

# Diabetes Severity Measured by Treatment Control Status and Number of Anti-diabetic Drugs Affects Presenteeism Among Workers With Type 2 Diabetes

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## Research Article

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# Abstract

**Background:** The number of people with diabetes is increasing and resulting in major economic losses. Presenteeism accounts for the majority of economic losses, so measures against presenteeism are important. This study investigated the relationship between severity of type 2 diabetes and presenteeism.

**Methods:** A cross-sectional study was conducted among workers over 40 years of age. Participants were classified as normal group or diabetic treatment group using their medical examination results and health insurance claims data. Diabetic treatment groups were described by degree of treatment control: Good (HbA1c <7%), Intermediate ( $7\% \leq \text{HbA1c} < 8\%$ ), and Poor ( $8\% \leq \text{HbA1c}$ ). Therapy type was also divided into monotherapy and combination therapy. Logistic regression analysis was performed to predict presenteeism loss using the Quantity and Quality method.

**Results:** Data on 13271 workers were analyzed. Presenteeism loss was significantly higher in all treatment control groups compared with the normal group, particularly for the intermediate and poor control groups. The monotherapy group did not differ from the normal group, but presenteeism loss was significantly higher in the combination therapy group than the normal group.

**Conclusions:** Presenteeism loss in workers with diabetes may be affected by diabetes severity, and even if treatment control was good, presenteeism loss could occur when the number of anti-diabetic drugs was high. Therefore, it is important to provide early intervention and continuous support as a preventive measure against not only diabetes and diabetes-related complications but also presenteeism.

## Background

The number of people with diabetes is increasing. According to global reports of the International Diabetes Federation (IDF), 463 million people were diagnosed with diabetes in 2019. It is estimated that the number will increase to 578 million by 2030 and 629 million by 2045 if effective measures are not taken.<sup>1</sup>

The increasing number of people diagnosed with diabetes constitutes a significant economic loss for employees, employers, and society. The American Diabetes Association has estimated the economic cost of diabetes in the United States every five years since 1997,<sup>2-6</sup> and the latest (2017) cost was \$ 32.7 billion.<sup>6</sup> Similar estimates have also been made in European countries.<sup>7-11</sup> However, most studies have estimated losses according to the number of only those diagnosed with diabetes, and they have not included undiagnosed patients. The IDF reports that almost half of all adults with diabetes worldwide have not been diagnosed, and therefore including those individuals would further increase the losses.<sup>12</sup>

Economic costs of illness consist of direct and indirect costs. Absenteeism and presenteeism, which are included in indirect costs, are often evaluated as productivity losses due to workers' health problems. Absenteeism refers to "absence from work due to health problems," while presenteeism is defined as "health-related productivity loss while at paid work".<sup>13</sup>

According to a survey of employees of large US companies, presenteeism due to diabetes accounted for 62% of the total costs and 87% of the indirect costs of diabetes.<sup>14</sup> Therefore, as a measure of diabetes in society as a whole—and in companies—it is important not only to reduce medical costs but also to take measures against presenteeism, which accounts for the majority of all health-related economic losses. Particularly, it is expected that the number of individuals working while being treated for diabetes will increase due to social changes such as the extension of retirement age because of the declining birthrate and aging population in Japan. Prevention of chronic diseases—including diabetes—and measures against presenteeism are becoming more and more important in the workplace.

Many studies have pointed out that diabetes causes presenteeism, but there were some problems in that undiagnosed diabetes was not included, and treatment status analysis was not always performed. Therefore, we defined the classification of diabetes for Japanese workers according to the results of medical examinations and using health insurance claims data, and we analyzed the relationship between diabetes status and presenteeism. We reported that presenteeism occurred significantly in the diabetic drug treatment group compared with that in the normal group, but no presenteeism occurred in the untreated diabetic group.<sup>15</sup> It is suggested that the cause of presenteeism in the diabetic drug treatment group could be the influence of the severity of diabetes and the influence of the diabetic drug itself.

The severity of diabetes is evaluated by “treatment control status” according to test values such as fasting blood glucose and hemoglobin A1c (HbA1c), and of course, these test values are affected by the diabetic drugs. In non-insulin dependent states such as type 2 diabetes mellitus, if exercise or diet does not improve glycemic control, monotherapy is started. If treatment control is not possible, patients are treated with two or more drugs.<sup>16</sup> Thus, it is considered appropriate to express the severity of diabetes in terms of treatment control status according to test values and number of anti-diabetic drugs. It is difficult to distinguish between the influence of the severity and the influence of the drug itself.

As a background to the occurrence of presenteeism due to diabetes, previous studies have investigated the direct causes such as hypoglycemia,<sup>17-21</sup> the number of tolerability issues with anti-diabetic drugs such as hypoglycemia, constipation or diarrhea, nausea or vomiting, headache, weight gain, edema, urinary tract infection, etc,<sup>22</sup> complications of diabetic neuropathy,<sup>23-26</sup> diabetes-associated stress,<sup>27,28</sup> and complications of mood disorders such as depression.<sup>29,30</sup> However, few studies have investigated the relationship with severity. Thus, we investigated the relationship between two severities—the treatment control status and the number of anti-diabetic drugs—and presenteeism for type 2 diabetes mellitus.

## Methods

A cross-sectional study was conducted of workers aged 40 or over from 7 private companies in various industries such as electrical appliances, pharmaceuticals, the wholesale industry, and the food industry in Japan. The data were obtained from the results of annual medical examinations in each company in 2016, questionnaire surveys conducted with workers, and health insurance claims. According to Article 44

(2) of the Occupational Safety and Health Regulations, blood tests are a legal requirement for those aged 40 or over in medical examinations. In addition, the prevalence of diabetes increases with age, and prevalence under 40 years is approximately one-third that of those in their 40s.<sup>31</sup> For these reasons, we considered that including workers under 40 would affect the analysis, and therefore we limited our focus to those aged 40 or over in this study. In conducting this study, we explained the purpose to the management and workers via e-mail, intranet homepage, or the Safety and Health Committee, and the consent of the workers was obtained. The research protocol was approved by the Ethics Committee of Medical Research, University of Occupational and Environmental Health, Kitakyushu, Japan.

## **Classification of participants**

On the basis of the diabetes diagnosis criteria of the Japan Diabetes Society,<sup>32</sup> the participants with fasting blood glucose of less than 110 mg/dL and HbA1c [National Glycohemoglobin Standardization Program (NGSP)] (hereinafter HbA1c) of less than 6.0% were defined as the normal group. From the health insurance claims, if participants had taken anti-diabetic drugs from 3 months before the questionnaire through to the response month, they were classified as being in a diabetic treatment group regardless of their blood tests. Participants with insulin treatment were also included in the diabetic treatment group. In addition, information on the diagnosis name and prescription content was also collected from the health insurance claims. The reason for confirming the prescription history for 3 months was that the prescription of anti-diabetic drugs is mostly for 90 days or less in Japan.<sup>33</sup> Regarding insulin treatment, some previous studies reported that it was a factor in the occurrence of presenteeism,<sup>28,34</sup> but no significant difference was found in the insulin treatment group in our previous studies.<sup>15</sup> Thus we considered that insulin had almost no effect and decided to include it in the diabetic treatment group in this study. We excluded participants with data for only one test and those with casual blood glucose instead of fasting blood glucose because both fasting blood glucose and HbA1c were used. In addition, type 1 diabetes and other specified diabetes were excluded. We did not consider typical symptoms of diabetes such as dry mouth or polyuria.

Treatment control targets are the same in the United States<sup>16</sup> and Japan<sup>32</sup> where the target for prevention of complications is HbA1c <7%, and if it is difficult to strengthen the treatment due to side effects such as hypoglycemia, the target is HbA1c <8%. Therefore, we divided participants into three groups according to treatment control targets: good control group—HbA1c <7%; intermediate control group—7% ≤ HbA1c <8%; and poor control group—8% ≤ HbA1c. In addition, the number of anti-diabetic drugs was considered and classified as monotherapy group or combination therapy group if the participants were taking two or more drugs. Currently, some compounding drugs for diabetes are used, and participants taking these compounding drugs were included in the combination therapy group as two types of drugs were essentially prescribed.

## **Presenteeism**

We defined productivity loss due to presenteeism as “presenteeism loss” and evaluated the loss using the Quantity and Quality (QQ) method.<sup>35</sup> The evaluation using this method was performed through the following steps. First, we asked whether participants had any health problems or conditions during their work in the past month. If the answer was “no,” the presenteeism loss was set to zero. If the answer was “yes,” we asked the participants to identify their health problems from a list of 14 conditions and to select the one condition that most affected their work. If the conditions did not affect their work, the presenteeism loss was also set to 0. The 14 conditions were as follows: (1) troubled by allergies (e.g. hay fever); (2) skin diseases/itchiness (e.g. eczema, atopic dermatitis); (3) disorders caused by infections (e.g. cold, influenza, gastroenteritis); (4) gastrointestinal disorders (e.g. recurrent diarrhea, constipation); (5) pain in arm and leg joints or lack of mobility (e.g. arthritis); (6) back pain; (7) painful neck or stiff shoulder; (8) headaches (e.g. migraine, chronic headache); (9) tooth trouble (e.g. toothache); (10) mental health problems (e.g. depression, anxiety); (11) insomnia, insufficient sleep; (12) a sense of weariness or fatigue; (13) eye problems (e.g. loss of vision, eyestrain, dry eye, glaucoma); and (14) other.

Second, we asked participants to describe the quantity and quality of the work when they had the identified problem compared with those when they had no problems. The answers were scored from 0 (unable to work at all) to 10 (normal). Finally, presenteeism loss was calculated using the following equation:

$$\text{Presenteeism loss} = 100 - \text{Quantity (range: 0–10)} \times \text{Quality (range: 0–10)}$$

In our previous study,<sup>15</sup> the top 10% with a presenteeism loss score of 51 or higher, was defined as high presenteeism loss, and the top 20%, with a score of 36 or higher, was defined as moderate presenteeism loss, but similar results were obtained with these two indicators. Therefore, only 36 or higher was defined as presenteeism loss in this study.

## **Analysis**

Participant characteristics were summarized using means and standard deviations (SDs) for continuous variables and percentages for categorical variables. The presenteeism loss was calculated in each treatment control group compared with that of the normal group, and was also calculated for each therapy type compared with that of the normal group. Furthermore, the presenteeism loss in each treatment control group of combination therapy was also calculated. We performed logistic regression analysis with each treatment control group, number of anti-diabetic drugs, and each treatment control group of combination therapy as the independent variable, and presenteeism loss using the QQ method, that is, 36 or higher as the dependent variable. For all analyses, the normal group was the reference category, and age, sex, company, and occupation were adjusted. Adjusted odds ratios (aORs) and corresponding 95% confidence intervals (CIs) were calculated. In all analysis, *p*-values <0.05 were considered statistically significant. All analyses were performed using STATA Version 16 (StataCorp LLC, College Station, TX).

## Results

A total of 22,930 workers aged 40 years or older were selected. We excluded 8,825 patients who did not provide both fasting blood glucose and HbA1c in their medical examinations, 583 who had deficiencies in the questionnaire survey, 13 who were diagnosed with type 1 diabetes or other specified diabetes, 230 whose treatment status was unknown and 8 patients whose prescription was unknown in the treatment group. We then analyzed 13,271 participants. The participants were classified into 11,494 in the normal group and 485 in the diabetic treatment group (Fig. 1).

Table 1 shows the characteristics of the participants. Among the diabetic treatment groups, 300 were in the “good control” group, 105 in the “intermediate control” group, and 80 in the “poor control” group. In addition, 190 participants were receiving monotherapy, and 146 of them were in the good control group. There were 295 individuals in the combination therapy group (including those taking compounding drugs), and the proportion of combination therapy increased in the intermediate and poor control groups.

### *Occurrence of presenteeism loss for each treatment control status*

The odds of presenteeism loss were significantly higher in all control groups, the good control group (aOR 1.47, 95%CI 1.11–1.95,  $p<0.01$ ), the intermediate control group (aOR 1.92, 95%CI 1.24–2.97,  $p<0.01$ ), and the poor control group (aOR 1.81, 95%CI 1.08–3.02,  $p=0.02$ ) than in the normal group. In particular, the odds were higher in the intermediate and poor control groups (Table 2).

### *Occurrence of presenteeism loss for number of anti-diabetic drugs*

There was no significant difference between the monotherapy and the normal group, but the odds of presenteeism loss were significantly higher in combination therapy (aOR 1.81, 95%CI 1.38–2.38,  $p<0.01$ ). Regarding each treatment control group of combination therapy, the odds of presenteeism were significantly higher in all groups, the good control group (aOR 1.54, 95%CI 1.05–2.27,  $p=0.03$ ), the intermediate control group (aOR 2.12, 95%CI 1.26–3.54,  $p<0.01$ ), and the poor control group (aOR 2.09, 95%CI 1.22–3.59,  $p<0.01$ ). In particular, the odds were higher in the intermediate and poor control groups (Table 3).

## Discussion

In our previous study<sup>15</sup>, the diabetic drug treatment group had a significantly higher presenteeism loss compared with that of the normal group, and therefore we focused on two severities, “treatment control status” and “number of anti-diabetic drugs.” Here we investigated the relationship between these severities and presenteeism loss for type 2 diabetes mellitus.

Our results suggested that presenteeism loss was less likely to occur with monotherapy, but combination therapy could cause the loss even when treatment control was good, and further loss could occur when treatment control became poor, specifically  $HbA1c \geq 7\%$ .

### ***Occurrence of presenteeism loss for severity of diabetes***

There are several possible factors that cause presenteeism loss due to the severity of diabetes. Poor treatment control tends to cause typical diabetic symptoms such as dry mouth and polydipsia,<sup>36</sup> and these symptoms may cause presenteeism. In addition, poor treatment control and longer treatment periods increase the risk of developing diabetes-related complications such as heart disease, cerebrovascular disease, neuropathy, nephropathy, and retinopathy.<sup>16,37-40</sup>

It can be difficult to control treatment over a long time period, and therefore multiple prescriptions may be required.<sup>16</sup> Although we did not identify symptoms or complications in this study, these could be present in the case of intermediate and poor treatment control, or when the treatment period has been long and multiple prescriptions have been required for treatment control.

Diabetes treatment often causes diabetes-associated stress, including stress due to poor glycemic control, and concerns about the need to continue treatment, future complications and costs.<sup>41</sup> In particular, the psychological burden of the poor control group may be large.<sup>42,43</sup> Diabetes is often associated with mental health challenges such as depression and anxiety.<sup>44,45</sup> Presenteeism loss is likely to occur due to the diabetes-associated stress and the complications of the mental difficulties,<sup>28,29,30</sup> which may be due to the severity of diabetes treatment causing presenteeism through psychiatric symptoms.

If poor control continues, more anti-diabetic drugs may be used in an attempt to improve control or dosage might be increased. In this study, this was true because the proportion of combination therapy was higher in the poor control group. The previous study reported that as the number of tolerability issues associated with anti-diabetic drugs such as hypoglycemia, gastrointestinal symptoms, weight gain, edema, etc. increased, presenteeism loss was more likely to occur,<sup>22</sup> and combination therapy may increase these issues compared with monotherapy.<sup>46</sup> Furthermore, combination therapy may cause issues that are unlikely to occur with monotherapy. For example, dipeptidyl peptidase IV inhibitors<sup>47,48</sup> and sodium-glucose cotransporter 2 inhibitors,<sup>49</sup> which are currently the mainstream prescriptions in Japan, are unlikely to cause hypoglycemia by themselves, but it is reported that the combined use of sulfonylureas and insulin is more likely to cause hypoglycemia, and the guidelines also draw attention to this likelihood.<sup>32</sup>

Thus, there was no significant difference between the monotherapy and normal group and the loss that occurred; although this was higher in the combination therapy group in this study. The presenteeism loss may have occurred through tolerability issues due to the increase in the number and dose of anti-diabetic drugs. Another factor is simply the burden of increasing the number of oral doses and the number of tablets taken at one time.

### ***Use of the results***

As diabetes becomes more severe, in addition to the direct effects of poor glycemic control, the number of anti-diabetic drugs and dosages increase, causing multiple tolerability issues and diabetes-associated stress. This may then lead to a vicious cycle of reduced exercise and diet behavior, medication adherence, and treatment satisfaction, resulting in further poor glycemic control.<sup>41,50,51</sup> As our findings suggested that the severity of diabetes might cause presenteeism loss, from the perspective of workplace health and productivity management intervention efforts in the workplace should be considered. Specifically, it is important to detect borderline diabetes early and intervene as soon as possible from this stage. Supporting diet and exercise therapy means that even if type 2 diabetes mellitus is diagnosed, it is not necessary to start an anti-diabetic drug. If an anti-diabetic drug is prescribed, continuous support must be provided to reduce factors that hinder the continuation of treatment and glycemic control so that the treatment can be continued and controlled by monotherapy. Diabetes treatment is linked to psychological burden, and therefore it is also necessary to consider providing regular mental health support.<sup>16</sup>

## **Strengths And Limitations**

This study revealed that the severity of diabetes might have a significant effect on the relationship between diabetes and presenteeism. Many previous studies of these relationships selected participants and evaluated treatment status through e-mail and using the Internet. However, in this study, we used objective data based on the results of medical examinations and health insurance claims data.

There were several limitations to this study. First, the duration of diabetes was not taken into consideration. In general, longer durations of the condition mean greater possibility of having diabetic complications such as neurosis, retinopathy, and nephropathy. Second, we did not consider the typical diabetic symptoms and the coexistence of diseases other than diabetes, which could affect presenteeism loss. Third, the evaluation index of presenteeism loss using the QQ method is a self-administered survey, which reflects the participants' subjectivity so that presenteeism loss may be over- or underestimated. Forth, this study was a cross-sectional study, which means that recent changes in treatment content have not been captured. Fifth, because this study targeted workers in large companies with very high health literacy, it is difficult to generalize our results to small and medium-sized companies.

## **Conclusion**

Our results found that there was an association between the severity of diabetes measured by treatment control status and number of treatments, and occurrence of presenteeism loss. Higher severity was more likely to cause loss among the diabetic drug treatment groups. It was also suggested that even if treatment control was good, the loss could occur when the number of anti-diabetic drugs was high. Therefore, in the workplace, it is important to provide early intervention and continuous support as a preventive measure against diabetes and diabetes-related complications of workers, and also as a measure against presenteeism, which causes large losses for companies.

## **Abbreviations**

IDF: International Diabetes Federation

HbA1c: hemoglobin A1c

NGSP: National Glycohemoglobin Standardization Program

QQ: Quantity and Quality

SD: standard deviation

aOR: Adjusted odds ratio

CI: confidence interval

BMI: body mass index

## **Declarations**

### **Ethics approval and consent to participate**

This study was approved by the ethics committee of the University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, and was conducted in full accordance with the World Medical Association Declaration of Helsinki. We explained the study protocol and Informed consent was obtained from all participants.

### **Consent for publication**

Not applicable

### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors' contributions**

TM, TN, MN, KM designed the research. TM, TN, KF completed the data analysis. TM drafted the initial manuscript, and all authors assisted with data interpretation and reviewed and revised the manuscript. All authors commented on drafts of the report.

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## Tables

Table 1. Baseline characteristics of the participants

	Normal group n = 11,494	Good control group n =300	Intermediate control group n = 105	Poor control group n=80
Age, years, mean (SD)	49.0 (5.7)	53.3 (5.2)	53.2 (4.9)	51.3 (5.1)
Gender, %				
Male	76.9	95.7	92.4	93.7
Female	23.1	4.3	7.6	6.3
Occupation, %				
Managerial	39.7	42.1	41.3	26.9
Clerical	15.9	10.2	10.9	11.9
Sales	20.5	34.6	26.1	46.3
Research & Development	10.5	4.3	7.6	3.0
Engineering	4.6	3.1	3.3	1.5
Production line	8.1	4.7	8.7	10.4
Other	0.8	0.8	2.2	0
Smoking status, %	20.1	31.7	31.4	28.8
BMI (kg/m <sup>2</sup> ), mean (SD)	23.0 (3.1)	26.5 (4.3)	26.8 (3.8)	28.1 (3.9)
Fasting blood glucose (mg/dL), mean (SD)	91.6 (7.6)	118.9 (20.3)	142.1 (25.2)	184.0 (46.9)
HbA1c (NGSP) (%), mean (SD)	5.4 (0.3)	6.3 (0.4)	7.4 (0.3)	9.2 (1.4)
Therapy type, %				
Monotherapy	0	52.3	31.4	17.5
Combination therapy	0	47.7	68.6	82.5
Quantity of work, mean (SD)	9.0 (1.7)	8.9 (1.7)	8.7 (2.1)	8.7 (2.2)
Quality of work, mean (SD)	8.9 (1.8)	8.9 (1.8)	8.6 (2.1)	8.4 (2.4)
Presenteeism loss, mean (SD)	16.8 (24.4)	17.6 (24.8)	21.8 (27.7)	22.7 (30.7)

Presenteeism loss = 100 - Quantity (range: 0–10) × Quality (range: 0–10)

SD, standard deviation; BMI, body mass index; HbA1c, hemoglobin A1c,

NGSP, National Glycohemoglobin Standardization Program, Combination therapy, 2 or more anti-diabetic drugs

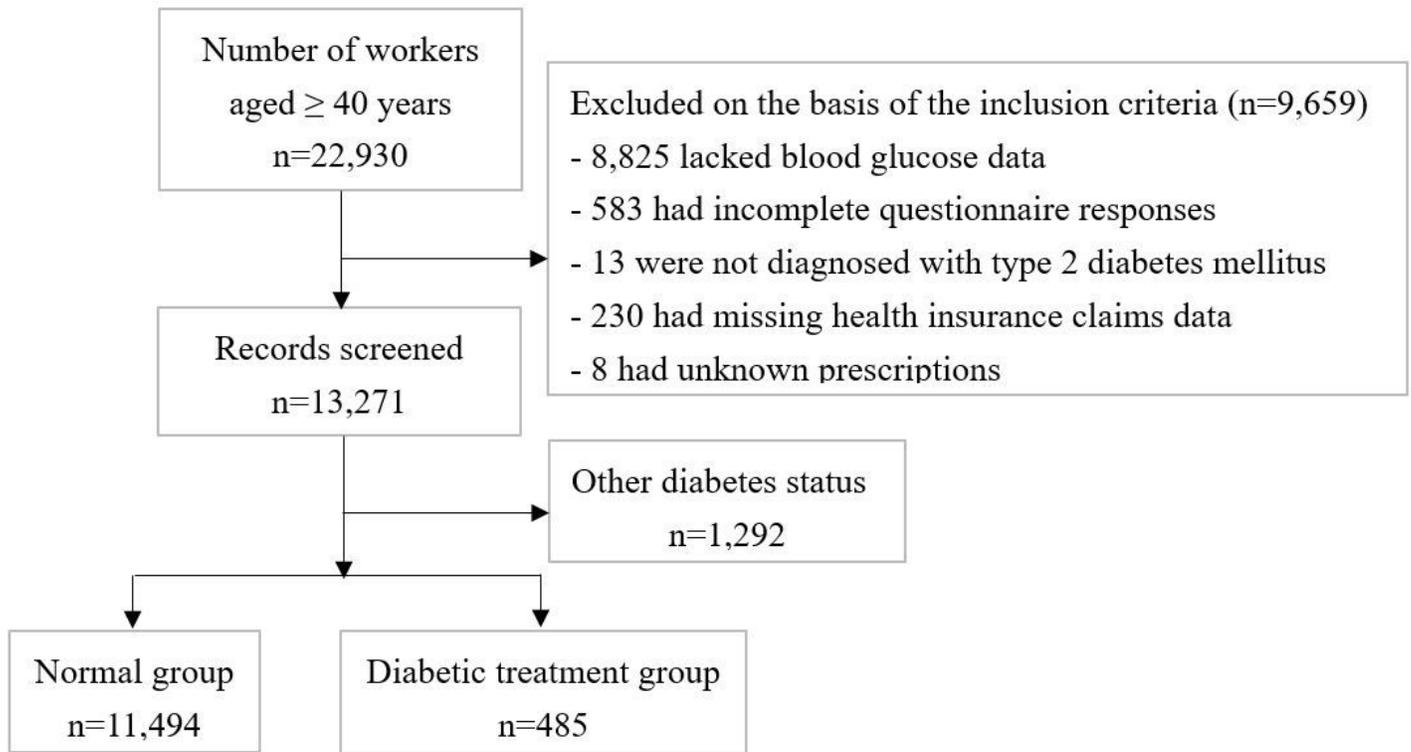
Table 2. Relationship between each treatment control and presenteeism loss

	n	mean (SD) of QQ	Presenteeism loss			
			%	aOR	95% CI	<i>p</i> -value
Normal group	11494	16.8 (24.4)	24.2	reference		
Good control group	300	17.6 (24.8)	27.3	1.47	1.11–1.95	0.008
Intermediate control group	105	21.8 (27.7)	34.3	1.92	1.24–2.97	0.004
Poor control group	80	22.7 (30.7)	33.8	1.81	1.08–3.02	0.024
Models adjusted for sex, age, company and occupation.						
Presenteeism loss, productivity loss due to presenteeism; SD, standard deviation						
QQ, Quantity and Quality; aOR, adjusted odds ratio; CI, confidence interval						

Table 3. Relationship between the number of anti-diabetics and presenteeism loss

	n	mean (SD) of QQ	Presenteeism loss			
			%	aOR	95% CI	<i>p</i> -value
Normal group	11494	16.8 (24.4)	24.2	reference		
Monotherapy group	190	17.1 (24.1)	26.8	1.34	0.94–1.91	0.103
Combination therapy group	295	20.8 (27.9)	31.9	1.81	1.38–2.38	<0.001
Good control group	154	18.3 (25.6)	27.9	1.54	1.05-2.27	0.029
Intermediate control group	74	23.9 (29.0)	36.5	2.12	1.26-3.54	0.004
Poor control group	67	23.3 (31.3)	35.8	2.09	1.22-3.59	0.007
Models adjusted for sex, age, company and occupation.						
Presenteeism loss, productivity loss due to presenteeism; SD, standard deviation						
QQ, Quantity and Quality; aOR, adjusted odds ratio; CI, confidence interval						

# Figures



**Figure 1**

Participant classification flowchart