## A Population Perspective on Diabetes Prevention

Whom should we target for preventing weight gain?

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**OBJECTIVE** — To examine the influence of obesity and prevention of weight gain on the incidence of type 2 diabetes.

**RESEARCH DESIGN AND METHODS** — We examined participants in the San Antonio Heart Study, a prospective population-based study of Mexican Americans and non-Hispanic whites residing in San Antonio, Texas. BMI was stratified into four categories: normal ( $<25 \text{ kg/m}^2$ ), overweight ( $\ge 25 \text{ kg/m}^2$  and  $< 30 \text{ kg/m}^2$ ), obese ( $\ge 30 \text{ kg/m}^2$  and  $< 35 \text{ kg/m}^2$ ), and very obese ( $\ge 35 \text{ kg/m}^2$ ). The number and proportion of incident cases prevented by targeting each BMI category were estimated. In addition, we calculated the decrease in risk of developing type 2 diabetes associated with weight gain prevention across both the BMI and age spectra.

**RESULTS** — Preventing normal individuals from becoming overweight would result in the greatest reduction in incidence of type 2 diabetes. This would result in a 62 and 74% reduction in the incidence of type 2 diabetes in Mexican Americans and non-Hispanic whites, respectively. Preventing the entire population from gaining, on average, 1 BMI unit would result in a reduction in incidence of type 2 diabetes of 12.4 and 13.0% in Mexican Americans and non-Hispanic whites, respectively.

**CONCLUSIONS** — The majority of cases of type 2 diabetes were in individuals who were overweight or mildly obese with a family history of type 2 diabetes. Public health resources should be directed toward the prevention of weight gain among normal and overweight individuals in order to prevent the maximum number of cases of type 2 diabetes.

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he U.S. is in the midst of dual epidemics, one of obesity (1–4) and one of type 2 diabetes (5–8). Obesity is a well-established risk factor for type 2 diabetes (9–13). Although there are other risk factors for type 2 diabetes, it is likely that the epidemic of obesity will be the most important factor for the subsequent rise in the incidence and prevalence of type 2 diabetes. Prevention of type 2 diabetes is an important public

health challenge. Recent results from the Diabetes Prevention Program indicate the effectiveness of lifestyle changes and treatment with metformin on the prevention of type 2 diabetes in all categories of BMI (14). However, it is arguable that such results may not be possible on a population level. The best way to prevent type 2 diabetes may be to prevent individuals from gaining weight in the first place. Thus, it is important to determine the fol-

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Abbreviations: SES, socioeconomic status.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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lowing: 1) Where along the diabetes risk spectrum do most cases of diabetes in a population develop? and 2) Where along the risk spectrum would weight gain prevention have the greatest impact on reducing the incidence of type 2 diabetes? To address these issues, we analyzed data from the San Antonio Heart Study. a population-based study of diabetes and cardiovascular disease in Mexican Americans and non-Hispanic whites residing in San Antonio, Texas. We examined where along the obesity and age spectrum most cases of type 2 diabetes develop. In addition, we examined what effect weight gain prevention would have on the incidence of type 2 diabetes in different parts of the obesity and age spectrum.

## RESEARCH DESIGN AND

**METHODS** — The San Antonio Heart Study is a population-based study of diabetes and cardiovascular disease in Mexican Americans and non-Hispanic whites. The study initially enrolled 3,301 Mexican Americans and 1,857 non-Hispanic white men and nonpregnant women in two phases between 1979 and 1988. Participants were 25-64 years of age at enrollment and were randomly selected from low-income (barrio), middleincome (transitional), and high-income (suburb) neighborhoods in San Antonio, Texas. A 7- to 8-year follow-up to examine the incidence of type 2 diabetes and cardiovascular disease began in 1987 and was completed in the fall of 1996. A total of 3,682 individuals (73.7% of survivors) from the two phases completed the follow-up examination.

The study protocol was approved by the institutional review board at the University of Texas Health Science Center at San Antonio, and all subjects gave informed consent. Descriptions of the survey procedures used have been published previously (15–17). Height, weight, and systolic and diastolic blood pressures (random-zero sphygmomanometer; Hawksley-Gelman, London)

were measured as previously described (18-21). BMI was calculated as weight (kg) divided by height (m) squared and was used as an index of overall adiposity. The ratios of waist-to-hip circumference and subscapular-to-triceps skinfold were used as measures of body fat distribution. Socioeconomic status (SES) was assessed at baseline using the Duncan Socioeconomic Index (22,23). Ethnicity was determined using a previously published algorithm that considers parental surnames and birth places, stated ethnicity of grandparents, and the participant's preferred ethnic identity when that ethnic identity indicated a distinct national origin (24). Family history of type 2 diabetes was assessed via self-report questionnaire responses indicating whether either parent or a sibling had diabetes.

Blood chemistry measurements were made in San Antonio at the Division of Clinical Epidemiology laboratory. Fasting plasma glucose concentration; fasting serum insulin and total, LDL, and HDL cholesterol; and triglyceride concentrations were determined as previously described (25). Glucose and insulin concentrations were also measured 2 h after a standardized 75-g oral glucose load (26).

Subjects were considered to have type 2 diabetes if they met the 1997 American Diabetes Association (27) plasma glucose criteria (fasting glucose value of ≥126 mg/dl or a 2-h postload value of ≥200 mg/dl). Subjects who gave a history of diabetes and who were under treatment with either insulin or oral antidiabetic agents were also considered to have diabetes, regardless of their plasma glucose levels. Diabetic subjects who were not taking insulin were considered to have type 2 diabetes. Those taking insulin were considered to have type 2 diabetes if they had a BMI >27 kg/m<sup>2</sup> and age of onset >30 years. Individuals who did not meet American Diabetes Association criteria at baseline but did meet criteria at follow-up were defined as incident cases.

To examine the influence of overweight and obesity on the incidence of type 2 diabetes, we examined BMI as a categorical and as a continuous variable. BMI was stratified into four categories: normal ( $<25 \text{ kg/m}^2$ ), overweight ( $\geq25 \text{ kg/m}^2$  and  $<30 \text{ kg/m}^2$ ), obese ( $\geq30 \text{ kg/m}^2$  and  $<35 \text{ kg/m}^2$ ), and very obese ( $\geq35 \text{ kg/m}^2$ ) (28). To estimate the number and proportion of incident cases that would be prevented by targeting each

BMI category, we multiplied the number of individuals who were nondiabetic at baseline in a particular BMI category by the incidence rate in the next-lowest BMI category. The difference between this incidence and the actual incidence of type 2 diabetes would be the number of cases that would be prevented if individuals in that BMI category had not gained enough weight to move into the next-highest BMI category. To determine the influence of preventing the entire population from gaining 1 BMI unit, we multiplied the number of individuals at each BMI unit (kg/m<sup>2</sup>) by the incidence rate in the nextlowest BMI unit and then summed the rates. The difference between this incidence and the actual incidence of type 2 diabetes would be the number of cases that would be prevented if all individuals were prevented from gaining enough weight to move to the next-highest BMI

We also examined the effects of age and family history of type 2 diabetes on the effects of weight gain prevention on diabetes incidence. We used logistic regression to estimate the decrease in risk of developing type 2 diabetes associated with prevention of increases in various BMI units. Age, family history, and BMI were included in each model. BMI values were inverse-transformed to more closely approximate a normal distribution and to improve the fit of the model to the data. These analyses were conducted separately for Mexican Americans and non-Hispanic whites.

Statistical analyses were performed using SAS statistical software (29). We used  $\chi^2$  to determine statistical differences in proportions. We used t tests to determine statistical differences in means.

**RESULTS**— A total of 226 of 1,996 Mexican Americans and 69 of 1.232 non-Hispanic whites had developed type 2 diabetes at follow-up (mean 7.5 years). The baseline risk factors for type 2 diabetes, stratified by ethnicity and diabetes incidence status, are presented in Table 1. Among Mexican Americans, individuals who developed type 2 diabetes were older, had a lower SES, and were more likely to live in a barrio neighborhood compared with those who did not develop type 2 diabetes. Those who developed type 2 diabetes also had higher BMI at baseline; weighed more; had higher subscapular-to-tricep skinfold ratio; had

higher fasting glucose, 2-h glucose, fasting insulin, systolic and diastolic blood pressure, and triglycerides; and had lower HDL cholesterol. Among non-Hispanic whites, individuals who developed type 2 diabetes were older and more likely to live in a transitional neighborhood compared with those who did not develop type 2 diabetes (Table 1). Those who developed type 2 diabetes also had higher BMI; were heavier; had a higher subscapular-totricep skinfold ratio; had higher fasting glucose, 2-h glucose, fasting insulin, systolic and diastolic blood pressure, total cholesterol and triglycerides; and had lower HDL cholesterol.

Table 2 presents the incidence of type 2 diabetes, along with the relative risk of developing type 2 diabetes, by BMI category at baseline and stratified by ethnicity. The overall incidence of type 2 diabetes was 11.3% in Mexican Americans and 5.6% in non-Hispanic whites. This difference was seen particularly in individuals with BMI <30 kg/m². The relative risk of BMI category increased as BMI increased.

Table 3 presents the number and percentage decrease in the incidence of type 2 diabetes if individuals in a targeted population, based on BMI category, are prevented from gaining enough weight to be categorized in the next-highest BMI category. In Mexican Americans, preventing individuals from increasing from obese to very obese would result in a 25% reduction in the incidence of type 2 diabetes in that group. This would reduce the overall incidence in Mexican Americans by 5.8%, from 11.3 to 10.6%. Preventing individuals from increasing from overweight to obese would result in a 47% reduction in the incidence of type 2 diabetes in the obese group. This would reduce the overall incidence of type 2 diabetes in Mexican Americans by 14.2%, from 11.3 to 9.5%. Preventing individuals from increasing from normal to overweight would result in a 62% reduction in type 2 diabetes in this group. This would reduce the overall incidence of type 2 diabetes in Mexican Americans by 22.6%, from 11.3 to 8.7%.

In non-Hispanic whites, preventing individuals from increasing from obese to very obese would result in an 11% reduction in incidence of type 2 diabetes in that group (Table 3). This would reduce the overall incidence in non-Hispanic whites by 1.4%, from 5.6 to 5.5%. Preventing

Table 1—Baseline risk factors for incidence of diabetes stratified by ethnicity and diabetes incidence status

	Mexican Americans ( $n = 1,996$ )			Non-Hispanic whites $(n = 1,232)$		
Variables	Diabetic	Nondiabetic	P value	Diabetic	Nondiabetic	P value
Age (years)	47.7	42.0	< 0.001	48.3	44.5	0.007
Sex (% male)	38.0	41.8	0.288	47.8	44.4	0.574
SES*	42.3	46.5	0.009	61.5	61.5	0.995
Neighborhood (%)						
Barrio	54.0	40.8	0.001	_	_	0.017
Transitional	25.7	26.0	0.001	56.5	41.9	0.017
Suburb	20.4	33.1	0.001	43.5	58.1	0.017
BMI (kg/m²)	31.4	27.5	< 0.001	29.8	25.4	< 0.001
Weight (lbs)	178.6	160.1	< 0.001	192.3	161.5	< 0.001
Subscapular-to-tricep ratio	1.44	1.33	0.008	1.39	1.14	0.003
Fasting glucose (mg/dl)	96.8	87.4	< 0.001	100.0	87.5	< 0.001
Fasting insulin (mg/dl)	21.9	13.2	< 0.001	20.7	11.1	< 0.001
2-h glucose (mg/dl)	140.4	106.1	< 0.001	135.8	100.1	< 0.001
Systolic blood pressure (mmHg)	123.2	114.6	< 0.001	122.8	113.2	< 0.001
Diastolic blood pressure (mmHg)	75.0	71.7	< 0.001	75.2	70.3	< 0.001
HDL cholesterol (mg/dl)	44.8	51.8	< 0.001	45.1	55.8	< 0.001
LDL cholesterol (mg/dl)	126.0	123.1	0.244	131.4	123.6	0.083
Total cholesterol (mg/dl)	203.4	201.5	0.502	216.6	203.1	0.009
Triglycerides (mg/dl)	181.8	140.1	< 0.001	221.8	122.2	< 0.001

<sup>\*</sup>Duncan Socioeconomic Index

individuals from increasing from overweight to obese would result in a 61% reduction in incidence of type 2 diabetes in the obese group. This would reduce the overall incidence of type 2 diabetes in non-Hispanic whites by 20.3%, from 5.6 to 4.5%. Preventing individuals from increasing from normal to overweight would result in a 74% reduction in type 2 diabetes in this group. This would reduce the overall incidence of type 2 diabetes in non-Hispanic whites by 29.0%, from 5.5 to 4.0%.

We also examined the number and percentage of type 2 diabetes cases re-

duced if BMI in the entire population is prevented from increasing by 1 BMI unit. For Mexican Americans, the incidence of type 2 diabetes would be reduced by 12.4%, from 11.3 to 9.9%. For non-Hispanic whites, the incidence of type 2 diabetes would be reduced by 13.0%, from 5.6 to 4.9%.

Figure 1 presents the estimated decrease in the risk of developing type 2 diabetes associated with preventing a 1-kg/m² increase in BMI. In Mexican Americans with a family history of type 2 diabetes, the greatest impact would be on those aged ≥55 years and primarily in the

overweight category, where the incidence would be reduced by  $\sim 3\%$ . Similarly, in Mexican Americans without a family history of type 2 diabetes, the greatest effect would be in the same area of the age and BMI spectra, although with a smaller decrease in diabetes incidence. In non-Hispanic whites, with or without a family history of type 2 diabetes, the greatest effect would be in those in the obese category. Again, the effect would be higher in those with a family history, where the incidence would be reduced by 2.5% compared with  $\sim 2\%$  in those without a family history.

Table 2—Incidence of type 2 diabetes and relative risk of developing type 2 diabetes by BMI category and stratified by ethnicity

BMI category (kg/m²)	Number in BMI category	7.5-year incidence (%)	Relative risk	Proportion of population*	Proportion of incident cases†
Mexican Americans					
<25	633	3.8	1.0‡	633/1,996 (31.7)	24/226 (10.6)
$\geq$ 25 to $<$ 30	809	10.1	2.7	809/1,996 (40.5)	82/226 (36.3)
$\geq$ 30 to $<$ 35	352	19.3	5.1	352/1,996 (17.6)	68/226 (30.1)
≥35	202	25.7	6.8	202/1,996 (10.1)	52/226 (23.0)
Non-Hispanic whites					
<25	621	1.6	1.08	621/1,232 (50.4)	10/69 (14.5)
$\geq$ 25 to $<$ 30	420	6.4	4.0	420/1,232 (34.1)	27/69 (39.1)
≥30 to <35	141	16.3	10.1	141/1,232 (11.4)	23/69 (33.3)
≥35	50	18.0	11.2	50/1,232 (4.1)	9/69 (13.0)

Data are n/n (%), unless otherwise noted. \*Number in BMI category/total population by ethnic group; †number of incident cases in BMI category/total incident cases by ethnic group; ‡reference category for Mexican Americans; §reference category for non-Hispanic whites.

Table 3—Number and percentage decrease in incidence of type 2 diabetes if targeted population, based on BMI category, is prevented from increasing to next-highest category

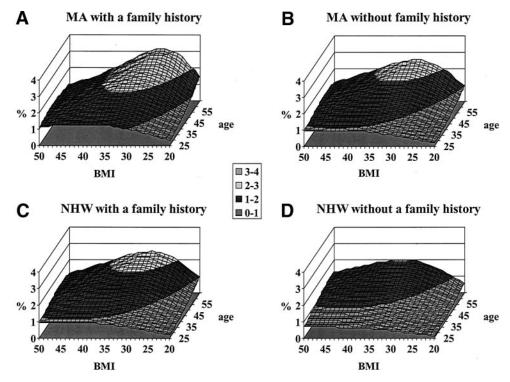
	Percent decrease in incidence of type 2 diabetes according to baseline BMI category	Number of reduced incident cases (proportion of overall incident cases)	Reduced overall incidence rate (from 11.3% in Mexican Americans and 5.6% in non-Hispanic whites)
Mexican Americans			
Obese to very obese*	25	13 (5.8)	10.6
Overweight to obese	47	32 (14.2)	9.5
Normal to overweight	62	51 (22.6)	8.7
Non-Hispanic white			
Obese to very obese*	11	1 (1.4)	5.5
Overweight to obese	61	14 (20.3)	4.5
Normal to overweight	74	20 (29.0)	4.0

Data are % or n (%). \*Very obese  $\geq$  35 kg/m<sup>2</sup>; obese  $\geq$  30 kg/m<sup>2</sup> and < 35 kg/m<sup>2</sup>; overweight  $\geq$  25 kg/m<sup>2</sup> and < 30 kg/m<sup>2</sup>.

**CONCLUSIONS** — Results from the San Antonio Heart Study and other studies indicate the presence of epidemics of both type 2 diabetes and obesity in the U.S. (1,2,5–8). This study examined what part of the overweight-obesity spectrum was most responsible for the diabetes epidemic. This study also examined

the expected decrease in the incidence of type 2 diabetes that would result if prevention of increases in BMI in various areas of the overweight-obesity spectrum had occurred. Finally, this study examined the expected decrease in the incidence of type 2 diabetes after controlling for age and family history of type 2 dia-

betes. Results from this study indicate that most cases of type 2 diabetes result from individuals who are overweight or obese (BMI 25–35 kg/m<sup>2</sup>). In Mexican Americans, targeting those who are normal and preventing them from becoming overweight would be most effective. In non-Hispanic whites, targeting those who



**Figure 1**—Estimated decrease in risk of developing type 2 diabetes over the 7- to 8-year follow-up associated with preventing a  $1\text{-kg/m}^2$  increase in BMI. The model used for each calculation is as follows: estimated incidence rate =  $1/(1+e^{1-0.3068}+0.0454\times age+0.4598\times family \text{ history}+0.4712\times ethnicity}-126.8\times (1/BMI))$  from a logistic regression model fit to San Antonio Heart Study data predicting the incidence of type 2 diabetes, where family history = 1 if the subject reported having a parent or sibling with diabetes and 0 otherwise, and ethnicity = 1 if Mexican Americans and 0 if non-Hispanic white. The figures present the difference between the estimated incidence rate for each combination of values for ethnicity, family history, age, and BMI and the incidence rate for the same combination of values, except that  $1\text{-kg/m}^2$  is subtracted from BMI. A: Mexican Americans with a family history of type 2 diabetes. B: Mexican Americans without a family history of type 2 diabetes. C: Non-Hispanic whites with a family history of type 2 diabetes. D: Non-Hispanic whites without a family history of type 2 diabetes.

are normal or overweight and preventing them from becoming overweight or obese would be most effective. This indicates that targeting type 2 diabetes preventive programs at individuals in these categories would have the most dramatic effect on the overall incidence of type 2 diabetes and would be most beneficial in reducing the burden of type 2 diabetes.

Obesity is a strong risk factor for the development of type 2 diabetes that has been seen in multiple ethnic groups (7,10). It is interesting that in this study, increasing BMI had more of an effect on type 2 diabetes incidence in non-Hispanic whites than Mexican Americans. This is because Mexican Americans were more likely to develop diabetes at a lower BMI compared with non-Hispanic whites. This may be a result of increased insulin resistance in nondiabetic Mexican Americans compared with non-Hispanic whites (30). This may also be a reflection of a differential correlation of BMI and body fat distribution in the two ethnic

The results of this study have strong public health implications. Although targeting subpopulations may be controversial, in an age of limited resources and soaring health care costs, it is important to identify where we can have the most effect in reducing obesity and subsequently the incidence of type 2 diabetes. Based on the results of this study, targeting those individuals who are normal and overweight from becoming overweight and obese, respectively, seems to be most effective in preventing diabetes.

There are a number of assumptions of this study. One is that there is a causal relationship between BMI and diabetes. Based on the large number and consistency of studies, we feel that such a causal relationship has been established. This study is a hypothetical comparison of the incidence of type 2 diabetes in individuals at baseline in the San Antonio Heart Study and the incidence of type 2 diabetes if these same individuals had not gained various amounts of weight before entering this study. We acknowledge that we have not adjusted for confounding factors related to both weight gain and diabetes. Prevention of weight gain would affect such factors as hypertension and cholesterol, which are related to diabetes incidence.

This study also assumes that costeffective weight prevention programs on a population or subpopulation level are feasible. With the difficulty in maintaining weight loss, weight gain prevention may be a more feasible strategy in preventing diabetes. In addition, we have not evaluated the issue of cost in these analyses. Finally, we admit that we did not adjust for other factors such as exercise and diet, for which we did not have reliable data, that may significantly influence these results.

Another limitation of this study was that we have measures of obesity at only two points in time: at baseline and follow-up examinations. It would be more informative to have measures of obesity at multiple time points in order to achieve a more accurate assessment of duration of obesity on type 2 diabetes incidence. This study also examines only 7- to 8-year incidence of diabetes among adults. It may be beneficial to target those at younger ages for several reasons: first, they may be more physically able to maintain current weight or even lose weight; and second, they may have a longer life expectancy in which to develop complications from

Finally, we certainly do not want to lessen the importance of weight loss in all overweight categories. Although from the population perspective, more cases of type 2 diabetes may be prevented by targeting individuals who are overweight or mildly obese, individuals who are very obese may benefit greatly from weight reduction.

We conclude that the majority of cases of type 2 diabetes were from individuals who were overweight or mildly obese and who were not from the upper end of the obesity spectrum. Public health resources should be directed at preventing normal and overweight individuals from becoming overweight and obese in order to prevent the maximum number of type 2 diabetes cases at the population level.

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