Clinical Pain Research

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Analysis of Japanese nationwide health datasets: association between lifestyle habits and prevalence of neuropathic pain and fibromyalgia with reference to dementia-related diseases and Parkinson's disease

https://doi.org/10.1515/sjpain-2023-0010
Received January 21, 2023; accepted June 27, 2023;
published online July 13, 2023

Abstract

Objectives: Chronic pain is defined as pain that persists or recurs for more than 3 months. This study focuses on neuropathic pain (NP) and fibromyalgia (FM) which are chronic pain states, and aims to identify lifestyle habits associated with their prevalence. Other neurological disorders are also analyzed as references.

Methods: Association between the variable referring to disease prevalence (number of claims for reimbursement of marker drugs) and the variable for lifestyle habits/health examination results (collected from insured individuals aged 40–74 years) was determined by analyzing Japanese nationwide datasets, which were collected in 2018 and aggregated by prefecture. Pregabalin, donepezil, and levodopa were used as marker drugs for the chronic pain states, dementia-related diseases (Alzheimer's disease and Lewy body dementia) and Parkinson's disease (PD), respectively. Pearson's correlation analysis and multiple linear regression analysis were conducted.

Results: Variables showing correlation coefficient ($|r|$)>0.5 were put into the multiple linear regression. Exercise habits (β=−0.3182), smoking habits (0.3218), daily drinking (0.2683), and alanine aminotransferase>51 U/L (0.2309) were finally incorporated in the equation for pregabalin (R^2=0.7268). Walking speed (−0.4543) and daily drinking (0.5077) were incorporated in the equation for donepezil (R^2=0.5718).

Conclusions: The prevalence of chronic pain states is associated with lifestyle habits, just like the dementia-related diseases. Exercise in daily life is negatively associated with the prevalence of the chronic pain states, although excessive alcohol drinking, smoking, and high serum ALT are positively associated with it. The prevalence of PD seems less associated with lifestyle habits.

Keywords: dementia-related diseases; fibromyalgia; health examination; lifestyle habits; neuropathic pain; Parkinson's disease

Introduction

All residents in Japan (around 126 million in 2018) are, in principle, need to be enrolled in public health insurance based on the universal health coverage policy. When an insured patient is prescribed drugs from a medical provider, he/she pays co-payment to the provider. The provider, then, submits claims for reimbursement of the remaining portion of drug price. This procedure makes it possible to grasp the number of claims for drugs prescribed in Japan, and the Ministry of Health, Labor and Welfare (MHLW) of Japan has constructed National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB Open Data Japan), a nation-wide database which exhaustively covers number of claims for reimbursement of individual drugs. This database also contains millions of health check-up results of insured persons and their dependents aged 40–74 years [1, 2]. The data have been aggregated by prefecture (administrative unit). Due to the rich individuality of 47 prefecture each in terms of people's lifestyle habits based on

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Japanese geographical (bow-shaped land wide in both east-west and north-south directions) and historical features, analysis of prefecture-based datasets is an efficient research approach to identify the factors associated with the target of interest health issues. We have recently conducted a prefecture-based ecological study using this database with "marker drug", the drug at the position of first-line recommendation in the therapeutic guideline for target of interest disease. The number of reimbursement claims for the marker drug (uroselective α_1 receptor blocker) per unit population was used for prevalence of the target of interest disease (benign prostatic hyperplasia [BPH]). The study has identified critical lifestyle habits (e.g., exercise in daily life) and health examination result (e.g., high blood pressure) associated with BPH prevalence [3].

International Association for the Study of Pain (IASP) defined chronic pain as pain that persists or recurs for more than 3 months for the International Classification of Diseases (ICD-11) [4]. The present study focuses on neuropathic pain (NP) and fibromyalgia (FM) which are chronic pain states. NP is caused by lesions or diseases of the somatosensory system [5] and associated with a variety of conditions, including diabetes and viral infections [6], with an estimated prevalence of 6.9–10.0 % of the general population [7]. FM is characterized by medically unexplained widespread pain and often accompanied by comorbidities including sleep disorder and fatigue [8]. It is common as prevalence in the general population is estimated to be between 2 and 10 % [9]. Although several drugs including pregabalin (a ligand for the $\alpha_2\delta$ subunit of voltage-gated calcium channel) have been used for the management of NP and FM symptoms [10], their efficacies are limited [11, 12]. For example, only a small portion of FM patients are adherent to taking the currently available drugs for more than one year due to either lack of efficacy or side effects [13]. In the light of high prevalence and difficulties in their treatment, the chronic pain states (NP and FM) are a serious burden for individuals and the social health care system [14]. The purpose of this ecological study is, thus, to verify or explore the lifestyle habits/health examination results associated with the prevalence of the chronic pain states by prefecture-based analysis of NDB Open Data Japan. Other neurological diseases, dementia-related diseases (Alzheimer's disease and Lewy body dementia) and Parkinson's disease (PD), were also assessed for reference.

Materials and methods

Study design

This cross-sectional ecological study investigates an association between the lifestyle habits/health examination results variables and the variables regarding the prevalence of target of interest diseases (i.e., number of claims for reimbursement of marker drugs per 1,000 population) by Pearson's correlation analysis and multiple linear regression analysis with 47 Japanese prefectures as the unit. The Research Ethics Committee of the International University of Health and Welfare (Fukuoka, Japan) approved this study (reference number: 22-Ifh-049).

Marker drugs referring to prevalence of diseases

Pregabalin for the chronic pain states (NP and FM), donepezil for dementia-related diseases (Alzheimer's disease and Lewy body dementia), and levodopa for PD, which are at the position of the mainstay in clinical guidelines in Japan and approved specifically for the treatment of relevant disease by Japanese authority (Ministry of Health, Labour and Welfare), are used as marker drugs. Number of claims for reimbursement of the marker drug per 1,000 population was used as the variable referring to the prevalence of each target of interest disease. Pregabalin, a ligand for $\alpha_2\delta$ subunit of neuronal calcium channel, has been approved for the treatment of NP (including postherpetic neuralgia and painful diabetic polyneuropathy) and FM, but not for other categories of pain such as inflammatory pain in Japan. It is at the position of first-line recommendation for both NP [15, 16] and FM [17, 18] in many countries including Japan. Although pregabalin has been used as also an antiepileptic drug in the European Union and the United States [19], it is approved only for the treatment of NP/FM but not for epilepsy in Japan [20]. This indication specificity in Japan makes pregabalin valuable in the study focusing on the prevalence of NP and FM. Another gabapentinoid, gabapentin was not used as a marker drug, because it has been approved only for the therapy of epilepsy in Japan. Donepezil, an acetylcholinesterase inhibitor, is reported to be effective in treating patients with Alzheimer's disease [21] and Lewy body dementia [22]. The use of donepezil for treating those two dementia-related diseases (Alzheimer's disease and Lewy body dementia) is covered by health insurance in Japan. Levodopa, a precursor of dopamine, is the most effective medication available for treating motor symptoms and half of the patients with PD receives levodopa monotherapy between 2008 and 2016 [23].

Variables and data sources

The present study used the datasets collected in 2018 and published on the webpages managed by Japanese ministries. Data referring to diseases prevalence, i.e. number of claims for reimbursement of the marker drugs (pregabalin for the chronic pain states, donepezil for the dementia-related diseases, and levodopa for PD) per 1,000 male population, were acquired from "the 5th NDB Open Data Japan" which contains total number of 1.9 billion claims [1].

NDB Open Data Japan also contains data on health check-ups and answers to lifestyle habits-related questions. In Japan, public health insurers need to provide a specific health checkup, including questions regarding lifestyle habits, for insured individuals aged 40–74 years. The 6th NDB Open Data Japan contains more than 29 million eligible adults who participated in the check-up in 2018 [2]. Thus, data corresponding to lifestyle habits variables, i.e., percentage of respondents who selected each answer option in the questions regarding lifestyle habits, were also from the 6th NDB Open Data Japan [2]. Data corresponding to health examination results, i.e., the prefecture level average values of health check-up results, were also from the 6th NDB Open Data Japan [2].

Because the lifestyle habits and health examination results data aggregated by prefecture are influenced by age composition of

Table 1: Variables for analysis and data sources.

Category	Variables	Abbreviation	Unit	
Marker drugs	Number of claims for reimbursement of pregabalin/population	Pregabalin	n/1,000 people	[1]
	Number of claims for reimbursement of donepezil/population	Donepezil	n/1,000 people	
	Number of claims for reimbursement of levodopa/population	Levodopa	n/1,000 people	
Health examination	Average body mass index (BMI)	BMI	kg/m^2	[2]
	Average serum HbA_{1c}	Serum HbA_{1c}	%	
	Average serum high density lipoprotein cholesterol (HDL-C)	Serum HDL-C	mg/dL	
	Average serum low density lipoprotein cholesterol (LDL-C)	Serum LDL-C	mg/dL	
	Average serum alanine aminotransferase (ALT)	Serum ALT	U/L	
	Average creatinine clearance (Ccr)	Ccr	mL/min	
	Average estimated glomerular filtration rate (eGFR)	eGFR	mL/min/ 1.73 m^2	
	Positive result in urine protein test	Urine protein	% of men	
	Average serum hemoglobin	Serum hemoglobin	g/dL	
	Average systolic blood pressure (BP)	Systolic BP	mmHg	
	Abnormal finding in electrocardiogram test	ECG	% of men	
Lifestyle habits-related questions	Are you under any medication for high blood pressure? (Y/N)	Antihypertensive medication	% yes	
	Are you under insulin injections or other medications to reduce blood glucose level? (Y/N)	Antidiabetic medication	% yes	
	Are you under medication to reduce cholesterol level? (Y/N)	Antihyperlipidemic drug	% yes	
	Have you ever been diagnosed as stroke (e.g., cerebral hemorrhage, cerebral infarction) or got treated for it? (Y/N)	History of stroke	% yes	
	Have you ever been diagnosed as heart disease (e.g., angina, myocardial infarction) or got treated for it? (Y/N)	History of heart disease	% yes	
	Have you ever been diagnosed with chronic kidney failure or got treated (e.g., dialysis) for it? (Y/N)	History of kidney failure	% yes	
	Have you ever been diagnosed as anemic? (Y/N)	History of anemia	% yes	
	Are you a habitual cigarette smoker (a total of over 100 cigarettes or for over six months) at present? (Y/N)	Smoking habits	% yes	
	Have you gained 10 kg or more compared to your body weight when you were 20 years-old? (Y/N)	Body weight gain	% yes	
	Have you been doing sweaty exercise (30 min or more per session and two days or more per week) for over a year? (Y/N)	Exercise habits	% yes	
	Have you been walking or doing any equivalent amount of physical activity over an hour per day in everyday life? (Y/N)	Walking habits	% yes	
	Is your walking speed faster than the speed of those of almost the same age and of the same gender? (Y/N)	Walking speed	% yes	
	What is your condition when you chew your meal? (Chew anything/Sometimes hard to chew/Hardly chew)	Chewing condition	% chew anything	
	Is your eating speed faster than others? (Faster/Ordinary/Slower)	Fast eating speed	% faster	
	Do you eat snacks other than three meals? (Y/N)	Snack habits	% yes	
	Do you skip breakfast three times or more per week? (Y/N)	Skipping breakfast	% yes	
	How often do you drink alcohol? (Every day/Sometimes/Rarely or never)	Daily drinking	% every day	
	How much do you drink in terms of sake per day? 180 mL of sake is equivalent to 500 mL of beer. (<180 mL/180–360 mL/360–540 mL/540 mL <)	A small amount of drinking	% <180 mL of sake	

All data were collected in 2018 and have been made public by Japanese ministries. Health condition-and lifestyle habits-related variables are standardized by age using the Japanese demographic composition [24] as the standard population. Y, yes; N, no; n, number.

prefectural residents, they are standardized for age using the formula: Standardized data=($\sum$ age-specific raw data in a 5-year age group × standard population in that age group)/(total population in standard population), where the Japanese demographic composition [24] is used as the standard population. Table 1 summarized the variables and data sources used in this study.

Statistical analysis

Statistical analysis was conducted with BellCurve for Excel version 3.20 (Social Survey Research Information Co., Ltd., Tokyo, Japan). The association between lifestyle habits/health examination results variables and variables for prevalence of target of interest diseases was investigated. Pearson's correlation coefficients (r) for all possible pairs of the variables were determined and their statistical significances were tested with t-test. The variables with r of 0.5 or larger as absolute value were screened as candidate explanatory variables for inclusion in the multiple regression equations where number of claims for marker drugs per 1,000 population were used as response variables. The stepwise selection with the criteria set at $p<0.2$ was then performed to determine the explanatory variables for final inclusion in the regression model. Principal component analysis was applied to the variables (exercise habits, smoking habits, daily drinking, and ALT>51 U/L) which were included in the regression model for pregabalin. The p values less than 0.05 were regarded as statistically significant.

Results

Correlation analysis

The correlations between the marker drug variables (pregabalin, donepezil, and levodopa) and lifestyle habits/health examination results variables are shown in Table 2. The variables with $|r|>0.5$ by Pearson's correlation analysis are marked with bold face. Pregabalin showed a significantly positive correlation with serum ALT>51 U/L, antihypertensive medication, antidiabetic medication, and smoking habits, and daily drinking, and a significantly negative correlation with serum LDL-C>140 mg/dL, urine protein positive, history of anemia, exercise habit, walking speed, body weight gain, chewing condition, fast eating speed, snack habits, and a small amount of drinking. Donepezil exhibited a significantly positive correlation with systolic BP>140 mmHg, smoking habits, and daily drinking, and a significantly negative correlation with body weight gain, exercise habits, walking habits, walking speed, chewing condition, and skipping breakfast habits. Levodopa showed a significantly negative correlation with serum HbA_{1c}>6.5 %.

Multiple linear regression analysis

Multiple linear regression equations were developed using the variables with $|r|>0.5$. The explanatory variables, which remained in the stepwise selection, were finally included in the regression model. Table 3 presents the regression coefficients of the equations. Exercise habits, smoking habits, daily drinking, and ALT>51 U/L were included in the equation for pregabalin (R^2=0.7268, $p<0.001$). Multicollinearity was not suspected, as variance inflation factor (VIF) was 2.3901 or less for these variables. Walking speed and daily drinking were included in the equation for donepezil (R^2=0.5718, $p<0.001$). Multicollinearity was not suspected because VIF was 1.0577 for these variables. The equation for levodopa was not constructed because no explanatory variable did not show $|r|>0.5$ in the correlation analysis. Principal component analysis was performed on the variables (exercise habits, smoking habits, daily drinking, and ALT>51 U/L) which were included in the regression model for pregabalin. Table 4 presents factor loadings and eigenvalues of each principal component. Only one principal component (PC1) was with eigenvalues greater than 1.0, which explained about 56 % of the total variance.

Discussion

The prefecture-based analysis of NDB Open Data Japan demonstrates that the prevalence of NP and FM, which are chronic pain states, is significantly associated with lifestyle habits/health examination results, suggesting that the chronic pain states seem a type of lifestyle-related disorder. Especially, exercise in daily life is negatively associated with its prevalence, although daily alcohol drinking, smoking, and high ALT value are positively associated with it.

There have been few previous reports which proved a significant effect of exercise on the incidence of the chronic pain states, although evidence suggests that physical exercise is an intervention that may reduce pain severity and improve the quality of life in patients who have already developed symptoms [25, 26]. In the present study, the correlation and regression analyses show that exercise habits are negatively associated with the prevalence of the chronic pain states.

There have been mixed previous study results regarding the influence of alcohol drinking on the prevalence of chronic pain. A dose-response meta-analysis has shown that alcohol consumption at any doses is inversely associated with the chronic pain prevalence [27]. A review of a bunch of cohort studies has demonstrated that alcohol abstinence is one of risk factors for incidence of FM [28]. Excessive alcohol consumption seems to have a precipitative effect on the incidence of chronic pain. For example, long-term excessive alcohol consumption causes damages to nerves and produces painful peripheral neuropathy [29]. A cross-sectional study has shown that excessive alcohol consumption is one of predictors for the presence of chronic pain [30]. A cohort study has demonstrated that chronic alcohol drinking enhances the incidence of pain disorders [31]. In the present study, the result of correlation analyses suggests that the

Table 2: The correlations between marker drugs (prevalence of diseases) and lifestyle habits/health examination results variables.

Category	Variables	Chronic pain states	Dementia-related diseases	PD
		Pregabalin	**Donepezil**	**Levodopa**
Marker drugs	Pregabalin	1	**0.6935**[c]	0.1631
	Donepezil	**0.6935**[c]	1	0.3581[b]
	Levodopa	0.1631	0.3581[b]	1
Health examination[a]	BMI>25	0.1732	−0.1981	−0.0531
	Serum HbA_{1c}>6.5 %	0.1289	−0.1968	−0.3653[b]
	Serum HDL-C<40 mg/dL	−0.0150	−0.0524	0.0262
	Serum LDL-C>140 mg/dL	−0.3612[b]	−0.1831	0.1508
	Serum ALT>51 ng/ML	**0.5294**[c]	0.0872	−0.0488
	Urine protein positive	−0.4039[c]	−0.0132	0.0658
	Systolic BP>140 mmHg	0.3843[c]	0.4926[c]	0.2213
	ECG abnormal finding	0.0018	−0.0740	0.0434
Lifestyle[a]	Antihypertensive medication	0.4472[c]	0.1340	−0.1024
	Antidiabetic medication	0.3927[c]	0.2004	−0.0365
	Antihyperlipidemic drug	−0.1074	−0.2249	−0.0666
	History of stroke	−0.1567	−0.1663	−0.1162
	History of heart disease	0.1258	−0.0939	0.1481
	History of kidney failure	−0.2592	−0.1576	−0.1001
	History of anemia	−0.3333[b]	−0.1750	0.2147
	Smoking habits	**0.7515**[c]	0.4525[c]	0.0719
	Body weight gain	−0.4633[c]	−0.4859[c]	−0.0017
	Exercise habits	**−0.6126**[c]	**−0.5380**[c]	0.0078
	Walking habits	−0.1941	−0.3746[c]	0.1495
	Walking speed	−0.4182[c]	**−0.5728**[c]	0.0025
	Chewing condition	−0.3432[b]	−0.3418[b]	−0.0853
	Fast eating speed	**−0.5649**[c]	−0.1489	0.0969
	Snack habits	−0.3492[b]	0.0841	0.2079
	Skipping breakfast habits	−0.2331	−0.3241[b]	−0.1997
	Daily drinking	**0.6253**[c]	**0.6138**[c]	0.1526
	A small amount of drinking	−0.4713[c]	−0.0958	0.2853

Bold face represents |r|>0.5 by Pearson's correlation analysis. [a]Values, that are age standardized for the age range of 40–74 years, are used as lifestyle-habits/health examination results variables. CI, confidence interval; [b]p<0.05; [c]p<0.01 by t-test.

association between alcohol drinking habits and prevalence of the chronic pain states is biphasic, because a small amount of alcohol drinkers and daily drinkers are significantly associated with reduction and increase of the prevalence, respectively. This result is consistent with the frequently reported biphasic effect of alcohol on health. For example, those drinking low-to-moderate amounts of alcohol show a decreased risk of mortality while heavy drinkers have an increased risk [32, 33].

Previous studies have shown that smoking habits are associated with higher risk for prevalence of the chronic pain states. For example, a large-scale questionnaire study in patients with type 2 diabetes demonstrates that smoking habits are the most clearly associated with the prevalence of painful diabetic neuropathy [34]. A large prospective cohort study demonstrates a significant positive association between smoking habits and development of new cases of FM [35]. In accordance with those reports, the correlation and regression analyses in the present study demonstrate that smoking habits is tightly correlated to the prevalence of the chronic pain states.

High serum ALT (a deviation enzyme from hepatocytes) level is the only test item showing $|r|$ larger than 0.5 in the correlation analysis among the health examination results in the present study. It also showed a significant positive effect in the regression analysis. The relationship between liver function and chronic pain has not been sufficiently investigated, although a study has suggested that chronic hepatitis B carriage may increase the risk of FM [36]. Notably, the present study suggests that liver function is significantly associated with the prevalence of the chronic pain states.

Dementia-related diseases (Alzheimer's disease and Lewy body dementia) are used as references based on previous studies which have proved that prevalence of dementia is tightly associated with lifestyle habits. Namely, there is considerable evidence that individuals with healthy lifestyle habits such as avoidance of smoking [37], physically

Table 3: Multiple regression equations assess the association between disease prevalence-related variables and lifestyle habits/health examination results variables.

Response variables	Explanatory variables and constant term	B with 95 % CI	p-Value	β	VIF	R^2
Pregabalin	Exercise habits	−173.6 (−282.8 to −64.4)	0.0026[b]	−0.3182	1.5123	0.7268 p<0.001
	Smoking habits	206.4 (45.0–367.8)	0.0134[a]	0.3218	2.3901	
	Daily drinking	120.5 (33.9–207.1)	0.0075[b]	0.2683	1.4041	
	ALT>51	793.1 (68.5–1,517.8)	0.0327[a]	0.2309	1.6800	
	Constant term	−2,596.7 (−9,215.2–4,021.7)	0.4329			
Donepezil	Walking speed	−65.3 (−94.7 to −35.9)	<0.001[b]	−0.4543	1.0577	0.5718 p<0.001
	Daily drinking	71.0 (42.4–99.7)	<0.001[b]	0.5077	1.0577	
	Constant term	2,588.7 (574.4–4,603.0)	0.0130[a]			

The explanatory variables, which remained in the stepwise selection, were finally included in the regression model. CI, confidence interval; B, partial regression coefficient; β, standardized partial regression coefficient indicating the impact of one individual variable, independent of scales of the variables; VIF, variance inflation factor; R^2, coefficient of determination; [a]p<0.05; [b]p<0.01 by t-test. Negative B and β values indicate inverse correlation.

Table 4: Principal component analysis on the life habits-related variables which were included in the regression model for pregabalin.

Variable	PC1	PC2	PC3	PC4
	Factor loading based on principal component analysis			
Exercise habits	−0.6674	0.6037	0.3882	0.1984
Smoking habits	0.8932	0.1441	−0.1676	0.3915
Daily drinking	0.7403	−0.2500	0.6218	−0.0526
ALT>51 U/L	0.6578	0.6983	−0.0784	−0.2711
Eigenvalue	2.224	0.935	0.572	0.269
Proportion, %	55.60	23.38	14.29	6.72
Cumulative, %	55.60	78.99	93.28	100.00

PC, principal component.

active [38], moderate alcohol consumption [39], and healthy diet [40] are associated with a substantially lower prevalence of Alzheimer's disease, the most common form of dementia [41, 42]. On the other hand, physical inactivity [43], smoking [44], unhealthy diet [45], mid-life hypertension [46], and alcohol drinking above the recommended amounts [24] are established as risk factors for the incidence of Alzheimer's disease. Being consistent with these evidences, the correlation analysis in the present study showed that systolic BP>140 mmHg, smoking habits, and daily drinking were positively associated with the prevalence of the dementia-related diseases and that exercise habits and walking speed were negatively associated with the prevalence. These results confirms that the analysis of prefecture-based datasets in NDB Open Data Japan provides an appropriate and efficient research approach to identify the factors associated with the target of interest health issues.

PD is also used as a reference disease based on the generally sparse and weak evidence regarding the correlation between lifestyle habits and the prevalence of PD [47]. For example, there have been conflicting study results for the influence of alcohol intake on the prevalence of PD [48, 49]. A meta-analysis study found no association between BMI and the prevalence of PD [50]. Being consistent with these weak evidences, the present study did not detect a strong correlation between PD prevalence and lifestyle/health examination results, unlike the chronic pain states and the dementia-related diseases. Notably, smoking habits are not correlated with PD prevalence (r=0.0719), being contrary to the significant correlation shown for the chronic pain states (r=0.7515) and the dementia-related diseases (r=0.4525). This could be in line with the previous several epidemiological studies which demonstrated even an preventive effect of smoking habits on the incidence of PD [47, 48].

There are limitations in the present study. First, the correlation analyses conducted in the present study only demonstrate a covariation between the variables (lifestyle-related variables and disease prevalence-related variables). It should be noted that the covariation does not necessarily mean a cause-and-effect relationship between the variables. Second, the unit of data corresponding to lifestyle habits/health examination results is not individual but region (prefecture). It should be noted that the association between the variables at the prefecture level is not necessarily

applicable to the individual level. Third, stratified analysis by gender was not conducted, because the data of number of claims for reimbursement of individual drugs are not distinguished by gender in the NDB Open Data Japan. Fourth, the present study excluded the variables, which even showed statistical significance in the correlation analysis with coefficient values of 0.5 or less, from the multiple regression equations. It remains to be possible that such variables are associated with the disease prevalence.

Conclusions

The present study confirms that the analysis of prefecture-based datasets in NDB Open Data Japan is appropriate and efficient for identifying the factors associated with the target of interest health issues. The results demonstrate that the prevalence of NP and FM, which are chronic pain states, is tightly associated with lifestyle/health examination results, just like the dementia-related diseases. Exercise in daily life is negatively associated with the prevalence of the chronic pain states, although excessive alcohol drinking, smoking, and high serum ALT are positively associated with it. The prevalence of PD seems less associated with lifestyle habits.

Acknowledgments: We would like to thank Editage (www.editage.jp) for English language editing.
Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Research funding: Authors state no funding involved.
Competing interests: Authors state no conflict of interest.
Ethical considerations: The Research Ethics Committee of the International University of Health and Welfare (Fukuoka, Japan) approved this study (reference number: 22-Ifh-049).

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