Seasonal Variations in the Achievement of Guideline Targets for HbA_{1c}, Blood Pressure, and Cholesterol Among Patients With Type 2 Diabetes: A Nationwide Population-Based Study (ABC Study: JDDM49)

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OBJECTIVE

Precise monthly achievement rates for reaching guideline targets for HbA_{1c}, blood pressure (BP), and lipid levels remain unknown. We evaluated achievement rates on a monthly basis in persons with type 2 diabetes mellitus (T2DM) and explored related factors.

RESEARCH DESIGN AND METHODS

This retrospective study initially analyzed data on 104,601 persons with T2DM throughout Japan. Patients whose HbA_{1c}, BP, and LDL cholesterol were measured ≥12 times during a 24-month period were included. We evaluated monthly achievement rates. Achieved targets were defined as HbA_{1c} <7%, BP <130/80 mmHg, and LDL cholesterol <100 mg/dL. Achievement of all targets was expressed as the "all ABC achievement."

RESULTS

A total of 4,678 patients were analyzed. The achievement rates of all ABC, HbA_{1c}, BP, and LDL cholesterol were lowest in winter, with those for systolic BP (SBP) being particularly low (all ABC, summer 15.6%, winter 9.6%; HbA_{1c}, 53.1%, 48.9%; SBP, 56.6%, 40.9%; LDL cholesterol, 50.8%, 47.2%). In winter, age ≥65 years (odds ratio 0.47 [95% CI 0.34–0.63]) was independently related to decreased achievement rates for SBP, BMI ≥25 kg/m^2 (BMI 25–30 kg/m^2, 0.45 [0.29–0.70]; BMI ≥30 kg/m^2, 0.35 [0.22–0.57]), and diabetes duration ≥10 years (0.53 [0.37–0.76]) were independently related to lower achievement rates for HbA_{1c}. Insulin use and sulfonylurea use were independently associated with the decreased all ABC achievement rates in both summer and winter.

CONCLUSIONS

The all ABC achievement rate for guideline targets changed on a monthly basis. Seasonal variations in the all ABC achievement rate should be considered when managing T2DM in ordinary clinical practices.

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The goal of treatment of type 2 diabetes mellitus (T2DM) is to reduce the incidence of cardiovascular (CV) events and improve the prognosis. In T2DM, comprehensive control of blood glucose levels, blood pressure (BP), and lipid levels was reported to lead to a decreased number of CV events and an improved prognosis (1). Conversely, some large-scale clinical trials reported different results for CV outcome and mortality in the achievement of the same HbA_{1c} target (2–4). A similar phenomenon was reported for BP (5,6) and lipid levels (7,8); therefore, target values are difficult to establish and should be revised as necessary. Currently, various academic societies have established target values as guidelines for blood glucose levels (9), BP (10), and lipid levels (11). Some recent statements have defined target values as ranges. In 2018, the American College of Physicians recommended in an evidence-based guidance statement (12) that T2DM should be treated to achieve an HbA_{1c} level between 7% and 8% rather than 6.5% to 7%, as previously recommended.

The reason for the different results for CV outcome and mortality in those persons having achieved the same target values might be that values were measured at different time points and frequencies in many large-scale clinical trials. Differences may also be due to seasonal variations (13–15), with worse values during the winter and more favorable values during the summer. To improve the prognosis of patients with T2DM, values should be evaluated at time points that would account for seasonal variations. It is important to intensify treatment when control worsens and to prevent adverse events such as hypoglycemia (16) and low BP (17) when the control is satisfactory. However, the achievement rates necessary to formulate effective specific treatment strategies remain unknown.

In the current study, we evaluated for the first time rates of achieving guideline targets for HbA_{1c}, BP, and LDL cholesterol on a monthly basis in patients with T2DM and explored factors affecting the achievement rates.

RESEARCH DESIGN AND METHODS

Patients

Thirty-eight medical clinics or general/university-affiliated hospitals specializing in diabetes care volunteered to participate in this study. These clinics were located in different areas in Japan (latitude variations of hospitals [degrees North], 26°12′44″–43°11′46″). They all used the same software, which was specifically developed for the Japan Diabetes Clinical Data Management (JDDM) Study Group to incorporate patient records from January 2013 to December 2014. Details of the JDDM and CoDiC were described previously (18).

The inclusion criteria were patients whose HbA_{1c}, BP, and LDL cholesterol levels were measured ≥12 times during the 2-year period; who were ≥20 years of age and <75 years of age; and who had received a diagnosis of T2DM based on criteria in the "Report of the Committee of the Japan Diabetes Society on the Classification and Diagnostic Criteria of Diabetes Mellitus" (19). Exclusion criteria were irregular clinic visits; visit intervals of >2 months; type 1 diabetes; hemodialysis for end-stage renal failure; and no information on antidiabetic drugs, antihypertensive agents, lipid-lowering agents, antiplatelet drug use, current smoking status, alcohol drinking status, family history of diabetes, or diabetes duration.

Of the 104,601 registered patients in 38 medical clinics, 4,678 were included in the analysis after excluding 82,092 patients with diabetes whose HbA_{1c}, body weight, or BP were not measured ≥12 times over the 2 years, who had irregular clinic visits, or who had visit intervals of >2 months. Also excluded were 4,152 patients under <20 years old or ≥75 years old, 1,275 patients with type 1 diabetes or end-stage renal failure on hemodialysis, and 12,404 patients whose LDL cholesterol level was not measured ≥12 times within 2 years or had no available information on use of antidiabetic drugs, antihypertensive agents, lipid-lowering agents, or antiplatelet drugs; current smoking status; alcohol drinking status; family history of diabetes; or diabetes duration (Supplementary Fig. 1).

The ethics committee of the JDDM, which also included outside members such as lawyers and ethics experts, approved the current study. The JDDM operates as an aggregate organization under the supervision of the central analytical facility and an ethics committee. All patients provided informed consent at each participating institute in accordance with the Guidelines for Epidemiological Studies of the Ministry of Health, Labor and Welfare of Japan.

Measurements

HbA_{1c}, expressed in National Glycohemoglobin Standardization Program units, was measured by high-performance liquid chromatography. Plasma glucose was measured by a glucose-oxidase method. BP was measured at each local medical institution according to the recommendations of the Japanese Ministry of Health, Labor, and Welfare. Plasma total cholesterol, HDL cholesterol, and triglycerides (TGs) were assessed with standard enzymatic spectrophotometric techniques. Plasma LDL cholesterol was calculated by the Friedewald equation or β-quantification methods (20). The estimated glomerular filtration rate (eGFR) was calculated with the MDRD formula. Clinical data (duration of diabetes; BMI; smoking status [never, current]; alcohol drinking status [never, current]; use of antidiabetic drugs, antihypertensive agents, and lipid-lowering agents; family history of diabetes) were obtained from medical records and a questionnaire.

Definitions

T2DM was defined according to fasting plasma glucose (FPG) concentration of ≥200 mg/dL or the provision of pharmacological treatment. In patients with an FPG concentration between ≥126 and <200 mg/dL, the measurement of FPG was repeated at another time. If the second FPG value was also ≥126 mg/dL, a diagnosis of T2DM was confirmed. Those with an FPG concentration <126 mg/dL underwent a standard oral glucose tolerance test (75 g of glucose over 2 h), and if FPG concentration was ≥126 mg/dL and/or 2-h plasma glucose concentration was ≥200 mg/dL, patients were considered to have T2DM. Hypertension was defined as systolic BP (SBP) ≥140 mmHg, diastolic BP (DBP) ≥90 mmHg, and/or the current use of antihypertensive agents based on the criteria of the American Heart Association and the American College of Cardiology (21,22). Dyslipidemia was defined as abnormal values for one or more from among HDL cholesterol <40 mg/dL, LDL cholesterol ≥120 mg/dL, TGs ≥150 mg/dL, and/or the current use of lipid-lowering agents based on criteria in

the Japan Atherosclerosis Society Guidelines (23).

Summer was defined as June, July, and August, and winter as December, January, and February. The mean values for HbA_{1c}, SBP, DBP, and LDL cholesterol measured in the summer (2 years) and winter (2 years) were calculated for each patient by the same methods.

Achievements of targets were defined as HbA_{1c} <7% (9), SBP <130 mmHg, and DBP <80 mmHg (10) according to the American Diabetes Association, and LDL cholesterol <100 mg/dL according to the American Association for Clinical Endocrinologists (11). Achievement rates for both HbA_{1c} <8% and HbA_{1c} <7% were analyzed. In this study, the proportion of achievement of all guideline targets for HbA_{1c}, SBP, DBP, and LDL cholesterol was expressed as the "all ABC achievement rate." "A" stands for HbA_{1c}, "B" for BP, and "C" for LDL cholesterol. This study was carried out by the Japan Diabetes Clinical Data Management (JDDM) Study Group as part of the JDDM study; therefore, we named this study ABC Study: JDDM49.

Study Outcome

The primary objective was to evaluate the all ABC achievement rate for each month (Fig. 1*A*). Secondary objectives included evaluation of the achievement rates for HbA_{1c}, SBP, DBP, and LDL cholesterol for each month (Fig. 1*B*); the all ABC achievement rates in summer and winter (Fig. 1*C*); and the achievement rates for HbA_{1c}, SBP, DBP, and LDL cholesterol, respectively, in summer and winter (Fig. 1*D*). The factors affecting the all ABC achievement rate in summer and winter as well as those affecting the achievement rates for HbA_{1c}, SBP, DBP, and LDL cholesterol individually in summer and winter were also studied (Table 2). Objectives also included the following evaluations for the summer and winter: the proportion of patients in the BP target groups (SBP <130 mmHg and DBP <80 mmHg; SBP ≥130 mmHg; or DBP ≥80 mmHg) for each HbA_{1c} target group (HbA_{1c} <7% or ≥7%) (Supplementary Fig. 2*A*), the proportion of patients in the LDL cholesterol target groups (LDL cholesterol <100 mg/dL or ≥100 mg/dL) for each HbA_{1c} target group (Supplementary Fig. 2*B*), and the proportion of patients in the BP target groups for each LDL cholesterol target group (Supplementary Fig. 2*C*).

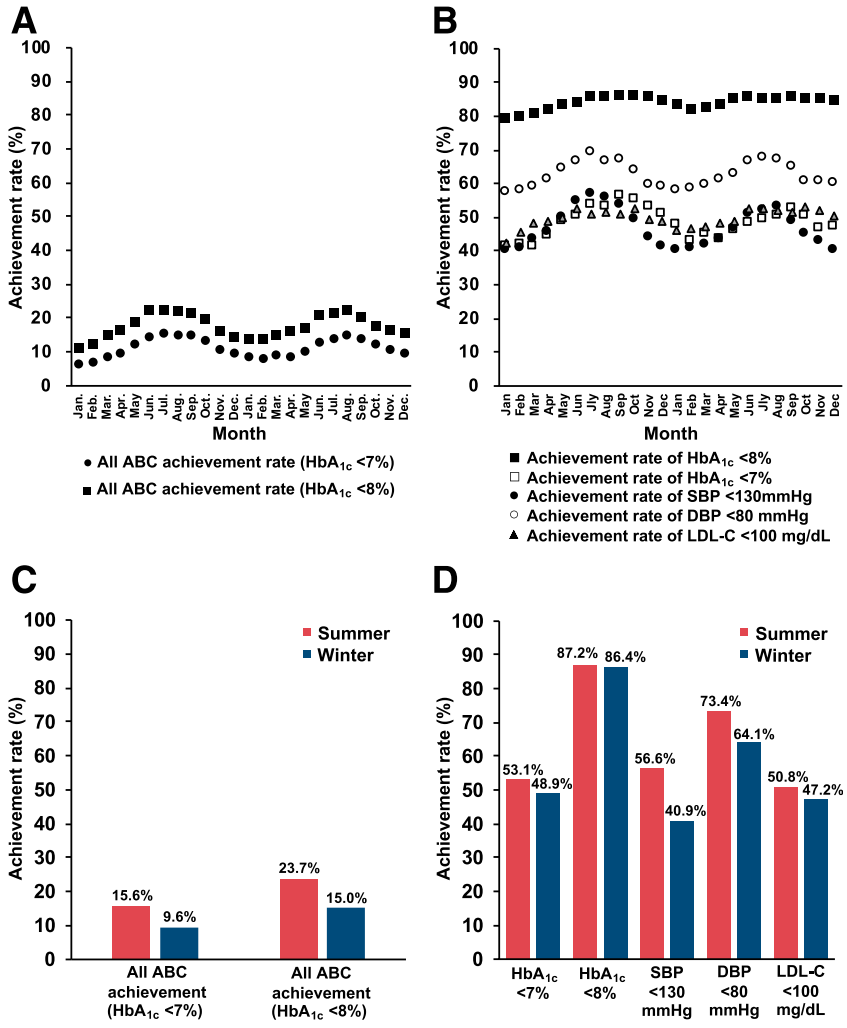

Figure 1—Achievement rates for all ABC, HbA_{1c}, BP, and LDL cholesterol throughout the year (*A* and *B*) and in summer and winter (*C* and *D*). *A*: All ABC (HbA_{1c} [<7% or <8%], BP, and LDL cholesterol) achievement rates monthly over a period of 2 years. *B*: Monthly achievement rates for HbA_{1c}, BP, and LDL cholesterol over a 2-year period. *C*: All ABC achievement rates in summer and winter in a 2-year period. *D*: Achievement rates for HbA_{1c} (<7% or <8%), SBP, DBP, and LDL cholesterol in summer and winter in a 2-year period. LDL-C, LDL cholesterol.

Statistical Methods

Patients' characteristics and results are presented as the mean ± SD or the median with the interquartile range, as appropriate according to data distribution. Multiple logistic regression analysis was used to determine the independent associations between achievement of all ABC, HbA_{1c}, SBP, DBP, and LDL cholesterol targets, respectively, in summer and winter, and the variables of sex, age, diabetes duration, family history of diabetes, BMI, eGFR, history of hypertension, antihypertensive agent use, history of dyslipidemia, lipid-lowering agent use, antiplatelet drug use, insulin use, sulfonylurea (SU) use, metformin use, dipeptidyl peptidase 4 (DPP-4) inhibitor use, glucagon-like peptide 1 (GLP-1) receptor agonist use, glinide use, α-glucosidase inhibitor use, thiazolidinedione use, current smoking status, and current alcohol drinking status (Table 2). Age, diabetes duration, BMI, and eGFR were included as quadrichotomous variables. For the BMI, which was included as a covariate, the average BMI for summer and winter, respectively, was used for multiple logistic regression analysis. Separate models were constructed using the following dependent variables: in summer and winter, achievement of *1*) all ABC, *2*) HbA_{1c} <7%, *3*) SBP <130 mmHg, *4*) DBP <80 mmHg, and *5*) LDL cholesterol <100 mg/dL. The results were

expressed as an odds ratio with 95% CI. A P value <0.001 was considered significant. Data analyses were performed using the Statistical Package for the Social Sciences version 22.0 software (IBM, Armonk, NY).

RESULTS

Baseline Characteristics of Study Participants

A total of 4,678 patients were analyzed. Table 1 shows the characteristics of the study participants. The mean ± SD age of participants was 61.3 ± 9.4 years, and the mean HbA_{1c} was 57.2 ± 13.5 mmol/mol (mean % HbA_{1c} 7.4 ± 1.2%). The prevalence of study participants ever diagnosed with hypertension or dyslipidemia was 65.3% or 83.7%, respectively.

Achievement Rates of All ABC, HbA_{1c}, BP, and LDL Cholesterol in All Seasons

The achievement rates for all ABC (Fig. 1*A*), HbA_{1c}, BP, and LDL cholesterol varied seasonally (Fig. 1*B*). The achievement rate for HbA_{1c} <8% was the highest, followed by that for DBP <80 mmHg (Fig. 1*B*). Equivalent achievement rates for HbA_{1c} <7%, SBP <130 mmHg, and LDL cholesterol <100 mg/dL were found (Fig. 1*B*). The achievement rates for all ABC (Fig. 1*C*), HbA_{1c}, SBP, DBP, and LDL cholesterol (Fig. 1*D*) in the summer were higher than in the winter. Differences between the achievement rates in summer and winter were the largest for SBP (Fig. 1*D*).

Factors involved in the decrease in achievement rates for all ABC, HbA_{1c}, BP, or LDL cholesterol were revealed by the multiple logistic regression analysis (Table 2). In winter, BMI ≥25 kg/m^2 and diabetes duration ≥10 years were independently related to lower achievement rates for HbA_{1c}. Age ≥65 years was independently related to the decreased achievement rate for SBP in winter. No obvious factor was related to the decreased achievement rate for LDL cholesterol in winter. The proportions of patients who achieved HbA_{1c}, BP, or LDL cholesterol targets within each HbA_{1c} target group, BP target group, or LDL cholesterol target group in summer and winter are shown in Supplementary Fig. 2.

Table 1—Baseline characteristics of the study population

Data	
No. of patients	4,678
Male/female, *n*	2,948/1,730
Age (years)	61.3 ± 9.4
Latitude variation of hospitals (degrees North)	26°12′44″–43°11′46″
Diabetes duration (years)	12.6 ± 8.6
Hypertension, *n* (%)	3,055 (65.3)
Dyslipidemia, *n* (%)	3,914 (83.7)
Glycemic control	
Casual blood glucose (mg/dL)	161.4 ± 63.6
HbA_{1c} (mmol/mol)	57.2 ± 13.5
HbA_{1c} (%)	7.4 ± 1.2
No. of HbA_{1c} measurements in 2 years (times/2 years)	19.0 ± 3.7
BP (mmHg)	
Systolic	133.8 ± 16.0
Diastolic	77.3 ± 11.5
No. SBP measurements in 2 years (times/2 years)	19.0 ± 3.7
No. DBP measurements in 2 years (times/2 years)	19.0 ± 3.7
Lipid profile (mg/dL)	
TG	122 (85–180)
LDL cholesterol	107.0 ± 29.7
HDL cholesterol	54.8 ± 14.5
No. LDL cholesterol measurements in 2 years (times/2 years)	17.8 ± 4.0
BMI (kg/m^2)	
Baseline	25.5 ± 4.3
Summer mean	25.3 ± 4.4
Winter mean	25.4 ± 4.3
eGFR (mL/min/1.73 m^2)	74.4 ± 20.1
First visit, *n* (%)	
January	3,701 (79.1)
February	715 (15.3)
March	85 (1.8)
Others	177 (3.8)
Antidiabetic drugs	
Insulin, *n* (%)	1,127 (24.1)
SU, *n* (%)	1,916 (41.0)
Metformin, *n* (%)	2,206 (47.2)
DPP-4 inhibitors, *n* (%)	2,161 (46.2)
GLP-1 receptor agonists, *n* (%)	143 (3.1)
Glinides, *n* (%)	180 (3.8)
α-Glucosidase inhibitors, *n* (%)	762 (16.3)
Thiazolidinediones, *n* (%)	593 (12.7)
Antihypertensive agents, *n* (%)	2,314 (49.5)
Antihypertensive agent use for hypertension (%)	75.8
Lipid-lowering agents, *n* (%)	2,468 (52.8)
Lipid-lowering agent use for dyslipidemia (%)	63.1
Antiplatelet drugs, *n* (%)	433 (9.3)
Current smokers, *n* (%)	609 (13.0)
Current alcohol drinking, *n* (%)	966 (20.6)

Values are mean ± SD or median (25th–75th percentiles) unless otherwise indicated.

CONCLUSIONS

This is the first clinical study to assess the monthly achievement rates for guideline targets for HbA_{1c}, BP, and LDL cholesterol and the all ABC achievement rate in those with T2DM. We retrospectively assessed data on patients with T2DM whose HbA_{1c}, BP, and LDL cholesterol were measured ≥12 times during a 2-year period.

The results showed that the achievement rates for guideline targets for HbA_{1c}, BP, and LDL cholesterol and the all ABC achievement rate varied seasonally (Fig. 1*A* and *B*). The analysis of achievement rates by season (summer and winter) indicated that the all ABC achievement rate was highest in the summer (June, July, August) and lowest in the winter (December, January, February) (Fig. 1*C*). As to guideline targets

Table 2—Multiple logistic regression analysis for achievement of All ABC, HbA_{1c}, BP, and LDL cholesterol guideline targets in summer and winter

	All ABC		HbA_{1c} <7%		SBP <130 mmHg		DBP <80 mmHg		LDL-C <100 mg/dL	
	Summer	Winter	Summer	Winter	Summer	Winter	Summer	Winter	Summer	Winter
Female sex	0.73 (0.61–0.88)*	1.10 (0.88–1.38)	0.77 (0.67–0.89)*	0.87 (0.75–1.00)	0.94 (0.82–1.07)	1.16 (1.01–1.34)	2.61 (2.21–3.09)*	3.04 (2.61–3.55)*	0.61 (0.53–0.69)*	0.72 (0.63–0.83)*
Age										
<45 years (reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
46–55 years	0.86 (0.53–1.38)	0.84 (0.47–1.52)	0.86 (0.63–1.18)	1.03 (0.75–1.41)	1.03 (0.76–1.39)	0.76 (0.56–1.03)	0.86 (0.63–1.17)	0.98 (0.72–1.34)	1.12 (0.82–1.51)	1.04 (0.77–1.42)
56–65 years	1.17 (0.76–1.82)	0.99 (0.57–1.70)	1.11 (0.82–1.49)	1.33 (0.98–1.80)	1.01 (0.76–1.35)	0.65 (0.48–0.87)	1.79 (1.33–2.40)*	2.14 (1.59–2.89)*	1.29 (0.97–1.73)	1.30 (0.97–1.75)
≥65 years	1.31 (0.84–2.06)	1.21 (0.69–2.11)	1.41 (1.04–1.92)	1.76 (1.28–2.41)*	0.79 (0.59–1.07)	0.47 (0.34–0.63)*	3.52 (2.55–4.84)*	3.78 (2.76–5.18)*	1.52 (1.13–2.06)	1.45 (1.07–1.97)
Diabetes duration										
<1 year (reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1–5 years	0.68 (0.43–1.06)	0.84 (0.45–1.54)	1.15 (0.80–1.67)	0.79 (0.55–1.15)	0.99 (0.69–1.40)	0.69 (0.48–0.99)	1.02 (0.70–1.48)	0.80 (0.56–1.16)	1.06 (0.74–1.52)	1.13 (0.78–1.63)
5–10 years	0.58 (0.37–0.90)	0.74 (0.40–1.36)	0.85 (0.59–1.23)	0.62 (0.43–0.89)	0.92 (0.65–1.31)	0.63 (0.44–0.90)	0.93 (0.64–1.35)	0.62 (0.43–0.90)	1.11 (0.78–1.59)	1.18 (0.82–1.70)
≥10 years	0.63 (0.41–0.97)	0.94 (0.52–1.70)	0.66 (0.47–0.94)	0.53 (0.37–0.76)*	0.96 (0.69–1.35)	0.77 (0.55–1.10)	1.31 (0.91–1.88)	1.02 (0.71–1.45)	1.12 (0.79–1.58)	1.23 (0.86–1.75)
Family history of diabetes	0.92 (0.75–1.13)	1.19 (0.93–1.51)	0.89 (0.76–1.04)	0.94 (0.80–1.10)	1.23 (1.06–1.44)	1.12 (0.96–1.30)	1.40 (1.17–1.69)*	1.34 (1.13–1.59)*	0.77 (0.66–0.90)*	0.86 (0.74–1.01)
BMI										
<18.5 (kg/m^2) (reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
18.5–25 (kg/m^2)	0.76 (0.48–1.18)	0.81 (0.45–1.44)	1.09 (0.73–1.61)	0.71 (0.46–1.10)	0.59 (0.39–0.90)	0.79 (0.52–1.20)	0.86 (0.50–1.47)	1.10 (0.67–1.82)	0.67 (0.46–0.99)	0.71 (0.47–1.08)
25–30 (kg/m^2)	0.48 (0.30–0.77)	0.52 (0.28–0.95)	0.65 (0.43–0.97)	0.45 (0.29–0.70)*	0.45 (0.29–0.69)*	0.61 (0.40–0.94)	0.60 (0.35–1.04)	0.83 (0.50–1.37)	0.62 (0.42–0.92)	0.69 (0.45–1.05)
≥30 (kg/m^2)	0.39 (0.23–0.66)*	0.43 (0.22–0.86)	0.50 (0.32–0.77)	0.35 (0.22–0.57)*	0.31 (0.20–0.49)*	0.43 (0.27–0.68)*	0.42 (0.24–0.75)*	0.64 (0.38–1.09)	0.60 (0.39–0.91)	0.68 (0.43–1.06)
eGFR										
<30 mL/min/1.73 m^2 (reference)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
30–60 mL/min/1.73 m^2	1.04 (0.49–2.21)	0.64 (0.27–1.48)	0.82 (0.47–1.42)	0.91 (0.52–1.60)	1.24 (0.74–2.09)	1.04 (0.60–1.79)	0.36 (0.15–0.87)	0.37 (0.17–0.80)	1.36 (0.79–2.33)	1.27 (0.74–2.17)
60–90 mL/min/1.73 m^2	0.91 (0.44–1.92)	0.68 (0.30–1.56)	0.76 (0.44–1.32)	0.81 (0.47–1.40)	1.08 (0.65–1.80)	1.05 (0.61–1.80)	0.24 (0.10–0.58)	0.24 (0.11–0.52)*	1.44 (0.84–2.45)	1.28 (0.75–2.17)
≥90 mL/min/1.73 m^2	0.78 (0.36–1.69)	0.66 (0.28–1.58)	0.55 (0.31–0.97)	0.57 (0.33–1.01)	0.93 (0.55–1.58)	0.89 (0.51–1.55)	0.21 (0.09–0.51)*	0.26 (0.12–0.55)*	1.53 (0.88–2.65)	1.43 (0.83–2.47)
Hypertension	0.38 (0.28–0.51)*	0.15 (0.09–0.26)*	0.99 (0.81–1.20)	1.13 (0.93–1.38)	0.19 (0.15–0.23)*	0.11 (0.09–0.14)*	0.24 (0.20–0.30)*	0.20 (0.16–0.25)*	0.97 (0.80–1.17)	1.04 (0.86–1.26)
Antihypertensive agent use	2.16 (1.58–2.94)*	4.87 (2.78–8.53)*	1.28 (1.06–1.56)	1.06 (0.87–1.29)	1.91 (1.59–2.30)*	2.84 (2.26–3.56)*	1.81 (1.49–2.21)*	2.16 (1.77–2.62)*	1.32 (1.09–1.59)	1.15 (0.96–1.39)
Dyslipidemia	0.44 (0.34–0.58)*	0.35 (0.25–0.50)*	0.53 (0.43–0.65)*	0.58 (0.47–0.71)*	0.93 (0.77–1.13)	0.79 (0.65–0.96)	0.86 (0.68–1.08)	0.89 (0.72–1.09)	0.31 (0.26–0.38)*	0.30 (0.25–0.37)*
Lipid-lowering agent use	2.51 (2.00–3.16)*	3.05 (2.24–4.16)*	1.40 (1.20–1.63)*	1.41 (1.21–1.65)*	1.28 (1.11–1.49)	1.42 (1.21–1.66)*	0.92 (0.78–1.10)	0.90 (0.77–1.06)	3.65 (3.13–4.24)*	3.89 (3.34–4.54)*
Antiplatelet drugs	1.19 (0.91–1.56)	1.43 (1.04–1.98)	0.89 (0.71–1.12)	0.96 (0.77–1.21)	1.23 (0.99–1.52)	1.38 (1.11–1.71)	2.11 (1.56–2.86)*	1.92 (1.48–2.48)*	1.02 (0.82–1.26)	0.99 (0.80–1.23)
Antidiabetic drugs										
Insulin use	0.41 (0.32–0.53)*	0.30 (0.22–0.42)*	0.18 (0.15–0.22)*	0.17 (0.14–0.21)*	0.61 (0.52–0.71)*	0.67 (0.56–0.79)*	1.06 (0.88–1.28)	1.17 (0.98–1.40)	1.02 (0.87–1.19)	1.01 (0.86–1.18)
SU use	0.60 (0.50–0.73)*	0.54 (0.42–0.69)*	0.35 (0.30–0.41)*	0.31 (0.26–0.36)*	0.84 (0.73–0.97)	0.83 (0.71–0.96)	1.06 (0.89–1.25)	1.09 (0.93–1.27)	0.91 (0.79–1.04)	0.84 (0.73–0.97)
Metformin use	0.96 (0.80–1.15)	0.88 (0.70–1.11)	0.92 (0.80–1.06)	0.93 (0.81–1.07)	0.89 (0.78–1.02)	0.83 (0.72–0.95)	1.00 (0.85–1.17)	0.88 (0.76–1.02)	1.40 (1.23–1.60)*	1.46 (1.28–1.67)*
DPP-4 inhibitor use	0.90 (0.75–1.07)	0.83 (0.66–1.03)	0.71 (0.62–0.82)*	0.77 (0.67–0.88)*	1.02 (0.89–1.16)	0.97 (0.85–1.11)	0.90 (0.77–1.05)	0.81 (0.69–0.93)	1.24 (1.09–1.42)	1.19 (1.04–1.36)
GLP-1 receptor agonists use	0.31 (0.14–0.69)	0.36 (0.14–0.90)	0.25 (0.16–0.38)*	0.26 (0.17–0.42)*	0.78 (0.53–1.13)	0.70 (0.47–1.04)	0.84 (0.56–1.27)	0.68 (0.46–1.01)	1.18 (0.81–1.71)	0.95 (0.65–1.38)
Glinide use	0.87 (0.56–1.35)	0.71 (0.41–1.25)	0.63 (0.45–0.89)	0.76 (0.54–1.08)	1.02 (0.73–1.43)	1.09 (0.78–1.54)	1.07 (0.72–1.60)	1.28 (0.88–1.86)	1.00 (0.72–1.39)	0.84 (0.60–1.17)
α-Glucosidase inhibitor use	1.06 (0.85–1.33)	1.14 (0.86–1.51)	1.22 (1.02–1.46)	1.13 (0.95–1.36)	1.18 (0.99–1.40)	0.94 (0.79–1.12)	1.44 (1.17–1.78)*	1.36 (1.12–1.64)	1.07 (0.90–1.27)	1.01 (0.85–1.19)
Thiazolidinedione use	1.50 (1.18–1.91)*	1.15 (0.84–1.57)	1.07 (0.88–1.30)	1.13 (0.93–1.38)	1.28 (1.05–1.55)	0.90 (0.73–1.10)	1.36 (1.08–1.72)	1.37 (1.11–1.70)	1.55 (1.27–1.89)*	1.54 (1.27–1.87)*
Current smoker	1.05 (0.81–1.36)	1.20 (0.87–1.66)	0.80 (0.65–0.98)	0.94 (0.76–1.16)	1.28 (1.05–1.57)	1.00 (0.81–1.22)	1.46 (1.16–1.84)	1.34 (1.08–1.66)	1.08 (0.88–1.31)	1.01 (0.83–1.23)
Current alcohol drinking	1.12 (0.89–1.40)	0.99 (0.75–1.32)	1.31 (1.09–1.58)	1.26 (1.05–1.52)	1.11 (0.93–1.33)	1.20 (1.00–1.44)	0.74 (0.60–0.90)	0.89 (0.74–1.08)	1.19 (1.00–1.43)	1.20 (1.01–1.43)

Values given are odds ratio (95% CI). *$P < 0.001$. LDL-C, LDL cholesterol.

for HbA_{1c}, BP, and LDL cholesterol, the achievement rate for SBP was particularly low in the winter (Fig. 1*D*).

Our results further support existing data showing that there are seasonal variations in blood glucose, BP, and lipid levels (13). However, the limitation of previous studies was that these parameters were measured only once or twice a year. These parameters have been reported to be controlled by various factors, including physical activity (24,25), eating behaviors (25), insulin resistance (26), and body composition (27). Since a previous study (28) reported that resting sympathetic nerve activity varies seasonally, with peak levels evident in winter, the seasonal variation in sympathetic activity may contribute to the all ABC achievement rate. Temperature was also reported to be the most influential factor in seasonal variations in these parameters (13,24). Although this study did not compare achievement rates between the southern and northern areas of Japan, the pattern of seasonal variations in achievement rates can be expected to differ depending on the climate pattern. In fact, in a country with minimal monthly temperature variations, HbA_{1c} variations were reported to be small throughout the year (29). Regarding BP, since it was reported that SBP increases by 5.7 mmHg every time the temperature decreases by 10°C regardless of latitude (30), the seasonal variation in the achievement rate may be smaller in areas with small temperature differences between summer and winter, such as southern areas in Japan. On the other hand, during the winter holidays, in particular the New Year holidays, people are customarily physically inactive because of snow and temperature drops, and they traditionally indulge in salty meals, such as soup. Body weight tends to increase over holidays (31), which may be a factor in the yearly increased levels of HbA_{1c}, BP, and lipids among persons with T2DM. In fact, HbA_{1c} and cholesterol levels were reported to be increased during winter holiday periods (32). Another study (33) reported that adult outpatients in a tropical country have a circannual pattern of HbA_{1c} values reflecting holiday celebrations in the preceding 3 months. These reports may explain why it is more difficult for patients with diabetes to meet targets in winter.

This study explored and evaluated factors affecting the rates for the achievement of guideline targets for HbA_{1c}, BP, and LDL cholesterol on a monthly basis. In the winter, advanced age was found to be an independent factor for the lower SBP achievement rate. Since the SBP achievement rate was particularly low in winter, these results may be an important factor in lowering the all ABC achievement rate in winter. Among patients of advanced age, atherosclerosis might have prevented meeting BP goals in winter. Atherosclerosis impairs vasodilatability and CV autonomic function (34), and the effectiveness of functions for regulating BP decreases. Therefore, BP increases may be due to the exacerbation of various factors affecting BP in the winter, further decreasing the rate of achieving BP targets. BMI $\geq$25 kg/m^2 and diabetes duration $\geq$10 years were independently associated with the decreased achievement rates for HbA_{1c} in winter. Obese patients with T2DM and/or those with diabetes of a long duration may experience large changes in physical activity and food intake in winter.

The analysis according to antidiabetic drug use revealed that insulin use and SU use were independently associated with decreased all ABC achievement rates in both summer and winter. Insulin and SU are administered to patients whose hyperglycemia is relatively difficult to treat. In fact, Table 2 shows that these drugs were independently associated with decreased HbA_{1c} achievement rates. Interestingly, insulin use was independently associated with a lower achievement rate for SBP. Thus, physicians should pay more attention to the all ABC achievement rates throughout the year in patients using these drugs.

A recent investigation of the prognosis of T2DM (35) showed that in patients with T2DM, the percentage of preventable CV events was approximately one-third even if the patient succeeded in smoking cessation in addition to appropriate control of blood glucose, BP, and lipid levels. Causes may be long-term glycemic variability (36,37), long-term BP variability (38,39), and long-term lipid level variability (40), which are residual risk factors for CV events and were not evaluated.

The design and methods of this study had several strengths. First, the study included data only on patients with T2DM whose HbA_{1c}, BP, and LDL cholesterol levels were measured $\geq$12 times during a 2-year period. Second, patients with T2DM (n = 4,678) from throughout Japan (latitude variation of hospitals [degrees North] 26°12′44″–43°11′46″) were analyzed. This study also has some limitations. First was its retrospective design, which carries the risk of selection bias. Second, the number of study patients was small, and participants were a subgroup from a prior study. Third, medication adherence was not considered during the 2-year period. Fourth, the effects of temperature, physical activity, food intake including salt intake, and cultural factors on the achievement rates were not examined. In addition, although the range of the latitudes of the locations of the study hospitals were disclosed, individual hospital data were not disclosed so that we could not examine the effects of latitude differences on achievement rates. Fifth, participants included patients with T2DM who were under treatment for comorbidities such as arterial hypertension and dyslipidemia. Sixth, the basis of treatment for Japanese patients with diabetes differs from that for Caucasian patients, such as metformin use and DPP-4 inhibitor use.

In summary, this study showed that in patients with T2DM, the achievement rates for blood glucose, BP, and lipid target levels varied seasonally, and that the achievement rates for these parameters were lowest in winter. The individual background of each patient would also affect achievement rates. It is important to take seasonal variations in the all ABC achievement rate into consideration in managing patients in ordinary clinical practice. Furthermore, it could be expected that intensifying treatment for each value in the winter might lead to the prevention of CV events. A large-scale clinical trial needs to be conducted to verify which intervention to reduce seasonal variations would lead to the greatest decrease in CV events in the near future.

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