Hemoglobin A₁c as a Diagnostic Tool for Diabetes Screening and New-Onset Diabetes Prediction

A 6-year community-based prospective study

Sung Hee Choi, MD, PhD1,2
Tae Hyuk Kim, MD1
Soo Lim, MD, PhD2
Kyong Soo Park, MD, PhD1
Hak C. Jang, MD, PhD1,2
Nam H. Cho, MD, PhD2

OBJECTIVE—Various cutoff levels of hemoglobin A₁c (A1C) have been suggested to screen for diabetes, although more consensus about the best level, especially for different ethnicities, is required. We evaluated the usefulness of A1C levels when screening for undiagnosed diabetes and as a predictor of 6-year incident diabetes in a prospective, population-based cohort study.

RESEARCH DESIGN AND METHODS—A total 10,038 participants were recruited from the Ansung-Ansan cohort study. All subjects underwent a 75-g oral glucose tolerance test at baseline and at each biennial follow-up. Excluding subjects with a previous history of diabetes (n = 572), the receiver operating characteristic curve was used to evaluate the diagnostic accuracy of the A1C cutoff. The Cox proportional hazards model was used to predict diabetes at 6 years.

RESULTS—At baseline, 635 participants (6.8%) had previously undiagnosed diabetes. An A1C cutoff of 5.9% produced the highest sum of sensitivity (68%) and specificity (91%). At 6 years, 895 (10.2%) subjects had developed incident diabetes. An A1C cutoff of 5.6% had the highest sum of sensitivity (59%) and specificity (77%) for the identification of subsequent 6-year incident diabetes. After multivariate adjustment, men with baseline A1C ≥ 5.6% had a 2.4-fold increased risk and women had a 3.1-fold increased risk of new-onset diabetes.

CONCLUSIONS—A1C is an effective and convenient method for diabetes screening. An A1C cutoff of 5.9% may identify subjects with undiagnosed diabetes. Individuals with A1C ≥ 5.6% have an increased risk for future diabetes.
of the survey area for at least 6 months before testing, and sufficient mental and physical ability to participate. Participants were recruited from the residents of two Korean communities within 60 km of Seoul. Ansan is a representative rural farming community that had a population of 132,906 in 2000 (14). Of 7,192 eligible individuals in Ansan, 5,018 were surveyed (70% response rate) using a cluster-sampling method stratified by age, sex, and residential district. Ansan is a representative urban community that had a population of 554,998 in 2000 (14). We successfully recruited 5,020 subjects from 124,775 eligible subjects (4.0%) using a random-sampling method of the local telephone directory.

At baseline, we excluded 572 (5.7%) individuals with known type 2 diabetes and 91 who had an unknown glucose status. Among 9,375 (4,415 men and 4,960 women) participants without a previous history of diabetes, 635 (6.8%) were newly diagnosed with type 2 diabetes at the baseline examination. Of 8,740 remaining nondiabetic subjects, 3,022 from Ansung and 2,923 from Ansan) were included and underwent repeated examinations during the 6-year follow-up period. The recall rate was 85.7% at the 2-year follow-up examination, 74.9% at year 4, and 66.7% at year 6. To deal with the bias arising from missing data, we used a data-deletion method and found that there was no significant bias caused by loss to follow-up.

Informed written consent was obtained from all participants. The study protocol was approved by the ethics committee of the Korean Center for Disease Control and the Ajou University School of Medicine Institutional Review Board.

Throughout the study, the same trained researchers and instruments were used to collect the data. Anthropometric parameters and blood pressure were measured by standard methods. The fasting plasma concentrations of glucose, insulin, total cholesterol, triglycerides, HDL cholesterol, and high-sensitivity C-reactive protein (hsCRP) were measured in a central laboratory. After an 8- to 14-h overnight fast, all subjects underwent a 2-h 75-g OGTT at inclusion and biennially. A1C level was measured using high-performance liquid chromatography (Variant II; BioRad Laboratories, Hercules, CA). Pancreatic β-cell function and insulin resistance were calculated by the homeostasis model assessment (HOMA-β and HOMA-IR, respectively).

**Definition**
For both baseline and during follow-up, the definition of diabetes was based on plasma glucose results during the 75-g OGTT, defined according to the 1997 ADA criteria: FPG concentration ≥7.0 mmol/L (126 mg/dL) or 2-h plasma glucose ≥11.1 mmol/L (200 mg/dL) or current treatment by oral antidiabetes drugs or insulin (15). A family history of diabetes was coded if there was at least one diabetic first-degree relative. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or taking antihypertensive medication.

**Statistical analysis**
The data are presented as means ± SD, as numbers and percentages, or as a relative risk (RR) with 95% CIs. Fasting insulin, triglycerides, and hsCRP concentrations and HOMA-β and HOMA-IR were normalized by logarithmic transformation. The means were compared by Student's t tests or by ANCOVA. For qualitative variables, the results are expressed as percentages and were compared by c² or by logistic regression. Pearson correlation analysis was used to determine the relationships between A1C level and plasma glucose concentration. The diagnostic properties of the specific threshold levels of A1C were evaluated by calculating the sensitivity, specificity, and positive and negative predictive value by the receiver operating characteristic (ROC) curve. To decide optimal-cutoff A1C, we were referencing the Youden-Index (J = max[(sensitivity(c) + specificity(c) − 1), for all possible cutoff values c]) (16).

Risk of new-onset diabetes according to the A1C cutoff was modeled using the Cox proportional hazards model, after adjusting for age, and using those variables with P ≤ 0.25 in the age-adjusted comparison between the diabetic and nondiabetic groups. We first examined the age-adjusted effects of the A1C cutoff on the 6-year incidence of diabetes (model A). Model B comprised model A with additional adjustment for anthropometric and social parameters. Model C was the adjusted model B plus triglyceride, HDL cholesterol, and hsCRP concentrations and HOMA-β and HOMA-IR. The final Cox models fulfilled the proportional hazards assumption.

We compared the predictive performance of A1C level and FPG concentration as continuous variables using the ROC curves and by calculating the area under the curves. For detecting undiagnosed diabetes at baseline by ROC curve analysis, we used the baseline data of participants without a previous history of diabetes. For incident diabetes after the 6-year follow-up, we used the 6-year follow-up data of participants who were nondiabetic at baseline and who had completed the 6-year follow-up. MedCalc software was used to calculate the ROC curves; the significance of differences between areas under these curves was calculated as shown elsewhere (17). All other analyses were performed using SPSS software (version 12.0; SPSS, Chicago, IL). Significance was defined as P < 0.05 for two-sided tests.

**RESULTS**

**Baseline characteristics**
Of 9,375 participants without a previous history of diabetes, 635 (6.8%) subjects revealed previously undiagnosed diabetes at the baseline 75-g OGTT test (Table 1). The clinical characteristics of participants with and without undiagnosed diabetes at baseline are shown in Supplementary Table 1. At baseline, the Pearson correlation coefficients were 0.759 between A1C level and FPG and 0.673 between A1C level and 2-h plasma glucose (all P < 0.001).

Table 1 showed the different characteristics between diabetic converters versus nondiabetic subjects. Over 6 years, 895 (10.2%) subjects developed new type 2 diabetes, and the mean follow-up periods were 5.68 ± 0.99 years. After adjusting for age, BMI, waist circumference, blood pressure, FPG, and 2-h plasma glucose, A1C level, fasting insulin, HOMA-IR, total cholesterol, triglycerides, and hsCRP concentrations were higher in those who developed diabetes. In both sexes, a family history of diabetes, hypertension, and urban residence (Ansan) were more frequent in the incident diabetic group.

**A1C cutoff for detecting undiagnosed diabetes and predicting progression to diabetes**
Table 2 shows the sensitivity, specificity, and positive and negative predictive values of A1C level for detecting undiagnosed diabetes and predicting 6-year incident diabetes at A1C cutoff values of 5.0–6.6%. For detecting undiagnosed diabetes, an A1C cutoff of 5.9% produced the maximum sum of sensitivity (68%)}
**HbA1c for diabetes screening and prediction**

Table 1—Baseline characteristics of men and women who developed or did not develop diabetes at 6 years

|                     | Not diabetic at follow-up | Diabetic at follow-up | Age-adjusted P |
|---------------------|---------------------------|-----------------------|----------------|
| n                   | 2,328                     | 478                   |                |
| Age (years)         | 51.1 ± 8.4                | 52.5 ± 8.7            | <0.001         |
| BMI (kg/m²)         | 24.1 ± 2.8                | 24.8 ± 3.1            | <0.001         |
| Waist circumference (cm) | 83 ± 7                 | 85 ± 8                | <0.001         |
| Systolic blood pressure (mmHg) | 116 ± 16             | 121 ± 17              | <0.001         |
| Diastolic blood pressure (mmHg) | 76 ± 11                | 78 ± 11               | <0.001         |
| FPG (mmol/L)       | 4.7 ± 0.5                 | 5.1 ± 0.6             | <0.001         |
| 2-h glucose (mmol/L) | 6.1 ± 1.6               | 8.0 ± 1.9             | <0.001         |
| A1C (%)            | 5.3 ± 0.3                 | 5.6 ± 0.5             | <0.001         |
| Fasting insulin (pmol/L) | 35.8 ×± 25.4         | 38.3 ×± 28.1           | 0.016          |
| HOMA-IR            | 1.2 ×± 0.9                | 1.4 ×± 1.1            | <0.001         |
| HOMA-β             | 105.3 ×± 123.4           | 84.5 ×± 223.2         | <0.001         |
| Total cholesterol (mmol/L) | 5.0 ± 0.9               | 5.1 ± 1.0             | <0.001         |
| HDL cholesterol (mmol/L) | 1.2 ± 0.3               | 1.1 ± 0.3             | 0.026          |
| Triglycerides (mmol/L) | 1.6 ×± 1.2             | 1.9 ×± 1.2            | <0.001         |
| hsCRP (mg/dL)      | 0.12 ×± 0.57             | 0.14 ×± 0.42          | 0.005          |
| Serum creatinine (mg/dL) | 1.0 ± 0.2              | 1.0 ± 0.2             | 0.072          |
| Hypertension (%)   | 8.6                       | 14.9                  | <0.001         |
| Family history of diabetes (%) | 9.2                     | 14.0                  | <0.001         |
| Smoker (%)         | 46.1                      | 48.2                  | 0.319          |
| Living in urban area (Ansan) (%) | 50.1                  | 61.7                  | <0.001         |
| Sporting activity (≥1 per week) (%) | 39.2                 | 38.7                  | 0.929          |
| Alcohol intake (≥60 Kcal per day) (%) | 45.2               | 49.3                  | 0.053          |
| Child with birth weight ≥4 kg (%) | —                   | —                    | —              |

Data are means ± SD, geometric mean ×± SD, or column percentage. Comparisons are adjusted for age.

and specificity (91%) by ROC analysis. The positive and negative predictive values of this cut point were 54 and 98%, respectively.

For predicting incident diabetes at 6 years, an A1C level of 5.6% was the optimal cutoff; the sensitivity, specificity, and positive and negative predictive values of this cut point were 59, 77, 31, and 91%, respectively.

To test the A1C cut points to predict future diabetes, we tested reliability by randomly dividing our cohort into the two groups. Half of the cohort was used to define the cut point and the other half to test reliability by calculating the incidence and adjusted RRs. The incidences and RRs were 31.7, 37.6, 46.5, 53.3, 58.9, 67.6, and 89.7% and 4.9, 5.9, 8.9, 10.8, 13.8, and 51.5 at the A1C cutoff of 5.6, 5.7, 5.8, 5.9, 6, 6.2, and 6.6%, respectively.

**A1C level and prediction of new-onset diabetes**

The RR of new-onset diabetes in subjects whose A1C levels were above or below 5.6% was assessed using the Cox proportional hazards model (Table 3). In the age-adjusted model (model A), an A1C cutoff ≥5.6% predicted incident diabetes in both men and women with a RR of 3.4 (95% CI 2.9–4.1) in men and 4.6 (3.7–5.7) in women (both P < 0.001). This increased risk remained after additional adjustment for other confounding factors (model C).

Because the A1C level displayed a significant interaction with sex and FPG concentration, we stratified by sex and performed subgroup analysis in the subjects with impaired fasting glucose (IFG) (Table 3; Supplementary Table 2). A total of 457 participants had IFG at baseline, and 138 subjects developed incident diabetes during the 6 years. In IFG group at baseline, an A1C level of 5.8% produced the highest sum of sensitivity and specificity for predicting new-onset diabetes at 6 years (Supplementary Table 3). After multivariate adjustment, those with an A1C level ≥5.8% had a 3.5-fold increased risk of incident diabetes in men and 5.2-fold increased risk in women. The RR of incident diabetes increased as baseline A1C level increased in both the group with normal glucose tolerance and with IFG, respectively (Supplementary Table 2).

**ROC curves**

Figure 1 shows the ROC curves representing the sensitivity and specificity of the A1C levels in detecting undiagnosed diabetes (Fig. 1A) and predicting new-onset diabetes (Fig. 1B) at each possible A1C cutoff level. The analysis indicated a high predictive value for A1C level in screening for undiagnosed diabetes and in predicting future diabetes.

For the identification of undiagnosed diabetes in the entire study population of 9,375 subjects, the areas under the curve for A1C level were similar with that for FPG concentration (0.85 [95% CI 0.84–0.87] vs. 0.88 [0.86–0.89]; P = 0.14). The optimal FPG cutoff for predicting undiagnosed diabetes was 5.5 mmol/L (99 mg/dL), with 70% sensitivity and 94% specificity (Fig. 1A, dotted line).

For predicting new-onset diabetes after the 6-year follow-up, the area under the curve for A1C level was significantly greater than that for FPG concentration (0.74 [95% CI 0.72–0.76] vs. 0.69 [0.67–0.71]; P < 0.001). For FPG concentrations, the cutoff value of 4.8 mmol/L (87 mg/dL) yielded the maximum sum of sensitivity (62%) and specificity (67%) in
predictions for new-onset diabetes (Fig. 1B, dotted line).

CONCLUSIONS—The main finding of this study is that the A1C assay was useful as a screening test for type 2 diabetes and as a predictor of future diabetes. In our population, an A1C cutoff of 5.9% was able to identify people with undiagnosed diabetes, and individuals with an A1C ≥ 5.6% had an increased risk for progression to type 2 diabetes independent of other confounding factors.

This was a large, prospective cohort study that used stringent criteria to diagnose diabetes and to evaluate the usefulness of A1C level in diabetes screening and in the prediction of new-onset diabetes. In this homogenous population-based study, we applied the OGTT to all participants and used the same instruments and personnel for all clinical and biochemical assessments during the 6 years.

Use of the A1C level in the diagnosis of or screening for diabetes has been debated for many years. Most A1C assays, such as the National Glycohemoglobin Standardization Program (18), are standardized, and recent expert committee reports suggest an A1C cutoff of 6.5% for diagnosing diabetes (11). For screening a general population, the A1C level has several advantages over the currently used FPG concentration or 2-h glucose concentration after an OGTT. The A1C assay does not need a fasting or timed sample. It is a better indicator of chronic glycemic level, has less preanalytic instability (19), and has a more consistent relationship with diabetic microvascular complications than does FPG concentration (20,21). However, concerns remain about the risk of underdiagnosing people with overt diabetes when using an A1C cutoff of 6.5% (12).

Several cross-sectional studies have evaluated the accuracy of the A1C cutoffs in screening for diabetes. In analysis of the National Health and Nutrition Examination Survey data, Buell et al. (9) reported that an A1C level of 5.8% showed the highest sensitivity (86%) and specificity (92%) in identifying undiagnosed diabetes when using FPG concentration as the diagnostic test for type 2 diabetes. In the current study, the definition of diabetes was based on plasma glucose results from the 75-g OGTT, and the A1C value of 5.9% was appropriate for detecting undiagnosed type 2 diabetes in this Korean cohort population. In a Japanese study of OGTT results in 1,904 people, an A1C cut point of 5.6% identified undiagnosed type 2 diabetes, and this value is used as a supplementary diagnostic criterion by the Japanese Diabetes Society (10).

Only a few studies have investigated the utility of A1C level in predicting new-onset diabetes. Recent Japanese and French cohort studies reported that A1C level is effective in predicting type 2 diabetes (22,23) but was less sensitive and specific than FPG concentration for predicting FPG-defined diabetes (22). This might be because many people with an abnormal 2-h glucose concentration after an OGTT have a normal FPG concentration (24). We used OGTT to

Table 2—Sensitivity, specificity, and positive and negative predictive value of increasing A1C cutoff levels for detecting undiagnosed diabetes and for predicting the incidence of type 2 diabetes at the 6-year follow-up

| A1C cutoff (%) | Baseline undiagnosed diabetes Predictive value | Incident diabetes after 6 years of follow-up Predictive value |
|----------------|-----------------------------------------------|-------------------------------------------------------------|
|                | Sensitivity | Specificity | Positive | Negative | Sensitivity | Specificity | Positive | Negative |
| 5.0 (–1.00 SDs above normal mean) | 0.972 | 0.115 | 0.074 | 0.982 | 0.962 | 0.121 | 0.162 | 0.947 |
| 5.1 (–0.75 SDs above normal mean) | 0.956 | 0.185 | 0.079 | 0.98 | 0.935 | 0.198 | 0.171 | 0.945 |
| 5.2 (–0.50 SDs above normal mean) | 0.945 | 0.279 | 0.087 | 0.986 | 0.886 | 0.302 | 0.184 | 0.937 |
| 5.3 (–0.25 SDs above normal mean) | 0.915 | 0.390 | 0.098 | 0.984 | 0.827 | 0.419 | 0.201 | 0.932 |
| 5.4 (0.00 SDs above normal mean) | 0.887 | 0.506 | 0.115 | 0.984 | 0.768 | 0.547 | 0.231 | 0.930 |
| 5.5 (0.25 SDs above normal mean) | 0.866 | 0.616 | 0.141 | 0.984 | 0.682 | 0.665 | 0.265 | 0.922 |
| 5.6 (0.50 SDs above normal mean) | 0.822 | 0.717 | 0.174 | 0.982 | 0.594 | 0.769 | 0.313 | 0.914 |
| 5.7 (0.75 SDs above normal mean) | 0.770 | 0.797 | 0.216 | 0.979 | 0.508 | 0.847 | 0.370 | 0.907 |
| 5.8 (1.00 SDs above normal mean) | 0.720 | 0.862 | 0.274 | 0.977 | 0.420 | 0.908 | 0.448 | 0.898 |
| 5.9 (1.25 SDs above normal mean) | 0.676 | 0.907 | 0.344 | 0.975 | 0.333 | 0.947 | 0.527 | 0.889 |
| 6.0 (1.50 SDs above normal mean) | 0.619 | 0.933 | 0.411 | 0.971 | 0.263 | 0.967 | 0.586 | 0.881 |
| 6.2 (2.00 SDs above normal mean) | 0.523 | 0.968 | 0.544 | 0.965 | 0.152 | 0.987 | 0.677 | 0.868 |
| 6.6 (3.00 SDs above normal mean) | 0.372 | 0.992 | 0.771 | 0.956 | 0.051 | 0.999 | 0.885 | 0.856 |

Table 3—The RR of incident type 2 diabetes at the 6-year follow-up in Cox proportional hazards models based on A1C status at baseline

| A1C ≥ 5.6% (vs. <5.6%) in the entire study population | Men | | Women | |
|------------------------------------------------|--------| | | |
| RR (95% CI) | P | | RR (95% CI) | P |
| Model A* | 3.44 (2.87–4.13) | <0.001 | 4.60 (3.75–5.66) | <0.001 |
| Model B* | 3.17 (2.62–3.84) | <0.001 | 4.00 (3.24–4.95) | <0.001 |
| Model C* | 2.41 (1.98–2.93) | <0.001 | 3.06 (2.46–3.81) | <0.001 |
| A1C ≥ 5.8% (vs. <5.8%) in subjects with IFG | | | | |
| Model A* | 3.15 (2.13–4.64) | <0.001 | 6.29 (3.03–13.05) | <0.001 |
| Model B* | 3.57 (2.36–5.41) | <0.001 | 5.99 (2.83–12.66) | <0.001 |
| Model C* | 3.47 (2.27–5.29) | <0.001 | 5.15 (2.39–11.11) | <0.001 |

There was significant interaction between A1C and sex. The interaction between A1C and FPG was also significant. *Age adjusted. †Model A and waist circumference, family history of diabetes, living in urban area, hypertension, smoking, and alcohol intake were adjusted. ‡Model B and triglycerides (log), HDL cholesterol, HOMA-IR (log), HOMA-B (log), and hsCRP (log) were adjusted.
HbA1c for diabetes screening and prediction

define diabetes and found that A1C level was independently related to an increased risk of new-onset diabetes, even in those with IFG at baseline. The predictive value of the A1C level was greater than that of the FPG concentration.

Determining the optimal A1C cutoff for diabetes screening is somewhat arbitrary because the risk of diabetes is continuous over a range of glycemic measures. To maximize the diagnostic efficiency, the optimal A1C cutoff should be considered in balancing both sensitivity and specificity. Despite the A1C cutoff value of 5.6% for identifying individuals with increased risk of future diabetes, as was chosen by the Youden Index, it showed only 31% of the positive predictive value. However, we considered the clinical situation because diabetes is a common disease and the action for prevention is highly beneficial and does relatively little harm to healthy subjects. Our study has some limitations. All participants were enrolled from Korean rural and urban communities of homogeneous ethnic background, and it is debatable whether these results can be generalized. Although racial differences in A1C level have been suggested (25), the significance of any differences is not clear, and the use of different A1C values according to ethnicity is not currently recommended. However, after multivariate adjustment of confounders, A1C level remained as an independent predictor of incident diabetes. In addition, the stringency of our study method and prospective follow-up of a large community-based cohort for 6 years made our results stronger than those of other studies.

In conclusion, we found that A1C level was effective and convenient for diabetes screening. An A1C cutoff of 5.9% may identify a high proportion of people with undiagnosed type 2 diabetes. Individuals with A1C ≥ 5.6% have an increased risk for future diabetes, and early preventive intervention could be helpful.

Acknowledgments—This study was supported by the National Genome Research Institute, Korean Center for Disease Control and Prevention (contract nos. 2001-2003-348-6111-221, 2004-347-6111-213, and 2005-347-2400-2440-215). The funding source had no role in the collection of data or in the decision to submit the manuscript for publication.

No potential conflicts of interest relevant to this article were reported.

S.H.C. wrote and edited the manuscript. T.H.K. performed the statistical analysis and wrote the manuscript. S.L. contributed to discussion and statistical analysis. K.S.P. and T.H.K. reviewed and edited the manuscript. N.H.C. was the principal investigator of the project, collected and researched data, designed and performed the cohort study, and wrote the manuscript.

References
1. Cowie CC, Rust KF, Ford ES, et al. Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. Diabetes Care 2009;32:287–294
2. Chan JC, Malik V, Jia W, et al. Diabetes in Asia: epidemiology, risk factors, and pathophysiology. JAMA 2009;301:2129–2140
3. Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. Diabetes Care 1992;15:815–819
4. American Diabetes Association. Standards of medical care in diabetes. 2009. Diabetes Care 2009;32(Suppl. 1):S13–S61
5. UK Prospective Diabetes Study Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998;332:854–865
6. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE. Defining the relationship between plasma glucose and HbA1c: analysis of glucose profiles and HbA1c in the Diabetes Control and Complications Trial. Diabetes Care 2002;25:275–278
7. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. Ann Intern Med 2004;141:413–420
8. Tapp R, Tikellis G, Wong TY, Harper CA, Zimmet PZ, Shaw JE; Australian Diabetes Obesity and Lifestyle Study Group. Longitudinal association of glucose metabolism with retinopathy: results from the Australian Diabetes Obesity and Lifestyle (AusDiab) study. Diabetes Care 2008;31:1349–1354
9. Buell C, Kermah D, Davidson MB. Utility of A1C for diabetes screening in the 1999–2004 NHANES population. Diabetes Care 2007;30:2233–2235
10. Nakagami T, Tominaga M, Nishimura R, et al. Is the measurement of glycated hemoglobin A1c alone an efficient screening test for undiagnosed diabetes? Japan National Diabetes Survey. Diabetes Res Clin Pract 2007;76:251–256
11. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009;32:1327–1334
12. Kramer CK, Araneta MR, Barrett-Connor E. A1C and diabetes diagnosis: the Rancho Bernardo Study. Diabetes Care 2010; 33:101–103
13. Cho NH, Jang HC, Choi SH, et al. Abnormal liver function test predicts type 2 diabetes: a community-based prospective study. Diabetes Care 2007;30:2566–2568
14. STAT-Korea. Census. Daejeon, Korea, Korean National Statistical Office, 2003
15. Report of 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 1997;20:1183–1197
16. Youden WJ. Index for rating diagnostic tests. Cancer 1950;3:32–35
17. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837–845
18. Miedema K. Towards worldwide standardisation of Hba1c determination. Diabetologia 2004;47:1143–1148
19. Little RR, Rohlfing CL, Tennill AL, Connolly S, Hanson S. Effects of sample storage conditions on glycated hemoglobin measurement: evaluation of five different high performance liquid chromatography methods. Diabetes Technol Ther 2007;9:36–42
20. Sabanayagam CLG, Liew G, Tai ES, et al. Relationship between glycated haemoglobin and microvascular complications: is there a natural cut-off point for the diagnosis of diabetes? Diabetologia 2009; 52:1279–1289

21. Wong TY, Liew G, Tapp RJ, et al. Relation between fasting glucose and retinopathy for diagnosis of diabetes: three population-based cross-sectional studies. Lancet 2008; 371:736–743

22. Droumaguet C, Balkau B, Simon D, et al.; DESIR Study Group. Use of HbA1c in predicting progression to diabetes in French men and women: data from an Epidemiological Study on the Insulin Resistance Syndrome (DESIR). Diabetes Care 2006;29:1619–1625

23. Sato KK, Hayashi T, Harita N, et al. Combined measurement of fasting plasma glucose and A1C is effective for the prediction of type 2 diabetes: the Kansai Healthcare Study. Diabetes Care 2009;32: 644–646

24. Harris MI, Eastman RC, Cowie CC, Flegal KM, Eberhardt MS. Comparison of diabetes diagnostic categories in the U.S. population according to the 1997 American Diabetes Association and 1980-1985 World Health Organization diagnostic criteria. Diabetes Care 1997;20:1859–1862

25. Herman WH, Ma Y, Uwaifo G, et al.; Diabetes Prevention Program Research Group. Differences in A1C by race and ethnicity among patients with impaired glucose tolerance in the Diabetes Prevention Program. Diabetes Care 2007;30:2453–2457