incidence of prediabetes was much higher (21.0 %/5.9 years) than DM2, with a crude incidence of 37.7/1,000 PY. Age- and sex-adjusted prediabetes incidence (Figure 1) was 44.5/1,000 PY in the follow-up cohort. As with DM2 incidence, prediabetes incidence in WATCH women (47.0/1,000 PY) was slightly, but non-significantly, higher than in men (41.8/1,000 PY) and increased with age.

Associations of DM2 and pre-diabetes with risk factors, depicted by crude incident rate ratios (IRRs) and age- and sex- adjusted univariate HRs, are presented (Table 2). Among individual cardiometabolic risk factors, BMI ≥ 25 kg/m², increased waist circumference, and prediabetes glucose or HbA1c demonstrated the greatest hazards for DM2. The age and sex adjusted hazard for DM2 was approximately six times greater in participants with MetS than in those without MetS. In contrast, crude IRRs and univariate HRs for cardiometabolic risk factors were much lower for prediabetes than for DM2; only BMI ≥ 30 kg/m², elevated triglycerides, and abdominal obesity in women were significant predictors. The presence of any two cardiometabolic risk factors (excluding elevated FPG or HbA1c) nearly doubled the

risk (HR 1.93) for prediabetes. HRs for sex-adjusted age and age-adjusted sex (Table 3) showed that age, but not sex, was a significant predictor for DM2 and prediabetes.

Independent effects of covariates on DM2 and prediabetes incidence were assessed by multivariable hazard ratios (Table 3). Model 1 of Table 3 included classic risk factors of age, sex, history of smoking, family history of diabetes, obesity (BMI ≥ 30 kg/m²), impaired fasting glucose, and MetS as a surrogate measure of insulin resistance. In this model, age, impaired fasting glucose, and MetS were the only significant predictors of DM2; family history of diabetes and obesity were additional significant predictors of prediabetes.

Model 2 of Table 3 included age, sex, and individual risk factors specific to MetS. In this model, three cardiometabolic risk factors present at baseline independently increased risk for DM2: abdominal obesity (HR 2.36), high triglycerides (HR 1.91), and prediabetes (elevated fasting glucose or HbA1c; HR 4.66). However, advancing age (HR 1.03) and abdominal obesity (HR 1.66) were the only risk factors to independently increase risk for prediabetes. Although male sex appeared to be significant ($p = 0.046$), the upper level of the 95% CI approached 1.0 ($p = 0.996$).

Discussion

In this population-based study analyzing prevalence, incidence, and risk factors for DM2 in western AN people, we found low DM2 prevalence and incidence compared to the general U.S. population and American Indian populations in the contiguous 48 states. Prevalence findings are consistent with prior reports in this population (3, 5, 20), but this is the first report with sufficient power to report population-based incidence rates in this population. Prevalence and incidence of prediabetes, however, indicated by either elevated fasting glucose or HbA1c, were much higher than those for DM2. Increasing age, MetS, and prediabetes were significant independent predictors for DM2 incidence. Significant independent predictors for prediabetes included increasing age, family history of diabetes, and MetS (Table 3, Model 1). Controlling for age and sex, abdominal obesity was the only independent predictor for prediabetes among the factors that comprise MetS (Table 3, Model 2).

National diabetes registry surveillance conducted by the Centers for Disease Control and Prevention in 2011 estimated age-adjusted diabetes incidence as 7.6/1,000 PY among the general U.S. population (21), an incidence rate which is higher than that of our western AN population (4.3/1,000 PY) and does not include undiagnosed diabetes. National Health and Nutrition Examination (NHANES) data show that diabetes incidence varies by race and/or ethnicity and has been consistently higher among U.S. Hispanics and Blacks than among Whites (22). Incidence among U.S. Whites in 2011 was reported at 7.0/1,000 PY, while it was 11.1/1,000 PY among U.S. Hispanics and 12.4/1,000 PY among U.S. Blacks (22); thus, our data indicate that the western AN population has the lowest DM2 rate of U.S. ethnic groups reported to date.

Although no comparable population-based longitudinal data exist for other AN regions, 4.5% DM2 prevalence in WATCH is lower than prevalence reported by the ANDR for the

south central region (5.8%) or for two regions in southeastern (6.4% and 11.0%) Alaska (2). As indicated previously, ANDR estimates of incidence may be higher because they are based on higher risk individuals; rates also include all AN ethnicities. South central Alaska registry estimated incidence is also lower than that of U.S. whites. In contrast, studies in American Indian communities report high diabetes prevalence (23,24). The Strong Heart Study reported prevalence among American Indians in Arizona, Oklahoma, and the Dakotas as 72%, 42%, and 46% (23). Overall diabetes incidence among these American Indian communities was much higher than for any other reported U.S. racial/ethnic group, ranging from 23.4/1,000 PY in those with normal glucose levels at baseline to 66.1/1,000 PY in those with prediabetes at baseline (24). However, prediabetes prevalence in these American Indian communities (14%, 19%, and 19%, respectively) was much lower than the WATCH prevalence of 29.7%.

The WATCH prevalence of prediabetes was much higher than that of the WATCH DM2 prevalence and was more closely aligned with the 35% prevalence found in the 2011 U.S. general population (25). In 2005–2008, prediabetes prevalence among U.S. Whites, Mexican Americans, and Blacks was similar (35%, 35%, and 36%, respectively). However, among American Indians age 15 years in 2001–2004, prediabetes prevalence was estimated at only 20%, consistent with the Strong Heart Study findings (3).

Reasons for the low DM2 prevalence and incidence in the presence of higher prevalence and incidence of prediabetes among western AN people are of interest. Risk factors in the AN population are similar to those of other U.S. populations, with age, obesity, prediabetes, and MetS (i.e., insulin resistance) being significant predictors for DM2. Obesity prevalence in WATCH (31%) is similar to 2003–2004 NHANES data for U.S. Whites (36%), but lower than that seen in Blacks (68.6%) and Mexican Americans (50.1%) who have higher rates of diabetes incidence (26). Obesity prevalence for WATCH men (20%) is lower than that for all other U.S. ethnic groups (Whites 33.9%, Blacks 39.4%, and Mexican Americans 33.3%). Thus, lower prevalence of obesity may be one explanation for the lower rate of DM2 in western AN men.

Prevalence and incidence of DM2 are similar in men and women, despite the lower prevalence of obesity in men, a finding that is unique to this population. In previous analyses, we found that obesity in western AN women does not have strong relationships with many other associated DM2 risk factors (27); this finding is consistent with the data in the current study, which show similar DM2 rates in men and women. The comparatively low prevalence of MetS in WATCH men (13.5%) and women (21.8%) suggests lower prevalence of insulin resistance in both western AN men and women. Nationally, 2003–2006 NHANES data documented MetS prevalence in U.S. Whites as 37.2% in men and 31.5% in women. Among Mexican Americans, prevalence was 33.2% in men and 40.6% in women, and among Blacks, prevalence was 25.3% in men and 38.8% in women (28). Thus, the low rate of DM2 can be attributed in part to the low prevalence of insulin resistance in this population.

Another unique observation in this study population is the very low DM2 incidence in the presence of a higher incidence of prediabetes that is similar in men and women, despite the

higher prevalence of obesity in the women. Although incidence of DM2 in western AN people with prediabetes is higher than in those with normal glucose values, rates of DM2 incidence remain low in this population. This finding suggests that both men and women in this population remain in the prediabetic range for long periods of time. Worldwide, prediabetes prevalence is generally lower than diabetes prevalence (29). However, our study population reflects U.S. national prevalence with a higher proportion of prediabetes than diabetes (30). The major difference is a much lower DM2 prevalence and a greater DM2-to-prediabetes prevalence ratio (30, 31). The current paradigm for development of type 2 diabetes suggests that obesity and/or insulin resistance lead to impaired glucose tolerance, and the resultant beta cell failure leads to development of DM2 (32, 33, 34). It is possible that in western AN people, beta cell function is resistant to deterioration. Further studies are warranted to understand the protective factors that may lower DM2 incidence in this population.

Diet and lifestyle have changed rapidly among western AN people (35, 36, 37). Traditional lifestyles were very active, accompanied by a diet lower in calories from saturated fats and simple carbohydrates (35,37). Diminished physical activity along with greater consumption of convenience foods has likely contributed to the current rates of obesity and prediabetes (35, 36, 37, 38, 39). Concern is justified that reduced physical activity and less traditional diet practices may override any propensity for low insulin resistance and robust beta cell function and that DM2 rates will continue to rise in this AN population. Nutrition and physical activity are important upstream factors that will be examined more closely in this cohort to determine their role in DM2 and prediabetes risk. Currently, programs promoting traditional foods consumption and less reliance on processed foods have gained momentum in AN communities (40), calling attention to the importance of healthy food choices and physical activity. Dissemination of our findings highlights the need for health providers to address overweight as well as screen and treat cardiovascular disease risk factors well before diabetes is diagnosed.

The primary limitations of the current study were the relatively short duration of the follow up and small number of cases of DM2. Although generalizations must be made with caution, especially when convenience sampling methods are used, the WATCH cohort is representative of the western AN population, and no significant demographic or risk factor differences have been observed between the total WATCH cohort and the follow-up cohort (14). While the small number of cases limits the analysis of risk factor associations and decreases the precision of the estimates of prevalence and incidence, the study is strengthened by the increased sample size achieved through cohort consolidation and use of identical surveillance criteria and methods. As this is a relatively young cohort that will generate more cases as the participants age, future studies are likely to allow for more detailed analyses. Cardiometabolic risk factors may reflect upstream socio-behavioral factors that deserve attention in future studies.

In summary, while DM2 prevalence and incidence are low among western AN people, statewide data suggest rising rates. Although rates of conversion from prediabetes to DM2 also appear low, prevalence and incidence of prediabetes are high. Thus, lifestyle changes may begin to override any cultural, environmental, or genetic protective factors.

Interventions minimizing risk for prediabetes, obesity, and other DM2 risk factors, while maximizing protective factors that prevent conversion, are needed to prevent major increases in DM2 prevalence and incidence among western AN people.

ACKNOWLEDGMENTS

The WATCH study was funded in part by an American Recovery and Reinvestment Act Administrative Supplement to a grant funded by the National Center for Research Resources (NCRR), National Institutes of Health (NIH; P20 RR16430). The Alaska-Siberia Project (ASP) was funded by the National Institute of Diabetes and Digestive and Kidney Diseases [R21DK44592], and the Center for Alaska Native Health Research (CANHR) was funded through the NCRR COBRE [P20 RR016430 and R01 DK074842] mechanisms. Alaska Education and Research Toward Health (EARTH) was funded by the National Cancer Institute [CA88958 and CA96095]. Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) was funded by the National Heart, Lung, and Blood Institute [U01 HL64244]. Additional Federal funding was received from the NCRR and the National Center for Advancing Translational Sciences, NIH, through the Clinical and Translational Science Awards Program, a trademark of the U.S. Department of Health and Human Services, part of the Roadmap Initiative, "Re-Engineering the Clinical Research Enterprise (Grant # UL1RR031975); the National Institute of Diabetes and Digestive and Kidney Diseases (DK097307); and the Centers of Biomedical Research Excellence (P30GM103325). Funds were also made available by the President of the University of Alaska through unrestricted donations by British Petroleum and ConocoPhillips. In addition, Dr. Jolly was supported by a career development award (1K23DK091363-03) from the NIH. We thank Rachel Schaperow, MedStar Health Research Institute, for editing the manuscript.

APPENDIX

WATCH Component Studies

Alaska-Siberia Project (ASP) investigators: S.O. Ebbesson, C.D. Schraer, P.M. Risica, A.I. Adler, L. Ebbesson, A.M. Mayer, E.V. Shubnik of, J. Yeh, O.T. Go, D.C. Robbins.

Center for Alaska Native Health Research (CANHR) investigators: G.V. Mohatt (deceased), B.B. Boyer, B. Luick, C. Lardon, A. Bersamin, D. O'Brien, S. Hopkins.

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Figure 1. Age- and sex-adjusted incidence of diabetes and prediabetes in the WATCH cohort and in men and women stratified by age group
 PY=person-years, DM=diabetes, PreDM=prediabetes, WATCH=Western Alaska Tribal Collaborative for Health.

Table 1
WATCH Follow-up Cohort Baseline Risk Factors in Adults 18 years, by Sex and Region

Risk factors	WATCH (n=2,754)	Men n=1,218 (44%)	Women n=1,536 (56%)	p- value	NS n=1,335 (48.5%)	YK n=1,419 (51.5%)	p-value
Mean age in years (sd)	41.4 (16.03)	41.2 (16.02)	41.5 (16.04)	0.619	41.6 (16.25)	41.1 (15.82)	0.417
	n (%)	n (%)	n (%)	--	n (%)	n (%)	--
History of smoking	1,917 (70.2)	966 (79.8)	951 (62.5)	<0.001	1,069 (80.4)	848 (60.4)	<0.001
Family history of diabetes	178 (6.5)	55 (4.5)	123 (8.0)	<0.001	12 (0.9)	166 (11.7)	<0.001
BMI overweight	877 (32.1)	416 (34.5)	461 (30.3)	<0.001	405 (30.8)	472 (33.4)	
BMI obese	845 (31.0)	241 (20.0)	604 (39.6)		377 (28.7)	468 (33.1)	<0.001
Abdominal obesity	1,055 (39.0)	200 (16.8)	855 (56.6)	<0.001	392 (30.4)	663 (46.9)	<0.001
High blood pressure	964 (35.0)	462 (37.9)	502 (32.7)	0.004	435 (32.6)	529 (37.3)	0.010
Low HDL cholesterol	480 (18.0)	160 (13.6)	320 (21.4)	<0.001	292 (19.9)	228 (16.2)	0.013
High triglycerides	503 (18.8)	212 (18.1)	291 (19.4)	0.374	319 (25.2)	184 (13.1)	<0.001
Prediabetes Glucose or HbA1c	782 (29.7)	389 (33.4)	393 (26.8)	<0.001	310 (24.1)	472 (35.2)	<0.001
Metabolic syndrome	485 (18.1)	159 (13.5)	326 (21.8)	<0.001	208 (16.4)	277 (19.7)	0.030
Total prevalent diabetes	124 (4.5)	53 (4.4)	71 (4.6)	0.733	47 (3.5)	77 (5.4)	0.016
Undiagnosed diabetes	48 (39%)	27 (50.9)	21 (29.6)	0.016	17 (36.2)	31 (40.3)	0.650

Notes: Missing values for any risk factor 3%; n=number; significance= $p < 0.05$. Definitions: NS=Norton Sound; YK=Yukon Kuskokwim; sd=standard deviation; History of smoking=past or current cigarette use; family history of diabetes limited to 1st degree relatives; BMI overweight=25%–29.9%; BMI obese 30 kg/m²; abdominal obesity = waist >40 inches (>99 cm) in men, >35 inches (>102 cm) in women; high blood pressure 130/85 mmHg; a diagnosis of hypertension in the medical record, and/or use of prescription antihypertensive medications; low HDL cholesterol <40 mg/dl (<1.03 mmol/l) in men, <50 mg/dl (<1.29 mmol/l) in women; high triglycerides 150 mg/dl (1.7 mmol/l); elevated fasting glucose 100 mg/dl (5.6 mmol/l); metabolic syndrome 3 metabolic syndrome risk factors. Among total prevalent diabetes, n =124; undiagnosed diabetes = baseline fasting glucose 126 mg/dl (7.0 mmol/l) or HbA1c 6.5% and diabetes not diagnosed prior to baseline.

Diabetes and Prediabetes Crude Incidence Rate Ratios and Age- and Sex-Adjusted Hazard Ratios Associated with Selected Risk Factors in Adults 18 Years

Table 2

Risk Factor	DM Inc/ 1,000 PY (n)	Crude IRR for DM	HR for DM (95% CI)	PreDM Inc/1,000 PY (n)	Crude IRR for PreDM	HR for PreDM (95% CI)
Smoking history						
No	4.8 (20)			35.7 (101)		
Yes	2.9 (33)	0.62	0.70 (0.39–1.23)	38.5 (285)	1.08	1.07 (0.85–1.34)
Family history DM						
No	3.5 (^a)			37.4 (369)		
Yes	2.7 (^a)	0.78	0.95 (0.23–3.93)	44.5 (19)	1.19	1.68 (1.06–2.68)
Blood pressure						
<130/85 mmHg	1.9 (20)			33.5 (252)		
130/85 mmHg ^b	6.5 (33)	3.37	2.00 (1.07–3.72)	49.3 (137)	1.47	1.10 (0.87–1.38)
BMI						
<25 kg/m ²	0.9 (5)			32.9 (135)		
25–29.9 kg/m ²	3.7 (19)	4.34	4.18 (1.56–11.20)	36.5 (128)	1.11	1.04 (0.82–1.33)
30 kg/m ²	6.2 (28)	7.16	6.76 (2.59–17.66)	47.8 (124)	1.46	1.50 (1.17–1.92)
Waist circumference						
M 102cm; F 88cm	1.8 (17)			33.0 (227)		
M>102cm; F>88cm	6.2 (34)	3.53	3.68 (1.93–7.01)	47.2 (152)	1.43	1.65 (1.32–2.06)
HDL cholesterol						
M 40mg/dl; F 50mg/dl	2.7 (34)			38.3 (315)		
M >40mg/dl; F >50mg/dl	5.5 (14)	2.01	2.78 (1.48 – 5.21)	32.9 (53)	0.86	1.01 (0.76–1.34)
Triglycerides						
<150 mg/dl	2.3 (28)			34.9 (288)		
150 mg/dl	7.3 (21)	3.19	2.86 (1.62–5.05)	50.2 (80)	1.44	1.34 (1.05–1.72)
Prediabetes						
FPG <100 mg/dl						
HbA1c <5.7%	1.4 (16)			--		

Risk Factor	DM Inc/ 1,000 PY(n)	Crude IRR for DM	HR for DM (95% CI)	PreDM Inc/1,000 PY (n)	Crude IRR for PreDM	HR for PreDM (95% CI)
FPG 100–125 mg/dl HbA1c 5.7–6.4%	8.5 (37)	5.97	4.52 (2.44–8.35)	--	--	--
Metabolic syndrome ^c						
No	1.7 (21)			35.3 (323)		
Yes	12.0 (28)	7.28	5.75 (3.21–10.30)	50.2 (80)	1.80	1.88 (1.38–2.58)

Sample size and person-years vary based on data available for each risk factor. Participants with missing values were not included in the calculation of rates (3% missing values for any risk factor).

Abbreviations: *N(n)*=number; PY=person-years; DM=diabetes mellitus; Inc=incidence; IRR=incident rate ratio; HR=hazard ratio (age and sex adjusted); CI=confidence interval; preDM=prediabetes; mmHg=millimeters mercury; BMI=body mass index; kg/m²= kilograms per meters squared; M=male, F=female; cm=centimeters; mg/dl=milligrams per deciliter. Metabolic syndrome = 3 or more metabolic syndrome components, in accordance with 2002 National Cholesterol Education Program guidelines (National Cholesterol Education Program. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (ATP III), executive summary). Washington, DC: National Heart, Lung, and Blood Institute, National Institutes of Health, 2002. Retrieved from <http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf>. Accessed August 29, 2013

^a Suppressed due to at least one category cell containing n <5.

^b Blood pressure 130/85 mmHg also includes hypertension documented in medical record or prescribed anti-hypertension medication.

^c All metabolic syndrome components excluding fasting glucose.

Table 3

Predictors of Diabetes and Prediabetes Independent of Age and Sex, Classic and Metabolic Syndrome Risk Factor Models

Risk Factor	DM Hazard Ratio (95% CI)	p- value	PreDM Hazard Ratio^a (95% CI)	p- value
Age	1.05 (1.03–1.07)	<0.001	1.03 (1.02–1.04)	<0.001
Sex (referent men)	1.22 (0.70–2.13)	0.479	0.96 (0.78–1.17)	0.658
<i>Model 1, Classic Risk Factors</i>				
Age	1.04 (1.02–1.06)	<0.001	1.03 (1.02–1.03)	<0.001
Sex (referent men)	1.00 (0.55–1.84)	0.997	0.88 (0.71–1.09)	0.232
History of smoking	0.72 (0.39–1.31)	0.279	1.08 (0.85–1.36)	0.541
Family history of diabetes	0.40 (0.05–2.92)	0.365	1.75 (1.10–2.79)	0.019
BMI obesity	1.17 (0.59–2.29)	0.657	1.36 (1.06–1.74)	0.016
Prediabetes	3.29 (1.64–6.61)	<0.001	--	--
Metabolic syndrome	2.85 (1.31–6.21)	0.009	1.59 (1.13–2.24)	0.009
<i>Model 2, Metabolic Syndrome Risk Factors</i>				
Age	1.04 (1.01–1.06)	0.001	1.03 (1.02–1.03)	<0.001
Sex (referent men)	0.94 (0.49–1.83)	0.861	0.79 (0.62–1.00)	0.046
Hypertension	1.21 (0.62–2.39)	0.579	0.99 (0.78–1.27)	0.964
Abdominal obesity	2.36 (1.15–4.84)	0.019	1.66 (1.30–2.10)	<0.001
Low HDL-cholesterol	1.62 (0.83–3.17)	0.158	0.89 (0.65–1.22)	0.472
High triglycerides	1.91 (1.03–3.54)	0.042	1.23 (0.94–1.61)	0.125
Prediabetes	4.66 (2.29–9.49)	<0.001	--	--

Model 1: Adjusted for age, sex, history of smoking, family history of diabetes, body mass index (BMI) ≥ 30 kg/m², impaired fasting glucose 100–125 mg/dl (5.6–6.9 mmol/l), and metabolic syndrome (≥ 3 metabolic syndrome risk factors).

Model 2: Adjusted for age; sex; hypertension (blood pressure $\geq 130/85$ mmHg at baseline, hypertension diagnosis in the medical record, or prescribed antihypertensive medication); abdominal obesity (waist circumference ≥ 40 inches [≥ 102 cm] in men, ≥ 35 inches [≥ 88 cm] in women); low HDL-cholesterol <40 mg/dl (<1.03 mmol/l) in men, <50 mg/dl (<1.29 mmol/l) in women; high triglycerides ≥ 150 mg/dl (≥ 1.7 mmol/l); and prediabetes = fasting glucose ≥ 100 mg/dl (≥ 5.6 mmol/l) or HbA1c $\geq 5.7\%$ (≥ 39 mmol/mol).

Abbreviations: DM=diabetes mellitus, Pre-DM=prediabetes, CI=confidence interval, significance $p<0.05$.

^aExcludes elevated fasting glucose.