

Relationships between Diabetes and Medical and Dental Care Costs: Findings from a Worksite Cohort Study in Japan

Reiko IDE^{1*}, Tsutomu HOSHUYAMA², Donald John WILSON³,
Ken TAKAHASHI² and Toshiaki HIGASHI¹

¹Department of Work Systems and Health, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan, 1–1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan

²Department of Environmental Epidemiology, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan, 1–1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan

³Department of Environmental Toxicology, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan, 1–1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807-8555, Japan

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Abstract: The purpose of this study was to evaluate the relationships between diabetes and medical and dental care costs from a 5-yr prospective observation of Japanese workers. The data were derived from health and dental examinations and health insurance claims of 4,086 workers aged 40–54 yr. At baseline, the subjects were assigned to four categories: known diabetes; undiagnosed diabetes; impaired fasting glucose (IFG); and non-diabetic. The differences in health care costs among the non-diabetics, IFG and undiagnosed diabetes groups were not seen at baseline, but the costs incurred by the subjects with undiagnosed diabetes substantially increased thereafter. Over 5 yr of the study period, compared with the non-diabetic group, subjects with known diabetes incurred 3.9- and 2.9-fold higher annual inpatient and outpatient costs, respectively, while subjects in the undiagnosed diabetes group incurred 3.0- and 1.6-fold higher costs, respectively. There were no significant associations between annual dental care costs and diabetic status. The excess costs of medical care among subjects with diabetes were attributable to diabetes itself, heart disease and cerebrovascular disease, but not cancer. Among middle-aged workers, diabetics incurred significantly greater medical care costs than non-diabetics, whereas IFG was not associated with higher costs.

Key words: Diabetes, Impaired fasting glucose, Medical care costs, Dental care costs, Longitudinal study

Introduction

The increasing prevalence of diabetes around the world seems unrelenting¹. Consequently, the economic burdens of diabetes and its complications are mounting. Although many studies have reported excess medical costs for individuals with diabetes^{2–8}), relatively few studies have focused on working-age populations. The medical and productivity costs for employees with dia-

betes were reported to be 2.5-fold higher than those for control subjects in patients aged 46–55 yr²). From productivity and economic perspectives, it is important to evaluate the burden of diabetes, especially in people of working age.

Japan has a national health insurance system to ensure that everyone can receive necessary health care, and in principle every resident of Japan is enrolled in some form of health insurance plan⁹). Fees for medical and dental services are standardized nationwide under this system. The costs and utilization of health services associated with inpatient, outpatient and dental care can

*To whom correspondence should be addressed.
E-mail: r-ochide@med.uoeh-u.ac.jp

be calculated on the basis of claims over given periods, because such claims accurately reflect most of the costs for medical and dental services. The prevalence of diabetes is increasing in Japan, and the National Health and Nutrition Survey reported that 8.2 million Japanese adults had diabetes in 2006, compared with 7.4 million adults in 2002. In a study of community-dwelling Japanese individuals with hypertension and/or diabetes over a 10-yr period, Nakamura *et al.* reported that people with diabetes alone and those with both hypertension and diabetes had 2.3- and 2.4-fold higher personal medical expenditures, respectively, compared with people who had neither disorder. However, some true cases of diabetes may have been misclassified in that study because diabetes cases were only identified by a known history of diabetes⁷⁾.

Diabetes complications have a substantial impact on the medical costs of diabetes patients. Diabetes has been established as an important risk factor for periodontal disease and subsequent tooth loss, but surprisingly few longitudinal studies have examined the relationship between diabetes and dental care costs. The purpose of this study was to evaluate the relationships between diabetes and medical and dental costs from a 5-yr prospective observation of workers. We assessed the medical and dental care costs of subjects with known diabetes (history of diabetes), undiagnosed diabetes [fasting plasma glucose (FPG) >125 mg/dl without history of diabetes] or impaired fasting glucose (IFG; FPG 110–125 mg/dl)¹⁰⁾, especially in relation to non-diabetics.

Methods

Study design and data collection

The base population consisted of civil service officers (about 25,000) from a prefecture in southwestern Japan. These officers were responsible for administering various social welfare programs managed by a mutual aid association, which covers health insurance and welfare pensions, in accordance with Japanese government regulations. They received yearly periodic health examinations and biennial oral examinations, and the data analyzed in this study were derived from examinations conducted between April 2000 and March 2001. This period was chosen because the Japanese fiscal year begins in April and ends in March. Because periodic worksite health examinations are mandatory in Japan, almost all the subjects had completed this health examination at the time of the study. The check-up items included: height and weight measurements; blood pressure; chest X-ray; and blood tests including FPG and triglyceride (TG). Information on personal smok-

ing habits and the medical history of some diseases was obtained from a self-administered questionnaire during the oral examination. Periodontal status was defined using the Community Periodontal Index¹¹⁾, and a score of 4 was assigned as severe periodontitis. We also collected data on the utilization and costs of health care, including medical and dental care costs, obtained from health insurance claims made between April 2000 and March 2005. These included the expenses for inpatient, outpatient and dental components. For each claim in the inpatient and outpatient component records, only the main diagnosis was evaluated, even if the patient was suffering from other diseases simultaneously. The Japanese Health Insurance system utilizes the diagnosis based on the International Classification of Disease which is called “119 Classification” (hereafter referred to as “the 119 Classification”). An individual claim of health service is submitted from health providers monthly, which is entered in the form of each claim. The costs are summed up from the health insurance claims by ID numbers, according to periods, components, or diseases. Both the health and dental examination data were linked with the files of the health insurance claims by ID numbers. This study was reviewed and approved by the Ethics Committee of Medical Care and Research, University of Occupational and Environmental Health, Japan.

Study subjects

Of 11,813 eligible subjects who were registered with the mutual aid association for the full study period, 8,546 subjects completed both the health and oral examinations at baseline. Because most workers retire at 60 yr of age in Japan, only subjects aged 40–54 yr as of April 1, 2000, were analyzed in this study ($n=4,107$). Other exclusions were 21 subjects who had missing data for FPG, TG, height, body weight, systolic blood pressure or diastolic blood pressure. The remaining 4,086 subjects (males: 2,757; females: 1,329) were finally analyzed. All of the subjects completed 4-yr follow-up after baseline.

Statistical analysis

At baseline, we divided the subjects into the following four categories: known diabetes (history of diabetes); undiagnosed diabetes (FPG >125 mg/dl without history of diabetes); IFG (FPG 110–125 mg/dl); and non-diabetics (FPG <110 mg/dl)¹⁰⁾. Annual health care costs (inpatient, outpatient and dental components) were estimated by analysis of variance (ANOVA). For p -value estimation, a logarithmic transformation was used to make the data more symmetric and homoscedastic. If the costs were 0, the logarithmic transformations were

undertaken after replacing 0 with 1. Dunnett's procedure was used for multiple comparisons to identify groups whose costs differed significantly from the costs of the non-diabetic group. Crude admission and visit rates were calculated as the percentages of subjects who had ever been admitted to or visited health care institutions during the study period, respectively. The odds ratios (ORs) and 95% confidence intervals (CIs) of the effects of diabetic status on institutional admission and visits were estimated by a multiple logistic regression model taking the values for the non-diabetic group as references. The following variables were considered as potential confounders and included in the model: age (in 5-yr age groups: 40–44, 45–49 and 50–54); sex; smoking status (either current or past, or never); body mass index (BMI; ≥ 25 or < 25); hypertension (either systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 , or neither), hyperlipemia (TG ≥ 150 or < 150). BMI was calculated as body weight (kg) divided by the square of the body height (m^2).

First, the annual total health care costs per capita in each year after baseline were estimated for the four groups according to diabetic status. Second, the relationships of diabetic status with the utilization and annual costs of inpatient, outpatient and dental care were analyzed. Annual costs were estimated by dividing the cumulative amount for the study period by the number of subjects who were completely followed for

5 yr. Finally, medical care costs, including both inpatient and outpatient costs, were calculated for each of diabetes (code 402 of the 119 Classification) and the following diseases that were possibly related to diabetes: hypertension (901); heart disease (902 and 903); cerebrovascular disease (904 to 908); and cancer (201 to 205). The above calculations were executed using Statistical Analysis System Proc GLM and LOGISTIC Version 9.1 (SAS Institute, Cary, NC).

Results

The subjects had a mean age of 46.9 yr, and 67.5% were men. The proportions of subjects with IFG, undiagnosed diabetes and known diabetes were 4.9%, 2.1% and 2.9%, respectively, with higher prevalence in males (Table 1). The diabetes groups were likely to have a history of liver or heart disease. The proportion of male subjects with severe periodontitis among the non-diabetics, IFG, undiagnosed diabetes and known diabetes groups were 11.4%, 13.6%, 18.5% and 24.7%, respectively, and significantly differ between four groups ($p < 0.001$).

Figure 1 shows the adjusted annual health care costs per capita according to diabetic status in each year. At baseline, the annual health care costs for subjects with known diabetes were higher than those for non-diabetics ($p < 0.001$) and there were no differences among the

Table 1. Characteristics of the study subjects according to diabetic status at baseline

Diabetic status	Male					Female				
	Non-diabetic	IFG	Undiagnosed diabetes	Known diabetes	p value ¹⁾	Non-diabetic	IFG	Undiagnosed diabetes	Known diabetes	p value ¹⁾
	FPG (mg/dl)	<110	110–125	>125		<110	110–125	>125		
n	2,417	162	81	97		1,265	37	6	21	
Mean age (SD)	46.7 (4.0)	47.7 (3.9)	48.2 (4.3)	48.5 (3.9)	<0.001	46.7 (3.9)	48.3 (4.6)	47.7 (4.9)	49.9 (3.3)	<0.001
FPG (SD)	92.1 (7.7)	115.4 (4.4)	158.4 (35.2)	149.8 (51.8)	<0.001	88.4 (7.5)	115.2 (4.6)	138.5 (13.3)	172.5 (64.9)	<0.001
Smoking status (%)										
Current	51.5	43.2	51.9	56.7	0.422	1.9	0.0	0.0	4.8	0.696
Past	17.1	19.8	14.8	13.4		0.8	0.0	0.0	0.0	
BMI ≥ 25 (%)	26.1	38.3	37.0	25.8	0.001	13.8	43.2	16.7	23.8	<0.001
Hypertension (%)	17.3	32.7	28.4	21.7	<0.001	7.2	24.3	50.0	19.1	<0.001
Hyperlipemia (%)	31.8	37.0	55.6	44.3	<0.001	6.5	13.5	33.3	33.3	<0.001
History of liver disease (%)	4.6	4.3	4.9	10.3	0.109	2.4	2.7	16.7	14.3	0.008
History of heart disease (%)	1.5	1.2	3.7	6.2	0.007	0.9	5.4	0.0	4.8	0.035
Severe periodontitis (%)	11.4	13.6	18.5	24.7	<0.001	5.8	5.4	0.0	9.5	0.708
No. of missing teeth (SD)	1.6 (2.6)	2.2 (4.2)	3.2 (3.9)	3.4 (4.6)	<0.001	1.8 (2.5)	2.0 (2.7)	0.8 (0.8)	2.8 (4.1)	0.231

IFG=impaired fasting glucose; FPG=fasting plasma glucose; SD=standard deviation.

¹⁾ p values were calculated by analysis of variance, χ^2 test, or Fisher's exact test.

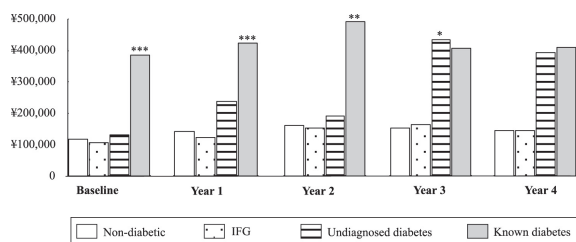


Fig. 1. Health care costs per person according to diabetic status.

IFG=impaired fasting glucose.

Health care costs were adjusted for age, sex, smoking status, BMI, hypertension, and hyperlipemia.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, significant difference versus the non-diabetic group for multiple post-hoc comparisons with Dunnett's correction, after the data were logarithmically transformed.

other three groups. In year 3, the costs for the undiagnosed diabetes group were higher than those for the non-diabetic group ($p = 0.025$), and similar to the level for subjects with known diabetes. Thus, the difference between the subjects with undiagnosed and known diabetes disappeared within 4 yr. Over 5 yr, the adjusted annual health care costs for the non-diabetic, IFG, undiagnosed diabetes and known diabetes groups were ¥144,085, ¥138,095, ¥277,876 and ¥422,763, respectively. The costs for subjects with undiagnosed and known diabetes were significantly higher than those for non-

diabetics (for undiagnosed diabetes: $p = 0.014$; for known diabetes: $p < 0.001$).

Table 2 shows the annual mean costs and utilization rates of inpatient, outpatient and dental components according to diabetic status. The admission rates of subjects with undiagnosed diabetes (OR, 2.05; 95%CI, 1.32–3.18) and known diabetes (OR, 2.70; 95%CI, 1.86–3.93) were higher than that of the non-diabetic group. Furthermore, the annual inpatient costs for subjects with undiagnosed and known diabetes were 3.0- and 3.9-fold higher than that of the non-diabetic group, respectively ($p < 0.001$ for both). Subjects with known diabetes had the highest annual outpatient costs, which were 2.9-fold higher than the costs of the non-diabetic group ($p < 0.001$). For the dental component, there were no significant associations of visit rates or annual costs with diabetic status. The annual dental visit rates of the non-diabetics were highest, although this trend did not reach significance. For subjects with IFG, the visits and costs of each component displayed similar patterns to those of the non-diabetics.

The annual medical costs for the disease classifications according to diabetic status are listed in Table 3. A worse diabetic status resulted in increased annual medical costs for subjects with known diabetes, and these costs were much higher than those for non-diabetics (¥128,671 vs. ¥886, $p < 0.001$). Regarding both heart and cerebrovascular diseases, the annual medical costs

Table 2. Mean health care costs and utilization according to diabetic status

	Diabetic status				p value ¹⁾
	Non-diabetic	IFG	Undiagnosed diabetes	Known diabetes	
	FPG	<110 mg/dl	110–125 mg/dl	>125 mg/dl	
n	3,682	199	87	118	
Inpatient					
Cumulative admission rate (%) ²⁾	22.1	28.6	41.4	47.5	
Odds ratio (95%CI) ³⁾	1.00 (reference)	1.27 (0.92–1.75)	2.05 (1.32–3.18)	2.70 (1.86–3.93)	
Annual hospital cost (¥) (SE) ^{3, 4)}	41,812 (4,573)	40,856 (12,112)	126,990* (18,033)	164,475* (15,644)	<0.001
Outpatient					
Cumulative visit rate (%) ²⁾	97.8	97.0	96.6	100.0	
Odds ratio (95%CI) ³⁾	1.00 (reference)	0.75 (0.32–1.77)	0.71 (0.22–2.33)	-	
Annual outpatient cost (¥) (SE) ^{3, 4)}	79,626 (4,256)	77,746 (11,273)	123,831 (16,784)	233,665* (14,560)	<0.001
Dental care					
Cumulative visit rate (%) ²⁾	86.2	81.9	80.5	82.2	
Odds ratio (95%CI) ³⁾	1.00 (reference)	0.79 (0.54–1.15)	0.76 (0.44–1.31)	0.79 (0.49–1.29)	
Annual dental care cost (¥) (SE) ^{3, 4)}	22,646 (658)	19,493 (1,743)	27,055 (2,595)	24,624 (2,251)	0.433

IFG=impaired fasting glucose; FPG=fasting plasma glucose; 95%CI=95% confidence interval; SE=standard error.

* $p < 0.001$, significant difference versus the non-diabetic group for multiple post-hoc comparisons with Dunnett's correction, after the data were logarithmically transformed.

¹⁾ p values were calculated by analysis of variance, after the data were logarithmically transformed.

²⁾ Crude rate (subjects who received care at least once between April 2000 and March 2005).

³⁾ Adjusted for sex, age, smoking status, BMI, hypertension, and hyperlipemia.

⁴⁾ Per capita.

Table 3. Mean medical care costs for disease classifications according to diabetic status

	Diabetic status	Non-diabetic	IFG	Undiagnosed diabetes	Known diabetes	<i>p</i> value ¹⁾
	FPG	<110 mg/dl	110–125 mg/dl	>125 mg/dl		
Annual medical care cost (¥) ^{2–4)}						
Diabetes (SE)		886 (1,141)	11,552** (3,022)	43,456** (4,500)	128,671** (3,904)	<0.001
Hypertension (SE)		18,106 (785)	20,833 (2,080)	29,588 (3,096)	25,492 (2,686)	0.085
Heart disease (SE)		5,434 (1,446)	4,615 (3,831)	3,515 (5,703)	25,630* (4,948)	0.041
Cerebrovascular disease (SE)		6,841 (2,068)	7,029 (5,476)	4,989 (8,153)	69,369* (7,073)	0.066
Cancer (SE) ⁵⁾		3,383 (1,513)	5,261 (4,008)	11,677 (5,968)	4,738 (5,177)	0.110

IFG=impaired fasting glucose; FPG=fasting plasma glucose; SE=standard error.

* $p < 0.05$, ** $p < 0.001$, significant difference versus the non-diabetic group for multiple post-hoc comparisons with Dunnett's correction, after the data were logarithmically transformed.

¹⁾ p values were calculated by analysis of variance, after the data were logarithmically transformed.

²⁾ This cost includes inpatient and outpatient care.

³⁾ Adjusted for sex, age, smoking status, BMI, hypertension, and hyperlipemia.

⁴⁾ Per capita.

⁵⁾ This includes cancers of the stomach, colon, rectum, liver, and lung.

for subjects with known diabetes were highest (for heart disease: $p = 0.039$; for cerebrovascular disease: $p = 0.030$). There were no clear differences for cancer medical costs.

Discussion

In this cohort study of 4,086 Japanese workers, we found that diabetic individuals incurred significantly higher health care costs than non-diabetics, while IFG was not associated with higher costs. Compared with the non-diabetic group, subjects with known diabetes incurred 3.9- and 2.9-fold higher annual inpatient and outpatient costs, respectively, while subjects in the undiagnosed diabetes group incurred 3.0- and 1.6-fold higher costs, respectively. Many of the excess costs of medical care among subjects with diabetes were caused by diabetes itself, but some was also attributable to cardiovascular disease (CVD), which is considered to be complications of diabetes.

Individuals with undiagnosed diabetes may notice an initial manifestation of diabetes, which subsequently leads to disease progression. In our study, similar health care costs were seen among the non-diabetic, IFG and undiagnosed diabetes groups at baseline, and the costs of the subjects with undiagnosed diabetes gradually increased thereafter to reach the levels of subjects with known diabetes within 4 yr. A primary care cohort study of type 2 diabetic patients with A1C <7% at baseline suggested that 28% of the patients had disease progression at 1 yr follow-up¹²⁾. Of the progressors, 62% were being treated with glucose-lowering medications. However, in our study, we could not conclude that the increasing cost in the undiagnosed diabetes group was associated with the diabetes progression.

A 10-yr follow-up study in Japan reported that medical costs for subjects with a self-reported history of diabetes were approximately 2-fold higher than those for subjects without either hypertension or diabetes⁷⁾. Even with a shorter follow-up period, our results indicated that the medical costs for subjects with known diabetes were 3.3-fold higher than those for the non-diabetic group. Overall, medical costs are typically 2-3-fold higher for subjects with diabetes than for non-diabetics.

A few studies have provided patient level estimates of the direct medical costs of patients with hyperglycemia below the diabetic threshold^{6, 8)}. They found that individuals with hyperglycemia incurred significantly higher medical costs than individuals with normal glucose, but the difference between the IFG group and the normal glucose group was not clear-cut. Age-, sex- and comorbidity-adjusted medical costs of subjects with FPG values in the range of 110–125 mg/dl were approximately 4% higher than those of subjects with FPG values of <100 mg/dl⁶⁾. Owing to the large sample size, the association is likely to be significant. Patients with both IFG (100–125 mg/dl) and possible impaired glucose tolerance were more costly than those with normoglycemia (\$7,003 vs. \$6,208, $p < 0.001$), while the costs were similar between subjects with isolated IFG and those with normoglycemia (\$6,171 vs. \$6,208)⁸⁾. Our findings showed that individuals with IFG did not incur higher costs than non-diabetics, suggesting that most of workers with IFG may have not converted to diabetes yet within 4-yr when cost is the focus.

Complications at the macrovascular level have been linked to diabetes, and subjects with diabetes are more likely to suffer from CVD¹³⁻¹⁵⁾. Previous studies have reported that CVD accounts for the large majority of diabetic complication costs^{3, 16, 17)}. Diagnosis of dia-

betes more than doubled the inpatient cost of cardiac disease and tripled the inpatient cost of cerebrovascular disease over 8 yr of follow-up¹⁷). The nationally representative study in the U.S. demonstrated that diabetes with macrovascular comorbid conditions are associated with both increased health care cost and lost productivity cost¹⁸). Our results demonstrated a higher prevalence of heart disease in subjects with known diabetes at baseline, and this may translate into the excess costs of CVD. It appears that heart and cerebrovascular diseases had no effect for subjects with undiagnosed diabetes during the study period. Although it is probable that CVD is considered to be a complication of diabetes, there may not have been a sufficient period of time between the onset of diabetes and the subsequent occurrence of CVD.

Recently, an elevated risk of cancer in diabetic patients has been reported. In a large-scale population-based cohort study in Japan, a past diagnosis of diabetes was associated with an increased risk of total cancer¹⁹). In the present study, there was no clear relationship between diabetic status and incremental medical costs due to cancer.

However caution is necessary when interpreting these results because the diagnosis for each instance of medical care use was based only on the main diagnosis, even if the patient was simultaneously suffering from other diseases. There were no significant differences in the hypertension costs among the different diabetes groups, although a lower proportion of subjects with known diabetes had hypertension than those with IFG and undiagnosed diabetes. One possibility is that more frequent medical visit for diabetes and CVD treatment may mask additional services given for hypertension.

Periodontal disease is more frequent and severe in diabetic individuals. Diabetic patients may reach a more significant extent of periodontal disease than non-diabetic controls, even in the absence of bacterial growth²⁰). As expected, our findings showed that the proportion of patients with severe periodontitis increased with worsening diabetic status. However, non-diabetics visited dental clinics most frequently during the 5-yr study period. A previous finding that US adults with diabetes were less likely to have seen a dentist than those without diabetes²¹). Dental care utilization may reflect the level of health concerns rather than oral conditions.

The present findings should be considered in the context of some limitations. First, the study population was a specific group of civil service officers aged 40–55 yr working in one prefecture in Japan, and health insurance systems and health services differ among countries. Thus, it is difficult to determine how applicable the

findings may be to other populations. However, given homogeneity with respect to important confounders and availability of accurate information, we suppose that the observed associations are valid estimates of the effects of diabetic status on health care costs²²). Second, we could not distinguish between types 1 and 2 diabetes. Because onset of type 1 diabetes usually occurs before the age of 30 yr²³), the individuals with undiagnosed diabetes in our study likely have had type 2 diabetes. Finally, as mentioned above, the diagnosis for each instance of medical care use was based only on the main diagnosis.

In summary, we have confirmed the presence of increased health care costs for diabetic individuals using 5-yr follow-up worksite cohort data. IFG was not found to be associated with higher costs. The health care costs of subjects with undiagnosed diabetes reached levels similar to those of known diabetics within 4 yr. Diabetes may increase the medical care costs for hypertension and CVD, even in middle-aged adults. Diabetes and related complications present considerable monetary burdens to health insurance providers. More promotion of the prevention of diabetes among people of working age should be encouraged in order to reduce health care cost, and this may also lead to better work productivity and quality of working life.

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References

- 1) Wild S, Roglic G, Green A, Sicree R, King H (2004) Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* **27**, 1047–53.
- 2) Ramsey S, Summers KH, Leong SA, Birnbaum HG, Kemner JE, Greenberg P (2002) Productivity and medical costs of diabetes in a large employer population. *Diabetes Care* **25**, 23–9.
- 3) Brandle M, Zhou H, Smith BR, Marriott D, Burke R, Tabaei BP, Brown MB, Herman WH (2003) The direct medical cost of type 2 diabetes. *Diabetes Care* **26**, 2300–4.
- 4) O'Brien JA, Patrick AR, Caro J (2003) Estimates of direct medical costs for microvascular and macrovascular complications resulting from type 2 diabetes mellitus in the United States in 2000. *Clin Ther* **25**, 1017–38.
- 5) Morsanutto A, Berto P, Lopatriello S, Voinovich D, Gelisio R, Mantovani LG (2004) Major diabetes com-

- plications have an impact on total annual medical cost of type 2 diabetes. *Diabetes Care* **27**, 1841–2.
- 6) Nichols GA, Brown JB (2005) Higher medical care costs accompany impaired fasting glucose. *Diabetes Care* **28**, 2223–9.
 - 7) Nakamura K, Okamura T, Kanda H, Hayakawa T, Okayama A, Ueshima H (2006) Medical costs of patients with hypertension and/or diabetes: a 10-year follow-up study of National Health Insurance in Shiga, Japan. *J Hypertens* **24**, 2305–9.
 - 8) Nichols GA, Arondekar B, Herman WH (2008) Medical care costs one year after identification of hyperglycemia below the threshold for diabetes. *Med Care* **46**, 287–92.
 - 9) Watanabe Y (1996) The health insurance system in Japan. *Pacing Clin Electrophysiol* **19**, 1117–21.
 - 10) World Health Organization (1999) Definition, Diagnosis and Classification of Diabetes Mellitus and Its Complications. Part 1: Diagnosis and Classification of Diabetes Mellitus. World Health Organization, Geneva.
 - 11) Ainamo J, Barmes D, Beagrie G, Cutress T, Martin J, Sardo-Infirri J (1982) Development of the World Health Organization (WHO) community periodontal index of treatment needs (CPITN). *Int Dent J* **32**, 281–91.
 - 12) Pani LN, Nathan DM, Grant RW (2008) Clinical predictors of disease progression and medication initiation in untreated patients with type 2 diabetes and A1C less than 7%. *Diabetes Care* **31**, 386–90.
 - 13) Fuller JH, Shipley MJ, Rose G, Jarrett RJ, Keen H (1980) Coronary-heart-disease risk and impaired glucose tolerance. The Whitehall study. *Lancet* **315**, 1375–6.
 - 14) Jeerakathil T, Johnson JA, Simpson SH, Majumdar SR (2007) Short-term risk for stroke is doubled in persons with newly treated type 2 diabetes compared with persons without diabetes: a population-based cohort study. *Stroke* **38**, 1739–43.
 - 15) Lee CM, Huxley RR, Lam TH, Martiniuk AL, Ueshima H, Pan WH, Welborn T, Woodward M (2007) Prevalence of diabetes mellitus and population attributable fractions for coronary heart disease and stroke mortality in the WHO South-East Asia and Western Pacific regions. *Asia Pac J Clin Nutr* **16**, 187–92.
 - 16) Glauber HS, Brown JB (1992) Use of health maintenance organization data bases to study pharmacy resource usage in diabetes mellitus. *Diabetes Care* **15**, 870–6.
 - 17) Brown JB, Nichols GA, Glauber HS, Bakst AW (1999) Type 2 diabetes: incremental medical care costs during the first 8 years after diagnosis. *Diabetes Care* **22**, 1116–24.
 - 18) Fu AZ, Qiu Y, Radican L, Wells BJ (2009) Health care and productivity costs associated with diabetic patients with macrovascular comorbid conditions. *Diabetes Care* **32**, 2187–92.
 - 19) Inoue M, Iwasaki M, Otani T, Sasazuki S, Noda M, Tsugane S (2006) Diabetes mellitus and the risk of cancer: results from a large-scale population-based cohort study in Japan. *Arch Intern Med* **166**, 1871–7.
 - 20) Campus G, Salem A, Uzzau S, Baldoni E, Tonolo G (2005) Diabetes and periodontal disease: a case-control study. *J Periodontol* **76**, 418–25.
 - 21) Tomar SL, Lester A (2000) Dental and other health care visits among U.S. adults with diabetes. *Diabetes Care* **23**, 1505–10.
 - 22) Rothman KJ, Greenland S, Lash TL (2007) Study Design and Conduct. In: *Modern Epidemiology*, 3rd Ed., Rothman KJ, Greenland S, Lash TL (Eds.), 128–47, Lippincott Williams & Wilkins, Philadelphia.
 - 23) Nishimura R, Tajima N, Matsushima M, LaPorte RE (1998) Puberty, IDDM, and death in Japan. Diabetes Epidemiology Research International Study Group. *Diabetes Care* **21**, 1674–9.