Psychiatry Research 273 (2019) 551–558

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Breakfast consumption and the risk of depressive symptoms: The Furukawa Nutrition and Health Study

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ARTICLE INFO

Keywords:
Depression risk
Breakfast
Prospective studies
Japanese

ABSTRACT

Breakfast consumption has been suggested to influence mood, but prospective evidence on this issue is limited. We prospectively investigated the association between the frequency of breakfast consumption and the risk of depressive symptoms in Japanese employees. Participants were 716 employees aged 19–68 years who were free from depressive symptoms and mental disorders at baseline and who attended the 3-year follow-up survey. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale. The frequency of breakfast consumption was categorized into "daily", "5–6 times/week", "3–4 times/week", "1–2 times/week", or "≤1 times/week". Logistic regression was used to estimate odds ratios of depressive symptoms according to breakfast consumption adjusted for dietary and lifestyle factors. Participants who consumed breakfast ≤1 times/week had an increased risk of depressive symptoms compared to those who ate breakfast every day, even after adjusting for other dietary factors (multivariable-adjusted odds ratio 2.92; 95% confidence interval, 1.37–6.22) The risk of depressive symptoms tended to increase with decreasing frequency of breakfast consumption (P for trend = 0.02). The omission of breakfast is related to increased risk of depressive symptoms among Japanese employees, independently of other dietary and non-dietary factors.

1. Introduction

Depression is a common mental health problem in the general population that reduces work productivity, lowers quality of life, and increases mortality (Doris et al., 1999). Given these immense burdens, modifiable targets for the prevention of mental disorders are now urgently needed (Sarris et al., 2015). Scientific evidence suggests that breakfast consumption has various benefits, including not only somatic benefits, but also to mental health, via the lowering of cortisol levels (Smith, 2002; Witbracht et al., 2015) and the regulation of the hepatic circadian clock (Tahara and Shibata, 2016). Cortisol is a steroid hormone that is released in response to stress. High cortisol levels are related to an increase in inflammatory cytokines, which affect neurotransmitters by lowering serotonin (Miller et al., 2009), and to the suppression of immune functions (Segerstrom and Miller, 2004). Thus, higher cortisol levels have been regarded as a risk condition for subsequent depression (Herbert, 2013). In addition, while a disruption to circadian rhythms is thought to be a contributing factor to depression (Boyce and Barriball, 2010), peripheral clock genes in the liver and intestine are reset by breakfast (Kagawa, 2012). Emerging evidence suggests that the timing of food intake or nutrients is a potent regulator of the hepatic circadian clock, and this regulation can be more powerful than the suprachiasmatic nucleus-mediated regulation of the peripheral clock, which can be phase-entrained by time-scheduled feeding instead of the normal light–dark cycle (Tahara and Shibata, 2016). These scientific data draw attention to the relation between depressive status

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https://doi.org/10.1016/j.psychres.2019.01.069
Received 20 April 2018; Received in revised form 25 December 2018; Accepted 23 January 2019
Available online 24 January 2019

and breakfast consumption.

Many studies have investigated the association between the frequency of breakfast and depressive symptoms. The majority (Smith, 1998, 1999; Allgower et al., 2001; Smith, 2003; Fulkerson et al., 2004; Gollub and Weddle, 2004; Nakao and Yano, 2006; Ahadi et al., 2016; Xu et al., 2016; Kwak and Kim, 2017; Lee, Han, et al., 2017; Lee, Park, et al., 2017), but not all (Kawada et al., 2009; Huang et al., 2017), have reported a beneficial association. However, most of these studies were conducted using a cross-sectional design (Smith, 1998, 1999; Allgower et al., 2001; Smith, 2003; Fulkerson et al., 2004; Gollub and Weddle, 2004; Kawada et al., 2009; Xu et al., 2016; Kwak and Kim, 2017; Lee, Han, et al., 2017; Lee, Park, et al., 2017), and only a few prospective studies (Nakao and Yano, 2006; Huang et al., 2017) have yet been reported. Furthermore, most of these studies (Allgower et al., 2001; Fulkerson et al., 2004; Gollub and Weddle, 2004; Nakao and Yano, 2006; Kawada et al., 2009; Xu et al., 2016; Kwak and Kim, 2017) have failed to account for potentially important factors, such as other aspects of diet (e.g., nutrients and foods) and health-related behaviors (e.g., physical activity and sleep duration). Although breakfast skippers are likely to lead an unhealthy lifestyle (Ahadi et al., 2016; Lee, Han, et al., 2017) and might have lower dietary intakes of nutrients (Tietyen and Fleming, 1995; Gollub and Weddle, 2004) than regular breakfast eaters, it has remained unclear whether the association between breakfast and depressive symptoms reflects nutritional factors and/or lifestyle confounders or the consumption of breakfast itself. In addition, prospective studies on this issue are limited due to the one- or two-year follow-up period and assessment of breakfast consumption only at baseline (Nakao and Yano, 2006; Huang et al., 2017), small sample size (n = 376) (Huang et al., 2017), or failure to exclude participants with depression at baseline (Nakao and Yano, 2006).

To address these issues, we investigated the prospective association of the frequency of breakfast consumption at baseline with depressive symptoms using a three-year follow-up survey, with adjustments made for a wide range of dietary and lifestyle factors.

2. Methods

2.1. Data and study population

As part of the Japan Epidemiology Collaboration on Occupational Health Study, the Furukawa Nutrition and Health Study, a nutritional epidemiological survey, was conducted at during periodic health examinations among workers from two factories of a manufacturing company and its affiliated companies in Chiba and Kanagawa Prefectures. Details of the study procedure have been described elsewhere (Miki et al., 2015). Prior to the health check-up, all employees (n = 2828) in these companies were invited to take part in the survey and asked to fill out two types of survey questionnaires (one for diet and the second for overall health-related lifestyle in general). We also obtained health examination data, including the results of anthropometric and biochemical measurements and information on disease history. Written informed consent was obtained from each participant.

Of 2828 health check-up attendees at baseline, 2162 agreed to participate (response rate = 76%). Of these, 2151 participants completed questionnaires assessing diet and health-related lifestyles at the baseline survey. We initially excluded 610 participants with depressive symptoms (CES-D ≥ 16) and 100 participants with a history of severe diseases at the baseline survey. We further excluded 41 participants with missing data on outcome, exposure and covariates at the baseline survey. Of the remaining 1400 participants, 898 (64%) participants responded to the three-year follow-up survey. We further excluded 3 participants with missing data with the Center for Epidemiological Studies Depression Scale (CES-D) score (Radloff, 1977; Shima et al., 1985) at the follow-up survey. Finally, we excluded 179 participants who engaged in night or rotating shift work at baseline, leaving 716 participants (622 men and 94 women aged 19–68 years) for analysis (Fig. 1). We excluded participants with night or rotating shift work because (1) they are at higher risk of depression (Lee, Myung, et al., 2017); (2) breakfast was self-defined, and participants who work the night or on a rotating shift may be misclassified as breakfast skippers if they regarded breakfast as a meal during traditional breakfast hours and not the meal they ate when they woke up; and (3) the number of participants engaged in night or rotating shift work was small.

2.3. Assessment of depressive symptoms

Depressive symptoms were assessed using a Japanese version (Shima et al., 1985) of the CES-D scale (Radloff, 1977). This scale consists of 20 items addressing 6 typical symptoms of depression experienced during the preceding week, including depressed mood, guilt or worthlessness, helplessness or hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance. Each item is scored on a scale of 0 to 3 according to the frequency of the symptom, and the scores are then summed to give the total CES-D score, which ranges from 0 to 60. The criterion validity of the CES-D scale has been well established among both Western (Radloff, 1977) and Japanese (Shima et al., 1985) participants. Participants with a CES-D score ≥ 16 are considered to have depressive symptoms (Radloff, 1977). A cutoff of ≥19, which has been suggested as more suitable for Japanese workers (Wada et al., 2007), was also assessed. In addition, we examined the association between breakfast frequency at baseline and change in CES-D score from baseline to three years later using a follow-up survey.

2.4. Assessment of breakfast consumption

Participants were asked to provide information concerning the frequency of breakfast consumption on the lifestyle questionnaire by responding to the following question: How often do you have breakfast a week? They had five response options: <1 time/week, 1–2 times/week, 3–4 times/week, 5–6 times/week, or daily.

To assess consistent exposure status over the duration of follow-up, participants who had breakfast every day at both baseline and follow-up were categorized as “maintained daily breakfast” whereas those who reported low breakfast consumption (<every day) on both surveys were categorized as “maintained non-daily breakfast.” We divided participants into daily or non-daily breakfast frequency groups because our study population included a relatively small number in the non-daily breakfast categories (n = 237) for both the baseline and follow-up surveys. In order to confirm the robustness of our findings regardless of cutoff points used to classify breakfast frequency groups, we conducted a sensitivity analysis using other cutoff points (i.e., breakfast consumption ≥5 times/week or <5 times/week).

2.5. Dietary assessment

Dietary habits during the preceding one-month period were assessed using a validated brief self-administered diet history questionnaire (BDHQ) (Kobayashi et al., 2012). Dietary intake for energy and nutrients were estimated using an ad hoc computer algorithm for the BDHQ (Kobayashi et al., 2011), with reference to the Standard Tables of Food Composition in Japan (Science and Technology Agency, 2005, 2010).

2.6. Assessment of other variables

Marital status, job grade, night and rotating shift work, overtime work, smoking, alcohol drinking, sleep duration, physical activity during work/housework or when commuting to work, and leisure-time physical activity were asked about in the survey questionnaire. Physical activity during work/housework or when commuting and leisure time were expressed as the sum of metabolic equivalents (METs) multiplied by the duration of time (in hours) across physical activities with

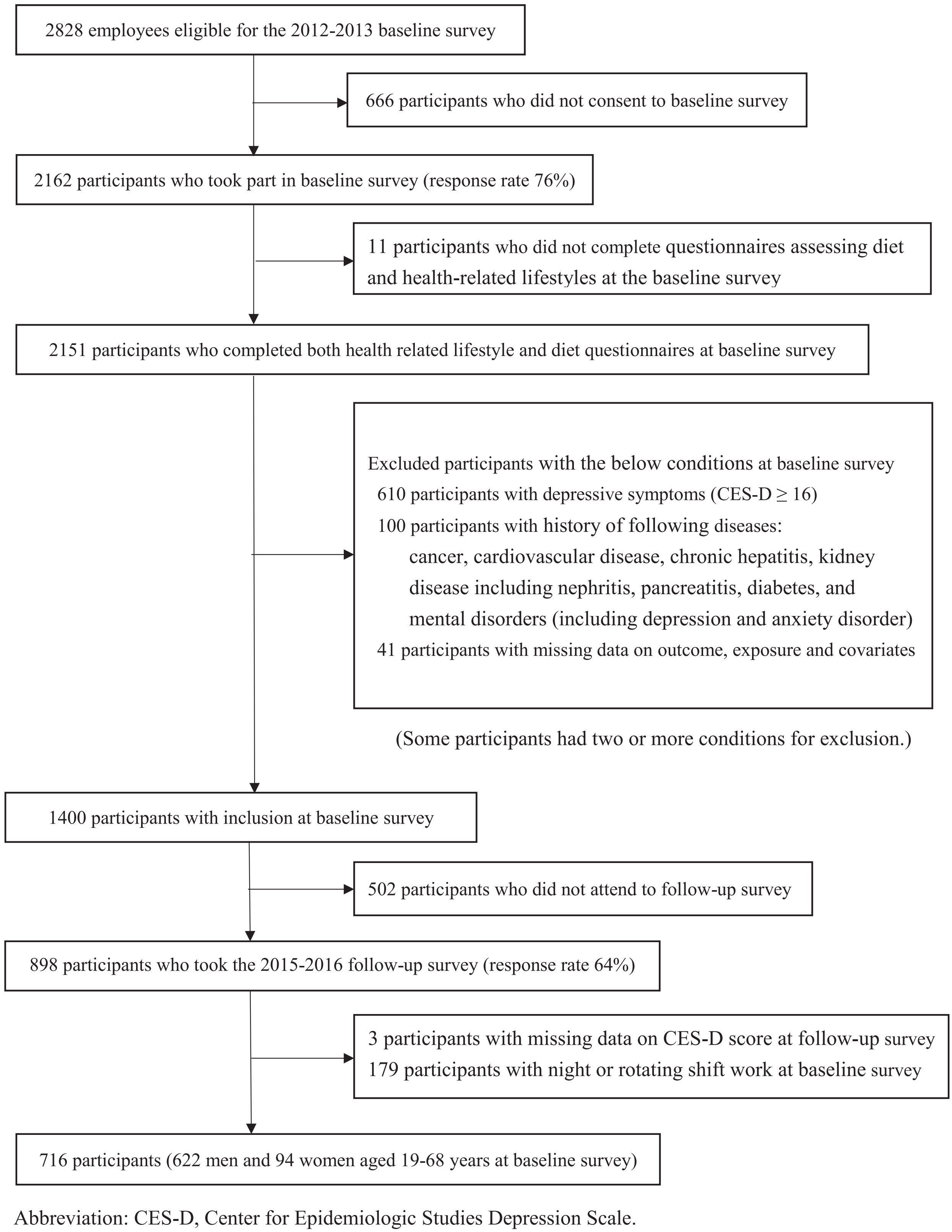

Fig. 1. Flowchart of study protocol.

different levels. Psychological work environment was also assessed via the Japanese version of the Job Content Questionnaire (Karasek et al., 1998), and the job strain score was calculated according to a standard procedure. Body height and weight were assessed to the nearest 0.1 cm and 0.1 kg, respectively, in a standardized procedure with participants wearing light clothes and without shoes. Body mass index was calculated as weight in kilograms divided by the square of height in meters (kg/m^2).

2.7. Statistical analysis

Data were expressed as means (standard deviation) and percentages for continuous variables and categorical variables. The trend association between confounding factors and the frequency of breakfast consumption at baseline was tested using linear regression analysis for continuous variables and the Mantel–Haenszel chi-square test for categorical variables, assigning ordinal numbers 1–5 to the categories of the frequency of breakfast consumption (daily, 5–6 times/week, 3–4 times/week, 1–2 times/week, and ≤1 times/week, respectively).

To examine the prospective association between the frequency of breakfast consumption at baseline and the risk of depressive symptoms, we performed multiple logistic regression analysis and calculated the odds ratios (ORs) and 95% confidence intervals (CIs) of depressive symptoms for the frequency of breakfast consumption at baseline, using those who had breakfast daily as the reference group. The first model was adjusted for age, sex, and works. The second model was further adjusted for marital status, job grade, overtime work, job strain, physical activity at work/housework or when commuting to work, leisure-time physical activity, smoking, alcohol drinking, sleep duration, body mass index, and total energy intake. In addition, the third model was further adjusted for intake of carbohydrate, fat, protein, folate, vitamin B6, vitamin B12, $n-3$ polyunsaturated fatty acids, magnesium, and zinc, which have been shown to be associated with decreased depressive symptoms (Woo et al., 2006; Gilbody et al., 2007; Sanchez-Villegas et al., 2007; Oishi et al., 2009; Skarupski et al., 2010; Wolfe et al., 2011; Li, Lv, et al., 2017; Li, Li, et al., 2017). To control for baseline depressive status, we further adjusted for CES-D scores at baseline. All models were adjusted for baseline values of all potential confounding variables (as described earlier). We checked the collinearity when we examined the associations after fully adjusting the covariates and confirmed that no variables were to be omitted because of collinearity in our analysis.

In order to confirm the robustness of association between frequency of breakfast consumption and depressive symptoms, multiple linear regression analysis was used to examine the association between frequency at baseline and change in CES-D score from baseline to follow-up survey. With prolonged follow-up, the misclassification of dietary exposure increases due to dietary changes over time, which cannot be captured by baseline assessment (Willett, 1998). Thus, we examined the prospective association between the repeated frequency of breakfast over time and the development of depressive symptoms as a sensitivity analysis to assess consistent exposure status by using baseline and follow-up surveys. The comparison of participants with repeatedly high frequency breakfast with those with repeatedly low frequency can provide a better estimate of dietary status because it is highly likely that these participants were truly high or truly low over long durations (Willett, 1998). Changes in exposure status over time are a mix of true variation and measurement error (Willett, 1998); thus, these estimates may not be reliable. Therefore, we decided not to present results of changes in exposure status over time and focused on consistent exposure status (i.e., the comparison of participants whose breakfast frequency is repeatedly high with those whose frequency is repeatedly low). A two-sided P value < 0.05 was considered statistically significant in all analyses. All analyses were performed using Stata version 12.1 (StataCorp, College Station, TX, USA).

3. Results

Table 1 shows the baseline characteristics of study participants according to their baseline frequency of breakfast consumption. Compared with participants who ate breakfast daily, those who skipped breakfast were characterized as younger, more likely to be unmarried, engaged in a low-ranking job position, and a current smoker. Mean values of dietary intake of total energy, carbohydrate, folate, magnesium, and zinc decreased with a less regular consumption of breakfast (P for trend <0.05).

Of the 716 participants without depressive symptoms at baseline, 112 participants (15.6%) were newly identified as having depressive symptoms at the follow-up survey three years later. The ORs of new-onset depressive symptoms according to the baseline frequency of the breakfast consumption are shown in Table 2. In an age-, sex-, and workplace-adjusted model (model 1), participants who had breakfast <1 times/week had higher depressive symptoms than those who ate breakfast daily at baseline. Further adjustment for other covariates (model 2) strengthened the association. The results were virtually unchanged after additional adjustment for the intake of depression-related nutrients (model 3). This finding remained statistically significant after further adjustment for baseline CES-D score (model 4). Participants who had breakfast <1 times/week had higher depressive symptoms than those who ate breakfast daily. The multivariable-adjusted ORs (95% CI) of developing depressive symptoms for those who had breakfast <1 times/week was 2.92 (1.37–6.22), compared with those who had breakfast daily (P for trend = 0.02) (model 4). Additionally, a high frequency of breakfast skipping at baseline was associated with a greater increase in CES-D scores from baseline to follow-up survey. In the multiple linear regression, the estimated mean difference of change in CES-D score for those who had breakfast <1 times/week was 1.69 higher compared with those who had breakfast daily ($P = 0.049$). The estimated regression coefficient of change in CES-D score (95% CI) for those who had breakfast <1 times/week versus those who had breakfast daily was 1.69 (0.01–3.36) (Table 3).

We found a statistically significant positive association between the repeated omission of breakfast and the development of depressive symptoms (supplemental Table 1). In the age-, sex-, and workplace-adjusted model (model 1), participants who maintained non-daily breakfast (i.e., ≤6 times/week) during the follow-up period had higher odds of developing depressive symptoms compared with those who maintained daily breakfast at both baseline and three years. Following further adjustment for other covariates (model 2), the association was strengthened. The results were virtually unchanged after the additional adjustment for intake of depression-related nutrients (model 3). Moreover, we confirmed a statistically significant positive association after further adjustment for baseline CES-D scores (model 4). The multivariable-adjusted ORs (95% CI) of developing depressive symptoms for those who maintained non-daily breakfast were 1.85 (1.02–3.37) compared with those who maintained daily breakfast. Similar associations were observed in sensitivity analysis using other cutoff points (i.e., breakfast consumption ≥5 times/week or <5 times/week), although the association was not statistically significant when a cutoff point (CES-D scale score of ≥16) was used in the definition of depressive symptoms, as shown in supplemental table 2. The multivariable-adjusted ORs (95% CI) of developing depressive symptoms for participants who had breakfast ≥5 times/week at both baseline and follow-up were 1.71 (0.86–3.39) compared with those who had breakfast less often (<5 times/week) at both surveys.

4. Discussion

In this prospective analysis, we found that the omission of breakfast is related to an increased risk of depressive symptoms in a Japanese employee population, even after controlling for a wide range of dietary and lifestyle factors. The present study is one of only a few prospective studies addressing the longitudinal association between the frequency of breakfast and depressive symptoms.

To date, the majority of cross-sectional studies (Smith, 1998, 1999; Allgower et al., 2001; Smith, 2003; Fulkerson et al., 2004; Gollub and Weddle, 2004; Ahadi et al., 2016; Tajik et al., 2016; Xu et al., 2016; Kwak and Kim, 2017; Lee, Han, et al., 2017; Lee, Park, et al., 2017), but not all (Kawada et al., 2009), have observed a positive relation between skipping breakfast and depressive symptoms. Cross-sectional data cannot differentiate whether the frequency of breakfast is a predictive

Table 1
Baseline characteristics of participants by categories of the frequency of breakfast consumption at baseline[a].

	Frequency of breakfast consumption at baseline daily	5–6 times/week	3–4 times/week	1–2 times/week	<1 time/week	*P*-trend[a]
Number of participants	520	79	19	37	61	
Age (mean ± s.d., year)	43.5 ± 8.9	38.0 ± 8.6	39.2 ± 8.0	40.1 ± 9.4	38.2 ± 8.5	<0.001
Sex (women, %)	14.2	11.4	15.8	16.2	3.3	0.07
Site (survey in April 2012, %)	59.6	57.0	36.8	64.9	54.1	0.43
Marital status (married, %)	77.3	44.3	84.2	70.3	47.5	<0.001
Job grade (low, %)	59.8	82.3	57.9	67.6	70.5	0.04
Overtime work (≥30 hours/month, %)	25.2	31.7	21.1	29.7	27.9	0.50
Job strain (mean ± s.d.)	0.45 ± 0.10	0.45 ± 0.10	0.46 ± 0.10	0.46 ± 0.10	0.44 ± 0.07	0.91
Physical activity at work and housework or on commuting to work (≥20 METs-hours/day, %)	10.0	10.1	5.3	16.2	14.8	0.18
Leisure-time physical activity (≥10 METs-hours/week, %)	31.5	31.7	42.1	29.7	24.6	0.41
Smoking status (current, %)	21.4	16.5	26.3	37.8	47.5	<0.001
Alcohol drinking (current[b], %)	55.6	45.6	68.4	56.8	44.3	0.21
Sleep duration (<6 hours/day, %)	33.3	41.8	36.8	40.5	27.9	0.93
BMI (mean ± s.d., kg/m^2)	22.9 ± 3.0	22.4 ± 3.2	23.4 ± 3.7	22.7 ± 3.3	22.8 ± 3.1	0.75
CES-D score (mean ± s.d)	7.9 ± 4.0	8.9 ± 4.3	8.1 ± 3.2	8.4 ± 4.6	8.5 ± 3.8	0.13
Daily dietary intake (mean ± s.d., per day)						
Total energy (kcal)	1827 ± 470	1724 ± 410	1849 ± 334	1477 ± 440	1563 ± 509	<0.001
Carbohydrate (% energy)	54.5 ± 7.4	54.9 ± 7.9	51.6 ± 9.3	51.9 ± 7.4	53.2 ± 9.4	0.03
Fat (% energy)	24.3 ± 5.3	24.9 ± 5.1	25.4 ± 4.8	24.7 ± 5.8	24.7 ± 6.0	0.37
Protein (% energy)	14.0 ± 2.4	13.9 ± 2.1	13.6 ± 2.2	13.7 ± 2.2	13.5 ± 2.6	0.14
Folate (µg/1000 kcal)	176 ± 59	162 ± 46	152 ± 39	162 ± 49	160 ± 67	0.006
Vitamin B6 (mg/1000 kcal)	0.63 ± 0.14	0.60 ± 0.11	0.62 ± 0.14	0.63 ± 0.15	0.60 ± 0.15	0.24
Vitamin B12 (µg/1000 kcal)	4.4 ± 2.0	4.4 ± 1.8	4.6 ± 1.6	4.1 ± 1.6	4.3 ± 2.0	0.67
N-3 polyunsaturated fatty acids (% energy)	1.18 ± 0.29	1.18 ± 0.32	1.21 ± 0.23	1.19 ± 0.31	1.21 ± 0.34	0.41
Magnesium (mg/1000 kcal)	130 ± 24	124 ± 21	125 ± 24	126 ± 19	123 ± 28	0.010
Zinc (mg/1000 kcal)	4.2 ± 0.6	4.3 ± 0.6	4.1 ± 0.6	4.0 ± 0.5	4.1 ± 0.7	0.040

Abbreviations: s.d., standard deviation, BMI, body mass index; METs; Metabolic Equivalents.

[a] On the basis of the Mantel–Haenszel χ^2 test for categorical variables and linear regression analysis for continuous variables, assigning ordinal numbers 1–5 to categories of the frequency of breakfast consumption.

[b] Alcohol consumption of at least one day per week.

Table 2
Odds ratios and 95% confidence intervals for depressive symptoms according to categories of the frequency of breakfast consumption at baseline[a].

	Frequency of breakfast consumption at baseline daily	5–6 times/week	3–4 times/week	1–2 times/week	<1 time/week	P for trend[a]
CES-D (15/16)						
Participants with/without depressive symptoms	70/450	17/62	4/15	4/33	17/44	
Model 1[b]	1.00 (ref)	1.57 (0.85–2.88)	1.50 (0.48–4.72)	0.74 (0.25–2.17)	2.16 (1.15–4.05)	0.053
Model 2[c]	1.00 (ref)	1.88 (0.98–3.60)	1.49 (0.44–5.04)	0.76 (0.24–2.39)	2.56 (1.26–5.19)	0.03
Model 3[d]	1.00 (ref)	2.03 (1.04–3.97)	1.57 (0.45–5.50)	0.87 (0.27–2.79)	2.74 (1.32–5.68)	0.019
Model 4[e]	1.00 (ref)	1.67 (0.82–3.40)	1.54 (0.39–6.05)	0.76 (0.22–2.61)	2.92 (1.37–6.22)	0.02
CES-D (18/19)						
Participants with/without depressive symptoms	41/479	9/70	4/15	3/34	12/49	
Model 1[b]	1.00 (ref)	1.25 (0.57–2.75)	2.69 (0.84–8.63)	0.95 (0.28–3.26)	2.31 (1.11–4.78)	0.03
Model 2[c]	1.00 (ref)	1.37 (0.59–3.18)	2.24 (0.64–7.80)	1.06 (0.28–3.95)	2.68 (1.17- 6.13)	0.03
Model 3[d]	1.00 (ref)	1.44 (0.60–3.42)	2.51 (0.68–9.28)	1.37 (0.36–5.23)	2.99 (1.27–7.05)	0.011
Model 4[e]	1.00 (ref)	1.04 (0.41- 2.59)	2.66 (0.63–11.19)	1.20 (0.29–4.96)	2.84 (1.17–6.91)	0.02

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; ref, reference.

[a] Based on multiple logistic regression analyses, assigning ordinal numbers of 1–5 to the categories of the frequency of breakfast consumption at baseline.

[b] Adjusted for age (year, continuous), sex, and works (survey in April 2012 or in May 2013).

[c] Adjusted for age (year, continuous), sex, works (survey in April 2012 or in May 2013), marital status (married or other), job grade (low, middle, or high), overtime work (<10 h/month, 10 to <30 h/month, or ≥30 h/month), job strain (quartile), physical activity at work and housework or in commuting to work (<3 METs-h/day, 3 to <7 METs-h/day, 7 to <20 METs-h/day, or ≥20 METs-h/day), leisure-time physical activity (not engaged, > 0 to <3 METs-h/week, 3 to <10 METs-h/week, or ≥10 METs-h/week), smoking (never-smoker, quitter, current smoker consuming <20 cigarettes/day, or current smoker consuming ≥20 cigarettes/day), alcohol drinking (nondrinker, drinker consuming 1–3 days/month, weekly drinker consuming <1 *go*/day, 1 to <2 *go*/day, or ≥2 *go*/day; one *go* contains approximately 23 g of ethanol), sleep duration (<6 h/day, 6 to 6.9 h/day, or ≥7 h/day), body mass index (kg/m^2, continuous), and total energy intake (kcal/day, continuous).

[d] Model 3 additionally adjusted for intake of carbohydrate (% energy, continuous), fat (% energy, continuous), protein (% energy, continuous), folate (µg/1000 kcal, continuous), vitamin B6 (mg/1000 kcal, continuous), vitamin B12 (µg /1000 kcal, continuous), *n*-3 polyunsaturated fatty acids (% energy, continuous), magnesium (mg/1000 kcal, continuous), and zinc (mg/1000 kcal, continuous).

[e] Model 3 + CES-D score at baseline (continuous) were further adjusted for.

factor or a consequence of depression, which underscores the need to investigate the relation between the frequency of breakfast and depressive status using prospective data. Yet few prior studies have prospectively investigated the association between them. A one-year prospective follow-up study among Japanese workers observed that irregular breakfast (<3 days/week) was a significant predictor of major depression in the following year compared with a more regular breakfast (≥3 days/week breakfast) (Nakao and Yano, 2006). Another

Table 3
Multiple linear regression model showing association between breakfast consumption at baseline and change in CES-D score[a].

	Regression coefficient[c]	95% confidence intervals	*P* value[b]
Baseline breakfast: daily	reference		
Baseline breakfast: 5–6 times/week	0.18	−1.28, 1.64	0.81
Baseline breakfast: 3–4 times/week	0.45	−2.27, 3.18	0.75
Baseline breakfast : 1–2 times/week	−0.57	−2.61, 1.48	0.59
Baseline breakfast: <1 time/week	1.69	0.01, 3.36	0.049

Abbreviation: CES-D, Center for Epidemiologic Studies Depression Scale.
[a] Change in CES-D score was calculated by subtracting CES-D score at baseline from the score at the follow-up survey.
[b] Based on multiple linear regression analysis.
[c] Adjusted for age (year, continuous), sex, and works (survey in April 2012 or in May 2013), marital status (married or other), job grade (low, middle, or high), overtime work (<10 h/month, 10 to <30 h/month, or ≥30 h/month), job strain (quartile), physical activity at work and housework or in commuting to work (< 3 METs-h/day, 3 to < 7 METs-h/day, 7 to < 20 METs-h/day, or ≥ 20 METs-h/day), leisure-time physical activity (not engaged, > 0 to <3 METs-h/week, 3 to <10 METs-h/week, or ≥10 METs-h/week), smoking (never-smoker, quitter, current smoker consuming <20 cigarettes/day, or current smoker consuming ≥20 cigarettes/day), alcohol drinking (nondrinker, drinker consuming 1–3 days/month, weekly drinker consuming <1 *go*/day, 1 to <2 *go*/day, or ≥2 *go*/day; one *go* contains approximately 23 g of ethanol), sleep duration (< 6 h/day, 6 to 6.9 h/day, or ≥ 7 h/day), body mass index (kg/m^2, continuous), total energy intake (kcal/day, continuous) and dietary intake of carbohydrate (% energy, continuous), fat (% energy, continuous), protein (% energy, continuous), folate (µg/1000 kcal, continuous), vitamin B6 (mg/1000 kcal, continuous), vitamin B12 (µg /1000 kcal, continuous), *n*-3 polyunsaturated fatty acids (% energy, continuous), magnesium (mg/1000 kcal, continuous), and zinc (mg/1000 kcal, continuous).

small prospective study failed to find a significant association between the frequency of breakfast and depressive status (Huang et al., 2017). The present prospective study, which adjusted for a wide range of dietary and non-dietary potential confounders, confirmed the protective role of breakfast consumption against depressive symptoms by using baseline and the repeated assessment of breakfast consumption over time.

Although skipping breakfast has been linked to nutrient inadequacies (Tietyen and Fleming, 1995; Gollub and Weddle, 2004), most prior studies on this issue have not investigated the potential role of nutritional factors as major mediators between breakfast intake and depressive status (Allgower et al., 2001; Fulkerson et al., 2004; Gollub and Weddle, 2004; Nakao and Yano, 2006; Kawada et al., 2009; Ahadi et al., 2016; Xu et al., 2016; Kwak and Kim, 2017; Lee, Han, et al., 2017; Lee, Park, et al., 2017). We observed that the mean dietary intake of carbohydrate, folate, magnesium, and zinc (nutrients that have been suggested to decrease depressive symptoms; (Gilbody et al., 2007; Oishi et al., 2009; Li, Lv, et al., 2017; Li, Li, et al., 2017)) was lower for those who skipped breakfast than for those who ate breakfast regularly (P for trend < 0.05). However, the observed association between skipping breakfast and depressive risk did not materially change after further adjustment for macronutrients and micronutrients that were linked to mood (Woo et al., 2006; Gilbody et al., 2007; Sanchez-Villegas et al., 2007; Oishi et al., 2009; Skarupski et al., 2010; Wolfe et al., 2011; Li, Lv, et al., 2017; Li, Li, et al., 2017), suggesting that the relation was not entirely mediated through nutritional factors. In addition, we further explored the possibility that the association with breakfast consumption could be confounded by other health-related behaviors, but we still observed a significant relation between the frequency of breakfast intake and the risk of depressive symptoms after adjusting for various lifestyle confounders. Therefore, skipping breakfast may be related with increased risk of depressive symptoms, independently of other dietary and non-dietary factors.

The mechanism linking breakfast consumption to depressive symptoms is unclear, but several possibilities have been suggested. When the blood glucose concentration falls due to night-time fasting, adrenalin and cortisol are released (Fishbein and Pease, 1994). High cortisol was associated with an increase in inflammatory cytokines, which affects neurotransmitters (e.g., serotonin) (Miller et al., 2009), and also with the suppression of immunity functions (Segerstrom and Miller, 2004). After consuming breakfast, the level of cortisol steadily decreased and reset activity in the hypothalamic-pituitary-adrenal (HPA) axis, whereas skipping breakfast was associated with elevated cortisol levels and overactivity in the HPA axis (Witbracht et al., 2015), which have been linked to depression (Miller et al., 2009; Herbert, 2013). In fact, observational studies have reported that those who consume breakfast regularly have lower cortisol levels than those who rarely consume it (Smith, 2002), have a healthy immune system (Li et al., 2007), and tend to be relaxed rather than tense or anxious (Rice and Duncan, 1985). The association between breakfast consumption and depressive symptoms can also be ascribed to the effect of meal timing on the peripheral circadian clock system (Kagawa, 2012). Evidence suggests that circadian rhythm disruptions are implicated in the underlying pathophysiology of depression (Boyce and Barriball, 2010), and peripheral clock genes in the liver and intestine are reset by breakfast (Kagawa, 2012).

The strengths of this study are its prospective design, the use of validated methodologies to assess nutrient intake (i.e., the BDHQ) and depressive symptoms (i.e., CES-D score), and the consideration of various dietary and lifestyle factors. Some limitations warrant mentioning. First, the large loss to follow-up (36% did not participate in the follow-up questionnaire) may have introduced selection bias. However, such bias may be unlikely because the baseline characteristics including breakfast frequency and CES-D score did not materially differ according to their participation status at follow-up survey (Supplemental Table 3). The reason for the decreased participation in the follow-up survey was mainly due to the downsizing of the factories and relocation of workers to other sites after the 2011 great earthquake in East Japan. Second, we assessed depressive symptoms at baseline and at a three-year follow-up survey, but we did not assess them during the follow-up. The status of depressive symptoms during the follow-up period might have influenced the association of breakfast frequency with the subsequent development of depressive symptoms, which cannot be captured with the use of assessment at baseline and three years later during the follow-up survey. Third, breakfast consumption assessed at baseline might not accurately represent a long-term habitual diet. However, we confirmed the relation with baseline breakfast consumption by showing that participants who did not maintain a daily breakfast routine over time had higher odds of depressive symptoms than those who maintained a daily breakfast routine through the use of repeated assessments of breakfast consumption during the follow-up period. Fourth, a good quality breakfast has been associated with depression (Ferrer-Cascales et al., 2018); thus, it was worth investigating breakfast contents or quality, but the present study lacked these data. Fifth, despite the adjustment for numerous potential confounders, we cannot rule out the possibility that the observed associations are due to unmeasured confounders and residual confounding. Finally, because the present study was conducted among workers in a Japanese manufacturing company, caution is required when generalizing the findings.

In conclusion, this prospective study suggests that skipping breakfast was related to an increased risk of depressive symptoms in a Japanese population. This association remained even after controlling for several dietary and lifestyle factors. The observed association requires confirmation in long-term prospective studies.

Authors' contributions

T. Mizoue and A.N. designed the research. T. Miki, M.E., K. Kuwahara, T.K., S.A., I. Kashino, H.H., K. Kurotani, I. Kabe, A.N., and T. Mizoue conducted the research. T. Miki performed statistical analysis, wrote the manuscript, and had primary responsibility for the final content. All authors were involved in the revision process and approved the final version of the manuscript.

Conflict of interest

The authors declare no conflicts of interest. M.E., T.K., and I. Kabe are health professionals employed by the Furukawa Electric Corporation.

Acknowledgments

We thank Fumiko Zaizen, Rie Ito, Hiroko Tsuruoka, and Akiko Makabe (Furukawa Electric Corporation) as well as Ayami Kume, Sachiko Nishihara, Yuho Mizoue, Saeko Takagiwa, Maki Konishi, Rika Osawa, and Yuriko Yagi (National Center for Global Health and Medicine) for their help with the data collection.

This study was supported by the Grant-in-Aid for Japan Society for the Promotion of Science (JSPS) Fellows Number 17J00166, JSPS KAKENHI Grant Numbers 25293146, 25702006, Practical Research Project for Life-Style related Diseases including Cardiovascular Diseases and Diabetes Mellitus (15ek0210021h0002) from the Japan Agency for Medical Research and Development, and the Industrial Health Foundation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.01.069.

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