Current status of achieving blood pressure target and its clinical correlates in Japanese type 2 diabetes (JDDM45)

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ABSTRACT
Aims/Introduction: To investigate the current status of achieved blood pressure levels in association with the number of antihypertensive drug classes as of 2013, and to explore the clinical correlates with achievement of target blood pressure in a large-scale cohort of Japanese individuals with type 2 diabetes.

Materials and Methods: A nationwide survey was carried out including 12,811 individuals with type 2 diabetes. Participants were divided by achieved blood pressure, <130/80 or 140/90 mmHg, and the number of drug classes taken.

Results: The percentages achieving a blood pressure of <130/80 or 140/90 mmHg were 52.0% and 86.1%, respectively. The prevalence of hypertension, if defined as ≥130/80 mmHg, became 67.9%. Among participants taking antihypertensive drugs, a blood pressure of <130/80 or <140/90 mmHg was 46.7% and 83.2%, respectively. The percentages of <130/80 mmHg were 55.9% without drugs, 47.1% on one drug, 42.5% on two drugs, 47.2% on three drugs and 56.8% on four or more drugs, respectively. The most prescribed drugs were renin-angiotensin system inhibitors, followed by calcium channel blockers, diuretics and beta-blockers. The multiple logistic regression analysis showed that a blood pressure <130/80 mmHg was associated with lower values in age, body mass index, albuminuria and glomerular filtration rate, higher proportions on targets for glycosylated hemoglobin A1c and lipids, and less retinopathy.

Conclusions: In type 2 diabetes, hypertension is common, and just 52% achieved <130/80 mmHg, indicating a difficulty in blood pressure lowering. This was correlated with difficulties in glycemic and lipid management, obesity, and vascular complications, implying this clustering to be a serious problem.

INTRODUCTION
High blood pressure (BP) is reported in over two-thirds of patients with type 2 diabetes mellitus, but the details of prevalence are unclear. Hypertension and type 2 diabetes mellitus are inextricably linked1,2, and BP lowering is often difficult in individuals with type 2 diabetes mellitus as compared with those without diabetes3,4. Treatment with antihypertensive drugs has been developed during the past two decades, and several studies have recently shown an improved trend of BP lowering, not only in non-diabetic individuals, but also in diabetes patients5-9. Several clinical trials have shown intensive BP lowering in type 2 diabetes mellitus to be extremely beneficial for reducing cardiovascular events, renal function loss and all-cause death10-13. Currently, tighter BP control might be disseminating widely5-9,14; therefore, it is important to clarify the current status of BP lowering in type 2 diabetes mellitus patients in terms of future healthcare strategies. However, just a few studies have reported the percentage of patients achieving the target BP5-6, what factors are correlated with the achievement of target BP6, how the number of antihypertensive drug classes to be taken is distributed5 or the percentages of achieved...
target BP with respect to the number of antihypertensive drug classes. In the present study, we aimed at investigating the current status of achieving BP levels in association with the number of antihypertensive drug classes as of 2013, and explored the clinical correlates to the achievement of target BP in a large-scale cohort of Japanese individuals with type 2 diabetes mellitus.

METHODS

Study population

A multicenter study was carried out encompassing 27 medical clinics (i.e., general practitioners) from different areas throughout Japan, including urban and rural areas from north to south (as mentioned in the Acknowledgments), using the same software to incorporate patient records to carry out scientific activities as part of the Japan Diabetes Clinical Data Management Study Group. The group consists of medical doctors specializing in diabetology who have volunteered to dedicate their time to recording clinical data of the attending patients with diabetes in daily clinical practice. The study was carried out in primary care settings. Individuals with diabetes who visited the clinic from May to August in 2013 and had received treatment for more than 1 year before this study, which included education on diet and exercise, and medication for controlling blood glucose, BP and lipids according to the guidelines by the Japan Diabetes Society (JDS), were enrolled (Figure 1). The patients who did not visit regularly or had visit intervals of ≥2 months were not included. Patients with secondary hypertension were excluded on the basis of interview, clinical manifestations and measurements of hormones if necessary. Patients with end-stage renal failure requiring dialysis or type 1 diabetes were excluded.

The patients who met the aforementioned criteria regularly attending the clinic every 1–2 months, and who had available data for urinary albumin and serum creatinine (Cr) were entered in the present study (n = 12,811; Figure 1). Treatment goals recommended by the JDS were a glycosylated hemoglobin A1c (HbA1c) value of <7.0% (53 mmol/mol), BP of <130/80 mmHg, and serum concentrations of low-density lipoprotein (LDL) cholesterol <3.1 mmol/L (120 mg/dL), triglycerides <1.7 mmol/L (150 mg/dL) and high-density lipoprotein cholesterol ≥1.0 mmol/L (40 mg/dL). The JDS and Japanese Society for Hypertension guidelines recommended using antihypertensive drugs initially from renin–angiotensin system inhibitors (RASI), followed by the addition of calcium channel blockers (CCB) or low-dose thiazide diuretics, and beta-blockers. The dose administered of each antihypertensive drug was principally the standard dose, except for thiazide diuretics, which were used at a low dose, and optimal dose amounts were used if the standard dose was not adequate with or without the use of other classes. Two drugs from the same antihypertensive class were not allowed. The study protocol was approved by the ethics committees of the Japan Diabetes Clinical Data Management and each clinic. All patients provided informed consent, and the study was carried out in accordance with the Helsinki Declaration II.

Measurements

BP was measured with an appropriately sized cuff in the sitting position after resting for at least 5 min, using an automated
standardized BP device. BP was measured three times on the three visits during the study period and the average was used. The concomitant use of antihypertensive drugs was noted, where antihypertensive drugs were basically not changed during the study period. Non-fasting blood samples were drawn and analyzed to measure serum creatinine and lipids at local laboratories once during the period. The normal values were the same. HbA1c was measured by high performance liquid chromatography (normal range 4.6–6.2%), which has been certified by the American National Glycohemoglobin Standardization Program. Serum and urinary concentrations of Cr were measured by an enzymatic method. Urinary albumin was measured using random urine samples by a turbidimetric immunoassay. The urinary albumin excretion rate was measured using the albumin-to-creatinine ratio (ACR). Normoalbuminuria, microalbuminuria, and macroalbuminuria were defined as an ACR <30 mg/g Cr, ACR ≥30 and <300 mg/g Cr, and ACR ≥300 mg/g Cr, respectively. The glomerular filtration rate (GFR) was estimated (eGFR) using the following equation by the Japanese Society of Nephrology: eGFR (mL/min/1.73 m²) = 194 × serum Cr−1.094 × age−0.287 × 0.739 (if female). LDL cholesterol was calculated by Friedewald’s formula. With regard to treatment of diabetes, patients were divided into groups by treatment of diet alone, hypoglycemic tablets or insulin. Cardiovascular disease (CVD) included coronary artery disease and ischemic stroke, including coronary, cerebrovascular and carotid revascularization, which was diagnosed by the doctor who treated the CVD and was noted in the medical record. Diabetic retinopathy was diagnosed after pupillary dilation by an ophthalmologist.

The BP target in the present study was <130/80 mmHg in accordance with the guidelines by the JDS and Japanese Society for Hypertension15. As the recent BP target by the 8th Joint National Committee guidelines was <140/80 mmHg for individuals with diabetes16, we analyzed in parallel the present data using an additional BP target of <140/80 mmHg. The number of antihypertensive classes was recorded, and the classes were categorized as RASI, CCB, diuretics, beta-blocker and others. The diuretics included thiazides, loop diuretics and the mineralocorticoid receptor antagonist, spironolactone; these were not divided, but the diuretics being taken were mostly thiazides. Spironolactone was not used as the first choice of diuretic because of the risk of hyperkalemia, gynecomastia and reduction of libido. The combined drug of RASI with a low-dose thiazide diuretic was counted as one RASI and one diuretic. The pill number and the dose were not collected. Participants were divided by achieving or not achieving BP levels, and the number of antihypertensive drug classes taken. Clinical characteristics were compared between participants achieving or not achieving a BP <130/80 mmHg; this analysis was carried out separately in participants with and without the use of antihypertensive drugs. The combination of antihypertensive drug classes in association with the percentage of achieving a BP of <130/80 mmHg was also investigated.

Statistical analysis
Data were expressed as the mean ± standard deviation if normally distributed, otherwise as the median and interquartile range. The significance of the differences between the two groups was determined by χ²-tests for categorical variables, and Student’s t-test for continuous variables. Triglycerides and albuminuria were logarithmically transformed before the analysis because of the skewed distribution. Multivariate logistic regression analysis was carried out to explore variables associated with achieving the BP target (<130/80 mmHg). A P-value of <5% (two-tailed) was considered significant. All analyses were carried out with the statistical software package SPSS (SPSS Japan, Tokyo, Japan).

RESULTS
Table 1 shows the number and percentages of participants by the number of antihypertensive drug classes taken. The percentage with a BP of <130/80 was 52.0%, and the prevalence of hypertension was 67.9% (8,702/12,811) if hypertension was defined as ≥130/80 mmHg or treated. Among the 5,463 patients treated with antihypertensive drugs, just 46.7% achieved a BP of <130/80 mmHg. The achievement rates of a BP of <130/80 mmHg by the number of antihypertensive drugs were 55.9% (4,109/7,384) without drugs, 47.1% (1,187/2,519) on one drug, 44.5% (828/1,860) on two drugs, 47.2% (394/834) on three drugs and 56.8% (142/234) on four or more drugs. The most prescribed drug was RASI, followed by CCB, diuretics and beta-blockers, which was in accordance with the guidelines by the Japanese Society for Hypertension and JDS.

The clinical characteristics between participants who achieved and did not achieve a BP of <130/80 mmHg were compared between those who took antihypertensive drugs and those who did not take them, and are shown in Table 2. In participants without the use of antihypertensive drugs, those who achieved a BP of <130/80 mmHg were characterized by lower body mass index (BMI) and HbA1c, lower insulin-use, lower values of systolic/diastolic BP, pulse pressure, LDL cholesterol, triglycerides, and ACR; higher value of high-density lipoprotein cholesterol; and lower percentages with retinopathy as compared with participants who did not achieve the target BP. The achievement rates in terms of HbA1c and lipid targets were significantly higher in participants who achieved a BP of <130/80 mmHg. Similarly, in participants who used antihypertensive drugs, those who achieved a BP of <130/80 mmHg were characterized by older age, lower BMI and HbA1c, lower insulin-use, lower values of systolic/diastolic BP, pulse pressure, LDL cholesterol, triglycerides, ACR and eGFR, lower percentage of retinopathy and higher achievement rates for HbA1c and lipid targets.

Among participants using antihypertensive drugs, the use of each antihypertensive drug class in association with the rate of achieving the target BP (<130/80 mmHg) is shown in Table 3. In participants taking one drug, the percentage on target was

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### Table 1 | Number and percentage of participants achieving the blood pressure levels of <130/80 or <140/90 mmHg by the number of antihypertensive drug classes

| No. antihypertensive drug classes | 0  | 1  | 2  | 3  | ≥4  | Total | Participants taking antihypertensive drugs |
|----------------------------------|----|----|----|----|-----|-------|---------------------------------------------|
| **Target <130/80 mmHg**          |    |    |    |    |     |       |                                             |
| On target                        |    |    |    |    |     |       |                                             |
| Systolic BP (mmHg)               |    |    |    |    |     |       |                                             |
| Diastolic BP (mmHg)              |    |    |    |    |     |       |                                             |
| Not on target                    |    |    |    |    |     |       |                                             |
| **Total**                        |    |    |    |    |     |       |                                             |
| RASI (%)                         |    |    |    |    |     |       |                                             |
| CCB (%)                          |    |    |    |    |     |       |                                             |
| Diuretics (%)                    |    |    |    |    |     |       |                                             |
| Beta-blocker (%)                 |    |    |    |    |     |       |                                             |
| Others (%)                       |    |    |    |    |     |       |                                             |
| **Target <140/90 mmHg**          |    |    |    |    |     |       |                                             |
| On target                        |    |    |    |    |     |       |                                             |
| Systolic BP (mmHg)               |    |    |    |    |     |       |                                             |
| Diastolic BP (mmHg)              |    |    |    |    |     |       |                                             |
| Not on target                    |    |    |    |    |     |       |                                             |
| **Total**                        |    |    |    |    |     |       |                                             |

Total n = 12,811. BP, blood pressure; CCB, calcium channel blocker; RASI, renin–angiotensin system inhibitor.

### Table 2 | Comparison of clinical characteristics in participants who achieved and did not achieve target blood pressure <130/80 mmHg in those who took and those who did not take antihypertensive drugs

|                                                  | In participants without use of antihypertensive drugs (n = 7,348, 57.4%) | In participants with use of antihypertensive drugs (n = 5,463, 42.6%) |
|--------------------------------------------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------|
|                                                  | BP on target (n = 4,109, 32.1%) | BP not on target (n = 3,239, 25.3%) | P-value                   | BP on target (n = 2,551, 19.9%) | BP not on target (n = 2,912, 22.7%) | P-value |
|                                                  |                                |                                 |                          |                             |                                       |          |
| **Men (%)**                                      | 62.1                          | 64.6                            | <0.05†                   | 61.7                        | 59.7                                | NS†      |
| **Age (years)**                                  | 63.1 ± 11.3                   | 63.5 ± 11.3                     | NS‡                      | 67.7 ± 9.7                  | 67.0 ± 10.7                         | <0.05‡   |
| **BMI (kg/m²)**                                  | 24.0 ± 4.0                    | 25.1 ± 4.2                      | <0.001†                  | 25.4 ± 4.2                  | 25.9 ± 4.3                          | <0.001†  |
| **HbA1c (%)**                                    | 7.0 ± 0.8                     | 7.1 ± 0.9                       | <0.001‡                  | 7.0 ± 0.8                   | 7.2 ± 0.9                           | <0.001‡  |
| **HbA1c (mmol/mol)**                             | 50.1 ± 3.6                    | 54.1 ± 3.6                      | <0.001‡                  | 53.1 ± 3.6                  | 55.1 ± 3.6                          | <0.001‡  |
| **Known duration of diabetes (years)**           | 13.3 ± 8.9                    | 13.6 ± 8.6                      | NS§                      | 15.2 ± 9.5                  | 15.1 ± 8.9                          | NS§      |
| **Diet/hypoglycemic tablets/insulin (%)**         | 337 ± 293/834 (82/715/203)    | 280 ± 220/745 (87/683/23.1)     | <0.05†                   | 196 ± 1733/615 (77/681/242)   | 233 ± 1841/832 (80/634/286)         | <0.01†   |
| **Systolic BP (mmHg)**                           | 119 ± 8                       | 136 ± 9                         | <0.001†                  | 120 ± 7                     | 137 ± 8                             | <0.001†  |
| **Diastolic BP (mmHg)**                          | 68 ± 7                        | 78 ± 8                          | <0.001†                  | 67 ± 8                      | 76 ± 9                              | <0.001   |
| **Pulse pressure (mmHg)**                        | 50 ± 8                        | 58 ± 11                         | <0.001†                  | 53 ± 8                      | 61 ± 11                             | <0.001   |
| **LDL cholesterol (mg/dL)**                      | 56.4 ± 15.2                   | 55.0 ± 15.4                     | <0.001†                  | 53.4 ± 14.0                 | 53.2 ± 14.3                         | NS§      |
| **Triglycerides (mg/dL)‡**                       | 111.0 (770–1620)              | 122.0 (840–1770)                | <0.001†                  | 122.0 (870–1750)            | 127.0 (890–1840)                    | <0.01†   |
| **Albuminuria (mg/g Cr)§**                       | 100.0 (580–2240)              | 132.0 (720–3820)                | <0.001†                  | 160.0 (810–4850)            | 208.0 (970–8000)                    | <0.001†  |
| **Normo-/micro-/macroalbuminuria (%)**           | 802.0/173.2/23                | 699.0/247.5/5.5                 | <0.001†                  | 653.0/280/67                | 582.0/315/103                       | <0.001†  |
| **eGFR (mL/min/1.73 m²)**                        | 73.9 ± 21.1                   | 74.3 ± 19.8                     | NS‡                      | 67.0 ± 21.6                 | 69.4 ± 20.0                         | <0.01†   |
| **Retinopathy (%)**                              | 23.2                          | 31.3                            | <0.001†                  | 34.4                        | 39.7                                | <0.01†   |
| **History of CVD (%)**                           | 12.7                          | 14.1                            | NS‡                      | 23.4                        | 25.1                                | NS‡      |
| **HbA1c on target (%)**                          | 54.9                          | 48.3                            | <0.001†                  | 54.9                        | 48.3                                | <0.001†  |
| **Lipids on target (%)**                         | 44.0                          | 37.0                            | <0.001†                  | 37.7                        | 32.6                                | <0.001†  |
| **Both A1c and lipids on target (%)**            | 25.5                          | 19.2                            | <0.001†                  | 22.6                        | 16.1                                | <0.001†  |

Total n = 12,811. All the data were available except for 279 data for lipids (2.2%). †The χ²-test. ‡Student’s t-test. §Median and interquartile range are given. †Mann–Whitney U-test. BMI, body mass index; BP, blood pressure; Cr, creatinine; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA1c, glycosylated hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, not significant.
Taking 1 class (\(\text{HbA1c} = 0.84 (0.74 \text{–} 1.00)\))

Taking any drug (\(\text{HbA1c} = 1.37 (1.23 \text{–} 1.53)\))

Taking 2 classes (\(\text{HbA1c} = 1.48 (1.25 \text{–} 1.75)\))

Antihypertensive drug use (\(\text{HbA1c} = 0.95 (0.88 \text{–} 1.01)\))

No. antihypertensive drug classes (\(\text{HbA1c} = 1.14 (1.06 \text{–} 1.26)\))

Statistical analyses were carried out by \(\chi^2\)-tests. CCB, calcium channel blocker; RASI, renin–angiotensin system inhibitor; NS, not significant.

**DISCUSSION**

In the present multicenter-based study dealing with a large number of Japanese patients with type 2 diabetes mellitus, the prevalence of hypertension was 67.9% (\(\geq 130/80\) mmHg or treated) and 49.4% (\(\geq 140/90\) mmHg or treated). Among participants taking antihypertensive drugs, percentages of a BP of \(<130/80\) or \(\geq 140/90\) mmHg were 46.7% and 83.2%, respectively. Furthermore, among patients not taking antihypertensive drugs, just 55.9% achieved a BP of \(<130/80\) mmHg. These figures show that hypertension is quite common in type 2 diabetes mellitus, and lowering the BP to \(<130/80\) mmHg in type 2 diabetes mellitus is difficult.
There have been several clinical epidemiological studies on the rate of achieving BP target, while methodological differences are unavoidable in these evaluations. Egan et al. reported that the rate of a BP of $<140/90$ mmHg in diabetes patients with treated hypertension was 48% in 1990 ($n = 783$) and 62% in 2000 ($n = 842$). The corresponding rates in all adult treated-hypertensive participants were 54% and 69%, respectively. This showed an improvement in achieving BP target both in participants with and without diabetes, and persisting difficulty in lowering BP for participants with diabetes. Nilsson et al. also demonstrated from data of the Swedish National Diabetes Registry that the rate of achieving a BP of $<130/80$ mmHg in treated-hypertensive patients with type 2 diabetes mellitus was 13% in 2005 ($n = 57,645$), which improved to 17% in 2007 ($n = 96,801$) and to 20% in 2009 ($n = 145,158$). They found that the decrease in BP levels was associated with an increase in antihypertensive drug treatment and a decrease in BMI. Cummings et al. investigated the correlates of a BP of $<130/80$ mmHg, including covariates such as race, calendar year, exercise intensity, household income, education and medical adherence, for 5,217 hypertensive diabetes patients. They found that the calendar year of 2007 relative to 2003 was significantly correlated with achieving a BP of $<130/80$ mmHg independent of other covariates, although the achievement rate of a BP of $<130/80$ mmHg was low at 30–43%. Comparatively, the rates of achieving a BP of $<140/90$ and 130/80 mmHg in the present study were much higher. The reason might be that the present study was carried out in 2013, which was more recent than the aforementioned studies, and was carried out with Japanese participants. Ethnic differences might affect the prevalence and BP control, which was shown previously.

Few epidemiological studies were carried out to analyze the relationship between BP target achievement and clinical parameters in detail. We found that the achievement of a BP target of $<130/80$ mmHg was associated with younger age, lower BMI, on target for HbA1c and lipids, lower albuminuria, and the absence of retinopathy. The finding was prominent in participants not taking antihypertensive drugs. These findings simply show that individuals who achieved the target BP could easily achieve targets for HbA1c and lipids, and were less complicated. In contrast, individuals failing to achieve the target BP often have difficulties in glycemic and lipid controls, which can lead to developing microvascular complications. These findings might indicate a link with the difficulties in achieving the three treatment targets. The mechanisms related to the link are likely to include insulin resistance in the nitric oxide pathway, the stimulatory effects of hyperinsulinemia on the sympathetic drive, smooth muscle growth and sodium–fluid retention, and the excitatory effects of hyperglycemia on the renin–angiotensin–aldosterone system. Retinopathy, albuminuria and CVD were associated with failure to achieve BP targets. The clustering of cardiovascular risk factors and difficulties in achieving each treatment target in type 2 diabetes mellitus patients is a very serious problem in daily practice. The association of albuminuria with a difficulty in achieving BP target could be because albuminuria is a marker for endothelial dysfunction and organ damage, which are known to be caused by elevated blood glucose and blood pressure levels. These findings highlight that more aggressive multifactorial treatment strategies are required for treatment-resistant individuals with type 2 diabetes mellitus. The finding of CVD and lower eGFR being positively correlated with achieving target BP was presumably driven on statistics due to aggressive BP treatment for individuals with a history of CVD and severe renal impairment.

Curiously, in all participants, antihypertensive drug use was not associated with achieving the target BP. In participants taking antihypertensive drugs, the achievement rates of target BP of $<130/80$ mmHg by the number of antihypertensive drugs were 47.1% on one drug, 44.5% on two drugs, 47.2% on three drugs and 56.8% on four or more drugs. Only a few studies previously reported the number of antihypertensive drugs in type 2 diabetes mellitus, but none reported the relationship with achieving BP levels in detail. Although the number of antihypertensive drugs remained significant in achieving target BP among participants using antihypertensive drugs in the multiple regression analysis, increasing the number of drugs was not in proportion to the increase in the achieving rate. These findings show that the use of drugs with increasing the number might not simply translate into achieving the target BP.

There were some limitations to the present study. First, we could not take the dose of drugs into account in this epidemiological study, although the standard dose was principally administered. Second, we did not take the measure of adherence to the drugs into account. Poor medication adherence is an important problem in type 2 diabetes mellitus, which contributes to the treatment outcomes. The patients in the present study attended the clinic regularly every 1–2 months, as is standard in any clinic in Japan run by general practitioners, and data were not self-reported but were derived from medical records; therefore, poor adherence might not largely affect the main result. Third, we should acknowledge the clinic-to-clinic variation in the measurement of BP and laboratory tests in terms of the device and other conditions caused by a multicenter study design. Fourth, we did not distinguish spironolactone from thiazide diuretics. Although the use of spironolactone was rare in the present study, spironolactone has been recently reported as useful for patients with type 2 diabetes mellitus, and the aggressive challenge to use it might be beneficial and should be investigated in the future. Fifth, we should acknowledge a possible participation bias. The primary care setting could represent the outpatients seen by GPs in Japan. However, the rate of achieving target BP in the present participants might be better than in those seen by GPs not specializing in diabetes care; or alternatively, medical doctors specializing in diabetes might have more complicated patients. The aforementioned potential weaknesses might be offset by the large and
representative nature of this nationwide study. The strength was that the measurements of BP were obtained on three different days. We found that, in addition to RASI in patients taking two different antihypertensive drug classes, the rate on target was significantly higher than the rate of not on target in users of beta-blockers and diuretics, but this was not the case with CCB users. This might indicate that beta-blockers and diuretics are more effective than CCB in addition to RASI. However, the results are simply reflected by the decision of each doctor regarding what drug should be added to each individual patient. These were likely derived from the individual’s data and doctor’s intention. This was an observational study and not designed to search for the effects of drug class. We acknowledge that these limitations inherent to such an observational study call for future randomized studies.

In conclusion, hypertension is quite common, and lowering BP to <130/80 mmHg is still at the moment difficult in patients with type 2 diabetes mellitus. Increasing the number of antihypertensive drugs did not translate into increasing the rate of achieving the target BP in proportion. A difficulty in achieving a BP of <130/80 mmHg was related to difficulties in glycemic and lipid management, obesity, and vascular complications, implying this clustering to be a serious problem in daily practice.

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DISCLOSURE
The authors declare no conflict of interest.

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APPENDIX 1

Japan Diabetes Clinical Data Management study group

The following clinics from the Japan Diabetes Clinical Data Management study group contributed to the present study: Ajihara Clinic (Fukushima), Asiya Chuou Hospital (Fukuoka), HEC Science Clinic (Kanagawa), Izumino Clinic (Ibaraki), Iwasaki Clinic (Yamaguchi), Jiyugaoka Medical Clinic (Hokkaido), Jiyugaoka Yamada Clinic (Hokkaido), Kato Clinic (Shizuoka), Kawai Clinic (Ibaraki), Kudo Clinic (Aomori), Kurihara Clinic (Hokkaido), Miyazawa Clinic (Hokkaido), Oishi Clinic (Kyoto), Okada Clinic (Fukuoka), Seino Clinic (Fukushima), Sugimoto Clinic (Fukuoka), Takai Clinic (Niigata), Takaki Clinic (Fukuoka), Isahaya Clinic (Okinawa), Takamura Clinic (Tokyo), Toshiba Rinkan Hospital (Kanagawa), Tsutsumi Hospital (Kumamoto), Wakamatsu memorial hospital (Kagoshima) and Yagi Clinic (Okinawa).