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ORIGINAL RESEARCH

Annual direct cost of dry eye in Japan

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Background: This study was performed to estimate the annual direct cost incurred by dry eye patients, which includes expenses for treatment and drugs, as well as the cost of punctal plugs.

Methods: The study group consisted of 118 dry eye patients aged 20 years or older who visited any of the 15 medical care facilities that participated in this prospective cohort dry eye study. We estimated annual direct costs from outpatient medical records and survey questionnaires obtained from patients.

Results: Of the total patients enrolled, 10 were men and 108 women, and their average age was 64.1 ± 11.2 years. The number of hospital visits made by patients was 5.8 ± 3.6 per year. Among those who used ophthalmic solutions, the numbers of bottles used per year were as follows: 32.1 ± 20.8 bottles of hyaluronic acid ophthalmic solution (87 patients), 53.1 ± 42.2 bottles of artificial tears (40 patients), and 33.2 ± 23.2 bottles of over-the-counter eyedrops (15 patients). In patients with punctal plugs, 4.1 ± 3.9 plugs were used annually. The annual drug cost was 32,000 ± 21,675 Japanese yen (323 ± 219 US dollars). The clinical cost was 16,318 ± 9961 Japanese yen (165 ± 101 US dollars). The total direct costs including punctal plug treatment amounted to 52,467 ± 38,052 Japanese yen (530 ± 384 US dollars).

Conclusion: Although treatment modalities for dry eye in Japan were different from those in the US and in European countries, the direct cost of dry eye patients in Japan was comparable with that reported in those countries. Considering the high prevalence of dry eye, the direct cost of this chronic condition may be significant.

Keywords: burden of disease, cost, dry eye, eyedrops, quality of life

Introduction

Dry eye is recognized as a common eye disease with a high prevalence in many countries, including Japan.[1,2] Although dry eye rarely leads to blindness or visual impairment, the condition exerts a key influence on quality of life (QOL) and imposes a burden on patients.[3–5] Miljanovic et al reported that patients with dry eye syndrome have more difficulty in reading, performing professional work, using a computer, watching television, and driving, as compared with those without dry eye.[6] Utility assessment is a formal method for quantifying the relative impact of a given health state or disease on patient lives, which is defined on a continuous scale from 0 to 1, where 0 corresponds to the worst possible QOL weight (equal to death) and 1 corresponds to the best possible QOL weight (equal to perfect health). Schiffman et al reported that the mean utility score of moderate dry eye was 0.81 and that of severe dry eye was 0.72.[7] Hence, there appears to be a considerable burden of dry eye disease based on both its prevalence and patient morbidity.

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In addition to impairment of QOL, the financial burden can be a cause of concern for patients with dry eye.[1,8–11] Financial burden consists of direct costs, including medical fees and drug expenses, and indirect costs, including absence from work and decreased productivity. Studies to estimate the direct and indirect costs of dry eye have been conducted in European countries and in the US.[1,8–11] The average annual direct costs of dry eye have been reported to be 600 US dollars in studies from six European countries.[8] In addition, the indirect financial burden in the form of work absences and decreased productivity cannot be overlooked, with studies showing that patients with dry eye lose 2–5 working days per year and work with the symptoms for more than 6 months.[10,11]

Assessing multiple aspects of the burden of this disease appears to be important from the perspective of medical care assessment or medical economics. The Dry Eye Survey Group consisting of 15 facilities, mostly affiliated with the National Hospital Organization in Japan, has been conducting a multicenter prospective cohort study on dry eye patients to investigate the effect of the disease from the patient perspective. This article reports the results of analysis on the direct costs of dry eye patients in Japan.

Materials and methods

This study was performed as part of a multicenter cohort study being conducted at 15 facilities comprising 13 affiliate hospitals of the National Hospital Organization, Keio University, and Tokyo Dental College (see Appendix). The subjects enrolled in the study were dry eye patients aged 20 years and older who visited any of the facilities. The diagnostic criteria used in this study complied with those defined by the Japanese Dry Eye Society, with a slight modification (Table 1).[12] All cases with definite dry eye according to the criteria were enrolled in the study. The principles of the World Medical Association Declaration of Helsinki were followed. Each subject was given a thorough explanation of the purpose of the study and all procedures involved, and the subjects provided written informed consent prior to enrollment. Approval for this research was granted by the Committee for the Protection of Human Subjects at each hospital.

Table 1 Diagnosis criteria for dry eye for this study

Having subjective symptoms due to dry eye	
Abnormality in tear function	
1. Schirmer's I testing (without anesthesia)	<5 mm
2. Tear film break-up time	<5 seconds
Positive when either of 1 or 2 is applicable	
Abnormality in corneal and conjunctival epithelium	
1. Fluorescein staining score (range 0–9)	>3
2. Rose bengal staining score (range 0–9)	>3
Positive when either of 1 or 2 is applicable	

Notes: The criteria primarily complied with those defined by Japanese Dry Eye Society with a slight modification.[12] Definite dry eye was diagnosed when all conditions were met.

The cases were registered between April 2005 and March 2008, with a total of 158 cases being initially registered. For the registered cases, information on ocular findings from the responsible physicians was collected. One year after registration in the cohort study, clinical data were collected from each facility. Information on drug expenses and number of hospital visits was also collected from the patients through a survey questionnaire. For this particular report, we analyzed the prescribed drugs and number of hospital visits in one year based on clinical data and patient questionnaire data collected during registration and one year later. Twelve patients were excluded because clinical data at one year after registration could not be obtained from the facilities. Twenty-eight patients were excluded because the survey questionnaire at one year was not returned. Consequently, we used the data from 118 subjects for analysis.

All medical costs are uniformly standardized by the social medical insurance system in Japan. Medical costs associated with dry eye were calculated based on the Japanese Social Insurance Medical Fee Payment for 2008. Based on hospital visits in one year, doctor fees were calculated assuming that an examination, slit-lamp biomicroscopy, and vital staining for corneal and conjunctival epithelium were performed at each hospital visit, and that a Schirmer's test, intraocular pressure measurement, and corrected vision testing were performed once a year. Costs for punctal plugs were calculated from the data based on the number of punctal plugs inserted. Drug costs were the one-year total of the basic preparation charges, charges for issuing prescriptions, and drug costs. The ophthalmic solutions focused on were hyaluronic acid eyedrops, artificial tears, chondroitin sulfate eyedrops, steroid eyedrops, nonsteroidal anti-inflammatory drug eyedrops, and antimicrobial eyedrops and ointments. In the case of patients using over-the-counter eyedrops, numbers of units and expenses were calculated approximately from questionnaires because the details could not be found in outpatient medical records. The direct cost consists of the medical and drug costs, and the expenses of plug insertion.

Results

The age of the 118 patients (10 men, 108 women) enrolled in the study ranged from 33 to 84 years with an average of

64.1 ± 11.2 years. Of these 118 patients, 47 had Sjögren's syndrome. Accordingly, some patients with Sjögren's syndrome visited the internal medicine department and the ophthalmology department on the same day. There were no ocular comorbidities, such as glaucoma and retinal disorders, which might affect the frequency of hospital visits. Results of clinical tests for dry eye at the time of enrollment and one year later are shown in Table 2. There were no statistically significant differences in the results of clinical tests between enrollment and one year later ($P > 0.05$, Mann-Whitney test).

The annual number of hospital visits made by the 118 patients in the study was 5.8 ± 3.6 (range 1–19). With regard to treatment modalities, hyaluronic acid ophthalmic solutions were used by 73.7% of patients, artificial tears in by 33.9% of patients, antimicrobials by 15.3% of patients, steroids by 18.6% of patients, nonsteroidal anti-inflammatory drugs by 7.6% of patients, chondroitin sulfate eyedrops by 9.3% of patients, and over-the-counter eyedrops by 12.7% of patients (Table 3). Punctal plugs were used by 11 patients (9.3%), whereas there were no cases treated with other surgical procedures, such as surgical punctal occlusion or tarsorrhaphy. Among those who used the respective ophthalmic solutions, the numbers of bottles used per year were as follows: 32.1 ± 20.8 bottles of hyaluronic acid ophthalmic solution (87 patients), 53.1 ± 42.2 bottles of artificial tears (40 patients), and 33.2 ± 23.2 of over-the-counter eyedrops (15 patients). In patients with punctal plugs, 4.1 ± 3.9 plugs were used annually.

From these data, the annual clinical cost was estimated to be 16,318 ± 9961 Japanese yen (165 ± 101 US dollars, calculated based on the yen-US dollar exchange rate in March, 2008, Table 4). The pharmacological cost was 32,000 ± 21,675 Japanese yen (323 ± 219 US dollars) per year, and the cost of punctal plugs was 4149 ± 17,876 Japanese yen (42 ± 181 US dollars). The mean annual cost per patient was 52,467 ± 38,052 Japanese yen (530 ± 384 US dollars).

Table 2 Characteristics of patients with dry eye in the survey

	At enrollment	One year later
Results of clinical tests (worse eye; n = 118)		
Schirmer's testing (mm)	3.7 ± 2.8	4.4 ± 3.5
Tear film break-up time (sec)	3.7 ± 1.7	3.8 ± 1.6
Fluorescein staining score (range 0–9)	1.9 ± 1.6	2.1 ± 1.7
Rose bengal staining score (range 0–9)	2.0 ± 2.0	2.0 ± 1.9

Notes: Results are expressed as the mean ± standard deviation. There were no statistically significant differences in results of clinical tests between enrollment and one year later ($P > 0.05$, Mann-Whitney test).

Table 3 Treatment modalities for dry eye patients in the survey

	Number of users (%)	Units used annually in users
Ophthalmic solutions		
Hyaluronic acid	87 (73.7%)	32.1 ± 20.8
Artificial tears	40 (33.9%)	53.1 ± 42.2
Antimicrobial drops	18 (15.3%)	13.8 ± 18.3
Steroidal drops	22 (18.6%)	18.4 ± 16.5
NSAID drops	9 (7.6%)	13.9 ± 9.0
Chondroitin sulfate	11 (9.3%)	26.3 ± 17.5
OTC eyedrops	15 (12.7%)	33.2 ± 23.2
Punctal plugs	11 (9.3%)	4.1 ± 3.9

Note: Numbers of units used for treatment are expressed as the mean ± standard deviation.
Abbreviations: NSAID, nonsteroidal anti-inflammatory drug; OTC, over-the counter.

Discussion

In the current study, the annual direct costs for dry eye in Japan were estimated to be 52,467 Japanese yen (530 US dollars), which included clinical costs of 16,318 Japanese yen (165 US dollars), pharmacological costs of 32,000 Japanese yen (323 US dollars), and costs of punctal plugs of 4149 Japanese yen (42 US dollars). It should be noted that treatment modalities for dry eye in Japan are different from those in the US and in European countries. Topical immunosuppressants, such as cyclosporine, and oral medications have not been approved for clinical use in the treatment of dry eye in Japan. Instead, hyaluronic acid eyedrops and artificial tears have been used as the major treatment modalities for dry eye. As shown in Table 3, other treatment modalities, such as steroid eyedrops, over-the-counter eyedrops, and punctual plugs, were concurrently used in some cases. Recently, two new topical agents for treating dry eye, diquafosol tetrasodium 3% and rebamipide 2%, have been approved for clinical use in Japan. These new drugs may alter the preferred practice patterns for the treatment of dry eye, but were not approved at the time of this study.

Clegg et al reported the results of the annual cost of dry eye patients in six European countries by using statistical data and interviews (Table 5).[8] Although there was a marked difference between the lowest amount of 273 US dollars in

Table 4 Direct costs for dry eye per year in the survey (Japanese yen)

Types of costs	Annual costs (mean ± SD, range)
Clinical costs	16,318 ± 9961 (range 2864–53,084)
Drug costs	32,000 ± 21,675 (range 4816–135,944)
Costs for punctal plugs	4149 ± 17,876 (range 0–152,320)
Mean direct cost per patient	52,467 ± 38,052 (range 7680–294,858)

Abbreviation: SD, standard deviation.

Table 5 Annual costs for dry eye in various countries

Country	Costs (US$)	Reference
France	273	Clegg et al[8]
Germany	536	Clegg et al[8]
Italy	645	Clegg et al[8]
Spain	765	Clegg et al[8]
Sweden	415	Clegg et al[8]
UK	1100	Clegg et al[8]
US	456	Pflugfelder[1]
US	11–355*	Enzenauer et al[9]
US	221**	Reddy et al[10]
Japan	530	MIZUNO(current study)

Notes: *Drug costs only; **Clinical costs only.

France and the highest amount of 1100 US dollars in the UK, the average expense of 622 US dollars was almost the same as that estimated in our study. The result in the US reported by Pflugfelder of 446 US dollars was also comparable.[1] Enzenauer et al reported that the annual cost in the particular case of ophthalmic solutions was 11–355 US dollars, which was in the same range as our results, though there is a difference arising from the type of ophthalmic solutions used.[9] Gayton estimated that 7–10 million Americans spend an average of 320 US dollars per year on artificial tears.[13] Reddy et al reported that the average doctor fees per year was 211 US dollars.[10] Although there are differences in preferred treatment modalities for dry eye among countries, there is no marked difference between the costs in the countries compared.

There are possible limitations to our research. In this study, 39% of patients had dry eye associated with Sjögren's syndrome. The predominance of females (92%) in the study is partly explained by this comorbidity, although dry eye is usually more common in women than in men. Further, this study was a hospital-based survey rather than a population-based survey. One of the clinical issues associated with dry eye is that many of the patients have not received medical management.[1,2] Therefore, it should be noted that the subjects in the study may not be representatives of the majority of patients with dry eye.

There are several studies of other eye diseases that indicate a concern about direct financial burden. It was reported that the direct costs of glaucoma in stage 4 were 2464 US dollars in the US, with approximately half of that amount spent on drugs.[14] Schmier et al reported that yearly expenditures for latanoprost and travoprost in the US were 1360 US dollars and 1278 US dollars, respectively.[15] The expenses for diabetic retinopathy are 1118 US dollars in the US,[16] and for age-related macular degeneration are 7349 Euros in France, 12,445 Euros in Germany, and 5732 Euros in Spain.[17] Expenditures on other eye diseases are high in comparison with the direct financial burden of dry eye. Drugs for dry eye are comparatively inexpensive and surgical remedies are generally not undertaken except for punctal plugs. However, when considering the high prevalence of this condition, the direct cost of this chronic condition may be significant.

Although not examined in this study, the indirect financial burden of dry eye is equally important, with 7% of patients obliged to change jobs and 11% forced to cut back on their working hours.[10] The subjective symptoms inherent in the disease, including eye discomfort for more than 6 months, contribute to the necessity of taking 2–5 days off from work in a year. In the present study, we have shown that patients with dry eye visit the hospital on average 5.8 times a year. When this time is converted into opportunity cost, it turns out to be approximately 500 US dollars. Although there are differences in indirect financial burden due to economic conditions, working conditions, and calculation methods, depending on each country, this cost is a cause of concern for the patients and cannot be overlooked. The estimation of indirect financial burden of dry eye should be investigated in the future.

The research method used here does not involve an assessment of outcomes and is called cost analysis. Moreover, other methods include cost utility analysis using utility and quality-adjusted life years, and cost effectiveness analysis based on specific outcomes (eg, life years and treatment results) and costs. Although cost analysis is easy to implement, it has a disadvantage in that it cannot be used to determine directly the distribution of medical resources and relative effectiveness of a given strategy for a specific treatment. Therefore, the burden of disease and treatment assessments using cost effectiveness analysis and cost utility analysis are topics for future investigation.

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Disclosure

The authors report no conflicts of interest in this work.

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Appendix

The Dry Eye Survey Group of National Hospital Organization in Japan

The following individuals and National Hospital Organizations participated in the study:

H Negishi, A Hayashi, Chiba Medical Center, Chiba; Terada H Tachikawa, Disaster Medical Center; T Katsuta, K Fujiike, S Hatou, Tokyo Medical Center, Tokyo; Y Yamada, Tokyo Hospital, Kiyose; H Hirose, K Toura, Nagoya Medical Center, Nagoya; M Yamamoto, N Yoshida, N Kawagoe, Kyoto Medical Center, Kyoto; Y Otori, Y Saito, Y Sakamoto, Osaka National Hospital, Osaka; T Nakamura, Kure Medical Center and Chugoku Cancer Center, Kure; M Kogiso, Zentsuji National Hospital, Zentsuji; H Enaida, T Nagatomi, Kyusyu Medical Center, Fukuoka; A Takehara, S Kubota, E Niiro, Ureshino Medical Center, Ureshino; H Aoki, Kumamoto Medical Center, Kumamoto; N Miyamura, H Hayashida, Nagasaki Medical Center, Ohmura; M Kaido, M Dogru, K Tsubota, Keio University School of Medicine, Tokyo; S Den, J Shimazaki, Tokyo Dental College, Chiba; M Yamada, Y Mizuno, G Hanazono, K Tsunoda, Y Miyake, National Institute of Sensory Organs, Tokyo Medical Center, Tokyo.

ClinicoEconomics and Outcomes Research Dove

ORIGINAL RESEARCH

Impact of dry eye on work productivity

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Background: The purpose of this study was to evaluate the impact of dry eye on work productivity of office workers, especially in terms of presenteeism.

Methods: A total of 396 individuals aged ≥20 years (258 men and 138 women, mean age 43.4 ± 13.0 years) were recruited through an online survey. Data from 355 responders who did not have missing values were included in the analysis. They were classified into the following four groups according to the diagnostic status and subjective symptoms of dry eye: a definite dry eye group; a marginal dry eye group; a self-reported dry eye group; and a control group. The impact of dry eye on work productivity was evaluated using the Japanese version of the Work Limitations Questionnaire. The cost of work productivity loss associated with dry eye and the economic benefits of providing treatment for dry eye were also assessed.

Results: The degree of work performance loss was 5 65% in the definite dry eye group, 4.37% in the marginal dry eye group, 6.06% in the self-reported dry eye group, and 4.27% in the control group. Productivity in the self-reported dry eye group was significantly lower than that in the control group ($P < 0.05$). The annual cost of work productivity loss associated with dry eye was estimated to be USD 741 per person.

Conclusion: Dry eye impairs work performance among office workers, which may lead to a substantial loss to industry. Management of symptoms of dry eye by providing treatment may contribute to improvement in work productivity.

Keywords: burden of disease, dry eye, presenteeism, quality of life

Introduction

Although the prevalence of dry eye varies among the reports, it is widely recognized that dry eye is a chronic eye disorder that is highly prevalent in many countries, including Japan.[1,2] Although the probability of dry eye causing blindness or permanent visual impairment is low, it is considered to have a significant impact on the daily and social lives of affected patients.[3–5] Miljanovic et al reported that patients with dry eye syndrome had more difficulty reading, carrying out professional work, using a computer, watching television, and driving compared with those without dry eye.[6] Utility assessment is a formal method for quantifying the relative impact of a given health state or disease on patient lives, which is defined on a continuous scale from 0 to 1, where 0 corresponds to the worst possible quality of life weight (equal to death) and 1 corresponds to the best possible quality of life weight (equal to perfect health). Schiffman et al reported that the utility of moderate dry eye was 0.81 and that of severe dry eye was 0.72.[7] The burden of dry eye disease from both the prevalence and patient morbidity standpoints appears to be considerable.

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The disease burden can be divided into three categories, ie, direct costs such as medical fees; indirect costs such as low employment, absence from work, and impaired productivity; and a decrease in quality of life. Given that dry eye is highly prevalent among people of working age as well as in the elderly, its impact on work productivity is considered to be substantial. Moreover, it has been reported that the incidence of dry eye is particularly high in workers using visual display terminals, including laptops, tablets, electronic readers, and smartphones.[8–10] Based on this background, it would appear worthwhile to evaluate work productivity in patients with dry eye, but few studies have been conducted from this viewpoint.

Loss of work productivity may occur through either absenteeism (absence, early leaving) or presenteeism. Presenteeism is a concept proposed by Auren in 1955[11] to describe productivity loss when employees come to work but are not fully productive. In a study on the burden of dry eye disease, Reddy et al reported that patients with dry eye take 2–5 days off work annually, while they were present at work having symptoms for 191–208 days annually, indicating that presenteeism is a greater issue than absenteeism among those having dry eye.[12]

Patel et al conducted a study to evaluate presenteeism in patients with a diagnosis of dry eye using the Work Productivity and Activity Impairment Questionnaire, and found that those with higher scores of the Ocular Surface Disease Index, which were obtained by a questionnaire concerning subjective symptoms of dry eye, had a greater loss of work productivity.[13] However, because this study did not include any subjects without dry eye, comparison of presenteeism against healthy individuals was not possible. In the present study, we evaluated the impact of dry eye on presenteeism using the Japanese version of the Work Limitations Questionnaire (WLQ-J, Sompo Japan Healthcare Services Inc, Tokyo, Japan) which is an established tool for evaluation of presenteeism.[14–16] Furthermore, the cost of work productivity loss associated with dry eye and economic benefits of providing treatment for dry eye were also assessed.

Materials and methods

Subjects

Using the general consumer panel (approximately 1,396,000 persons registered) run by Cross Marketing Inc (Tokyo, Japan), an Internet online survey was carried out targeting office workers aged ≥20 years. The survey is based on the WLQ-J, a questionnaire consisting of 25 questions. Questions concerning the background of participants, such as age and gender, diagnostic status of dry eye, and 12 questions concerning their subjective symptoms were also asked. Of 618 individuals who initially showed an intention to participate in the study, 396 responded and answered the questions during the study period. The study period was between June 10, 2011 and July 4, 2011. Those who were engaged in medical services, eye-related industry, and market research were excluded from participating in the present study. The study was conducted in accordance with the Declaration of Helsinki of the World Medical Association, and the Ethical Guidelines for Epidemiology Research issued by the Ministry of Education, Culture, Sports, Science, and Technology and the Ministry of Health, Labour, and Welfare of Japan (July 17, 2002). The study was reviewed by a nonprofit organization, the MINS Institutional Review Board, through Nielsen Company Japan (Tokyo, Japan), which organized the questionnaire survey, and was conducted appropriately in accordance with their advice on the clinical study.

Participants were divided into subgroups according to their diagnostic status and subjective symptoms of dry eye. Those who had consulted an ophthalmologist in the past and received a diagnosis of dry eye were defined as having dry eye. Moreover, participants were asked whether or not they had subjective symptoms of dry eye within the past month according to the following 12 criteria: eyes get tired easily; have eye mucus; eyes feel gritty; eyes feel heavy; eyes feel dry; eyes feel uncomfortable; eyes feel painful; have tears without reason; have blurry eyesight; eyes feel itchy; feel the light dazzling; eyes are often reddened. Those who met more than five criteria were defined as having subjective symptoms according to the report of Toda et al.[17] Based on the results, participants were classified into the following four groups: definite dry eye group, ie, those who have both symptoms and a diagnosis; marginal dry eye group, ie, those who have a diagnosis but no symptoms; self-reported dry eye group, ie, those who have symptoms but no diagnosis; and a control group, ie, those who have neither symptoms nor a diagnosis.

Evaluation of work performance loss using WLQ-J

Loss of work performance was evaluated using the WLQ-J, which is a questionnaire consisting of 25 items to estimate the degree to which health problems interfere with specific aspects of work performance and the impact of these work limitations on productivity by calculating scores using a specific algorithm. In addition to a total score to evaluate overall work performance, we also calculated subscale

scores to evaluate four aspects of work limitations, ie, time management, and physical, mental/interpersonal, and output demands.

Calculation of cost of work productivity loss and economic benefits of treatment

Data on the average annual wage in Japan from the Basic Survey on Wage Structure 2010 released by the Japanese Ministry of Health, Labour, and Welfare[18] and the degree of work performance loss associated with dry eye as measured by the WLQ-J were used to calculate the cost of work productivity loss due to dry eye. We previously estimated the annual direct cost incurred by dry eye patients, which includes the expenses for medical consultation, drug costs including over-the counter drugs, and cost of punctal plugs.[19] The direct cost of dry eye in Japan was weighed against the cost of work productivity loss to evaluate the economic benefits of providing treatment for dry eye. Values in Japanese yen were converted to US dollars using the currency exchange rate as of June 26, 2011 (1 yen = 0.0124 dollars).

Statistical analysis

Dunnett's test was used for comparison of the degree of work performance loss in each group, with a P value of <0.05 considered to be statistically significant.

Results

Participants

A total of 396 individuals (258 men [65.2%] and 138 women [34.8%]) aged 43.4 ± 13.0 (mean ± standard deviation) years responded to the survey. The age distribution was as follows: 175 (44.2%) were aged 20–39 years; 170 (42.9%) were aged 40–59 years; and 51 (12.9%) were aged ≥60 years. Of the responders, 355 who did not have missing values were enrolled and classified into four groups according to a diagnosis and subjective symptoms of dry eye. Consequently, 69 were in the dry eye group, 128 were in the marginal dry eye group, 80 were in the self-reported dry eye group, and 78 were in the control group. There was no significant difference in terms of age or gender among the groups (Table 1).

Impact of dry eye on work performance

The degree of work performance loss according to diagnostic status and symptoms of dry eye was 5.65% in the definite dry eye group, 4.37% in the marginal dry eye group, 6.06% in the self-reported dry eye, and 4.27% in the control group. Work performance in the self-reported dry eye group was significantly lower than that in the control group ($P < 0.05$, Figure 1). The subscale scores for the four aspects (time management, physical demands, mental/interpersonal, and output demands) were also calculated. Although the mental/interpersonal score was significantly lower in the definite dry eye group ($P < 0.05$) and the self-reported dry eye group ($P < 0.01$), no significant difference was observed among the other groups (Figure 2).

Cost of work productivity loss associated with dry eye

The cost of work productivity loss associated with dry eye was calculated. The differences in work productivity compared with the control group was 1.38%, 0.10%, and 1.79% in the definite dry eye group, the marginal dry eye group, and the self-reported dry eye group, respectively. Given that the average annual wage in Japan is currently USD 57,873 according to the Basic Survey of Wage Structure 2010 released by the Japanese Ministry of Health, Labour, and Welfare,[18] the cost of work productivity loss per person in each group was calculated as USD 799, USD 58, and USD 1036, respectively. Based on the difference in costs between the definite dry eye group and the control group, the cost of work productivity loss per person associated with dry eye was considered to be USD 799.

Table 1 Background of participants (n = 355)

	Definite dry eye group	Marginal dry eye group	Self-reported dry eye group	Control group	*P*-value
Participants (n)	69	128	80	78	
Gender (men/women)	41/28	87/41	47/33	57/21	0.168[b]
Age (years)[a]	42.9 ± 12.4	42.5 ± 12.9	42.8 ± 12.5	41.8 ± 11.0	0.944[c]
Age distribution (years)					
20–39	31	63	37	33	0.289[b]
40–59	30	51	32	42	
≥60	8	14	11	3	

Notes: [a]Values are expressed as the mean ± standard deviation; The following statistical analyses were used for comparisons between groups: [b]Chi-square test; [c]analysis of variance.

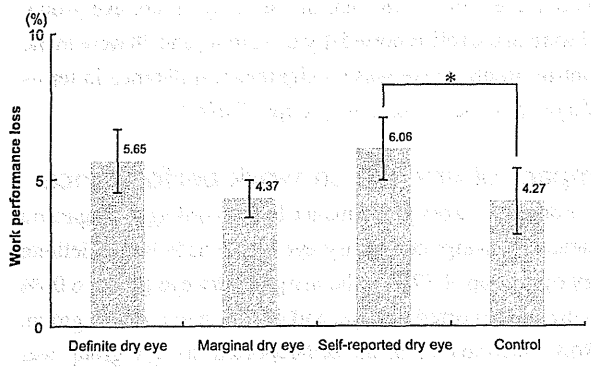


Figure 1 Work performance loss in each group.
Notes: The degree of work performance loss was 5.65% in the definite dry eye group, 4.37% in the marginal dry eye group, 6.06% in the self-reported dry eye group, and 4.27% in the control group. Productivity in the self-reported dry eye group was significantly lower than that in the control group. *$P < 0.05$ (Dunnett's test). Error bar shows 95% confidence interval.

Moreover, although participants in both the definite dry eye group and the marginal dry eye group were diagnosed as having dry eye, they are different in terms of the presence of subjective symptoms. Therefore, we assumed that the difference in work performance loss between the definite dry eye group and the marginal dry eye group was due to impaired work performance because symptoms of dry eye were not controlled. Multiplying this difference (1.28%) by the average annual wage resulted in USD 741. Given that it has been reported that the annual cost for treatment of dry eye in Japan is USD 651,[19] it is shown that benefits of providing treatment for dry eye equal or outweigh the cost incurred by productivity loss.

Discussion

Available objective survey instruments to evaluate presenteeism include the WLQ, Stanford Presenteeism Scale, and Work Productivity and Activity Impairment Questionnaire, for each of which reliability and validity have been established. WLQ is a measurement tool developed by Lerner et al (Tufts Medical Center, Boston, MA) to assess work productivity loss associated with health problems, and has been used for chronic conditions, such as depression, osteoarthritis, back pain, migraine, and epilepsy.[14–16]

In the present study, we evaluated the impact of dry eye on presenteeism among office workers using WLQ-J. The degree of work performance loss by WLQ-J was 5.65% in the definite dry eye group and 6.06% in the self-reported dry eye group, showing higher scores compared with the control group, and there was a significant difference between the self-reported dry eye group and the control group. This revealed that subjective symptoms of dry eye led to an impairment in work performance among office workers. On the other hand, the degree of work performance loss in the marginal dry eye group was 4.37%, which was comparable with that in the control group, suggesting that presenteeism

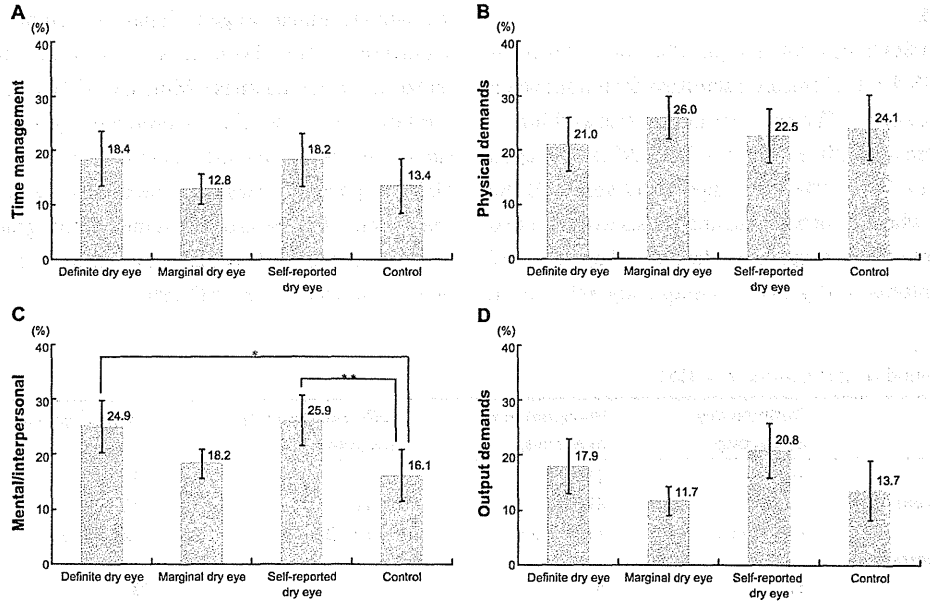


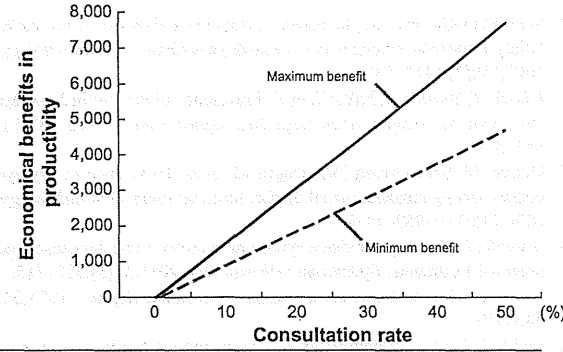
Figure 2 Work productivity loss by subscale scores for four aspects of work limitations, ie, time management (**A**), physical demands (**B**), mental/interpersonal (**C**), and output demands (**D**).
Notes: The mental/interpersonal score was significantly lower in the definite dry eye group ($P < 0.05$) and the self-reported dry eye group ($P < 0.01$). *$P < 0.05$; **$P < 0.01$ (one-way analysis of variance; Tukey or Games-Howell test was used for multiple comparisons). Error bar shows 95% confidence interval. Participants who had missing values (11 in group 1; 15 in group 2; four in group 3; 11 in group 4) were excluded from the analysis.

may not be affected when subjective symptoms of dry eye have lessened due to treatment, even when the diagnosis has been established.

When work productivity loss was converted into an amount of money, the annual difference between the definite dry eye group and the control group was USD 799. This indicates that dry eye poses a significant disease burden on individual office workers. Moreover, the amount of money for work productivity loss caused by uncontrolled subjective symptoms as calculated by the difference between the definite dry eye group and the marginal dry eye group was USD 741 annually, which is equivalent to the annual medical treatment cost for treating dry eye in Japan of USD 651. This suggests that providing treatment to control symptoms of dry eye can be justified from the viewpoint of medical costs in addition to other benefits, such as enhancing daily function and improving quality of life.

According to longitudinal data from the labor force survey (February, 2011) issued by the Statistics Bureau, the Ministry of Internal Affairs and Communications, and a statistics training institution, the number of employees in Japan is estimated to be 62,940,000.[20] Of these, 87.5% are office workers who use personal computers.[21] Therefore, it is estimated that there are 55,070,000 office workers in Japan who use personal computers at work. Since the incidence of dry eye among visual display terminal workers in Japan has been reported to be between 23%[8] and 32.3%,[9] office workers with dry eye are estimated to number between 12,666,100 and 17,790,000. When the cost of work performance loss associated with uncontrolled dry eye is assumed to be USD 741 based on the difference between the definite dry eye group and the marginal dry eye group in the present study, the annual loss of productivity associated with dry eye in Japan is estimated to be USD 9386–15,386 million (12,666,100–20,770,000 × USD 741/year).

One of the clinical issues associated with dry eye is that many of the patients have not received medical management.[1,2,22] In the present study, the degree of work performance loss was most prominent in the self-reported dry eye group, which included those who had symptoms of dry eye but who had not been diagnosed. This indicates that the consultation rate for patients with dry eye is generally low. Given that it is estimated that there are 12,666,100–20,770,000 office workers with dry eye in Japan, the economic benefits produced by medical treatment and subsequent increased productivity will reach USD 939–1539 million if 10% of the office workers with dry eye received medical treatment, and USD 4694–7693 million when 50% of them received medical treatment (Figure 3).



Consultation rate (%)	0	10	20	30	40	50
Minimum benefit	0	939	1,878	2,817	3,755	4,694
Maximum benefit	0	1,539	3,078	4,617	6,156	7,695

(Unit: USD million)

Figure 3 Economic benefits in productivity from providing treatment for dry eye.
Note: When 50% of office workers with dry eye received treatment, the economic benefits were estimated to be USD 4694–7693 million.

The present study shows that office workers with symptoms of dry eye had work performance loss, which can lead to a substantial loss in work productivity. It was also shown that the medical cost for the treatment of dry eye outweighs the loss of productivity, producing economic benefits Thus, it is very important to provide treatment for dry eye, because it not only improves quality of life for individual office workers, but also contributes to vitalization of the entire industry. In view of this, it may be important to enhance awareness of dry eye among office workers by educational activities.

Disclosure

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Understanding Measurements of Vitality in Patients with Chronic Kidney Disease: Connecting a Quality-of-Life Scale to Daily Activities

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Abstract

Background: Many patients with chronic kidney disease (CKD) suffer from fatigue caused by anemia, but that anemia can be reversed. Successful treatment can be measured as a decrease in fatigue and an increase in energy or vitality, particularly on the vitality (VT) subscale of the SF-36. Changes in VT scores are most commonly interpreted in terms of minimally important differences or standardized effect sizes, but neither a minimally important difference nor a standardized effect size provides information about how patients' activities are affected. Therefore, we analyzed the association between differences in VT scores and a variable that is meaningful to patients and to society the frequency of going out.

Study Design: Questionnaire survey. Analyses of differences among participants at bseline, and analyses of differences within participants over time.

Setting and Participants: CKD patients who were not on dialysis and were involved in a study of anti-anemia therapy.

Predictor: VT scores.

Outcome: Frequency of going out.

Measurements: VT scores and the frequency of going out.

Results: At baseline, higher VT scores and younger age were associated with going out more often, while sex and the presence of diabetic nephropathy were not associated with the frequency of going out. Greater changes in VT scores over time were associated with greater changes in the frequency of going out, in univariate and multivariate analyses.

Conclusions: At baseline, VT was associated with the frequency of going out. Increases in VT were also associated with increases in the frequency of going out. These results show how VT scores can be linked to daily activities that are important to individual patients and to society.

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Introduction

Anemia causes fatigue in predialysis patients with chronic kidney disease (CKD). That fatigue is alleviated when Hb levels increase after treatment with erythropoiesis-stimulating agents (ESAs). The effects of such treatment are often measured as self-reported decreases in fatigue and increases in energy or vitality. In a recent review of 14 studies, Gandra et al. [1] concluded that ESAs can increase self-reported levels of energy, and a review by Leaf and Goldfarb came to a similar conclusion [2].

In this context, one question is how scores on the vitality (VT) subscale of the SF-36 should be interpreted. Changes in VT scores are most commonly interpreted in terms of minimally important differences [3] or standardized effect sizes [4]. Minimally important differences are cutoff points; they can be used to distinguish treatments that have a pre-specified magnitude of effect from those that do not. Standardized effect sizes such as Cohen's d

Table 1. Demographic and clinical characteristics, and the frequency of going out.

	n (%), or mean ± SD
Sex	
M	144 (46.6)
F	165 (53.4)
Age (years)	64.7±11.8
<65	138 (44.7)
≥65	171 (53.3)
Underlying Disease	
Chronic glomerulonephritis	135 (43.7)
Diabetic nephropathy	67 (21.7)
Other	107 (34.6)
Weight (kg)	56.46±11.06
Hemoglobin (g/dL)	9.17±0.83
Ferritin (ng/mL)	128.6±203.8
TSAT (%)	31.02±12.29
Serum creatinine (mg/dL)	3.55±1.07
Ccr (mL/min)	18.79±6.67
VT	64.1±21.2
Frequency of going out	
Almost never	31 (10.0)
1–2 days a week	100 (32.4)
3–4 days a week	78 (25.2)
5 or more days a week	100 (32.4)
Total	309 (100)

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express the magnitude of an effect in standard-deviation units and are often interpreted as "small," "large," etc. By itself, however, neither a minimally important difference nor a standardized effect size provides information about how differences in vitality affect CKD patients' lives.

For example, in a recently reported randomized controlled trial, patients with chronic kidney disease were given an ESA, with one of two possible Hb targets [5]. The between-group difference in the change from the baseline value was 4.8 points on the VT scale, which is very close to the minimally important difference of 5 points that was suggested by Bjorner et al. [6]. That difference was also statistically significant ($p = 0.025$) However, when we ask what that difference means, then the p value of course gives no answer, and the minimally important difference is interpretable only in terms of the population-level phenomena by which it was originally defined.

Interpretability is recognized as an important characteristic of patient-reported outcomes [7], and the impact of anemia treatment on the quality of life of pre-dialysis CKD patients has been studied [8–10], but connections between VT scores and daily life are still obscure. Therefore, we analyzed the association between differences in VT scores and a variable that is not generally considered to be a direct manifestation of health-related quality of life, but is nonetheless meaningful to patients and to society: the frequency of going out (we translate the Japanese *gai-shutsu* as "going out"). This paper shows how differences in VT scores, both differences between participants at baseline and differences over time within participants, could be used to predict differences in the frequency of going out.

Methods

Data from those patients in Akizawa et al.'s study [5] whose quality-of-life (QOL) questionnaires at baseline and also at 12 weeks after the start of drug administration were complete, without regard to the group to which they were assigned, were analyzed. VT was measured with 4 question items and scored on a scale from 0 to 100, with higher scores reflecting greater vitality [11]. The questionnaires also included one question asking about the frequency of going out. That question had four choices as responses. "I almost never go out", "I go out one or two days each week", "I go out three or four days each week", and "I go out five or more days each week"

The relationship at baseline between VT score and the frequency of going out was analyzed, as was the relationship between changes in VT scores and changes in the frequency of going out.

This study was approved by the Institutional Review Boards at Ikegami General Hospital, the Medical Corporation of Showakai, and Kochi Takasu Hospital. All participants gave written informed consent.

Statistical Analysis

Analyses of data collected at baseline. To analyze the relationship at baseline between VT score and the frequency of going out, two logistic-regression models were used. In both models, the dependent variable was the baseline frequency of going out, which had been dichotomized into low frequency (fewer than three times each week) and high frequency (three or more times each week).

In the simple model (model A), there was only one independent variable: the baseline VT score. In the more complex model (model B), sex, age, and the presence or absence of diabetic nephropathy were included as covariates.

Analyses of changes over time. To model the association between changes in VT scores and changes in the frequency of going out, logistic regression was again used.

There were two independent variables one was the change in VT score, and the other was that change expressed as a standardized effect size and then categorized (SES) [4]. The SES of the change in VT score was computed as follows. (individual score at 12 weeks − individual score at baseline)/standard deviation of the scores at baseline.

SES results are often interpreted in terms of categories, and for this study five categories of SES were defined. The values most commonly used as "borders" between SES categories are 0.2, 0.5, and 0.8 [4]. Using those three criteria, we defined the highest category as "greater than or equal to 0.8", the next lower category as "from 0.5 to 0.8", and the next lower category as "from 0.2 to 0.5" SES values less than 0.2 include both very small positive effects and also all negative effects. Therefore, to separate the positive effects from the negative effects, we defined the two lowest categories as "from 0 to 0.2" and "less than 0" This gave a total of five categories.

The dependent variable was the change in the frequency of going out, after it had been dichotomized into "increase" and "no increase"

Two simple models, each of which had only one independent variable (either the change in VT score (model C1) or the category of SES (model C2)), were tested. More complex models were also used, in which sex, age, and the presence or absence of diabetic

Table 2. Analyses of data collected at baseline: associations of VT score and frequency of going out.

	β	Standard Error	Wald χ^2	Odds ratio	95% CI	*P*
Model A						
Intercept	−0.87	0.38	–	–	–	–
VT score as continuous variable	0.019	0.01	10.63	1.02	1.01–1.03	0.001
Model B						
Intercept	0.76	0.78	–	–	–	–
VT score as continuous variable	0.02	0.01	10.44	1.02	1.01–1.03	0.001
Age	−0.03	0.01	7.91	0.97	0.95–0.99	0.005
Sex (Male)	0.24	0.26	0.91	1.28	0.77–2.12	0.340
Diabetic nephropathy yes/no (non-diabetic nephropathy)	0.31	0.30	1.05	1.36	0.76–2.44	0.305

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nephropathy were included as covariates (models D1 and D2). Finally, the more complex models were used again, but after exclusion of data from the participants who at baseline were in the lowest category of going out (models E1 and E2). They were excluded because of concern that increases from the lowest category might have been caused by regression toward the mean.

For all analyses, alpha = 0.05 (two-sided), and 95% confidence intervals are shown.

Results

Usable data were obtained from 144 men and 165 women (Table 1).

Data Collected at Baseline

At baseline (Table 2), higher VT scores were associated with going out more often. Age was also associated with going out, but sex and diabetic nephropathy were not.

Changes Over Time

Greater changes in VT scores were associated with greater changes in the frequency of going out (Table 3), with both the univariate model (model C1) and the multivariate models (models D1 and E1). In the multivariate models, none of the covariates had a p value less than 0.05.

Figure 1 shows, for each SES category, the proportion of respondents in that category whose frequency of going out

Table 3. Associations between the change in VT scores and the improvement in the frequency of going out (VT change score as the independent variable).

	β	Standard Error	Wald χ^2	Odds ratio	95%CI	*P*
Model C1						
intercept	−1.23	0.14	–	–	–	–
VT change score (Continuous)	0.03	0.01	13.80	1.03	1.01–1.05	<0.001
Model D1 (covariates: age, sex, diabetic nephropathy)						
Intercept	−2.28	0.83	–	–	–	–
VT change score (Continuous)	0.02	0.01	14.26	1.03	1.01–1.05	<0.001
Age	0.02	0.01	1.95	1.02	0.99–1.04	0.162
Sex (Male)	−0.09	0.29	0.09	0.92	0.52–1.63	0.769
Diabetic nephropathy yes/no (non-diabetic nephropathy)	−0.06	0.34	0.03	0.94	0.48–1.84	0.855
Model E1: Same as Model D1 except patients at the floor at baseline were excluded to avoid regression to the mean						
Intercept	−2.17	0.91	–	–	–	
VT change score (Continuous)	0.02	0.01	7.65	1.02	1.01–1.04	0.005
Age	0.02	0.01	1.25	1.02	0.99–1.04	0.263
Sex (Male)	−0.30	0.33	0.86	0.74	0.39–1.40	0.354
Diabetic nephropathy yes/no (non-diabetic nephropathy)	−0.11	0.39	0.08	0.90	0.42–1.92	0.783

doi:10.1371/journal.pone.0040455.t003

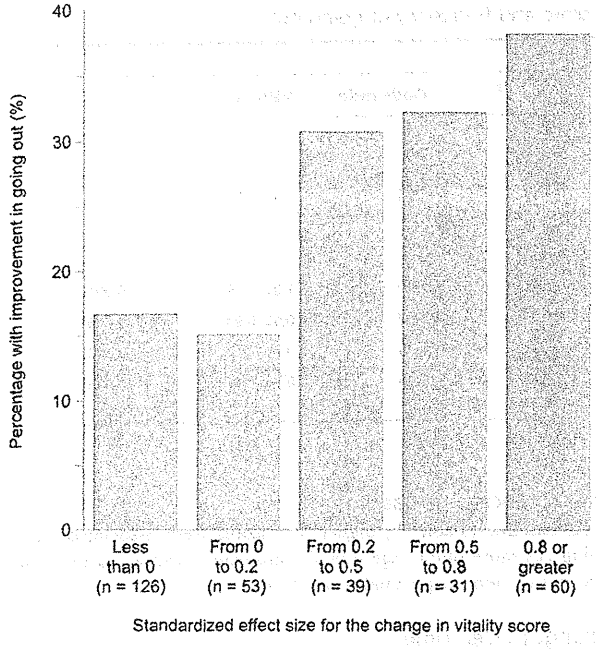

Figure 1. Relationship between the SES categories of changes in VT scores and the proportion of participants who had improvement in the frequency of going out. Comparing the group with the greatest increase in VT score to the group with a decrease and to the group with almost no increase, the Figure shows that more than twice as many people in the former group reported improvement in their frequency of going out. That is, groups with greater increases in VT scores had more peole who reported increases in the frequency of going out.
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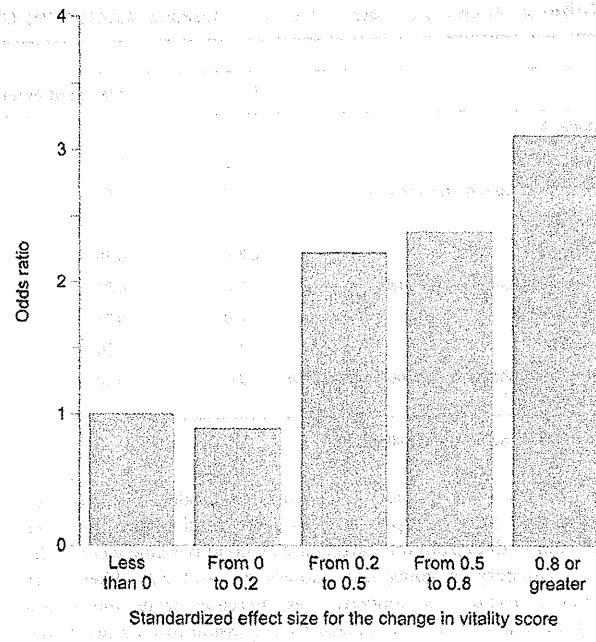

Figure 2. Association between changes in VT scores and changes in the frequency of going out. The independent variable is the categories of SES (SES of "<0" as the reference standard). This Figure shows the results from model C2, in which the change in VT score was the only independent variable. Greater changes in VT scores were clearly associated with going out more frequently
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increased. The frequency of going out increased in approximately 15% of those whose SES was less than 0.2, and it increased in more than 30% of those whose SES was greater than or equal to 0 2 In these data, an SES of 0.2 was equal to a change in VT score of 4 2 points.

Figures 2, 3, and 4 show odds ratios and adjusted odds ratios for increases in the frequency of going out The SES category of "less than zero" was the reference category For both the univariate and the multivariate models, the patterns are similar to that shown in Figure 1 None of the covariates in models C2, D2, or E2 had a p value less than 0.05

Discussion

The results of the analyses of the baseline data show that VT was associated with the frequency of going out, and the results of the analyses of changes over time show that increases in VT were associated with increases in the frequency of going out.

We expect that documenting such associations will be particularly important for patient-centered clinical practice, in which it is necessary to "translate" risk reductions, numbers needed to treat, and QOL scores into more concrete terms to help patients understand their meaning and also to give healthcare workers insights into patients' lives outside the context of the clinical encounter

Reports of QOL scores have become common in many clinical fields, including clinical nephrology [8], but such reports do not often give clear ideas about how the scores can be interpreted. For example, patients may be told that treatment of their anemia can be expected to increase their VT score by about 5 points (as found by Akizawa [5]), but of course that alone is not very informative It raises the question "What does a 5-point increase mean?" Some previous studies have approached such questions via the concept of the minimally important difference. For example, Bjorner et al. [6] quantified the effects of various medical conditions on VT scores, as well as the association between VT scores and life events such as job loss, hospitalization, and death. On the basis of their results, they proposed that 5 points be used as the minimally important difference for groups with below-average VT scores. Applying that criterion, we might expect treatment of anemia to result in a group-level difference in VT scores that would be important.

Another common approach to QOL scores involves expressing differences in standard-deviation units. As noted by Norman et al. [12], minimally detectable differences are often about 0.5 SDs. In this study, a VT score difference of about 5 was within the 0.2 to 0 4 range of standardized effect size that is usually called "medium" or "moderate" [2]

Nonetheless, whether we focus on minimally important differences (quantified by disease and by life events) or on thresholds in standard-deviation units, the implications from a patient's perspective can still be vague. Thus, attention should also be paid to the link between VT scores and effect indicators that are more immediately understandable to patients and more directly relevant to social policies. We examined the frequency of *gai-shutsu* as one such effect indicator

Interpretation of the present results therefore depends greatly on the meaning of the term *gai-shutsu*. While we translate it into English as "going out", it should be kept in mind that *gai-shutsu* is generally not used to describe any and all instances of leaving one's home. Instead, it is generally used to describe instances of leaving

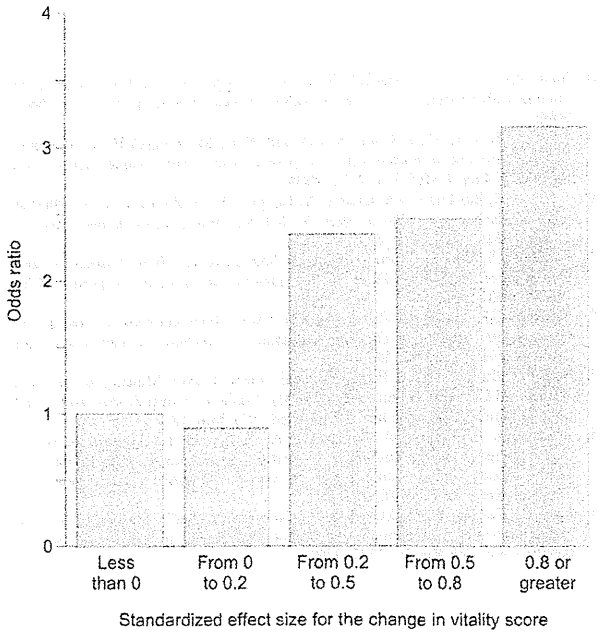

Figure 3. Association between changes in VT scores and changes in the frequency of going out. The independent variable is the categories of SES (SES of "<0" as the reference standard) This Figure shows the results from model D2, which included age, sex, and the presence or absence of diabetic nephropathy as covariates. The odds ratios are almost exactly the same as those shown in Figure 2, which indicates that the association of increases in VT scores with going out more frequently was robust even after likely confounders were accounted for.
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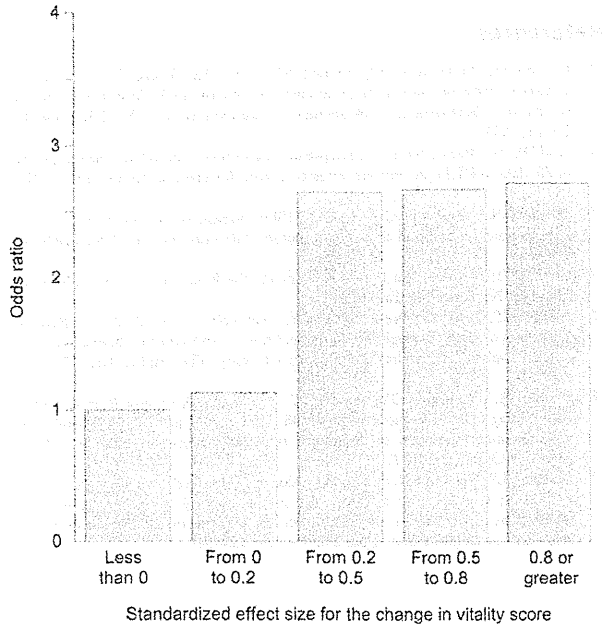

Figure 4. Association between changes in VT scores and changes in the frequency of going out. The independent variable is the categories of SES (SES of "<0" as the reference standard). This Figure shows the results from model E2, which was same as Model D2 except that patients whose values were at the floor at baseline were excluded. Compared with the results of model E2 (Figure 3), the most noteworthy difference is that the magnitude of the association was somewhat attenuated in the highest of the four categories of VT increase. We interpret this result as indicating that the strong association between increases in VT scores and increases in the frequency of going out was not caused by regression to the mean.
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either one's home or one's workplace for a non-obligatory activity Thus, it generally does not include going to work or to school. It might also not include going to a clinic or a hospital for a pre-scheduled outpatient appointment. In such a situation one would probably not use the general term *gai-shutsu*, but would instead mention the destination explicitly. *Gai-shutsu* can include going out alone, but it also covers many activities done in groups.

With that meaning in mind, these results provide a basis for seeing changes in VT scores as indicators of patients' daily lives. In particular, among older people in Japan and in Japanese society generally, social isolation and the loosening of family and community ties are becoming important problems. The proportion of elderly people living alone increased from 4 3% for men and 11.2% for women in 1980 to 9 7% for men and 19 0% for women in 2005 [13]

Any resulting tendency toward social isolation might be alleviated by interventions promoting activities outside the home. It is reasonable to expect that unemployed elderly people who go out (in the sense of *gai-shutsu*, as described above) are less likely to burden their family or social-service agencies. Increases in vitality might provide a foundation for increasing *gai-shutsu*, which would be both individually and socially beneficial. Another implication of the present work is that such improvements might be expected from medical interventions, and specifically from the treatment of anemia [2]

One important caveat derives from the fact that this study was a type of secondary analysis. The data were originally collected as part of a randomized trial of two different targets for anti-anemia therapy, and the opportunity to use them for the present purpose was incidental. Therefore these results must not be taken as definitive and conclusive. Because future confirmatory work is still required, these results can instead be seen as suggestive of a possibly important association. They can also be used to guide the design of future prospective research.

Such prospective studies are realistic and they should be done. Going out is not very commonly measured, but use of the SF-36 is now well-established in Japan, and it is widely used in contexts ranging from in-hospital RCTs to community-based observational studies [14,15]. The many ongoing and planned uses of the SF-36 will result in VT scores being recorded, and plans can be made prospectively to use those scores as sources of information about how often people go out Plans can also be made to include, as an important part of future studies, measurements of the frequency of going out. If the results of the present study are confirmed, then information about connections between VT and *gai-shutsu* might expand the possibilities for interpreting the results of a wide range of clinical interventions and social-welfare programs. Asking about the frequency of *gai-shutsu* is of course not the only way to explore the meaning of VT scores, and we hope that other work will continue putting clinical measurements into concrete and easily understood terms.

Author Contributions

Conceived and designed the experiments: SF SM Performed the experiments: TA YT Analyzed the data. SF SM Wrote the paper: SF Gave advice regarding results from the preceding clinical trial. TA YT

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Sex differences in the change in health-related quality of life associated with low back pain

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Abstract
Purpose To examine the sex differences in the impact of low back pain (LBP) on health-related quality of life among community-dwelling persons from a nationwide sample.
Methods Our analysis enrolled 2,358 participants from among 3,477 randomly selected subjects in Japan The cumulative days each individual experienced LBP were prospectively measured over 1 month. The Physical Component Summary (PCS) and Mental Component Summary (MCS) in the Short Form 8-item Health Survey were evaluated before and after the study period. Sex differences in the impact of the cumulative number of LBP days on PCS and MCS scores were evaluated using linear regression analysis.
Results Among the 2,170 participants with complete data, the prevalence of LBP in women (32%) was higher than that in men (25%) during the study period. One-day increases in LBP days were associated with greater decreases in PCS scores among men than among women (−0.72 vs. −0.29, sex difference $P < 0.001$). In contrast, no relationship was noted between the number of LBP days and the change in MCS score for either sex after adjustment.
Conclusions Although a greater incidence of LBP was noted in women, health-related quality of life was more seriously affected in men with the same number of days with LBP in the month.

Keywords Low back pain · Sex differences · SF-8 · PCS · MCS

Abbreviations

LBP	Low back pain
HRQOL	Health-related quality of life
HDS	Health Diary Study
SF-8	Medical Outcome Study Short Form 8-item Health Survey

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PCS Physical health component summary
MCS Mental health component summary
LOWESS Locally weighted scatter plot smoothing

Introduction

An important goal of healthcare is prolonging life while maintaining its quality. Although recent decades have seen an increase in the prevalence of chronic diseases, evaluation of the status of patients suffering from such conditions remains insufficient, in part due to the insensitivity of traditional outcome measures, such as mortality and morbidity. Among various proposed solutions, health-related quality of life (HRQOL) has recently gained recognition as a more sensitive, and thus more suitable, measure of chronic care outcome [1, 2].

Low back pain (LBP) is a major public health concern; there is a high prevalence of LBP in the general population, which creates an economic burden on society through increased utilization of health services [3–5] and, on a more individual level, causes poor physical health overall [6]. An analysis of eight datasets involving over 15,000 patients showed that the impact of musculoskeletal conditions on physical health in HRQOL was similar to or greater than that of other common chronic conditions, including cardiovascular conditions, cerebrovascular/neurological conditions, and visual impairment [1].

Researchers have recently reported sex differences in various aspects of LBP. Studies have shown that the prevalence of LBP is higher in women than in men, and women with LBP are more likely to seek care and to take sick leave than men [7–10]. Biological studies exploring the reasons for these phenomena have found that women tend to have lower pain thresholds and tolerance nociceptive stimuli than men [11, 12]. In contrast, some psychological studies have found men to have a greater increase in negative mood than women when exposed to the same degree of pain [13, 14]. These inconsistent findings make the overall influence of LBP on HRQOL uncertain.

Several studies have found that gender is related to HRQOL in subjects with LBP. Generally, these studies show that women with LBP have worse physical health scores than men with LBP [15]. Bingefors et al. [16] further examined the sex differences in the eight components of Short Form 36 and reported that women had worse physical function scores than men, while men tended to report worse in bodily pain and general health scores than women Due to their cross-sectional design, however, these studies do not reveal information concerning the sex differences in the impact of LBP on HRQOL. Using the nationwide data of the Health Diary Study, in which the participants documented their daily health events and symptoms, we investigated the sex differences in HRQOL changes in response to LBP.

Materials and methods

Study sample

We used data obtained from the Health Diary Study (HDS), which aims to describe the frequency of health-related events, symptoms, and care-seeking behaviors in a nationwide sample of the Japanese population [17]. Study participants kept a health diary for 1 month during which they documented all health symptoms and related healthcare use every day between October 1 and 31, 2003, and completed pre- and post-diary questionnaires.

The HDS study was designed to represent the Japanese population based on a panel of 210,000 households registered with Japan Statistics & Research Co., Ltd. The sample process involved two steps: selecting persons willing to participate and then resampling the selected persons to represent the Japanese population. In the first step, the whole registered panel was stratified by residential area size (metropolitan areas, cities with 100,000 or more residents, cities under 100,000 residents, and rural areas), and a total of 5,387 households were randomly selected from these strata and contacted to assess their willingness to participate in the study. Of the 1,857 households that agreed to participate in the study, 1,464 households containing 3,852 individuals were resampled to attain a sample population structure representing the general Japanese population. By the end of the study, 3,477 participants (87.8%) from 1,286 households had completed the health diary and both pre- and post-diary questionnaires. Because this study focused on HRQOL associated with LBP, we limited our sample to persons aged between 18 and 75, for whom the HRQOL scale included in the study was designed [18]. We also excluded persons who were hospitalized during the survey period. The final sample included 2,358 individuals. The HDS protocol was approved by the Research Ethics Committee of the Kyoto University Graduate School of Medicine.

Variables

Cumulative number of LBP days

The cumulative number of LBP days was defined as the total number of days during the 1-month study period in which a participant documented in his or her diary "pain" or any other unusual feeling in either the back or lumbar region. The number of LBP days ranged from 0 to 31.