Improving health risks by replacing sitting with standing in the workplace

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Received: September 27, 2017 / Accepted: January 16, 2018

Abstract This study examined the association between health-related risks and sitting time in three different domains covering a worker’s typical life. We investigated the beneficial effect of replacing sitting time with standing/walking time in the workplace using the isotemporal substitution model (ISM). The survey was administered through the Internet. We recruited 11,729 Japanese workers by approximating industry ratios based on the 2015 Japan Labor Force Survey. The sitting times of specific domains, i.e., while working (during working time), workday leisure time, and non-workday leisure time were collected by a validated questionnaire. We used multiple logistic regression analyses to determine associations between health-related risks and sitting time. Using the ISM approach, we estimated associations when we replaced sitting with standing/walking in the workplace, and included a model that examined subgroups of workers with and without exercise habits. The analyses involved 9,524 workers (43.4 ± 11.1 years). The longest sitting time (>7.7 h) while working (during working time) was associated with significant odds ratios (ORs) of diabetes (OR = 1.41, 95% CI 1.05-1.90), hyperlipidemia (1.58, 1.23-2.01) when compared to the shortest sitting time (<3.8 h). Replacing 1 h/day of sitting with an equal amount of standing/walking at the workplace was associated with a 4% decrease in risk for hyperlipidemia and 7% for heart disease. Furthermore, these results were noticeable for workers with non-exercise habits. In conclusion, this study suggests that, especially in the workplace, extended sitting time is associated with the risk of disease, and that replacing occupational sitting with standing can effectively reduce the risk of disease in workers, particularly for those with non-exercise habits.

Keywords: occupational health, sitting time, workplace, isotemporal substitution model

Introduction

Long sitting time is a significant public health concern. Epidemiological studies show that long periods of sitting is associated with metabolic disease\(^1\) and adversely affects mental health\(^3\). It also affects all-cause mortality\(^6\) independent of physical activity. In recent years, because of a sedentary work environment and increased automation, workers now spend about one third to one half of their work time sitting\(^5\). If we consider sitting time in the workplace as a deleterious health exposure factor, then time spent sitting during work has important occupational and public health implications\(^9\). Although previous studies have shown that occupational sitting time was associated with a higher health risk\(^7,9\), other studies have not shown an association between occupational physical activity and risk of disease\(^10,11\). Furthermore, some studies\(^12,13\) found an increased risk of disease in active workers compared to sedentary workers. Thus, whether occupational sitting time increases health risk is still controversial. A systematic review\(^14\) of the various techniques for measuring sitting time is needed to help explain the discrepancies.

Recently, we developed the Worker’s Living Activity-time Questionnaire (WLAQ), which primarily evaluates a worker’s sedentary behavior. Our previous studies\(^15,16\) and another study\(^17\) showed that asking for the percentage of time rather than the absolute length of time spent sitting improved the questionnaire’s properties. The WLAQ allowed us to measure time spent sitting and standing/walking separately during three different domains: while working, workday leisure time, and non-workday leisure time. In this study, we extend our earlier finding that to fully understand the relationship between sitting time in the workplace and health-related risks for workers, it is important to obtain prevalence estimates of the total amount of time spent sitting. Identifying the relationship between sitting time and health-related risks may provide answers for dealing with such risks. Hence, the first purpose of this study was to examine the association between
health-related risks and sitting time in three domains in a sample of Japanese workers from a range of employment sectors using the WLAQ. Clarifying to what extent each type of physical activity, including sitting or standing/walking in the workplace, is related to risk of disease can lead to development of evidence-based recommendations regarding physical activity in the workplace.

The isotemporal substitution model (ISM) can examine the effects of displacing one type of activity with another type of activity for an equal amount of time. In general, individuals spend each 24-hour day occupied in various physical activities, and a decrease in any specific activity requires an equal time substitution with another activity. The greatest advantage of the ISM is that it considers interdependence and substitution effects; its results are more reflective of real life with better interpretability compared to typical models.

Although in the field of sedentary behavior research, almost all studies using the ISM are based on data collected via an accelerometer, the ISM is also applicable to research using questionnaires. However, when applying the ISM, the total amount of activity time must be determined. Conventional questionnaires, such as the International Physical Activity Questionnaire (IPAQ), do not include the concept of “total time” making them difficult to incorporate into the ISM. On the other hand, the WLAQ can calculate the total time of a worker’s three typical domains. With regard to our secondary purpose, the present study focuses on the estimated replacement effects of occupational sitting time on health-related risks using the ISM. To our knowledge, the association between sitting time in different domains and health-related risks has not been investigated using the ISM approach.

Methods

Participants and procedures. This cross-sectional survey started in 2016 with participants answering a self-completed questionnaire that was administered through the Internet. We recruited participants with the goal of sampling a wide range of employment types based on the composition ratio of employed persons according to gender, age group (20 to 65 years old) and industry type listed in the 2015 Japan Labor Force Survey (Ministry of Internal Affairs and Communications). Data were collected through an internet-based investigation using a research company with a voluntary registrant of approximately 11,300,000 people. The research company randomly sent e-mail invitations for participation to enrolled workers. The workers then agreed to participate in health-related surveys, and they earned points available through the Internet according to their answer status. Through the Internet, 11,729 people responded. After carefully evaluating the responses, we excluded 1,573 respondents due to inappropriate answers or lack of data. We also excluded 632 of the part-time employees to equalize working hours for statistical purposes. Finally, 9,524 participants were selected for this study. This study was conducted in accordance with the guidelines proposed in the Declaration of Helsinki. The Ethics Committee of the National Institute of Occupational Safety and Health, Japan, reviewed and approved the study protocol (H2742). All participants were provided web-based informed consent.

Socio-demographic attributes. The socio-demographic variables included gender, age, type of employment (regular staff, temporary worker, contract employee, entrusted employee, others), presence or absence of shift work and type of industry (16 categories) based on the Japanese Ministry of Internal Affairs and Communications.

Exposure variables. The WLAQ is a self-administered questionnaire that can measure time spent sitting and walking (including standing) separately in three different domains covering a worker’s typical weekly life, such as while working, weekday leisure time, and non-working day leisure time. Briefly, the WLAQ asks the participant for the proportion of time spent sitting or walking/standing in a particular time period (e.g., total work time per day). The WLAQ also asks for bedtime, rising time, work start time and work end time on a typical day in the previous month. From this information, we can calculate the number of minutes per day participants spent sitting or walking/standing for each of the three domains. The proportion of each activity (sitting, walking/standing) was multiplied by the total minutes of each domain (working time, weekday leisure time, and non-working day leisure time). The WLAQ has been shown to have acceptable reliability and validity.

Health-related risks. Smoking status was categorized as current smoker, ex-smoker or non-smoker. Frequency of alcohol drinking was categorized as non-consumption, once or twice per week, three to five times per week or more than six times per week. Participants self-reported their history of treatment for hypertension, diabetes, hyperlipidemia, stroke, heart disease, cancer and depression received from medical institutions over the past year and their medication information (hypertension, diabetes, hyperlipidemia). We assessed each participant’s depressive symptoms using the Center for Epidemiologic Studies Depression Scale (CES-D). Developers of the CES-D indicate that scores at or above 16 points are suggestive of depression.

Statistical Analyses. Continuous data are expressed as mean ± standard deviation (SD). The Student’s unpaired t-tests were used to compare the differences between male and female. Categorical data are represented as n (%) with data analyzed using the chi-square test. A Kruskal-Wallis test was used to demonstrate a significant difference between industry categories in sleep time, commute...
time, working time and leisure time over a 24 h day. The total sample was categorized into tertiles of sitting time within each domain: working time (<3.8 h, 3.8-7.7 h, >7.7 h), leisure time in a workday (<2.9 h, 2.9-4.6 h, >4.6 h) and non-workday (<8.0 h, 8.0-11.6 h, >11.6 h). We then conducted multiple logistic regression analyses to examine independent relationships between health-related risks and sitting time within the three domains. We also examined the substitution effects of replacing sitting time with standing/walking time in the workplace using the ISM. This analysis assumes that any given time spent in one activity will lead to an isotemporal displacement of another activity while total time is kept constant. For example, in this study, to estimate the effect of substituting 1 h/day of sitting with 1 h/day of standing/walking in the workplace, sitting time is removed from the model and adjusted for total working time. Detailed analysis of ‘subgroup with exercise habit’, defined by the Ministry of Health, Labour and Welfare as continual exercise for at least 30 minutes per day 2 days per week over a year or more, was performed by ISM. In the present study, we defined hypertension, diabetes, hyperlipidemia, heart disease, cancer, depression and depressive symptoms as health-related risks, and considered participants as having one of these seven health-related risks if they were diagnosed within 1 year or were currently taking medication for the risk. In the multiple logistic regression analysis, age, gender, smoking, alcohol, exercise habits and shift work were adjusted as confounders. Odds ratios (ORs) and 95 % confidence intervals (CIs) were calculated for each variable. All statistical analyses were performed using SAS, version 9.3 (SAS Institute Japan, Tokyo, Japan) and results were considered significant at \( P < 0.05 \).

### Results

Table 1 lists the industry component ratios from the 2015 Japan Labor Force Survey and the present study. The industry component ratios of our participants closely resembled the component ratios of the 16 industry types

| Industry                                | Labor Force Survey (24) | Present study |
|-----------------------------------------|-------------------------|---------------|
|                                        | n  | %        | n      | %        |
| Agriculture and Forestry                | 224 | 3.50%    | 163    | 1.70%    |
| Construction                            | 491 | 7.70%    | 675    | 7.10%    |
| Manufacturing                           | 1033 | 16.30%   | 1624   | 17.10%   |
| Information and Communications          | 218 | 3.40%    | 453    | 4.80%    |
| Transport and Postal activities         | 326 | 5.10%    | 493    | 5.20%    |
| Wholesale and Retail trade              | 1067 | 16.80%   | 1469   | 15.40%   |
| Finance and Insurance                   | 170 | 2.70%    | 260    | 2.70%    |
| Real estate and goods rental and leasing | 131 | 2.10%    | 184    | 1.90%    |
| Scientific research, professional and technical services | 225 | 3.50% | 336    | 3.50%    |
| Accommodations, eating and drinking services | 390 | 6.10% | 498    | 5.20%    |
| Living-related and personal services    | 238 | 3.80%    | 313    | 3.50%    |
| Education, learning support             | 308 | 4.90%    | 593    | 6.20%    |
| Medical, Health care and Welfare        | 812 | 12.80%   | 1441   | 15.10%   |
| Compound services                       | 65  | 1.00%    | 103    | 1.10%    |
| Services, N.E.C                         | 423 | 6.70%    | 596    | 6.30%    |
| Government                              | 225 | 3.50%    | 323    | 3.40%    |
| **Total**                               | 6346 | 100.00%  | 9524   | 100.00%  |

\( ^{a} \) Ten thousand persons
in Japan.

Table 2 shows the general characteristics of the participants. Entire working hours account for 40% of daily life, sitting time at work occupies more than half (53.1%) of working hours. The sitting times for the other domains were 59.0% sitting during leisure time on a workday and 60.3% during a non-workday. The average sleep time on a work day was 6.6 h with no significant gender difference (male: 6.5 ± 1.6 h; female: 6.7 ± 1.6 h). However, there were significant differences between male and female in domain-specific times and health-related risks. Working time, sitting time while working, workday leisure time, and non-workday sitting time were significantly greater for males than for females (P < 0.005).

Fig. 1 displays the proportion of a 24 h day occupied by the four specific domains in each industry (A) and the percentage of sitting time while working and on a non-workday (B). In Fig. 1 (A), there was a significant difference among industry categories in sleep time, commute time, working time and leisure time. The industries with the longest working times were “information and communications” (10.0 ± 1.6 h), “construction” (9.9 ± 1.9 h), “manufacturing” (9.8 ± 1.8 h) and “finance and insurance” (9.8 ± 2.1 h). Illustrated in Fig. 1 (B), the percentages of sitting times were significantly different among industries during both working (P < 0.001) and non-workday (P = 0.026). The industry with the longest sitting time at work was “information and communications” (8.1 ± 2.5 h), and the shortest was “accomodations, eating and drinking services” (2.5 ± 3.2 h).

Table 3 shows logistic regression models for the association between sitting time and health-related risks in each domain. When fully adjusted by age, gender, smoking status, alcohol status, exercise habits, shift work, and

| Table 2. Characteristics of the study participants. |
|-----------------------------------------------|
|                                      Total   |  Male   |  Female |
|-----------------------------------------------|
| **Number (%)**                               | 9,524 (100) | 5,193 (54.5) | 4,331 (45.5) |
| **Age, year**                                | 43.4 ± 11.1 | 44.8 ± 10.9 | 41.6 ± 11.2 |
| **Working time, hours**                      | 9.6 ± 2.1 | 10.3 ± 1.9 | 8.7 ± 2.1 |
| **Sitting time during working time, hours**  | 5.1 ± 3.9 | 5.5 ± 4 | 4.6 ± 3.7 |
| **Leisure time on workday, hours**           | 6.6 ± 2.7 | 5.8 ± 2.4 | 7.5 ± 2.7 |
| **Sitting time during leisure time on workday, hours** | 3.9 ± 2.3 | 3.5 ± 2.1 | 4.2 ± 2.4 |
| **Leisure time on non-workday, hours**       | 15.9 ± 2.6 | 16.1 ± 2.4 | 15.6 ± 2.8 |
| **Sitting time on non-workday, hours**       | 9.6 ± 3.8 | 9.9 ± 3.9 | 9.2 ± 3.7 |
| **Smoking status**                            | 2,410 (25.3) | 1,710 (18.0) | 700 (7.4) |
| Current smoker                               | 1,893 (19.9) | 1,319 (13.8) | 574 (6.0) |
| Ex-smoker                                    | 5,221 (54.8) | 2,164 (22.7) | 3,057 (32.1) |
| **Alcohol status**                            | 4,273 (49.6) | 2,104 (22.1) | 2,619 (27.5) |
| Non-consumption                              | 2,001 (21.0) | 1,086 (11.4) | 915 (9.6) |
| Once or twice per week                        | 1,021 (10.7) | 686 (7.2) | 335 (3.5) |
| Three to five times per week                 | 1,779 (18.7) | 1,317 (13.8) | 462 (4.9) |
| More than six times per week                  | 875 (9.2) | 675 (7.1) | 200 (2.1) |
| **Diabetes**                                 | 341 (3.6) | 286 (3.0) | 55 (0.6) |
| **Hypertension**                             | 550 (5.8) | 417 (4.4) | 133 (1.4) |
| **Hyperlipidemia**                           | 58 (0.6) | 47 (0.5) | 11 (0.1) |
| **Heart disease**                             | 79 (0.8) | 33 (0.4) | 46 (0.5) |
| **Depression**                                | 323 (3.4) | 192 (2.0) | 131 (1.4) |
| **Depressive symptoms**                      | 2,628 (27.6) | 1,371 (14.4) | 1,257 (13.2) |

Values are presented as n (%) or mean ± standard deviation. Abbreviations: *Significant differences were observed between male and female (p < 0.05).
industry type in model 3, the longest sitting time during working time (> 7.7 h) was associated with significant ORs of diabetes (OR = 1.41, 95% CI 1.05-1.90), hyperlipidemia (OR = 1.58, 95% CI 1.23-2.01) when compared to the shortest sitting time (< 3.8 h). On the other hand, there were significant ORs only of diabetes in leisure time on a workday (OR = 1.36, 95% CI 1.04-1.78) and of CES-D on a non-workday (OR = 1.21, 95% CI 1.08-1.37). These results were not changed when participants were limited to between 40 and 65 years old.

The results of the ISM are displayed in Table 4. The substitution model suggests that, reallocating 1 h/day from sitting time to 1 h/day standing/walking time in the workplace was associated with a 4% lower risk of hyperlipidemia and an even greater risk reduction of 7% for heart disease. Table 5 shows a detailed analysis of subgroups. The replacement benefits of sitting time with standing/walking time in the workplace were associated with a 4% lower risk of hyperlipidemia and an 11% lower risk of heart disease only in participants with non-exercise habits. In contrast, substituting 1 h/day of sitting time with standing/walking time did not seem to be sig-
Table 3. Analysis of logistic regression in 3 time domains, adjusted by variables associated with sitting time and disease.

|                      | Working time | Leisure time on workday | Non-workday |
|----------------------|--------------|-------------------------|-------------|
|                      | ≤ 3.8h (n = 3160) | 3.8h - 7.7h (n = 3170) | 7.7h (n = 3194) | ≤ 2.9h (n = 3225) | 2.9h - 4.6h (n = 3164) | 4.6h (n = 3135) | ≤ 8.0h (n = 2766) | 8.0h - 11.6h (n = 3703) | 11.6h (n = 3055) |
| Hypertension         |              |                         |             |              |                         |             |              |                         |             |
| (n = 875)            |              |                         |             | Model 1      | 1.00                   | 1.31 (1.10-1.56) | 1.34 (1.13-1.60) | 1.00                   | 1.00                   | 1.25 (1.05-1.50)         |
|                      |              |                         |             | Model 2      | 1.00                   | 1.18 (0.98-1.42)  | 1.15 (0.95-1.38) | 1.00                   | 1.00                   | 1.08 (0.89-1.36)          |
|                      |              |                         |             | Model 3      | 1.00                   | 1.20 (0.99-1.46)  | 1.21 (0.99-1.47) | 1.00                   | 1.00                   | 1.09 (0.91-1.32)          |
|                      |              |                         |             |              |                         |             |             |              |                         |             |
| Diabetes             |              |                         |             |              |                         |             |             |              |                         |             |
| (n = 341)            |              |                         |             | Model 1      | 1.00                   | 1.26 (0.94-1.67)  | 1.64 (1.25-2.14) | 1.00                   | 1.00                   | 1.36 (1.04-1.78)          |
|                      |              |                         |             | Model 2      | 1.00                   | 1.16 (0.86-1.55)  | 1.41 (1.07-1.86) | 1.00                   | 1.00                   | 1.14 (0.87-1.51)          |
|                      |              |                         |             | Model 3      | 1.00                   | 1.16 (0.86-1.56)  | 1.41 (1.05-1.90) | 1.00                   | 1.00                   | 1.15 (0.87-1.52)          |
|                      |              |                         |             |              |                         |             |             |              |                         |             |
| Heart disease        |              |                         |             |              |                         |             |             |              |                         |             |
| (n = 341)            |              |                         |             | Model 1      | 1.00                   | 1.59 (1.27-1.99)  | 1.67 (1.34-2.09) | 1.00                   | 1.00                   | 1.13 (0.91-1.40)          |
|                      |              |                         |             | Model 2      | 1.00                   | 1.49 (1.18-1.88)  | 1.50 (1.19-1.89) | 1.00                   | 1.00                   | 1.06 (0.77-1.20)          |
|                      |              |                         |             | Model 3      | 1.00                   | 1.47 (1.16-1.87)  | 1.58 (1.23-2.01) | 1.00                   | 1.00                   | 0.97 (0.73-1.28)          |
|                      |              |                         |             |              |                         |             |             |              |                         |             |
| Cancer               |              |                         |             |              |                         |             |             |              |                         |             |
| (n = 79)             |              |                         |             | Model 1      | 1.00                   | 1.75 (0.86-3.56)  | 2.07 (1.04-4.13) | 1.00                   | 1.00                   | 1.17 (0.62-2.21)          |
|                      |              |                         |             | Model 2      | 1.00                   | 1.51 (0.74-3.10)  | 1.72 (0.85-3.46) | 1.00                   | 1.00                   | 1.03 (0.41-1.53)          |
|                      |              |                         |             | Model 3      | 1.00                   | 1.72 (0.82-3.64)  | 2.04 (0.97-4.32) | 1.00                   | 1.00                   | 0.97 (0.54-1.53)          |
|                      |              |                         |             |              |                         |             |             |              |                         |             |
| Depression           |              |                         |             |              |                         |             |             |              |                         |             |
| (n = 323)            |              |                         |             | Model 1      | 1.00                   | 1.47 (0.82-2.64)  | 1.67 (0.95-2.96) | 1.00                   | 1.00                   | 1.02 (0.54-1.63)          |
|                      |              |                         |             | Model 2      | 1.00                   | 1.45 (0.81-2.63)  | 1.98 (1.10-3.55) | 1.00                   | 1.00                   | 1.04 (0.54-1.62)          |
|                      |              |                         |             | Model 3      | 1.00                   | 1.27 (0.69-2.33)  | 1.82 (0.97-3.42) | 1.00                   | 1.00                   | 1.00 (0.52-1.59)          |
|                      |              |                         |             |              |                         |             |             |              |                         |             |
| Depressive symptoms  |              |                         |             |              |                         |             |             |              |                         |             |
| (n = 2628)           |              |                         |             | Model 1      | 1.00                   | 0.86 (0.66-1.13)  | 0.95 (0.73-1.24) | 1.00                   | 1.00                   | 1.11 (0.84-1.47)          |
|                      |              |                         |             | Model 2      | 1.00                   | 0.92 (0.69-1.21)  | 0.99 (0.76-1.30) | 1.00                   | 1.00                   | 1.12 (0.85-1.49)          |
|                      |              |                         |             | Model 3      | 1.00                   | 0.89 (0.67-1.18)  | 0.92 (0.69-1.22) | 1.00                   | 1.00                   | 0.99 (0.89-1.11)          |

Values are presented as odds ratio (OR) and (95% confidence interval). The significant OR (95% confidence interval) are indicated in the table by boldface values. Model 1 was not adjusted; Model 2 was adjusted for age, gender, smoking (0: ex-smoker and non-smoker, 1: smoker), alcohol (0: non-consumption, 1: once or twice per week, three or five times per week and over the six times per week), exercise habits and shift work (0: absence of shift work, 1: presence of shift work). Model 3 was additionally adjusted for industry types (0: no, 1: yes). In Models 2 and 3, non-workday does not include shift work as a confounder.
Health benefit of isotemporal replacement of sitting with standing

In contrast, our results are based on the calculated time spent sitting and should contribute to a deeper understanding of the association between worker’s sitting time in the workplace and health-related risks. Our logistic regression analysis also included the other specific domains. As a result, we found that sitting time during leisure time on a workday was only associated with diabetes. Similarly, the present analysis showed that the longest sitting time (>11.6 h) on a non-workday was only associated with depressive symptoms as measured by the CES-D.

The mechanisms of too much sitting affecting health-related risks are not fully known, but several previous studies have suggested that prolonged sitting results in increased plasma triglyceride levels, decreased levels of high-density lipoprotein cholesterol and decreased insulin sensitivity, which appear to reduce metabolic and vascular health. It has also been suggested that sitting behavior affects metabolic functions such as reducing glycemic-control and increasing the risk of type 2 diabetes. Although the present study showed that prolonged sedentary time on a non-workday increased depressive symptoms, the causal factors remain unknown.

One more challenging finding that the ISM approach allowed us to consider for the first time in this cross-sectional study was that reallocating 1 h/day of sitting time with 1 h/day of standing/walking in the workplace could have health benefits by decreasing the risk of hyperlipidemia by 4% and heart disease by 7%. The ISM controls significantly associated with any health risks (e.g., hyperlipidemia: OR = 0.98, 95% CI 0.93-1.03; heart disease: OR = 1.06, 95% CI 0.92-1.23) in participants with exercise habits. (Table 4, Table 5)

**Discussion**

The novel finding in this study is that a long time sitting during work is significantly associated with an increased risk of diabetes and hyperlipidemia. Furthermore, replacing 1 h/day of sitting with an equal amount of standing/walking in the workplace was associated with a 4% decrease in risk for hyperlipidemia and a 7% decrease for heart disease. Interestingly, this phenomenon was especially apparent in workers with non-exercise habits.

The prominent results of this study, showing the significant association between sitting time during work and risk of diabetes and hyperlipidemia, are consistent with previous studies that suggest an adverse association between sitting time during specific domains, including work, metabolic syndrome and diabetes. Those previous studies were adjusted for general physical activity, and the results suggest that occupational sitting time may be a potential independent factor effecting health outcomes. However, those studies evaluated sitting time using a ‘categories scale’ (i.e low, moderate, high), which likely lacked sensitivity for detecting the specific relationship between sitting time at work and health outcomes. In contrast, our results are based on the calculated time spent sitting and should contribute to a deeper understanding of the association between worker’s sitting time in the workplace and health-related risks. Our logistic regression analysis also included the other specific domains. As a result, we found that sitting time during leisure time on a workday was only associated with diabetes. Similarly, the present analysis showed that the longest sitting time (>11.6 h) on a non-workday was only associated with depressive symptoms as measured by the CES-D.

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One more challenging finding that the ISM approach allowed us to consider for the first time in this cross-sectional study was that reallocating 1 h/day of sitting time with 1 h/day of standing/walking in the workplace could have health benefits by decreasing the risk of hyperlipidemia by 4% and heart disease by 7%. The ISM controls

| Table 4. Isotemporal substitution models for disease in all participants. |
|-----------------------------|-----------------------------|-----------------------------|
|                             | Sitting time | Standing/walking time | Total time |
|                             | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Hypertension                  |             |                 |             |
| Partition                    | 1.01 (0.98-1.04) | 1.00 (0.97-1.02) | - |
| Replacement/substitution      | Dropped     | 0.99 (0.97-1.01) | 1.00 (0.96-1.04) |
| Diabetes                     |             |                 |             |
| Partition                    | 1.04 (1.00-1.08) | 1.01 (0.97-1.05) | - |
| Replacement/substitution      | Dropped     | 0.99 (0.96-1.02) | 1.04 (0.98-1.10) |
| Hyperlipidemia                |             |                 |             |
| Partition                    | 1.04 (1.01-1.08) | 0.98 (0.95-1.01) | - |
| Replacement/substitution      | Dropped     | **0.96 (0.94-0.98)** | 1.03 (0.98-1.08) |
| Heart disease                 |             |                 |             |
| Partition                    | 1.02 (0.94-1.11) | 0.92 (0.86-0.99) | - |
| Replacement/substitution      | Dropped     | **0.93 (0.87-0.99)** | 0.92 (0.80-1.06) |
| Cancer                       |             |                 |             |
| Partition                    | 1.10 (1.00-1.21) | 1.03 (0.93-1.14) | - |
| Replacement/substitution      | Dropped     | 0.97 (0.91-1.04) | 1.02 (0.91-1.15) |

Values are presented as odds ratio (OR) and (95% confidence interval). The significant OR (95% confidence interval) are indicated in the table by boldface values. Model was adjusted for age, gender, smoking status, alcohol status, exercise habits, shift work and industry types (0: no, 1: yes).
### Table 5. Isotemporal substitution models for disease by exercise habits.

|                    | Non-exercise habits (n = 7,708) | Exercise habits (n = 1,816) |
|--------------------|----------------------------------|----------------------------|
|                    | Sitting time                     | Standing/walking time       | Total time (working time) | Sitting time | Standing/walking time | Total time (working time) |
|                    | OR (95% CI)                      | OR (95% CI)                 | OR (95% CI)               | OR (95% CI) | OR (95% CI)           | OR (95% CI)               |
| **Hypertension**   |                                  |                              |                           |                                  |                          |
| Partition          | 1.01 (0.98-1.04)                 | 0.98 (0.96-1.01)             | -                         | 1.04 (0.97-1.11)                 | 1.05 (0.99-1.12)         |
| Replacement/substitution | Dropped                        | 0.98 (0.96-1.01)             | 0.99 (0.95-1.04)           | Dropped                        | 1.02 (0.98-1.07)         | 1.05 (0.96-1.15)         |
| **Diabetes**       |                                  |                              |                           |                                  |                          |
| Partition          | 1.04 (0.99-1.08)                 | 0.99 (0.95-1.04)             | -                         | 1.05 (0.95-1.17)                 | 1.08 (0.98-1.18)         |
| Replacement/substitution | Dropped                        | 0.98 (0.94-1.01)             | 1.03 (0.96-1.10)           | Dropped                        | 1.02 (0.98-1.07)         | 1.05 (0.96-1.15)         |
| **Hyperlipidemia** |                                  |                              |                           |                                  |                          |
| Partition          | 1.03 (1.00-1.07)                 | 0.97 (0.94-1.00)             | -                         | 1.10 (1.01-1.19)                 | 1.05 (0.97-1.13)         |
| Replacement/substitution | Dropped                        | **0.96 (0.93-0.98)**         | 1.00 (0.95-1.06)           | Dropped                        | 0.98 (0.93-1.03)         | 1.16 (1.04-1.30)         |
| **Heart disease**  |                                  |                              |                           |                                  |                          |
| Partition          | 1.03 (0.94-1.14)                 | 0.88 (0.82-0.95)             | -                         | 1.11 (0.85-1.44)                 | 1.14 (0.89-1.46)        |
| Replacement/substitution | Dropped                        | **0.89 (0.83-0.96)**         | 0.89 (0.76-1.04)           | Dropped                        | 1.06 (0.92-1.23)         | 1.03 (0.76-1.38)         |
| **Cancer**         |                                  |                              |                           |                                  |                          |
| Partition          | 1.12 (1.00-1.25)                 | 1.04 (0.92-1.18)             | -                         | 1.07 (0.89-1.29)                 | 1.02 (0.85-1.22)         |
| Replacement/substitution | Dropped                        | 0.97 (0.89-1.04)             | 1.05 (0.92-1.19)           | Dropped                        | 0.99 (0.87-1.12)         | 0.96 (0.75-1.23)         |

Values are presented as odds ratio (OR) and (95% confidence interval). The significant OR (95% confidence interval) are indicated in the table by boldface values. Model was adjusted for age, gender, smoking status, alcohol status, shift work and industry types (0: no, 1: yes).
for the confounding effect of total working time; hence, the observed associations between on-the-job sitting and standing/walking are independent of total working time. Interestingly, the above health benefits were not seen in workers with exercise habits. These findings are consistent with Matthews et al.29 demonstrating the health benefits associated with replacing sitting time with an equal amount of different types of physical activity in less active (<2 hrs/d overall activity) and more active (>2 hrs/d) participants. Although, this previous study did not focus on exercise habits, but on total activity time, only the less active participants, who replaced one hour per day of sitting with an equal amount of given physical activity, were associated with lower mortality. These findings suggest that, especially in less activity people, replacement of sitting time with a more physically active lifestyle may bring additional health benefits.

Almost all previous studies28,30 using ISM showed that replacing sedentary time with any physical activity, from light-intensity to moderate-vigorous physical activity, was an effective strategy for improving health outcomes such as body mass index,30,31 waist circumference,29,31 and metabolic outcomes.2,23 These previous studies primarily targeted the reduction of sitting and promotion of physical activity. Another large-scale epidemiological study34 using the ISM approach replaced sedentary time with standing time and showed a 3% decrease in mortality. Furthermore, Katzmarzyk et al.35 used a non-substitutional approach and reported that the proportion of daily time spent standing is associated with a lower OR for all-cause and cardiovascular disease mortality among physically-inactive participants only. Our study is in line with these previous studies, and we believe that replacing sitting with standing/walking is a good first step and a more realistic goal for workers with non-exercise habits in a work environment.

The first major strength of our study was the large worker population and wide range of employment sectors that were encompassed. Thus, our findings could be generalized to most Japanese workplaces. Secondly, the validated WLAQ provided continuous time outcome data for use with the ISM and allowed us to examine the replacement effect of sitting time with standing/walking time in the workplace. Most previous studies incorporating the ISM have used accelerometer data to assess sedentary time, because analyzing the accelerometry output can reveal the length of time spent on each activity during specific domains, and also total activity time. Our study also had some limitations. First, although our results are based on a large cross-section of Japanese workers, the data was collected in an internet setting. Data collection through the internet runs the risk of questionable legitimacy if the contents are not properly maintained. Furthermore, the sample collection through the internet survey was not random. These limitations may influence some of the associations obtained between sitting time and health-related risks. Second, lifestyles associated with health risk, such as eating behavior, were not adjusted for multiple logistic regression analysis, which may also influence the results. In addition, it is not possible to determine causality, because this study only carried out a cross-sectional examination. Therefore, further studies are needed to clarify these issues.

In conclusion, in this sample of Japanese employees, sitting time comprised 56.8% of total work time, 58.2% of leisure time on a workday and 60.3% of a non-workday. In the present study, sitting during working time was associated with an increased risk of diabetes and hyperlipidemia. In addition, replacing 1 h/day of sitting while working with 1 h/day of standing/walking was associated with a decreased risk of hyperlipidemia and heart disease, and these replacement effects were evident particularly among workers with non-exercise habits. Certainly, an expanded experimental study is needed to fully understand the mechanisms of these associations. However, our results provide new insight into the potential effects of reallocating sitting time during work that may be used for promoting worker’s health guidelines. It also may give direction to intervention studies examining the appropriate amount of time that should be reallocated.

Conflict of Interests

All authors report no conflict of interests relevant to this manuscript. The authors declare that the results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

Acknowledgments

This study was supported by an Industrial Disease Clinical Research Grant from the Ministry of Health, Labour and Welfare, Government of Japan (150903-01). We thank Dr. Hiroyuki Sasai of the University of Tokyo for his support with this study.

References

1) Bertrais S, Beyeme-Ondoua JP, Czernichow S, Galan P, Hercberg S and Oppert JM. 2005. Sedentary behaviors, physical activity, and metabolic syndrome in middle-aged French subjects. Obes Res 13: 936-944.
2) Grantveld A and Hu FB. 2011. Television viewing and risk of type 2 diabetes, cardiovascular diseases, and all-cause mortality: a meta-analysis. JAMA 15: 2448-2455.
3) Teychenne M, Ball K and Salmon J. 2010. Physical activity, sedentary behavior and depression among disadvantaged women. Health Educ Res 25: 632-644.
4) Katzmarzyk PT, Church TS, Craig CL and Bouchard C. 2009. Sitting time and mortality from all causes, cardiovascular disease, and cancer. Med Sci Sports Exerc 41: 998-1005.
5) Stamatakis E, Ekelund U and Wareham NJ. 2007. Temporal trends in physical activity in England: the Health Survey for England 1991 to 2004. Prev Med 45: 416-423.
population. *Int J Behav Med* 11: 219-224.
7) Mummery WK, Schofield GM, Steele R, Eakin EG and Brown WJ. 2005. Occupational sitting time and overweight and obesity in Australian workers. *Am J Prev Med* 29: 91-97.
8) Hu G, Tuomilehto J, Borudulin K and Jousilahti P. 2007. The joint associations of occupational, commuting, and leisure-time physical activity, and the Framingham risk score on the 10-year risk of coronary heart disease. *Eur Heart J* 28: 492-498.
9) Simons CC, Hughes LA, van Engelnd M, Goldbohm RA, van den Brandt PA and Weijenberg MP. 2013. Physical activity, occupational sitting time, and colorectal cancer risk in the Netherlands cohort study. *Am J Epidemiol* 177: 514-530.
10) Thune I and Lund E. 1997. The influence of physical activity on lung-cancer risk: a prospective study of 81,516 men and women. *Int J Cancer* 70: 57-62.
11) Bak H, Petersen L and Sorensen TI. 2004. Physical activity in relation to development and maintenance of obesity in men with and without juvenile onset obesity. *Int J Obes Relat Metab Disord* 28: 99-104.
12) Steindorf K, Friendenreich C, Linseinen J, Rohrmann S, Rundle A, Veglia F, Vines P, Johnsen NF, Tjonneland A, Overvad K, Raaschou-Nielsen O, Clavel-Chapelon F, Bouter-Ruault MC, Schulz M, Boeing H, Trichopoulou A, Kalapothaki V, Koliva M, Krogh V and Palli D. et al. 2006. Physical activity and lung cancer risk in the European Prospective Investigation into Cancer and Nutrition Cohort. *Int J Cancer* 119: 2389-2397.
13) Johansson S, Rosengren A, Tsipogianni A, Ulvenstam L, Wiklund I and Wilhelmsen L. 1988. Physical activity as a risk factor for primary and secondary coronary events in Goteborg, Sweden. *Eur Heart J* 9 Suppl L: 8-19.
14) van Uffelen JG, Wong J, Chau JY, Van der Ploeg HP, Riphaard CM, Owen N, Ainsworth BE, Healy GN and Gardiner PA. 2017. Replacement effects of sedentary time on metabolic risk. *Diabetes* 56: 2655-2667.
15) Matsuo T, Sasai H, So R and Ohkawara K. 2016. Percentagemethod improves properties of workers’ sitting- and walking-time questionnaire. *J Epidemiol* 26: 405-412.
16) Matsuo T, So R, Sasai H and Ohkawara K. 2017. Evaluation of Worker’s Living Activity-time Questionnaire (UNIOSH-WLAQ) primarily to assess workers’ sedentary behavior. *Sangyo Eiseigaku Zasshi* 59: 219-228.
17) Chau JY, Van Der Ploeg HP, Dunn S, Kurko J and Bauman AE. 2012. Validity of the occupational sitting and physical activity questionnaire. *Med Sci Sports Exerc* 44: 118-125.
18) Mekary RA, Willett WC, Hu FB and Ding EL. 2009. Isotemporal substitution paradigm for physical activity epidemiology and weight change. *Am J Epidemiol* 170: 519-527.
19) Statistics Bureau. 2015. *Labour Force Survey* 2015. http://www.stat.go.jp/english/data/roudou/index.htm.
20) Radloff LS. 1977. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1: 1385-1401.
21) Ministry of Health, Labour and Welfare. 2015. National Health and Nutrition Examination Survey (NHANES) in 2015. http://www.mhlw.go.jp/file/04-Houdouhappyou-10904750-Kenkyoukouyou-Gantsaiakukoukou.pdf.
22) Hu FB, Leitzmann MF, Stampfer MJ, Colditz GA, Willett WC and Rimm EB. 2001. Physical activity and television watching in relation to risk for type 2 diabetes mellitus in men. *Arch Intern Med* 161: 1542-1548.
23) Hu FB, Li TY, Colditz GA, Willett WC and Manson JE. 2003. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 289: 1785-1791.
24) Hu G, Qiao Q, Silventoinen K, Eriksson JG, Jousilahti P, Lindström J, Valle TT, Nissinen A and Tuomilehto J. 2003. Occupational, commuting, and leisure-time physical activity in relation to risk for Type 2 diabetes in middle-aged Finnish men and women. *Diabetologia* 46: 322-329.
25) Tremblay MS, Colley RC, Saunders TJ, Healy GN and Owen N. 2010. Physiological and health implications of a sedentary lifestyle. *Appl Physiol Nutr Metab* 35: 725-740.
26) Hamilton MT, Hamilton DG and Zderic TW. 2007. Role of low energy expenditure and sitting in obesity, metabolic syndrome, type 2 diabetes, and cardiovascular disease. *Diabetes* 56: 2655-2667.
27) Healy GN, Clark BK, Winkler EA, Gardiner PA, Brown WJ and Matthews CE. 2011. Measurement of adults’ sedentary time in population-based studies. *Am J Prev Med* 41: 216-227.
28) Matthews CE, Moore SC, Sampson J, Blair A, Xiao Q, Kendall SK, Hollenbeck A and Park Y. 2015. Mortality benefits for replacing sitting time with different physical activities. *Med Sci Sports Exerc* 47: 1833-1840.
29) Ekblom-Bak E, Ekblom Ö, Bergström G and Börjesson M. 2016. Isotemporal substitution of sedentary time by physical activity of different intensities and bout lengths, and its associations with metabolic risk. *Eur J Prev Cardiol* 23: 967-974.
30) Falconer CL, Page AS, Andrews RC and Cooper AR. 2015. The potential impact of displacing sedentary time in adults with type 2 diabetes. *Med Sci Sports Exerc* 47: 2070-2075.
31) Hamer M, Stamatakis E and Steptoe A. 2014. Effects of substituting sedentary time with physical activity on metabolic risk. *Med Sci Sports Exerc* 46: 1946-1950.
32) van der Berg JD, van der Velden JPMH, de Waard EAC, Bosma H, Savelberg HHCM, Schaper NC, van den Bergh JPW, Geusens PPM, Schram MT, Sep SJS, van der Kallen CJH, Henry RMA, Dagnelie PC, Eussen SJPM, van Dongen MCJM, Kühler S, Kroon AA, Stehouwer CDA and Koster A. 2017. Replacement effects of sedentary time on metabolic outcomes: The Maastricht study. *Med Sci Sports Exerc* 49: 1351-1358.
33) Buman MP, Winkler EA, Kurka JM, Hekler EB, Baldwin CM, Owen N, Ainsworth BE, Healy GN and Gardiner PA. 2014. Reallocating time to sleep, sedentary behaviors, or active behaviors: associations with cardiovascular disease risk biomarkers, NHANES 2005-2006. *Am J Epidemiol* 179: 323-334.
34) Stamatakis E, Rogers K, Ding D, Berrigan D, Chau J, Hamer M and Bauman A. 2015. All-cause mortality effects of replacing sedentary time with physical activity and sleeping using an isotemporal substitution model: a prospective study of 201,129 mid-aged and older adults. *Int J Behav Nutr Phys Act* 12: 121.
35) Katzmarzyk PT. 2014. Standing and mortality in a prospective cohort of Canadian adults. *Med Sci Sports Exerc* 46: 940-946.