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Examining Trends in Prediabetes and its Relationship with the Metabolic Syndrome in U.S. Adolescents, 1999–2014

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Abstract

Introduction—Prediabetes is a reversible state of glycemic abnormalities that is frequently associated with obesity and the metabolic syndrome (MetS). There has been controversy over determining the most effective methods of determining prediabetes status in adolescents. We sought to investigate temporal trends in prediabetes prevalence among U.S. adolescents using two definitions and evaluate relationships with obesity and a MetS-severity score.

Methods—We evaluated data from 5418 non-Hispanic-white, non-Hispanic-black, and Hispanic adolescents aged 12–19 participating in the National Health and Nutrition Examination Survey 1999–2014 with complete data regarding MetS and hemoglobin A1c (HbA1c). Prediabetes status was defined by American Diabetes Association (ADA) criteria: fasting glucose 100–125 mg/dL or HbA1c 5.7%–6.4%. MetS severity was assessed with a MetS-severity Z-score.

Results—Prevalence of prediabetes as defined by HbA1c abnormalities significantly increased from 1999–2014, while prevalence of prediabetes as defined by fasting glucose abnormalities showed no significant temporal trend. There were variations in these trends across different racial/ethnic groups. MetS Z-score was overall more strongly correlated with HbA1c, fasting insulin, and the homeostasis-model-of-insulin-resistance than was BMI Z-score. These correlations were true in each racial/ethnic group with the exception that in non-Hispanic-white adolescents, in whom the MetS Z-score was not significantly correlated to HbA1c measurements.

Conclusion—We found conflicting findings of temporal trends of U.S. adolescent prediabetes prevalence based on the ADA's prediabetes criteria. The increasing prevalence of prediabetes by HbA1c assessment is concerning and raises the urgency for increased awareness and appropriate measures of prediabetes status among physicians and patients.

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Statement of Human and Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Statement of Informed Consent: Informed consent was obtained from all patients for being included in the study.

Introduction

Prediabetes is a state of abnormal blood sugar elevation that is not yet classifiable as type 2 diabetes mellitus (T2DM). The American Diabetes Association (ADA) uses 3 different criteria to define prediabetes: fasting glucose between 100 mg/dL and 125 mg/dL, hemoglobin A1c (HbA1c) between 5.7% and 6.4%, and oral glucose tolerance test (OGTT) 2-hour glucose between 140 mg/dL and 200 mg/dL (also called impaired glucose tolerance) (1). A significant rise in U.S. adolescent prediabetes from 1999–2008 was previously reported (2). Without treatment, there is a strong possibility of progression from prediabetes to T2DM within 7 years (3). However, with therapeutic intervention, prediabetes is reversible (4, 5). With the validation of early intervention, it is of great priority to identify and treat prediabetes in adolescents.

Prediabetes in adolescents has multiple upstream causative factors, including obesity and the metabolic syndrome (MetS)(6, 7). MetS is a cluster of clinical abnormalities featuring central obesity, hypertension, hyperglycemia, hypertriglyceridemia, and low HDL. We previously reported that MetS, as diagnosed by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) and characterized by the MetS Severity Score (MetS Z-score) had low sensitivity in identifying adolescents with pre-diabetes as determined by impaired oral glucose tolerance (8). We also recently reported temporal decrease in MetS severity among adolescents that occurred despite an increase in BMI over time (9), raising questions regarding which of these was more strongly associated with prediabetes.

Our goals in the present study were 1) to evaluate whether the trend of increasing prediabetes had continued from 1999 through 2012, 2) whether any such trends were consistent between the definitions of prediabetes using fasting glucose and HbA1c, and 3) whether these markers of prediabetes and fasting insulin as a marker of insulin resistance (10) correlated more strongly with BMI z-score or MetS severity. Understanding the temporal trends in prediabetes and its potential causative factors among U.S. adolescents is important for evaluating how the U.S. is responding to the obesity epidemic and its associated health risks (11). Potential links between MetS severity and markers of prediabetes may aid in determining additional prediabetes screening indicators for clinicians to identify and treat at-risk youth.

Methods

Data was obtained from the Center for Disease Control's National Health and Nutrition Examination Survey (NHANES 1999–2014). NHANES is a series of surveys conducted in two-year waves that represents a cross-sectional, national, stratified, multistage probability, random selection of non-institutionalized U.S. civilians. Consenting participants answered questionnaires, as well as underwent clinical measurements and lab work. Laboratory measurements were obtained using the controlled protocols and equipment as specified by the CDC NHANES databook (12). The National Center for Health Statistics ethic review board approved of this study. The study design from 1999–2006 including oversampling of adolescents, and Mexican Americans; beginning in 2007, the study discontinued

oversampling of adolescents and changed oversampling of Mexican Americans to include the entire Hispanic population.

We analyzed data from participants aged 12–19 with complete data regarding MetS and prediabetes. Of the 14775 individuals in this age group, 9223 participants did not meet inclusion criteria due to incomplete fasting MetS data. Laboratory samples were collected on scheduled morning participants; afternoon participants were not scheduled for fasting laboratory studies. Fasting status was taken into account in designing sample weights to reflect a nationally representative sample. Of the participants who did complete the morning laboratory collection, 1714 participants had incomplete HbA1c data. Participants were excluded on the basis of pregnancy (n=181), physician diagnosed diabetes (n=73), and having either fasting glucose or HbA1c measures which would clinically classify someone as diabetic (n=76). Multiple participants were excluded for failure to meet more than one of the inclusion criteria; the total number of participants excluded was 9357. Prediabetes was evaluated using the HbA1c criteria and fasting glucose criteria. HbA1c levels greater than or equal to 39 mmol/molHb (5.7%) and less than or equal to 46 mmol/molHb (6.4%) corresponded to prediabetes. Fasting glucose levels greater than or equal to 100 mg/dL and less than or equal to 125 mg/dL corresponded to prediabetes (1). In assessing the relationship of BMI Z-score and MetS Z-score as potential upstream causes of prediabetes, we also assessed fasting insulin measures as an indicator of the state of insulin resistance (10). We assessed informed knowledge of prediabetes diagnosis by evaluating by the question “Have you ever been told by a doctor or other health professional that you have any of the following: prediabetes, impaired fasting glucose, impaired glucose tolerance, borderline diabetes or that your blood sugar is higher than normal but not high enough to be called diabetes or sugar diabetes?”. This question was incorporated into the diabetes questionnaire beginning in 2005.

MetS severity score (MetS Z-score) was calculated for participants using the series of Metabolic Syndrome Severity Z-Score formulae(<http://mets.health-outcomes-policy.ufl.edu/calculator/>)(13–17). This set of formulae were derived previously from data from non-Hispanic-white, non-Hispanic-black, and Hispanic adolescents age 12–19 years participating in NHANES 1999–2010(13). We used confirmatory factor analysis on individual sex- and racial/ethnic groups, generating equations to calculate a Z-score estimating the severity of MetS. The score evaluates BMI Z-score, fasting glucose, fasting triglycerides, HDL, and systolic blood pressure with different loading factors to account for differences in MetS across specific racial/ethnic and sex groups.

From 2007–2012, physical activity was assessed as minutes per week of moderate to vigorous physical recreational activity per day. Participants were first asked if they did any vigorous/moderate-intensity sports, fitness, or recreational activities that cause large increase in breathing or heart rate like running or basketball for at least 10 minutes continuously. If they answered yes, they were further questioned for how many minutes per typical day they do these activities.

Statistical significance was defined as $P < 0.05$. Statistical analysis was performed using SAS (version 9.4, Cary, NC). Trends in continuous clinical and laboratory measurements

were assessed via linear regression, while trends in prevalence of binary outcomes were assessed with logistic regression. All models accounted for the complex survey design of NHANES in obtaining population-based estimates; specifically, fasting weights were applied to ensure that the sample was nationally representative and used only those with appropriate fasting status for accurate lab assessments of measures such as glucose and triglycerides. The natural log transformation was used for measures with a highly skewed distribution.

Results

Participant characteristics

We analyzed data from 5418 participants who completed laboratory measurements and were eligible for prediabetes and MetS evaluation (Table 1). Of those participants, there were 1551 non-Hispanic whites, 1726 non-Hispanic blacks, and 2141 Hispanics. Mean age (standard error) was 15.5 years (0.05); the sample was 51.5% male, and had a mean BMI Z-score of 0.61 and had 36.5 minutes of moderate activity daily. Compared to participants lacking fasting laboratory studies, included participants did not differ with respect to age, BMI-Z, overall physical activity or moderate or vigorous physical activity.

Prevalence and trends in prediabetes by HbA1c

Prevalence of prediabetes as diagnosed by HbA1c levels increased over time in U.S. adolescents overall ($P < 0.0001$) (Table 2). The overall prevalence was 1.87% in 1999–2000 and 4.99% in 2013–2014 (Figure 1). This trend was observed in all three racial/ethnic groups ($P < 0.0001$). Likewise, this increasing trend in prediabetes defined by HbA1c was also significant by sex (Table 2). Total prevalence of HbA1c prediabetes in overall U.S. adolescents was 4.4% from 1999–2014. Prevalence varied by race/ethnicity: non-Hispanic white 1.29%, non-Hispanic black 9.34%, Hispanic 2.98%.

The mean HbA1C measurement was 31 mmol/molHb (5.03%) in 1999–2000 and 31 mmol/molHb (5.16%) in 2013–2014. Regression analysis showed a significant increasing trend in HbA1c measurements over time ($P < 0.0001$). This trend was observed in non-Hispanic blacks ($P < 0.0001$) and Hispanics ($P < 0.0001$) and less so among non-Hispanic whites ($P < 0.05$).

Prevalence and trends in prediabetes by fasting glucose

The prevalence of prediabetes by fasting glucose has varied over time, but no systematic trends were observed in the overall U.S. adolescent population (Figure 1). This was true for all three race/ethnicity groups (Table 2). Total prevalence of fasting glucose prediabetes in overall U.S. adolescents was 15.5% from 1999–2014. Prevalence varied by race/ethnicity: non-Hispanic white 15.0%, non-Hispanic black 9.9%, Hispanic 20.1%. Similarly and as previously reported (9), mean fasting glucose measurements did not change over time in U.S. adolescents overall. These findings were true for males and females and all three race/ethnicity groups (Table 2).

Fasting insulin measurements are rising over time

Fasting insulin measurements increased over time in U.S. adolescents overall ($P < 0.0001$) (Table 2). The mean fasting insulin was 10.6 mIU/L in 1999–2000 and 14.6 mIU/L in 2013–2014. This trend was seen in all racial/ethnic groups $P < 0.01$.

Metabolic syndrome severity score and BMI Z-score are linked with fasting insulin and HbA1C

To address potential upstream causes of the increase in HbA1c-determined prediabetes, we estimated correlations of MetS severity score and BMI z-score with HbA1C and fasting insulin. MetS severity score was strongly correlated with fasting insulin levels as a marker of insulin resistance ($r = 0.50$, $P < 0.0001$), but was less correlated with HbA1C levels ($r = 0.08$, $P = 0.001$) (Figure 2). Further analysis revealed a significant MetS Z-sex interaction in the relationship between MetS Z and log-fasting insulin ($P = 0.006$), with males exhibiting more significant interactions, compared to females (Table 3). MetS Z-score was significantly correlated with insulin and HbA1c for non-Hispanic blacks and Hispanics (all $P < 0.01$ or $P < 0.0001$); however for non-Hispanic whites this correlation was statistically significant only with fasting insulin ($P < 0.0001$) and not with HbA1c ($P = 0.1277$).

BMI Z-score was also positively correlated with HbA1c levels ($r = 0.10$, $P < 0.01$) and fasting insulin levels ($r = 0.52$, $P < 0.0001$) (Table 3). MetS Z-score exhibited higher slope estimates than did BMI Z for fasting insulin but not for HbA1c. These higher slope estimates for MetS Z vs. BMI-Z with fasting insulin were true for all racial/ethnic groups. There was a significant BMI-Z – sex interaction in the relationship between BMI-Z and log-fasting insulin ($P < 0.0001$), with stronger associations between BMI-Z and log insulin in males vs. females. The BMI Z-score was not significantly associated to HbA1c in non-Hispanic whites ($P = 0.173$), but it was associated in non-Hispanic blacks and Hispanics ($P = 0.020$, 0.015 respectively).

Physician reported prediabetes among those with laboratory-determined prediabetes

Finally, we assessed for relationships between prediabetes status and adolescents reporting whether a physician had ever told them they had prediabetes. Between 2005 and 2014, 176 participants had prediabetes as defined by HbA1c abnormalities. Of these, only 3 (1.70%) reported that a physician told them that they had prediabetes. In that same time period, 440 participants had prediabetes as defined by elevated fasting glucose; only 5 (1.14%) were told by a physician that they had prediabetes.

Discussion

There has been controversy in determining the optimal method to identify prediabetes in U.S. adolescents (18–20). Our nationally-representative findings from NHANES suggested that prediabetes as defined by HbA1c measures have been increasing in U.S. adolescents over time. We were surprised to see that there was no temporal change in the prevalence of elevated fasting glucose over the same time. Indeed, there was wide variability in the prevalence of elevated fasting glucose, including an abrupt decrease between '07–'08 and '09–'10, which occurred without change in laboratory assay and is of unclear

significance. The wave-to-wave consistency of the prevalence of prediabetes by HbA1c leads one to believe that this is a legitimate trend. At the same time, the NHANES participant self-reported data suggested that there was either a significant under-diagnosis or poor patient understanding of prediabetes, with only 1% of adolescents reporting having been told by a physician that they had prediabetes. These findings encourage the need to understand adolescent prediabetes, its epidemiologic trends, and associated markers that could aid in identifying prediabetes in at-risk youth.

Our discrepant findings regarding temporal trends of U.S. adolescent prediabetes as defined by HbA1c and impaired fasting glucose are only in agreement in demonstrating that prediabetes prevalence has not decreased from 1999–2014. The discrepancies in these measures highlight the complex relationship between HbA1c and glucose measures when defining prediabetes in adolescents. This paradox is one shared by previous studies, which have shown poor agreement among the ADA's three different prediabetes criteria (18, 21–23). All three measures are flawed in that they lack validation in the pediatric population (24), emphasizing the need to corroborate prediabetic measures in children and adolescents.

HbA1c measurements have advantages over measurements of fasting insulin and fasting glucose in that HbA1c is more reflective of long-term changes in blood sugar, has standardized assays and is subject to less clinical variability (18, 19, 24–26). With the development of HbA1c as a diagnostic tool for prediabetes, an added benefit among adolescents is increased prediabetes screening without compromise in accuracy due to non-fasting status and thus may not require a repeat visit (22). Certainly, both measures of prediabetes that we evaluated have been shown to correlate strongly with adverse outcomes (27, 28). Given these reasons, we believed that the temporal trend of increasing HbA1c measures in U.S. adolescents is a legitimate cause for concern. This was corroborated by temporal increases in fasting insulin, suggesting an increase in insulin resistance in U.S. adolescents from 1999–2014, with insulin resistance being an avenue toward development of poor glucose control (10).

With further interest in the potential causes of this trend in HbA1c-determined prediabetes, we investigated how HbA1c, fasting glucose and fasting insulin (as factors associated with prediabetes), were associated with obesity and MetS severity. MetS Severity is associated with childhood obesity and is a significant risk factor for prediabetes and progression to T2DM (6, 29). We had previously found that while childhood obesity measured by mean BMI Z-score had increased over time, there had been a decrease in MetS severity among adolescents, largely due to improvements in lipid measures (9).

Our findings in the current study demonstrated that, compared to BMI Z-score, the MetS Z-score had stronger correlations with fasting insulin in all racial/ethnic groups. Despite this finding, there was evidence that the relationship between MetS and HbA1c value was not strong, with overall low correlations between MetS Z-Score and HbA1c. Furthermore, MetS Z-score levels decreased over the same time period that HbA1c levels increased. This poorer correlation between MetS-Z and HbA1c, compared to the correlation between MetS-Z and fasting insulin, is consistent with our previous finding that MetS severity corresponded poorly with glucose intolerance (8). Overall, it would appear that while MetS and obesity

may in part explain this increasing trend of prediabetes, these factors are only two of multiple factors, given the low association of both with these markers of prediabetes.

There are racial/ethnic differences in MetS and HbA1c measurements (30–33). However, HbA1c measurements increased over time for all three racial/ethnic groups analyzed, further emphasizing the need for concern and its utility across different races. Confirmatory factor analysis had been performed for the MetS Z-score to account for racial/ethnic and sex differences in MetS (13). In the current study, the correlation of MetS Z-score with HbA1c was only significant among non-Hispanic-black and Hispanic adolescents and not among non-Hispanic-white adolescents. This may be because non-Hispanic-white adolescents had a greater prevalence of undiagnosed pathologies that cause HbA1c elevations independent of insulin resistance such as Type I diabetes and MODY (34–36). However, the MetS Z-score was significantly correlated with fasting insulin for all three racial/ethnic groups analyzed. Thus, an elevated MetS Z-score should not be completely disregarded as a possible indicator for prediabetes screening in non-Hispanic-white adolescents.

Among adolescents with measured prediabetes, we found an unfortunately small number who reported that their physician had informed them regarding prediabetes. While the cause of this is unclear (and potentially due to a lack of testing, informing or remembering regarding prediabetes), this may nevertheless serve as a call for vigilance in preventive care. If the course of prediabetes is not altered, patients are at risk for future T2DM and cardiovascular disease (37). Studies have shown that lifestyle modifications can improve measures used to diagnose prediabetes and reverse the prediabetic state (38). Reversal of the prediabetes could in turn save the patient and our health care economy millions of U.S. dollars (39), but clearly requires discovery of prediabetes status among at-risk patients.

Our study had multiple limitations. The ADA definitions of prediabetes that we evaluated in this study were based on extrapolation from adult data and lack validation in the pediatric population (24). Studies have suggested that the HbA1c cutoffs are set too high for adolescent patients and would result in an underestimate of prediabetes prevalence (40). In the context of our study, the systematic underestimate of adolescent prediabetes would likely not change the finding that there was a rising trend over time. We were only able to evaluate a small subset of adolescents evaluated in NHANES, though the non-fasting weights of the complex survey design enabled us to evaluate these as a nationally-representative sample. We were also limited by the cross-sectional nature and scope of NHANES in our ability to study causality.

In sum, we found conflicting trends of increasing prediabetes as diagnosed using HbA1c but no change in trend of prediabetes as defined by fasting glucose among U.S. adolescents from 1999–2014. Trends in obesity may in part explain this increasing trend of prediabetes. Refined screening indications for adolescents at risk for prediabetes are necessary. There also needs to be increased awareness of prediabetes status among U.S. adolescents, their medical providers, and the general public. These are issues of great concern because proper intervention can greatly improve the health of at-risk adolescents and potentially save millions in the national healthcare economy.

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Figure 1. Prediabetes prevalence versus time

The bars show weighted frequency prediabetes with 95% confidence intervals as determined by either fasting glucose or HbA1c, adjusted for age and sex. Logistic regression analysis showed that odds of having HbA1C prediabetes was increasing over time (odds ratio reported in figure). There were no temporal trends in fasting glucose prediabetes prevalence.

Figure 2. Correlation of fasting insulin and HbA1c measurements with the MetS Z-score and the BMI Z-score

Fasting insulin (log-transformed) and HbA1C are both significantly positively correlated with the overall U.S. adolescent population. MetS Z-score analyses yielded higher slopes than BMI Z-score analyses.

Table 1

Participant characteristics by race/ethnicity and study period

	Total	Non-Hispanic White	Non-Hispanic Black	Hispanic	Mean Age ^a (SE)	%Male ^a (SE)
1999–2000	910	203	249	458	15.36 (0.13)	54.01 (2.66)
2001–2002	920	291	301	328	15.42 (0.10)	49.32 (2.63)
2003–2004	895	234	359	302	15.57 (0.18)	52.37 (2.77)
2005–2006	836	220	291	325	15.51 (0.10)	51.95 (2.76)
2007–2008	435	145	112	178	15.69 (0.14)	49.21 (3.69)
2009–2010	517	182	109	226	15.37 (0.13)	51.31 (3.38)
2011–2012	430	128	168	134	15.31 (0.15)	53.00 (2.87)
2013–2014	475	148	137	190	15.55 (0.12)	51.16 (2.38)
Total	5418	1551	1726	2141	15.48 (0.05)	51.47 (1.04)

^aWeighted, SE = standard error

Racial/ethnic specific data regarding prediabetes prevalence and laboratory measures over time. Overall data and data by race/ethnicity are adjusted for age and sex; by sex data are adjusted for age.

Table 2

Diagnoses prevalence vs. time			Lab values vs. time		
Odds Ratio (95% CI)*			Mean Difference (95% CI)**		
HbA1c prediabetes	Fasting glucose	prediabetes	HbA1c	Fasting glucose	Fasting Insulin (log-transformed)
Overall	increasing 1.250 (1.159,1.348)	no change 0.961 (0.919,1.004)	increasing 0.017 (0.011,0.024)	no change -0.068 (-0.209,0.072)	increasing 0.050 (0.036,0.064)
Males	increasing 0.1,220 (1.112, 1.338)	no change 0.960 (0.910,1.013)	increasing 0.011 (0.002,0.020)	no change -0.113 (-0.283,0.057)	increasing 0.052 (0.032,0.072)
Females	Increasing 1.297 (1.147, 1.467)	no change 0.963 (0.896,1.034)	increasing 0.024 (0.016,0.0325)	no change -0.019 (-0.217,0.179)	increasing 0.048 (0.030,0.067)
Non-Hispanic White	increasing 1.296 (1.001,1.677)	no change 0.929 (0.866,0.996)	increasing 0.015 (0.005,0.024)	no change -0.145 (-0.324,0.035)	increasing 0.048 (0.025,0.071)
Non-Hispanic Black	increasing 1.190 (1.119,1.266)	no change 1.009 (0.914,1.114)	increasing 0.018 (0.009,0.027)	no change 0.038 (-0.250,0.327)	increasing 0.039 (0.020,0.059)
Hispanic	increasing 1.291 (1.136,1.468)	no change 1.003 (0.949,1.060)	increasing 0.022 (0.013,0.030)	no change 0.047 (-0.122,0.217)	increasing 0.055 (0.037, 0.073)

* Odds ratio comparing consecutive sampling periods. Values greater than 1 indicate an increase in rate of prediabetes; bold indicates statistical significance (p < 0.05).

** Mean difference between two consecutive sampling periods. Values greater than 0 indicate a mean increase in measurements; bold indicates statistical significance (p < 0.05).

Linear regression of log fasting insulin and HbA1C, modeling separately as a function of MetS Z-score and BMI Z-score overall and by race/ethnicity and gender.

Table 3

	n	MetS Z-Score			BMI Z-Score					
		HbA1c		Fasting Insulin		HbA1c		Fasting Insulin		
		Slope Estimate (CI)	r	Slope Estimate (CI)	r	Slope Estimate (CI)	r	Slope Estimate (CI)	r	
All										
	Overall	5033	0.027* (0.011, 0.043)	0.077	0.456†*** (0.424, 0.488)	0.497	0.025* (0.013, 0.037)	0.095	0.355†*** (0.331, 0.379)	0.522
	Males	2639	0.014 (−0.010, 0.038)	0.045	0.515** (0.471, 0.558)	0.550	0.021 (0.005, 0.036)	0.084	0.384** (0.349, 0.419)	0.567
	Females	2394	0.041* (0.019, 0.062)	0.114	0.441** (0.389, 0.493)	0.484	0.031* (0.014, 0.047)	0.114	0.315** (0.281, 0.349)	0.467
NHW										
	Overall	1477	0.018 (−0.005, 0.041)	0.055	0.419** (0.375, 0.464)	0.480	0.012 (−0.005, 0.029)	0.055	0.326** (0.293, 0.359)	0.500
	Males	783	0.012 (−0.020, 0.044)	0.032	0.524** (0.463, 0.585)	0.577	0.012 (−0.009, 0.034)	0.055	0.380** (0.332, 0.428)	0.575
	Females	694	0.023 (−0.009, 0.055)	0.063	0.364** (0.284, 0.444)	0.415	0.012 (−0.011, 0.034)	0.045	0.256** (0.207, 0.305)	0.401
NHB										
	Overall	1542	0.074** (0.047, 0.100)	0.167	0.546** (0.490, 0.602)	0.534	0.045** (0.023, 0.066)	0.141	0.392** (0.354, 0.431)	0.534
	Males	849	0.0600* (0.018, 0.101)	0.126	0.523** (0.433, 0.612)	0.501	0.039* (0.011, 0.067)	0.122	0.386** (0.336, 0.437)	0.539
	Females	693	0.089** (0.052, 0.127)	0.226	0.560** (0.482, 0.638)	0.575	0.055* (0.026, 0.085)	0.182	0.381** (0.314, 0.449)	0.514
Hispanic										
	Overall	2014	0.036* (0.015, 0.057)	0.110	0.507** (0.461, 0.553)	0.534	0.031** (0.016, 0.047)	0.122	0.397** (0.351, 0.444)	0.561
	Males	1007	0.029 (−0.002, 0.060)	0.084	0.530** (0.467, 0.594)	0.547	0.023 (0, 0.045)	0.095	0.388** (0.325, 0.451)	0.562

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		MetS Z-Score				BMI Z-Score			
		HbA1c		Fasting Insulin		HbA1c		Fasting Insulin	
		Slope Estimate (CI)	r	Slope Estimate (CI)	r	Slope Estimate (CI)	r	Slope Estimate (CI)	r
n									
Females		0.041 [*] (0.012,0.070)	0.118	0.517 ^{***} (0.459, 0.575)	0.559	0.044 [*] (0.021, 0.067)	0.167	0.406 ^{**} (0.355, 0.456)	0.563

[†] significant interaction between MetS Z and sex

^{*} p<0.01;

^{**} >0.0001