American Diabetes Association Diabetes Diagnostic Criteria, Advancing Age, and Cardiovascular Disease Risk Profiles

Results from the Third National Health and Nutrition Examination Survey

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OBJECTIVE — To evaluate age-specific effects on diabetes prevalence estimates resulting from the American Diabetes Association (ADA) recommendation against use of the oral glucose tolerance test (OGTT), we contrasted the prevalence of two mutually exclusive groups: undiagnosed diabetes according to ADA criteria (no report of diabetes and fasting glucose [FG] ≥126 mg/dl) and isolated postchallenge hyperglycemia (IPH) (FG <126 mg/dl and OGTT ≥200 mg/dl), a group designated to have diabetes by World Health Organization (WHO) criteria but not ADA criteria.

RESEARCH DESIGN AND METHODS — The weighted age-specific ratios of undiagnosed diabetes:IPH were calculated for 2,844 subjects aged 40–74 years without reported diabetes who had both FG and OGTT. A ratio >1.0 indicated that the proportion of undiagnosed diabetes was greater than that of IPH. Mean levels of HbA_{1c} and cardiovascular disease (CVD) risk factors were contrasted among people with undiagnosed diabetes and IPH and those without either abnormality ("nondiabetic").

RESULTS — Both undiagnosed diabetes and IPH increased with age, but age-specific undiagnosed diabetes:IPH ratios decreased from 5.49 in the 40–44 age-group to 0.77 in the 70–74 age-group. Regression analysis showed a significant ($P = 0.006$) negative association between age and these ratios. Mean HbA_{1c} was 7.1% in the undiagnosed diabetes group and differed significantly from that of the IPH and nondiabetic groups (5.6 and 5.3%, respectively). Individuals with undiagnosed diabetes had less favorable triglycerides, BMI, and HDL cholesterol compared with people with IPH.

CONCLUSIONS — Compared with WHO criteria, the ADA criteria underestimate glucose abnormalities more with increasing age. However, compared to those with undiagnosed diabetes, individuals with IPH had a mean HbA_{1c} level that is considered in the nondiabetic range, and this group had significantly more favorable levels of several key CVD risk factors. These findings suggest that the ADA criteria, although underestimating the abnormalities of postchallenge hyperglycemia that occur frequently with increasing age, appear to be effective at identifying a group of individuals with both unfavorable CVD risk factor profiles and evidence of long-term exposure to hyperglycemia.

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Abbreviations: ADA, American Diabetes Association; CVD, cardiovascular disease; FG, fasting glucose; IFG, impaired fasting glucose; IPH, isolated postchallenge hyperglycemia; NHANES III, Third National Health and Nutrition Examination Survey; OGTT, oral glucose tolerance test; TG, triglycerides; WHO, World Health Organization.

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

In 1997, the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus of the American Diabetes Association (ADA) recommended changes to the criteria for diagnosing diabetes (1). These changes included a reduction in the fasting glucose (FG) threshold that is diagnostic of diabetes from 140 to 126 mg/dl and a recommendation against use of the oral glucose tolerance test (OGTT) to ascertain undiagnosed diabetes. The Expert Committee recommended that ADA criteria replace the previously accepted World Health Organization (WHO) criteria, which call for use of the OGTT (2), and that the ADA criteria be used both clinically as well as in epidemiologic studies.

In the same report, the Expert Committee showed that the prevalence of undiagnosed diabetes in U.S. adults aged 40–74 years was reduced from 6.34% under WHO criteria to 4.35% under the ADA criteria. However, the Expert Committee did not address two important issues: *1)* whether the decrease in the prevalence of undiagnosed diabetes under the ADA criteria was similar across all age-groups, and *2)* if levels of HbA_{1c} and cardiovascular disease (CVD) risk factors were similar in people with FG ≥126 mg/dl (undiagnosed diabetes by ADA criteria) and those with isolated postchallenge hyperglycemia (IPH) (FG <126 and OGTT ≥200). The latter group would have been considered diabetic by both the 1985 WHO criteria (2) as well as revised provisional criteria published by a WHO consultation group in 1998 (3). The IPH group is not considered diabetic by ADA criteria.

For this article, "isolated postchallenge hyperglycemia" is solely a descriptive term used to define a group of individuals with a combination of fasting and postchallenge glucose values whose prevalence, HbA_{1c}, and CVD risk factor profiles are important to evaluate in light of the ADA criteria, which rely on FG only.

Table 1—*Frequency of ADA diabetes, isolated postchallenge hyperglycemia, and nondiabetic individuals, NHANES III, 1988–1994*

Age-group (years)	ADA diabetes*		IPH†		Nondiabetic‡		Age-specific ratio of ADA diabetes:IPH and 95% CI	
	n§	%¶	*n*§	%¶	*n*§	%¶		
40–44	21	1.92	3	0.35	551	97.93	5.49	0, 11.92
45–49	22	3.85	11	0.84	355	95.31	4.58	0, 10.09
50–54	21	4.14	13	2.14	331	93.72	1.93	0.20, 3.66
55–59	24	6.35	16	3.77	293	89.88	1.68	0.21, 3.15
60–64	37	7.96	29	7.60	383	84.44	1.05	0.44, 1.64
65–69	28	5.16	22	4.00	321	90.84	1.29	0.18, 2.40
70–74	26	6.99	31	9.05	306	83.96	0.77	0.27, 1.27
Total	179	4.73	125	3.27	2,540	92.00	1.44	1.00, 1.88

Data are means. *Fasting glucose ≥126 mg/dl, †fasting glucose <126 mg/dl and postchallenge glucose ≥200 mg/dl, ‡fasting glucose <126 mg/dl and postchallenge glucose <200 mg/dl, §unweighted, ¶weighted age-specific prevalence.

RESEARCH DESIGN AND METHODS

The Third National Health and Nutrition Examination Survey (NHANES III) was conducted from 1988 to 1994 and included a home interview followed by a physical examination conducted in a mobile examination center (4). Fasting plasma glucose values were obtained from subjects who were examined in the morning, and an OGTT was performed on a subset of subjects aged 40–74 years who did not report diabetes during the home interview. Data on HbA_{1c} and a number of established CVD risk factors were also collected from these fasting subjects. These data included serum total cholesterol, HDL and LDL cholesterol, serum triglycerides (TG), and BMI. Criteria for selection of the 2,844 subjects aged 40–74 years with both FG and OGTT values have been reported in detail, as have laboratory protocols for collection of anthropometric measures and for processing of blood (5,6). In brief, venous whole blood was collected into a vacuum tube containing the glycolytic inhibitors potassium oxalate and sodium fluoride and was centrifuged immediately at 1,500*g* for 10 min. The plasma was frozen at −70°C, shipped on dry ice to the University of Missouri Diabetes Diagnostic Laboratory, and stored at −70°C until analysis. Plasma glucose was measured using a modified hexokinase enzymatic method. Both within-assay and between-assay quality-control procedures were used; the coefficient of variation of the method was 1.6–3.7% during the 6 years of the study (6).

Age-specific prevalence of undiagnosed diabetes (FG ≥126 mg/dl) and IPH (FG <126 mg/dl and OGTT ≥200 mg/dl) were calculated. For the purposes of this analysis, the term "glucose abnormality" refers to either FG ≥126 mg/dl or OGTT ≥200 mg/dl, and the term "nondiabetic" refers to individuals with FG <126 mg/dl and postchallenge glucose <200 mg/dl. Age-specific ratios and 95% CIs (7) contrasting undiagnosed diabetes and IPH (undiagnosed diabetes:IPH ratio) were calculated to determine if these ratios were consistent across age and if they were significantly different from unity. Consistent values for this ratio across age would indicate that the overall decrease in prevalence of undiagnosed diabetes reported by the Expert Committee occurred with similar frequency across age. Whether the ratio values differ from 1.0 is an indication of the frequency with which undiagnosed diabetes was present relative to IPH. Thus, a ratio value >1.0 indicates that undiagnosed diabetes occurred more frequently than IPH, a ratio ~1.0 indicates that the two are about equally represented, and a ratio <1.0 indicates that IPH occurs more frequently than undiagnosed diabetes. Regression analysis was used to test whether age (in 5-year intervals with 40–44 as the reference) significantly predicted the magnitude of these ratios.

HbA_{1c} and CVD risk factors were examined among individuals with undiagnosed diabetes and IPH and the nondiabetic group. Because NHANES III is based on a complex sampling design, SUDAAN (8) software was used to incorporate sampling weights into statistical analyses.

RESULTS

Table 1 shows the unweighted age-specific number of individuals with undiagnosed diabetes and IPH and nondiabetic individuals, as well as weighted age-specific U.S. prevalence estimates of these groups. A total of 179 people had undiagnosed diabetes, and 125 had IPH. IPH occurred infrequently in the younger age-groups, with a total of only 14 cases before age 50. Among adults aged 40–74, the overall prevalence of undiagnosed diabetes according to ADA criteria is 4.73%, and the prevalence of IPH in U.S. adults is 3.27%.

The prevalence of both undiagnosed diabetes and IPH increases with age. At younger ages, the ADA criteria appeared to identify most glucose abnormalities: that is, younger individuals rarely had IPH. For example, although 1.92% of subjects aged 40–44 had undiagnosed diabetes, only 0.35% had IPH. However, as age increased, the prevalence of IPH increased faster than undiagnosed diabetes such that the separate prevalence of undiagnosed diabetes and IPH converged and then crossed in older age. In the 60–64 age-group, the prevalence of both undiagnosed diabetes and IPH was ~8%, indicating that similar proportions of individuals in this age-group would be identified as diabetic as would be missed under the ADA criteria because of the focus on FG. In the 70–74 age-group, the prevalence of IPH exceeded the prevalence of undiagnosed diabetes (9.05 vs. 6.99%), suggesting that in this age-group, IPH occurred at least as frequently as undiagnosed diabetes, and possibly more frequently.

The age-specific ratios of undiagnosed diabetes:IPH showed a clear pattern with age. The ratio in the 40–44 age-group was 5.49 but decreased to 0.77 in the 70–74 age-group, indicating that the prevalence of undiagnosed diabetes relative to IPH decreased with age. Despite the large ratios in the 40–49 age-groups (5.49 and 4.58, respectively), the CIs for these ratios included 1.0, indicating that these estimates were not significantly different from unity. Despite the trend with age, the relatively small number of individuals with both undiagnosed diabetes and IPH resulted in CIs about each age-specific ratio that included 1.0.

The curves presented in Fig. 1 provided the best fit to prevalence estimates of undiagnosed diabetes and IPH, as measured by r^2 values, and emphasize important patterns in the prevalence of these groups as a function of age. If x increasing age-groups are represented as integers 1, 2, 3…7, the equation of the curve for prevalence of undiagnosed diabetes was y =

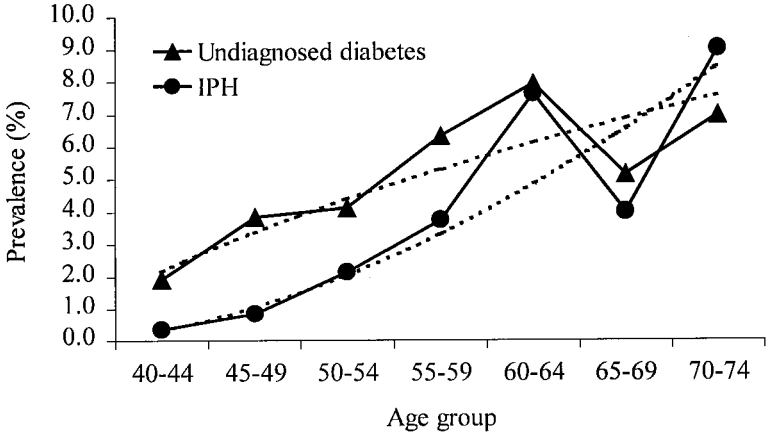

Figure 1—*Age-specific prevalence of undiagnosed diabetes and IPH (solid lines), NHANES III, 1988–1994. The dotted curves show trends in prevalence of undiagnosed diabetes and IPH with increasing age.*

$2.18x^{0.64}$, and the curve for prevalence of IPH was $y = 0.33x^{1.67}$. The equations for undiagnosed diabetes and IPH had r^2 values of 0.84 and 0.94, respectively, indicating that the majority of variability in prevalence of both groups could be explained by age, with slightly more variance explained by age among those with IPH. Importantly, the curves converge and then cross in old age, suggesting that the prevalence of undiagnosed diabetes and IPH were similar in old age. Linear regression analysis that used the age-specific undiagnosed diabetes:IPH ratios as the dependent variable revealed a significant, negative association with age. The intercept of the regression equation was 5.48, estimating the undiagnosed diabetes:IPH ratio for the 40–44 age-group, and is similar to the estimate in Table 1. These analyses yielded a β coefficient associated with age of −0.77 ($P = 0.006$), indicating a significant decrease in the undiagnosed diabetes:IPH ratio with increasing age. This negative association indicated that the ADA criteria for ascertainment of glucose abnormalities results in these abnormalities being ascertained relatively less frequently in older adults compared with WHO criteria.

Table 2 shows weighted mean levels of HbA_{1c} and established CVD risk factors among people with undiagnosed diabetes and IPH and nondiabetic individuals. In general, CVD risk factors were worst among people with undiagnosed diabetes, intermediate in the IPH group, and most favorable in the nondiabetic group. As expected, individuals with IPH were significantly older than both those with undiagnosed diabetes and nondiabetic individuals. Despite their older age, individuals with IPH had more favorable measures of TG, HDL cholesterol, and BMI than individuals with undiagnosed diabetes. However, the IPH group had worse serum total cholesterol, TG, and BMI than nondiabetic individuals. HDL cholesterol was similar in the IPH and nondiabetic groups, and LDL cholesterol did not differ between groups. When analysis of CVD risk factors was adjusted for age differences between the groups, results were unchanged.

As expected, mean FG was highest in the undiagnosed diabetes group and was significantly higher than levels in the IPH and nondiabetic groups (172, 111, and 97 mg/dl, respectively). Similarly, postchallenge glucose was elevated in both the undiagnosed and IPH groups but was considerably lower in the nondiabetic group. Of particular interest were mean levels of HbA_{1c}. Although the difference in HbA_{1c} between the IPH and nondiabetic groups was statistically significant (5.6 vs. 5.3%), the mean of both of these groups falls in the range defined as normal by the ADA (<6%). In contrast, mean HbA_{1c} was considerably higher among people with undiagnosed diabetes (7.1%) and was significantly higher than HbA_{1c} in both the IPH and nondiabetic groups. Of the undiagnosed diabetes group, 67% had $HbA_{1c} \geq 6\%$, compared with 23% of the IPH group and 5% of the nondiabetic group.

CONCLUSIONS — Implications of the ADA criteria for ascertainment of diabetes at different ages have not been reported. An age-associated underestimation of glucose abnormalities under the ADA criteria is possible because it is known that advancing age is a major diabetes risk factor and because old and new reports suggest that IPH is common in older age (9,10). Of equal importance is evaluation of the relationship of undiagnosed diabetes and IPH to HbA_{1c} and CVD risk factors. It is important to examine these characteristics in the two groups because people with IPH were not counted as diabetic in the diabetes prevalence estimates reported by the Expert Committee.

Our findings show that compared with the WHO criteria, FG-based ADA criteria tend to underestimate glucose abnormalities more in older age than in younger age. Our results indicate that although the ADA criteria identified most abnormalities under age 50 years, underestimation of these abnor-

Table 2—*Mean levels of HbA_{1c} and CVD risk factors among individuals with ADA diabetes and IPH and nondiabetic individuals, NHANES III, 1988–1994*

Risk factor	ADA diabetes*	IPH†	Nondiabetic‡	*P*¶	*P*§
Age (years)	57.8	62.4	53.7	<0.001	<0.001
Total cholesterol (mg/dl)	216	230	215	<0.01	<0.001
HDL cholesterol (mg/dl)	41	51	51	<0.001	NS
LDL cholesterol (mg/dl)	131	139	137	NS	NS
TG (mg/dl)	245	199	143	<0.001	<0.001
Fasting glucose (mg/dl)	172	111	97	<0.001	<0.001
2-h glucose (mg/dl)	269	233	110	<0.001	<0.001
HbA_{1c} (%)	7.1	5.6	5.3	<0.001	<0.001
BMI (kg/m^2)	31.5	29.1	27.0	<0.01	<0.01

Data are means. *Fasting glucose ≥126 mg/dl, †fasting glucose <126 mg/dl and postchallenge glucose ≥200 mg/dl, ‡fasting glucose <126 mg/dl and postchallenge glucose <200 mg/dl, ¶difference in means between ADA diabetes and IPH, §difference in means between IPH and nondiabetic individuals.

malities in older age may be as high as 50%. This is attributable to the large number of older individuals with FG <126 mg/dl who have postchallenge glucose ≥200 mg/dl. The magnitude of underestimation of diabetes between the ADA and WHO criteria that we report in the older age-groups in NHANES III is consistent with results from the Cardiovascular Health Study, a cohort of adults aged >65 years, which recently demonstrated a 50% underestimation of diabetes prevalence in older adults comparing the ADA with WHO criteria (10). Our findings are also consistent with results from Rancho Bernardo (a cohort of adults aged 50–89 years), which showed that of new cases of glucose abnormalities, 48% of men and 72% of women had IPH (11).

However, recent studies have not uniformly demonstrated decreases in diabetes prevalence in older adults when ADA criteria are compared with WHO criteria. The DECODE study group showed an increase in diabetes in older adults, while the Hoorn Study of adults aged 50–75 years showed similar numbers of diabetic subjects under the two classification schemes (12,13). The findings of the DECODE study group of increased diabetes prevalence under the ADA criteria can be explained by important differences in statistical methods between DECODE and other groups (14). However, differences in analytic methods do not explain the findings from the Hoorn Study, indicating that further studies are needed to determine the basis for differences in the prevalence of IPH between cohorts of older adults in the U.S. and Europe.

Although NHANES III is a nationally representative sample of U.S. adults, the weighted prevalence estimates of people with undiagnosed diabetes and IPH were generated from small numbers of individuals (n = 125 for diabetes and n = 179 for IPH). It is important to emphasize that weighted cells based on small numbers have large variances, even after weighting has increased the cell size. Exacerbating the methodological limitations associated with working with small numbers is the fact that, consistent with our hypothesis, IPH does not occur frequently in the younger age-groups. However, the decreasing ratio of undiagnosed diabetes:IPH with increasing age is consistent with the idea that IPH is more common in older than in younger adults and provided empirical support for our hypothesis. Further supporting our hypothesis were results from regression analyses that clearly showed a significant negative association between age and the ratio of undiagnosed diabetes:IPH. These analyses confirmed that when only FG is used, glucose abnormalities are ascertained less frequently in older, compared with younger, adults.

Despite the high prevalence of IPH in some populations of older adults (10,11), physical and metabolic characteristics of this group have been poorly described. We showed that, compared with individuals with undiagnosed diabetes, those with IPH had significantly lower BMI and TG and significantly higher HDL cholesterol. This suggests that, for at least some CVD risk factors, people with IPH have more favorable CVD risk factor profiles than those with undiagnosed diabetes, supporting use of the ADA criteria with respect to identifying individuals with unfavorable levels of these factors. Of equal importance, the IPH group had significantly lower HbA_{1c} than the undiagnosed diabetic group (7.1 vs. 5.6%), lending further support to the ADA criteria in identifying people with evidence of long-term exposure to hyperglycemia.

Despite the ability of the ADA criteria to distinguish important differences between the undiagnosed diabetic and IPH groups, it is important to note that the IPH group had higher serum total cholesterol, TG, and BMI than the nondiabetic group. This indicates that for some CVD risk factors, people with IPH appear to have less favorable CVD risk factor profiles than individuals without a postchallenge glucose abnormality. Adjustment for age differences between the IPH and nondiabetic groups did not abolish these differences. Although HbA_{1c} was statistically higher in the IPH group compared with the nondiabetic group, both means were clearly low. These findings support specificity of the ADA criteria with respect to excluding persons without evidence of long-term hyperglycemia from classification as having undiagnosed diabetes. The slightly higher mean HbA_{1c} levels in the IPH group and the greater proportion of the IPH group with HbA_{1c} ≥6% might be explained by the older age of this group and the fact that glycation of proteins increases with aging (15,16). However, adjustment for age did not abolish the statistical difference in HbA_{1c} between the IPH and nondiabetic groups, indicating that postchallenge hyperglycemia is associated with a small, but statistically significant, increase in HbA_{1c}.

Worse CVD risk factor profiles in IPH, compared with nondiabetic, individuals may have played a role in recent studies that showed increased risk of CVD and mortality among those with IPH. A prospective study in the Rancho Bernardo cohort showed that among women aged 50–89 years, those with IPH had increased 7-year risk of fatal CVD and heart disease compared with nondiabetic women, indicating the potential impact of IPH on health outcomes in old age (11). This general result was echoed by a European group that showed individuals with IPH had a mortality ratio of 1.6 compared with nondiabetic individuals (17).

When interpreting results from the latter studies, it is important to consider that people with IPH may constitute a heterogeneous group of individuals, some of whom may be at increased risk of CVD and mortality and others whose risk factor profiles do not differ significantly from older adults without glucose abnormalities. Presence or absence of impaired fasting glucose (IFG) (110 ≤ FG <126) is one characteristic that may help distinguish the heterogeneity of health risk among people with IPH. Our results showed that the mean FG among IPH individuals was 111 mg/dl. The subset of IPH individuals who also have IFG may carry much of the health risk that has been observed in prospective studies that show increased risk of CVD and mortality among people with IPH (11,17). Prospective examination of this hypothesis has not been reported and should be a topic of future investigation.

If IFG is shown to predict adverse health outcomes more effectively than IPH, then intervention among people with IFG (who can be identified easily in the clinical setting), rather than screening using the OGTT, might be an effective way of reducing CVD and mortality among people who do not meet the ADA FG cutpoint for diabetes. This strategy is supported by evidence suggesting that diabetic vascular complications begin not only at FG levels <126 mg/dl but also at levels <110 mg/dl (18,19).

In summary, we showed that, compared with WHO criteria, the FG-based ADA criteria underestimate glucose abnormalities more as age increases. We also showed that individuals with undiagnosed diabetes as defined by the ADA criteria have significantly worse CVD risk factors than individuals with IPH and that mean HbA_{1c} in the IPH group was in the normal range. The ADA criteria appear to identify individuals with unfavorable levels of several CVD risk factors and evidence of long-term hypergly-

cemia. Future research should continue to evaluate the ADA criteria in both younger and older adults, with a focus on identifying whether IFG, a measure easily collected in the clinical setting, plays a role in previously observed associations between IPH and adverse health outcomes.

References

1. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 20:1183–1197, 1997
2. World Health Organization: *Diabetes Mellitus: Report of a WHO Study Group*. Geneva, World Health Org., 1985 (Tech. Rep. Ser., no. 727)
3. Alberti KGMM, Zimmet PZ, for the WHO Consultation: Definition, diagnosis and classification of diabetes mellitus and its complications. Part I: diagnosis and classification of diabetes mellitus Provisional Report of a WHO consultation. *Diabet Med* 15:539–553, 1998
4. National Center for Health Statistics: *Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988–1994*. Hyattsville, MD, National Center for Health Statistics, 1994 (*Vital and Health Statistics* Ser. 1, no. 32)
5. Harris MI, Flegal KM, Cowie CC, Eberhardt SM, Goldstein DE, Little RR, Weidmeyer HM, Byrd-Holt DD: Prevalence of diabetes, impaired fasting glucose and impaired glucose tolerance in U.S. adults: the Third National Health and Nutrition Examination Survey, 1988–1994. *Diabetes Care* 21:518–524, 1998
6. National Center for Health Statistics: *NHANES III Reference Manuals and Reports. CD ROM*. Hyattsville, MD, Centers for Disease Control and Prevention, 1996
7. Hansen MH, Hurwitz WN, Madow WG: *Sample Survey Methods and Theory: Methods and Applications*. Vol. 1. New York, Wiley, 1953, p. 514
8. Shah BV, Barnwell BG, Bieler GS: *SUDAAN User's Manual, Release 7.0*. Research Triangle Park, NC, Research Triangle Institute, 1996
9. Andres R: Aging and diabetes: symposium on diabetes mellitus. *Med Clin North Am* 55: 835–846, 1971
10. Wahl PW, Savage PJ, Psaty BM, Orchard TJ, Robbins JA, Tracy RP: Diabetes in older adults: comparison of 1997 American Diabetes Association classification of diabetes mellitus with 1985 WHO classification. *Lancet* 352:1012–1015, 1998
11. Barrett-Connor E, Assiamira F: Isolated post-challenge hyperglycemia and the risk of fatal cardiovascular disease in older women and men. *Diabetes Care* 21: 1236–1239, 1998
12. DECODE Study group, on behalf of the European Diabetes Epidemiology Study group: Will new diagnostic criteria for diabetes mellitus change phenotype of patients with diabetes? Reanalysis of European Epidemiological data. *BMJ* 317:371–375, 1998
13. De Vegt F, Dekker JM, Stehouwer CDA, Nijpels G, Bouter LM, Heine RJ: The 1997 American Diabetes Association criteria versus the 1985 World Health Organization criteria for the diagnosis of abnormal glucose tolerance: poor agreement in the Hoorn Study. *Diabetes Care* 21:1686–1690, 1998
14. Resnick HE, Harris TB: New diagnostic criteria for diabetes mellitus result in fewer cases in older adults. *BMJ* 318:531, 1999
15. Schleicher ED, Wagner E, Nerlich AG: Increased accumulation of the glycoxylation product N-carboxymethyllysine in human tissues in diabetes and aging. *J Clin Invest* 99:457–468, 1997
16. Brownlee M, Cerami A, Vlassara H: Advanced glycosylation end products in tissue and the biochemical basis of diabetic complications. *N Engl J Med* 318:1315–1321, 1988
17. Balkau B: New diagnostic criteria for diabetes and mortality in older adults. *Lancet* 353:68–69, 1999
18. Standl E, Schnell O, Balletshofer B, Schleicher E, Muhr D, Ziegler AG, Hasbbeck M: Influence of diabetes mellitus on the heart and macrovascular mortality. *Diabetologia* 40 (Suppl. 2):125–126, 1997
19. Bjørnholt JV, Erikssen G, Aaser E, Sandvik L, Nitter-Hauge S, Jervell J, Erikssen J, Thaulow E: Fasting blood glucose: an underestimated risk factor for cardiovascular death. *Diabetes Care* 22:45–49, 1999