Rapid Rise in the Incidence of Type 2 Diabetes From 1987 to 1996

Results From the San Antonio Heart Study

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Background: The prevalence of type 2 diabetes has increased in the early part of the 20th century, particularly in developing countries. There is now evidence that the prevalence also continues to increase in developed countries, including the United States. However, it is unknown whether this increase is due to a rise in the incidence of diabetes or to decreasing diabetic mortality or both.

Methods: Participants in the San Antonio Heart Study, who were nondiabetic at baseline and who returned for a 7- to 8-year follow-up examination, were examined for secular trends in the incidence of type 2 diabetes. Risk factors for diabetes, such as obesity, were also examined. Patients were enrolled in the San Antonio Heart Study from 1979 to 1988 and 7- to 8-year incidence of diabetes was determined from 1987 to 1996.

Results: A significant secular trend in the 7- to 8-year incidence of type 2 diabetes was observed in Mexican Americans (5.7% for participants enrolled in 1979 to 15.7% for participants enrolled in 1988). In non-Hispanic whites, the incidence increased from 2.6% for participants enrolled in 1980 to 9.4% for participants enrolled in 1988 ($P = .07$). After adjusting for age and sex, the secular trend remained significant in Mexican Americans and borderline significant in non-Hispanic whites. This indicates that between 1987 and 1996 the 7- to 8-year incidence of type 2 diabetes approximately tripled in both ethnic groups. The overall secular trend also remained significant after adjusting for additional risk factors for diabetes, such as obesity. A rising secular trend in obesity was also observed.

Conclusions: There has been a significant increasing secular trend in the incidence of type 2 diabetes in Mexican Americans and a borderline significant trend in non-Hispanic whites participating in the San Antonio Heart Study. Unlike other cardiovascular risk factors such as lipid levels, cigarette smoking, and blood pressure, which are either declining or under progressively better medical management and control, and unlike cardiovascular mortality, which is also declining, obesity and type 2 diabetes are exhibiting increasing trends. Thus, obesity and diabetes could easily become the preeminent US public health problem.

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PARTICIPANTS AND METHODS

The San Antonio Heart Study is a population-based study of diabetes and cardiovascular disease in Mexican Americans and non-Hispanic whites. Participants were enrolled in 2 phases between 1979 and 1988 and included Mexican American and non-Hispanic white men and nonpregnant women. The participants were 25 to 64 years of age at enrollment and were randomly selected from low-, middle-, and high-income neighborhoods in San Antonio, Tex. The sampling procedure used was the same in both phases of the study. A 7- to 8-year follow-up to determine the incidence of type 2 diabetes and cardiovascular disease began in October 1987 and was completed in the fall of 1996.

A total of 5158 participants were seen at baseline (3301 Mexican Americans and 1857 non-Hispanic whites). Of these, 2343 Mexican Americans and 1339 non-Hispanic whites returned for follow-up (71.4%). Three hundred forty-eight of the Mexican Americans and 108 of the non-Hispanic whites were either diabetic at baseline, or had unknown diabetes status at either baseline or follow-up, and are therefore excluded from the present analyses. The incidence estimates are thus based on 1995 Mexican Americans and 1231 non-Hispanic whites who were nondiabetic at baseline and whose diabetes status was known at follow-up.

Descriptions of the survey procedures used at the baseline and follow-up examinations have been published previously.8-10 Plasma glucose level was determined after a 12-hour fast and 2 hours after a standard oral glucose load. Fasting serum lipid, lipoprotein, and insulin concentrations, along with blood pressure, height, weight, subscapular and triceps skinfolds, were measured at baseline and follow-up as previously described.10-12 Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Obesity was defined as a BMI of 27 or greater. Socioeconomic status was assessed at baseline using the Duncan Socioeconomic Index.13,14 A higher score indicates a higher socioeconomic level. Chronic disease at baseline was defined as self-reported heart attack, cancer, gallbladder disease, or stroke, or angina based on the Rose questionnaire. Ethnic group was determined using a previously published algorithm that considers parental surnames and birthplaces, stated ethnicity of grandparents, and participant’s preferred ethnic identity when it indicates a distinct national origin.15

Subjects were considered to have type 2 diabetes if they met the 1997 American Diabetes Association plasma glucose criteria (≥7.0 mmol/L [≥126 mg/dL] for fasting glucose and ≥11.1 mmol/L [≥200 mg/dL] for 2-hour glucose).12 Subjects reporting a history of diabetes and receiving treatment with insulin or oral antidiabetic agents were also considered to have diabetes regardless of their plasma glucose levels. Only 10 of the 293 incident cases were diagnosed solely on the basis of taking antidiabetic medication. The remaining 283 met plasma glucose criteria. Subjects with diabetes 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 greater than 27 and age at onset older than 30 years. Impaired glucose tolerance (IGT) was defined according to the 1997 American Diabetes Association criteria (nondiabetic, but with a 2-hour glucose level between 7.8 and 11.0 mmol/L [140-199 mg/dL]) as was impaired fasting glucose (nondiabetic, but with a fasting glucose level between 6.1 and 6.9 mmol/L [110-123 mg/dL]).

Statistical analyses were performed using SAS statistical software (SAS Institute Inc, Cary, NC). The Cochran-Armitage procedure was used to test for significant trends in crude incidence. This procedure tests for trends in binominal proportions across levels of a single factor or covariate and is appropriate for a contingency table where 1 variable has 2 levels and the other variable is ordinal. Secular trends were also assessed using logistic regression analysis with date of enrollment included as an independent risk factor. Odds ratios for the date of enrollment were calculated for intervals of 1 year (365.25 days). For years in which fewer than 40 patients of a given ethnic group were enrolled, the annual diabetes incidence rates are unstable and may not be representative of the incidence in that year and therefore were not presented in the figures. However, since statistical analyses were based on date as a continuous variable in days, all data were used in the logistic regression and Cochran-Armitage statistical analyses. The criterion for both entrance and retention in the logistic regression model was .05.

We were concerned about the possibility that, with the passage of time, people with greater diabetic risk might be increasingly likely to return for follow-up. For example, if individuals with a family history of diabetes were increasingly likely to return for follow-up owing to increased awareness compared with those without a family history, this could have artifactually produced an increasing incidence trend. We therefore examined trends in the ratios of baseline risk factors in those who returned for follow-up vs those who did not return. For continuous variables the ratio of means was examined for trends over time and for dichotomous variables the ratio of proportions was similarly examined. In addition, a logistic regression model was used to predict whether an individual returned for follow-up as a function of whether he or she had a given risk factor. An interaction term between the risk factor and the date of enrollment was used to test whether there was a significant difference in secular trends in risk factors among those who returned and those who did not return for the follow-up examination.

RESULTS

Figure 1 and Figure 2 present the crude 7- to 8-year incidence of type 2 diabetes according to year of enrollment for Mexican Americans and non-Hispanic whites.
A total of 225 Mexican Americans and 68 non-Hispanic whites developed diabetes during the follow-up period. The Cochran-Armitage test for trend was significant for Mexican Americans ($P = .001$) and borderline significant for the non-Hispanic whites ($P = .07$). In Mexican Americans, the 7- to 8-year incidence increased from 5.7% for participants initially enrolled in 1979 to 15.7% for those enrolled in 1988. In non-Hispanic whites, the 7- to 8-year incidence increased from 2.6% for participants initially enrolled in 1980 to 9.4% for those enrolled in 1988.

Figures 1 and 2 reveal a lower incidence of type 2 diabetes in 1987 compared with the preceding and following years for both Mexican Americans and non-Hispanic whites. This is probably because in 1987 only participants from high-income (suburb) neighborhoods were enrolled. As seen in Figure 3, for both ethnic groups neighborhood had a powerful effect on incidence, which was lower in the suburbs compared with the middle-income (transitional) and low-income (barrio) neighborhoods. We therefore controlled for neighborhood effects in subsequent analyses.

Table 1 presents the logistic regression models for the incidence of type 2 diabetes. For the model containing date of enrollment only (model 1), this variable was highly statistically significant ($P < .01$). The odds ratio of 1.08 indicates that on average the odds of developing diabetes for individuals enrolled in a given year was 8% higher than for individuals enrolled in the preceding year. Age, sex, ethnic group, neighborhood, and date of enrollment were forced into all subsequent models (models 2-10), including the stepwise regressions. With these variables included (model 2), the odds ratio for date of enrollment increased to 1.10 and remained statistically sig-
significant. Age, ethnic group, and neighborhood were also significant predictors of diabetes. Body mass index, IGT, impaired fasting glucose, fasting glucose, and 2-hour glucose were all significantly associated with development of diabetes after adjusting for age, sex, ethnic group, and neighborhood. Despite adjustment for this extensive panel of risk factors, date of enrollment remained significantly associated with diabetes incidence and, in fact, its odds ratio tended to increase with adjustment for each risk factor. In particular, even though neighborhood was highly associated with risk of future diabetes, date of enrollment remained a highly significant predictor of diabetes (models 2-10). Stepwise logistic regression was used to determine the best-predicting model for type 2 diabetes.

Since obesity is a strong risk factor for diabetes, a possible explanation for the secular trend in the incidence of type 2 diabetes could be a secular increase in the mean weight of the population. Table 2 presents logistic regression models for obesity (defined as BMI > 27). Date of enrollment was significantly associated with obesity whether entered into the model alone (model 1) or along with age, sex, ethnic group, and neighborhood (model 2). However, the secular trend in obesity does not appear to fully account for the secular trend in diabetes, since, as shown in Table 1, model 3, year of enrollment continued to be significantly predictive of diabetes even after allowing for the effects of BMI.

We were concerned about possible biases that could produce artifactual trends in diabetes incidence. If, for example, there was a difference in diabetes risk factors between those who returned for follow-up and those who did not return, and if this differential changed with time such that subjects with more diabetes risk factors were progressively more likely to return, an artifactual trend could be produced. To address this possibility, we examined the ratio of risk factor levels in returnees and nonreturnees (ratio of means for continuous variables and ratio of proportions for dichotomous variables) (Table 3). With one exception, none of these ratios showed a rising trend, ie, progressively increasing risk among the returnees relative to nonreturnees. For example, although BMI was highly predictive of future diabetes (Table 1), the mean BMI among those who returned relative to those who did not remained constant over time. Similarly, there was no tendency for returnees to become pro-

![Figure 3. Seven- to 8-year incidence of type 2 diabetes by ethnicity and type of neighborhood. P = .001, Mexican American group; P = .01, non-Hispanic white group (χ² test).](image)

Table 1. Odds Ratios for Various Risk Factors for the Development of Type 2 Diabetes Estimated From Logistic Regression Models

<table>
<thead>
<tr>
<th>Variable†</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Stepwise NGT Only</th>
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<tbody>
<tr>
<td>Day of enrollment (365.25) (f)</td>
<td>1.08‡</td>
<td>1.10‡</td>
<td>1.09‡</td>
<td>1.09‡</td>
<td>1.09‡</td>
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<td>1.12‡</td>
<td>1.19‡</td>
<td>1.14‡</td>
<td>1.18‡</td>
<td>1.13‡</td>
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<tr>
<td>Age (10-y interval) (f)</td>
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<td>1.56‡</td>
<td>1.58‡</td>
<td>1.59‡</td>
<td>1.59‡</td>
<td>1.31‡</td>
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<td>0.96</td>
<td>1.01</td>
<td>0.95</td>
<td>0.95</td>
<td>1.03</td>
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<td>0.66‡</td>
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<td>0.95</td>
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<td>Ethnicity (MA vs NHW) (f)</td>
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<td>1.72‡</td>
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<td>2.13‡</td>
<td>1.73‡</td>
<td>1.99‡</td>
<td>1.98‡</td>
<td>1.59‡</td>
<td>2.02‡</td>
<td>1.62‡</td>
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<td>1.93‡</td>
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<td>1.33‡</td>
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<tr>
<td>BMI (5 kg/m²)</td>
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<td>...</td>
<td>1.81‡</td>
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<td>...</td>
<td>...</td>
<td>1.48‡</td>
<td>1.54‡</td>
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<td>Family history</td>
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<td>SES (25 U)</td>
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<td>...</td>
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<td>IGT</td>
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<td>...</td>
<td>7.62‡</td>
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<td>Fasting glucose (0.6 mmol/L [10 mg/dL])</td>
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<td>2-h glucose (1.7 mmol/L [30 mg/dL])</td>
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<tr>
<td>Subscapular/triceps skinfolds ratio</td>
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<td>...</td>
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<td>...</td>
<td>...</td>
<td>0.98</td>
<td>...</td>
</tr>
</tbody>
</table>

* NGT indicates normal glucose tolerance; MA, Mexican American; NHW, non-Hispanic white; M, male; F, female; BMI, body mass index; SES, socioeconomic status; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; NA, not applicable; and ellipses, variable not included in the model.
†† indicates forced into all models.
‡‡ indicates less than .01.
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gressively enriched with individuals who had reported a family history of diabetes at baseline. Only the ratio of IGT in returnees relative to nonreturnees progressively increased over time. We therefore examined the secular trend among those with normal glucose tolerance at baseline (Table 1). A secular trend was still present in those with normal glucose tolerance at baseline. The best-fitting model using stepwise regression, with date of enrollment, age, sex, ethnic group, and neighborhood forced into the model, included elevated BMI, elevated fasting glucose level, and elevated 2-hour glucose level. Thus, even excluding those with IGT, the secular trend remained highly significant.

Our results indicate an increasing secular trend in the 7- to 8-year incidence of type 2 diabetes occurring from 1987 to 1996. The test for trend was highly significant for Mexican Americans (P < .001), while for non-Hispanic whites it was of borderline significance (P = .07). Since the magnitude of the trend was similar in the 2 ethnic groups, the borderline significance in whites may be due to the smaller number of cases in this ethnic group.

As expected, BMI was a significant predictor of type 2 diabetes. Moreover, a significant rising secular trend was also found for BMI. Since several studies have reported a rising rate of obesity in the US population, this is not surprising. However, the secular trend in diabetes incidence remained significant even after allowing for the contribution of BMI in the regression model. This indicates that rising BMI contributes to, but does not totally account for, the secular trend in diabetes incidence. Other factors must therefore have contributed to this trend. However, even though a number of other risk factors were found to contribute significantly to diabetes incidence, the trend remained significant even after controlling for these factors.

Although we examined a number of potential risk factors for this trend, there are factors that we did not assess. Such factors include changes in physical activity and dietary habits. Although it may seem that the likely mechanism by which these factors affect diabetes incidence is by increasing the rate of obesity in a population, it is also possible that these factors could have contributed independent of their association with obesity.

A potential concern was that a changing pattern in diabetic risk factors between those who returned for follow-up and those who did not return might have biased the results. In the analyses of the ratio of risk factors levels such as age, BMI, socioeconomic status, ethnicity, and family history of diabetes, no increase among the returnees relative to the nonreturnees was seen with time. The only increase over time was seen in IGT status. However, after stratifying by IGT status, a secular trend remained in those without IGT. Though it is difficult to account for all potential confounding factors, none of the ones of which we examined could account for the trend.

Declining mortality among cases could cause prevalence to rise even if incidence remained unchanged. Using the NHANES data from 1971-1993, Gu et al. found that diabetic subjects have experienced declines in mortality, although these declines were not as steep as in nondiabetic individuals. Nelson et al. also reported that case-fatality in Pima Indian diabetic subjects has decreased since the 1970s. Thus, a rise in prevalence could be a result of diabetic subjects living longer. However, the rising trend in diabetes incidence that we observed provides evidence that the rise in prevalence is at most only partially due to a decrease in diabetic mortality.

Only a few previous recent studies have examined secular trends in the incidence of type 2 diabetes. Knowler et al. used data acquired from the Arizona Pima Indians in which incidence of diabetes was compared over two 10-year time periods, 1965 to 1975 and 1975 to 1985. Averaged over the 10-year periods, the incidence rates increased by about 50% in most age and sex groups. In our study, the age-, sex-, ethnicity- and neighborhood-adjusted incidence of diabetes approximately tripled in 9 years. Although it is difficult to compare such different populations, it seems that the secular trend was con-

Table 2. Odds Ratios for Obesity (BMI $\geq$ 27 kg/m²) Estimated From Logistic Regression Models*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day of enrollment (365.25 d)</td>
<td>1.05 (1.03-1.07)</td>
</tr>
<tr>
<td>Age (10-y interval)</td>
<td>1.27 (1.21-1.34)</td>
</tr>
<tr>
<td>Sex (M vs F)</td>
<td>1.38 (1.23-1.55)</td>
</tr>
<tr>
<td>Ethnic group (MA vs NHW)</td>
<td>2.41 (2.14-2.72)</td>
</tr>
</tbody>
</table>

* BMI indicates body mass index; CI, confidence interval; MA, Mexican American; NHW, non-Hispanic white; M, male; F, female; and ellipses, variable not included in the model.

Table 3. Ratio of Risk Factors in Participants Who Returned for Follow-up vs Those Who Did Not*

<table>
<thead>
<tr>
<th>Year Enrolled</th>
<th>Age, y</th>
<th>BMI</th>
<th>SES</th>
<th>% MA</th>
<th>% IGT</th>
<th>% With Family History†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>1.02</td>
<td>1.00</td>
<td>1.25</td>
<td>0.94</td>
<td>0.84</td>
<td>1.52</td>
</tr>
<tr>
<td>1980</td>
<td>1.06</td>
<td>0.96</td>
<td>1.05</td>
<td>1.04</td>
<td>0.55</td>
<td>1.02</td>
</tr>
<tr>
<td>1981</td>
<td>1.05</td>
<td>1.00</td>
<td>1.07</td>
<td>1.01</td>
<td>0.78</td>
<td>1.00</td>
</tr>
<tr>
<td>1982</td>
<td>1.08</td>
<td>1.01</td>
<td>1.01</td>
<td>1.02</td>
<td>1.06</td>
<td>0.78</td>
</tr>
<tr>
<td>1984</td>
<td>1.07</td>
<td>1.03</td>
<td>1.02</td>
<td>1.58</td>
<td>0.79</td>
<td>1.92</td>
</tr>
<tr>
<td>1985</td>
<td>1.09</td>
<td>1.03</td>
<td>1.05</td>
<td>0.99</td>
<td>1.28</td>
<td>0.94</td>
</tr>
<tr>
<td>1986</td>
<td>1.16</td>
<td>1.00</td>
<td>0.99</td>
<td>1.00</td>
<td>1.10</td>
<td>0.93</td>
</tr>
<tr>
<td>1987</td>
<td>1.07</td>
<td>1.00</td>
<td>1.00</td>
<td>1.09</td>
<td>1.06</td>
<td>1.09</td>
</tr>
<tr>
<td>1988</td>
<td>1.06</td>
<td>1.01</td>
<td>1.03</td>
<td>0.92</td>
<td>1.43</td>
<td>1.22</td>
</tr>
</tbody>
</table>

* Ratio of means for continuous variables and ratio of proportions for dichotomous variables. BMI indicates body mass index; SES, socioeconomic status; MA, Mexican American; and IGT, impaired glucose tolerance.
† Defined as having a parent or a sibling with type 2 diabetes.
‡ Logistic regression models were created to predict return to follow-up. The predicting variables (independent variables) included year of enrollment, each diabetes risk factor (one at a time), and the interaction between the risk factor and year of enrollment. The statistical significance of the coefficient for the interaction term was used to test for trend.
siderably steeper in our study than in the Pima study. A limitation of the Pima study is the possibility of selective outmigration of Pimas with more admixture of whites, leaving behind those with more Native American admixture. Since white admixture is associated with a decreased risk of diabetes, this may have contributed to an apparent rise in the incidence of diabetes.

A study in Rochester, Minn, used a population-based retrospective design to examine temporal trends in diabetes. All medical records of residents in the Rochester area were reviewed from 1945 to 1989. Cases were defined as those with type 2 diabetes aged 45 or older. Age-adjusted 5-year incidence rates rose 47% for men and 26% for women between 1960-1965 and 1985-1989. Glucose values and case definitions were standardized throughout the study. However, this study only included individuals receiving health care during this period. Thus, increased health care utilization could have contributed to an apparent rise in incidence.

Results from the Morbidity and Mortality Weekly Report showed that between 1980 and 1994 the incidence of self-reported cases of type 2 diabetes increased by 48%. Using data from NHANES, annual incidence increased from 2.5 per 1000 persons in 1980 to 3.7 per 1000 persons in 1994. However, these data were self-reported and included only those receiving medical care during this period.

A study in the Cincinnati, Ohio, area was conducted to determine if there was a rise in the incidence of adolescent non-insulin-dependent diabetes mellitus (type 2) between 1982 and 1995. Study participants were identified as those who received care at the Children's Hospital Medical Center, the only pediatric facility in the Greater Cincinnati area. Thus, the case ascertainment was believed to be complete. Children with insulin-dependent diabetes mellitus (type 1) and maturity-onset diabetes of the young were excluded. The incidence of adolescent type 2 diabetes increased from 0.7 per 100 000 in 1982 to 7.2 per 100 000 in 1994, providing additional evidence of an increasing secular trend in the incidence of type 2 diabetes.

A rising trend in the incidence of diabetes will have a significant impact on public health. The mortality, morbidity, and economic costs of diabetes are all exceptionally high. In addition, the association between diabetes and cardiovascular disease is well established. Cardiovascular disease mortality has been declining nationwide since the 1960s, including Mexican Americans in Texas. However, unlike cardiovascular disease risk factors, such as lipid levels and cigarette smoking, which are either declining or under progressively better medical management and control, our data indicate rising trends for diabetes and obesity. Thus, the rate of decline of cardiovascular disease may be halted or reversed with a rising trend in diabetes and obesity. This indicates the increasing significance of diabetes as a cause of morbidity and mortality and the need for better prevention strategies for diabetes.

Thus, we conclude there has been an increasing secular trend in the incidence of type 2 diabetes in Mexican Americans and non-Hispanic whites participating in the San Antonio Heart Study. There has been much speculation in the literature about an increasing trend in the prevalence of type 2 diabetes. It was unknown, however, whether this trend was due to an increase in the incidence of type 2 diabetes, particularly given that mortality among diabetic subjects is known to be declining. Results from this study support the hypothesis that a rising incidence is the primary cause of the rise in prevalence of type 2 diabetes. Considering the morbidity, mortality, and economic costs caused by this disease, an increase in its incidence has profound public health significance.

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