Moving to an A1C-Based Diagnosis of Diabetes Has a Different Impact on Prevalence in Different Ethnic Groups

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OBJECTIVE — To compare screen-detected diabetes prevalence and the degree of diagnostic agreement by ethnicity with the current oral glucose tolerance test (OGTT)-based and newly proposed A1C-based diagnostic criteria.

RESEARCH DESIGN AND METHODS — Six studies (1999–2009) from Denmark, the U.K., Australia, Greenland, Kenya, and India were tested for the probability of an A1C ≥6.5% among diabetic case subjects based on an OGTT. The difference in probability between centers was analyzed by logistic regression adjusting for relevant confounders.

RESULTS — Diabetes prevalence was lower with the A1C-based diagnostic criteria in four of six studies. The probability of an A1C ≥6.5% among OGTT-diagnosed case subjects ranged widely (17.0–78.0%) by study center. Differences in diagnostic agreement between ethnic subgroups in the U.K. study were of the same magnitude as between-country comparisons.

CONCLUSIONS — A shift to an A1C-based diagnosis for diabetes will have substantially different consequences for diabetes prevalence across ethnic groups and populations.

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Recently, an international expert committee report recommended a shift in the diagnostic tool for diabetes from the 75-g oral glucose tolerance test (OGTT) to A1C (1), thereby proposing replacement of the current World Health Organization (WHO) criteria (2). More specifically, an A1C threshold of ≥6.5% was recommended, as this value has been shown to be strongly related to retinopathy (1). In their report, the international expert committee emphasizes that it is premature to establish separate diagnostic thresholds based on race/ethnicity and that the new diagnostic criterion is likely to identify different individuals than those identified by the WHO criteria (1). Previous studies have shown A1C levels in individuals with impaired glucose tolerance or diabetes to differ by race and ethnicity (3–5). We aimed to compare diabetes prevalence and the degree of diagnostic agreement between the OGTT- and A1C-based definitions by race/ethnicity in six different countries. Below, the term diabetes is referring to diabetes assessed by one OGTT or one A1C at screening.

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RESEARCH DESIGN AND METHODS

— Six studies including populations from different ethnic origins were included in the analysis (6–11). Populations from Denmark (Inter99 study), the U.K. (Whitehall II study, phase 7), Australia (The Australian Diabetes, Obesity and Lifestyle Study [AusDiab]), Greenland (Inuit Health in Transition Study), Kenya, and India (Chennai Urban Rural Epidemiology Study [CURES]) were included.

Data were collected during the period 1999–2009. Participants were excluded if they had missing OGTT or A1C measurements or known diabetes (self-reported). In the Inter99 study, 5.6% were not of Danish nationality and were excluded from the analyses. In the Whitehall II study, whites were included in the main analysis, whereas south Asian (4.2%) and black (1.9%) participants were analyzed in a subsidiary analysis. In the AusDiab study, only individuals born in Australia or New Zealand who spoke English at home and were not of Aboriginal/Torres Strait Islander origin were included (76.2%). In the Inuit Health in Transition Study, only Inuit participants were included in the analysis (95.5%). The participants in the study from Kenya were all black, and participants in the CURES study were all of Indian origin. A total of 23,094 participants were included in this analysis.

Participants were categorized into four groups based on their OGTT results (diabetes or no diabetes) and A1C levels (<6.5% or ≥6.5%). Exact 95% CIs were calculated for proportions (12). The probability of an A1C ≥6.5% among diabetic case subjects based on an OGTT was calculated. This probability is effectively the sensitivity of an A1C cut point of 6.5% with the WHO criteria as the gold standard. The magnitude of the difference in probability between centers was analyzed using logistic regression analysis adjusted for relevant confounders (age, sex, BMI, waist circumference, and smoking). A1C assays were aligned to the Diabetes Control and Complications Trial assay at each study center according to local labora-

Table 1—*Background characteristics and diabetes prevalence by OGTT and A1C diagnostic criteria in different ethnic groups*

	Denmark	U.K.	Australia	Greenland	Kenya	India
	Inter99	Whitehall II (phase 7)	AusDiab	Inuit Health in Transition		CURES
Study period	1999–2001	2002–2004	1999–2000	2005–2009	2005–2006	2001–2004
n	5,932	4,563	7,800	2,321	296	2,182
Age (years)	46.2 ± 7.9	60.5 ± 5.9	50.9 ± 14.4	44.1 ± 14.6	37.6 ± 10.6	38.8 ± 12.6
Male subjects (%)	49.7 (48.4–51.0)	73.9 (72.6–75.2)	44.4 (43.3–45.5)	43.4 (41.4–45.5)	44.6 (38.8–50.5)	46.0 (43.9–48.1)
BMI (kg/m^2)	26.2 ± 4.5	26.5 ± 4.2	26.9 ± 4.9	26.4 ± 5.1	22.1 ± 4.6	23.0 ± 4.0
Waist circumference (cm)	86.5 ± 13.2	93.2 ± 12.0	90.6 ± 13.8	91.9 ± 13.3	79.9 ± 12.2	83.0 ± 11.4
Current smoker (%)	36.0 (34.8–37.2)	6.8 (6.1–7.6)	16.3 (15.5–17.2)	66.1 (64.1–68.0)	10.5 (7.3–14.6)	18.6 (17.0–20.3)
Fasting plasma glucose (mmol/l)	5.5 ± 0.8	5.3 ± 0.7	5.4 ± 0.7	5.7 ± 0.8	4.5 ± 0.9	5.1 ± 1.7
2-h plasma glucose (mmol/l)	6.2 ± 2.1	6.5 ± 2.0	6.2 ± 2.2	5.9 ± 2.4	5.6 ± 1.7	7.0 ± 3.5
A1C (%)	5.8 ± 0.5	5.2 ± 0.5	5.1 ± 0.4	5.7 ± 0.4	5.0 ± 0.6	5.9 ± 1.2
Diabetes by OGTT (%)	4.2 (3.7–4.8)	3.7 (3.2–4.3)	4.0 (3.6–4.4)	7.0 (6.0–8.1)	3.4 (1.6–6.1)	10.2 (9.0–11.6)
Diabetes by A1C (%)	6.7 (6.1–7.3)	1.0 (0.7–1.3)	0.7 (0.5–0.9)	3.9 (3.1–4.7)	1.4 (0.4–3.4)	12.9 (11.5–14.4)
A1C ≥6.5% given diabetes by OGTT (%)	42.6 (36.4–49)	25.0 (18.7–32.3)	17.0 (13.0–21.7)	29.6 (22.7–37.3)	20.0 (2.5–55.6)	78.0 (72.0–83.3)
Diabetes by OGTT given A1C ≥6.5% (%)	27.0 (22.7–31.7)	91.3 (79.2–97.6)	98.1 (90.1–100)	53.3 (42.5–63.9)	50.0 (6.8–93.2)	61.9 (56.0–67.6)

Data are means ± SD and proportions (95% CI). Diabetes by OGTT: fasting plasma glucose ≥7.0 mmol/l or 2-h plasma glucose ≥11.1 mmol/l. Diabetes by A1C: A1C ≥6.5%.

tory guidelines (assay details in the online appendix at http://care.diabetesjournals.org/cgi/content/full/dc09-1843/DC1).

RESULTS — The prevalence of diabetes was lower in four of six studies (Whitehall II, AusDiab, Inuit Health in Transition, and Kenya) with the A1C diagnostic criterion than with the OGTT (Table 1). The probability of a person having an A1C ≥6.5% given the presence of diabetes according to the OGTT differed by study center (range 17.0–78.0%). Overall, the magnitude of this difference between centers was independent of differences in age and sex distributions. Further adjustment for BMI, waist circumference, and smoking reduced the magnitude of the difference between some centers, but the overall difference remained significant ($P < 0.0001$). Pairwise comparisons between centers on this difference in probability were significant. Exceptions were the contrasts between Whitehall II and Greenland, and the comparisons between Kenya on the one hand and Inter99, Whitehall II, AusDiab, and Greenland on the other. These results did not change when adjusting for age, sex, BMI, waist circumference, and smoking.

We also performed a subsidiary analysis on the south Asian ($n = 204$) and black ($n = 91$) minority groups in the Whitehall II study. The differences in agreement between the two diagnostic criteria for diabetes between these ethnic subgroups within Whitehall matched those observed between populations in the main analysis (online appendix). Disregarding differences in study size, the overall prevalence of diabetes was 18% lower with an A1C-based diagnostic test for diabetes. The corresponding probability of A1C ≥6.5% among diabetic case subjects based on an OGTT was 43.5%.

CONCLUSIONS — The diabetes prevalence was more likely to be lower than higher when replacing the OGTT diagnostic criteria with A1C. The rate was 63% higher in the Inter99 study, while it was 82% lower in the AusDiab study. These differences are quite substantial and may in part be due to methodological differences.

There was also a significant discrepancy in the magnitude of the OGTT and A1C diabetes diagnosis overlap between study populations of different ethnic origins, even after adjusting for age, sex, BMI, waist circumference, and smoking. However, the differences between the white populations of Inter99, Whitehall II, and AusDiab were also significant and of the same magnitude, suggesting that part of the discrepancy in overlap can be ascribed to difference in study methodology such as the A1C assay method. On the other hand, the subsidiary analysis of the south Asian and black minorities compared with the white majority group of Whitehall II indicates that discrepancies are at least partly due to ethnic differences.

The lack of a significant difference in the pairwise comparisons between the Kenyan population and four of five other studies does not rule out a true difference in the probability of A1C ≥6.5% among OGTT-diagnosed diabetic case subjects but may be due to the limited number of individuals in the Kenyan data.

Although we cannot dismiss the possibility that part of the observed diagnostic inconsistency is due to methodological differences between studies, we can conclude that the proposed shift to A1C as the diagnostic tool for diabetes is likely to have a substantially different impact on diabetes prevalence in different populations, partly due to differences in race/ethnicity. However, future analyses on ethnic differences between studies using the same methodology are needed.

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