Prevalence, Diagnosis, and Treatment of Impaired Fasting Glucose and Impaired Glucose Tolerance in Nondiabetic U.S. Adults

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OBJECTIVE — To estimate the rates of prevalence, diagnosis, and treatment of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).

RESEARCH DESIGN AND METHODS — A representative sample of the U.S. population (the National Health and Nutrition Examination Survey [NHANES]) from 2005–2006 including 1,547 nondiabetic adults (>18 years of age) without a history of myocardial infarction was assessed to determine the proportion of adults who met the criteria for IFG/IGT, and the proportion of IFG/IGT subjects who: *1*) reported receiving a diagnosis from their physicians; *2*) were prescribed lifestyle modification or an antihyperglycemic agent; and *3*) were currently on therapy. We used multivariable regression analysis to identify predictors of diagnosis and treatment.

RESULTS — Of the 1,547 subjects, 34.6% (CI 30.3–38.9%) had pre-diabetes; 19.4% had IFG only; 5.4% had IGT only, and 9.8% had both IFG and IGT. Only 4.8% of those with pre-diabetes reported having received a formal diagnosis from their physicians. No subjects with pre-diabetes received oral antihyperglycemics, and the rates of recommendation for exercise or diet were 31.7% and 33.5%, respectively. Among the 47.7% pre-diabetic subjects who exercised, 49.4% reported exercising for at least 30 min daily.

CONCLUSIONS — Three years after a major clinical trial demonstrated that interventions could greatly reduce progression from IFG/IGT to type 2 diabetes, the majority of the U.S. population with IFG/IGT was undiagnosed and untreated with interventions. Whether this is due to physicians being unaware of the evidence, unconvinced by the evidence, or clinical inertia is unclear.

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An estimated 26% of the U.S population (54 million) suffered from impaired fasting glucose (IFG) as of 2003 (1), and an estimated 15.8% (32 million) had impaired glucose tolerance (IGT) in 1994 (2). In 2002, a randomized clinical trial (the Diabetes Prevention Project [DPP]) demonstrated that lifestyle modification and oral antihyperglycemics, specifically metformin, can delay or prevent progression to type 2 diabetes (3). Conse-

quently, in 2005 the American Diabetes Association (ADA) recommended the oral antihyperglycemic, metformin, and lifestyle modification for those with IFG and/or IGT (4).

Those with IFG, IGT, or both are at greater risk for cardiovascular disease than those with normal glucose metabolism, though their glycometabolic abnormalities do not yet qualify for a diagnosis of type 2 diabetes (5–9). Since type 2 diabetes is associated with even

greater cardiovascular risk than pre-diabetes, preventing type 2 diabetes may improve cardiovascular outcomes regardless of the impact on other cardiovascular risk factors. The DPP has demonstrated that progression of IFG/IGT to type 2 diabetes can be prevented or delayed by lifestyle modification and pharmacological interventions (3).

No studies to date have quantified the combined prevalence of IFG and IGT and their rates of diagnosis and treatment. In addition, no studies have examined the rates of adherence to these therapies. Using data obtained from a nationally representative sample of the U.S. population three years after publication of the DPP (the National Health and Nutrition Examination Survey [NHANES] IV), we assessed the proportion of adults who met the criteria for IFG/IGT, and the proportion of IFG/IGT subjects who: *1*) reported receiving a formal diagnosis from their physicians; *2*) reported having lifestyle modification or an oral hypoglycemic agent recommended; and *3*) were actively doing lifestyle modification or using an oral hypoglycemic agent.

RESEARCH DESIGN AND METHODS

Data source
NHANES is a cross-sectional survey of the health and nutrition of the noninstitutionalized, household-dwelling U.S. population conducted by the National Center for Health Statistics and by the Centers for Disease Control and Prevention (10,11). The survey consists of two components: the in-home interview and the mobile exam center, which performs several laboratory tests including the fasting plasma glucose (FPG) test and the 2-hr oral glucose tolerance test (OGTT). The in-home survey collects demographic and clinical information, including the subject's age, race, sex, medical history, therapy, and lifestyle variables such as the frequency and duration of exercise and dietary habits.

Population

NHANES has collected data in 2-year cohorts since 1999. The 2005–2006 sample from NHANES IV, the most recent publicly available version, was used in this study. We restricted our analyses to the subjects in the subsample that had morning examinations since they were the only subjects who had valid FPG and OGTT testing. We also excluded from our analyses subjects aged <18 years, those with diagnosed or undiagnosed diabetes, and those with a history of myocardial infarction (MI).

Study variables and definitions

The current ADA definition for IFG is blood glucose 100–125 mg/dl after an 8-h fast (12). When the IFG category was initially introduced by the ADA, IFG was defined as 110–125 mg/dl after fasting. In 2003, the ADA lowered the threshold of IFG to better capture those who met the World Health Organization's (WHO) criteria for IGT. WHO defines IGT as a glucose level of 140–199 mg/dl 2 h after a glucose load (13). We compared the estimates of the prevalence of pre-diabetes using the old and the new fasting blood glucose criterion.

Subjects were asked if their physicians have ever told them that they have "borderline diabetes, pre-diabetes, impaired fasting glucose, or impaired glucose tolerance." A prior diagnosis of pre-diabetes was considered to be a "yes" to any of the four terms.

The ADA recommends metformin alone as the antihyperglycemic of choice based upon the DPP results. However, because NHANES does not indicate the class of antihyperglycemic used for IFG/IGT, we could only determine whether any antihyperglycemic medication was given. Lifestyle modification included either exercise, diet modification, or both. Subjects who averaged at least 30 min of vigorous or moderate activity daily for the previous 30 days were considered "compliant" with ADA recommendations for treatment of IFG/IGT (4). Vigorous activity was defined as activity that causes "heavy sweating or large increases in breathing or heart rate." Moderate activity was defined as activity that causes "moderate sweating or slight to moderate increases in breathing or heart rate." Subjects were asked if they maintained their activity levels over the last year relative to the last 30 days. Provider recommendation for diet modification included reporting either counseling to reduce weight or counseling to reduce fat/calorie intake, or both. NHANES did not indicate the chronological order of the physician recommendations and the actual change in exercise or diet, so it was not possible to determine if lifestyle behaviors changed in response to the recommendations.

Statistical analyses

The associations between subject demographics and medical conditions and the presence of pre-diabetes were examined using the χ^2 statistic for categorical predictor variables and logit modeling for continuous predictor variables. Sampling weights were used to provide estimates that are representative of the U.S. population; all percentages presented are weighted. Most variables analyzed had little missing data (<4%), but 16.7% of subjects were missing data for either income, education, or both. Therefore, multiple imputation was used to more accurately account for the high level of missing data for all analyses involving these two variables (14). Multivariable logistic regression was used to examine independent predictors of treatment and adherence to lifestyle modification therapies. Independent variables in the model included sex, race, education, insurance status, and the percent of poverty level. All statistical analyses were performed using the STATA software (version 10.0; StataCorp LP, College Station, TX).

RESULTS

Study population

The NHANES 2005–2006 cohort included 2,425 subjects aged 18 years or older in the morning examination (fasting) sample. From this sample, 878 were excluded from our analysis: 87 because they had had a prior MI (since we were interested in pre-diabetes and diabetes as coronary artery disease risk factors); 659 because they had missing OGTT data; 16 because they had diagnosed diabetes; and 116 because they had undiagnosed diabetes (based on FPG and/or OGTT testing). Subjects who were on oral medications or receiving insulin for their diagnosed diabetes were excluded from OGTT testing; hence, only 16 subjects were excluded for diagnosed diabetes and 116 for undiagnosed diabetes. These exclusions resulted in a sample of 1,547 subjects in the study. By applying sample weights to make the results representative of the nondiabetic U.S. population without a history of MI, we estimate that about 34.6% (CI 30.3–38.9%) of nondiabetic U.S. adults had pre-diabetes. Of the pre-diabetic subjects, 84% met IFG criteria, 44% met IGT criteria, and 28% met both. Using the 1997 ADA criteria for IFG (110–125 mg/dl) resulted in 43% fewer subjects meeting the criteria for IFG, reducing the estimate of the prevalence of pre-diabetes in nondiabetic U.S. adults from 34.6 to 19.8% (Table 1).

Demographics and medical conditions

The subjects' demographic characteristics and medical conditions are reported in Table 2. Those with pre-diabetes had substantially higher cardiovascular risk, with a mean Framingham 10-year risk for cardiovascular events of 8.5% (CI 6.0–10.6%), which was almost twice that of normoglycemic subjects (5.2% [CI 3.9–6.4%], $P < 0.001$) (15,16).

Only 3.4% of the entire study sample reported a prior diagnosis of "impaired fasting glucose, impaired glucose tolerance, borderline diabetes, or pre-diabetes" (Table 2). Of those reporting a diagnosis, 38.5% no longer met the pre-diabetes criteria (either due to resolution or misdiagnosis); 61.5% had unresolved pre-diabetes. No diagnosed pre-diabetic subjects reported receiving oral antihy-

Table 1—Prevalence of pre-diabetes in 2005–2006 of a nationally representative sample of 1,547 nondiabetic U.S. adults using older vs. newer ADA criteria

	1997 ADA criteria	2003 ADA criteria
	(110 < FPG ≤125)	(100 < FPG ≤125)
Pre-diabetes	19.8 (16.3–23.3)	34.6 (30.3–38.9)
IFG only	4.5 (3.0–6.0)	19.4 (16.3–22.4)
IGT only	11.8 (9.2–14.3)	5.4 (3.5–7.3)
IFG and IGT	3.5 (2.1–4.9)	9.8 (7.5–12.0)

Pre-diabetes = having either IFG or IGT.

Table 2—Demographic and medical information for the study population (a nationally representative sample of 1,547 nondiabetic U.S. adults in 2005–2006)*

Demographics	Normoglycemic	Pre-diabetes	*P* value
n	963	584	
Age (mean)	39.6 (38.0–41.3)	49.3 (46.8–51.9)	<0.001
Male (%)	43.1 (40.9–45.3)	59.0 (53.3–64.6)	<0.001
Race (%)			
White	72.5 (67.2–77.7)	69.1 (61.1–77.2)	>0.2
Black	11.8 (7.9–15.6)	10.4 (6.4–14.4)	
Hispanic	10.8 (8.6–13.0)	14.4 (9.7–19.1)	
Other/multiracial	5.0 (2.4–7.5)	6.0 (2.7–9.3)	
Insured (%)	79.7 (74.0–85.3)	80.5 (75.1–85.8)	>0.2
Current cigarette smoking (%)	29.8 (24.5–35.2)	19.7 (14.6–24.8)	<0.001
Education (%)			
<High school	12.3 (9.3–15.4)	19.7 (15.1–24.4)	<0.001
High school graduate	24.7 (20.7–28.8)	24.4 (20.3–28.5)	
>Some college	62.9 (57.2–68.7)	55.9 (50.4–61.3)	
Income (%)			
<Poverty level	9.3 (7.0–11.6)	10.1 (7.2–13.0)	>0.2
100–200% of poverty level	17.4 (12.3–22.4)	20.4 (14.7–26.2)	
>200% poverty level	73.3 (68.1–78.6)	73.3 (68.1–76.5)	
BMI (mean)	26.8 (26.3–27.4)	30.7 (29.7–31.8)	<0.001
Blood pressure (mean ± SD, mmHg)			
Systolic	116.8 (115.4–118.1)	125.2 (123.5–127.1)	<0.001
Diastolic	67.9 (66.5–69.3)	70.0 (68.8–71.2)	0.013
Cholesterol (mean ± SD, mg/dl)			
Total	194.4 (190.0–198.7)	202.6 (197.1–208.1)	0.004
HDL	57.1 (55.9–58.3)	53.1 (51.6–54.6)	<0.001
Past medical history of pre-diabetes (%)	1.7 (1.1–2.4)	4.8 (3.1–6.5)	0.003
Interventions (%)			
Exercise recommended only	23.7 (19.5–30.0)	31.7 (23.3–40.2)	<0.001
Diet recommended only	16.6 (12.4–20.7)	27.4 (20.3–34.5)	<0.001
Mean 10-year cardiovascular risk (mean)	5.2 (3.9–6.4)	8.3 (6.0–10.6)	<0.001
Hemoglobin A1C (mean)	5.1 (5.1–5.2)	5.4 (5.4–5.5)	<0.001
Fasting serum glucose (mean, mg/dl)	91.2 (90.6–91.9)	105 (104.2–105.9)	<0.001
2-h postglucose load test (mean, mg/dl)	92.8 (90.8–94.8)	128.9 (125.5–132.4)	<0.001

*The study population is a 2005–2006 nationally representative sample of nondiabetic U.S. adults. Statistical significance was tested using χ^2 testing for differences in percentages and *t* testing for differences in means.

perglycemic medications (CI 0–10.8%). Multivariable analysis found that subjects who had pre-diabetes tended to be older, male, and Mexican American (Table 3).

Recommendations for and practice of diabetes prevention behaviors

Of pre-diabetic subjects, 31.7% (CI 23.3–40.2%) reported receiving counseling for exercise, 33.4% (CI 26.4–40.5%) for diet, and 25.9% (CI 17.9–34.5%) for both (Table 4). Of those who reported exercising, only about half reported achieving the ADA IFG/IGT guidelines of at least 30 min daily. Rates of recommendations for and practice of diabetes prevention behaviors were similar when the 1997 ADA criteria for IFG (FPG of 110–125 mg/dl) were applied.

CONCLUSIONS — This study is the first to publish a combined estimate of IFG/IGT and explore its contemporary diagnosis and treatment patterns in a national sample. Using NHANES data gathered roughly 3 years after the publication of the DPP, we found that the majority of people with IFG and/or IGT are undiagnosed and untreated with interventions that the DPP suggests can substantially reduce progression to type 2 diabetes, reducing the risk of both microvascular and macrovascular complications.

Delays in the adoption of effective new therapies have been commonly reported. However, given the significant potential benefits of metformin and lifestyle modification, the very low level of detection and intervention are concerning. In the DPP randomized trial, lifestyle modification and metformin reduced the incidence of type 2 diabetes by 58 and 38%, respectively, in just 3 years (15–17).

We found similar rates of prevalence of IFG and IGT in reports from earlier time periods (1,2) and found a combined prevalence of 34.6% nondiabetic U.S. adults. Consistent with prior studies, relative to normoglycemic subjects, pre-diabetic subjects in this cohort tended to be older, male, Mexican American, hypertensive, hyperlipidemic, and have substantially greater overall 10-year cardiovascular risk.

Disappointingly, only 3.4% of pre-diabetes individuals reported that their physicians diagnosed them with pre-diabetes. This extremely low rate could in part be due to incomplete recollection by subjects or because physicians did not emphasize the importance of pre-diabetes to their patients. Another likely explanation is that physicians do not adequately screen for and diagnose pre-diabetes, resulting in marked underdiagnosis of pre-diabetes. For instance, physicians did not recommend lifestyle modification to pre-diabetic subjects any more intensively than normoglycemic subjects. In addition, not one subject reported receiving metformin, suggesting that physicians were either unaware of metformin's benefits, were hesitant to prescribe it, or were unaware the subject had pre-diabetes; however, it is also possible that many physicians are aware of the DPP findings, but found its results unconvincing.

Three years after the DPP, however, subjects reported that lifestyle interventions were recommended to less than one-third of pre-diabetic subjects. Of pre-diabetic subjects, less than half reported exercising, less than two-thirds reported recent attempts at weight and/or diet control, and 44% reported both. Though it could be argued that the recent formal guidelines may improve upon practice at the time of study (our NHANES cohort

Table 3—*Independent associations with the presence of pre-diabetes (a 2005–2006 nationally representative sample of 1,546 nondiabetic U.S. adults)*

Predictors	Unadjusted association		Adjusted associations*	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Male	1.90 (1.54–2.34)	<0.001	2.30 (1.75–3.01)	<0.001
Age (per decade of life)	1.46 (1.38–1.55)	<0.001	1.58 (1.45–1.72)	<0.001
Race (ref = white)				
Black	0.93 (0.68–1.26)	>0.2	1.15 (0.86–1.54)	>0.2
Mexican American	1.47 (1.00–2.17)	0.05	1.96 (1.10–3.48)	0.03
Other/multiracial	1.26 (0.70–2.27)	>0.2	1.54 (0.82–2.88)	0.16
Insured	1.05 (0.76–1.46)	>0.2	0.99 (0.68–1.45)	>0.2
Education (ref = some college or more)				
High school graduate	1.11 (0.81–1.53)	>0.2	0.92 (0.67–1.26)	>0.2
<High school	1.80 (1.42–2.29)	<0.001	1.28 (0.96–1.71)	0.09
Income (ref = >200% poverty)				
<Poverty level	1.15 (0.78–1.70)	>0.2	1.29 (0.84–1.99)	>0.2
100%–200% poverty level	1.24 (0.75–2.05)	>0.2	1.12 (0.63–2.00)	>0.2

*Independent associations in a multiple logistic regression model controlling for all listed variables. OR, odds ratio; ref, reference.

was from 2005–2006 and U.S. Preventive Services Task Force and ADA guidelines were published around this time), most evidence suggests that passive dissemination of national guidelines is ineffective in changing clinical practice.

While substantial evidence has demonstrated the benefits of early glycemic control in reducing the incidence of type 2 diabetes, whether early glycemic control significantly reduces cardiovascular outcomes has been debated. However, unlike most studies of early or intensive antihyperglycemic medication interventions, intervention with a lifestyle modification in pre-diabetes substantially improved cardiovascular risk factors in the DPP (such as blood pressure and lipids), making it likely that such interventions will improve cardiovascular outcomes (18). It is also possible that lowering the lifetime glycemic burden by early intervention could reduce long-term cardiovascular outcomes, as seen in the 17-year follow-up of the Diabetes Control and Complications Trial (DCCT) (19). Finally, the cardiovascular risk associated with overt type 2 diabetes is substantially greater than the cardiovascular risk associated with pre-diabetes, suggesting that delaying or preventing type 2 diabetes should improve both cardiovascular and microvascular outcomes regardless of the direct impact on other cardiovascular risk factors (20).

The limitations of our study include large amounts of missing data for smoking, particularly when calculating the Framingham risk score. In addition, the rates of physician diagnosis were dependent on subject self-report and were not verified by chart abstraction; consequently the rates of diagnosis and treatment of IFG/IGT may have been underreported. Also, only subjects reporting pre-diabetes were asked about whether they were on oral hypoglycemic medications, so some additional subjects may have been treated that were not captured in our results. NHANES also does not report the chronological order of diagnosis, recommendation, and treatment. Finally, the ADA 2003 criteria for IFG resulted in a dramatic increase in the number of people being diagnosed with IFG and has been controversial; many physicians may dis-

Table 4—*Subject-reported recommendations for and practice of diabetes prevention behaviors for 584 subjects with pre-diabetes in a 2005–2006 nationally representative sample of U.S. adults**

Interventions	Reported diabetes prevention behavior	Reported receiving a recommendation for a diabetes prevention behavior	Of those reporting receiving a recommendation, % reporting diabetes prevention behavior
Exercise (%)	47.7 (43.2–52.2)	31.7 (23.3–40.2)	70.0 (61.7–78.4)
Vigorous exercise, of those exercising (%)	47.2 (39.9–54.5)	†	†
Moderate exercise, of those exercising (%)	22.5 (17.7–27.3)	†	†
Mean METs, of those exercising	5.2 (5.0–5.4)	†	†
Exercise >30 min daily, of those exercising	49.4 (43.6–55.1)	†	†
Change in exercise in past year, for all pre-diabetics			
Increased activity	22.5 (17.7–27.3)	†	†
Same activity	56.2 (51.0–61.4)	†	†
Decreased activity	21.2 (16.5–26.0)	†	†
Control their diet or weight (%)	62.1	33.5 (26.4–40.5)	86.0 (79.4–92.5)
Control weight (%)	51.9 (47.1–56.6)	27.4 (20.3–34.5)	72.2 (62.6–81.9)
Reduce fat/calories (%)	53.9 (48.3–60.0)	29.0 (21.8–36.2)	83.2 (77.0–90.0)
Diet + exercise (%)	44.4 (40.7)	25.9 (17.2–34.5)	69.1 (61.0–77.3)
Oral antihyperglycemic	0 (0–10.8)‡	†	†

*Data were only available on patient behavior, if recommendation for exercise was given at all. NHANES did not indicate the chronological order of the physician recommendations and the actual change in exercise or diet so it is not possible to determine if lifestyle behaviors changed in response to recommendations. Applying WHO IFG criteria (FPG 110–125) showed similar results. †Rates of recommendation for these specific exercise categories were not reported in NHANES. ‡Only available for those with diagnosed pre-diabetes.

agree with this lower threshold for diagnosis. However, the 20% of the population who met 1997 ADA pre-diabetes criteria had similar results of recommendation and compliance with lifestyle modification measures as did those who met the new ADA pre-diabetes criteria.

Three years after a landmark study demonstrated that early diagnosis of and intervention of pre-diabetes can substantially reduce progression to type 2 diabetes, the majority of people with IFG and/or IGT were undiagnosed and untreated. Whether this is due to physicians being unaware of the evidence, unconvinced by the evidence, or clinical inertia is unclear. Consideration should be given to national policies to improve upon this situation such as public and provider education programs.

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