# Associations of Abdominal Muscle Area with 4-Year Change in Coronary Artery Calcium Differ by Ethnicity Among Post-Menopausal Women

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**Objective:** To examine the association of abdominal muscle area with coronary artery calcium (CAC) presence, extent, and progression in a multi-ethnic cohort of older, community-dwelling post-menopausal women.

**Design and Setting:** Cross-sectional and longitudinal population-based cohort.

**Participants:** The sample comprised 179 non-Hispanic White women, 116 Filipina women and 144 African American women, all without known CVD, who underwent chest and abdominal computed tomography (CT) scans twice about four years apart for abdominal muscle and fat, as well as CAC.

**Main Outcome Measures:** CAC presence, extent and progression.

**Results:** There was a significant interaction of ethnicity with baseline oblique muscle area (p-for-interaction .01), and marginally significant interactions with baseline total and paraspinal muscle for change in CAC (p-for-interactions both .09). Among Filipina women, each standard deviation (SD) greater total muscle area was associated with a 26% (95% CI (-43%, -4%), $P$=.02) reduced rate of change in CAC; higher paraspinal and oblique muscle area were associated with a 24% (-38%, -6%, $P$=.01) and a 37% (-53%, -16%, $P$=.0002) reduced rate of change in CAC, respectively. These associations were not significant in African American or non-Hispanic White women. There were no significant associations of abdominal muscle with CAC presence or extent, nor were there significant ethnicity by muscle interactions in these models.

**Conclusions:** Among Filipina women, greater abdominal muscle mass is associated with a decreased rate of CAC progression. Higher muscle mass may be important for this group in reducing CVD outcomes. *Ethn Dis*. 2015;25(4):435-442; doi:10.18865/ed.25.4.435

**Keywords:** Abdominal Muscle, Muscle Mass, Coronary Artery Calcium, Ethnicity, Race

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## Introduction

Deterioration of muscle mass and strength is associated with aging,[1,2] and related to cardiovascular disease (CVD) risk factors[3-5] and mortality.[6-8] Additionally, muscle plays an important role in glucose metabolism and insulin sensitivity.[9] Previous studies have found loss of muscle mass and strength among those with glucose dysregulation and insulin resistance,[10-12] as well as metabolic syndrome.[13] As a modifiable risk factor, muscle loss can be prevented and muscle strength improved with resistance training,[14] which can also improve insulin resistance[15] and glucose disposal.[9] Furthermore, insulin resistance has been previously associated with coronary artery calcium (CAC).[16] Taken together, this is important evidence of the potential role of muscle in preventing metabolic syndrome, type 2 diabetes, and clinical CVD, as well as subclinical CVD, which is an established risk factor for both clinical CVD and type 2 diabetes mellitus (DM).

Compared with research on regional adiposity, far less attention has been paid to the potential role of regional skeletal muscle, in particular abdominal muscle area measured by computed tomography, as it relates to clinical and subclinical CVD. Jensky et al[17] found that total abdominal lean muscle was significantly inversely associated with CAC presence and thoracic artery calcium (TAC) presence. After additional model adjustment, the association with TAC remained significant while the association with

CAC was attenuated to marginal significance. However, in the Multi-Ethnic Study of Atherosclerosis,[18] total abdominal muscle area was not significantly associated with TAC, CAC or aortic artery calcium (AAC).

Thus, to further assess the potential relationship between lean muscle and CVD, we examined the association of abdominal muscle area with CAC presence, extent and progression over approximately four years in a group of older, community-dwelling, post-menopausal non-Hispanic White women, African American women, and Filipina women. We also examined whether any of these associations differed by ethnicity. As women are at increased risk of CVD after transitioning to menopause and body composition changes often occur during this period, we chose to study the associations of abdominal muscle with CAC in post-menopausal women of different ethnicities.

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## Methods

### Study Participants

The Rancho Bernardo Study (RBS) is a prospective cohort study of community-dwelling middle-to-upper class adults of predominantly northern European (Caucasian) ancestry established between 1972 and 1974, when 82% of the adult residents of a San Diego, California suburb first participated in a survey of heart disease risk factors. Further details of recruitment and inclusion/exclusion criteria for the original cohort can be found elsewhere.[19,20] Since then, the participants of this study have been followed periodically, with the eighth examination (the baseline for this study) taking place between 2001-2002. At this visit, participants aged ≥ 55 years who had no known CVD had electron beam computed tomography (CT) scans of the chest and abdomen performed so that the extent of CAC could be determined and abdominal body composition could be measured.

Additionally, a group of Filipina women from the University of California – San Diego (UCSD) Filipino Women's Health Study and African American women from the Health Assessment Study of African American Women (HASAAW) cohorts were recruited in 1994-1999 as ethnic comparison groups to the Rancho Bernardo study using the same research protocol, staff, and diagnostic laboratories. The samples included community-dwelling women aged 40-84 years who self-identified as Filipina and women aged 50-87 years who self-identified as African American. More detailed inclusion and exclusion criteria for the Filipina and African American women have also been described elsewhere.[21,22]

Filipina and African American women aged ≥55 years and free of known CVD in 2001-2002 were also invited to have CT scans performed. Using these scans and appropriate software for making the measurements, data on abdominal muscle and CAC were available on a total of 439 RBS, UCSD Filipino Women's Health Study and HASAAW participants: 179 post-menopausal White women, 116 post-menopausal Filipina women, and 144 post-menopausal African American women.

Participants were mailed invitation letters to have a CT scan at the follow-up tenth examination (2005-2006), regardless of current CVD status. At this follow-up exam, CT scans were repeated on non-Hispanic White, Filipina and African American participants who returned. From these scans, we generated data on change in CAC, which was available on 330 of the 439 women participants from the 8th examination (baseline for this study): 150 White women, 91 Filipina women, and 89 African American women.

The RBS, as well as the UCSD Filipino Women's Health and HASAAW studies, were approved by the Institutional Review Board of the University of California, San Diego; all participants gave written informed consent at both examinations.

### Measurement of Covariates

Information on age, sex, smoking status, physical activity, medical

history, and medication use was obtained via standard self-administered or interviewer-administered questionnaires. Body mass index was calculated using weight in kilograms divided by height in meters squared. Systolic and diastolic blood pressures were measured twice in seated participants at rest for at least five minutes, and the average of two readings was used. Morning fasting blood samples were obtained by venipuncture after a requested 12-hour fast. Fasting plasma glucose, total cholesterol, HDL cholesterol, and triglycerides were measured by standard methods, and low-density cholesterol (LDL) was calculated using the Friedewald equation.

Diabetes was defined as self-report of physician diagnosis, anti-diabetes medication use, or fasting glucose ≥ 126 mg/dL. Hypertension was defined as self-report of physician diagnosis, and anti-hypertensive medication use, or systolic blood pressure ≥ 140 mm Hg, or diastolic blood pressure ≥ 90 mm Hg measured in the clinic. Physical activity was assessed by asking whether the participant currently exercised three or more times per week. This simple question was indirectly validated by showing a positive association with HDL-cholesterol and an inverse association with resting pulse rate. Further details on covariate measurements can be obtained from the lead author.

## Measurement of Coronary Artery Calcium

An Imatron C-150 ultrafast computed tomography scanner (Imatron, San Francisco, Calif.) that produced contiguous thin-section sections was used to obtain the images of the chest and abdomen. Cardiac scans were electrocardiographically triggered to the R-R interval, and images were obtained at end-diastole usually during a single breath-hold. CAC was scored according to the Agatston method[23] by specially trained technicians. Further details on CAC measurement in this cohort have been published.[24]

## Measurement of Abdominal Muscle and Fat

Abdominal tissue areas were measured from the baseline CT scans by three experienced analysts working on networked workstations running muscled segmentation software on the MIPAV platform (MIPAV Version 4.1.2, NIH). A transverse cross section slice of 6 mm thickness was selected at the umbilicus (~L4 – L5 disc spaces) for analysis of abdominal fat, including subcutaneous, visceral and intermuscular fat. Muscle segmentation was also performed on 4 separate muscle groups: psoas, paraspinal, oblique, and rectus abdominus. Fat area was obtained using the voxel count that fell within the threshold of -190 to -30 Hounsfield Units (HU). Lean area was obtained using the voxel count that fell within the threshold of 0 to 100 HU. The left and right side muscle groups were averaged together to obtain the psoas, paraspinal, rectus abdominus, and oblique muscle areas. Total abdominal muscle was defined by summing over the left and right for each muscle group. Further details on abdominal muscle and fat measurements have been published elsewhere.[25]

## Statistical Analysis

Univariate associations of ethnicity with CVD risk factors were examined using ANOVA, chi-square or Kruskal-Wallis tests as appropriate. In particular, as triglycerides and CAC amount were skewed, Kruskal-Wallis tests were used. Total abdominal, psoas, paraspinal, oblique and rectus abdominus muscle areas were modeled as per standard deviation increment in all models. Staged multivariate logistic regression models were used to examine the association of each of the four muscle groups with CAC presence and progression in separate models. To estimate the association of muscle and CAC for each ethnic group, global models included a separate term for the muscle-CAC association for each ethnic group, ie, models were not stratified by ethnicity. CAC presence was defined as Agatston score at the baseline visit >0. CAC progression was defined using the Hokanson method,[26] and participants were defined as having binary CAC progression if the square root of (follow-up CAC volume – baseline CAC volume) ≥2.5 $cm^3$.

Staged multivariate linear regression models were used to determine the association of muscle groups with CAC extent (or amount) and CAC change as continuous outcomes. CAC extent was defined as ln(Agatston score at baseline exam + 1), and CAC change was defined as ln((follow-up exam Agatston score – baseline exam Agatston score)/baseline exam Agatston score). Since these outcomes were natural log transformed, we used the transformation $(e^{\beta} - 1)*100$ to convert the beta coefficients and confidence limits into percents.

Interactions between ethnicity and muscle groups for CAC presence, extent and progression were tested on an additive scale in linear regression models for CAC extent and 4-year change in CAC, and on a multiplicative scale in logistic regression models for CAC presence and progression as binary outcomes.

*P*<.05 were considered statistically significant and SAS V 9.2 (Cary, N.C.) was used for all analyses.

# Results

## Characteristics and Ethnic Differences in Abdominal Muscle

Baseline characteristics and risk factors differed significantly across ethnicity for all factors (Table 1). CAC presence and CAC extent were highest in Filipina women, followed by White women, and then African American women, although these unadjusted differences were not statistically significant *(P*=.08 and .09, respectively) (Table 1). Of the 330 women participants with CAC progression data available, and as defined by the Hokanson method, 89/150 (59%) White women, 59/91 (65%) Filipina women, and 33/89 (37%) African American women had CAC progression (yes vs no) between the baseline and follow-up visit, a median of four years later. White women had a median (quartile 1, quartile 3) natural log 4-year change in CAC of 1.02 (0.80, 1.34), African American women 0.92 (0.63, 1.16), and Filipina women 1.17 (0.98, 1.75). Figure 1 shows the total abdominal muscle area, as well as separate psoas, paraspinal, rectus abdominus, and oblique muscle areas, by ethnicity, adjusted for age and BMI. Ethnic groups differed significantly from each other in total abdominal (pairwise *P*<.001), psoas (pairwise *P*<.006), paraspinal (pairwise *P*<.001), oblique (pairwise *P*<.005), and rectus abdominus (pairwise *P*<.001) muscle areas, except White women and African American women for total abdominal *(P*=.58), paraspinal *(P*=.06), oblique *(P*=.58), and rectus abdominus *(P*=.07) muscle areas.

## Associations of Abdominal Muscle with CAC Presence, Extent, and Progression

There were no significant associations of total, psoas, paraspinal, rectus abdominus and oblique muscle areas with CAC presence or CAC extent, and there were no ethnicity by muscle interactions. Areas of the muscle groups were not associated with CAC progression (yes vs no), nor were there any interactions by ethnicity. Detailed data tables on these factors and interactions are available from the lead author.

**Table 1. Baseline characteristics by ethnicity**

| | White Women *n*=179 | African American Women *n*=144 | Filipina Women *n*=116 | *P* |
|---|---|---|---|---|
| Age, years | 66 ± 6 | 61 ± 8 | 59 ± 6 | <.001 |
| Ever smoke, *n* (%) | 97 (54) | 71 (49) | 13 (11) | <.001 |
| Exercise ≥ 3x/week, n (%) | 134 (75) | 86 (60) | 78 (67) | .01 |
| Body mass index, kg/m$^2$ | 26 ± 5 | 30 ± 6 | 25 ± 3 | <.001 |
| Visceral Fat, cm$^2$ | 61 ± 34 | 57 ± 28 | 69 ± 29 | .01 |
| Intermuscular Fat, cm$^2$ | 23 ± 11 | 21 ± 11 | 18 ± 7 | <.001 |
| LDL cholesterol, mg/dL | 122 ± 30 | 124 ± 36 | 133 ± 35 | .02 |
| HDL cholesterol, mg/dL | 67 ± 17 | 63 ± 16 | 53 ± 12 | <.001 |
| Triglycerides, mg/dL[a] | 119 (83, 164) | 78 (58, 113) | 138 (97, 190) | <.001 |
| Lipid-lowering medications, *n* (%) | 22 (19) | 23 (20) | 39 (34) | <.001 |
| Prevalent hypertension, *n* (%) | 80 (45) | 84 (58) | 63 (54) | .04 |
| Hypertension medications, *n* (%) | 52 (29) | 65 (45) | 37 (32) | .008 |
| Systolic blood pressure, mm Hg | 128 ± 19 | 137 ± 23 | 133 ± 21 | .003 |
| Diastolic blood pressure, mm Hg | 75 ± 8 | 78 ± 10 | 79 ± 10 | <.001 |
| Prevalent diabetes, *n* (%) | 6 (3) | 16 (11) | 37 (32) | <.001 |
| Fasting plasma glucose, mg/dL | 100 ± 27 | 98 ± 31 | 109 ± 38 | .02 |
| CAC presence, *n* (%) | 112 (63) | 84 (58) | 83 (72) | .08 |
| CAC amount, Agatston units [a] | 10 (0, 112) | 5 (0, 71) | 25 (0, 141) | .09 |

a. Median (Quartile 1, Quartile 3).

**Table 2. Association of baseline abdominal muscle with 4 year change in CAC by ethnicity[a]**

| | White Women Percent (95% CI); *P* | African American Women Percent (95% CI); *P* | Filipina Women Percent (95% CI); *P* | *P*-for-interaction |
|---|---|---|---|---|
| Total abdominal | 1.38 (-18.00, 25.33); .90 | 6.51 (-16.38, 35.66); .61 | -25.70 (-42.56, -3.90); .02 | .09 |
| Paraspinal | -1.65 (-17.56, 17.32); .85 | 2.53 (-15.16, 23.93); .79 | -23.51 (-37.68, -6.12); .01 | .09 |
| Psoas | 5.50 (-19.93, 39.02); .70 | 5.33 (-22.87, 43.85); .74 | -4.96 (-34.25,37.37); .79 | .89 |
| Rectus abdominus | 2.94 (-17.20, 27.97); .79 | 12.75 (-6.07, 35.34); .20 | 27.10 (-2.58, 65.83); .08 | .57 |
| Oblique | 3.56 (-16.30, 28.14); .75 | 4.50 (-18.86, 34.61); .73 | -37.06 (-52.69, -16.26); .002 | .01 |

a. Models are adjusted for age, ever smoking, exercise ≥ 3 times per week, prevalent diabetes, prevalent hypertension, BMI, HDL cholesterol, LDL cholesterol, triglycerides and fasting plasma glucose. Models included a separate term for each ethnic group for the muscle-CAC association to estimate this association within each ethnic group.

There was evidence for ethnicity by muscle group interactions for four-year change in CAC modeled as a continuous variable (Table 2). Specifically, the association of oblique muscle area with change in CAC differed significantly by ethnicity group (*P*=.01). Additionally, there were marginally significant interactions for total and paraspinal muscle areas with ethnicity for change in CAC (both *P*=.09). Direction of the associations was consistent for both the significant and marginally significant interactions. These associations were not significant in White women or African American women, but were strongly significant in Filipina women (Table 2). Among Filipina women, each standard deviation (SD) greater total abdominal muscle was associated

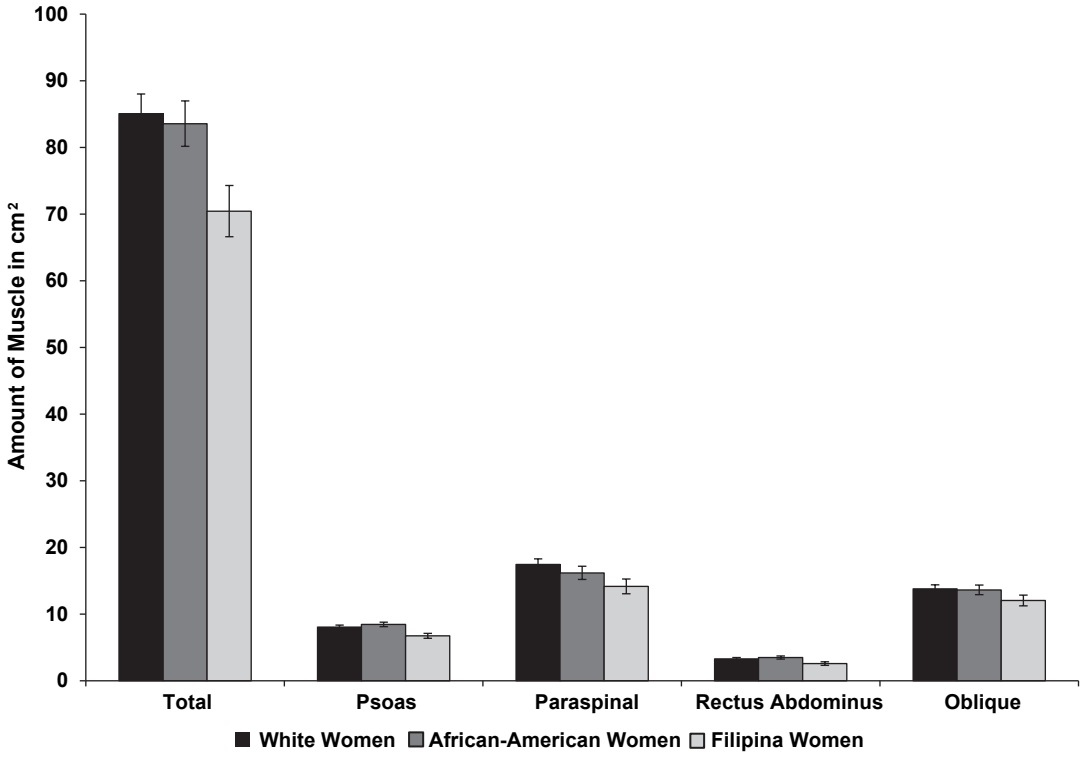


**Figure 1. Shows the area of total abdominal muscle, and each muscle group separately by ethnicity group, adjusted for age and body mass index. The y-axis is muscle area in centimeters squared, while the x-axis has groups of columns for muscle. The error bars are standard errors of the adjusted means.**

with a 26% reduced rate of four-year change in CAC *(P*=.02), independent of CVD risk factors. Each SD greater paraspinal muscle was associated with a 24% reduced rate of change in CAC, and oblique muscle was associated with a 37% reduced rate of four-year change in CAC, independent of CVD risk factors. Although there was not a significant interaction of ethnicity and rectus abdominus muscle *(P*=.57), greater rectus abdominus muscle area was marginally associated with greater rate of change in CAC in Filipina women *(P*=.08).

Further adjustment for lipid-lowering medications, intermuscular fat, or visceral fat did not materially change results of associations of baseline muscle groups with four-year change in CAC.

## Discussion

In a multi-ethnic sample of post-menopausal women from the Rancho Bernardo Study, UCSD Filipino Women's Health Study, and Health Assessment Study of African American Women (HASAAW), we found that the association of baseline abdominal muscle area with continuous four year change in CAC differed significantly by ethnicity, with muscle appearing to play a more significant role for Filipinas in CAC progression. There was also a marginally significant association of change in psoas muscle with change in CAC in Filipina women, although the interactions of muscle with ethnicity were not statistically significant in these cases. The associations of greater total abdominal, paraspinal, and oblique muscle area at baseline with a reduced rate of change in CAC among Filipinas may indicate that maintaining muscle is important for this group, and may be protective in progression of subclinical CVD and development of clinical CVD. Why these associations appeared to be more important among Filipinas as compared with the women of other ethnic groups is unclear and warrants further investigation. Visceral fat accumulation differs among ethnic groups, with Filipinos having a large accumulation relative to body size.[27] Visceral fat is also strongly associated with diabetes among Filipinos.[27] Thus, it could be that there are differences in muscle area that confer greater or less risk for other chronic diseases as well. To our knowledge, this is the first study to examine the associations of abdominal muscle area, and change in abdominal muscle area with CAC presence, amount and progression in a multi-ethnic cohort of post-menopausal women.

*… we found that the association of baseline abdominal muscle area with continuous four year change in CAC differed significantly by ethnicity, with muscle appearing to play a more significant role for Filipinas in CAC progression.*

The directionality of associations among Filipinas was not consistent in some cases, ie, greater baseline rectus abdominus muscle was marginally associated with greater, not reduced, change in CAC. However, given that this association was marginal, and that the interactions by ethnicity were not statistically significant, these particular results should be interpreted with caution. One potential explanation for these counter-intuitive findings could be that CAC progression could indicate an increase in density of the calcified plaques (meaning less lipid in the plaque) and thus increased plaque stabilization,[28-31] leading to lower risk for a CVD event. Adjustment for lipid lowering medications, which are associated with progression of CAC,[32,33] did not materially change the results in our study.

Despite adjustment for potential confounders and mediators, several muscle groups remained significantly associated with four year change in CAC among Filipinas, and interactions of ethnicity with muscle remained significant or marginally significant for change in CAC. Jensky et al[17] found, in a primarily Caucasian, self-referred clinic population of men and women, total abdominal lean muscle mass inversely associated with CAC presence (OR 0.80, 95% CI [0.3, 1.0]) and TAC presence (OR 0.34 95% CI [0.2, 0.7]), after adjustment for age, gender, family history of CHD, hypertension, dyslipidemia, diabetes and ever smoking. Among 1020 Caucasian, African American, Hispanic and Asian participants

from the Multi-Ethnic study of Atherosclerosis, abdominal muscle area was not significantly associated with CAC, AAC, or TAC.[18] In the current study, we did not find an association of abdominal muscle with CAC presence; measurements of TAC were not available. To our knowledge, these are the only studies in the literature examining these associations in similar study populations with similar methodology for muscle measurement.

Our study has several strengths as well as some limitations. Our study assesses an ethnically diverse population, and to our knowledge, is the first to examine the association of total abdominal muscle and separate muscle groups with CAC presence, extent and progression. It is also the first study to quantify and describe differences in abdominal muscle among different ethnic groups of post-menopausal women. This study has high-quality CT images, and has quantified not only total abdominal muscle and fat depots, but each of the four abdominal muscle groups. Additionally, since each of our ethnic groups had CT scans performed at the same location with the same CT scanners, and the CT scans were read by the same readers, we have consistent within-study results with which to make ethnic group comparisons. However, the sample size in each ethnic group is relatively small, so power is an issue for binary outcomes such as CAC presence, as well as possibly for the interactions. Some counter-intuitive results among Filipinas (ie, greater change in psoas muscle associated with greater progression of CAC) should be interpreted with caution, as *Ps* are not strictly statistically significant, and the ethnicity by muscle group interactions are not statistically significant in these cases. Our study consists of participants without clinically overt CVD at baseline, which is excellent for studying how muscle is associated with early, subclinical stages of CVD. However, the results may not be generalizable to a population with known CVD. Finally, residual confounding or unknown confounders could play a significant role, as in any observational study.

Given that loss in muscle mass and strength is associated with aging[1,2] and mortality,[6-8] and this can be modified and improved through resistance training,[14] the implications of the results from this study could be broad-reaching. Our study has shown that muscle area is independently associated, when accounting for CVD risk factors and even abdominal adiposity, with change in CAC over time among post-menopausal Filipina women, suggesting that increasing muscle mass could play a role in preventing subclinical and clinical CVD in this ethnic group. This may be especially true after the transition to menopause, when women often have accompanying changes in body composition, and are at increased risk for CVD. However, further larger studies are warranted to replicate and extend the current results, and to further ascertain whether increasing muscle mass could prevent or delay CVD.

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## Author Contributions

Research concept and design: Wassel, Barrett-Connor. Acquisition of data: Allison, Laughlin, Saad, Barrett-Connor, Wooten, Araneta. Data analysis and interpretation: Wassel, Saad, Wooten. Manuscript draft: Wassel, Allison, Laughlin, Wooten, Araneta. Statistical expertise: Wassel. Acquisition of funding: Wassel, Barrett-Connor, Wooten, Araneta. Administrative: Wooten. Supervision: Allison

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