



Long Working Hours and Risk of Ischemic Heart Disease Among Japanese Workers: The Jichi Medical School Cohort Study

Mayumi Saiki^{1,2}, Akizumi Tsutsumi³, Jian Li^{1,4}

¹Joe C. Wen School of Nursing, University of California Los Angeles, Los Angeles, CA, USA; ²School of Nursing, Vanderbilt University, Nashville, TN, USA; ³Department of Public Health, Kitasato University School of Medicine, Sagamihara, Japan; ⁴Departments of Environmental Health Sciences and Epidemiology, Fielding School of Public Health, University of California Los Angeles, Los Angeles, CA, USA

Objectives: Karoshi, or “death from overwork,” has been recognized for decades; however, epidemiological findings regarding long working hours (LWH) and ischemic heart disease (IHD) remain inconsistent. This study aimed to provide new evidence on the association between LWH and IHD, while accounting for job strain among Japanese workers, both male and female.

Methods: This study utilized data from 6670 workers participating in the Jichi Medical School Cohort Study. Baseline working hours were categorized as <5.0, 5.0 to 6.9, 7.0 to 8.9 (reference), 9.0 to 10.9, and ≥ 11.0 hr/day. Fatal and non-fatal incident IHD cases were determined during follow-up using International Classification of Diseases, 10th revision codes. Multivariable Cox proportional hazards models were used to examine associations, adjusting for socio-demographic factors, lifestyle behaviors, cardiometabolic characteristics, and job strain.

Results: During a mean follow-up of 12 years, 58 incident IHD cases (42 male and 16 female) were documented. Long working hours (≥ 11.0 hr/day) were significantly associated with an increased risk of IHD in the total sample (hazard ratio, 2.92; 95% confidence interval, 1.15 to 7.39), and the overall pattern of associations was similar in sex-stratified analyses.

Conclusions: These findings suggest that LWH independently increases the risk of IHD among Japanese workers, even after adjustment for job strain, underscoring the importance of managing working hours to reduce karoshi in both male and female workers.

Key words: Long working hours; Myocardial ischemia; Cohort studies; Japan

INTRODUCTION

Cardiovascular diseases (CVD), including ischemic heart disease (IHD), represent the leading cause of death globally, and

research supports that long working hours (LWH), defined as ≥ 55 hr/wk, are a moderate risk factor for IHD [1,2]. LWH have been reported to be particularly prevalent among male workers and those in early middle age; they are also more common in Southeast Asia, whereas prevalence is lower in Europe [2].

In Japan, several studies have examined the associations between LWH and IHD [3-6]. However, most studies have focused only on male workers [3,4,6]. Although one study included females, its sample was still male-dominant, with males accounting for 98% of participants [5]. Moreover, these studies did not reflect the recent increase in female employment in Japan, which has exceeded 80% [7]. Prior research has indicated that daily LWH ≥ 11 hours [3,6], weekly LWH ≥ 55 hours [5],

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Corresponding author: Jian Li

Departments of Environmental Health Sciences and Epidemiology, Fielding School of Public Health, 650 Charles E. Young Drive South, Los Angeles, CA 90095, USA

E-mail: jianli2019@ucla.edu

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and weekly LWH ≥ 61 hours [4] are significantly associated with an increased risk of IHD among male workers.

Another work-related psychosocial factor, job strain (i.e., high job demand and low job control) [8], has been shown to contribute to the global burden of CVD and IHD [9]. However, none of the previous studies assessed the independent effect of LWH while accounting for job strain [3-6]. Therefore, this investigation aimed to examine whether LWH are associated with IHD independently of job strain and whether these associations differ by sex among Japanese workers.

METHODS

Study Sample

Data were drawn from the Jichi Medical School (JMS) Cohort Study, which investigated lifestyle factors, socioeconomic factors, and CVD risk factors in the general Japanese population [10]. This multicenter study recruited participants aged ≥ 18 years from 12 rural districts. In total, 12 490 individuals participated at baseline, conducted between April 1992 and July 1995. Participants were followed through the end of December 2005. At baseline, participants completed a standardized questionnaire and underwent a physical examination [10]. During annual follow-up, information on new diagnoses of IHD was collected. Additional details have been reported elsewhere [10].

Among the 12 490 baseline participants, 4536 who were retired or unemployed and 141 with missing or zero working hours were excluded. An additional 729 participants with miss-

ing covariate data were excluded, yielding 7084 participants with complete covariate data. Participants with a history of angina, myocardial infarction, other heart diseases, stroke, or cancer were then excluded, resulting in a final analytic sample of 6670 participants (Figure 1).

Working Hours

Participants were interviewed about their work-related activities at baseline. They reported the average number of daily hours spent on work-related activities, which were summed to calculate total daily working hours. Daily working hours were then categorized into 5 groups: < 5.0 , 5.0 to 6.9, 7.0 to 8.9 (reference), 9.0 to 10.9, and ≥ 11 hours, in accordance with a previous study [6].

Covariates

All covariates were measured at baseline, including age (< 40 , 40–49, 50–59, 60–69, or ≥ 70 years), sex (male or female), age at completion of education (≤ 15 , 16–18, or ≥ 19 years), occupation (professional/technician/clerk, sales/service workers, farming/forestry/fishery, and security/transportation/communications/craft workers/laborers), managerial position (yes and no), smoking (lifetime non-smoker, former smoker, and current smoker), alcohol consumption (non-drinker, light drinker, and heavy drinker), exercise (continuous physical activity index calculated by multiplying activity duration and weight factors based on the intensity of different physical activities), hypertension (yes or no), diabetes mellitus (DM; yes and no), body mass index (BMI; continuous), total cholesterol (TC; continu-

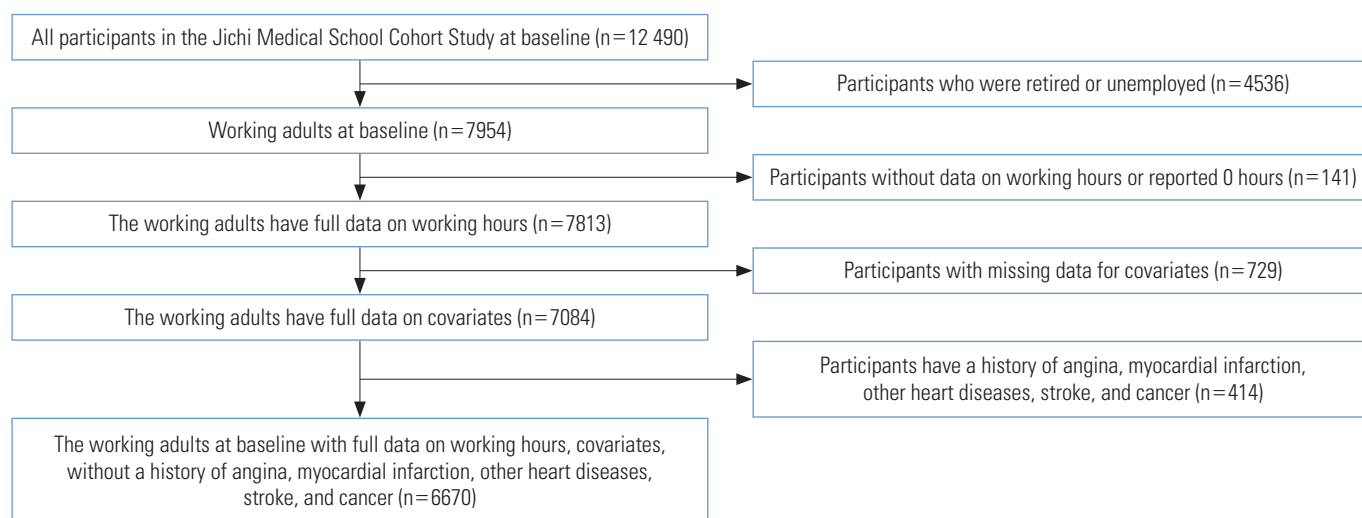


Figure 1. Flow chart of study sample selection.

ous), and community (12 rural districts). Job strain was defined as the ratio of job demand to job control (continuous); the total job demand score was divided by the total job control score, adjusted for differences in item counts [11].

Ascertainment of Ischemic Heart Disease

During follow-up, when an episode of IHD (non-fatal or fatal) was suspected, medical records from hospitals or death certificates from public health centers were obtained for review. Diagnoses were adjudicated by a diagnostic committee composed of radiologists, cardiologists, and neurologists. In line with prior research, IHD was defined as conditions with International Classification of Diseases, 10th revision codes I20 to I25 [1]. Total IHD cases were defined as the sum of non-fatal and fatal cases.

Statistical Analysis

First, descriptive statistics were generated to compare baseline characteristics across the 5 working-hours groups, using analysis of variance for continuous variables and chi-square tests for categorical variables. Multivariable Cox proportional hazards models were then fitted, with results reported as hazard ratios (HRs) and 95% confidence intervals (CIs). Statistical significance was set at p -value < 0.05 . In these analyses, deaths from causes other than IHD were censored, and fatal IHD events were censored in the analysis of non-fatal IHD. Unadjusted results were reported as model 0. Model 1 was adjusted for age, sex, age at completion of education, occupation, managerial position, smoking status, alcohol consumption, exercise, BMI, hypertension, DM, TC, and community, in accordance with a previous study [11]. Model 2 additionally adjusted for job strain.

An interaction term among working hours, sex, and job strain was included to test potential effect modification by sex and job strain. Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Ethics Statement

The study design and procedures were reviewed and approved by each municipal government and the Ethics Committee for Epidemiological Research at Jichi Medical School. Written informed consent was obtained from all participants.

RESULTS

Table 1 presents baseline characteristics stratified by working hours. Among the 6670 participants, most individuals across age groups worked 7.0–11.0 hr/day. Among those working ≥ 11.0 hr/day, the highest proportions were in the 40–49 and 50–59 age groups. Males were more prevalent than females in the longer working-hours categories. Participants working ≥ 11.0 hr/day were most frequently employed in farming, forestry, and fishing, followed by sales and service; occupational distributions are shown in Supplemental Material 1. Participants who were not in managerial positions or business owners generally worked longer hours. Most participants completed their education by age 18, and age at completion of education did not differ by working-hours category. Most participants were lifetime non-smokers or former smokers, and most were non-drinkers or light drinkers. Workers with longer working hours were less likely to exercise. No obvious differences were observed in BMI, TC, DM, or hypertension across working-hours categories. Participants with LWH expe-

Table 1. Characteristics of the study sample at baseline stratified by daily working hours (n=6670)

Characteristics	Daily working hours (hr)						<i>p</i> -value ¹
	Total	<5.0	5.0–6.9	7.0–8.9	9.0–10.9	≥ 11.0	
No. of participants	6670	190	516	2180	2339	1445	
Age (y)							<0.001
<40	720 (10.8)	11 (5.8)	64 (12.4)	242 (11.1)	235 (10.1)	168 (11.6)	
40–49	1840 (27.6)	37 (19.5)	103 (20.0)	606 (27.8)	657 (28.1)	437 (30.2)	
50–59	1972 (29.6)	37 (19.5)	113 (21.9)	649 (29.8)	722 (30.9)	451 (31.2)	
60–69	1954 (29.3)	89 (46.8)	206 (39.9)	627 (28.8)	674 (28.8)	358 (24.8)	
≥ 70	184 (2.8)	16 (8.4)	30 (5.8)	56 (2.6)	51 (2.2)	31 (2.2)	
Sex							<0.001
Male	3289 (49.3)	56 (29.5)	146 (28.3)	990 (45.4)	1312 (56.1)	785 (54.3)	
Female	3381 (50.7)	134 (70.5)	370 (71.7)	1190 (54.6)	1027 (43.9)	660 (45.7)	

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Table 1. Continued from the previous page

Characteristics	Daily working hours (hr)						p-value ¹
	Total	<5.0	5.0–6.9	7.0–8.9	9.0–10.9	≥11.0	
Occupation							<0.001
Professionals/technicians/clerks	879 (13.2)	20 (10.5)	60 (11.6)	381 (17.5)	228 (11.9)	140 (9.7)	
Sales/service workers	1379 (20.7)	57 (30.0)	113 (21.9)	364 (16.7)	455 (19.4)	390 (27.0)	
Farming/forestry/fishery	2642 (39.6)	92 (48.4)	247 (47.9)	759 (34.8)	931 (39.8)	613 (42.4)	
Security/transportation/communications/ craft workers/laborers	1770 (26.5)	21 (11.1)	96 (18.6)	676 (31.0)	675 (28.9)	302 (20.9)	
Manager/business owner							<0.001
No	4150 (62.2)	133 (70.0)	379 (73.5)	1433 (65.7)	1402 (59.9)	803 (55.6)	
Yes	2520 (37.8)	57 (30.0)	137 (26.6)	747 (34.3)	937 (40.1)	642 (44.4)	
Education (y)							0.331
≤15	2937 (44.0)	96 (50.5)	229 (44.4)	952 (43.7)	1001 (42.8)	659 (45.6)	
16–18	2940 (44.1)	77 (40.5)	227 (44.0)	949 (43.5)	1066 (45.6)	621 (43.0)	
≥19	793 (11.9)	17 (9.0)	60 (11.6)	279 (12.8)	272 (11.6)	165 (11.4)	
Job strain	0.87 ± 0.26	0.79 ± 0.28	0.80 ± 0.28	0.88 ± 0.27	0.88 ± 0.25	0.87 ± 0.24	<0.001
Smoking status							<0.001
Lifetime non-smoker	3829 (57.4)	129 (67.9)	373 (72.3)	1289 (59.1)	1248 (53.4)	790 (54.7)	
Former smoker	917 (13.8)	22 (11.6)	52 (10.1)	274 (12.6)	336 (15.7)	203 (14.1)	
Current smoker	1924 (28.9)	39 (20.5)	91 (17.6)	617 (28.3)	725 (31.0)	452 (31.3)	
Alcohol consumption (g/day)							<0.001
Non-drinker	3250 (48.7)	119 (62.6)	324 (62.8)	1083 (49.7)	1053 (45.0)	671 (46.4)	
Light drinker (<28.9)	1766 (26.5)	47 (24.7)	116 (22.5)	580 (26.6)	640 (27.4)	383 (26.5)	
Heavy drinker (≥28.9)	1654 (24.8)	24 (12.6)	76 (14.7)	517 (23.7)	646 (27.6)	391 (27.1)	
Exercise (physical activity index)	9.11 ± 3.74	17.25 ± 4.61	13.71 ± 2.88	10.68 ± 2.29	8.54 ± 2.14	4.96 ± 2.45	<0.001
Body mass index	22.99 ± 2.92	23.27 ± 3.16	22.97 ± 3.22	23.07 ± 2.95	22.94 ± 2.83	22.92 ± 2.87	0.299
Total cholesterol	189.31 ± 34.28	193.12 ± 33.61	189.60 ± 35.73	189.98 ± 34.71	189.25 ± 33.49	187.79 ± 34.43	0.194
Hypertension							0.118
No	5848 (87.7)	162 (85.3)	437 (84.7)	1904 (87.3)	2066 (88.3)	1279 (88.5)	
Yes	822 (12.3)	28 (14.7)	79 (15.3)	276 (12.7)	273 (11.7)	166 (11.5)	
Diabetes mellitus							0.367
No	6453 (96.8)	184 (96.8)	507 (98.3)	2109 (96.7)	2257 (96.5)	1396 (96.6)	
Yes	217 (3.3)	6 (3.2)	9 (1.7)	71 (3.3)	82 (3.5)	49 (3.4)	
Community							<0.001
1	577 (8.7)	21 (11.1)	51 (9.9)	207 (9.5)	167 (7.1)	131 (9.1)	
2	1668 (25.0)	42 (22.1)	170 (33.0)	517 (23.7)	672 (28.7)	267 (18.5)	
3	1135 (17.0)	38 (20.0)	95 (18.4)	374 (17.2)	372 (15.9)	256 (17.7)	
4	212 (3.2)	3 (1.6)	8 (1.6)	48 (2.2)	101 (4.3)	52 (3.6)	
5	833 (12.5)	20 (10.5)	55 (10.7)	264 (12.1)	281 (12.0)	213 (14.5)	
6	731 (11.0)	18 (9.5)	51 (9.9)	323 (14.8)	250 (10.7)	89 (6.2)	
7	149 (2.2)	9 (4.7)	21 (4.1)	66 (3.0)	32 (1.4)	21 (1.5)	
8	618 (9.3)	19 (10.0)	36 (7.0)	158 (7.3)	214 (9.2)	191 (13.2)	
9	200 (3.0)	2 (1.1)	11 (2.1)	69 (3.2)	74 (3.2)	44 (3.0)	
10	142 (2.1)	8 (4.2)	6 (1.2)	35 (1.6)	62 (2.7)	31 (2.2)	
11	96 (1.4)	3 (1.6)	2 (0.4)	17 (0.8)	33 (1.4)	41 (2.8)	
12	309 (4.6)	7 (3.7)	10 (1.9)	102 (4.7)	81 (3.5)	109 (7.5)	

Values are presented as number (%) or mean ± standard deviation.

¹Chi-square tests for categorical variables and analysis of variance for continuous variables were used to test differences between daily working hours.

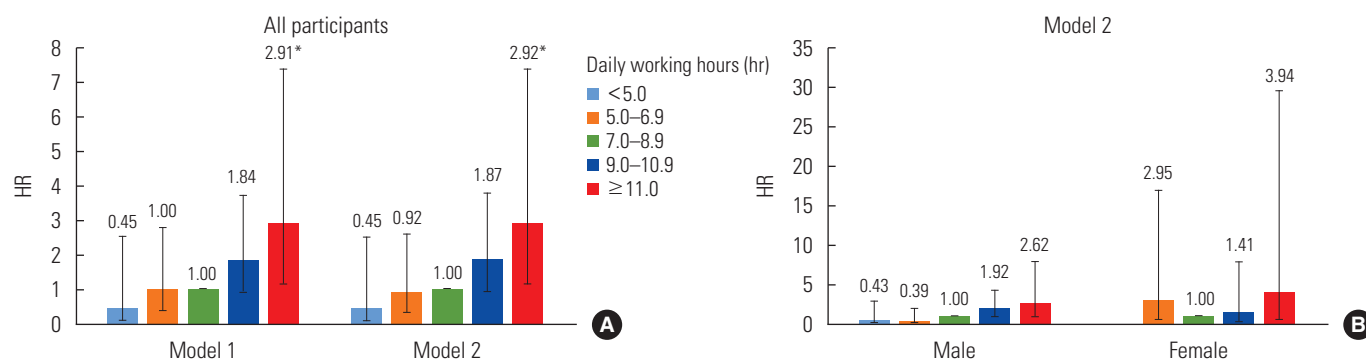


Figure 2. Hazard ratios (HRs) of ischemic heart disease by daily working hours (HR and 95% confidence intervals) for (A) all participant and (B) sex-stratified analysis (model 2). * $p < 0.05$.

rienced higher job strain.

During follow-up, 58 new IHD cases were identified, corresponding to an incidence rate of 0.73 per 1000 person-years. Total follow-up time was 79 809.86 person-years, with a mean follow-up of 12.08 years. The number of events and follow-up person-time by covariate categories are presented in Supplemental Material 2. The median time to IHD onset was 7.13 years. Figure 2 presents the HRs and 95% CIs for IHD. Working ≥ 11 hr/day was associated with an increased risk of IHD in the univariate model (Supplemental Material 3), and this association was further strengthened after adjustment in model 1 (HR, 2.91; 95% CI, 1.15 to 7.37). After additional adjustment for job strain in model 2, the association remained robust and statistically significant (HR, 2.92; 95% CI, 1.15 to 7.39), whereas job strain was not significantly associated with IHD risk (Supplemental Material 4).

The interaction between working hours and sex was not significant ($p = 0.54$). Results of the sex-stratified analyses are shown in Figure 2. Because the number of incident IHD cases was limited (42 in male and 16 in female), the associations did not reach statistical significance. However, a similar pattern was observed in both male and female, with elevated HRs among those working ≥ 11 hr/day (male: HR, 2.62; 95% CI, 0.88 to 7.83; female: HR, 3.94; 95% CI, 0.53 to 29.52) (Supplemental Material 3). In addition, the interaction between working hours and job strain was not significant ($p = 0.41$).

DISCUSSION

To our knowledge, this is the first study to examine the independent effect of LWH on IHD, beyond job strain, among Japanese workers. Previous studies have reported positive as-

sociations between LWH and IHD in this demographic [3-6]. The present findings indicate that LWH were independently associated with IHD after accounting for job strain. In this study, job strain was not significantly associated with IHD, which may suggest cultural differences in the explanatory value of job strain for IHD development between Western and Eastern working populations. Notably, the HR in model 2 did not attenuate after adjustment for job strain compared with model 1, indicating that any mediating effect of job strain was minimal. Furthermore, the moderating role of job strain between LWH and IHD risk was not supported, based on the non-significant interaction test.

Similar trends were observed in both male and female, consistent with previous Japanese studies reporting associations between LWH and IHD in male workers [3-6]. Additional analyses suggested no evidence of sex differences in the association between LWH and IHD ($p = 0.54$). Although the risk of IHD was increased in both male and female, the 95% CIs were wide because of the small number of incident cases. Our results add to the limited evidence on the risk associated with LWH among female workers in Japan and are consistent with prior evidence suggesting similar IHD risk related to LWH exposure in male and female ($p = 0.99$ for sex differences) [1].

A potential explanation for the effects of LWH on IHD may involve behavioral and physiological changes associated with LWH [1]. One behavioral pathway relates to meal selection. Research has shown that LWH may increase sodium intake due to the limited time available for cooking [12]. Additionally, the benefits of exercise are well documented; regular physical activity helps prevent atherosclerosis and improves cardiovascular health [13]. As shown in Table 1, workers with LWH were less likely to engage in exercise, which is a risk factor for IHD.

Regarding physiological changes, LWH may activate the sympathetic nervous system, leading to elevated blood pressure and increased heart rate [14]. Moreover, LWH are significantly associated with elevated high-sensitivity C-reactive protein levels [15] and a higher risk of glucose intolerance [16]. These conditions increase the risk of atherosclerosis and predispose individuals to IHD [17].

The strengths of this prospective study should be highlighted. First, the JMS Cohort Study was a multicenter study that recruited participants from 12 districts in Japan. Although most previous Japanese studies included predominantly male participants [3-6], the JMS Cohort Study included both male and female, enhancing generalizability to the Japanese population. Second, the JMS Cohort Study had a long follow-up duration (mean, 12.08 years). The median time to IHD onset was 7.13 years, suggesting that follow-up was sufficient to capture the latency between exposure to LWH and IHD development. Third, IHD diagnoses were adjudicated by a diagnostic committee using medical records and death certificates, which likely improved the accuracy of outcome classification. Fourth, Cox proportional hazards models were used to account for time-to-event outcomes and censoring. In addition, a broad set of covariates associated with IHD was included, minimizing potential confounding. Importantly, job strain was incorporated into the analyses, as described above. Finally, the 12-year follow-up enabled capture of incident IHD events, thereby improving statistical power.

The limitations of this study should also be addressed. First, data regarding working hours were collected only at baseline in the JMS Cohort Study; thus, changes in working hours, duration of exposure to LWH, timing, and shift patterns during the 12-year follow-up could not be assessed. This may have introduced bias by failing to capture cumulative exposure to LWH. Second, working hours were self-reported and may have been subject to recall bias. However, the validity and reproducibility of self-reported working hours are considered relatively high [18]. Third, the data were collected from 1992 to 2005, which may limit applicability to current working conditions. For example, the number of farmers has decreased substantially since 2005, from 2.2 million in 2005 to 1.2 million in 2023 [19].

The work-style reform law was enforced in Japan in 2019, and the proportion of full-time workers with LWH >60 hr/wk decreased from 17.0% in 2005 to 8.9% in 2022 [20]. The number of compensated work-related CVD cases (i.e., *karoshi*) also

showed a declining trend, from 330 cases in 2005 to 241 in 2024. These data suggest that policy-level interventions targeting LWH in Japan have substantially reduced work-related CVD cases compared with 20 years ago. The present results suggest that LWH are a significant factor in increasing IHD risk among Japanese workers, underscoring the importance of managing working hours to prevent *karoshi*.

NOTES

Data Availability

Due to the proprietary nature of the dataset and the need to protect study participant privacy, the raw data from the Jichi Medical School Cohort Study cannot be made openly available at this time. Further information about the data and conditions for access is available from Dr. Akizumi Tsutsumi (akizumi@kitasato-u.ac.jp) at Kitasato University School of Medicine. The authors will provide the SAS syntax supporting the conclusions of this article without undue reservation. Requests for access to the SAS syntax should be directed to Dr. Jian Li (jianli2019@ucla.edu) at the University of California, Los Angeles.

Supplemental Materials

Supplemental materials are available at <https://doi.org/10.3961/jpmph.25.577>.

Conflict of Interest

The authors have no conflicts of interest associated with the material presented in this paper.

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Author Contributions

Conceptualization: Li J, Tsutsumi A. Data curation: Tsutsumi A, Saiki M, Li J. Formal analysis: Saiki M, Li J. Funding acquisition: Li J, Saiki M. Methodology: Li J, Tsutsumi A, Saiki M. Project administration: Tsutsumi A, Li J. Visualization: Saiki M. Writing – original draft: Saiki M, Li J. Writing – review & editing: Saiki M, Tsutsumi A, Li J.

ORCID

Mayumi Saiki: <https://orcid.org/0000-0002-1648-6872>; Akizumi Tsutsumi: <https://orcid.org/0000-0003-0966-4869>; Jian Li: <https://orcid.org/0000-0003-2614-4291>

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