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Patterns of changes in overtime working hours over 3 years and the risk for progression to type 2 diabetes in adults with pre-diabetes

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ABSTRACT

No information exists regarding the effects of working hours on glucose metabolism in adults with pre-diabetes, a high-risk group for developing diabetes. Further, longitudinal patterns in working hours and their effects on glucose metabolism have not been described previously. We investigated the association between changes in overtime working hours over 3 years and the risk for progression to type 2 diabetes among adults with pre-diabetes. We analyzed patterns of overtime working hours from 2008 to 2011 among 18,172 workers in Japan (16,474 men, aged 30 to 64 years) with pre-diabetes in 2011 (baseline) using the sub-cohort data from the Japan Epidemiology Collaboration on Occupational Health Study. Participants were followed up to March 2016. Overtime working hours per month were self-reported annually in 2008–2011 and trajectory patterns were identified using group-based trajectory modeling. Type 2 diabetes was diagnosed by fasting or random plasma glucose test, hemoglobin A1c, and history of diabetes. Multivariable-adjusted hazard ratios of incident diabetes were calculated using Cox regression. We identified 3 distinct trajectories of overtime work: persistently short, long-to-short, and persistently long. During a mean follow-up of 3.5 years, 1613 participants (8.9%) developed diabetes. Compared with persistently short overtime working hours, no material increase in diabetes risk was observed for either long-to-short working hours or persistently long working hours. After adjustment for potential confounders, this association was materially unchanged. The results suggest that among individuals with pre-diabetes, persistently long working hours over 3 years were not associated with an increased risk of developing type 2 diabetes.

1. Introduction

Long working hours have been reported globally (Lee et al., 2007). Data show that long working hours are common in Asian countries with their rapid economic growth (Lee et al., 2007). Long working hours have been suggested to increase diabetes risk through sleep deprivation and leisure-time physical inactivity (Kivimäki et al., 2015); however, empirical data are still scarce, especially in Asia. Diabetes causes microvascular complications (Chatterjee et al., 2017); elevates the risk for various diseases, including cardiovascular disease (Emerging Risk Factors Collaboration et al., 2010) and dementia (Gudala et al., 2013); and thus results in loss of work ability (Breton et al., 2013) and income (Seuring et al., 2015). Therefore, it is important to confirm whether long working hours increase diabetes risk.

Published studies have shown inconsistent findings on the association between baseline working hours and diabetes in individual cohort studies (Bannai and Tamakoshi, 2014; Kivimäki et al., 2015). These inconsistent results may be partly ascribed to the use of only one-time point data (e.g., working hours in the past month (Kawakami et al., 1999), the past two to three months (Kuwahara et al., 2018), or unspecified period (Kivimäki et al., 2015). Working hours before this time point vary from person to person; this difference among individuals may have affected the association between baseline working hours and diabetes. To reduce the possibility of such dilution and to show

Abbreviations: BMI, body mass index; CI, confidence interval; HbA1c, hemoglobin A1c; J-ECOH, Japan Epidemiology Collaboration on Occupational Health

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clinically meaningful data, the identification of subgroups showing similar trajectories of working hours over time using repeated-measures data and comparing health outcomes across these subgroups (Allen et al., 2014; Nagin and Odgers, 2010) would be more useful than one-time measurements. However, no study has addressed this issue. Furthermore, no study has examined the working hours-diabetes association among adults with pre-diabetes, a high-risk group for diabetes development (Tabák et al., 2012). Given the high incidence rate of diabetes among pre-diabetic adults (Morris et al., 2013), it is critically important to identify modifiable risk factors, including long working hours, in adults with pre-diabetes to establish effective preventive strategies for diabetes.

Recently, we reported no association overall between baseline overtime work and the risk for diabetes among non-diabetic workers in Japan (Kuwahara et al., 2018) using 2008–2013 health data from the Japan Epidemiology Collaboration on Occupational Health (J-ECOH) Study. In the J-ECOH Study, working hours have repeatedly been measured at annual health examinations in subgroups, and the population size is large enough to study the association between working hours and diabetes risk among pre-diabetic adults (Uehara et al., 2014). Thus, the J-ECOH Study provides a unique opportunity to address the above-mentioned issues simultaneously. Here, we investigated the association of changes in overtime working hours over 3 years with and the risk of progression to diabetes among workers with pre-diabetes using 2008–2015 data from the J-ECOH Study.

2. Methods

2.1. Study setting

The J-ECOH Study is an ongoing multi-company-based study of workers from > 10 large-scale companies in Japan. We extracted data on annual health check-ups between April 2008 and March 2016 (fiscal year from 2008 to 2015) from the two participating companies for which annually measured data on overtime working hours were available. In Japan, annual health examinations are mandatory for workers under the Industrial Safety and Health Act (Ministry of Justice, Japan, 2009). The details of the J-ECOH Study (Hu et al., 2018) and the present sub-cohort to estimate the health effects of working hours (Kuwahara et al., 2014) have been explained previously.

The conduct of the J-ECOH Study was explained to each participating company before data collection via posters with the purpose and procedure of the study. Written informed consent from each participant was waived. Participants were allowed to refuse their participation. This procedure followed the ethical guidelines for observational studies in Japan. Study procedures were approved by the ethics committee of the National Center for Global Health and Medicine.

2.2. Study participants

At baseline (April 2011 to March 2012, fiscal year 2011), 51,261 workers (43,834 men and 7427 women) aged 30 to 64 years underwent health examinations. Of these, we extracted the data of 21,891 workers without cardiovascular diseases, cancer, psychiatric disease, or diabetes but with pre-diabetes defined as a fasting plasma glucose level of 100 to < 126 mg/dL and/or hemoglobin A1c (HbA1c) of 5.7 to < 6.5% (American Diabetes Association, 2018) at baseline. Subsequently, 1053 workers were excluded due to missing data on overtime work (n = 874) or covariates (n = 560) at baseline. We further excluded 1556 workers without information on overtime for at least 2-time points in 2008–2010. Lastly, 1108 were excluded due to no follow-up data on diabetes until March 2016. Finally, 18,174 workers (16,474 men and 1700 women) aged 30 to 64 years (mean: 47.6, standard deviation: 7.9) at baseline were included in this study. Some participants met more than one exclusion criteria.

2.3. Assessment of overtime working hours

Self-reported working hours were measured at baseline (2011) and for 3 years before baseline (2008–2010), resulting in a maximum of 4 measurements over 3 years. Overtime work was assessed differently in the 2 workplaces. At one workplace, monthly overtime working hours (< 45, 45 to < 60, 60 to < 80, 80 to < 100, and ≥100 h) were self-reported at the annual health examination; whereas, at the other company, daily working hours were self-reported. At this company, overtime working hours per month was defined as daily working hours minus 8 h multiplied by 20 days. We combined the overtime working hours of all the companies into 4 categories using 45, 80, and 100 h per month as cutoffs, as explained previously (Kuwahara et al., 2014).

2.4. Covariates

At the time of the health examinations, lifestyle factors, including smoking and sleep duration and personal medical history were confirmed using self-administered questionnaires. Body height and weight and blood pressure were measured objectively in a standard manner at each company. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or treatment for hypertension. At one company, other lifestyle factors (alcohol use and leisure-time exercise), work-related factors (occupational physical activity, job position, and type of department), and family history of diabetes were also assessed using the questionnaire at the health examinations (Kuwahara et al., 2014).

2.5. Biochemical measurements and assessment of type 2 diabetes

Blood glucose concentrations were measured using enzymatic or glucose oxidase electrode methods, and HbA1c was measured using high-performance liquid chromatography. All laboratories performing these tests were assigned high ratings (grade A) by external quality control agencies. We defined diabetes as a fasting plasma glucose level of ≥126 mg/dL, random plasma glucose level of ≥200 mg/dL, HbA1c of ≥6.5%, or current treatment or history of diabetes based on the 2018 criteria by American Diabetes Association (2018). If individuals with pre-diabetes at baseline developed diabetes after the baseline, she or he was considered to have progressed to type 2 diabetes.

2.6. Statistical analyses

To characterize the patterns of changes in overtime working hours over 3 years, we used group-based trajectory modeling (Nagin and Odgers, 2010) which uncovers hidden subgroups in longitudinal data (Nagin, 2005). We used this method rather than time-averaged and cumulative working hours over time because the latter cannot consider longitudinal changes in the target variable, which may play a role in pathophysiology (Allen et al., 2014). Additionally, we believe that a better understanding of working-hour patterns over time and their health effects may help workplace management. We decided to assess overtime work pattern over 3 years (4-time points) and defined baseline year as 2011. This is because group-trajectory modeling requires at least 3-time points and if we took longer periods of exposure assessment (e.g., over 4 years or more), this would result in fewer outcome assessment periods, leading to unstable results due to fewer incident cases. We did not use overtime work data during follow-up assessment period because follow-up period is different especially between adults who developed diabetes and those who did not, resulting in difficulty in the interpretation of the patterns extracted. Our analysis follows existing studies (Tielemans et al., 2015).

Of the 18,156 participants, 15,893 (87.4%) had data for all 4 overtime time points; the remaining participants (12.6%) had data for 3 of the 4 time points: 5.2% (n = 942) did not have data for 2010, 2.2%

(n = 392) did not have data for 2009, and 5.2% (n = 947) did not have data for 2008. Participants with missing data of overtime work during 2008–2011 were included in the analysis (Jones et al., 2001; Niyonkuru et al., 2013) but only available data were used for the model specification (Niyonkuru et al., 2013). Before the estimation, we combined the categories of overtime working hours of 80 to 99 h and ≥100 h in each year because the number of participants in the last category was small which led to unstable results. We assigned 23, 63, and 95 to the increasing categories of overtime work each year to perform trajectory modeling.

We determined the number and shape (linear, quadratic, and cubic) of overtime work trajectories based on the 2-stage approach (Nagin, 2005) as described elsewhere (Kuwahara et al., 2017). First, we repeated the modeling by changing the number of trajectory groups from 2 to 5. We treated overtime work as the dependent variable and age, sex, and workplace as the independent variables. Given the distribution of overtime work, we selected a censored normal model suited for continuous data (Jones et al., 2001; Nagin, 2005). The time of the health examinations during 2008–2011 was treated as a time scale (e.g., 2008 as 1 and 2011 as 4). We considered the Bayesian information criterion (an indicator for goodness of model fit) and the number of participants and incident cases of diabetes in each trajectory to determine the number of trajectory groups. The latter was considered because an insufficient number of participants or cases lead to unstable results. After determining the number of trajectories, we further repeated the modeling to determine the shape of trajectories, by changing the combinations of trajectory shapes. We selected to use the best-fit model in the 3 trajectory groups for the main analysis. The average posterior probability for each group was calculated to confirm whether classifying participants into distinctive groups was successful (≥0.70 indicates good discrimination).

We calculated person-years from the date of baseline examination to the date of the first diagnosis of diabetes at the follow-up examinations or the date of the last examination. Cox regression analysis was performed to assess the association between working hours and diabetes. In model 1, we adjusted for age (year, continuous), sex, and workplace. In model 2, we further adjusted for smoking (never, past, and current) and hypertension (yes and no). BMI (kg/m^2, continuous) was additionally adjusted for in model 3 and BMI and sleep duration (< 5, 5 to < 6, 6 to < 7, and ≥7 h per day) in model 4. In model 5, we adjusted for the factors in model 4 plus HbA1c at baseline; we adjusted for HbA1c alone because HbA1c and fasting glucose are highly correlated (Ketama and Kibret, 2015), raising a concern of over-adjustment when simultaneously adjusted for, and because HbA1c reflects long-term blood glucose levels and is more biologically stable than fasting glucose (International Expert Committee, 2009).

We further adjusted for baseline variables in one company in model 2 as follows: alcohol use (non-drinker, drinkers consuming < 1, 1 to < 2, and ≥2 *go* of Japanese sake equivalent; 1 *go* of Japanese sake contains approximately 23 g of ethanol), leisure-time exercise (< 150 and ≥150 min per week), occupational physical activity (sedentary, standing, walking, and fairly physically active), type of department (field-related and those not), job position (high and low), and family history of diabetes (yes and no).

We also estimated the combined association of sleep duration (< 6 or ≥6 h per day) at baseline and overtime working hours with diabetes to examine whether sleep duration may affect the overtime-diabetes association. We chose the cut point of 6 h for short sleep based on the existing knowledge (Shan et al., 2015) and to ensure enough sample size in each group. Although long sleep (≥8 or 9 h per day) may increase diabetes risk (Shan et al., 2015), in occupational settings of Japan, workers with long sleep are few (Kita et al., 2012). Moreover, we had not data on long sleep (≥8 h). Thus, we did not consider long sleep.

We repeated all analyses using more severe criteria for pre-diabetes, defined as fasting plasma glucose of 110 to < 126 mg/dL or HbA1c of 6.0 to < 6.5% (Heianza et al., 2012). All P-values (2-sided) < 0.05 was considered statistically significant. All statistical analyses were performed using Stata version 14.2 (Stata Corp, College Station, TX, USA).

Table 1
Distributions of overtime work hours per month according to patterns in overtime working hours during 2008–2011.

Fiscal year	2008	2009	2010	2011
Persistently short				
< 45 h	10,653 (93.8)	10,260 (90.3)	9666 (85.1)	10,202 (89.8)
45 to < 80 h	37 (0.3)	802 (7.1)	1075 (9.5)	1088 (9.6)
≥80 h	0 (0)	27 (0.2)	39 (0.3)	72 (0.6)
Missing	672 (5.9)	273 (2.4)	582 (5.1)	0 (0)
Long to short				
< 45 h	0 (0)	1732 (57.1)	2028 (66.9)	2664 (87.9)
45 to < 80 h	2679 (88.4)	1210 (39.9)	831 (27.4)	368 (12.1)
≥80 h	271 (8.9)	34 (1.1)	16 (0.5)	0 (0)
Missing	82 (2.7)	56 (1.9)	157 (5.2)	0 (0)
Persistently long				
< 45 h	565 (15.0)	527 (13.9)	247 (6.5)	148 (3.9)
45 to < 80 h	2301 (60.9)	2422 (64.1)	2627 (69.5)	2883 (76.3)
≥80 h	726 (19.2)	768 (20.3)	698 (18.5)	749 (19.8)
Missing	188 (5.0)	63 (1.7)	208 (5.5)	0 (0)

Data are shown as number (%).

3. Results

3.1. Descriptive data according to overtime working hours pattern

Three discrete trajectories were identified for overtime working hours over 3 years (Table 1). Nearly 60% of participants (n = 11,362, 62.3%) were classified into a group characterized by a persistently high proportion of short overtime work and thus named as “persistently short”. Of rest, the second major group (n = 3780, 20.8%) was characterized by a persistently large proportion of participants with long overtime working hours over the 3 years, thus labeled as “persistently long.” The last group (n = 3032, 16.7%) was characterized as a gradual decrease in the proportion of participants with long overtime work over the 3 years, and it was thus labeled as “short-to-long.” The average posterior probability of classification into each group of working hours was sufficiently high (0.99 for the persistently short group, 0.95 for the persistently long group, and 0.85 for the long-to-short group).

Participant characteristics at baseline according to the changes in working hours during 2008–2011 are shown in Table 2. Individuals with persistently short overtime working hours were slightly older and tended to be women, and they had a lower BMI but more hypertension than the other 2 groups. They tended to be non-smokers and to sleep enough hours. Baseline HbA1c levels were not materially different between the 3 groups.

Table 2
Characteristics of participants with pre-diabetes in 2011 according to trajectory patterns of overtime working hours during 2008–2011.

	Patterns in overtime work hours		
	Persistently short	Long to short	Persistently long
No. of participants (%)	11,362 (62.5)	3032 (16.7)	3780 (20.8)
Age, year	48.4 (8.2)	47.5 (7.9)	45.4 (6.8)
Men, n (%)	9703 (85.4)	3015 (99.4)	3756 (99.4)
Current smoking, n (%)	4190 (36.7)	1180 (38.9)	1420 (37.6)
Sleeping < 6 h/day, n (%)	5349 (47.1)	1601 (52.8)	2653 (70.2)
Hypertension, n (%)	2593 (22.8)	613 (20.2)	608 (16.1)
BMI, kg/m^2	24.1 (3.5)	24.2 (3.2)	24.2 (3.2)
HbA1c, %	5.7 (0.3)	5.7 (0.3)	5.7 (0.3)

Data are shown as mean (SD) or number (%).
BMI, body mass index; HbA1c, hemoglobin A1c.

Table 3
Trajectory patterns in overtime working hours and risk of type 2 diabetes among adults with pre-diabetes, data from the 2008–2015 Japan Epidemiology Collaboration on Occupational Health Study.

	Working hours pattern over 3 years		
	Persistently short	Long to short	Persistently long
N	11,362	3032	3780
Cases, n (%)	1034 (9.1)	282 (9.3)	297 (7.9)
Person-years	39,604	10,838	13,953
Incidence-rate/1000	26.1	26.0	21.3
Crude model	1 (reference)	0.99 (0.87, 1.13) $P = 0.94$	0.80 (0.70, 0.91) $P = 0.001$
Model 1[a]	1 (reference)	1.00 (0.87, 1.14) $P = 0.96$	0.86 (0.75, 0.98) $P = 0.021$
Model 2[b]	1 (reference)	1.02 (0.89, 1.16) $P = 0.79$	0.89 (0.78, 1.02) $P = 0.09$
Model 3[c]	1 (reference)	1.03 (0.90, 1.17) $P = 0.71$	0.91 (0.80, 1.04) $P = 0.17$
Model 4[d]	1 (reference)	1.03 (0.90, 1.18) $P = 0.69$	0.91 (0.80, 1.04) $P = 0.17$
Model 5[e]	1 (reference)	1.02 (0.90, 1.17) $P = 0.77$	0.99 (0.87, 1.13) $P = 0.89$

Data are shown as hazard ratio (95% confidence intervals).
[a] Adjusted for age (years, continuous), sex, and workplace at baseline.
[b] Adjusted for factors in model 1 plus baseline smoking (never, past, and current) and hypertension (yes and no).
[c] Adjusted for factors in model 2 plus baseline body mass index (kg/m^2, continuous).
[d] Adjusted for factors in model 3 plus sleep duration (< 5, 5 to < 6, 6 to < 7, and ≥7 h per day).
[e] Adjusted for factors in model 4 plus baseline HbA1c (%, continuous).

3.2. Association between patterns of overtime working hours and the risk for progression to type 2 diabetes from pre-diabetes

During a mean follow-up of 3.5 years with a total of 64,396 person-years, diabetes occurred in 1613 participants (8.9%). The associations between changes in working hours and diabetes onset are shown in Table 3. Compared with persistently short overtime working hours, neither persistently long overtime work nor long-to-short overtime work exhibited a significantly increased risk for progression to diabetes. The hazard ratios and 95% confidence intervals (CIs) of developing diabetes were 1.02 (95% CI 0.90, 1.17) for long-to-short overtime and 0.99 (95% CI 0.83, 1.13) for persistently long overtime when compared with persistently short overtime in model 5. When we further adjusted for alcohol use, leisure-time exercise, occupational physical activity, shift work, type of department, job position, and family history of diabetes using available data from one company (n = 16,392), the results were not materially different (Table 4).

When we examined the combined association of sleep duration at baseline and overtime work patterns with diabetes, persistently long overtime working hours with short sleep (< 6 h per day) were not associated with an increased risk for diabetes (Supplementary Table 1). When we repeated the all analyses using the more severe criteria for pre-diabetes, three overtime work hours patterns were identified among 5676 workers and we obtained similar results to the main findings (Supplementary Tables 2A to 2E).

4. Discussion

In this population-based study of working adults with pre-diabetes, we identified 3 heterogeneous patterns of change in overtime working hours over 3 years: persistently short, long-to-short, and persistently long. The present data showed that persistently long working hours did not increase the risk for progression to diabetes when compared with persistently short overtime working hours. This is the first study to estimate the effects of longitudinal working hours patterns on health outcomes.

Table 4
Association of overtime working hours pattern and diabetes risk with additional adjustment for lifestyles and work-related factors in one company (n = 16,392), data from the 2008–2015 Japan Epidemiology Collaboration on Occupational Health Study.

	Working hours pattern over 3 years		
	Persistently short	Long to short	Persistently long
N	9942	2853	3597
Cases (%)	836 (8.4)	256 (9.0)	282 (7.8)
Person-years	34,892	10,278	13,302
Incidence-rate/1000	24.0	24.9	21.2
Crude model	1 (reference)	1.04 (0.90, 1.20) $P = 0.58$	0.87 (0.76, 1.00) $P = 0.046$
Model 1[a]	1 (reference)	1.01 (0.88, 1.16) $P = 0.91$	0.90 (0.78, 1.03) $P = 0.12$
Model 2[b]	1 (reference)	1.04 (0.90, 1.20) $P = 0.59$	0.98 (0.85, 1.13) $P = 0.75$
Model 3[c]	1 (reference)	1.05 (0.91, 1.21) $P = 0.48$	0.99 (0.86, 1.14) $P = 0.88$
Model 4[d]	1 (reference)	1.05 (0.91, 1.22) $P = 0.48$	0.99 (0.86, 1.14) $P = 0.87$
Model 5[e]	1 (reference)	1.00 (0.87, 1.15) $P = 1.00$	1.02 (0.88, 1.17) $P = 0.83$

Data are shown as hazard ratios (95% confidence intervals) of progression from pre-diabetes to type 2 diabetes.
[a] Adjusted for age (years, continuous) and sex at baseline.
[b] Adjusted for factors in model 1 plus baseline hypertension (yes and no) and smoking (never, past, and current), alcohol use (non-drinker, drinker consuming < 1 *go*, 1 to < 2 *go*, ≥2 *go* of Japanese sake equivalent; 1 *go* of Japanese sake contains approximately 23 g of ethanol), leisure-time exercise (< 150 min and ≥150 min per week), occupational physical activity (sedentary, standing, walking, physically fairly active), shift work (yes and no), job position (high and low), field-related department (yes and no), and family history of diabetes.
[c] Adjusted for factors in model 2 plus baseline body mass index (kg/m^2, continuous).
[d] Adjusted for factors in model 3 plus baseline sleep duration (< 5, 5 to < 6, 6 to < 7, and ≥7 h per day).
[e] Adjusted for factors in model 4 plus baseline HbA1c (%, continuous).

The present data showed that neither persistently long working hours nor changes in working hours from long to short were associated with an increased risk for diabetes. This finding is compatible with a recent finding from a meta-analysis showing that baseline working hours were not associated with diabetes risk among workers with high socio-economic status (Kivimäki et al., 2015) because the present participants are mainly regular full-time employees in large companies, who usually have high socioeconomic status. Although the present study was designed to reduce the healthy worker effect (i.e., healthy workers, who are at low risk of developing diseases including diabetes, work longer hours than unhealthy workers, resulting in null finding for long overtime work) by including only workers with pre-diabetes and adjusting for health-related factors, a plausible reason for the null finding may be this effect. In this study, participants with persistently long overtime working hours tended to be healthier than participants with persistently short overtime hours; the prevalence of hypertension among workers with persistently long working hours (15.8%) was lower than in those with persistently short working hours (22.8%). Although we adjusted for risk factors for diabetes including hypertension, BMI, and smoking, effect of healthy worker might have remained. Alternatively, existing data have shown that body weight control is important to prevent the progression from pre-diabetes to diabetes (Khavandi et al., 2013). In the present study, BMI levels during 2008–2011 were not materially different across the 3 patterns of overtime work (data not shown). This may partly explain the observed null finding.

We previously found that long overtime working hours were

associated with an increased risk for diabetes when short sleep duration was combined (Kuwahara et al., 2018). In the present study, such an association was not found. This null finding may be explained by unstable results due to the small sample size when participants were divided by the combinations of working hours and sleep. Therefore, a conclusion cannot be drawn from the present data regarding the effect modification by sleep duration among high-risk groups.

The present study has some strengths including repeated measurements of both working hours and blood glucose markers, including blood glucose and HbA1c. Moreover, the identification of longitudinal patterns in working hours in a high-risk population provided a unique insight into the role of working hours in health outcomes.

Limitations of this study should be mentioned. First, working hours were not uniformly measured across participating companies. Nonetheless, we recently confirmed that self-reported overtime work and daily working hours assessed by similar questionnaires are highly correlated with registered working hours (i.e., high validity) and moderately reproducible among workers from the companies participating in the J-ECOH Study (Imai et al., 2016). Second, we assessed working hours only once a year. Thus, the reported overtime working hours at a single time point may not reflect true working hours throughout the year. However, we confirmed that self-reported monthly overtime working hours in the previous month were highly and positively correlated with the frequency of long overtime work (defined as ≥45 h per month) within the last 12 months (Spearman correlation 0.80, $P < 0.001$, $n = 174$); similar correlation was found between the company records of overtime hours in the previous month and total overtime work hours during the past 12 months (Spearman correlation 0.74, $P < 0.001$, $n = 170$) using data of the previous study (Imai et al., 2016) (data not shown in the original study). Third, we used simply categorized data of overtime work: < 45, 45 to < 80, and ≥80 h per month. Although self-reported overtime work are valid (Imai et al., 2016), if we had data of overtime work derived from company records, we could have estimated overtime work patterns more precisely. Fourth, although adults with long overtime work tended to work longer hours whereas adults with short overtime work tended to work shorter hours during the follow-up period (Supplementary Table 3), working hours during the follow-up period might have diluted the present results. Fifth, we estimated only the long-term effects of working hours. Therefore, a conclusion cannot be drawn regarding short-term or acute health effects. Sixth, "long to short" overtime group was not identified when severe criteria for pre-diabetes were applied. When we extracted a group "long to short" artificially as follows (1) ≥80 h per month in 2008 and 2009, 45 to < 80 h per month in 2010, and < 45 h per month in 2011, (2) ≥80 h per month in 2008, 45 to < 80 h per month in 2009 and 2010, and < 45 h per month in 2011, and (3) ≥80 h per month in 2008, 45 to < 80 h per month in 2009, < 45 h per month in 2010 and 2011, the numbers of workers in these groups were small: (1) $n = 10$, (2) $n = 19$, and (3) $n = 22$, respectively. We confirmed that all these adults were classified as "persistently long". Thus, we could not elucidate the risk in this "long to short" group when severe criteria of pre-diabetes were used. Given that "long to short" group constituted only 4.9% of "long to short" group (51 out of 1044 workers), "long to short" group may not have materially affected the risk in "persistently long" group. Seventh, glycemic conditions during 2008 to 2010 might have affected the overtime work–diabetes association. However, majority of participants had pre-diabetes persistently during 2008 to 2010 ($n = 9359$) and when analyzed among adults with persistent pre-diabetes during this period, the overtime work-diabetes association was not materially changed (Supplementary Table 4). Therefore, glycemic conditions during 2008 to 2010 may not have affected the present result. Eighth, follow-up period was relatively short in the present study. However, given the high conversion rate from pre-diabetes to diabetes (e.g., 5 to 10% per year) (Tabák et al., 2012) and high cumulative incidence in the present study (about 10% with 1600 cases), the follow-up period may not have affected the present conclusion. Ninth, the present sample size was large enough for main analysis but insufficient for subgroup analysis stratified by overtime work and sleep duration. Tenth, residual and unmeasured confounding factors (e.g., job demand and control, diet) may have influenced the association of working hours with diabetes. Further, during the study period, several notable events including the Great Recession of 2008–2009 and the Great East Japan Earthquake 2011 occurred, which may affect working hours and glycemic status. Nonetheless, we confirmed that proportion of overtime work and average levels of HbA1c and fasting glucose did not change materially during 2008–2012. Thus, these events may not have confounded the results significantly. Lastly, the participants were Japanese workers from large-scale companies in specific industries (electric machinery and apparatus manufacturing and steel) and the majority was male. Therefore, the present findings may not be generalizable to workers from different backgrounds (e.g., small- and middle-sized enterprises or other industries) and female workers.

5. Conclusion

This study showed that persistently long overtime working hours were not associated with an increased risk for progression from pre-diabetes to diabetes among Japanese workers. Effect modification by sleep deprivation should be investigated in a larger cohort study.

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Conflict of interest

T. Miyamoto, S. Yamamoto, T. Honda, and T. Nakagawa are occupational physicians at the participating companies. We declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2019.02.002.

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