Association between mandatory health examination attendance and diabetes treatment initiation among employees being treated for hypertension

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Abstract

Objectives: It is unclear whether mandatory health examination is effective for employees who are already being treated for chronic diseases. We focused on patients being treated for hypertension and evaluated the association between employer-based health examination attendance and diabetes treatment initiation.

Methods: Using a database that stores health insurance claims and health examination results of subscribers enrolled in society-managed health insurance plans in Japan, we identified employees aged 40-59 years who were being treated for hypertension when starting diabetes treatment from April 2012 to December 2016. A case-crossover analysis was conducted using 90, 180, and 270 days prior to diabetes treatment initiation as reference points and 90 days after the mandatory health examination as the exposure period. We conducted a subgroup analysis by hemoglobin A1c (HbA1c) level and frequency of outpatient blood glucose testing before the mandatory health examination.

Results: We identified 1464 individuals starting treatment for diabetes while on antihypertensive drugs. The overall odds ratio for starting diabetes treatment within 90 days of the health examination was 1.89 (95% confidence interval: 1.70-2.10). The subgroup analysis showed that this odds ratio increased as HbA1c level increased and as blood glucose testing frequency decreased.

Conclusions: Among employees starting treatment for diabetes while being treated for hypertension, employer-based mandatory health examination attendance was associated with initiation of diabetes treatment. The health examinations may be functioning as a complement to screening in outpatient settings.

Keywords
diabetes mellitus, hypertension, occupational health
1 | INTRODUCTION

The prevention of mortality and morbidity caused by cardiovascular disease (CVD) is a major objective in the treatment of hypertension. However, multiple CVD risk factors frequently coexist in individuals with hypertension. Diabetes mellitus (DM) is a common comorbidity, and the combination of hypertension and DM substantially increases the risk of CVD.1-4 Associations with increased risks of microvascular diseases such as nephropathy and retinopathy have also been suggested.5,6 Optimal management for patients with DM and hypertension, such as the target blood pressure, remains controversial. However, early diagnosis and treatment of DM is essential for individuals with hypertension.2-4,7,8

The implementation of effective preventive strategies is important in reducing the burden of non-communicable diseases including hypertension and DM.9 In Japan, annual employer-based health examinations for employees are mandated by the Industrial Safety and Health Act. Since the Act's implementation in 1972, items have been added to the mandatory health examination to meet the need for identifying non-communicable diseases among employees. In 2008, an amendment was made in accordance with the Act on Assurance of Medical Care for Elderly People, which required insurers to conduct health examinations focusing on metabolic syndrome for all insured persons aged 40-74 years. Although the cost-effectiveness of these mandatory health examinations is controversial, several studies have demonstrated the examinations' effectiveness.10,11

However, to date, there has not been a study that focused on employees being treated for chronic diseases. Hypertension is common among employees, and a considerable proportion of working people are already under treatment for the condition. Because primary care physicians providing treatment may also play a role in identifying DM in this population, it is unknown whether employer-based health examinations have any additional effect on the diagnosis and treatment of DM.

The aim of the present study was to evaluate the association between attending the employer-based mandatory health examination and DM treatment initiation among individuals being treated for hypertension in an outpatient setting. We also evaluated whether screening for DM and other conditions was being conducted in an outpatient setting in this population.

2 | MATERIALS AND METHODS

2.1 | Health examinations for employees in Japan

Under the Industrial Safety and Health Act, employers in Japan are obliged to ensure the safety and health of employees in the workplace.12 Employers must provide their employees with an annual health examination. The purpose of this health examination is to have employers assess the health status of their employees, and employees who are already under a physician's care must also comply. Results of these health examinations are reported to the employees, and employers are obligated to endeavor to provide health guidance by physicians or public health nurses to employees who require such guidance. The components of the health examination are specified by the Ordinance on Industrial Safety and Health and include urinalysis, chest X-ray, blood pressure measurement, and blood analysis.

2.2 | Data source

We used the JMDC Claims Database (JMDC Inc), a database of health insurance claims and health examination results in Japan. Under the universal health coverage system in Japan, everyone living in Japan must be enrolled in a health insurance plan; the plan in which individuals enroll is determined by their age and employment status. Society-managed health insurance, the National Health Insurance Association, and Mutual Aid Associations cover employees of large companies, small-to-medium companies, and the public sector, respectively, as well as their dependants. Citizens’ health insurance covers those who are self-employed or irregularly employed. The Late Elders’ Health Insurance is for those aged 75 years or older and those aged 65-74 years with certain disabilities. The services covered by insurance and their fees are set by the government and are the same for all plans.13,14 The JMDC Claims Database stores anonymous data provided by society-managed health insurance organizations. A subscriber can be followed as long as he/she continues to enroll in the same insurance scheme and the data are provided to JMDC. Subscriber information includes gender, employment status (employee or dependent), year and month of birth, and data provision period. All medical claims data on covered outpatient, inpatient, and pharmacy services are recorded. This includes consultations, drugs, and procedures. Drugs are classified according to the Anatomical Therapeutic Chemical Classification System, and diagnoses are recorded based on International Classification of Diseases 10th Revision codes. Health examination records in the database include the date of examination, health questionnaires, the presence of signs/symptoms, and the results of laboratory tests.

The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Institutional Review Board of the Graduate School of Medicine, The University of Tokyo. The requirement for informed consent was waived because of the anonymous nature of the data.
2.3 | Sample selection

Using data from the JMDC Claims Database from April 2012 to December 2016, we first identified subscribers meeting the following inclusion criteria: (a) born from May 1952 to March 1977; (b) insured employee; and (c) attended a health examination during the study period. From subscribers meeting all three criteria, we selected individuals with a diagnosis record of hypertension and continuous outpatient prescription of antihypertensive drugs. The codes used for the identification of these drugs are presented in Table S1. Continuous treatment was defined as having a prescription interval of ≤90 days, and individuals with missing data on the prescription date for antihypertensive drugs were excluded. We then identified those who started a medication for DM while being treated for hypertension. The codes used for the identification of these drugs are also presented in Table S1. We required individuals in the sample to be aged 40-59 years when the treatment for DM began and to have been on continuous antihypertensive medication for at least 360 days before treatment for DM. Those with missing data on the prescription date for medication for DM were excluded. Furthermore, we excluded individuals who had not attended a health examination within 360 days before the start of DM treatment. Individuals with no record of urine glucose, hemoglobin A1c (HbA1c), or blood sugar from health examinations within 360 days before the start of DM treatment were also excluded.

2.4 | Variables

We analysed the type of DM medication based on the claims record for the first treatment for DM. These medications were classified into eight groups \(^{15}\): sulfonylureas, biguanides, α-glucosidase inhibitors, dipeptidyl peptidase-4 inhibitors, sodium-glucose co-transporter-2 inhibitors, other non-insulin glucose-lowering agents (thiazolidinediones, glinides or glucagon-like peptide-1 receptor agonists), a combination of medications without insulin, and any treatment including insulin. Claims records were used to identify the frequency of HbA1c or glycoalbumin testing in an outpatient setting prior to the most recent health examination. In the Japanese fee schedule, there is a specific reimbursement for the outpatient management of lifestyle-related diseases conducted by primary care physicians at clinics or small hospitals (<200 beds). Claims records for this reimbursement prior to the health examination were also extracted. Antihypertensive agents were categorized into the following groups based on first prescription during the observation period \(^{16}\): angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs); calcium channel blockers; diuretics or β-blockers; a combination of ACE inhibitors/ARBs and calcium channel blockers; a combination of ACE inhibitors/ARBs and diuretics; a combination of calcium channel blockers and diuretics; a combination of ACE inhibitors or ARBs, calcium channel blockers and diuretics; and combination therapy including β-blockers. Using data on the most recent health examination prior to DM treatment, we calculated the interval between the health examination and initiation of DM treatment. The following examination results were extracted: presence of any subjective symptoms or objective signs, body mass index, waist circumference, systolic and diastolic blood pressures, HbA1c, fasting blood sugar, urine glucose, and urine protein. Questionnaire results for the following variables were also obtained: current smoking status, frequency of alcohol consumption, weight change of 3 kg or more in the last year, perception of healthier lifestyles (stage according to the Transtheoretical model), and intention to receive health guidance following the examination.

2.5 | Statistical analysis

We conducted a case-crossover analysis to evaluate the association between the time period after the health examination and the initiation of DM treatment. \(^{17}\) In the case-crossover design, exposure frequency during the window period before the outcome is compared with exposure frequencies during other reference times within an individual. Only the cases are included in the analysis, and the self-controlled nature of the design controls for confounding by time-independent characteristics. In this study, the initiation of treatment for DM was the outcome. Three reference time points were selected: 90, 180, and 270 days prior to the initiation of DM treatment. Considering the interval between the health examination and outpatient consultation, we set 90 days after the health examination as an exposure period. A schematic presentation of a case-crossover analysis is shown in Figure 1. A Mantel–Haenszel estimate treating each individual as a separate stratum was used to derive the odds ratio (OR) of the exposure. A subgroup analysis was conducted, categorizing individuals by frequency of glucose testing in an outpatient setting and

FIGURE 1 Schematic presentation of a case-crossover analysis. Each line represents a timeline of an individual, with shaded time representing the period after the health examination (exposure period). The initiation of diabetes treatment is indicated with a black triangle, and reference time points are indicated with white triangles.
by HbA1c level during the health examination. Individuals with missing HbA1c values were excluded from the subgroup analysis. We also performed the analyses limiting the sample to individuals with claims records for outpatient primary care management of lifestyle-related diseases.

We conducted several sensitivity analyses to test the robustness of the results. First, the exposure period was changed to 120, 60, and 30 days following the examination, and the interval of reference time points was altered to 60 days (60, 120, and 180 days prior to the initiation of DM treatment) in the main analysis to consider the effect of various lengths of time between the health examination and DM treatment initiation. Second, individuals who received at least one health examination with no laboratory tests (urine glucose, HbA1c, or blood sugar) during the 360 days prior to DM treatment initiation were excluded. Third, health examinations with no laboratory tests (urine glucose, HbA1c, or blood sugar) were excluded from the exposures. These analyses were performed to examine the possible impact of including health examinations that are unlikely to have affected DM treatment initiation in the exposure. Finally, a medication possession ratio ≥80% for antihypertensive drugs was added to the definition of patients under continuous hypertension treatment. A two-sided P value of less than 0.05 was considered statistically significant. IBM SPSS, Version 25 (IBM) was used for the statistical analyses.

3 | RESULTS

Figure 2 illustrates the sample selection process. From 760,963 subscribers, we identified 110,170 people who were on continuous treatment for hypertension (14.5%). Of these individuals, 4173 had started treatment of DM. There were 1464 people who met the inclusion criteria. Their average age was 51.9 years (standard deviation, 4.9 years), and 91% were male. The demographic characteristics of the study participants are presented in Table 1. For 29% of the sample, neither HbA1c nor glycoalbumin testing was conducted in an outpatient setting. Claims records for outpatient primary care management of lifestyle-related diseases were present for 1291 participants (88%). Tables 2 and 3 present the results of the most recent health examination. HbA1c was 6.5% or higher for 973 participants (66%), and fasting blood sugar was 126 mg/dL or greater for 737 participants (50%). The median interval between health examination and the initiation of DM treatment was 125 days (interquartile range: 50-235 days).

The results of the main analysis and the subgroup analysis are presented in Table 4. The overall OR of the health examination and 90 days following it was 1.89 (95% confidence interval [CI], 1.70-2.10), indicating a significant association between attending a health examination and the initiation of treatment for DM. When limiting the sample to individuals with claims records for outpatient primary care management of lifestyle-related diseases, the overall OR was 1.95 (95% CI, 1.75-2.19). In the subgroup analysis categorizing participants by frequency of glucose testing in an outpatient setting and HbA1c level at the health examination, the OR increased as HbA1c level increased and as frequency of glucose testing in an outpatient setting prior to the health examination decreased. The same trend was observed among participants with claims records for outpatient primary care management of lifestyle-related diseases.

In the sensitivity analyses, the overall ORs when changing the exposure period to 120, 60, and 30 days following the health examination were 1.95 (95% CI, 1.76-2.16), 2.03 (95% CI, 1.80-2.30), and 1.67 (95% CI, 1.39-2.00) respectively. When the reference time points were set at 60, 120, and 180 days prior to the initiation of DM treatment, the overall ORs with the exposure periods of 60 and 30 days were 1.88 (95% CI, 1.66-2.12) and 1.47 (95% CI, 1.23-1.76).

FIGURE 2 Selection of eligible patients starting treatment for diabetes mellitus while on continuous treatment for hypertension, using the JMDC Claims Database
respectively. In the analysis that excluded the periods after health examinations without laboratory tests from the exposure, the overall OR was 1.91 (95% CI, 1.72-2.12). Finally, the analysis excluding employees who received a health examination without laboratory tests and the analysis of employees with a medication possession ratio ≥0.8 showed ORs of 1.92 (95% CI, 1.73-2.14, n = 1403) and 1.92 (95% CI, 1.72-2.15, n = 1365) respectively.
In this study, we conducted a case-crossover analysis, which is one of the self-controlled study designs. In case-crossover studies, each case provides both exposure and control periods of its own. Confounders that are stable over time within an individual, such as genetic background, quality of care by primary care physicians, and patient adherence to treatment, are cancelled out. The inference is ‘why now?’ in cases, instead of ‘why me?’ in a cohort. The assumption is that there are no unobserved confounders that change with time. In the present study, however, we believe it is unlikely that another event that could induce the start of DM treatment coincided with time periods after the health examination. How long the effect of the health examination persisted was unknown. Therefore, considering the time it takes for individuals to receive their results, visit physicians, and begin treatment, we assumed the effective time period would be 90 days after health examination attendance. However, there may be additional effects in the longer term following periods of dietary and exercise therapies. Further study is required to evaluate such effects. The sensitivity analysis shortening this time to 30 days after the health examination resulted in a decrease in the OR. A possible explanation for this may be that some participants had not received the results of their health examination at 30 days.

As the case-crossover design requires, the target population was those who started treatment for DM. In addition, the focus of this study was individuals being treated for hypertension. These people appeared to be in good control in terms of their blood pressure; 46% had systolic blood pressure ≤130 mm Hg, and 73% had systolic blood pressure ≤140 mm Hg at the health examination. However, the frequency of testing for blood glucose was low; 46% were tested less than once per year or not tested at all. The frequency of testing did not increase in individuals with high HbA1c levels; 181 of 334 patients (54%) with HbA1c ≥ 7.5% were tested less than once per year or were not tested. This proportion did not change considerably when the study population was limited to individuals with claims records for outpatient primary care management of lifestyle-related diseases. Additionally, the examination results showed that 55% had no intention of receiving health guidance, and 33% were currently smokers.

### Table 2 (Continued)

| Frequency of alcohol consumption | n (%) |
|---------------------------------|-------|
| Every day                       | 394 (26.9) |
| Sometimes                       | 419 (28.6) |
| Rarely or never                 | 516 (35.2) |
| Missing                         | 135 (9.2)  |

| Weight change in a year         | n (%) |
|---------------------------------|-------|
| Yes                             | 435 (29.7) |
| No                              | 820 (56.0) |
| Missing                         | 209 (14.3) |

| Perception of healthier lifestyles | n (%) |
|-----------------------------------|-------|
| Precontemplation stage            | 169 (11.5) |
| Contemplation stage               | 469 (32.0) |
| Preparation stage                 | 227 (15.5) |
| Action stage                      | 141 (9.6)  |
| Maintenance stage                 | 242 (16.5) |
| Missing                           | 216 (14.8) |

| Intention to receive health guidance | n (%) |
|-------------------------------------|-------|
| Yes                                 | 376 (25.7) |
| No                                  | 801 (54.7) |
| Missing                             | 287 (19.6) |

### Table 3

**Blood pressure of employees identified from the JMDC Claims Database who started treatment for diabetes mellitus while on continuous treatment for hypertension (n = 1447)**

| Systolic blood pressure, mmHg | Diastolic blood pressure, mmHg | <80 | 80-84 | 85-89 | ≥90 | All |
|-------------------------------|--------------------------------|-----|-------|-------|-----|-----|
| <120                          |                                | 202 (14.0) | 45 (3.1) | 11 (0.8) | 5 (0.3) | 263 (0.3) |
| 120-129                       |                                | 181 (12.5) | 110 (7.6) | 74 (5.1) | 41 (2.8) | 406 (28.1) |
| 130-139                       |                                | 74 (5.1) | 116 (8.0) | 115 (7.9) | 98 (6.8) | 403 (27.9) |
| ≥140                          |                                | 25 (1.7) | 40 (2.8) | 65 (4.5) | 245 (16.9) | 375 (25.9) |
| All                           |                                | 482 (33.3) | 311 (21.5) | 265 (18.3) | 389 (26.9) | 263 (0.3) |

Note: Excludes 17 patients with missing data on blood pressure. Data shown as n (%).
For patients under treatment for a lifestyle-related disease, in addition to health guidance provided by insurers, primary care physicians play a role in comprehensive disease management. Reimbursement for this type of care was recorded for approximately 90% of the sample. However, our results suggest that this management may have been inadequate in some cases.

The overall OR of the time period following the mandatory health examination was 1.89, indicating that the examination was associated with a modification of the management of lifestyle-related diseases. In this group of individuals, the health examination may function as a complement to outpatient management. The subgroup analysis showed that the association was not significant for those with lower HbA1c and frequent testing of blood glucose in an outpatient setting, but the OR increased for patients with higher HbA1c and those with less frequent blood glucose testing. This suggests that the health examinations may be especially important for patients with poor control of blood glucose.

The policy implications of this study relate to the questions of whether employer-based mandatory health examinations are necessary for employees who are already under treatment and which items should be included in these examinations. For employees who are being treated for a diagnosed illness, primary care physicians may take on the responsibility of ensuring their health. Thus, the role of the health examinations may be questioned for these employees. However, the results of the present study suggest that these examinations are also beneficial for this population under the current healthcare system. Employer-based health examinations in this population should be continued or strengthened with more emphasis on identifying potential DM. Meanwhile, primary care by physicians may require improvement to identify DM while providing regular care for other conditions. In the present study, we did not evaluate long-term effects such as the occurrence of CVD, hemodialysis, or death, or the economic burden of such effects. Furthermore, the effects may differ for underlying diseases other than hypertension, such as dyslipidaemia and DM, and other targeted diseases such as cancer. It is necessary to consider these factors in the evaluation of the overall additional effect of health examinations.

Several limitations of the present study must be noted. First, the study included only individuals who started DM treatment during the study period. The effect of health examinations on behavioral change and the identification of milder conditions that do not lead to treatment could not be evaluated. Additionally, patients with extreme conditions leading to death or withdrawal from insurance during the study period were excluded. Second, the target population was those being treated for hypertension. We focused on these individuals to extract a relatively homogeneous sample with a common disease. However, the association may differ for patients with other conditions. Third, the results of the health examination may differ from conditions present at the initiation of DM treatment, causing misclassification in our subgroup analysis. Fourth, data on job categories and positions were not obtainable from the database. Further research is required to evaluate whether the associations found in this study differ according to job characteristics. Fifth, the study population was employees enrolled in society-managed health insurance plans. The results may not be generalizable to employees enrolled in other schemes because the characteristics of

### Table 4
Results of case-crossover analysis for the association between health examination and diabetes treatment initiation, stratified by frequency of glucose testing and HbA1c level

| Participants | HbA1c, % | Frequency of hemoglobin A1c or glycoalbumin testing in an outpatient setting | OR (95% CI) | n | OR (95% CI) | n | OR (95% CI) | n | OR (95% CI) | n |
|--------------|---------|-------------------------------------------------|-------------|---|-------------|---|-------------|---|-------------|---|
|              | <6.5    | Once in 90 d or more                            | 0.71 (0.39-1.29) | 67 | 0.69 (0.44-1.07) | 123 | 1.47 (1.03-2.11) | 137 | 0.98 (0.76-1.26) | 327 |
|              | 6.5-7.4 | Between once in 90 d and once in 360 d          | 1.00 (0.70-1.42) | 162 | 1.79 (1.36-2.37) | 205 | 2.68 (2.11-3.40) | 283 | 1.87 (1.60-2.20) | 650 |
|              | ≥7.5    | Less than once in 360 d or never                | 3.65 (2.07-6.45) | 51 | 3.27 (2.20-4.86) | 102 | 4.63 (3.42-6.28) | 181 | 4.01 (3.22-5.01) | 334 |
|              | All     | All                                             | 1.22 (0.96-1.56) | 316 | 1.55 (1.29-1.87) | 481 | 2.64 (2.26-3.08) | 667 | 1.89 (1.70-2.10) | 1464 |
| Primary carea | <6.5    | <6.5                                           | 0.80 (0.41-1.56) | 52 | 0.62 (0.38-1.00) | 111 | 1.56 (1.07-2.29) | 120 | 1.00 (0.76-1.31) | 283 |
|              | 6.5-7.4 | Between once in 90 d and once in 360 d          | 0.93 (0.63-1.39) | 134 | 1.77 (1.32-2.36) | 189 | 2.81 (2.18-3.61) | 255 | 1.90 (1.61-2.25) | 578 |
|              | ≥7.5    | Less than once in 360 d or never                | 3.75 (2.04-6.90) | 45 | 3.50 (2.33-5.27) | 97 | 4.75 (3.43-6.58) | 159 | 4.15 (3.28-5.25) | 301 |
|              | All     | All                                             | 1.27 (0.98-1.66) | 260 | 1.56 (1.28-1.89) | 440 | 2.75 (2.33-3.24) | 591 | 1.95 (1.75-2.19) | 1291 |

Abbreviations: CI, confidence interval; HbA1c, hemoglobin A1c; OR, odds ratio.
aIndividuals with claims records for outpatient primary care management of lifestyle-related diseases.
health management by employers may differ in smaller-scale workplaces. Additionally, the results may not be applicable to other forms of health examination, such as the Specific Health Checkups and Guidance provided to dependents or subscribers of the citizens’ health insurance. Finally, there remains a possibility of unmeasured time-varying confounders that coincided with the health examination.

5  |  CONCLUSION

Among employees who started treatment for diabetes in addition to hypertension, attending the employer-based mandatory health examination was associated with DM treatment initiation. Further studies would lead to identifying effective role of outpatient services and health examinations.

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DISCLOSURE

Approval of the research protocol: The study was approved by the Institutional Review Board of the Graduate School of Medicine, The University of Tokyo. Informed consent: The requirement for informed consent was waived because of the anonymous nature of the data. Registry and the registration no. of the study: N/A. Animal studies: N/A. Conflict of interest: HY1 and TJ have academic affiliations with the Department of Health Services Research, Graduate School of Medicine, The University of Tokyo, supported by Tsumura & Company. SO has academic affiliations with the Department of Eat-loss Medicine, Graduate School of Medicine, The University of Tokyo, supported by ITO EN. AO has academic affiliations with the Department of Prevention of Diabetes and Lifestyle-related Diseases, Graduate School of Medicine, The University of Tokyo, supported by Asahi Mutual Life Insurance Company. Tsumura & Company, ITO EN, and Asahi Mutual Life Insurance Company played no role in the design of the study; collection, analyses, or interpretation of data; writing of the manuscript; or decision to publish the results.

AUTHOR CONTRIBUTIONS

HY1 contributed to the conception and design, and the analysis and interpretation of the data. SO and AO contributed to the analysis and interpretation of the data. TJ contributed to the conception and design, and the interpretation of the data. HY2 contributed to the conception and design, and the acquisition and interpretation of the data. HY1 drafted the manuscript, and all other authors revised it for important intellectual content.

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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