Assessment of glycemic control in patients with type 2 diabetes mellitus treated with metformin–sulfonylurea combination: Results of a multicenter, cross-sectional, observational study in Korea

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ABSTRACT
Aims/Introduction: To assess the current status of glycemic control in patients with type 2 diabetes treated with a combination of metformin and sulfonylurea for >3 months, as measured by glycosylated hemoglobin (HbA1c).

Materials and Methods: Data on patient demographics, diabetic complications, HbA1c, fasting plasma glucose (FPG) and type of treatment were collected in this multi-center, cross-sectional, non-interventional study.

Results: From April 2008 to February 2009, 5,628 patients were recruited from 299 centers in Korea. Patients characteristics (mean ± SD) were as follows: age 58.4 ± 10.8 years, duration of diabetes 6.1 ± 4.7 years, body mass index 24.7 ± 2.9 kg/m², HbA1c 7.77 ± 1.22%, FBG 147.4 ± 46.5 mmol/L and FPG 164.0 ± 54.3 mmol/L. The most common diabetic complication was neuropathy (22.5%), followed by retinopathy (18.3%) and microalbuminuria (16.1%). Just 1,524 (27.1%) patients achieved HbA1c ≤ 7%. A higher number of patients (32.6%) treated by endocrinologists achieved HbA1c ≤ 7% than those treated by internists (24.4%) and primary care physicians (23.2%). In multivariate analyses, diabetic retinopathy (odds ratio 0.455, 95% confidence interval 0.341–0.606), nephropathy (odds ratio 0.639, 95% confidence interval 0.43–0.949), diabetes for ≥ 5 years (odds ratio 0.493, 95% confidence interval 0.4–0.606) and older age added by 1 year (odds ratio 1.019, 95% confidence interval 1.01–1.029) was significantly associated with achieving target HbA1c. In addition, treatment by endocrinologists rather than internists significantly increased chances of achieving target HbA1c (odds ratio 1.417, 95% confidence interval 1.146–1.751).

Conclusions: The majority of patients with type 2 diabetes in Korea had inadequate glycemic control, despite receiving a combination of metformin and sulfonylurea.

INTRODUCTION
Globally, an estimated 366.2 million people with diabetes existed in 2011, accounting for 8.3% of the world adult population, and this number is projected to increase to 551.8 million by 2030, which would represent 9.9% of world adult population1. In South East Asia, 71.4 million people had diabetes in 2011, and this number is estimated to increase to 120.9 million in 20301. The prevalence of diabetes in Korea is set to increase from its level of 3.3 million in 2010 to 4.3 million by 20302. In the past four decades, the prevalence of diabetes in Korea has increased from 1.5 to 9.9%3. A nationwide survey of Korean patients with diabetes reported a high
prevalence of diabetic complications, such as microalbuminuria (30.3%), retinopathy (38.3%), nephropathy (44.6%), coronary artery disease (CAD; 8.7%), cerebrovascular disease (CVD; 6.7%) and peripheral artery disease (PAD; 3.0%)4. The increasing prevalence of diabetes mellitus and its related complications have contributed to a substantial increase in morbidity and mortality in Korea4.

The international guidelines, including American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD) guidelines6, the American Association of Clinical Endocrinologists/American College of Endocrinology Diabetes Guidelines (AACE/ACE) guidelines7 and the Korean national guidelines8, suggest comprehensive management of patients with type 2 diabetes to maintain glycemic control, and reduce the risk of microvascular and macrovascular diabetes-related complications. According to the algorithm for medical management of type 2 diabetes, the ADA/EASD guidelines recommend initial therapy with lifestyle changes and then use of metformin (Met), followed by continuing timely augmentation of therapy with additional agents (including sulfonylureas [SU] and early initiation of insulin therapy)9. The combination of Met and SU (Met + SU) addresses both underlying defects in the disorder, insulin deficiency and insulin resistance. Earlier randomized controlled trials on Met + SU combination showed significant reductions in glycosylated hemoglobin (HbA1c) in patients with type 2 diabetes not controlled by monotherapy alone10,11. However, the results of these studies should be validated in the real-world practice, outside the controlled conditions of the randomized trials.

Evaluation of glycemic control in patients with type 2 diabetes receiving Met + SU would be very relevant for planning further treatment intensification strategies targeting improved diabetes control. However, there is a paucity of real-world data on the effect of Met + SU in type 2 diabetes patients in Korea. The Observational Registry Study to Explore the Current status of Glucose Control in type 2 Diabetes Mellitus Patients on Oral Hypoglycemic Agents (HbA1c Level in Type 2 Diabetes Patients on Oral Hypoglycemic Agents [ALIT]) study in Korea aimed to evaluate the current status of glycemic control in patients with type 2 diabetes receiving Met + SU therapy.

MATERIALS AND METHODS

Study Design and Objective

It was a multicenter, non-interventional, cross-sectional observational study carried out in 299 centers across Korea. The objective of the study was to explore the current status of glucose control in patients with type 2 diabetes receiving Met + SU, by assessing the HbA1c levels.

The present study was carried out in accordance with the Declaration of Helsinki (as revised in Edinburgh 2000)12 and all subsequent amendments, and guidelines for Good Epidemiological Practice in the USA13 and Europe14. The protocol was approved by the local ethics committees at each study site.

Investigators

The participating physicians were selected to obtain stratified physician groups from general hospitals, semi-hospitals and clinics. They included endocrinologists, internists and other primary care physicians. In context of the present study, endocrinologists were defined as members of the Korean Endocrine Society, and mainly worked in tertiary and secondary hospitals. Internists were defined as members of the Korean Association of Internal Medicine, and worked as primary care physicians. Other primary care physicians included general practitioners, including family physicians, and all doctors other than endocrinologists and internists.

Patients

The study included patients diagnosed with type 2 diabetes, who were being treated with Met + SU for >3 months, who had their HbA1c levels tested within the past 1 month before enrolment and who signed the data release consent form before the study. Exclusion criteria comprised patients who were participating in another clinical study, who received insulin within 3 months, and who had taken oral hypoglycemic agents other than SU and Met within the past 3 months.

Study Assessments

Data collected included patient demographics: diabetic complications (retinopathy, neuropathy, nephropathy, microalbuminuria, cardiovascular disease [CVD] and peripheral vascular disease [PVD]); diabetic comorbidities (hypertension, dyslipidemia related to total cholesterol [TC], low-density lipoprotein [LDL], high-density lipoprotein [HDL] and triglycerides [TG]); duration of diabetes; and HbA1c levels, fasting blood glucose (FBG) levels, fasting plasma glucose (FPG) levels and treatment details with oral hypoglycemic agents. Whether the patient had diabetic complications was identified by review of the patient’s medical records.

As per the post-hoc analysis, we analyzed three subgroups of patients who were treated by: (i) endocrinologists; (ii) internists; and (iii) other primary care physicians.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as frequencies and percentages. The average HbA1c values were summarized by mean ± SD, median, minimum and maximum levels. Statistical methods used included analysis of the variance (ANOVA) χ²-test, Wald χ²-test and t-test. The univariate and multivariate logistic regression analyses were carried out to test associations between patient characteristics and achievement of target HbA1c. All statistical tests were carried out using two-tailed tests at 5% level of significance or with adjustment if required. All statistical analyses were carried out using sas version 9.2 (SAS Institute Inc., Cary, NC, USA).
RESULTS

Patient Disposition
Between April 2008 and February 2009, a total of 5692 patients were enrolled. Of them, 5628 patients, excluding 64 patients who did not meet the eligibility criteria, were included in the analysis.

Met + SU Treatment Received By Patients
Of the total patients, 1,457 (25.9%) patients received fixed-dose combination of Met + SU in one pill. There were very few patients who received the following combination of treatment: SU + fixed-dose combination of Met + SU (41, 0.7%), Met + fixed dose combination of Met + SU (63, 1.1%) and SU + Met + fixed dose combination of Met + SU (11, 0.2%).

Patient Characteristics in Total Patients and Subgroups of Patients Treated By Different Physician Specialties
Table 1 presents data on patient characteristics, diabetic complications and comorbidities of total patients, as well as patient subgroups treated by different physician specialties. Of 5,628 patients, 3,099 (55.1%) were males. Mean age and body mass index (BMI) were 58.4 ± 10.8 years and 24.7 ± 2.9 kg/m², respectively. Mean HbA1c was 7.8 ± 1.2%, FBG was 147.3 ± 46.5 mmol/L and FPG was 164.0 ± 54.3 mmol/L. Diabetic neuropathy (22.5%) was the most common diabetic complication, whereas hypertension (59.2%) was the most common comorbidity. Mean duration of diabetes in total patients was 6.1 ± 4.7 years, whereas mean time to start combination therapy after diagnosis was 1256.9 ± 1424.2 days (mean time to start combination therapy in patients visiting endocrinologists, internists and other primary care physicians was 1311.2 ± 1510.5 days, 1226.2 ± 1327.0 days and 1406.2 ± 2,305 days, respectively (P = 0.3590).

Achievement of Target HbA1c
Data on target HbA1c achievement is presented in Figure 1. Just 27.1% of patients achieved HbA1c ≤7%. A higher number of patients (32.6%) treated by endocrinologists achieved HbA1c ≤7% than those treated by internists (24.4%) and other primary care physicians (23.2%; P < 0.0001).

Levels of HbA1c and Patient Characteristics
The details of HbA1c levels as per patient characteristics are presented in Table S1. Young age, long duration of diabetes, diabetic retinopathy, nephropathy, dyslipidemia related to total cholesterol, LDL and triglycerides were significantly associated with high HbA1c.

Factors Associated With HbA1c Target Achievement (HbA1c ≤7%) by Univariate and Multivariate Analysis
The strength and statistical significance of the association of patient characteristics with achievement of target HbA1c, as tested by univariate and multivariate logistic regression, is presented in Table 2. Findings of this analysis show that patients with older age added by 1 year significantly increased chances of achieving target HbA1c (adds ratio [OR] 1.019, 95% confidence interval [CI] 1.01–1.029). The presence of diabetic retinopathy (OR 0.455, 95% CI 0.341–0.606), nephropathy (OR 0.639, 95% CI 0.43–0.949) and diabetes for ≥5 years (OR 0.493, 95% CI 0.4–0.606) significantly decreased the odds of achieving target HbA1c.

When comparisons were made among the physician subgroups, patients being treated by endocrinologists had significantly increased chances of achieving target HbA1c.

DISCUSSION
In the present large, multicenter, cross-sectional observational study of patients with type 2 diabetes receiving Met + SU treatment in Korea, we observed that just 1,524 (27.1%) patients achieved HbA1c ≤7%. According to earlier studies in Korea, the percentage of treated patients with type 2 diabetes who achieved target HbA1c <7% was in the range of 35.7–43.9%. The present results suggest that almost three-quarters of patients with type 2 diabetes were not well controlled, despite being treated with Met + SU therapy. We also found that young age and diabetic complications, such as retinopathy, nephropathy and long duration of diabetes, were associated with a decreased chance of achieving target HbA1c. These data, which report underachievement of target HbA1c in treated patients, serve as an alert to physicians, and emphasize the need to prescribe intensive treatment for diabetes management.

Type 2 diabetes is an increasing epidemic in Asia, characterized by rapid rates of increase over short periods, onset at a relatively young age and low BMI. Patient characteristics of Korean patients with type 2 diabetes are known to be different than patients from Western countries. The low BMI in the present study (24.7 kg/m²) is comparable with a previous study reporting 60–80% of Korean patients having type 2 diabetes with BMI <25 kg/m². We found that BMI (OR 1.002, 95% CI 0.964–1.041, P = 0.7039) and abdominal circumference (OR 0.994, 95% CI 0.983–1.005, P = 0.2866) were not significantly associated with achievement of target HbA1c. In the present study, young age (OR 1.019, 95% CI 1.01–1.029, P < 0.0001) has been shown to be associated with decreased chances of achieving target HbA1c. Young patients have been associated with low glycemic control as compared with old patients, which might be due to the fact that young patients are less compliant with recommendations of diet, exercise and pharmacological treatment.

In Asian patients with type 2 diabetes, diabetes is associated with high rates of cardiovascular risk factors, leading to high morbidity, mortality and economic burden. Earlier studies in Korea reported chronic complications in patients with type 2 diabetes. A cross-sectional study in Korea of patients admitted to hospital reported a high prevalence of CVD (7.8%), stroke (8.4%) and retinopathy (35.2%). A study showed a high
### Table 1 | Characteristics of three subgroups of patients and total patients

| Characteristics                      | Endocrinology | Internal medicine | Family medicine and others | Total     | P-value  |
|--------------------------------------|---------------|-------------------|-----------------------------|-----------|----------|
|                                      |               |                   |                             |           |          |
|                                      |               |                   |                             |           |          |
| **Sex**                              |               |                   |                             |           |          |
| n                                    | 1,848         | 3,586             | 194                         | 5,628     |          |
| ** Male**                            | 976 (52.8)    | 2,016 (56.2)      | 107 (55.2)                  | 3,099 (55.1) | 0.0574*  |
| ** Female**                          | 872 (47.2)    | 1,570 (43.8)      | 87 (44.9)                   | 2,529 (44.9) |          |
| **Age (years)**                      |               |                   |                             |           |          |
| n                                    | 1,848         | 3,586             | 194                         | 5,628     |          |
| ** Mean ± SD**                       | 57.9 ± 11.0   | 58.6 ± 10.5       | 59.7 ± 13.1                 | 58.4 ± 10.8 | 0.0322†  |
|                                      |               |                   |                             |           |          |
| **Duration of diabetes (years)**     |               |                   |                             |           |          |
| n                                    | 1,598         | 3,336             | 117                         | 3,609     |          |
| ** Mean ± SD**                       | 65 ± 5.4      | 5.9 ± 4.2         | 7.0 ± 6.7                   | 6.1 ± 4.7 | <0.0001* |
|                                      |               |                   |                             |           |          |
| **Weight (kg)**                      |               |                   |                             |           |          |
| n                                    | 1,451         | 3,188             | 173                         | 4,812     |          |
| ** Mean ± SD**                       | 66.2 ± 11.0   | 66.7 ± 10.1       | 65.2 ± 11.4                 | 66.5 ± 10.5 | 0.0702†  |
|                                      |               |                   |                             |           |          |
| **Waist circumference (cm)**         |               |                   |                             |           |          |
| n                                    | 1,043         | 2,359             | 115                         | 3,517     |          |
| ** Mean ± SD**                       | 87.6 ± 9.3    | 89.7 ± 11.3       | 87.2 ± 10.3                 | 89.0 ± 10.8 | <0.0001† |
|                                      |               |                   |                             |           |          |
| **BMI (kg/m²)**                      |               |                   |                             |           |          |
| n                                    | 1,443         | 3,156             | 172                         | 4,771     |          |
| ** Mean ± SD**                       | 24.8 ± 3.1    | 24.7 ± 2.7        | 24.6 ± 3.7                  | 24.7 ± 2.9 | 0.2096†  |
|                                      |               |                   |                             |           |          |
| **HbA1c levels (%)**                 |               |                   |                             |           |          |
| n                                    | 1,848         | 3,586             | 194                         | 5,628     |          |
| ** Mean ± SD**                       | 7.6 ± 1.3     | 7.8 ± 1.1         | 8.1 ± 1.6                   | 7.8 ± 1.2 | <0.0001† |
|                                      |               |                   |                             |           |          |
| **FBG (mg/dL)**                      |               |                   |                             |           |          |
| n                                    | 862           | 1,740             | 137                         | 2,739     |          |
| ** Mean ± SD**                       | 142.2 ± 38.8  | 149.2 ± 47.3      | 156.2 ± 71.2                | 147.3 ± 46.5 | 0.0001†  |
|                                      |               |                   |                             |           |          |
| **FPG (mg/dL)**                      |               |                   |                             |           |          |
| n                                    | 600           | 1,203             | 36                          | 1,839     |          |
| ** Mean ± SD**                       | 158.2 ± 52.1  | 166.5 ± 54.7      | 176.9 ± 67.8                | 164.0 ± 54.3 | 0.0033†  |
|                                      |               |                   |                             |           |          |
| **Prevalence of complications**      |               |                   |                             |           |          |
| Diabetic retinopathy                 |               |                   |                             |           |          |
| n (%)                                | 362 (22.5)    | 497 (16.3)        | 24 (14.6)                   | 883 (18.3) | <0.0001* |
| Diabetic neuropathy                  |               |                   |                             |           |          |
| n (%)                                | 383 (23.1)    | 727 (22.5)        | 32 (17.7)                   | 1,142 (22.5) | 0.2468*  |
| Diabetic nephropathy                 |               |                   |                             |           |          |
| n (%)                                | 188 (11.3)    | 406 (13.4)        | 13 (7.3)                    | 607 (12.5) | 0.0121*  |
| Microalbuminuria                     |               |                   |                             |           |          |
| n (%)                                | 1629          | 2,696             | 156                         | 4,481     |          |
| CVD‡                                 |               |                   |                             |           |          |
| n (%)                                | 521 (31.5)    | 311 (10.5)        | 21 (11.5)                   | 547 (11.5) | 0.0106*  |
| PVD                                  |               |                   |                             |           |          |
| n (%)                                | 1,493         | 2820              | 177                         | 4,490     | <0.0001* |
| **Prevalence of comorbidities**      |               |                   |                             |           |          |
| Hypertension                         |               |                   |                             |           |          |
| n (%)                                | 1,747         | 3,417             | 186                         | 5,350     | <0.0001* |
|                                      |               |                   |                             |           |          |
|                                      |               |                   |                             |           |          |
prevalence of hypertension (43.2%), dyslipidemia (34.8%), macrovascular disease (10.8%) and microvascular disease (16.7%)\textsuperscript{21}. In another study, there was a high prevalence of complications: microalbuminuria 30.3%, retinopathy 38.3%, nephropathy 44.6%, CAD 8.7%, CVD 6.7% and PAD 3.0%\textsuperscript{4}. The prevalence of diabetic complications in the present study is in line with the earlier studies; that is, neuropathy 22.5%, retinopathy 18.3%, microalbuminurea 16.1%, nephropathy 12.5%, CVD 11.5% and PVD 3.8%. The prevalence of comorbidities in our studies is high: hypertension 59.2%, high TG 36.4%, high LDL 33.2% and low HDL 33.2%. The present study also showed that patients with diabetic complications, such as retinopathy, nephropathy and long duration of diabetes, were significantly associated with a decreased chance of achieving target HbA1c, which is in line with an earlier study\textsuperscript{22}.

Hence, reducing the diabetes complications should be a public health priority in Asian populations\textsuperscript{17}. Earlier studies, including the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS), have shown the importance of strict glycemic control to prevent and/or reduce the risk of these complications\textsuperscript{23,24}. In the ALIT study, the majority of patients (72.9%) did not achieve HbA1c \leq 7\%, despite receiving Met + SU treatment. The reported inadequate metabolic control in these patients suggests that current treatment regimens might be insufficient to reach glycemic target. Early and persistent intensification of antidia-

Table 1 (Continued)

| Characteristics | Departments | Total | P-value |
|----------------|-------------|-------|---------|
| | Endocrinology | Internal medicine | Family medicine and others |
| High TC | n | 1,608 | 3,219 | 171 |
| | n (%) | 299 (18.6) | 975 (30.3) | 40 (23.4) |
| High LDL | n | 1,536 | 2,952 | 149 |
| | n (%) | 494 (32.2) | 989 (33.5) | 54 (36.2) |
| Low HDL | n | 1,528 | 2,950 | 148 |
| | n (%) | 440 (28.8) | 707 (24.0) | 34 (23.0) |
| High TG | n | 1,585 | 3,064 | 164 |
| | n (%) | 529 (33.4) | 1,165 (38.0) | 60 (36.6) |

FBG, fasting blood glucose; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; SD, standard deviation. n = 5,628. Missing data – weight: 816; waist circumference: 2111; body mass index (BMI): 857; diabetic retinopathy: 797; diabetic neuropathy: 557; diabetic nephropathy: 757; microalbuminuria: 1147; cardiovascular disease (CVD): 873; peripheral vascular disease (PVD): 1,138; hypertension: 258; total cholesterol (TC): 630; low-density lipoprotein (LDL): 991; high-density lipoprotein (HDL): 1,002; TG: 815. Cut-offs used – hypertension: blood pressure \(>130/80 \text{mmHg}\); High TC: \(>240 \text{mg/dL (6.1 mmol/L)}\); High LDL: \(>100 \text{mg/dL (2.5 mmol/L)}\); high HDL: in males <40 mg/dL (1.0 mmol/L), in females <50 mg/dL (1.2 mmol/L); high triglycerides (TG): \(>150 \text{mg/dL (1.6 mmol/L)}\). \*Chi-square test. †Analysis of variance test. #Angina/myocardial infarction/chronic heart failure/stroke.

Figure 1 | Achievement of target glycosylated hemoglobin (HbA1c) in subgroup and total patients (\(\chi^2\) P-value <0.0001).
glycemic control is an approach that most likely will achieve opti-
mal glycemic control in patients with type 2 diabetes and help
prevent associated complications. According to the Korean
guidelines, another oral hypoglycemic agent (OHA) is added
to existing OHA, if patients do not reach the HbA1c target. How-
ever, in the current study, the time to start combination ther-
apy after diagnosis is approximately 3.5 years. This can be due
to the clinical inertia in up-titration of treatment dose and initi-
aton of additional therapies, which could lead to suboptimal
glycemic control rates. In an earlier study, 45.1% of patients treated by specialists, the proportions were 36.2%
and 62.7%, respectively. One of the possible explanations for
this result is that the phenotype of patients with diabetes was
different between hospitals and primary care units. Therefore,
patients cared by specialists might have more severe diabetes.
In the present study, patients visiting endocrinologists had
more diabetic complications compared with patient visiting
internists and other primary care physicians (Table 1).

It has also been observed that the proportion of patient visits
meeting the minimally acceptable levels of quality was better in
the diabetes clinic than the general medicine clinic (73% vs
7.0%); the rest of the values are by χ²-test.

Table 2 | Factors associated with glycosylated hemoglobin target achievement by univariate and multivariate analysis

| Factors                        | Unadjusted OR (95% CI) | P-value | Adjusted OR (95% CI) | P-value |
|--------------------------------|------------------------|---------|----------------------|---------|
| Sex (male/female)              | 1.115 (0.99–1.255)     | 0.0721  |                      |         |
| Age (per 1 year higher)        | 1.01 (1.005–1.016)     | 0.0003* | 1.019 (1.01–1.029)   | <0.0001 |
| BMI (per 1 kg/m² higher)       | 1.025 (1.003–1.048)    | 0.0263* |                      |         |
| Abdominal circumference (per 1 cm higher) | 0.998 (0.991–1.005) | 0.5450* |                      |         |
| Diabetic retinopathy (yes vs no) | 0.537 (0.447–0.646) | <0.0001 | 0.455 (0.341–0.606) | 0.0001 |
| Diabetic nephropathy (yes vs no) | 0.911 (0.785–1.056) | 0.2147  |                      |         |
| Microalbuminuria (yes vs no)   | 0.524 (0.422–0.659)    | <0.0001 | 0.639 (0.43–0.949)   | 0.0104 |
| CVD (yes vs no)                | 0.797 (0.65–0.978)     | 0.0294  |                      |         |
| PVD (yes vs no)                | 0.524 (0.352–0.782)    | 0.0013  |                      |         |
| Hypertension (yes vs no)       | 0.947 (0.839–1.07)     | 0.3834  |                      |         |
| Dyslipidemia high TC (yes vs no) | 0.683 (0.59–0.791)    | <0.0001 |                      |         |
| Dyslipidemia high LDL (yes vs no) | 0.925 (0.806–1.061) | 0.2658  |                      |         |
| Dyslipidemia low HDL (yes vs no) | 0.97 (0.837–1.126)    | 0.6911  |                      |         |
| Dyslipidemia high TG (yes vs no) | 0.945 (0.829–1.078) | 0.4002  |                      |         |
| Duration of diabetes (≥5 years vs <5 years) | 0.522 (0.462–0.591) | <0.0001 | 0.493 (0.4–0.606)    | <0.0001 |
| Physican groups                |                        |         |                      |         |
| Endocrinology vs family medicine and others | 1.604 (1.133–2.270) | 0.0077  |                      |         |
| Endocrinology vs internal medicine | 1.498 (1.324–1.695) | <0.0001 | 1.417 (1.146–1.751) | 0.0013 |
| Internal medicine vs family medicine and others | 1.070 (0.760–1.507) | 0.6971  |                      |         |

BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HbA1c, glycosylated hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; Met, metformin; OR, odds ratio; PVD, peripheral vascular disease; SD, standard deviation; SU, sulfonylurea; TC, total cholesterol; TG, triglycerides. n = 5,628. ²P-value | *Unpaired t-test; the rest of the values are by χ²-test.

The present study reports that mean HbA1c in patients visiting
dermatology, internists and other primary care physicians was 7.6, 7.8 and 8.1%, respectively (P < 0.0001). Earlier studies also reported that patients treated by endocrinologists showed significantly lower HbA1c levels than that patients visiting primary care units (8.3% vs 8.7%, P = 0.01)²⁸, (7.9% vs 8.3%, P < 0.0001)²⁷. As aforementioned, this result could partly reflect a lack of drug intensification in primary care units. Therefore, the same prescriptions between specialist care and primary care are important for this kind of comparison. In the present study, despite the same Met + SU prescriptions, achievement of target HbA1c with endocrinologists was significantly better than that with internists or other primary care physicians; that is, 32.6% of patients treated by endocrinologists achieved target HbA1c, as compared with 24.4% of patients treated by internists and 23.2% of patients treated by other primary care physicians. On the contrary, an earlier study in Japanese patients with type 2 diabetes showed that the proportion of patients treated by general practitioners with HbA1c levels <6.5% and <7.0% were 43.1% and 62.7%, respectively, whereas for the patients treated by specialists, the proportions were 36.2 and 56.4%, respectively²⁹. One of the possible explanations for this result is that the phenotype of patients with diabetes was different between hospitals and primary care units. Therefore, patients cared by specialists might have more severe diabetes. In the present study, patients visiting endocrinologists had more diabetic complications compared with patient visiting internists and other primary care physicians (Table 1).
However, the present study also had some limitations. In this observational study, there could be bias in hospital selection and potential confounders if any. Another limitation was the cross-sectional nature of the study, which did not allow long-term follow up in terms of further intensification of antidiabetic therapy. The measurements of lipid profile and other clinical measurements were carried out in different laboratories/hospitals, hence there can be interlaboratory variations in the measurements. The present study did not collect data on any self-monitoring of blood glucose by patients. In addition, our study evaluated two specific OHAs, Met and SU, and did not collect information on the dosage of each medication. Also, the study did not collect data on adherence/compliance to the Met + SU treatment for controlling glycemia.

In conclusion, the majority of patients with type 2 diabetes in Korea have inadequate glycemic control, despite receiving Met + SU. Intensification of antihyperglycemic therapy is necessary to ensure optimal glycemic control in patients with type 2 diabetes in Korea. Therefore, future longitudinal studies to assess glycemic control in Korean patients over various time durations after starting/intensifying treatments are warranted.

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REFERENCES
1. International Diabetes Federation. Diabetes Atlas 5th Edition [Article online], 2011. Available at: http://www.idf.org/ diabetesatlas/5e/the-global-burden Accessed on 4 February 2013.
2. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010; 87: 4–14.
3. Kim DJ. The epidemiology of diabetes in Korea. Diabetes Metab J 2011; 35: 303–308.
4. Lim S, Kim DJ, Jeong IK, et al. A nationwide survey about the current status of glycemic control and complications in diabetic patients in 2006: the Committee of the Korean Diabetes Association on the Epidemiology of Diabetes Mellitus. Korean Diabetes J 2009; 33: 48–57.
5. Kim JH, Kim DJ, Jang HC, et al. Epidemiology of micro- and macrovascular complications of type 2 diabetes in Korea. Diabetes Metab J 2011; 35: 571–577.
6. Nathan DM, Buse JB, Davidson MB, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2009; 32: 193–203.
7. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/ American College of Endocrinology consensus panel on type 2 diabetes mellitus: an algorithm for glycemic control. Endocr Pract 2009; 15: 540–559.
8. Ko SH, Kim SR, Kim DJ, et al. 2011 clinical practice guidelines for type 2 diabetes in Korea. Diabetes Metab J 2011; 35: 431–436.
9. Proks P, Reimann F, Green N, et al. Sulfonylurea stimulation of insulin secretion. Diabetes 2002; 51(Suppl 3): S368–S376.
10. Herrmann LS, Schersten B, Bitzen PO, et al. Therapeutic comparison of metformin and sulfonylurea, alone and in various combinations. A double-blind controlled study. Diabetes Care 1994; 17: 1100–1109.
11. Lewin A, Lipetz R, Wu J, et al. Comparison of extended-release metformin in combination with a sulfonylurea (glyburide) to sulfonylurea monotherapy in adult patients with type 2 diabetes: a multicenter, double-blind, randomized, controlled, phase III study. Clin Ther 2007; 29: 844–855.
12. Declaration of Helsinki. Article I.9. Helsinki, Finland: Adopted by the 18th World Medical Assembly, Helsinki, 1964 as amended by the 59th World Medical Assembly, Seoul, 2008. Available at: http://www.wma.net/en/30publications/ 10policies/b3/17cpdf Accessed on 19 February 2013.
13. International Society for Pharmacoepidemiology. Guidelines for Good Epidemiology Practices for drug, Device, and Vaccine Research in the United States. Revised in 2007, 1996. Available at: http://www.pharmacoepiorg/resources/ guidelines_08027cfm Accessed on 19 February 2013.
14. International Epidemiology Association Guidelines for Proper Conduct in Epidemiologic Research. Available at: http://webcasthrsagov/conferences/mcb/mchepi_2009/ communicating_research/Ethical_guidelines/ IEA_guidelinespdf Accessed on 19 February 2013.
15. Choi YJ, Kim HC, Kim HM, et al. Prevalence and management of diabetes in Korean adults: Korea National Health and Nutrition Examination Surveys 1998-2005. Diabetes Care 2009; 32: 2016–2020.
16. Kim SG, Choi DS. The present state of diabetes mellitus in Korea. J Korean Diabetes Assoc 2008; 51: 791–798.
17. Chan JC, Malik V, Jia W, et al. Diabetes in Asia: epidemiology, risk factors, and pathophysiology. JAMA 2009; 301: 2129–2140.
18. Kim DJ, Song KE, Park JW, et al. Clinical characteristics of Korean type 2 diabetic patients in 2005. Diabetes Res Clin Pract 2007; 77(Suppl 1): S525–S527.
19. Glasgow RE, Hampson SE, Strycker LA, et al. Personal-model beliefs and social-environmental barriers related to diabetes self-management. Diabetes Care 1997; 20: 556–561.

20. Lee KU, Park JY, Kim SW, et al. Prevalence and associated features of albuminuria in Koreans with NIDDM. Diabetes Care 1995; 18: 793–799.

21. Rhee SY, Chon S, Kwon MK, et al. Prevalence of chronic complications in Korean patients with type 2 diabetes mellitus based on the Korean national diabetes program. Diabetes Metab J 2011; 35: 504–512.

22. Janghorbani M, Amini M. Patterns and predictors of long-term glycemic control in patients with type 2 diabetes. ISRN Endocrinol 2012; 2012: 526824.

23. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993; 329: 977–986.

24. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000; 321: 405–412.

25. Vinik A. Advancing therapy in type 2 diabetes mellitus with early, comprehensive progression from oral agents to insulin therapy. Clin Ther 2007; 29 Spec No: 1236–1253.

26. Knecht LA, Gauthier SM, Castro JC, et al. Diabetes care in the hospital: is there clinical inertia? J Hosp Med 2006; 1: 151–160.

27. Shah BR, Hux JE, Laupacis A, et al. Diabetic patients with prior specialist care have better glycaemic control than those with prior primary care. J Eval Clin Pract 2005; 11: 568–575.

28. Leinung MC, Gianoukakis AG, Lee DW, et al. Comparison of diabetes care provided by an endocrinology clinic and a primary-care clinic. Endocr Pract 2000; 6: 361–366.

29. Arai K, Hirao K, Matsuba I, et al. The status of glycemic control by general practitioners and specialists for diabetes in Japan: a cross-sectional survey of 15,652 patients with diabetes mellitus. Diabetes Res Clin Pract 2009; 83: 397–401.

30. Ho M, Marger M, Beart J, et al. Is the quality of diabetes care better in a diabetes clinic or in a general medicine clinic? Diabetes Care 1997; 20: 472–475.

SUPPORTING INFORMATION
Additional Supporting Information may be found in the online version of this article:

Table S1| Glycosylated hemoglobin levels according to patient characteristics (n = 5,628)