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<tr>
<td>Author(s)</td>
<td>Kawamura, Taichi</td>
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<tr>
<td>Citation</td>
<td>Kyoto University (京都大学)</td>
</tr>
<tr>
<td>Issue Date</td>
<td>2018-05-23</td>
</tr>
<tr>
<td>URL</td>
<td><a href="https://doi.org/10.14989/doctor.k21266">https://doi.org/10.14989/doctor.k21266</a></td>
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Influence of comorbidities on the implementation of the fundus examination in patients with newly diagnosed type 2 diabetes

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Abstract

Aims

To investigate the influence of comorbidities on undergoing a diabetic eye examination in patients with newly diagnosed type 2 diabetes mellitus (T2DM).

Design

Retrospective cohort study

Methods

This was a retrospective cohort study using data from health insurance claims made between January 2005 and March 2013 in Japan. The primary outcome was implementation of the fundus examination that includes fundus photography, ophthalmoscopy and optical coherence tomography by a doctor within one year of initial drug therapy for Type2 Diabetes Mellitus (T2DM). We used multivariable logistic regression models with adjustment for demographic parameters to investigate the influence of comorbidities (hypertension and/or hyperlipidemia) on patients with T2DM receiving fundus examinations. We conducted an additional analysis
to investigate whether the site of treatment might influence the performance of fundus
examinations in patients with T2DM.

Results

A total of 6,492 patients were eligible for this analysis, of which 1,044 (16.1%) had
comorbidities and 2,212 (34.1%) received the fundus examination. In the multivariable
analysis, there was a significant association between comorbidities and a lower proportion of
examination implementation (odds ratio [OR], 0.57; 95% confidence interval [CI], 0.48–0.68;
P<0.001). The implementation proportion for patients treated for comorbidities and T2DM in
the same facility was also low (OR, 0.52; 95% CI, 0.43–0.63; P<0.001).

Conclusions

These results suggest that the proportion of taking fundus examination is low among patients
with comorbidities, especially in patients treated at the same facility for comorbidities and
T2DM. This may help to increase the proportion of T2DM patients receiving fundus
examinations.

Keywords
diabetes mellitus, diabetic retinopathy, eye examination, comorbidity, claims data
1. Introduction

Diabetic retinopathy (DR) is the second most common cause of visual disturbances in Japan [1]. DR is the initial diagnosis for approximately 40% of patients with type 2 diabetes mellitus (T2DM) [2]. The quality of life of patients is shown to decrease with increased severity of DR [3], and DR negatively affects family relationships and working life [4]. Although DR presents no symptoms in the early stages, the advanced stages such as proliferative DR, require ophthalmological treatment (e.g. laser photocoagulation or vitrectomy) [5]. These procedures can cause side effects, including night blindness, color vision changes, and visual loss following photocoagulation [6, 7].

Preventing the development and progression of DR via intensive glycemic control is important, especially for patients with newly diagnosed T2DM [8]. Intensive glycemic control achieves significant reduction in glycated hemoglobin (HbA1c) levels, as well as improvement in beta-cell function [9, 10]. However, a large reduction in blood glucose levels over a short period causes a temporary worsening of DR [11]. In addition, common comorbidities of DM include hypertension and hyperlipidemia, which are risk factors for DR [12, 13]. Tight blood pressure control and intensive hyperlipidemia therapy reduce the risk of DR [14-17]. Therefore, an early detection of DR is important for slowing the progression of the disease and for implementing an appropriate therapeutic strategy. Notably, previous studies report that the early detection of DR is important to prevent visual loss [18, 19].
The optimal method for detecting DR is an eye examination; the guidelines for DM care recommend an eye examination performed by an ophthalmologist once a year [20, 21]. In the UK, health services are largely free at the point of use [22]. The first contact for medical care is generally a general practitioner (GP) that can make the necessary referrals to primary care trusts. However, some people cannot see their GP when necessary. The large number of cases processed through the UK’s NHS Diabetic Eye Screening Programme for patients with DM resulted in the reduced prevalence of advanced stages of DR [23]. In the US, there are some federal medical insurance programs (e.g. Medicare and Medicaid) as well as private medical insurance. However, More than 10% of the population is uninsured even after the implementation of the Affordable Care Act, and have no access to primary care [24]. On another front, EyeCare America provides eye care for citizens aged 65 or older through ophthalmologists at no cost [25]. This program recommends that anyone diagnosed with diabetes visit an ophthalmologist. Japan has a universal healthcare system, and people can access medical care freely, including ophthalmologists [26]. Despite a cooperative approach between internal medicine and ophthalmology, with the aim of reducing the rate of drop-out from regular eye examinations [27], the proportion of patients receiving the necessary ophthalmological examinations remains low [28, 29]. Furthermore, one study reports that approximately 50% of patients with DM have never received an eye examination [30].

Previous studies report factors influencing the implementation of eye examinations in
patients with DM from analyses of health insurance claims’ data used for the reimbursement of medical fees. For example, a study that used a Kaiser Permanente database demonstrates that age, duration of DM, insulin usage, poor vision, and severe DR were associated with the likelihood of a follow-up eye examination [31]. Moreover, a study of elderly patients with DM used Medicare claims’ data to reveal that there are associations between the reduced occurrence of regular eye examinations and male sex, low mobility, living a long distance from an ophthalmologist, and a low cognitive function [32]. However, although it is imperative to conduct an ophthalmological examination to facilitate the early detection of DR, none of these studies focused on patients with an initial diagnosis of DM. Some previous surveys of patients with DM based on questionnaires might have had uncontrolled potential bias (e.g. recall biases) [33-38]. Furthermore, the related factors should be evaluated for each country independently, as medical circumstances, including the guidelines for DM care and medical policies differ for each country. To the best of our knowledge, no previous study has investigated the factors related to implementation of an eye examination in patients with newly T2DM using nation-wide health insurance claims data in Japan.

Using health insurance claims’ data in Japan, we evaluated the association between comorbidities and the proportion of patients with T2DM who received a fundus examination, which reveals the state of the retina in detail, within one year from initial drug therapy for T2DM. In particular, we focused on hypertension and hyperlipidemia.
2. Materials and Methods

2.1 Study Design and Data Source

This study was a retrospective cohort study using health insurance claims made between January 2005 and March 2013. Claims were anonymously obtained from the database of Japan Medical Data Center (JMDC) Ltd. (Tokyo, Japan). The population covered by the JMDC database consists of beneficiaries (employees and their dependents) in several health insurance unions across Japan in 2012. The claims provided inpatient and outpatient information, including demographics, diagnoses, drug prescriptions, and procedures. Diagnoses were categorized using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) diagnosis codes. Drugs were coded according to the Anatomical Classification of Pharmaceutical Products (ATC).

2.2 Study Patients

The cohort included patients aged >20 years diagnosed with T2DM (ICD-10 codes E10-14) between January 2005 and March 2013, and had been prescribed antidiabetic drugs (ATC codes: A10). The index month was defined as the first month in which the study patients had been diagnosed with DM and prescribed an antidiabetic drug. We excluded patients who were not prescribed an antidiabetic drug after the index month. In addition, we excluded patients without a 12-month follow-up period from the index month. Furthermore,
we selected the patients with newly diagnosed T2DM by reference to a previous study [39]. In particular, we excluded patients who had been diagnosed with DM or prescribed an antidiabetic drug during the nine months after registration in the database. In addition, patients with a definitive DR diagnosis prior to the index month were excluded. We also excluded patients who had undergone eye examinations (e.g. visual acuity or intraocular pressure), who had been diagnosed with eye diseases (ICD-10 codes H00-H59), or who had undergone an intervention for the eyes (e.g. cataract surgery or epilation) within the six months preceding the index month, in order to select patients who did not visit the ophthalmologist regularly. Lastly, we excluded patients without information regarding the facility at which DM treatment took place in the index month.

The study protocol was approved by the Ethics Committee Graduate School and Faculty of Medicine Kyoto University (R0288).

2.3 Measurements

In the present study, we utilized the following patients’ information from the health insurance claims data: sex, age, insulin usage during the index month, hospitalization during the index month, types of facilities for T2DM treatment in the index month (hospital or clinic with fewer than 20 beds [clinic]), comorbidities (hypertension and hyperlipidemia), and any other comorbidities within the six months preceding the index month (including large...
categories of ICD-10 codes), and implementation of the fundus examination. The fundus
examination included fundus photography, ophthalmoscopy and optical coherence
tomography. Comorbidities were defined by the therapeutic medication for each disease
within the six months preceding the index month (hypertension: ATC codes C02, C03, C07,
C08, and C09; hyperlipidemia: ATC code C10). In addition, we have extracted patients
diagnosed with DR. The diagnosis was defined by more than two times of diagnose for DR
within the six months.

2.4 Outcome

The primary outcome was implementation of the fundus examination within one year
from the index month.

2.5 Statistical analysis

Eligible patients were assigned to two groups: patients with either hypertension and/or
hyperlipidemia and patients without these comorbidities. The subject characteristics for each
group, including sex, age, hospitalization, insulin usage, types of facilities for T2DM
treatment in the index month, and occurrence of diseases within six months preceding the
index month, were described. We also described the comorbidities (hypertension and/or
hyperlipidemia) and elucidated whether the treatment facilities for DM were the same as the
facilities for the comorbidities. Data are presented as the mean ± standard deviation for continuous variables, and the frequency (percentage) for categorical variables. Continuous variables were compared using Mann–Whitney U tests and categorical variables were compared using chi-square tests. In addition, the proportion of patients who underwent a fundus examination within one year of the index month was also described for each group.

To identify independent variables in patients at the index month, univariate and multivariable logistic regression analyses were performed. Covariates for the regression model were selected based on previously reported associations between covariates (sex, age, and insulin usage) and the frequency of eye examinations. The model also included hospitalization and the types of facilities for T2DM treatment (hospital or clinic) during the index month. Furthermore, we included the occurrence of diseases within the six months preceding the index month as a covariate, in order to consider the influence of visiting hospital on the incidence of other diseases. The comorbidities of hypertension and hyperlipidemia were also added to the model.

We performed a sensitivity analysis using a subgroup from which patients who had visited both a hospital and clinic in the index month were excluded. To confirm the association between the incidence of comorbidities and the examination without these patients, we calculated adjusted odds ratios (ORs) for this subgroup using a multivariable logistic regression model.
We also investigated whether patients being treated for comorbidities and T2DM in the same facility influenced the likelihood of undergoing an eye examination. To confirm the influence of this factor, we calculated adjusted ORs using a multivariable logistic regression model with dummy variables that indicated whether facilities for the treatment of T2DM and comorbidities were identical. Patients who were prescribed an antidiabetic drug and received treatment for comorbidities at the same facility were referred to as “patients treated at the same facility”, while patients who were prescribed an antidiabetic drug and received treatment for comorbidities at different facilities were referred to as “patients treated at different facilities”.

Results are presented as ORs and corresponding 95% confidence intervals (CI). P<0.05 in a two-sided test was considered statistically significant. Data management and statistical analyses were performed using SPSS software, version 22 (IBM SPSS, Armonk, NY, USA).
3. Results

We analyzed data from 203,870 patients who had a record of DM between January 2005 and March 2013. Of the 6,492 patients with newly diagnosed T2DM who met the inclusion criteria, 1,044 (16.1%) were defined as patients with comorbidities and 5,448 (83.9%) were defined as patients without comorbidities (Fig. 1).

Table 1 shows the baseline characteristics of the patients with T2DM in each group. The mean age of the patients with comorbidities was older than that of the patients without comorbidities. In the index month, the proportion of patients who administered insulin was lower for the patients with comorbidities compared with those without comorbidities, and the proportion of hospitalized patients was higher for the patients with comorbidities compared with those without comorbidities. The types of facilities for T2DM treatment in the index month were approximately equally represented. The proportion of patients who presented with other diseases within the six months preceding the index month was higher in the patients with comorbidities compared with those without comorbidities. When considering the patients with comorbidities only (n=1,044), 862 (82.6%) had hypertension and 529 (50.7%) had hyperlipidemia. A total of 910 patients (87.2%) were treated at the same facility for both the T2DM and comorbidities, while 134 (12.8%) were treated at different facilities.

Table 2 describes the proportions of patients in each group who underwent a fundus examination within one year from the index month. In total, 2,212 patients (34.1%) received a
fundus examination, including 236 (22.6%) patients with comorbidities and 1,976 (36.3%) patients without comorbidities. Among those who received the fundus examination, more than 80% received it within 6 months. Of 2,212 patients taking fundus examination within one year, 880 patients were diagnosed with DR within one year (39.8%).

Table 3 shows the results of the univariate and multivariable logistic regression analyses. In the univariate analysis, comorbidities and all other variables were significantly associated with receiving the fundus examination. The multivariable analysis revealed that, compared with patients without comorbidities, patients with comorbidities were less likely to undergo a fundus examination (OR, 0.57; 95% CI, 0.48–0.68; P<0.001). Furthermore, male patients (OR, 0.69; 95% CI, 0.62–0.77; P<0.001), patients aged <61 years (OR, 0.81; 95% CI, 0.72–0.91; P=0.001), patients who were treated by a clinic (OR, 0.58; 95% CI, 0.52–0.65; P<0.001), and patients in whom other diseases occurred within the six months preceding the index month (OR, 0.88; 95% CI, 0.78–1.00; P<0.045) were less likely to have had the examination. Conversely, patients who self-administered insulin or were hospitalized were more likely to undergo the examination. In the sensitivity analysis restricted to patients who had not visited both a hospital and a clinic in the index month, there was a significant association between comorbidities and a lower proportion of examination implementation (OR, 0.57; 95% CI, 0.48–0.68; P<0.001), the same result obtained for the main analysis.

Table 4 describes the results of the multivariable logistic regression analysis including
dummy variables indicating patients treated at the same or different facilities for T2DM and comorbidities. Compared with the patients without comorbidities, the patients treated at the same facility were significantly less likely to have undergone a fundus examination (OR, 0.52; 95% CI, 0.43–0.63; P<0.001). Conversely, the likelihood of having undergone a fundus examination was not significantly different between the subgroup of patients treated at different facilities and the group of patients without comorbidities.
4. Discussion

This is the first study to use health insurance claims’ data to compare the implementation proportion of fundus examination between newly diagnosed T2DM patients with and without comorbidities.

The proportion of patients who received a fundus examination within one year from the index month was 34.1%. Notably, comorbidities were associated with a lower implementation proportion of the examination. Furthermore, patients who were male, aged <61 years, had visited a clinic, and who presented with other diseases within the six months preceding the index month were associated with a low implementation of the examination. Conversely, patients who self-administered insulin or were hospitalized during the index month were associated with a high implementation proportion of the examination.

Although the guidelines recommend an eye examination once a year, two-thirds of patients did not receive a fundus examination within one year of the index month. The result of this study was marginally higher than that of a previous study in Japan [28]. The efforts towards increasing the number of patients receiving the examination and the difference in the duration of the study period might have led to the differences in the results [27].

In the present study, comorbidities were associated with a lower implementation proportion of the examination in patients with T2DM. In an additional analysis, although the treatment of patients at different facilities for T2DM and comorbidities was not associated
with the examination, patients treated at the same facility showed a low implementation proportion of the examination. Several studies report that the types or expertise of physicians affect the incidence of regular eye examinations [34, 35, 40]. Some patients treated at the same facility for T2DM and comorbidities in this study would have been prescribed an antidiabetic drug by the same physician who prescribed the drug for comorbidities. Therefore, the competence of the physicians who prescribed the drugs for comorbidities might have influenced the occurrence of a fundus examination.

According to the multivariable analysis, insulin usage in the index month was related to a high implementation proportion of the fundus examination. This result is consistent with the findings of previous studies that focused on follow-up eye examinations in patients with DM [31, 33]. The reason that the implementation proportion of the examination was high in patients with insulin could be: 1 The patients might have had high HbA1c levels, 2 The patients might lower a hurdle of visiting hospital, 3 The patients might have taken a positive stance towards DM therapies. Although recent joint American and European guidelines for T2DM recommend initiating therapy with metformin [41], insulin is recommended as the initial drug for patients with high HbA1c levels [20, 42]. Therefore, patients who had started receiving insulin therapy might have had high HbA1c levels. High HbA1c levels constitute the most important risk factor for DR, and achieving long-term glycemic control is critical for reducing the risk of microvascular diseases [8, 12, 43]. In this case, because physicians would
have focused on the treatment of 2TDM first, they might not have diagnosed and treated other possible disorders. Thus, the proportion of insulin users might be high in patients without comorbidities. Also insulin usage might lower a hurdle of visiting hospital, and it might lead to a better chance of undergoing a fundus examination. In addition, differences in patients’ understanding of DM therapy would have influenced the consultation behavior. As patients with DM typically resist the initiation insulin therapy [44, 45], patients who accepted insulin therapy in the index month might have taken a positive stance towards DM therapy in general. It is presumed that the patients sufficiently understood the risk of DR associated with DM and the importance of the fundus examination for observing the state of the retina.

The age, sex and occurrence of diseases within six months are presumed to be patient-related factors that influenced the implementation of the examination. The association between patients who were male or aged <61 years and a low implementation proportion can be attributed to their work commitments, which might have decreased their availability for the examination. These results are consistent with the findings of previous studies [31, 32]. Furthermore, the occurrence of diseases within six months prior to the index month was related to a low implementation proportion of the examination. This might be because patients visiting physicians regularly may avoid further visits to the clinic. The hospitalization and type of facility would be factors related to health care providers that influence the implementation of the examination. In the multivariable analysis,
hospitalization during the index month was related to a high implementation proportion of the examination. This might have been because it is convenient to receive the examination during hospitalization, especially if the facilities for DM treatment and the department of ophthalmology are in the same building. As for the type of facility for the treatment of T2DM, clinics were associated with a lower implementation proportion of the examination. Differences in the medical care system, including medical staff and medical facilities for DM, between clinics and hospitals might have influenced the implementation.

The proportion of patients diagnosed with DR is consistent with a previous study [46]. In this study, we excluded type 1 diabetes mellitus (T1DM) because of the difference in the incidence and time to onset of DR in T1DM and in T2DM. The DR screening for patients with T1DM is recommended beginning 5 years after diagnosis [47].

The strength of the present study was in identifying patients with newly diagnosed T2DM and using the nationwide health insurance claims’ data. A previous Japanese study using health insurance claims’ data was conducted in a limited area and with a small sample size [28]. Our study, however, has several limitations. First, the data had a low proportion of elderly people and a high proportion of working people from urban areas. This bias in the data limits the ability to generalize our results. Therefore, additional studies considering age and area of residence are necessary to improve the general implications. Second, levels of HbA1c were not included in the analysis. However, this variable would not likely have influenced the
results of the study, as the levels of HbA1c are not associated with eye examinations [31].

Third, some of preferred variables could not be included in the analysis because of secondary use of data. We could include patients who were traceable at least one year from the initial treatment of diabetes in this study. However it was difficult to trace the same patients for the second consecutive year. To confirm the regular eye examination for consecutive years, further research is needed.

In conclusion, only one-third of patients received a fundus examination within one year from initial therapy for T2DM. Our findings suggest that patients with comorbidities show low implementation proportion of the fundus examination, especially in patients treated at the same facility for comorbidities and T2DM. This result could help to increase the proportion of T2DM patients receiving fundus examinations.

Acknowledgements

We are grateful to JMDC for allowing us to access their claims data. We would like to thank Editage (www.editage.jp) for English language editing.

Conflicts of Interest: T. Kawamura, Employee (Senju Pharmaceutical); I. Sato, Grant (K-CONNEX), Yearly Pay (K-CONNEX); H. Tamura, Grant (Findex), Lecture fees (Findex, Novartis, RIAM NPO); Y. M. Nakao, None; K. Kawakami, Honorarium (Behringer Ingelheim
Japan, Daiichi Sankyo, Eisai, Mitsubishi Tanabe Pharma, Novartis Pharmaceutical, Sanofi, Shionogi Pharmaceuticals, Takeda Pharmaceutical), Consultant fees (Kaken Pharmaceutical, Kyowa Hakko Kirin, Olympus, Otsuka Pharmaceuticals) and K. Kawakami is responsible for data acquisition from Japan Medical Data Center Ltd.


8. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional
treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK
9. Chen HS, Wu TE, Jap TS, Hsiao LC, Lee SH, Lin HD. Beneficial effects of insulin on
glycemic control and beta-cell function in newly diagnosed type 2 diabetes with severe
pancreatic beta-cell function and long-term glycemic control in newly diagnosed type 2
Arch ophthalmology, 1998;116:874-86.
progression of diabetic retinopathy in Japanese adults with type 2 diabetes: 8 year follow-up
fenofibrate on the need for laser treatment for diabetic retinopathy (FIELD study): a
14. Matthews DR, Stratton IM, Aldington SJ, Holman RR, Kohner EM. Risks of progression
of retinopathy and vision loss related to tight blood pressure control in type 2 diabetes


43. The effect of intensive treatment of diabetes on the development and progression of


Figure legends

Fig. 1 Flow diagram of the subject selection process
Table 1. Baseline characteristics of study patients (N = 6,492)

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<th>Patients with comorbidities* (N = 1,044)</th>
<th>Patients without comorbidities (N = 5,448)</th>
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<tbody>
<tr>
<td>Male sex</td>
<td>707 (67.7)</td>
<td>3,557 (65.3)</td>
</tr>
<tr>
<td>Age, years</td>
<td>54.3 ± 9.7</td>
<td>53.0 ±11.7</td>
</tr>
<tr>
<td>Age &lt; 61 years</td>
<td>783 (75.0)</td>
<td>3,980 (73.1)</td>
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<tr>
<td>Insulin use during the index month</td>
<td>86 (8.2)</td>
<td>844 (15.5)</td>
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<td>Hospitalization during the index month</td>
<td>110 (10.5)</td>
<td>410 (7.5)</td>
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<tr>
<td>Type of facility for the treatment of T2DM</td>
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</tr>
<tr>
<td>hospital</td>
<td>404 (38.7)</td>
<td>2,170 (39.8)</td>
</tr>
<tr>
<td>clinic</td>
<td>640 (61.3)</td>
<td>3,278 (60.2)</td>
</tr>
<tr>
<td>Presence of diseases within six months†</td>
<td>884 (84.7)</td>
<td>1,553 (28.5)</td>
</tr>
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</table>

Data are presented as the mean ± standard deviation or n (%). T2DM, type 2 diabetes mellitus.

*Comorbidities included hypertension and/or hyperlipidemia.

†Presence of diseases within six months prior to the index month (confirming large categories of ICD-10 codes)
Table 2. Proportion of patients who received fundus examinations within one year of the index month.

<table>
<thead>
<tr>
<th></th>
<th>Patients with comorbidities (N = 1,044)</th>
<th>Patients without comorbidities (N = 5,448)</th>
<th>Total (N = 6,492)</th>
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<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
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<tr>
<td>Fundus examination†</td>
<td>236</td>
<td>22.6</td>
<td>1,976</td>
</tr>
<tr>
<td>≤ 6 months</td>
<td>191</td>
<td>80.9</td>
<td>1,636</td>
</tr>
<tr>
<td>7-12 months</td>
<td>45</td>
<td>19.1</td>
<td>340</td>
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*Comorbidities included hypertension and/or hyperlipidemia.

†Proportion of patients who received a fundus examination within one year from the index month.
Table 3. Univariate and multivariable logistic regression models

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariable analysis</th>
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<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Comorbidity* (vs. without comorbidities)</td>
<td>0.51</td>
<td>0.44−0.60</td>
</tr>
<tr>
<td>Insulin use during the index month (vs. not used)</td>
<td>2.86</td>
<td>2.48−3.29</td>
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<tr>
<td>Hospitalization during the index month (vs. outpatients)</td>
<td>2.55</td>
<td>2.12−3.05</td>
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<tr>
<td>Male sex (vs. female sex)</td>
<td>0.67</td>
<td>0.61−0.75</td>
</tr>
<tr>
<td>Aged ≤60 years (vs. aged &gt;60 years)</td>
<td>0.75</td>
<td>0.67−0.85</td>
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<td>Type of facility for the treatment of T2DM</td>
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<tr>
<td>clinic (vs. hospital)</td>
<td>0.48</td>
<td>0.44−0.54</td>
</tr>
<tr>
<td>Presence of diseases within 6 months† (vs. without diseases within 6 months)</td>
<td>0.75</td>
<td>0.67−0.83</td>
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</tbody>
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CI, confidence interval; OR, odds ratio; T2DM, type 2 diabetes mellitus; P, P-value.

*Comorbidities included hypertension and/or hyperlipidemia.

†Presence of diseases (ICD-10 codes) within six months prior to the index month.
Table 4. Univariate and multivariable logistic regression models with dummy variables

<table>
<thead>
<tr>
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<th>Multivariable analysis</th>
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<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Patients treated at different facilities† (vs. patients without comorbidities*)</td>
<td>0.88</td>
</tr>
<tr>
<td>Patients treated at the same facility‡ (vs. patients without comorbidities)</td>
<td>0.52</td>
</tr>
<tr>
<td>Insulin use during the index month (vs. not used)</td>
<td>1.98</td>
</tr>
<tr>
<td>Hospitalization during the index month (vs. outpatients)</td>
<td>1.25</td>
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<tr>
<td>Male sex (vs. female sex)</td>
<td>0.69</td>
</tr>
<tr>
<td>Aged ≤60 years (vs. aged &gt;60 years)</td>
<td>0.81</td>
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<td>Type of facility for the treatment of T2DM</td>
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<tr>
<td>clinic (vs. hospital)</td>
<td>0.58</td>
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<tr>
<td>Presence of diseases within 6 months (vs. without diseases within 6 months)</td>
<td>0.88</td>
</tr>
</tbody>
</table>

CI, confidence interval; OR, odds ratio; T2DM, type 2 diabetes mellitus; P, P-value.

*Comorbidities included hypertension and/or hyperlipidemia.
†Patients who were not prescribed the antidiabetic drug at the same facility as the drug for treatment of hypertension and/or hyperlipidemia.

‡Patients who were prescribed the antidiabetic drug at the same facility where the drug for the treatment of hypertension and/or hyperlipidemia was prescribed.