OBSERVATIONS

What Is the Sensitivity and Specificity of Self-Report for Retinopathy Screening?

A wide range in screening rates for diabetic retinopathy by dilated ophthalmic examination has been reported in studies over the last decade (1–4). Comparisons of these rates should take into account the measure used to assess the condition (i.e., screened versus unscreened). Examples of measures include self-report by the individual, claims data for the service, or medical record abstraction of the desired information. Because goals for improvement of diabetes care (5) are based on studies using these reported rates, the sources of these data must be considered and described. Self-report by an individual relies on memory, correct discernment of a dilated versus undilated exam, and accurate identification of the screening behavior within the time frame in question. Claims data, on the other hand, can overestimate the rate of dilated exams under the code for a comprehensive ophthalmic examination. Furthermore, depending on the patient's health care coverage plan, the retinopathy screening may be a service that does not require a separate claim. Finally, abstraction of medical records may be a sensitive measure for a dilated ophthalmic examination; however, its specificity is dependent on a record system that captures and organizes the medical reports for retrieval and evaluation.

A recently published study by Basch et al. (6) reported that a telephone-based health education intervention was associated with a doubling in the rate of dilated ophthalmic examinations (54.7% screened in the intervention group vs. 27.3% in the standard care group) in a sample of African-American adults with diabetes. The main outcome for that randomized controlled trial was documentation from the medical record of receipt of a dilated eye examination. In addition, staff conducted telephone interviews to ascertain self-report of a dilated eye examination. The cross-classification of documented and self-reported screening status from that study is presented here in order to describe the accuracy (7) of self-report of a dilated eye examination.

Eligibility for the randomized trial specified that participants had not had a dilated eye examination in the previous 14 months. The current standard of diabetes care is for an annual dilated eye examination (8). A total of 280 African-Americans with diabetes from five New York City metropolitan area medical centers consented to be randomized and completed the study. Documentation of a dilated eye examination consisted of medical record abstraction by an auditor masked to group assignment. If in the telephone interview the subject reported having gone to an outside eye care provider and signed a medical release, then a form for provider documentation of the date of the most recent dilated eye examination was obtained. Because the documented outcome from the medical record would have superceded the patients' self-report as the primary outcome for this study, completion of the telephone interview was not a prerequisite for inclusion in the published report. There was no self-report for 32 subjects because of the staff's inability to contact the subjects by telephone, even after repeated attempts. Each of the remaining 248 subjects included in this current report had both self-report and accessible medical record documentation for eye examination status. Inaccessible medical records for seven subjects (three intervention subjects and four control subjects) were conservatively treated as a negative for the dichotomous categories of screened versus unscreened.

The telephone interviewer, masked to group assignment, asked, "When was the last time you had an eye exam in which the pupils were dilated?" Response options were: "less than 1 month," "1–12 months," "13–24 months," "more than 2 years," and "never." We allowed plus or minus 1 month for error in recall. Thus, if a person reported having an exam in the past 1–12 months, and documentation indicated an exam 13 months ago, the self-report was considered verified. Similarly, the self-report was allowed to underestimate the time since last exam.

Rates of self-reported and documented dilated eye examinations for the entire sample ($n = 248$) and for the intervention ($n = 119$) and control ($n = 129$) groups separately are as follows: self-report was 58.5% for total sample, with 75.6 vs. 42.6% for intervention and control groups, respectively; documentation of exam was 44.0% for total sample, with 60.5 and 28.7%, respectively, for intervention and control groups. The apparent overestimation due to self-report was 33% in the total sample (58.5 vs. 44%), 48% in the control group (42.6 vs. 28.7%), and 25% in the intervention group (75.6 vs. 60.5%). The sensitivity of self-report for the total sample was 94.5, with intervention subjects showing greater sensitivity in self-report. Specificity overall was 69.8, with intervention subjects at 55.3 and control subjects at 77.2.

Objective 5-13 of Healthy People 2010 (5) is to increase the proportion of adults with diabetes who have an annual dilated eye examination from a 2000 baseline of 47% to a goal of 75%. The baseline was derived from self-report data. The National Health Interview Survey (NHIS) rate for African-Americans was 43%, which is virtually the same as the self-report data for the sample of African-Americans assigned to the control group, where the overestimation compared with documentation was by 48% (5).

These data indicate that self-report of a dilated ophthalmic exam and the documentation from the medical record or provider confirmatory letter are not in complete agreement. In fact, the intervention group had much less difference between the two measures than the control group. This difference could be because of a greater awareness of what constitutes a dilated eye examination, a result of the telephone-based health education and the brief behavioral counseling to improve retinopathy screening rates. Thus, accuracy of self-report data may be improved with greater patient education about what constitutes a dilated eye examination.

Ascertaining the true condition of screened versus unscreened for each subject was beyond the scope of this study and is a limitation of this report. It is possible that a subject's self-report of having had a dilated eye examination was indeed factual, but medical records were misfiled or incomplete; the great majority (>90%) of subjects in this report, however, re-

ceived eye care from medical centers using a shared medical record for individuals among clinics. There is not an alternative gold standard measure for receipt of a dilated eye examination, absent the observation of the event. However, more advanced databases and electronic medical records should improve the accuracy of documentation in the near future, and this, in turn, will improve the benchmarking for retinopathy screening as a standard of diabetes care.

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Association Between Twin Pregnancy and Hyperglycemia in a Multiethnic Community in New Zealand

Human placental lactogen is higher in twin pregnancies than singleton pregnancies. Theoretically, this should increase insulin resistance and risk for gestational diabetes mellitus (GDM) (1). However, twin pregnancy has been found to be associated with a higher incidence of GDM in some studies (2,3) but not others (4,5). Polynesians have a high incidence of GDM (6), and we have investigated whether, in our multiethnic population, twin pregnancies are associated with a greater risk of GDM.

Locally, a universal screening policy using a nonfasting 50-g glucose challenge test (GCT) at 24–28 weeks is advocated (6), and if the fasting glucose is ≥5.5 mmol/l and/or the 2-h post–oral glucose tolerance test (OGTT) 75-g load is ≥9.0 mmol/l, GDM is diagnosed (7). If a suspicion of GDM occurs (e.g., previous GDM or evidence of macrosomia), then direct referral to OGTT can occur. All women with twin pregnancies are managed within specialist antenatal services. This study was approved as an audit by the hospital management.

The methods have been previously described (6). Data relating to GDM and twin pregnancies were manually extracted from the medical records from all 5,462 deliveries in South Auckland Hospitals with discharges between 1 March 1994 and 28 February 1995. A total of 509 (9.3%) records were not found, and 14 women had known diabetes. Data are shown as the means ± SD for twins versus singletons and are compared using ANOVA. Adjustment for age, weight, and parity was undertaken using ANCOVA. Parity is shown as median (interquartile range) and compared using the Mann-Whitney test. Proportions (*n*) were compared using the χ^2 test (Table 1).

Among the 4,939 deliveries, there were 54 (1.1%) twin pregnancies. There was no ethnic difference in incidence of twin pregnancies (Europeans 1.2% [20/1,643], Maori 0.8% [11/1,308], Pacific Is-

Table 1 —*Screening for GDM by ethnic group*

	Twin pregnancies	Singleton pregnancies	*P*
N	54	4,885	
Age (years)	29 ± 5	27 ± 6	0.012
% European	37.0	33.3	0.277
% Maori	20.4	26.6	
% Pacific Islander	38.9	31.0	
% Other	3.7	9.2	
Parity	2 (1–3)	1 (0–2)	0.007
Weight at booking (kg)	80.0 ± 21.0	74.7 ± 16.9	0.023
% Smokers	35.2	31.2	0.532
Weeks gestation at booking	17 ± 8	16 ± 9	0.718
Weeks gestation at OGTT	28 ± 4 (10)	30 ± 6 (391)	0.214
Weeks gestation at delivery	37 ± 3	40 ± 2	<0.001
% Screened GCT, OGTT	77.8 (42)	50.6 (2,473)	<0.001
First 1-h GCT result (mmol/l)	6.7 ± 1.3	6.0 ± 1.5	0.004
GCT after adjustment for age, weight, and parity	6.6	6.0	0.022
% Screen positive during GCT	17.9 (7)	12.6 (301)	0.319
% GDM on OGTT if screen positive (attended OGTT)	50.0 (2/4)	28.3 (66/233)	0.342
GDM among all women screened	11.9	5.1	0.051

Data are means ± SD, %, median (interquartile range), means ± SD (*n*), % (*n*), and % (*n*/*n*).

landers 1.4% [21/1,534], and others 0.4% [2/454]). No women with a twin pregnancy had a stillbirth. Women with a twin pregnancy were older (29 ± 5 vs. 27 ± 6 years, $P = 0.012$), more parous (2 [1–3] vs. 1 [0–2], $P = 0.007$), and weighed more at booking (80.0 ± 21.0 vs. 74.7 ± 16.9 kg, $P = 0.023$) at the same gestation (17 ± 9 weeks) than those with a singleton pregnancy but were otherwise similar.

Of the 2,515 women screened for GDM, 3 twin and 83 singleton pregnancies had no GCT before the OGTT: the proportion with GDM was similar among those having the OGTT (33.3 vs. 37.3%). Women pregnant with twins were more likely to be screened (77.8% [42] vs. 50.6% [2,473], $P < 0.001$), had a higher 1-h glucose challenge results (6.6 ± 1.3 vs. 6.0 ± 1.5; $P = 0.004$ before age, weight, and parity adjustment and $P = 0.022$ after), and were nonsignificantly more likely to have a positive screen on GCT (17.9% [7] vs. 12.6% [301], $P = 0.319$) and GDM on OGTT after a positive GCT (50.0% [2/4] vs. 28.3% [66/233], $P = 0.342$) than women with a singleton pregnancy, but numbers were small. Overall incidences of GDM were 11.9 and 5.1% ($P = 0.051$).

Our data confirm that twin pregnancies are associated with greater risk of GDM with relative hyperglycemia. Unfortunately, the numbers of women with a twin pregnancy and an OGTT were too few to show a significantly higher incidence of GDM overall. The greater screening for GDM among women with twin pregnancies should have reduced the difference in GDM risk between the two groups, with the likely lower threshold for screening for GDM in these women (although closed unit versus shared care practice could be a further explanation). It was unfortunate that there were insufficient numbers to look at the risk of GDM within ethnic groups, but the groups were well matched for this. These data support the hypothesis that twin pregnancies are more prone to GDM. If so, women with twin pregnancies should be tested for GDM not only at 24–28 weeks but also later on in pregnancy.

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A Case of Fulminant Type 1 Diabetes With Elevated Rheumatoid Factor and the Temporal Presence of Thyroid-Stimulating Hormone Receptor Antibody

Type 1 diabetes is divided into two subtypes: autoimmune and idiopathic diabetes (1). Recently, fulminant type 1 diabetes was identified as a novel subtype of idiopathic diabetes (2). Imagawa et al. (2), who first identified this subtype, hypothesized that the disorder is caused by nonautoimmune mechanisms, including viral infection of exocrine pancreatic tissue. This hypothesis was generated from the negative test results for diabetes-related antibodies in patients with fulminant type 1 diabetes.

Additional pieces of supporting evidence were the absence of hyperexpression of major histocompatibility complex class I molecules in islets and the presence of lymphocyte infiltration in exocrine pancreatic tissue without insulitis in biopsy specimens. Consequently, high serum amylase levels were the primary characteristics of patients with fulminant type 1 diabetes. However, the hypothesis mentioned above has not been universally accepted (3). We report a case of fulminant type 1 diabetes in a patient who had a normal level of serum amylase at the time of diagnosis along with increased rheumatoid factor and thyroid-stimulating hormone (TSH) receptor antibody levels.

A 22-year-old woman was admitted to our hospital with diabetic ketoacidosis. She suffered from a sore throat and headache 7 days before admission. Nausea, vomiting, and slight fever started 2 days before admission. She visited the emergency room with epigastric pain and thirst and was found to have a high glucose level. She was transferred to our hospital the next day for admission.

The patient was comatose when she arrived. Her plasma glucose level was 59.6 mmol/l. Her HbA_{1c} was 5.3%, within normal range. Urinary ketone was strongly positive. Arterial pH was 6.922, and bicarbonate was 1.9 mmol/l. Serum and urinary C-peptide levels were low, 0.24 ng/ml and 5.6 μg/day, respectively. She had no diabetes-related antibodies (GAD antibody, tyrosine phosphatase–like protein [IA-2] antibody, islet cell antibody, or insulin autoantibody). These findings were consistent with the characteristics of fulminant type 1 diabetes.

The patient's serum amylase level was 71 IU/l in the emergency room and 135 IU/l at the time of her admission to our hospital, but it rose to 761 IU/l the next day. The serum levels of other exocrine pancreatic enzymes lipase and trypsin also rose, although the levels of these two enzymes were not measured on the day of admission. These findings suggested that injury to exocrine pancreatic tissue indeed occurred in this subject. However, we considered this injury to be secondary, based on the initially normal amylase level and its subsequent rise.

This patient had HLA-DRB1*0405/*0405, DQA1*0303/*0303, DQB1*0405/*0405, the haplotype associated with type 1 diabetes in Japanese people. Furthermore, her immunological examinations after ad-

Table 1 —*Partial Spearman correlation coefficients of the relation between UAE and carotid IMT in type 2 diabetic and nondiabetic subjects*

Carotid IMT (mm)	UAE (mg/24 h)	*P*
Nondiabetic subjects ($n = 681$)		
Model 1	0.14	<0.001
Model 2	0.04	NS
Model 3	−0.01	NS
Type 2 diabetic subjects ($n = 57$)		
Model 1	0.31	0.02
Model 2	0.37	0.0056
Model 3	0.40	0.0049

Model 1 unadjusted; model 2 adjusted for age and sex; model 3 adjusted for age, sex, diastolic and systolic blood pressure, BMI, current smoking, plasma glucose, and total, LDL, and HDL cholesterol. NS, not significant.

mission showed elevated rheumatoid factor and the temporal presence of TSH receptor antibody. These findings suggested that her disease had the immunogenetic characteristics of an autoimmune disease but not against the endocrine pancreas.

Unlike previous cases of fulminant type 1 diabetes (4), this case was characterized by a late increase in serum amylase level and autoimmune characteristics. Therefore, although fulminant type 1 diabetes has been clinically identified, its etiology remains in question.

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Difference in the Relation Between Urinary Albumin Excretion and Carotid Intima-Media Thickness in Nondiabetic and Type 2 Diabetic Subjects

Microalbuminuria is an indicator of an increased cardiovascular risk in diabetic and nondiabetic populations (1,2). Predominantly based on studies in type 2 diabetic populations, it has been suggested that microalbuminuria is an early indicator of atherosclerosis (3). Whether, in nondiabetic subjects, microalbuminuria is an independent indicator of subclinical atherosclerosis or merely a reflection of the increased prevalence of cardiovascular risk factors remains a matter of debate (4). Therefore, in the present study, we investigated the relation between urinary albumin excretion (UAE) and intima-media thickness (IMT) in both a nondiabetic and a type 2 diabetic population.

Subjects were recruited on the basis of reproducible microalbuminuria (UAE once >10 mg/l in an early morning spot urine and at least once 15–300 mg/24 h in 2 × 24 h urine samples). The IMT was measured at the posterior wall of the left common carotid artery using radio frequency signal analysis obtained by M-mode ultrasonography. Type 2 diabetes was defined as currently using antidiabetic drugs or a fasting plasma glucose exceeding 6.1 mmol/l. A total of 481 men and 257 women with a mean age of 50 years were included. Adjusted for age and sex, UAE was related to diastolic and systolic blood pressure as well as BMI in diabetic ($n = 57$) and nondiabetic subjects ($n = 681$). All relations between UAE and these variables were stronger in the type 2 diabetic population. In both diabetic and nondiabetic subjects, a positive relation was present between UAE and IMT (Table 1). In nondiabetic subjects, this relation could no longer be demonstrated after correction for age, sex, and classical cardiovascular risk indicators. In contrast, in type 2 diabetes patients, the relation between UAE and IMT remained highly significant after risk factor correction.

This study shows that UAE is strongly related to subclinical atherosclerosis (assessed as IMT) in type 2 diabetes patients, whereas in healthy volunteers, the relation between UAE and IMT is predominantly a consequence of a clustering of cardiovascular risk indicators. The latter observation implies that if microalbuminuria proves to be an independent risk indicator for cardiovascular disease in the nondiabetic population, this is due to mechanisms other than enhanced atherosclerosis progression per se.

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Correlation of Serum Leptin Levels With Insulin Sensitivity in Patients With Chronic Hepatitis-C Infection

Diabetes is a less-recognized association of hepatitis-C virus (HCV) infection, although several recent studies provide data linking HCV infection and diabetes (1–5). To investigate whether patients with chronic HCV infection without evidence of cirrhosis have an increased risk of diabetes, we conducted a case-control study in 44 consecutive eligible patients with HCV infection and no clinical or histological evidence of cirrhosis and in 20 control subjects without liver disease who were matched by age, sex, and BMI. All 44 patients with chronic HCV infection had biochemical evidence of ongoing inflamation with elevated alanine aminotransferase activity and histologic confirmation. There was no evidence of decompensated liver disease. No patient received any antiviral, immunomodulatory, or immunosuppressive therapy. Immunoreactive insulin was determined by double-antibody radiomimmunosassay (Coat-a-count; Diagnostic Products, Los Angeles, CA). Serum leptin level was determined by the quantitative sandwich enzyme immunoassay technique (Quantikine R & D Human Leptin Immunoassay Systems). Insulin sensitivity was assessed by homeostasis model assessment (HOMA)-estimated insulin sensitivity with the formula that was defined by Matthews et al. (6).

The fasting serum insulin levels were significiantly elevated in patients with chronic HCV infection compared with control subjects (22.5 ± 7.9 vs. 9.0 ± 2.8, $P < 0.001$). Serum leptin levels were also significiantly elevated in patients with chronic HCV infection compared with control subjects (11.8 ± 4.3 vs. 6.0 ± 3.6, $P < 0.001$). Fasting serum leptin and insulin levels and HOMA-estimated insulin sensitivity were correlated in the whole group. There was a significant positive correlation between serum leptin and insulin ($r = 0.43$, $P <$ 0,001) and between leptin and HOMA-estimated insulin sensitivity ($r = 0.42$, $P <$ 0,01). Mehta et al. (5) reported the analysis of HCV infection and type 2 diabetes in the Third National Health and Nutrition Examination Survey. They reported that patients with HCV infection were more than three times as likely to have type 2 diabetes than those without HCV infection.

In conclusion, our study results suggest that HCV infection may serve as an additional risk factor for the development of type 2 diabetes due to insulin resistance and hyperleptinemia. Investigators from many disciplines will need to prospectively characterize the temporal sequence of HCV infection and type 2 diabetes, define the relationship with serious liver disease, and explicate the biological mechanisms.

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COMMENTS AND RESPONSES

Reduced Insulin Sensitivity in Mexican-Americans From San Antonio With Elevated Incidence of Type 2 Diabetes Compared With Mexicans From Mexico City

The interesting article by Burke et al. (1) in the September issue of *Diabetes Care* reports a higher incidence of type 2 diabetes among low-income Mexican-American residents in San Antonio, Texas, than in a comparable population

from Mexico City, Mexico. This difference was not accounted for by the potential mediating factors examined (BMI; waist circumference; fasting and 2-h post–glucose load insulin and glucose; fasting triglycerides and HDL cholesterol; and percentage of impaired glucose tolerance, impaired fasting glucose, or hypertension).

However, in our opinion, an important consideration is missing: the possible role of reduced insulin sensitivity in the high incidence of type 2 diabetes in San Antonio. Indeed, analysis of the data shown in Table 2 of the paper by Burke et al. indicates that both men and women who were residents in San Antonio had statistically significant higher 2-h glucose and 2-h insulin levels compared with men and women who were residents in Mexico City. The simultaneous increase in insulin and glucose levels suggests the occurrence of reduced insulin sensitivity.

Recently, we published a method that allows the quantitative measurement of insulin sensitivity from the insulin and glucose levels recorded at 0, 1, and 2 h during an oral glucose tolerance test (OGTT), or even (with minimal loss of sensitivity) from data recorded only at 0 and 2 h (2–4). Because the values of insulin and glucose at 0 h (i.e., in the fasting state) and at 2 h during OGTT are given in the article by Burke et al., it was possible for us to calculate insulin sensitivity. Our method is based on the following formula: $ISI(gly) = 2/[(INSp \times GLYp) + 1]$, where ISI(gly) indicates the insulin sensitivity index toward glycemia [our method also allows the measurement of insulin sensitivity toward blood free fatty acids (FFAs), or ISI(ffa)] and INSp and GLYp indicate insulinemic and glycemic areas, respectively, during OGTT for the person studied. Because this test is based on the "areas" during OGTT, it can be indicated as ISI(gly)-a. By using basal levels, instead of areas, we can measure the insulin sensitivity in the basal state, or ISI(gly)-b. Both the basal levels and areas are expressed by taking the "mean normal value" as 1 (i.e., by dividing the observed value by the mean normal value). In normal subjects, ISI(gly) is always ~1, with maximal variations among patients comprised between 0 and 2. ISI(gly), as well as the insulin sensitivity index toward blood FFAs, can be easily calculated through a computer program that is freely downloadable from the following website: http://users.iol.it/francesco.belfiore/index.htm.

Table 1 —*Insulin sensitivity indexes in comparable populations from Mexico City and San Antonio, based on data from Burke et al. (1)*

	Mexico City	San Antonio
Men		
ISI(gly)-b	0.60	0.61
ISI(gly)-a	0.62	0.55
Women		
ISI(gly)-b	0.56	0.59
ISI(gly)-a	0.49	0.41

As just mentioned, to measure insulin sensitivity with our method, the mean normal values of basal levels and areas of insulin and glucose are required. Because Burke et al. did not include a "normal" group in their study, we used as mean normal values for insulin and glucose those values reported in Table 1 of a previous article by the same authors (5); the values were obtained from 870 individuals of both sexes. Note, however, that the use of different mean normal values would equally affect the ISI(gly) values in both groups (Mexico City and San Antonio residents) and therefore would not alter the difference between them. Results of our analysis are shown here in Table 1.

These values of insulin sensitivity obtained with our index are derived from the mean values (and not from individual values) of insulin and glucose reported in Table 1 of the article by Burke et al. (1). Therefore, they cannot be statistically evaluated. However, because the reduced values of ISI(gly)-a that we found in the San Antonio population were derived from the "areas" that showed statistically significant difference between the two populations, these reduced values should be statistically significant. On the other hand, the ISI(gly)-b is derived from basal values of insulin and glucose, which changed in opposite directions in the two populations, thus annulling each others statistical significance.

Thus, because the value of ISI(gly) in normal subjects is always equal to 1, both of the populations studied have reduced insulin sensitivity. However, compared with Mexico City residents, the San Antonio population shows a more pronounced reduction in insulin sensitivity deduced from the areas during OGTT, i.e., during the absorption period (characterized by high insulin and glucose levels), but not in the basal state. This is true for both men and women. This observation, which in turn may depend on several factors, may contribute to explain the different incidence of diabetes between the two populations.

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Insulin Sensitivity Does Not Account for Differences in Type 2 Diabetes Incidence Between San Antonio, Texas and Mexico City, Mexico

We would like to thank Belfiore and Iannello (1) for their interesting questions regarding our study (2). We agree that lower insulin sensitivity in the San Antonio, Texas pop-

Table 1—*Age-adjusted baseline risk factors in Mexico City residents and San Antonio Mexican-Americans*

	Men		Women		
Risk factor	Mexico City (n = 578)	San Antonio (n = 129)	Mexico City (n = 801)	San Antonio (n = 244)	P for main effect of city
ISI-a	1.25*	1.18	1.08*	1.03	0.0101
ISI-b	1.15	1.15	1.10†	1.15	0.2954

*$P < 0.0001$, †$P < 0.01$ for city comparisons within sexes; there were no significant city-sex interactions.

ulation could have contributed to the elevated incidence in this population compared with the Mexico City, Mexico population. Drs. Belfiore and Iannello calculated their insulin sensitivity index using the mean fasting and 2-h insulin values from our study because the raw data were not available to them. To address this question, we calculated the two indexes from the individual fasting and 2-h insulin values. Two indexes were calculated: ISI-a, a measure of insulin sensitivity based on the areas under the oral glucose tolerance test curve and ISI-b, a measure of insulin sensitivity in the basal state. As seen in Table 1, ISI-a was significantly higher in Mexico City, whereas ISI-b was not, thus confirming the calculations of Belfiore and Iannello. As noted by Belfiore and Iannello, these associations, which parallel the fasting and 2-h insulin values in Mexico City, could reflect impaired insulin secretion rather than enhanced insulin sensitivity.

Controlling for either ISI-a or -b did not attenuate the odds ratios reflecting the excess incidence of diabetes in San Antonio (Table 2). Thus, these indexes of insulin sensitivity do not account for the difference in incidence between the two cities. However, because these indexes may not be perfectly correlated with insulin sensitivity measured by a more definitive method, e.g., the euglycemic clamp, we do not dispute that differences in insulin sensitivity may account for part of the incidence difference between the two cities.

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Table 2—*Age-, sex-, and risk factor–adjusted odds of developing type 2 diabetes in San Antonio Mexican-Americans compared with Mexico City residents*

	RR	P	95% CI
San Antonio versus Mexico City	1.84	<0.0001	1.36–2.46
ISI(gly)-a Mexico City (0.50)	0.47	<0.0001	0.39–0.58
San Antonio versus Mexico City	1.86	<0.0001	1.37–2.51
ISI(gly)-b (0.50)	0.50	<0.0001	0.41–0.61
San Antonio versus Mexico City	2.13	<0.0001	1.58–2.87

There were no significant city–risk factor interactions.

On Methods and Materials

Response to Parretti et al.

Parretti et al. (1) were very meticulous in assuring that their subjects had similar demographics and were glucose tolerant, healthy, and of similar gestational age. Of note is their finding of a mean fasting glucose value of 56.2 mg/dl and mean 24-h glucose values of 74.7 mg/dl. These results are substantially lower than those found by previous investigators who reported fasting plasma glucose concentrations between 78 and 80 mg/dl (2–4) and 24-h mean glucose concentrations between 85 and 96 mg/dl (2,5,6). Before one accepts the results of the study by Parretti et al. as representative of those of nondiabetic women in the third trimester, it seems appropriate to question whether differences in methodology might explain these seeming inconsistencies.

The meter (Accutrend α) that was used in their study is calibrated to give results equivalent to whole blood, not plasma glucose. Because the concentration of glucose in plasma is greater than that of red cells, the higher the hematocrit, the higher the plasma glucose corresponding to the same patient's whole-blood glucose concentration (7). For example, assuming a hematocrit of 35%, the plasma glucose equivalent of the fasting and overall daily mean glucose reported in the study were 65.4 and 87.0 mg/dl, respectively. Such a conversion brings the mean glucose concentrations reported by the authors into closer proximity with those reported by others.

In contrast with previous studies, the authors had patients check and report their own glucose level. The protocol required that each subject report a total of 15 blood glucose tests taken around the clock for 1 day every 2 weeks from 28 to 38 weeks. The Accutrend α has a memory capacity for only nine results and cannot be downloaded to a computer. Thus, it seems likely that the patients' results were self reported and not transcribed directly from the meter. Unless the investigators verified these results, either by direct observation or by running duplicate saved samples independently in the laboratory, the credibility of these results may legitimately be called into question.

Hopefully these comments will aid in the interpretation and application of the findings of this unique study.

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Response to Letter by Sacks

The response letter by Sacks (1) in this issue of *Diabetes Care* acknowledges that our study (2) was meticulous, but raises concerns as to the reliability of results, and reminds that hematocrit influences glucose values determined on whole blood. In this respect, some observations can be made.

First, the women involved in our study were absolutely free to leave the glucose profile monitoring program, which indeed was discontinued by a significant proportion of them (10%). This does not imply that the remainders were reliable but lends some credence to the fact that they performed and recorded the appropriate determinations at the right time. In addition, it is true that Accutrend α can only record the last nine values, but this allowed verification of determinations achieved in the night, which no doubt were those more likely to be skipped. Maybe hospitalization, as performed in previous studies, would positively contribute to obtaining precise plasma glucose determinations with reliable written results issued directly from the laboratory, but one may argue that the bias introduced by hospital stay in terms of lifestyle modifications (e.g., lack of physical activity) would in turn have some impact on the reliability of the results; also, the implications of hospitalization, in terms of both social costs and personal restrictions, would most probably limit, to a significant extent, the number of subjects available for such a study. More generally, if reliability of subjects enrolled in a study is questioned, then it would be tempting to suggest the absolute unreliability of many studies published thus far, as well as the fragility of most parameters on which clinical management relies, because it seems very difficult to achieve evidence that subjects enrolled in randomized controlled trials actually take their medications at the expected time with the expected continuity and, as for clinical practice, that pregnant women follow physicians' advice and prescriptions.

Second, the influence of hematocrit on whole-blood glucose determinations is well known, but we believe that this criticism, despite formal correctness, is beside the point. In fact, the conversion in plasma glucose equivalents, assuming a hematocrit of 35%, still shows that glucose concentrations documented in our study are lower than those reported by others, although to a lesser extent. In addition, it is undeniable that glycemic normalization achieved in pregnant diabetic patients is commonly accomplished by following indications provided by capillary blood glucose determinations, without taking into account adjustments for hematocrit. It is important to realize that the aim of our study was to explore third-trimester glucose values in a group of nondiabetic pregnant women, because we felt the striking contrast of treating diabetes in pregnancy in an attempt to normalize glycemia without defining normoglycemia. This paradox could also explain the strange high rate of macrosomia found in some studies, despite apparent glycemic rectification. We contributed to this definition with a study involving 51 women who carefully followed our indications with high compliance; all pregnancies reported in our study were uneventful and had maternal cardiovascular adaptation with consequent changes in hematocrit values. In this context, the fact that capillary blood instead of plasma glucose was determined make the results more clinically useful, because the treatment of diabetic pregnant women is, in most instances, based on fingerstick measurements. For these reasons, we believe that glycemic values reported in our study, appropriately defined as unique, can be regarded as a point of reference.

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Diabetes Care: Interventions in the Community

In the timely review by Renders et al. (1), phoning patients with reminders for follow-up visits is suggested as an intervention of possible value. In the studies quoted, this intervention had not been used in isolation. We recently completed a prospective study looking at the effectiveness of this single intervention in a primary care environment. We hypothesized that having a nurse call patients to remind them of their follow-up visit would be beneficial.

A total of 59 patients diagnosed with type 2 diabetes were recruited between July 1999 and January 2000 while attending outpatient diabetes teaching programs at the University of Alberta Hospitals. A nurse contacted the patients in the test group by telephone at 1, 3, 6, 9, and 12 months after attendance at the Metabolic Center to advise them of the need to attend follow-up visits with their family doctor at those intervals. Patients in the control group were not contacted or reminded of their need for follow-up visits with their physicians, other than a suggested follow-up visit at the time of discharge from the program. There was concern that obtaining information prospectively regarding how often patients in the control group visited their own physicians would undermine the control group. We obtained this information retrospectively. Patients were randomly allocated to either the test or the control group.

Subject characteristics were not significantly different between the two groups at study entry. The mean age in the control and experimental groups was 51.8 ± 12.2 and 54.2 ± 12.4 years, respectively. The duration of diabetes was 6.69 ± 8.5 and 4.21 ± 4.6 years in the control and experimental groups, respectively. In the control and experimental groups, 13.8 and 21.4% required insulin and 48.3 and 42.9% used oral hypoglycemic agents alone, respectively. The primary end point was glucose control as assessed by HbA_{1c}. Data are reported as the means ± SD. Student's *t* test was used for statistical analysis, with a significance level set at $P < 0.05$.

In total, 57 subjects completed the study. Our research nurse was successful in contacting patients in the test group regarding their visit 95% of the time. Despite telephone reminders, only 9 of the 28 test group participants completed follow-up visits with their family physicians at all time points (i.e., 1, 3, 6, 9, and 12 months), a success rate of only 32%. A further seven test group patients completed at least half of the expected follow up visits. A retrospective analysis of the control group subjects' attendance at their family doctor's office (21 of 29 doctor's offices responded to our query) indicated that the frequency of visits was not significantly different from that of the test group.

HbA_{1c} and lipid values were obtained for 85% of study participants at the study end. No significant difference was found between the HbA_{1c} or lipid values of the control and test groups. HbA_{1c} at entry was 7.6 ± 1.8 and 7.6 ± 1.8% for the control and test groups, respectively, and at 1 year, HbA_{1c} was 7.6 ± 1.8 and 7.5 ± 1.6%, respectively. Total cholesterol at entry was 5.16 ± 0.9 and 5.41 ± 1.3 mmol/l for the control and test groups, respectively, and at 1 year, it was 5.14 ± 1.0 and 5.06 ± 1.2 mmol/l, respectively. The relatively good lipid and HbA_{1c} values may have reduced our chance of seeing an effect.

The single intervention of providing telephone reminders did not significantly improve compliance, and there was no measurable improvement in diabetes care. Although it seemed reasonable to expect that reminding patients to see their physicians at recommended intervals would improve diabetic care, the study does not support this assumption. It is clear that more than simple telephone reminders are required.

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Response to Shandro et al.

We read with interest the letter from Shandro et al. (1) in this issue of *Diabetes Care*. In our systematic review, in which we reviewed the effectiveness of interventions targeted at health care professionals and/or the structure of care to improve the management of diabetes in primary care, outpatient, and community settings, only a few of the studies that were included sent reminders to patients for follow-up visits. In these studies, this intervention was usually combined with other interventions. Consequently, the effectiveness of this single intervention was difficult to assess.

The only study in which sending reminders to patients was used as a single intervention was the study carried out by Halbert et al. (2). In that study, the intervention affected process measures only in the short term. Its effectiveness on patient outcomes was not assessed.

The other studies included in the review investigated the effectiveness of multifaceted interventions, and sending reminders to patients for follow-up visits was combined with other professional or organizational interventions, or with patient education. These multifaceted interventions improved the process of care, and if they were combined with patient education or the enhancement of the role of nurses in diabetes care, they also resulted in improvements in patient outcomes.

Shandro et al. conclude in their study that simple telephone reminders are not enough to improve diabetes care. This supports the conclusion of our review that multifaceted interventions that facilitate structured and regular review of patients are effective in improving the process of diabetes care. In studies on the effectiveness of multifaceted interventions, little effort has been made to disentangle the effects of the various components. However, it seems that only

a combination of different elements is effective in improving diabetes care, but which specific combination is the most effective is not clear. The addition of patient education or a nurse to multifaceted interventions aimed at facilitating structured care seems to be of important additional value in improving patient outcomes as well as the process of care (3).

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