Trends in HbA1c Concentrations Among US Adults With Diagnosed Diabetes from 1999 to 2004

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\textbf{Running title:} HbA1c trends

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Glycated hemoglobin (HbA1c) is formed when glucose reacts nonenzymatically with amino acids on hemoglobin. Its concentration represents an integrated measure of glucose concentration during hemoglobin’s lifespan, which is about 2-3 months (1). Because HbA1c concentration predicts the risk for microvascular and macrovascular complications (2,3), it is used in the clinical setting to assess longer term glycemic control among people with diabetes mellitus. Generally, HbA1c concentrations <7% are regarded as acceptable glycemic control (4). About 44% of US adults with diagnosed diabetes had a concentration of HbA1c <7% during 1988-1994 compared with about 36%-37.0% during 1999-2000 (5, 6). More recently, data from the National Committee for Quality Assurance showed steady increases in the percentage of patients receiving annual testing for HbA1c and decreases in the percentage of patients with poor glycemic control from 2000 to 2006 (7). Our objective was to examine trends in glycemic control among US adults with diagnosed diabetes from 1999 to 2004 using nationally representative samples.

RESEARCH DESIGN AND METHODS
The National Health and Nutrition Examination Survey (NHANES) 1999-2004 included nationally representative samples of the noninstitutionalized, civilian US population selected using a multistage, stratified sampling design (8). Participants were asked “Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?” In addition, to answering “yes” or “no”, participants could report having “borderline” diabetes. Persons with borderline diabetes were excluded from further analysis.

Concentrations of glycated hemoglobin, measured as %HbA1c, were determined by using boronate affinity high-performance liquid chromatography on Primus CLC330 and Primus CLC385 instruments (Primus Corporation, Kansas City, MO). Interassay coefficients of variation were <3% (9). All measurements were performed at the Diabetes Diagnostic Laboratory at the University of Missouri-Columbia. The method was standardized to the reference method of the Diabetes Control and Complication Trial. A plot of the mean concentrations of two levels of HbA1c controls from 1999 to 2004 shows no evidence of drift. Analyses, done by using SUDAAN to account for the complex sampling design, were limited to participants aged >=20 years who attended the mobile examination center. Prevalence ratios were estimated using log-binomial regression analysis (10).

RESULTS
A total of 1334 participants with diagnosed diabetes had a measurement of HbA1c. The percentage of participants with diagnosed or undiagnosed diabetes whose diabetes had been diagnosed was 70.2% in 1999-2000, 66.9% in 2001-2002, and 73.0% in 2003-2004. The mean age and sex and racial or ethnic composition of the samples were similar for the three 2-year cycles.

In 2003-2004, the geometric mean concentration of HbA1c was significantly lower than in 1999-2000 (Table 1). The unadjusted percentage of participants with diagnosed diabetes who had a concentration of HbA1c <7% increased significantly from 37.0% (95% CI: 28.4, 45.7) in 1999-2000 to 56.8% (95% CI: 49.6, 64.0) in 2003-2004 (Table 1). These percentages were little affected by adjustment for age, sex, ethnicity, educational status, smoking status, hypertension, concentrations of total cholesterol, body mass index, waist circumference, treatment (no oral glucose-lowering medications or insulin, oral glucose-
lowering medications only, insulin only, both), and duration of diabetes in logistic regression (1160 participants with complete data). Compared with participants from NHANES 1999-2000, the adjusted prevalence ratios for having a concentration of HbA1c <7% were 1.32 (95% confidence interval [CI]: 0.98, 1.79) for participants from NHANES 2001-2002 and 1.46 (95% CI: 1.08, 1.97) for participants from NHANES 2003-2004 (p for linear trend = 0.010). The trends did not differ significantly between men and women.

Improvements in HbA1c were steadiest among whites but occurred primarily from 1999-2000 to 2001-2002 among African Americans and Mexican Americans. Despite these apparent differences, no significant differences in trends among the ethnic groups were found possibly due to limited statistical power. For the entire 6-year period, glycemic control was similar in men and women (p=0.235). However, white participants exhibited better control than African American (p=0.001) or Mexican American participants (p<0.001).

CONCLUSIONS

Although glycemic control as determined by a concentration of HbA1c <7% did not change significantly from 1988-1994 to 1999-2000 (5,6), it is encouraging that a significant improvement appears to have occurred from 1999-2000 to 2003-2004. After controlling for factors known to be associated with HbA1c (11-14), we still found a substantial increase in glycemic control suggesting that other factors must have been at work during the study period. A trend towards earlier detection of diabetes could have explained the improvement in glycemic control. However, we did not find evidence of such a trend during the study period. Therefore, it is conceivable that the concerted efforts of professional organizations and clinicians at improving glycemic control are bearing fruit. A variety of approaches can improve glycemic control (15-20). Learning whether these approaches or other factors may have positively impacted the recent trends in glycemic control could provide important lessons for effecting further improvements in glycemic control in the future.

Significant ethnic disparities in glycemic control were noted and are consistent with previously findings (21). The disparity in glycemic control stands in contrast to the results from some studies that showed no or little ethnic difference in annual testing for HbA1c (22,23).

Some limitations should be considered. We were unable to provide separate estimates of glycemic control for type 1 and type 2 diabetes. Sample sizes were inadequate to provide detailed estimates when the sociodemographic variables were considered simultaneously.

In conclusion, our results are consistent with other data suggesting that improvements in glycemic control have occurred among patients with diabetes in the United States. As welcome as the recent favorable trends in glycemic control are, additional efforts are needed to help the approximately 40% of patients with diabetes who do not have adequate glycemic control.
REFERENCES

HbA1c trends


Table 1—Unadjusted percentage of a HbA1c concentration <7% and unadjusted geometric mean concentration of HbA1c among US adults with diagnosed diabetes aged ≥20 years

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>HbA1c concentration &lt;7%</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N*</td>
<td>% (SE)†</td>
<td>N*</td>
<td>% (SE)†</td>
<td>N*</td>
<td>% (SE)†</td>
</tr>
<tr>
<td>Total</td>
<td>404</td>
<td>37.0 (4.3)</td>
<td>446</td>
<td>49.7 (3.6)</td>
<td>484</td>
</tr>
<tr>
<td>Men</td>
<td>203</td>
<td>37.0 (4.6)</td>
<td>224</td>
<td>46.6 (4.4)</td>
<td>244</td>
</tr>
<tr>
<td>Women</td>
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<td>37.0 (5.9)</td>
<td>222</td>
<td>52.7 (4.2)</td>
<td>240</td>
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<tr>
<td>White§</td>
<td>120</td>
<td>41.8 (6.5)</td>
<td>188</td>
<td>53.6 (4.2)</td>
<td>218</td>
</tr>
<tr>
<td>African American</td>
<td>110</td>
<td>28.1 (4.1)</td>
<td>101</td>
<td>44.2 (4.2)</td>
<td>104</td>
</tr>
<tr>
<td>Mexican American</td>
<td>132</td>
<td>28.9 (4.4)</td>
<td>118</td>
<td>42.4 (3.1)</td>
<td>138</td>
</tr>
<tr>
<td><strong>Geometric mean HbA1c concentration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N*</td>
<td>Geometric mean (SE)†</td>
<td>N*</td>
<td>Geometric mean (SE)†</td>
<td>N*</td>
<td>Geometric mean (SE)†</td>
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<td>Total</td>
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<td>7.60 (0.15)</td>
<td>446</td>
<td>7.24 (0.14)</td>
<td>484</td>
</tr>
<tr>
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<td>7.56 (0.13)</td>
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<td>7.37 (0.19)</td>
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<td>7.12 (0.14)</td>
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<td>White§</td>
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<td>7.34 (0.21)</td>
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<tr>
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<td>7.97 (0.18)</td>
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<td>7.95 (0.21)</td>
<td>118</td>
<td>7.62 (0.14)</td>
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</table>

NHANES = National Health and Nutrition Examination Survey.
*Unweighted sample size.
†Weighted percentage or mean.
‡P for linear trend determined from linear contrasts generated from orthogonal polynomial coefficients.
Results for race or ethnicity designation “other” not shown because of small sample size.

Interactions tested in log-binomial regression models for dichotomized concentration of HbA1c and linear regression model for log-transformed HbA1c.