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Grip Strength Cut Points for Diabetes Risk Among Apparently Healthy U.S. Adults

Elise C. Brown, PhD,[1] Duncan S. Buchan, PhD,[2] Samar Madi, MS,[3] Breanne Gordon, BS,[4] Dorin Drignei, PhD[3]

From the [1]Department of Public and Environmental Wellness, Oakland University, Rochester, Michigan; [2]Division of Sport and Exercise, Institute for Clinical Exercise and Health Science, University of the West of Scotland, Lanarkshire, Scotland; [3]Department of Mathematics and Statistics, Oakland University, Rochester, Michigan; and [4]Department of Interdisciplinary Health Sciences, Oakland University, Rochester, Michigan

Address correspondence to: Elise C. Brown, PhD, Department of Public and Environmental Wellness, Oakland University, 433 Meadow Brook Rd., Rochester MI 48309. E-mail: elisebrown@oakland.edu.

Introduction: Early detection screening tools are needed to aid in preventing vascular complications associated with type 2 diabetes. As low muscular strength is linked to increased diabetes risk, the purpose of this study is to establish muscular strength cut points for determining diabetes risk using a large, nationally representative U.S. sample.

Methods: Using the 2011–2012 and 2013–2014 National Health and Nutrition Examination Survey data, 5,108 participants aged 20–80 years (68.6% aged 20–50 years; young male participants, *n*=1,813, mean age=33.43 years; young female participants, *n*=1,692, mean age=33.39 years; older male participants, *n*=813, mean age=59.92 years; older female participants, *n*=790, mean age=60.45 years) and free of common diabetes comorbidities were included. Muscular strength was assessed using a handgrip dynamometer, and normalized by adjusting for body weight. A logistic regression for survey data controlling for covariates was used to determine normalized grip strength cut points. Diabetes risk was determined using American Diabetes Association diagnostic criteria. Analyses were conducted summer of 2019.

Results: Normalized grip strength significantly predicted diabetes (p=0.0332), and the cut points for detecting diabetes risk included 0.78 (young male participants), 0.57 (young female participants), 0.68 (older male participants), and 0.49 (older female participants). The risk percentages for diabetes and estimated rates reported for all subgroups were comparable, and the risk percentages included 6.84 (95% CI=5.32, 8.36; younger male participants), 7.49 (95% CI=5.87, 9.10; younger female participants), 5.76 (95% CI=2.34, 9.19, older male participants), and 4.27 (95% CI=2.44, 6.10; older female participants).

Conclusions: Normalized grip strength using the cut points proposed in this paper may be a useful screening tool for diabetes risk in apparently healthy, normotensive adults.

INTRODUCTION

Type 2 diabetes (T2DM) is linked to increased cardiovascular-related morbidity and mortality.[1,2] Undiagnosed prediabetes and T2DM in the U.S. in 2017 were estimated to cost $43.4 and $31.7 billion, respectively.[3] This economic burden highlights the need for better early T2DM detection efforts. T2DM is asymptomatic in initial stages of the disease, and a prompt diagnosis could prevent or delay vascular complications such as neuropathy.[4,5] Various studies have used aerobic fitness as an indicator of T2DM risk.[6–8] However, a limitation to this approach is the use of different assessment modalities like step test[6] and treadmill.[8] As within-subject predicted peak oxygen consumption values vary across aerobic modalities,[9] T2DM risk comparisons across studies is difficult.

Low muscular strength and quality are linked to increased cardiometabolic[10,11] and T2DM risk in adults.[12,13] Low muscular strength, when assessed using a handgrip dynamometer, in adulthood is associated with mortality.[14] Recent studies indicate that T2DM-related low muscular strength is linked to poor glycemic control and insulin resistance.[15,16] As HG dynamometers are portable, cost-effective, and require minimal training, the use of a handgrip test for detecting T2DM risk in adults could be implemented in clinical[17] and community settings.[18] This practice could enhance early detection of T2DM, identifying those who may benefit from interventions, and serve to monitor intervention effectiveness.

Muscular strength cut points for detecting cardiometabolic risk have been established in adults,[19–22] using handgrip dynamometers[19–21] and variable-resistance weight machines.[22] Similarly, handgrip cut points for detecting T2DM risk have also been established in U.S.[21] and

older Mexican adults.[23] Peterson et al.[21] recently established normalized HG cut points for T2DM or insulin resistance risk using 2011–2012 National Health and Nutrition Examination Survey (NHANES) data. However, the analyses included participants with known comorbidities of T2DM (e.g., cardiovascular disease), limiting the utility of the cut points in asymptomatic adults for prevention efforts. Therefore, the purpose of this study was to determine age- and sex-specific thresholds of MS, for accurate prediabetes and T2DM risk categorization among apparently health, normotensive U.S. adults.

METHODS

Study Population

This study used publicly available NHANES 2011–2012 and 2013–2014 data.[24] The NHANES is a nationally representative survey conducted to collect information about the health and nutritional status of individuals in all 50 U.S. states and DC. It uses a complex survey design consisting of four-stage clustering and stratification by groups of states. Further details of the survey methodology can be found elsewhere.[25] The data collection procedures for muscular strength and T2DM risk variables for the 2011–2012 and 2013–2014 NHANES surveys were approved by the NHANES Ethics Review Board, Hyattsville, MD. Informed consent was obtained from all participants prior to study involvement.

The 2011–2014 survey design is composed of data released in the 2-year cycles, 2011–2012 (n=9,756) and 2013–2014 (n=10,175). These two cycles were combined (N=19,931), and adults aged ≥20 years were retained (n=11,329). Only respondents who self-reported they were free from major medical conditions such as stroke, cardiovascular diseases (hypertension, heart

attack, coronary heart disease, and congestive heart failure), and cancer were retained (*n*=7,226). Participants with missing, *don't know* or *refused* responses on T2DM-related covariates were removed. The final sample size of 5,108 was used in analyses. The analyses were conducted in the summer of 2019.

Measures

Full details of data collection procedures have been reported elsewhere.[26–28] Briefly, participant demographics, health and medical history, and list of prescribed medications were obtained from a home interview. All other procedures took place in a mobile examination center, and were performed by trained personnel.

Race/ethnicity was categorized into six groups: Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and other race. Education and poverty were used to estimate SES. Education was categorized into five groups: less than 9th grade, 9th–12th grade with no diploma, high school graduate or equivalent, some college or associate degree, and college graduate or above. Poverty–income ratio (PIR) was used as a continuous measure of poverty.[29] PIR is a ratio of family income relative to poverty thresholds established by HHS, with a PIR <1 considered poverty.

In survey participants aged ≥6 years, muscular strength tests were conducted using a Takei Digital Grip Strength Dynamometer, Model T.K.K. 5401. Prior to data collection at each testing site, the dynamometer was calibrated using known standard weights. Participants were randomly assigned to a morning, afternoon, or evening testing session. This testing involved the squeezing of a handheld device to estimate overall muscular strength. If participants were unable to

complete the assessment with either hand, they were excluded from this test. When physical limitations were present in one hand (e.g., pain, stiffness, or surgery), only the non-limited hand was tested. Following the dynamometer adjustment for grip size, participants completed a sub-maximal practice trial. The test was conducted in a standing position unless they were unable to stand, and the dynamometer was held at thigh level with a fully extended elbow. Both hands were tested three times each, and, to align with American College of Sports Medicine guidelines,[30] the sum of the highest score (kg) on each hand was used in analyses. Exercise prior to the testing session was not controlled. Given the covariance between strength capacity and body weight, grip strength was normalized as strength per body weight as has been done previously.[20,22]

Body weight was measured in kg with participants wearing examination gowns. Standing height was measured in cm using a mechanical stadiometer with participant shoes removed. Height and weight were used to calculate BMI as weight (kg) divided by height squared (m^2). BMI was used as a measure of obesity. Waist circumference (WC) was measured to the nearest 0.1 cm with the tape measure positioned horizontally at the uppermost portion of the hip on the right side of the body. WC was used as a measure of abdominal obesity. Blood pressure was assessed in a seated position after resting for 5 minutes.

Blood collection procedures were performed by a trained phlebotomist. Fasting samples included glucose, HbA1c, triglycerides, total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. A total of 117–145 mL of blood was collected on each participant from an elbow, forearm, or hand vein. For oral glucose tolerance testing (OGTT),

after initial venipuncture, participants consumed 75mg of Trutol®, and completed a second venipuncture 2 hours later. Blood serum was immediately processed, stored, and shipped for analysis.

Prediabetes and T2DM risk were determined based on the American Diabetes Association diagnostic criteria.[31] High risk for T2DM was defined as fasting glucose ≥126 mg/dL, or 2-hour plasma glucose ≥200 mg/dL during OGTT, or HbA1c ≥6.5%. Moderate risk for T2DM (prediabetes criteria) was defined as fasting glucose between 100 mg/dL and 125 mg/dL, or 2-hour plasma glucose during 75-g OGTT 140–199 mg/dL, or HbA1c 5.7%–6.4%. In line with Peterson and collagues,[32] because it was not possible to determine which participants had type 1 diabetes, those who were diagnosed with diabetes, only taking insulin as a diabetes medication, and aged ≤30 years were excluded. A sensitivity analysis was conducted with these excluded participants included back in the analysis. Appendix File 1 provides notes on sensitivity analysis, sample weights, and receiver operating characteristics curves.

Sedentary behavior, alcohol use, and cigarette use were assessed as covariates. For sedentary behavior, minutes sedentary was used as a continuous variable and represented the total minutes per day the participant spent sitting. Alcohol use was based on yearly frequency of alcohol consumption, and was categorized into two categories: drank <12 drinks in the last year and drank >12 drinks in the last year. Cigarette use was based on the question: *Have you smoked at least 100 cigarettes in your entire life?* Respondents were categorized into two groups based on answering *yes* or *no*.

Statistical Analysis

All statistical analyses were performed using SAS, version 9.4. The following variables per age–sex category were presented as means and (SEs) incorporating the survey design for descriptive purposes: age, BMI, percentage with obesity, WC, percentage abdominal obesity, grip strength, normalized grip strength (NGS), HbA1c, percentage with T2DM, percentage with prediabetes, fasting glucose, 2-hour OGTT glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total cholesterol, triglycerides, systolic blood pressure, diastolic blood pressure, percentage that had ≥12 alcoholic drinks in 1 year, percentage that smoked ≥100 cigarettes in lifetime, sedentary activity minutes, PIR, education, and race/ethnicity. Proc surveymeans in SAS was used to obtain the means and SEs. To assess sex and age differences, multiple regression for survey data was used (SAS proc surveyreg) when the response variable was continuous, and logistic regression for survey data was used (SAS proc surveylogistic) when the response variable was binary. To retain the highest number of respondents as possible, the full sample 2-year mobile examination center exam weights were used in analyses (Appendix File 1).

To determine cut points for the NGS variable while controlling for sociodemographic, anthropometric, and lifestyle factors, a logistic regression for survey data based on the whole, final sample was used. The T2DM binary variable computed was the response variable and the covariates used are included in Table 1. NGS was continuous and “Survey Year” was an indicator variable for the 2011–2012 and 2013–2014 cycles. Proc surveylogistic (SAS, version 9.4) was used to obtain estimates and SEs accounting for the survey design. Once it was established that the NGS variable was significant, the same logistic regression model for T2DM was used further, except for the NGS continuous variable being replaced by a dichotomized NGS

variable at a value C. The Akaike information criterion (AIC) value for a range of C values was recorded, and the whole-sample optimal cut point C as the value that minimized the AIC was chosen (Appendix File 1).

The T2DM risk percentages were defined as the weighted percentages of respondents having NGS below the optimal cut point, in each age–sex category. The SEs of the risk percentages for T2DM were obtained using a jackknife variance estimation method for survey data.

The logistic regression model in Table 1 was also used for prediabetes, but the continuous NGS variable was statistically insignificant. Therefore, the cut point analysis for prediabetes was not reported.

RESULTS

Descriptive data for participant characteristics are presented in Table 2. Among the 5,108 study participants, 68.6% were aged 20–50 years (younger male participants, n=1,813, mean age=33.43 [SE=0.39] years; younger female participants, *n*=1,692, mean age=33.39 [SE=0.43] years; older male participants, *n*=813, mean age=59.92 [SE=0.35] years; older female participants, *n*=790, mean age=60.45 [SE=30] years). Briefly, sex and age differences were found for ethnicity/race, education, muscular strength, cardiometabolic risk factors, diabetes risk, and lifestyle variables, and age differences were evident for poverty.

Table 1 indicates that significant covariates for T2DM included NGS, sex, age, WC, race/ethnicity, PIR, education level, and minutes in sedentary activity. For prediabetes, the

results of the logistics regression model were similar to those for T2DM, except survey year was significant, and NGS, sex, PIR, education level, and minutes in sedentary activity were not significant.

For a given threshold C, a binary variable that identifies a respondent at risk of T2DM was created by comparing their NGS value with C. A logistic regression model with this binary variable as one of the predictors was then fitted and the AIC value was obtained. Thus, any threshold C corresponds to an AIC value. Figure 1 shows the threshold C varied between 0.40 and 0.90, along with the corresponding AIC values. The minimum AIC value was attained at threshold C=0.58, and was chosen as the whole-sample cut point. The computed z-score of this cut point for the whole-sample continuous NGS distribution was z= –1.44. The cut point for any subset of these data that still included a large number of respondents was defined as the point on the continuous NGS distribution of the subset corresponding to the above z-score.

For the older group, the risk percentages for T2DM and the estimated T2DM rates reported in Table 2 were comparable, and the corresponding population percentages were statistically equal. For the younger group, the risk percentages for T2DM were higher than the estimated T2DM rates, especially in female participants. However, these differences diminished substantially when the standard errors were considered. Indeed, the differences between the closest bounds of the 95% CIs for the population percentages reduce to 1.42% for younger males, and to 2.76% for younger female participants.

For the subset of each age–sex category, Table 3 shows the sample sizes, T2DM cut points, and T2DM risk percentages estimated using the survey design and weights. To assist healthcare professionals, corresponding body weights and handgrip values for each cut point are provided in Table 3. After adjusting for covariates, a respondent who was not screened out because of other health problems (e.g., cardiovascular disease) was at risk of T2DM if their NGS was below the cut points. For example, after adjusting for the above covariates, a male participant aged >50 years with no major systemic diseases, and an NGS=0.6, is at risk for T2DM.

DISCUSSION

This study established NGS cut points for detection of T2DM risk in adults free of common T2DM comorbidities. To the best of the authors' knowledge, this is the first study to use a large, U.S. nationally representative sample using American Diabetes Association criteria for T2DM and prediabetes, while screening out participants with common T2DM comorbidities. This approach increases the likelihood that the cut points are detecting T2DM risk and not risk of common comorbidities of T2DM. The results from this study can be used by clinicians and public health practitioners for T2DM prevention screening in normotensive, apparently healthy adults.

The NGS is an appropriate screening tool for apparently healthy adults for the detection of T2DM, but not prediabetes risk in U.S. adults. Although other studies using the NHANES have found prediabetes to be linked to low muscular strength in adults,[33,34] these studies did not screen out participants with cardiovascular disease, stroke, and cancer. This suggests that in prediabetes, low muscular strength may be related to other comorbidities. The cut points for T2DM risk in the

younger group was 0.78 for male and 0.57 for female participants. For the older group, the cut points were 0.68 for male and 0.49 for female participants. Other studies have also reported lower cut points for female and older adults.[21,22] One possible reason for the discrepancies in age–sex cut points could be related to variations in muscle mass with male[35] and young adults[36] having higher levels of lean mass compared with female and older adults, respectively.

When using the suggested NGS cut points in the current study, the differences in estimated T2DM risk and actual T2DM prevalence were statistically similar in both groups. However, in the younger group, especially in the female participants, the NGS cut points did not estimate T2DM risk as accurately as the older group. As older adults had significantly higher HbA1c, fasting glucose, and OGTT values compared with younger adults, it may be that NGS is more accurate for predicting T2DM in those with poorer glycemic control. Overall, the binary NGS variable proposed in this paper can be a useful screening tool for T2DM in adults.

Identification of the most relevant tools for public health and clinical T2DM screening that may prompt diagnostic tests is a high priority. Loss of muscular strength and mass in people with T2DM have a profound effect upon physical function impairment,[37,38] is evident in those newly diagnosed with T2DM, and is accelerated in those with higher HbA1c values or longer duration of T2DM.[37] Hyperglycemia through mitochondrial dysfunction[39,40] and insulin resistance through dysfunctional muscle protein synthesis and catabolism[41,42] are thought to mediate the relationship between T2DM and muscle loss. Early identification of T2DM-related low muscular strength may prevent further muscular impairment by prompting prevention/treatment interventions.

Previous studies have determined NGS cut points for cardiometabolic risk detection in adults.[20–22] However, limitations of these cut points included the use of population samples that were not representative,[20,22] non-standardized muscular strength assessment equipment,[22] and the inclusion of study participants with known T2DM comorbidities.[21] Peterson et al.[21] used the 2011–2012 NHANES data to identify NGS cut points for adults with T2DM, though their methods differ from those of this study in several ways. In the present study, data from the 2011–2012 and 2013–2014 cycles were combined, and respondents having other major systemic diseases (e.g., cardiovascular) were excluded. Therefore, the cut points proposed in the present study are more likely to predict the TD2 itself rather than other comorbidities. Additionally, these proposed cut points were obtained using a formal optimality method, based on AIC.

Considering the limitations of the previously proposed cut points, the strength of this study is that these NGS cut points have been proposed from individuals free of common T2DM comorbidities using a large, nationally representative U.S. sample. According to the recommendations by the U.S. Preventive Services Task Force for identifying T2DM in asymptomatic adults, the benefit of screening was unclear in those who were normotensive.[43] The findings from the present study highlight the value in using muscular strength testing in asymptomatic, normotensive individuals for the detection of increased risk of T2DM, aligning with the more broad screening recommendations of the American Diabetes Association.[44]

Limitations

This study also had several limitations. The proposed cut points were limited to two age categories, and a larger sample size would have enabled the determination of cut points for more

age groups. Nonetheless, the reduced sample size was expected given the rigorous screening process undertaken to remove participants with comorbidities. Given the known diurnal variations in muscular performance, randomized testing times may have affected grip strength performance.[45] Lastly, although the summation of grip strength values from dominant and non-dominant hands is in line with industry guidelines,[30] the inclusion of the non-dominant hand value may have reduced the maximal strength assessment and impacted the relationship with cardiometabolic variables.

CONCLUSIONS

In apparently healthy adults, low muscular strength is associated with increased risk of T2DM after controlling for known covariates. Established NGS cut points may be used in U.S. adults for the detection of increased risk of T2DM. This tool can easily be implemented in clinical or public health domains to aid in the detection of T2DM. Further work is needed to establish the accuracy of these proposed cut points over a period of time.

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LIST OF FIGURES

AIC, Akaike Information Criterion; C, constant at which the normalized grip strength is dichotomized; * indicates the cut point.

Table 1. Covariates Used in Logistic Regression Analysis to Determine Cut points; Analysis of Maximum Likelihood Estimates

	Type 2 diabetes				**Prediabetes**			
Parameter	**Estimate**	**SE**	**t-value**	**Pr > t**	**Estimate**	**SE**	**t-value**	**Pr > t**
Intercept	–8.9152	1.1715	–7.61	****<0.001**	–5.2353	0.6617	–7.91	****<0.001**
NGS	–0.8706	0.3911	–2.23	***0.0332**	0.4476	0.3369	1.33	0.1934
Survey year	0.0348	0.0673	0.52	0.6089	0.1094	0.0488	2.24	***0.0318**
Sex	0.2409	0.0882	2.73	***0.0102**	0.0562	0.0645	0.87	0.3898
Age	0.0638	0.0042	15.28	****<0.001**	0.0420	0.0026	15.97	****<0.001**
WC	0.0431	0.0080	5.41	****<0.001**	0.0274	0.0040	6.83	****<0.001**
Race/ethnicity (ref=other race)								
Mexican American	0.0715	0.1811	0.39	0.6956	0.1057	0.0970	1.09	0.2841
Other Hispanic	–0.0329	0.2090	–0.16	0.8760	–0.0797	0.1013	–0.79	0.4369
Non-Hispanic white	–0.9783	0.1622	–6.03	****<0.001**	–0.3169	0.0756	–4.19	****<0.001**
Non-Hispanic black	0.0035	0.2222	0.02	0.9875	0.1287	0.0645	2.00	0.0545
Non-Hispanic Asian	0.8717	0.1654	5.27	****<0.001**	0.4749	0.1124	4.23	****<0.001**
PIR	–0.1963	0.0623	–3.15	***0.0035**	–0.0393	0.0336	–1.17	0.2507
Education level (ref=college graduate or above)								
Less than 9th grade	0.2121	0.1541	1.38	0.1782	–0.0040	0.1341	–0.03	0.9764
9–12th grade (no degree)	0.4806	0.1918	2.51	***0.0175**	0.1799	0.1084	1.66	0.1067
High school graduate	–0.1505	0.1584	–0.95	0.3491	–0.0906	0.0869	1.04	0.3050
Some college or associates degree	–0.1320	0.1668	–0.79	0.4347	–0.0108	0.0679	–0.16	0.8746
Minutes in sedentary activity	0.0008	0.0003	2.43	***0.0208**	–0.0003	0.0002	–1.28	0.2083
Alcohol use	–0.0552	0.0818	–0.68	0.5043	–0.0804	0.0542	–1.48	0.1480
Smoking status	–0.0147	0.0767	–0.19	0.8497	0.0243	0.0433	0.56	0.5789

Notes: Boldface indicates statistical significance (**p*<0.05; ***p*<0.001).

NGS, normalized grip strength; WC, waist circumference; PIR, poverty to income ratio.

Table 2. Descriptive Statistics for Participant Characteristics

	Aged 20–50 years		Aged 50–80 years	
Parameter	**Males (n=1,813)**	**Females (n=1,692)**	**Males (n=813)**	**Females (n=790)**
Demographics				
Age (years)[b]	33.43 (0.39)	33.39 (0.43)	59.92 (0.35)	60.45 (0.30)
Ethnicity/Race (%)				
Mexican American[a,b]	12.32 (1.59)	10.43 (1.74)	5.92 (1.23)	4.02 (0.82)
Other Hispanic[b]	7.44 (1.10)	7.16 (1.03)	3.80 (0.59)	4.95 (0.89)
Non-Hispanic white[b]	61.04 (2.69)	61.03 (2.94)	76.01 (2.42)	77.45 (2.43)
Non-Hispanic black[a,b]	9.92 (1.25)	12.09 (1.60)	7.95 (1.28)	8.02 (1.34)
Non-Hispanic Asian[b]	5.75 (0.72)	6.22 (0.65)	3.97 (0.59)	3.82 (0.53)
Other race (including multi-racial)	3.53 (0.59)	3.07 (0.39)	2.34 (0.64)	1.74 (0.98)
Education (%)				
Less than 9th grade[a,b]	3.35 (0.47)	2.48 (0.38)	5.78 (1.09)	3.28 (0.55)
12th grade or less	10.69 (1.10)	8.66 (1.08)	8.50 (1.12)	9.25 (1.66)
High school graduate/GED or equivalent[a]	23.22 (1.71)	16.73 (1.42)	19.69 (1.80)	18.81 (1.57)
Some college or associate degree[a,b]	31.78 (1.61)	36.46 (1.66)	27.09 (2.40)	30.56 (2.32)
College graduate or above	30.96 (1.92)	35.68 (2.20)	38.95 (3.22)	38.10 (2.84)
Poverty income ratio[b]	2.82 (0.09)	2.79 (0.10)	3.45 (0.11)	3.42 (0.11)
Muscular strength				
Grip strength (kg)[a,b]	95.85 (0.46)	61.00 (0.30)	84.58 (0.99)	53.39 (0.45)
Normalized grip strength[a,b]	1.14 (0.01)	0.85 (0.01)	1.01 (0.01)	0.76 (0.01)
Cardiometabolic risk factors				
BMI (kg/m^2)	27.96 (0.18)	28.17 (0.26)	27.99 (0.35)	27.78 (0.29)
Obese (%)	29.54 (1.40)	32.23 (1.45)	29.13 (1.88)	30.33 (2.72)
Waist circumference (cm)[a,b]	97.28 (0.55)	93.48 (0.58)	102.45 (0.72)	95.18 (0.68)
Abdominal obesity (%)	33.14 (1.47)	56.45 (1.95)	51.51 (2.47)	68.51 (2.37)
Triglycerides (mg/dL)[a]	134.85 (4.31)	105.83 (6.25)	114.97 (5.76)	112.79 (3.96)

Total cholesterol (mg/dL)[a,b]	188.26 (1.48)	186.49 (1.23)	195.31 (1.50)	214.46 (1.89)
HDL cholesterol (mg/dL)[a,b]	46.99 (0.36)	57.38 (0.49)	51.09 (0.94)	63.20 (0.99)
LDL cholesterol (mg/dL)[b]	115.01 (1.29)	107.18 (1.60)	116.07 (2.03)	126.47 (2.09)
Systolic blood pressure (mmHg)[a,b]	118.07 (0.32)	111.27 (0.39)	126.11 (0.82)	122.30 (0.73)
Diastolic blood pressure (mmHg)[a,b]	70.66 (0.53)	68.08 (0.38)	72.88 (0.61)	70.41 (0.42)
Diabetes risk				
HbA1c (%)[a,b]	5.35 (0.01)	5.29 (0.01)	5.74 (0.05)	5.68 (0.03)
Glucose (mg/dL)[a,b]	99.84 (0.75)	94.94 (0.70)	108.78 (2.15)	103.14 (1.57)
2-h OGTT glucose (mg/dL)[b]	101.41 (1.74)	104.03 (1.77)	120.11 (4.49)	116.87 (2.29)
T2DM (%)[a,b]	2.93 (0.47)	2.41 (0.35)	11.19 (1.61)	7.26 (1.02)
Prediabetes (%)[a,b]	29.44 (1.70)	19.09 (1.26)	43.65 (2.61)	46.00 (2.18)
Lifestyle variables				
Minutes sedentary activity (minutes)	398.89 (8.45)	403.54 (7.47)	405.41 (9.21)	382.43 (10.01)
At least 12 alcoholic drinks/year (%)[a]	86.75 (1.61)	76.46 (2.04)	89.98 (1.20)	70.32 (2.63)
At least 100 cigarettes in lifetime (%)[a,b]	41.21 (1.40)	32.25 (1.96)	53.87 (3.28)	37.55 (2.37)

Notes: Boldface indicates statistical significance at the 0.05 level. All values are presented as mean (SE) unless otherwise noted.
[a]Sex differences in whole sample.
[b]Age differences between younger and older groups.

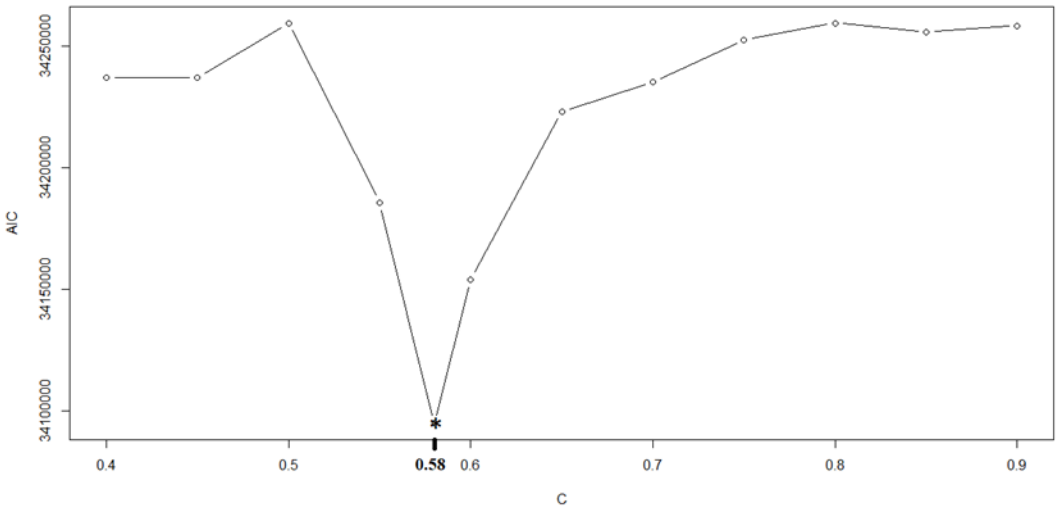
HDL, high-density lipoprotein; LDL, low-density lipoprotein; OGTT, oral glucose tolerance test, T2DM, type 2 diabetes.

Table 3. Diabetes Weighted Risk Percentages, Cut points, and Corresponding Grip Strength and Body Mass Values

	Aged 20–50 years				Aged 50–80 years			
Parameter	**M**	**GS value**	**F**	**GS value**	**M**	**GS value**	**F**	**GS value**
Sample size	1,813		1,692		813		790	
Type 2 diabetes								
Cut point	0.78		0.57		0.68		0.49	
Body mass (kg)								
50		39.0		28.5		34.0		24.5
55		42.9		31.4		37.4		27.0
60		46.8		34.2		40.8		29.4
65		50.7		37.1		44.2		31.9
70		54.6		39.9		47.6		34.3
75		58.5		42.8		51.0		36.8
80		62.4		45.6		54.4		39.2
85		66.3		48.5		57.8		41.7
90		70.2		51.3		61.2		44.1
95		74.1		54.2		64.6		46.6
100		78.0		57.0		68.0		49.0
105		81.9		59.9		71.4		51.5
110		85.8		62.7		74.8		53.9
115		89.7		65.6		78.2		56.4
120		93.6		68.4		81.6		58.8
125		97.5		71.3		85.0		61.3
130		101.4		74.1		88.4		63.7
135		105.3		77.0		91.8		66.2
140		109.2		79.8		95.2		68.6
145		113.1		82.7		98.6		71.1
150		117.0		85.5		102.0		73.5
155		120.9		88.4		105.4		76.0
160		124.8		91.2		108.8		78.4
165		128.7		94.1		112.2		80.9
170		132.6		96.9		115.6		83.3
175		136.5		99.8		119.0		85.8
180		140.4		102.6		122.4		88.2
185		144.3		105.5		125.8		90.7
Risk % diabetes (95% CI)	6.84 (5.32, 8.36)		7.49 (5.87, 9.10)		5.76 (2.34, 9.19)		4.27 (2.44, 6.10)	

GS, grip strength; M, male; F, female.

1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Appendix File 1. Statistical analysis notes related to sensitivity analysis, sample weights, and receiver operating characteristics curves.

Sensitivity Analysis

We performed a sensitivity analysis by including back in the sample the respondents younger than 30 years and who were told they have diabetes, as well as those not taking insulin or diabetic pills to lower blood sugar. The new sample size was n=5,142 and the whole-sample cut point changed to C=0.57. The cut points for specific age-sex categories become: 0.77 (younger males), 0.56 (younger females), 0.67 (older males) and 0.48 (older females). These results support the robustness of our analysis.

Sample Weights

After using our screening criteria, the final sample size was 5,108 among whom 366 were identified as having type 2 diabetes (according to the American Diabetes Association definition), and we used the full sample 2-year mobile exam center (MEC) exam weights in our analysis. There are two other sets of sample weights, the fasting subsample 2-year MEC weight and the oral glucose tolerance test (OGTT) subsample 2-year MEC weight. However, if we had used the fasting subsample 2-year MEC weight, a subset of 2,671 respondents had missing sample weights, among which 136 were classified as having type 2 diabetes since they had an HbA1c larger than 6.5%. Similarly, if we had used the OGTT subsample 2-year MEC weight, a subset of 2,812 respondents had missing sample weights, among which 144 were classified as having diabetes because they had a HbA1c larger than 6.5%. Therefore, using either of these two alternative sets of sample weights would have led to a dramatic reduction in the overall sample size, as well as in the number of respondents who would otherwise be classified as having diabetes. We performed analyses to determine if biased inference was an issue. For the respondents in the fasting subsample who had non-zero weights, the correlation coefficient between the full sample 2-year MEC exam weights and the fasting subsample 2-year MEC weights was 0.99, while the correlation coefficient between the full sample 2-year MEC exam weights and the OGTT subsample 2-year MEC weights was 0.98. These strong correlations suggest that such bias may be small.

Receiver Operating Characteristics Curves

Receiver operating characteristics (ROC) curves can be used to identify cut points for a continuous variable relative to a binary condition, e.g. by maximizing Youden's index and balancing sensitivity vs specificity (e.g., Zou et al., Circulation 2007; Koyama et al., BMC Res Notes 2016). However, they are not always appropriate for cut point selection, and there are papers in the literature looking into alternative methods. For example, Peterson et al. (Am J Prev Med 2016) suggested that "clinicians and public health experts may not agree that sensitivity and specificity are of equal consequence when screening children for risks of cardiometabolic diseases." As an alternative, they used conditional inference tree analyses and locally smoothing curves to select the cut points. A somewhat similar method for cut point detection based on locally smoothing curves has also been used for a diabetes study in adults (Peterson et al., Sports Med, 2016). The ROC curves and sensitivity-specificity at the cut points are almost exclusively applicable to a simple random sample, but it is not clear that such methods can be directly applied to survey data. For example, there is evidence in the literature (Yao et al., Statist. Med., 2015) that the area under the ROC curve (AUC) is better estimated when taking the survey

design into account. To reflect accurately the data collection process, in our paper we used only existing methods that incorporate the survey design. New methodological research will be needed to incorporate the survey design into the ROC curve itself in order to determine the appropriate cut points, as well as into the sensitivity-specificity measures and negative-positive predictive values at the resulting cut points. As an alternative, in this paper we chose an information-based method that incorporates the survey design in order to select the optimal cut points. Using information-based criteria such as minimizing the AIC is an established selection method in the statistics literature (e.g., Kutner et al. 2005, Applied Linear Statistical Models, 5th Ed., McGraw-Hill).

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