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The Comparative Efficacy of Lifestyle Intervention and Metformin by Educational Attainment in the Diabetes Prevention Program

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Abstract

Objective—Educational attainment is inversely associated with type 2 diabetes risk, but it is unknown whether education impacts individuals' diabetes prevention efforts. We examined the comparative efficacy of intensive lifestyle intervention and metformin by educational attainment among participants in the Diabetes Prevention Program (DPP), an ongoing U.S. multi-site trial beginning in 1996.

Methods—We studied 2,910 DPP participants randomized to receive lifestyle intervention, metformin, or placebo. Stratifying by educational attainment, diabetes incidence and relative risk reductions by treatment assignment were estimated using Cox proportional hazards regression.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

Results—47% of participants had completed college and 53% had not. Compared to placebo, lifestyle participants who had completed college demonstrated a 68% reduction in diabetes incidence (95% CI=56, 77), whereas those with less education experienced a 47% risk reduction (95% CI=29, 61). For metformin participants, college graduates experienced a 49% relative risk reduction (95% CI=33, 62), compared to 23% (95% CI=1, 41) among those with lower educational attainment. There was a statistically significant education-by-treatment interaction with incident diabetes ($p=0.03$).

Conclusions—Intensive lifestyle intervention and metformin have greater efficacy among highly educated individuals. Future efforts to deliver these treatments and study their dissemination may be more effective if tailored to individuals' educational background.

Keywords

diabetes prevention; socioeconomic status; educational attainment; lifestyle intervention; metformin

INTRODUCTION

Type 2 diabetes mellitus results in a tremendous public health and economic burden, affecting almost 12% of the U.S. adult population and costing approximately \$245 billion annually.^{1,2} Low socioeconomic status is a widely recognized risk factor for many health conditions, including diabetes.³ Among commonly measured socioeconomic indicators, educational attainment may have a particularly large impact on individuals' health.⁴ Many studies have reported that higher educational attainment is associated with a lower risk of diabetes—a finding that is consistent across different time periods, geographic regions, data sources, and study designs.⁵ This observed relationship between educational attainment and diabetes risk suggests that those with lower levels of education will bear a disproportionate burden of diabetes as the prevalence of this disease continues to grow.

Large randomized trials have demonstrated that intensive lifestyle interventions can effectively prevent or delay the onset of diabetes.^{6–8} The Diabetes Prevention Program (DPP) also found that metformin was effective at achieving the same outcome.⁸ Intensive lifestyle programs are designed to help participants lose weight by reducing caloric intake, altering the macronutrient composition of their diets, and promoting regular physical activity.^{6–8} Participants are expected to record their diet and activity behaviors in detailed logs—an activity that is associated with success at achieving relevant behavioral and metabolic endpoints.⁹ Understanding the concepts underlying these lifestyle changes, and then successfully enacting and recording them in logs, requires literacy and numeracy skills that are developed through formal education. Therefore, those with more formal education may have a relative advantage in preventing or delaying diabetes over those with lower levels of education. To date, no studies have explored whether the effects of diabetes prevention treatments differ by participants' educational attainment.

Using publicly available data from the Diabetes Prevention Program (DPP), we examined differences in diabetes incidence among all study participants according to their level of educational attainment. Specifically, the objective of this study was to determine whether

the efficacy of either active treatment in the DPP was greater among those with high educational attainment compared to those with lower levels of education.

MATERIALS AND METHODS

Participants

DPP participants were adults with a body mass index (BMI) of 24kg/m² or greater and a high clinical risk of developing diabetes (defined as having a fasting plasma glucose of 95–125mg/dL and a two-hour postload glucose of 140–199mg/dL). Of the 3,154 DPP participants available in the public use dataset (representing 97.5% of the total participants), those who lacked data on educational attainment were excluded (n=73). In the public use dataset, race/ethnicity was reported as Caucasian (referred to from this point forward as non-Hispanic White), African American, Hispanic, or Other. We excluded Asians and American Indians comprising the Other category because these demographic groups have divergent educational backgrounds and share a high diabetes risk (n=171).^{2,10} The final analytic sample included 2,910 participants.

Interventions

The design of the DPP has been described in-depth elsewhere.¹¹ Briefly, participants were randomly assigned to receive one of three interventions: metformin 850mg or placebo twice daily, or an intensive lifestyle intervention. The DPP lifestyle intervention was a goal-based diet and physical activity program designed to achieve and maintain 150 minutes per week of moderate physical activity and 7% weight loss from baseline. In addition, participants in the lifestyle group were given a goal for restricting the percent of total calories from fat (<25%) and for daily dietary intake (1,200–2000 kcal/day) based on their initial weight. The intensive lifestyle curriculum was delivered in 16 sessions over a 24 week period, with subsequent maintenance sessions either bimonthly or monthly. Participants randomized to the metformin and placebo groups received standardized written materials and an annual individual session focused on similar lifestyle recommendations, in addition to the medication or placebo tablets. The mean participant follow-up was 2.8 years.

Measures

The primary outcome was the development of diabetes, which was determined using quarterly fasting plasma glucose measurements or annual oral glucose tolerance tests. The following criteria were used to diagnose diabetes (fasting plasma glucose ≥126mg/dL or two-hour postload plasma glucose ≥200mg/dL). Plasma glucose testing was also performed when participants reported symptoms suggestive of diabetes. All participants with positive diabetes tests completed a repeat confirmatory test within six weeks according to the same diagnostic criteria. Participants with confirmed diabetes continued their study treatment unless their fasting plasma glucose exceeded 140mg/dL, at which point they stopped taking study medication and were referred to their usual physicians for treatment. The participants and investigators were blinded to glucose measurements unless they exceeded the threshold for discontinuing treatment.

Participants' educational attainment was determined at baseline by the following question: "What is the highest grade or year of school you have completed?" Response options included "No schooling," "6," and every year thereafter from 7 to "20+." For this analysis, educational attainment was dichotomized into <16 years ("< College") and ≥16 years ("College") based on this variable's distribution in the study population. Due to the high levels of formal education among DPP participants, we could not create additional categories that would more fully capture lower levels of educational attainment.

Six participant characteristics were considered potential confounders or effect modifiers of the relationship between educational attainment and diabetes incidence: age, sex, race/ethnicity, and baseline levels of BMI, fasting plasma glucose, and two-hour postload glucose. For each of these variables, we used the same categories that were reported in the primary DPP analysis,⁸ with the exception of race/ethnicity which consisted of non-Hispanic Whites, African Americans, and Hispanics/Latinos in this analysis. An additional covariate—medication adherence—was measured by quarterly pill counts among participants assigned to metformin and placebo arms, and was documented as either <80% or ≥80% of the prescribed dose. Using the 6-month interval adherence data available, we specified this variable in our analysis according to the method previously described by Walker, et al.¹²

Statistical Analysis

Summary statistics were used to characterize the study cohort with respect to all covariates. We used chi-square tests to examine the association between the covariates and educational attainment. The time to the outcome (i.e. diabetes incidence) was evaluated using the Kaplan-Meier product-limit method and compared using the log-rank test among various covariate groups. We used Cox proportional hazards regression to examine diabetes incidence, relative risk reductions by treatment assignment, and interactions between treatment assignment and covariates. Results from Cox models were stratified by educational attainment (< college and ≥ college) with adjustment for potential confounders (age, race/ethnicity, sex, BMI, fasting plasma glucose, and two-hour postload glucose) to estimate the risk reductions by treatment arm and their 95% confidence intervals. Age, BMI and glucose measures were treated as continuous variables in adjusted proportional hazards models. Income and employment status were not considered confounders because they are likely part of the causal pathway between educational attainment and incident diabetes. Therefore, these variables were not included in adjusted models. A sensitivity analysis included medication adherence in the multivariable Cox proportional hazards model comparing metformin to placebo, in addition to the other covariates. A p-value of <0.05 was considered significant for all statistical testing. Due to the nature of the research question examined here, no adjustments were made for multiple testings or multiple comparisons. All analyses were conducted using SAS, version 9.3 (SAS Institute, Cary, NC). This study was deemed exempt from review by the Temple University Institutional Review Board.

RESULTS

2,910 DPP participants met study inclusion criteria, with equivalent representation of all three randomized treatment arms [lifestyle intervention (n=960); metformin (n=983);

placebo (n=967)]. With respect to educational attainment, 47% of the cohort completed college and 53% had less formal education (Table 1). Only 6.7% did not complete high school (data not shown). Overall, half of the participants were aged 45–59 years, approximately two-thirds were women, and 39% were members of minority groups. Sixty-nine percent of the study cohort was obese. Participants with less than college completion were more likely to be older, female, and African American or Hispanic/Latino. Educational attainment was significantly associated with all sociodemographic characteristics and BMI. The incidence of diabetes by participant characteristics is presented in Table 2.

Among college graduates, the incidence of diabetes (cases/100 person-years) by treatment arm was as follows: placebo (10.3), metformin (6.0), and lifestyle (4.0). The corresponding diabetes incidence among those with less formal education was: placebo (8.2), metformin (7.5), and lifestyle (4.9), respectively (Figure 1). There was a statistically significant educational attainment-by-treatment arm interaction with incident diabetes ($p = 0.03$). Overall, participants in the lifestyle group experienced a 55% reduction in the incidence of diabetes (95% CI: 44–64) compared to placebo (data not shown). Relative to participants in the placebo arm, lifestyle participants who had completed college demonstrated a 68% risk reduction (95% CI: 56–77), whereas those with less than a college education experienced a 47% risk reduction (95% CI: 29–61) in adjusted models (Figure 1A). For metformin participants overall, there was a 30% reduction in incident diabetes (95% CI: 15–42) versus placebo (data not shown). In adjusted analyses, those who were college graduates experienced a 49% relative risk reduction (95% CI: 33–62), but those with lower educational attainment experienced only a 23% risk reduction (95% CI: 1–41). (Figure 1B) All differences in risk reduction between participants with at least a college education and those with lower educational attainment were statistically significant. The relative risk reduction between the lifestyle and metformin groups was stable in all models (Figure 1C), demonstrating that the heterogeneity of treatment effects was proportional across levels of educational attainment. The impact of educational attainment on treatment effects was also consistent across strata of the covariates, with college graduates demonstrating greater risk reductions than participants with lower educational attainment when comparing lifestyle or metformin treatments to placebo (Table 3).

Additional analyses were conducted, for which data are not shown. When comparing those with missing data for educational attainment to those included in this analysis, there was no substantive difference with respect to diabetes incidence. Nor was there a difference in the outcome among those in the “Other” race/ethnicity category compared to those included here. A sensitivity analysis that included medication adherence among metformin and placebo participants did not impact the significant interaction between education and treatment assignment in the multivariable model comparing metformin to placebo. In addition, this analysis failed to produce a statistically substantive change in the diabetes risk reduction between these two groups, regardless of the educational attainment level.

DISCUSSION

Among participants randomized to receive either intensive lifestyle intervention or metformin, college graduates experienced a greater reduction in diabetes incidence

compared to their less educated counterparts. The heterogeneity of treatment effects across education levels was proportional in all models. The relative reduction in diabetes incidence was always larger for lifestyle intervention than metformin, and was similar in both the low and high education groups. The influence of educational attainment on treatment efficacy was robust and consistent across all covariates, such that the lifestyle intervention and metformin were always more effective among those who completed college than those who had not.

This is the first study to examine the relationship between individuals' educational attainment and their success in diabetes prevention efforts. The Diabetes Prevention Program presents a unique opportunity to study this question, given its large number and diversity of participants, in addition to the long follow-up period. Previous longitudinal studies examining the association of educational attainment and diabetes risk have not done so in the context of a diabetes prevention trial.⁵ These prior studies describe the natural history of diabetes incidence by educational attainment, but do not provide insight into whether individuals' educational background impacts efforts to lower their diabetes risk. Another strength of our study is that it includes two cost-effective treatments known to prevent or delay the onset of diabetes that have the potential for widespread use in clinical and community-based settings.¹³

There are several potential mechanisms underlying the principal findings. The greater effect of lifestyle treatment among participants who completed college may suggest that this group could better adhere to the treatment than less educated participants. Self-monitoring dietary intake requires reading and understanding nutrition labels, measuring portions of food precisely, and using addition, multiplication, and division to determine the total calories and percent of total calories from fat. Although these cognitive skills are taught early in the U.S. educational system, those with higher levels of education likely have more experience using such skills and therefore have greater facility with them.¹⁴ This would give participants with higher educational attainment a relative advantage in completing these tasks more quickly and reliably than those with lower educational attainment. Self-monitoring frequency was associated with meeting the DPP weight loss goal of 7%;⁹ and weight loss was an important determinant of diabetes risk among participants.¹⁵ Therefore, the greater lifestyle treatment effect among college graduates may reflect their ability to self-monitor dietary behaviors more accurately compared to those with less education.

Greater educational attainment may have helped participants succeed in the lifestyle program in other ways. Because education is positively associated with income in this cohort (data not shown), college graduates had more resources that they could contribute to meeting the lifestyle intervention's goals. For example, such resources may have provided them greater access to fresh fruits and vegetables or gym facilities than those with less education. There are likely other mechanisms linking educational attainment and diabetes risk among the participants. The protective effect of education on health outcomes has long been recognized, and many have described potential mechanisms to explain this consistent finding.³ For example, there is evidence that education helps buffer individuals from psychological stress and depression¹⁶—two conditions known to alter glucose metabolism and raise diabetes risk.^{17,18} More generally, education also helps shape healthy social and

physical environments, including neighborhoods, work conditions, and social networks.¹⁹ Given the long follow-up of participants in this study, it is possible that educational attainment may have also influenced their diabetes risk in such indirect ways.

Metformin participants who completed college experienced a statistically significant reduction in diabetes incidence relative to placebo, which was smaller in magnitude and marginally significant for those with less education (Figure 1). Although one DPP analysis demonstrated that adherence to metformin was associated with lower diabetes incidence,¹² this variable did not mediate the greater treatment effect of metformin in college graduates compared to less educated participants in our sensitivity analysis. A larger literature examining the relationship between educational attainment and medication adherence has reported conflicting results.^{20,21}

Physicians can impact patients' health outcomes through a therapeutic relationship that includes effective communication about treatment preferences and consideration of medications' risks and benefits.²² Previous research has demonstrated that doctors communicate differently with patients according to their educational background, which may impact this therapeutic relationship. In their interactions with highly educated patients, doctors spend more time, provide more information, and better justify treatment decisions.²³ If interactions between DPP staff and participants followed the same pattern, highly educated participants may have received more medication counseling, which could influence their outcomes through mechanisms unrelated to adherence. Indeed, effective communication between providers and patients can indirectly improve their health outcomes by enhancing satisfaction, social support, and self-care skills.²⁴ The observed heterogeneity in metformin efficacy may also partly reflect the same socially patterned differences in psychobiologic and environmental exposures by educational background.²⁵

The fact that those with higher educational attainment experienced greater benefits from diabetes prevention treatments has implications for research, practice, and policy. As efforts to deliver the DPP lifestyle intervention multiply and the infrastructure for scaling this evidence-based intervention at the national level develops further,^{26,27} it is important that this program be responsive to the needs of diverse communities. Designing simpler protocols that require fewer literacy and numeracy skills represents one potential strategy to improve effectiveness among less educated populations. To the extent that underlying psychological stress and depression contribute to educational disparities in lifestyle treatment outcomes, further modifications to the protocol may include addressing these mental health needs. Although a lifestyle intervention cannot change social and physical environments, protocols could integrate local resources for healthy foods and activity to promote lifestyle change among those living in communities where such resources are scarce or under-recognized. Future research should develop and test novel adaptations of the DPP lifestyle intervention, specifically targeting populations with low educational attainment.

Improving physicians' communication about diabetes risk may help increase the effectiveness of metformin, particularly among less educated patients. In general, only a small percentage of adults with prediabetes know they have it (10.1%), which is lowest

among those who haven't completed 12 years of formal education (4.9%).²⁸ And previous studies have found that patients' lack of insight into an illness predicts poor medication adherence and disease-related outcomes.²⁹ These observations underscore the importance of enhanced communication between healthcare providers and patients to discuss diabetes risk and develop individually tailored treatment plans. In healthcare systems that increasingly value patient-centered care, doctors are encouraged to engage patients in such dialogue.^{30,31} In addition, new healthcare payment models that reward preventive services may motivate providers to focus more on diabetes prevention in at-risk patients.

This study has several limitations. First, it was not a prespecified subgroup analysis of the data. Although many post hoc subgroup analyses are motivated by inspection of the data, the research question examined here was designed *a priori* without having previously explored the data for this purpose. Subgroup analyses have a greater potential to yield "false positive" findings due to testing of several baseline characteristics.³² Educational attainment was the only moderating variable included in this analysis, which reduces the possibility that the significant findings were due to chance. Asians and American Indians were excluded, which may limit the generalizability of the findings to these groups.

The educational attainment variable used in our analysis represents a crude measure of this exposure. The DPP participants were much more educated (47% college graduates) than the general U.S. population (24% college graduates),³³ which precluded creating additional categories for our primary predictor variable. It is well documented that clinical trial participants are highly educated.³⁴ In fact, one study cited high educational attainment as the strongest predictor of being recruited to clinical trials.³⁵ Therefore, the DPP cohort studied here is not unusual in this regard. Despite not fully capturing lower levels of education in our analysis, this study is the first to establish an association between educational attainment and treatment outcomes in the DPP. College completion represents a relevant educational milestone for our study, because college graduates should have mastered the literacy and numeracy skills required to comply with the DPP intervention protocols. However, translational studies of the DPP that include more diverse populations should examine whether lower thresholds of educational attainment are associated with treatment outcomes.

CONCLUSIONS

Given the growing public health burden of diabetes, which disproportionately affects those with low educational attainment, there is an acute need to promote the reach and effectiveness of diabetes prevention treatments in diverse populations. Evidence presented here suggests that lifestyle interventions and metformin have higher efficacy among more educated individuals. This finding may reflect intervention designs that require literacy or numeracy skills developed through formal education. Differences in healthcare providers' communication with more educated versus less educated patients may be one possible explanation for the observed educational disparity in metformin efficacy. Future research should develop and test novel adaptations of the DPP lifestyle program to increase its effectiveness in disadvantaged communities. Interventions to enhance patients' understanding of diabetes risk and its treatment options should be considered as a strategy to improve global diabetes prevention efforts. Increasing interest in population health

management and changes in healthcare payment models may present opportunities for natural experiments in these areas.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Diabetes prevention is a major global public health priority
- College graduates are more likely to prevent diabetes than non-college graduates
- Both lifestyle intervention and metformin were more effective in college graduates
- Diabetes prevention efforts may be more successful if tailored to educational level

Figure 1. Incidence of Diabetes in the Diabetes Prevention Program by Treatment Arm and Educational Attainment

Figure 1A displays the comparison of lifestyle intervention vs. placebo. Figure 1B displays the comparison of metformin vs. placebo. Figure 1C displays the comparison of metformin vs. lifestyle intervention. The relative reduction in diabetes incidence, and the corresponding confidence intervals, were estimated using Cox proportional hazards regression adjusted for the following covariates: age, race/ethnicity, sex, BMI, fasting plasma glucose, and 2-hour postload glucose.

Table 1

Participant Characteristics by Educational Attainment at Baseline (N=2,910)

Characteristic	Educational Attainment ^a			
	Overall N (%) ^b	< College N (%) ^b	College N (%) ^b	P value ^c
Overall	2910 (100)	1543 (53)	1367 (47)	
Age (years)				<0.01
25–44	848 (29)	452 (29)	396 (29)	
45–59	1449 (50)	724 (47)	725 (53)	
60	613 (21)	367 (24)	246 (18)	
Sex				<0.01
Male	934 (32)	424 (28)	510 (37)	
Female	1976 (68)	1119 (72)	857 (63)	
Race/Ethnicity				<0.01
Caucasian	1761 (61)	801 (52)	960 (70)	
African American	642 (22)	377 (24)	265 (20)	
Hispanic/Latino	507 (17)	365 (24)	142 (10)	
Body mass index (kg/m ²) ^d	34.3 (6.7)	34.6 (6.9)	33.8 (6.5)	<0.01
Fasting plasma glucose (mg/dL)	107.2 (7.8)	107.1 (7.7)	107.4 (7.8)	0.35
2-hr postload glucose (mg/dL)	164.6 (17.1)	165.1 (17.3)	164.1 (16.8)	0.12

Data were collected at 27 U.S. medical centers between 1996 and 2001

^a Educational attainment was determined based on number of completed years of education and dichotomized into <16 years (< College) and 16years (College).

^b N represents the total number of participants in each cell and % is expressed as the column percentage for each category of educational attainment. For continuous variables, this column contains the mean (standard deviation) for the specified group.

^c P-values are for the difference between those with at least a college education and those with less than a college education across strata of the participant characteristic using chi-square tests (categorical variables) and t-tests (continuous variables).

^d Body mass index is based on participants' measured weight and height at baseline.

Table 2Incidence of Diabetes by Participant Characteristics^a

Variable	N (%)	Incidence (cases/100 person-yr)		
		Placebo	Metformin	Lifestyle
Overall	2910 (100)	9.2	6.8	4.5
Age (years)				
25–44	848 (29)	9.8	6.1	5.7
45–59	1449 (50)	9.1	6.7	4.4
60	613 (21)	8.4	7.8	2.9
Sex				
Male	934 (32)	10.4	7.1	4.3
Female	1976 (68)	8.6	6.6	4.6
Race/Ethnicity				
Caucasian	1761 (61)	8.6	6.8	4.7
African American	642 (22)	10.3	6.3	4.5
Hispanic/Latino	507 (17)	9.7	7.2	3.9
Body mass index (kg/m ²)				
<30	901 (31)	8.0	7.3	3.0
30–35	880 (30)	6.9	6.5	3.6
>35	1129 (39)	11.6	6.5	6.4
Fasting plasma glucose (mg/dL)				
95–109	1926 (66)	5.5	4.9	2.6
110–125	984 (34)	16.1	10.1	7.8
2-hr postload glucose (mg/dL)				
<154	952 (33)	6.0	3.7	1.8
154–173	988 (34)	9.1	6.2	4.1
174–199	970 (33)	12.3	10.1	7.5

Data were collected at 27 U.S. medical centers between 1996 and 2001

^aDiabetes incidence by treatment arm was estimated using Cox proportional hazards regression.

Table 3Reduction in Diabetes Incidence by Participant Characteristics and Educational Attainment^a

Participant Characteristic	Reduction in Incidence, % (95% CI)					
	< College Education			College Education		
	Lifestyle vs. Placebo	Metformin vs. Placebo	Lifestyle vs. Metformin	Lifestyle vs. Placebo	Metformin vs. Placebo	Lifestyle vs. Metformin
Age						
25–44 years	26 (–12 – 52)	35 (3 – 57)	–13 (–77 – 27)	57 (33 – 72)	57 (35 – 72)	–1 (–64 – 38)
45–59 years	50 (27 – 65)	24 (–5 – 45)	34 (2 – 55)	70 (56 – 80)	50 (30 – 64)	41 (10 – 61)
60 years	66 (41 – 81)	3 (–50 – 37)	65 (39 – 80)	80 (63 – 89)	36 (–3 – 60)	69 (43 – 83)
Sex						
Male	58 (34 – 73)	23 (–12 – 47)	45 (13 – 65)	74 (59 – 83)	49 (26 – 65)	48 (18 – 67)
Female	42 (21 – 58)	24 (–2 – 43)	25 (–5 – 46)	64 (48 – 75)	49 (30 – 63)	29 (–6 – 52)
Race/ethnicity						
White	39 (12 – 57)	10 (–25 – 35)	32 (1 – 53)	65 (51 – 76)	44 (24 – 58)	38 (10 – 58)
African American	48 (14 – 68)	37 (3 – 59)	17 (–41 – 51)	71 (50 – 83)	61 (38 – 75)	25 (–35 – 58)
Latino	62 (34 – 78)	32 (–6 – 57)	43 (0 – 68)	78 (60 – 88)	58 (27 – 75)	49 (–1 – 74)
Body mass index (kg/m ²)						
<30	60 (33 – 76)	–11 (–65 – 25)	64 (40 – 78)	75 (58 – 85)	26 (–10 – 50)	66 (42 – 80)
30–35	42 (5 – 64)	–7 (–59 – 29)	45 (11 – 66)	63 (39 – 78)	29 (–9 – 54)	48 (12 – 69)
35	45 (22 – 61)	51 (31 – 65)	–12 (–65 – 24)	65 (49 – 76)	67 (53 – 77)	–6 (–64 – 31)
Fasting plasma glucose (mg/dL)						
95–109	40 (11 – 60)	–11 (–56 – 21)	46 (20 – 64)	63 (44 – 76)	28 (–2 – 50)	49 (20 – 67)
110–125	52 (33 – 66)	37 (15 – 54)	24 (–9 – 47)	71 (58 – 80)	60 (44 – 71)	27 (–8 – 51)
2-hr postload glucose (mg/dL)						
<154	65 (37 – 81)	30 (–13 – 56)	50 (7 – 74)	79 (62 – 89)	55 (27 – 72)	54 (13 – 76)
154–173	45 (15 – 64)	24 (–12 – 48)	28 (–14 – 55)	67 (49 – 79)	51 (27 – 67)	34 (–7 – 59)
174–199	41 (16 – 59)	19 (–12 – 41)	28 (–3 – 50)	65 (48 – 76)	48 (26 – 63)	34 (–1 – 56)

Data were collected at 27 U.S. medical centers between 1996 and 2001

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Reduction in diabetes incidence was estimated using Cox regression models adjusted for age, race/ethnicity, sex, BMI, fasting plasma glucose, and plasma glucose 2 hours after an oral load when appropriate. All variables but race/ethnicity and sex were treated as continuous in the multivariable regression models.