HHS Public Access

Author manuscript

Prev Med. Author manuscript; available in PMC 2015 October 26.

Published in final edited form as:

Prev Med. 2014 June ; 63: 43–47. doi:10.1016/j.ypmed.2014.02.013.

Race, regionality and pre-diabetes in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study

Loretta T. Lee[a,*], **Anne W. Alexandrov**[a], **Virginia J. Howard**[b], **Edmond K. Kabagambe**[c], **Mary A. Hess**[a], **Rhonda M. McLain**[a], **Monika M. Safford**[d], and **George Howard**[b]

[a]UAB School of Nursing, The University of Alabama at Birmingham, 1720 2nd Ave South, Birmingham, AL 35294-1210, USA

[b]Ryals School for Public Health, The University of Alabama at Birmingham, 1720 2nd Ave South, Birmingham, AL 35294-0113, USA

[c]Division of Epidemiology, Department of Medicine, Vanderbilt University Medical Center, 2525 West End Ave, Suite 316 Room 2, Nashville, TN 37203, USA

[d]Department of Medicine, Division of Preventive Medicine, The University of Alabama at Birmingham, 1720 2nd Ave South Birmingham, AL 35294-0113, USA

Abstract

Objective—To determine the association between race, region and pre-diabetes.

Method—The study used 2003–2007 United States baseline data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study for this cross-sectional analysis. Participants in this study were 45 years or older at recruitment. Logistic regression was used to assess whether race and region are associated with pre-diabetes independent of demographics, socioeconomic factors and risk factors.

Results—Twenty-four percent of the study participants (n = 19,889) had pre-diabetes. The odds ratio (95% confidence interval) for having pre-diabetes was 1.28 (1.19–1.36) for blacks relative to whites and 1.18 (1.10–1.26) for people living in the Stroke Belt region relative to the other parts of the United States. The odds of having pre-diabetes for Stroke Belt participants changed minimally after additional adjustment for race (OR = 1.20; 1.13–1.28), age and sex (OR = 1.24; 1.16–1.32), socioeconomic status (OR = 1.22; 1.15–1.31) and risk factors (OR = 1.26; 1.17–1.35). In the adjusted model, being black was independently associated with pre-diabetes (OR = 1.19; 1.10–1.28).

Conclusion—The prevalence of pre-diabetes was higher for both blacks and whites living in the Stroke Belt relative to living outside the Stroke Belt, and the prevalence of pre-diabetes was higher for blacks independent of region.

[*]Corresponding author at: UAB School of Nursing, NB 542, The University of Alabama at Birmingham, 1720 2nd Ave South, Birmingham, AL 35294-1210, USA..

E-mail addresses: llee@uab.edu (L.T. Lee), annealex@uab.edu (A.W. Alexandrov), vjhoward@uab.edu (V.J. Howard), Edmond.kabagambe@vanderbilt.edu (E.K. Kabagambe), wright@uab.edu (M.A. Hess), rho211@uab.edu (R.M. McLain), msafford@uab.edu (M.M. Safford), ghoward@uab.edu (G. Howard).

Conflict of interest statement The authors declare that there are no conflicts of interest.

Keywords

Pre-diabetes; Stroke Belt region; Non-Stroke Belt region; REGARDS study; Type 2 diabetes; Diabetes; Odds ratios; Fasting blood glucose; Impaired glucose tolerance; Impaired fasting glucose

Introduction

Pre-diabetes is a new diagnostic category established by the Expert Committee on Diagnosis and Classification of Diabetes Mellitus as impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), defined as a fasting blood glucose level between 100 and 125 mg/dL (Anon, 2009). Individuals in a pre-diabetic state are at substantially higher risk for progression to type 2 diabetes (T2D), with up to 70% of individuals with pre-diabetes converting to a T2D diagnosis within ten years (Buysschaert and Bergman, 2011). Other major adverse effects of pre-diabetes include microvascular complications, and cardiovascular disease (Anon, 2007; Coutinho et al., 1999; Plantinga et al., 2010) highlighting the significant public health impact of this new disease category.

In the U.S. National Health and Nutrition Examination Survey (NHANES) III, 1988 to 1994 data revealed that among overweight adults aged 45 to 74 years, 23% of participants had pre-diabetes (Benjamin et al., 2003). Further, 12 million overweight adults, age 45 to 74 years were reported to have pre-diabetes in 2000 (Benjamin et al., 2003), with an upward trend to 57 million American adults in 2007 (Control and Prevention, 2011). Accordingly these statistics continued to worsen in 2010 with an estimated 79 million American adults having pre-diabetes as defined by fasting blood glucose or hemoglobin A1C (Control and Prevention, 2011).

A higher T2D prevalence has previously been reported in the Stroke Belt region of the southeastern US (Cushman et al., 2008; Howard, 1999) and the prevalence of T2D and cardiovascular disease have been shown to vary by race (Cowie et al., 2006; Cushman et al., 2008). The clustered high T2D prevalence area has been identified by the US Center for Disease Control and Prevention (CDC) as the Diabetes Belt and exists primarily in the Stroke Belt region (Barker et al., 2011). The prevalence of diabetes in the Diabetes Belt is 11% relative to 8.5% in the remaining US, with 24% of the population in the Diabetes Belt being black (Barker et al., 2011). Data from the Diabetes Belt reveal that the increased risk of T2D is attributable to known risk factors: 30% modifiable risks (i.e. lifestyle factors) and 37% non-modifiable risk factors (i.e. race) (Barker et al., 2011), yet few studies have investigated the association between biological, social, demographic, or geographic factors with a diagnosis of pre-diabetes. The identification of individuals who are at increased risk of pre-diabetes may provide a window of opportunity to improve the efficiency of screening for T2D. Subsequently progression to T2D from pre-diabetes can be prevented or delayed with early intervention (Rydén et al., 2007). Therefore, the authors sought to determine whether race and region are associated with pre-diabetes in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort.

Methods

Permission was obtained from the University of Alabama at Birmingham Institutional Review Board to conduct a cross-sectional study using data from the REGARDS study. Briefly, the REGARDS study is a prospective cohort study of 30,239 black and white community-dwelling residents aged 45 years and older. The overall goal of REGARDS is to better understand the contributors to the substantial racial and geographic disparities in stroke. By design the study included 56% of the cohort from residents of the Stroke Belt states (North Carolina, South Carolina, Georgia, Alabama, Mississippi, Tennessee, Louisiana, and Arkansas) and the remainder from the rest of the 40 contiguous US states. Also, the study oversampled blacks. Potential participants were sampled from a commercially available list, and recruited from 2003 to 2007 through a combination of mail and telephone. For those agreeing to participate (cooperation rate was 49%, participation rate 33%), using a computer-assisted telephone interview, trained interviewers obtained demographic information and medical history. A brief physical examination including blood pressure measurements, blood samples, and an electrocardiogram (ECG) was conducted in-person 3–4 weeks after the telephone interview. Consent was obtained verbally and later in writing. Follow-up for incident stroke events and cognitive assessment is ongoing. Details of the methods are available elsewhere (Howard et al., 2005).

Individuals who had not fasted (n = 4321; 14%) for 8–10 h at the time of blood collection were excluded from the analysis. Of those fasting, the diabetes status of the participants was trichotomized following the American Diabetes Association guidelines (Anon, 2009) as: normoglycemic with fasting glucose less than 100 mg/dL (n = 15,031, 72%); pre-diabetic with a fasting glucose between 100 and 125 mg/dL (n = 4858, 24%), or diabetic with a fasting glucose of 126 mg/dL or greater (n = 893, 4%). Since the focus of this study was on the differences between the normoglycemic and pre-diabetic strata, individuals with diabetes or a fasting glucose of 126 mg/dL or greater were also excluded from the analysis. Race was defined by self-report as black or white (with those reporting other race/ethnic membership excluded from REGARDS). Region was defined as Stroke Belt or non-Stroke Belt, with the Stroke Belt being defined as current residence in North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas or Louisiana. Socioeconomic status was defined according to annual household income and highest education level. Annual household income (<$20,000, $20,000–$34,000, $35,000–$74,000, and $75,000 and over) and education (less than high school, high school graduate, some college, or college graduate) were defined by self-report. Risk factors were defined as body mass index (BMI) (<18.5 kg/m^2, underweight; 18.5–25 kg/m^2, normal weight; 25–30 kg/m^2, overweight; and >30 kg/m^2, obese) and self-reported lifestyle characteristics (physical activity, smoking history, and alcohol use). Physical activity was defined by response to the computer assisted telephone interview question – “How many times per week do you engage in intense physical activity, enough to work up a sweat?”, categorized as none, 1–3 times a week, or 4 or more times a week. Smoking was categorized into strata of never, past and current smoker. Alcohol use was defined according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines as none, moderate (1–7 drinks/week for women and 1–14

drinks/week for men), and heavy drinker (8+ drinks/week for women and 15+ drinks/week for men) (Gunzerath et al., 2004).

Statistical analysis

Among individuals with no history of diabetes, logistic regression was used to assess the relationship between race and region with the prevalence of pre-diabetes in incremental models, first assessing the crude association, then considering the joint effect of race and region, then adjusting for demographic factors (age and sex), socio-economic status, and finally after adjustment for risk factors. Data were analyzed with Statistical Analysis System (SAS) software, version 9.1.

Results

A total of 19,889 subjects met inclusion and exclusion criteria, of which 24% were pre-diabetic, 36% were black, 44% were male and 55% were from the Stroke Belt. The mean (±SD) age for the sample was 64 ± 10 years. Table 1 presents the demographic, socioeconomic, and risk factors of study subjects dichotomized by race and region.

Regardless of the region of residence, pre-diabetes was more common in blacks compared to whites; in the Stroke Belt the prevalence was 31% in blacks and 24% in whites, in the non-Stroke Belt it was 25% in blacks and 20% in whites. The unadjusted odds ratio of having pre-diabetes was 1.28 (95% CI: 1.19–1.36) for blacks compared to whites, and 1.18 (95% CI: 1.10–1.26) for people living in the Stroke Belt region compared to the non-Stroke Belt of the United States (Table 2). Interestingly, within Stroke Belt subjects, odds ratios changed minimally after additional adjustment for race (OR = 1.20; 95% CI: 1.13–1.28), age and sex (OR = 1.24; 95% CI: 1.16–1.32) and socioeconomic status (OR = 1.22; 95% CI: 1.15–1.31) (Table 2). After adjusting for region; age and sex; socioeconomic status; and risk factors, black race was independently associated with pre-diabetes (OR = 1.19; 95% CI: 1.10–1.28).

Discussion

In this large national cohort study, the prevalence of pre-diabetes was higher for both blacks and whites living in the Stroke Belt, and the prevalence of pre-diabetes was higher for blacks than whites independently of region. Until recently, few studies provided support for regionality as a risk factor for diabetes, but work by the REGARDS investigators has shown that diabetes in blacks and whites is significantly more prevalent in those living within the Stroke Belt (Barker et al., 2011; Voeks et al., 2008). Others have identified states within the Stroke Belt that have multiple counties in close proximity where rates of diabetes are greater than 10%, describing what has previously been referred to as the Diabetes Belt (Barker et al., 2011). The higher prevalence of pre-diabetes in the Stroke Belt and diabetes in the Diabetes Belt may be related to the increased prevalence of risk factors such as obesity, sedentary lifestyle and lifestyle choices that include smoking or alcohol use. Thirty-three percent of the people living in the Diabetes Belt are obese relative to 25% of the remaining US (Barker et al., 2011). Moreover 31% of the people living in the Diabetes Belt lead a sedentary lifestyle relative to 25% for the rest of the country (Barker et al., 2011). There are limited data on the effect of smoking on pre-diabetes, although there is an abundance of

evidence related to the negative effects of smoking on diabetes (Willi et al., 2007; Xie et al., 2009). Further, the association between moderate or heavy alcohol consumption and pre-diabetes has not been studied but the most consistent finding is that no beneficial effect can be attributed to high alcohol consumption on diabetes (Carlsson et al., 2005). Pre-diabetes is an important risk factor for T2D and our findings suggested that pre-diabetes status may be a substantial contributor to racial and regional disparities that have been previously associated with a diagnosis of T2D. Because progression from pre-diabetes to T2D may be halted with appropriate treatment (Rydén et al., 2007), our findings highlight the need for early identification and treatment of pre-diabetes as a key target for future intervention to reduce racial and regional disparities related to diabetes.

Genetic variants associated with race may increase the risk of having pre-diabetes (Konen et al., 1999) and subsequently diabetes (Carnethon et al., 2002; Vassy et al., 2012). The *thrifty* gene hypothesis offers one explanation for the increased risk of pre-diabetes and T2D in blacks. Researchers continue to look for support or otherwise for the theory. The hypothesis posits that descendants of indigenous people of Africa may have a specific gene that makes them more susceptible to diabetes (Neel, 1962). According to Neel's theory over thousands of years ago indigenous populations who relied on hunting, fishing and farming for their nourishment experienced alternating periods of feast or famine. To adapt to the extreme challenges of feast or famine people developed a *thrifty* gene that is not natural in human beings but evolved in time of famine to allow them to store fat and prevent starvation. Accordingly, in contemporary westernized societies the unlimited access to food coupled with a sedentary lifestyle has caused the unnatural gene to become deleterious to descendants of Africa's indigenous population (Neel, 1962). Proponents of the thrifty gene hypothesis have examined other genes that provide support to the thrifty gene hypothesis for diabetes prevalence. The ancestral hypertension sensitive gene has been proposed by some researcher to be a *thrifty* gene (Li et al., 2011). Researchers have investigated the evolutionary ecology of the hyper-tension sensitive gene's (ancestral D allele of angiotensin-converting enzyme [ACE]) propensity for water and sodium retention and subsequently blood pressure regulation. The researchers concluded that the gene's sodium/water balance properties were directly related to the body's physiologic sweat response in the hot and arid climate of Africa. As descendants moved from the hot and arid climate of Africa the salt-sensitive D allele ACE gene became deleterious (Li et al., 2011). The *thrifty* gene hypothesis has also been proposed as a plausible explanation for the increased body mass index observed in Polynesian populations. The findings suggest that certain genes remain a strong candidate *thrifty* gene in the Pacific (Myles et al., 2011). Although Neel's theory is significant to understanding of the evolutionary history of diabetes some recent study dispels the long held idea that indigenous people may have a specific gene that makes them more susceptible to diabetes. Many of these studies provide alternative hypotheses for the *thrifty* gene hypothesis such as that of genetic drift and not positive selection (Speakman, 2006), the evolution of insulin resistance as a result of a socio-ecological and socio-nutritional adaptation rather than thriftiness (Watve and Yajnik, 2007) or the alteration of gene expression related to gross changes in maternal diet and subsequent metabolic impairment (Sebert et al., 2011). Moreover, research study suggests that the *thrifty* gene theory remains inconclusive and requires further investigation (Lazar, 2005; Southam et al., 2009), and

other research study offers a combination of the *thrifty* genotype and the *thrifty* phenotype hypotheses (Stoger, 2008) as an explanation for the increased prevalence of diabetes. The *thrifty* gene hypothesis may still play a role in understanding the prevalence of diabetes but such a role is less likely to be detected through genetic polymorphisms but rather functional studies (e.g. epigenetics). The findings showed that Stroke Belt whites carried a high prevalence of pre-diabetes, and while lifestyle may contribute to some of the risk associated with this; it remains unclear whether genetic variants in combination with other factors are at play in whites with pre-diabetes from the Stroke Belt. Few studies have identified the genetic variants of pre-diabetes or T2D in blacks. To date most of the genetic variants identified for T2D are from studies of European and Asian populations (Ng et al., 2013). Future work should consider the contribution of a wider variety of theoretically-sound socio-behavioral factors in combination with genetic findings to the development of pre-diabetes in both white and black subjects.

Strength of the study was the objective identification of pre-diabetes subjects by 8–10 hour fasting blood glucose between 100 and 125 mg/dL, instead of relying on self-report. Additionally, the large sample size provided the study with adequate power. While the study aim was limited to understanding the prevalence of pre-diabetes and its association with race and regionality after adjusting for sex and age; education and income; and BMI, physical activity, smoking history and alcohol use, previous work by the REGARDS investigators focused on lifestyle factors and co-morbid findings, identifying unhealthy eating habits (Newby et al., 2012), higher incidences of transient ischemic attack (TIA) symptoms (Judd et al., 2013), renal dysfunction/failure (McClellan et al., 2006), cognitive impairment (Tsivgoulis et al., 2009), heart disease (Howard et al., 2011), heavy drinking (Judd et al., 2011), and smoking (Howard et al., 2011) as well as poorer control of blood pressure, hyperlipidemia, and blood glucose associated with African American race and living in the Stroke Belt region of the US. These findings are physiologically consistent with a finding of pre-diabetes, and subsequently T2D, providing an association with pathogenesis.

Study limitations

Study limitations extend to the methods used for the REGARDS study, including use of self-report socioeconomic data, and self-report lifestyle choices (physical activity, smoking history, and alcohol consumption) that may have contributed to the selection of responses that were considered socially desirable, instead of an accurate reflection of socioeconomic state and lifestyle choices. Additionally, the highly rural Stroke Belt region carries high rates of poverty among blacks many of whom lack telephone access and were therefore excluded from participating in REGARDS: therefore, it is unclear whether the findings are representative of this group. The study was also limited by its cross-sectional design, with data collection occurring at only one point in time.

Conclusion

In summary this study provides support for the role of racial and regional variations in prevalence pre-diabetes. Conversely there may be other factors present in the southeast region of the US that lead to an increased risk of pre-diabetes more than that which can be explained by regional and racial variation. We should also consider the possibility that

region and race here may not be causal but simply correlates of causal variables such as blood pressure, hyperlipidemia, medication use, etc. Regardless of the mechanism, the study is important because prioritizing screening for pre-diabetes by race and region could be useful. Because pre-diabetes is a stage in the diabetes continuum where interventions have been shown to be effective to prevent or delay diabetes (Anon, 2010; Scragg et al., 2004) it is imperative to identify risk factors for pre-diabetes. The identification of race and regionality as risk factors for pre-diabetes may allow for early prioritization of interventions that focus on the southeast region of the US. Prevention or delayed progression of pre-diabetes to diabetes in the southeast region of the US may decrease the morbidity and mortality of diabetes in the US.

Living in the US Stroke Belt is associated with an increased prevalence of pre-diabetes in both blacks and whites. Pre-diabetes is a risk factor for T2D and it may be contributing to the increased risk for T2D for those living within the Stroke Belt. Practitioners must identify pre-diabetes as one of the most significant opportunities for clinical intervention to reduce subsequent T2D diagnoses. While the study does not fully explain physiologic, behavioral, and socioeconomic mechanisms for pre-diabetes, it suggests the need for future work that aims to determine causal mechanisms ripe for intervention within the southeastern Stroke Belt region of the US.

Acknowledgments

The REGARDS research project is supported by a cooperative agreement U01 NS041588 from the National Institute of Neurological Disorders and Stroke, National Institutes of Health, and Department of Health and Human Service (U01 NS041588). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Neurological Disorders and Stroke or the National Institutes of Health. Representatives of the funding agency have been involved in the review of the manuscript but not directly involved in the collection, management, analysis or interpretation of the data. The authors thank the other investigators, the staff, and the participants of the REGARDS study for their valuable contributions. A full list of participating REGARDS investigators and institutions can be found at http://www.regardsstudy.org.

The authors thank Dr. Rita Jablonski, Associate Professor at the UAB School of Nursing, University of Alabama at Birmingham for her valuable contribution of writing assistance and proof reading the article.

References

The prevalence of retinopathy in impaired glucose tolerance and recent-onset diabetes in the Diabetes Prevention Program. Diabet. Med. 24:137–144.

Diagnosis and classification of diabetes mellitus. Diabetes Care. 32(Suppl. 1):S62–S67. [PubMed: 19118289]

Standards of medical care in diabetes—2010. Diabetes Care. 33(Suppl. 1):S11–S61. [PubMed: 20042772]

Barker LE, Kirtland KA, Gregg EW, Geiss LS, Thompson TJ. Geographic distribution of diagnosed diabetes in the U.S.: a diabetes belt. Am. J. Prev. Med. 2011; 40:434–439. [PubMed: 21406277]

Benjamin SM, Valdez R, Geiss LS, Rolka DB, Narayan KM. Estimated number of adults with prediabetes in the US in 2000: opportunities for prevention. Diabetes Care. 2003; 26:645–649. [PubMed: 12610015]

Buysschaert M, Bergman M. Definition of prediabetes. Med. Clin. North Am. 2011; 95:289–297. vii. [PubMed: 21281833]

Carlsson S, Hammar N, Grill V. Alcohol consumption and type 2 diabetes. Diabetologia. 2005; 48:1051–1054. [PubMed: 15864527]

Carnethon MR, Palaniappan LP, Burchfiel CM, Brancati FL, Fortmann SP. Serum insulin, obesity, and the incidence of type 2 diabetes in black and white adults: the atherosclerosis risk in communities study: 1987–1998. Diabetes Care. 2002; 25:1358–1364. [PubMed: 12145235]

Control, C.F.D., Prevention. National Diabetes Fact Sheet: National Estimates and General Information on Diabetes and Prediabetes in the United States, 2011, 3. US Department of Health and Human Services, Centers for Disease Control and Prevention; Atlanta, GA: 2011.

Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. Diabetes Care. 1999; 22:233–240. [PubMed: 10333939]

Cowie CC, Rust KF, Byrd-Holt DD, et al. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health and Nutrition Examination Survey 1999–2002. Diabetes Care. 2006; 29:1263–1268. [PubMed: 16732006]

Cushman M, Cantrell RA, Mcclure LA, et al. Estimated 10-year stroke risk by region and race in the United States: geographic and racial differences in stroke risk. Ann. Neurol. 2008; 64:507–513. [PubMed: 19067365]

Gunzerath L, Faden V, Zakhari S, Warren K. National institute on alcohol abuse and alcoholism report on moderate drinking. Alcohol. Clin. Exp. Res. 2004; 28:829–847. [PubMed: 15201626]

Howard G. Why do we have a stroke belt in the southeastern United States? A review of unlikely and uninvestigated potential causes. Am. J. Med. Sci. 1999; 317:160–167. [PubMed: 10100689]

Howard VJ, Cushman M, Pulley L, et al. The reasons for geographic and racial differences in stroke study: objectives and design. Neuroepidemiology. 2005; 25:135–143. [PubMed: 15990444]

Howard G, Cushman M, Kissela BM, et al. Traditional risk factors as the underlying cause of racial disparities in stroke: lessons from the half-full (empty?) glass. Stroke. 2011; 42:3369–3375. [PubMed: 21960581]

Judd SE, Mcclure LA, Howard VJ, Lackland DT, Halanych JH, Kabagambe EK. Heavy drinking is associated with poor blood pressure control in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. Int. J. Environ. Res. Public Health. 2011; 8:1601–1612. [PubMed: 21655140]

Judd SE, Kleindorfer DO, Mcclure LA, et al. Self-report of stroke, transient ischemic attack, or stroke symptoms and risk of future stroke in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study. Stroke. 2013; 44:55–60. [PubMed: 23233382]

Konen JC, Summerson JH, Bell RA, Curtis LG. Racial differences in symptoms and complications in adults with type 2 diabetes mellitus. Ethn. Health. 1999; 4:39–49. [PubMed: 10887461]

Lazar MA. How obesity causes diabetes: not a tall tale. Science. 2005; 307:373–375. [PubMed: 15662001]

Li X, Sun X, Jin L, Xue F. Worldwide spatial genetic structure of angiotensin-converting enzyme gene: a new evolutionary ecological evidence for the thrifty genotype hypothesis. Eur. J. Hum. Genet. 2011; 19:1002–1008. [PubMed: 21559052]

Mcclellan W, Warnock DG, Mcclure L, et al. Racial differences in the prevalence of chronic kidney disease among participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study. J. Am. Soc. Nephrol. 2006; 17:1710–1715. [PubMed: 16641151]

Myles S, Lea RA, Ohashi J, et al. Testing the thrifty gene hypothesis: the Gly482Ser variant in PPARGC1A is associated with BMI in Tongans. BMC Med. Genet. 2011; 12:10. [PubMed: 21244673]

Neel JV. Diabetes mellitus: a “thrifty” genotype rendered detrimental by “progress”? Am. J. Hum. Genet. 1962; 14:353–362. [PubMed: 13937884]

Newby PK, Noel SE, Grant R, Judd S, Shikany JM, Ard J. Race and region have independent and synergistic effects on dietary intakes in black and white women. Nutr. J. 2012; 11:25. [PubMed: 22500645]

Ng MC, Saxena R, Li J, et al. Transferability and fine mapping of type 2 diabetes loci in African Americans: the Candidate Gene Association Resource Plus Study. Diabetes. 2013; 62:965–976. [PubMed: 23193183]

Plantinga LC, Crews DC, Coresh J, et al. Prevalence of chronic kidney disease in US adults with undiagnosed diabetes or prediabetes. Clin. J. Am. Soc. Nephrol. 2010; 5:673–682. [PubMed: 20338960]

Rydén L, Standl E, Bartnik M, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Eur. Heart J. 2007; 28:88–136. [PubMed: 17220161]

Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes Care. 2004; 27:2813–2818. [PubMed: 15562190]

Sebert S, Sharkey D, Budge H, Symonds ME. The early programming of metabolic health: is epigenetic setting the missing link? Am. J. Clin. Nutr. 2011; 94:1953s–1958s. [PubMed: 21543542]

Southam L, Soranzo N, Montgomery SB, et al. Is the thrifty genotype hypothesis supported by evidence based on confirmed type 2 diabetes- and obesitysusceptibility variants? Diabetologia. 2009; 52:1846–1851. [PubMed: 19526209]

Speakman JR. Thrifty genes for obesity and the metabolic syndrome—time to call off the search? Diab. Vasc. Dis. Res. 2006; 3:7–11. [PubMed: 16784175]

Stoger R. The thrifty epigenotype: an acquired and heritable predisposition for obesity and diabetes? Bioessays. 2008; 30:156–166. [PubMed: 18197594]

Tsivgoulis G, Alexandrov AV, Wadley VG, et al. Association of higher diastolic blood pressure levels with cognitive impairment. Neurology. 2009; 73:589–595. [PubMed: 19704077]

Vassy JL, Durant NH, Kabagambe EK, et al. A genotype risk score predicts type 2 diabetes from young adulthood: the CARDIA study. Diabetologia. 2012; 55:2604–2612. [PubMed: 22782289]

Voeks JH, Mcclure LA, Go RC, et al. Regional differences in diabetes as a possible contributor to the geographic disparity in stroke mortality: the REasons for Geographic and Racial Differences in Stroke Study. Stroke. 2008; 39:1675–1680. [PubMed: 18388336]

Watve MG, Yajnik CS. Evolutionary origins of insulin resistance: a behavioral switch hypothesis. BMC Evol. Biol. 2007; 7:61. [PubMed: 17437648]

Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA. 2007; 298:2654–2664. [PubMed: 18073361]

Xie X-T, Liu Q, Wu J, Wakui M. Impact of cigarette smoking in type 2 diabetes development. Acta Pharmacol. Sin. 2009; 30:784–787. [PubMed: 19434055]

Table 1

Characteristics of the pre-diabetes study participants by race and region. REGARDS, United States, 2003–2007.[a]

Subjects	Stroke Belt region		Non-Stroke Belt region	
	Blacks	Whites	Blacks	Whites
n	3596	7399	3516	5378
Male	1278 (36%)	3323 (44%)	1346 (38%)	2816 (52%)
Highest education				
<High school	657 (18%)	554 (7%)	517(15%)	249 (5%)
High school graduate	1010 (28%)	1892 (26%)	971 (27%)	1166 (22%)
Some college	928 (26%)	2037 (28%)	1009 (29%)	1373 (25%)
College graduate	999 (28%)	2914 (39%)	1015 (29%)	2587 (48%)
Income				
<$20,000	895 (25%)	1654 (22%)	733 (21%)	487 (9%)
$20,000–$34,000	979 (27%)	2409 (33%)	933 (26%)	1125(21%)
$35,000–$74,000	322 (9%)	1526 (21%)	1014 (29%)	1826 (34%)
>$75,000	436 (12%)	938 (13%)	417 (12%)	1328 (25%)
Refused to disclose	964 (27%)	872 (11%)	419 (12%)	612 (11%)
Body mass index (kg/m^2)				
Underweight (<18.5)	43 (1%)	92 (1%)	45 (1%)	63 (1%)
Normal (18.5–25)	717 (20%)	2345 (32%)	734 (21%)	1607 (30%)
Overweight (25–30)	1195 (33%)	2961 (40%)	1300 (37%)	2248 (42%)
Obese (30+)	1624 (45%)	1979 (27%)	1427 (41%)	1445 (27%)
Physical activity				
None	1196 (34%)	2230 (31%)	1286 (37%)	1568 (30%)
1–3 times/week	1315 (37%)	2684 (37%)	1263 (36%)	1974 (37%)
4+ times/week	1023 (29%)	2390 (33%)	917 (27%)	1762 (33%)
Smoking history				
Never	1734 (49%)	3374 (46%)	1509 (43%)	2495 (47%)
Past	1186 (33%)	2988 (41%)	1357 (39%)	2273 (42%)
Current	655 (18%)	1016 (14%)	637 (18%)	589 (11%)
Alcohol (NIAAA)				
None	2579 (73%)	4274 (59%)	2242 (66%)	2400 (45%)
Moderate (1–7 drinks/week for women, 1–14 drinks/week for men)	859 (24%)	2633 (36%)	1068 (31%)	2565 (48%)
Heavy (8+ drinks/week for women, 15+ drinks/week for men)	93 (3%)	389 (5%)	106 (3%)	333 (6%)
Pre-diabetes	1107 (31%)	1766 (24%)	84 (25%)	1091 (20%)

Note: REGARDS = Reasons for Geographic and Racial Differences in Stroke study. NIAA = National Institute on Alcohol Abuse and Alcoholism, kg/m^2 = kilogram per square meter.

[a]Findings based on 19,889 pre-diabetes and no pre-diabetes REGARDS participants.

Table 2

Adjusted logistic regression models for pre-diabetes by race and region from the REGARDS cohort baseline data, United States, 2003–2007.

	Odds ratio (95% confidence interval)				
	Unadjusted	**Race + region[a]**	**Sex + age[b]**	**Income + education[c]**	**Risk factors[d]**
Region (Stroke Belt compared to non-Stroke Belt)	1.18 (1.10,1.26)	1.20 (1.13,1.28)	1.24 (1.16,1.32)	1.22 (1.15,1.31)	1.26 (1.17,1.35)
Race (black compared to white)	1.28 (1.19,1.36)	1.29 (1.21,1.38)	1.36 (1.27,1.46)	1.33 (1.24,1.43)	1.19 (1.10,1.28)

[a] Adjusts for race and region.

[b] Adjusts for race, region plus demographics (age and gender).

[c] Adjusts for race, region, demographics plus socioeconomic status (education and income).

[d] Adjusts for race, region, demographics, socioeconomic status and diabetes risk factors (body mass index, physical activity, smoking history, and alcohol use).