Determining whether periodic health checkups have any preventive effect on deterioration in health among middle-aged adults: A hazards model analysis in Japan

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Abstract
Objectives: We aimed to examine the long-term impact of periodic health checkups (PHCs) on health outcomes among middle-aged adults.
Methods: We used longitudinal data from 29,770 individuals (15,399 men and 14,371 women) aged 50–59 years in the baseline year (2005), obtained from a population-based 14-wave survey. PHC participants were defined as those who underwent PHCs for the first three consecutive waves, and we investigated the onset of inpatient care for five types of non-communicable diseases (diabetes, heart disease, stroke, hypertension, and dyslipidemia) as well as poor self-rated health and problems in the activities of daily living in the subsequent 11 waves. Cox-proportional hazards models were used to estimate the impact of PHCs on health outcomes by employing the propensity score matching (PSM) method.
Results: Participation in PHCs was closely related to a respondent’s socio-economic status and health behavior. After controlling for these factors by PSM, the hazard models showed that PHCs postponed the onset of inpatient care for hypertension (hazard ratio, 0.56; 95% confidence interval: 0.36–0.85) among men, but PHCs had no impact on any other health outcomes in men or women.
Conclusions: The preventive impact of PHCs on health deterioration is generally limited among middle-aged adults. Future studies should address policy measures to enhance the effectiveness of PHCs.

KEYWORDS
activities of daily living, Cox-proportional hazard model, non-communicable disease, periodic health checkups, propensity score matching, self-rated health

1 | INTRODUCTION

Periodic health checkups (PHCs), or periodic/annual medical examinations, have been a fundamental part of public health policy for decades. PHCs aim to detect the presence of diseases and the risk factors for diseases with the purpose of reducing morbidity and mortality.1 Notably, workplace PHCs have been considered a key element for occupational health and workers’ well-being. However, the preventive effect of PHCs on health deterioration remains controversial. With regard to its impact on mortality, longitudinal studies have shown that participation in
PHCs is associated with a lower mortality rate,\textsuperscript{2–4} whereas other studies have been skeptical of such benefit.\textsuperscript{5,6} Recent systematic surveys, which focused on randomized controlled trials, concluded that PHCs tended to have little or no effect on the risk of mortality,\textsuperscript{7} which contrasts with the findings of previous review articles that demonstrated a beneficial effect of PHCs on the dispensation of subsequent medical care and more general health outcomes.\textsuperscript{7,8}

A challenging issue in examining the impact of PHCs on health outcomes is the endogeneity or self-selection of participation in PHCs. Previous studies have shown that the likelihood of participation in PHCs is associated with many factors, including an individual’s socioeconomic status (SES),\textsuperscript{9,10} health literacy,\textsuperscript{11} and lifestyle\textsuperscript{12} in addition to sex, age, and other sociodemographic factors. Without controlling for these factors, the estimation results cannot be used to assess the effects of PHCs.

This endogenous issue should be addressed explicitly, especially in Japan. The Japanese Industrial Safety and Health Act obliges each firm, regardless of its size, to provide PHCs to its employees;\textsuperscript{13} non-regular employees are often exempted from this practice. Meanwhile, self-employed workers, family workers, and dependent spouses of employees are encouraged to participate in PHCs provided by the municipalities, but their participation is voluntary. Accordingly, regular full-time employees are more likely to participate in PHCs than are precarious employees and other individuals.\textsuperscript{14,15} Occupational status is closely related to other SES factors, such as educational attainment and income, and is also associated with lifestyle and health behavior such as smoking, alcohol consumption, and physical activity.\textsuperscript{16–18} Hence, participation in PHCs may serve as a proxy for an individual’s SES and its related factors. If this is the case, any observed correlation between PHCs and health may be substantially confounded by them.

In this study, we aimed to examine the impact of PHCs on health outcomes among middle-aged individuals using a population-based, fourteen-wave survey conducted in Japan. This study is expected to provide new insights into the relevance of PHCs in two ways.

First, it focused on whether, and the extent to which, PHCs would delay the onset of inpatient care for non-communicable diseases (NCDs), unlike most previous studies that focused on the mortality rate, which likely matters later in life. Middle-aged adults are likely to be exposed to increasing risks of NCDs,\textsuperscript{19} which may lead to disparities in health in older adults. One previous study examined the association between PHCs and the risk of NCDs, but it was a cross-sectional study targeting adults with disabilities.\textsuperscript{20} We further considered the impact of PHCs on self-rated health (SRH), which represents general health conditions\textsuperscript{21,22} and activities of daily living (ADL), thus affecting the health-related quality of life.\textsuperscript{23} We examined whether, and to what extent, participation in PHCs would postpone the onset of poor SRH and ADL problems.

Second, this study explicitly assessed how the endogeneity of PHCs influences the evaluation of their effectiveness. Because it is difficult to conduct randomized controlled trials, two approaches were applied to address this issue. First, we controlled for potential confounders when estimating the Cox-proportional hazards model. Second, we applied the propensity score matching (PSM) method to these hazard models, regressing on the sample matched sets of PHC participants and non-participants who had similar propensity scores.\textsuperscript{24} We compared the estimation results with those of two previous studies\textsuperscript{3,4} that used PSM methods to examine the impact of PHCs in different data settings.

In these statistical analyses, we aimed to evaluate the experience of successive participation in PHCs over the first three waves to obtain a more reliable estimate of the impact of participation in PHCs on health outcomes.

2 | METHODS

2.1 | Study sample

In this study, we used data obtained from a nationwide fourteen-wave panel survey, “The Longitudinal Survey of Middle-aged and Elderly Persons,”\textsuperscript{25} conducted by the Japanese Ministry of Health, Labour and Welfare (MHLW) every year from 2005 to 2016. Japan’s Statistics Law required the survey to be reviewed from statistical, legal, ethical, and other viewpoints. We obtained survey data from the MHLW with its official permission; therefore, the current study did not require ethical approval.

The first wave of the survey was conducted among individuals aged 50–59 years (born between 1946 and 1955). A total of 34,240 individuals responded (response rate: 83.8%). The second to 14th waves of the survey were conducted each year from 2006 to 2018, and 20,677 individuals were retained in the fourteenth wave of the survey.

2.2 | Inclusion and exclusion criteria

We focused on the respondents who remained at least until the third wave, in order to know their experience in PHC participation over the first three waves. Then, we removed respondents who had already started receiving inpatient care in the first three waves for each NCD, because we could not identify the timing of the onset of inpatient care. For poor SRH and ADL problems, we similarly removed respondents who had already received inpatient care at least once in the first three waves.
In total, the longitudinal data of 29,770 respondents (15,399 men and 14,371 women) were used in this study. The number of respondents used in statistical analysis for each health outcome ranged from 15,467 (dyslipidemia) to 29,369 (ADL problems) (see Table 2 for more detail). We divided respondents into two groups: PHC participants (who participated in PHCs successively over the first three waves) and non-participants (others).

### 2.3 Periodic health checkups

During the survey, the respondents were asked whether they had participated in PHCs—including the “Ningen Dock” (the comprehensive health checkup system)—in the previous year. We constructed a binary variable for PHCs by allocating 1 to respondents who participated in PHCs successively over the first three waves (2005–2007) and 0 to others.

### 2.4 Health outcomes

We considered the onset of inpatient care for five types of NCDs (diabetes, heart disease, stroke, hypertension, and dyslipidemia) as well as SRH and ADL. We focused on the onset of inpatient care rather than the initial diagnosis or onset of outpatient care, despite the availability of both data in the survey. This is because the initial diagnosis and the onset of outpatient care may represent detection of illness or the start of medical intervention induced by the reported PHC results rather than their health outcomes. We defined the timing of the onset of inpatient care as the wave in which the respondents answered at the first time in the survey that they had an experience of hospitalization over the past one year. Thus, the onset of inpatient care in this study was based on the respondents’ self-report. Regarding SRH, the respondents were asked to rate their current health condition as follows: 1 (very good), 2 (good), 3 (somewhat good), 4 (somewhat poor), 5 (poor), or 6 (very poor). We constructed a binary variable for poor SRH by allocating 1 to those who chose 4–6 and 0 to the rest of the respondents. We also constructed a binary variable for ADL problems by allocating 1 to those who answered that they needed assistance in at least one of the 10 ADLs (such as walking, getting in and out of bed, and getting into and out of a chair).

### 2.5 Potential confounders

As potential confounders, we considered (i) educational attainment, household spending, and occupational status as SES factors; (ii) smoking, alcohol consumption, and no physical activity as health behavior; and (iii) age, all of which were evaluated in the third wave. For educational attainment, we constructed binary variables for graduating from junior high school, high school, junior college, college, or above. We also merged the respondents who graduated from other schools and those who did not respond to the questions in one group and constructed a binary variable for them. Household spending was adjusted for household size by dividing it by the square root of the number of household members. We categorized them into quartiles and constructed binary variables for each quartile. For respondents who did not answer questions about household spending, we allocated a binary variable to unanswered questions. For occupational status, we constructed binary variables for managers, regular employees, non-regular (or precarious) employees (such as part-time, temporary, and contract workers), others, and not working. Moreover, we constructed binary variables for smoking, alcohol consumption, and no physical activity by allocating 1 to respondents who answered that they were currently smoking, consuming alcohol almost every day, and not performing physical activity, respectively, and 0 to the rest of the respondents. Finally, we constructed binary variables for each age group in the third wave.

### 2.6 Descriptive analysis

For descriptive analysis, we compared SES and health behavior between PHC participants and non-participants, and then compared the prevalence of the onset of inpatient care for each NCD, poor SRH, and ADL problems in the third and fourteenth waves between the two groups.

### 2.7 Propensity score matching

For PSM, we initially computed the propensity scores by estimating the logistic regression model to explain the PHCs based on a respondent’s SES and health behavior. Then, we conducted simple nearest-neighbor matching with one neighbor without caliper. We matched each PHC participant with a non-participant whose propensity score was closest to that of the participant. Some non-participants may have had two or more matching participants, while others may have had no matches and were excluded from the analysis. We counted the number of matches for each non-participant and used it as the frequency weight in estimating Cox-proportional hazard model (Model 3), which will be explained below. We allocated one as a frequency weight to each PHC participant.
2.8 Cox-proportional hazard model analysis

In the regression analysis, we estimated three Cox-proportional hazards models (Models 1–3) to compute the hazard ratio (HR), with its corresponding 95% confidence interval (CI), for the onset of inpatient care for each NCD, poor SRH, and ADL problems in men and women. We defined the duration of follow-up as the length between the third and follow-up waves; for example, the fifth wave corresponded to the duration of two years.

Model 1 estimated the HR for each health outcome, adjusted only for baseline age. Model 2 additionally controlled for SES and health behavior. Model 3 replaced the original sample with the sample matched by PSM using the number of matches as the frequency weight, in addition to controlling for baseline age, SES factors, and health behavior. In this model, we also estimated the robust variances that accounted for clustering within the matched sets.27 The Stata software package (Release 17) was used for all statistical analyses.

We conducted two supplementary analyses. First, we examined how the results depended on the definition of PHC participation. To this end, we redefined PHC participants as those who underwent health checkups at least once over the first three waves and checked the robustness of the estimation results. Second, in addition to separate analyses for men and women, we directly examined sex differences using the entire sample. Specifically, we included a binary variable for women and its interaction term with PHC in regression models and examined their statistical significance.

| PHC participants | Non-participants | All |
|------------------|------------------|-----|
| Sex              |                  |     |
| Men              | 8907 (62.0%)     | 5464 (38.0%) | 14371 (100%) |
| Women            | 7720 (50.1%)     | 7679 (49.9%) | 15399 (100%) |
| Occupational status |              |     |
| Manager          | 939 (63.8%)      | 532 (36.2%) | 1471 (100%) |
| Regular employee | 7302 (78.6%)     | 1993 (21.4%) | 9295 (100%) |
| Non-regular employee | 3640 (56.1%) | 2843 (43.9%) | 6483 (100%) |
| Self-employed    | 1326 (36.1%)     | 2349 (63.9%) | 3675 (100%) |
| Other            | 952 (40.5%)      | 1399 (59.5%) | 2351 (100%) |
| Not working      | 2468 (38.0%)     | 4027 (62.0%) | 6495 (100%) |
| Educational attainment |              |     |
| Junior high school | 2618 (47.1%) | 2935 (52.9%) | 5553 (100%) |
| High school      | 9549 (56.0%)     | 7498 (44.0%) | 17047 (100%) |
| Junior college   | 1196 (55.4%)     | 963 (44.6%) | 2159 (100%) |
| College or above | 3090 (66.5%)     | 1556 (33.5%) | 4646 (100%) |
| Other or unanswered | 174 (47.7%) | 191 (52.3%) | 365 (100%) |
| Household income |                  |     |
| 1st quartile     | 3111 (50.6%)     | 3200 (52.0%) | 6148 (100%) |
| 2nd quartile     | 3951 (57.8%)     | 2991 (43.8%) | 6836 (100%) |
| 3rd quartile     | 3714 (61.2%)     | 2432 (40.1%) | 6064 (100%) |
| 4th quartile     | 4492 (61.9%)     | 2857 (39.4%) | 7259 (100%) |
| Unanswered       | 1359 (49.5%)     | 1663 (50.5%) | 2743 (100%) |
| Health behavior  |                  |     |
| Smoking          | 4357 (53.4%)     | 3800 (46.6%) | 8157 (100%) |
| Alcohol consumption | 5371 (60.0%) | 3588 (40.0%) | 8959 (100%) |
| No physical activity | 15841 (56.1%) | 12374 (43.9%) | 28215 (100%) |
| Age at baseline (years) | $M$ 54.7 ($SD$ 2.7) | $M$ 54.7 ($SD$ 2.7) | $M$ 54.7 ($SD$ 2.7) |
| $N$              | 16627 (55.9%)    | 13143 (44.1%) | 29770 (100%) |
3 | RESULTS

3.1 | Descriptive analysis

Table 1 summarizes the key features of PHC participants and non-participants evaluated in the third wave, showing that 55.9% of the study sample were PHC participants. For each item in the category, we examined the presence of bias toward PHCs. Initially, we computed the proportions of PHC participants and non-participants for each category. As seen in this table, men, regular employees, higher educational attainment, and higher household spending tended to be associated with PHCs, while women, self-employed, not working, lower educational attainment, and lower household spending tended to be associated with no PHCs. None of the three types of unhealthy behavior had any bias.

Table 2 compares the onset of inpatient care for each NCD as well as poor SRH and ADL problems between PHC participants and non-participants in the fourth to fourteenth waves among men and women. We did not adjust for other factors and ignored the differences in the timing of events. In men, PHCs were negatively associated with the risks of diabetes, stroke, hypertension, poor SRH, and ADL problems and were positively (albeit p > .05) associated with dyslipidemia. In women, no association was observed except for the risk of problems in performing ADLs, which was negatively associated with PHCs.

3.2 | Propensity score matching

To explain the PHCs to compute the propensity scores, we estimated the logistic regression models. Table 3 summarizes the estimation results of the logistic regression models, showing that PHCs were negatively associated with occupational status other than regular employees, lower educational attainment, and lower household spending for both men and women. PHCs were also negatively associated with smoking in both men and women. The results in Table 3 suggest that a higher propensity score corresponded to higher SES and non-smoking status.

Figure 1 compares the histograms of the computed propensity scores between PHC participants and non-participants for both men and women. In men, the distribution of scores was substantially asymmetric between the two groups. The scores were remarkably clustered at

| Table 2 | Medical care experiences over the fourth and fourteenth waves by participants and non-participants in periodic health checkups over the first three waves |
|---|---|---|---|---|---|
| | All | PHC participants | Non-participants | Difference in proportion |
| | N | N | Onsets | Proportion (A) | N | Onsets | Proportion (B) | (B) − (A) | SE | p |
| Men | | | | | | | | | | |
| Diabetes | 8796 | 5963 | 175 | (2.9%) | 2833 | 108 | (3.8%) | 0.9% | (0.4%) | .029 |
| Heart disease | 8433 | 5741 | 276 | (4.8%) | 2692 | 137 | (5.1%) | 0.3% | (0.5%) | .577 |
| Stroke | 8241 | 5624 | 143 | (2.5%) | 2617 | 102 | (3.9%) | 1.4% | (0.4%) | <.001 |
| Hypertension | 8246 | 5622 | 179 | (3.2%) | 2624 | 109 | (4.2%) | 1.0% | (0.5%) | .023 |
| Dyslipidemia | 8091 | 5505 | 53 | (1.0%) | 2586 | 15 | (0.6%) | −0.4% | (0.2%) | .079 |
| Cancer | 7754 | 5245 | 437 | (8.3%) | 2509 | 168 | (6.7%) | −1.6% | (0.6%) | .012 |
| Poor SRHa | 12 161 | 7712 | 979 | (12.7%) | 4449 | 677 | (15.2%) | 2.5% | (0.7%) | <.001 |
| ADLb problems | 14 204 | 8846 | 265 | (3.0%) | 5358 | 201 | (3.8%) | 0.8% | (0.3%) | .014 |
| Women | | | | | | | | | | |
| Diabetes | 8183 | 4563 | 66 | (1.4%) | 3620 | 66 | (1.8%) | 0.4% | (0.3%) | .179 |
| Heart disease | 7849 | 4394 | 65 | (1.5%) | 3455 | 52 | (1.5%) | 0.0% | (0.3%) | .926 |
| Stroke | 7664 | 4297 | 60 | (1.4%) | 3367 | 48 | (1.4%) | 0.0% | (0.3%) | .914 |
| Hypertension | 7610 | 4266 | 96 | (2.3%) | 3344 | 81 | (2.4%) | 0.2% | (0.3%) | .622 |
| Dyslipidemia | 7376 | 4160 | 43 | (1.0%) | 3216 | 27 | (0.8%) | −0.2% | (0.2%) | .394 |
| Cancer | 7028 | 3941 | 231 | (5.9%) | 3087 | 175 | (5.7%) | −0.2% | (0.6%) | .731 |
| Poor SRH | 13 226 | 6770 | 840 | (12.4%) | 6456 | 833 | (12.9%) | 0.5% | (0.6%) | .392 |
| ADL problems | 15 165 | 7635 | 316 | (4.1%) | 7530 | 368 | (4.9%) | 0.7% | (0.3%) | .026 |

aSelf-rated health.

bActivities of daily living.
TABLE 3 Estimation results of logistic regression models to explain the successive participation in periodic health checkups over the first three waves

| Occupational status          | Men HR (95% CI) | Women HR (95% CI) |
|------------------------------|-----------------|-------------------|
| Regular employee             | 1               | 1                 |
| Manager                      | 0.48* (0.42, 0.55) | 0.30* (0.23, 0.38) |
| Non-regular employee         | 0.37* (0.33, 0.42) | 0.37* (0.33, 0.41) |
| Self-employed                | 0.15* (0.14, 0.17) | 0.17* (0.14, 0.20) |
| Other job                    | 0.22* (0.18, 0.27) | 0.19* (0.16, 0.22) |
| Not working                  | 0.17* (0.15, 0.20) | 0.17* (0.15, 0.19) |

| Educational attainment       | Men HR (95% CI) | Women HR (95% CI) |
|------------------------------|-----------------|-------------------|
| College or above             | 1               | 1                 |
| Junior high school           | 0.62* (0.55, 0.70) | 0.73* (0.62, 0.85) |
| High school                  | 0.91*** (0.83, 1.00) | 0.84*** (0.73, 0.97) |
| Junior college               | 0.93 (0.72, 1.20) | 0.92 (0.78, 1.08)  |
| Other                        | 0.75 (0.55, 1.03) | 0.60** (0.42, 0.85) |

| Household spending           | Men HR (95% CI) | Women HR (95% CI) |
|------------------------------|-----------------|-------------------|
| 4th quartile [highest]       | 1               | 1                 |
| 1st quartile                 | 0.65* (0.58, 0.73) | 0.82* (0.74, 0.90) |
| 2nd quartile                 | 0.80* (0.72, 0.90) | 0.96 (0.87, 1.06)  |
| 3rd quartile                 | 0.93 (0.83, 1.04) | 0.99 (0.90, 1.10)  |
| Unanswered                   | 0.59* (0.51, 0.68) | 0.68* (0.60, 0.77) |

| Health behavior              | Men HR (95% CI) | Women HR (95% CI) |
|------------------------------|-----------------|-------------------|
| Smoking                      | 0.73* (0.68, 0.79) | 0.60* (0.54, 0.67) |
| Alcoholic consumption        | 1.06 (0.98, 1.14) | 0.90*** (0.81, 1.00) |
| No physical activity         | 1.27** (1.06, 1.51) | 0.99 (0.86, 1.14)  |
| 14 371                       | 15 399          |

Abbreviations: CI, confidence interval; HR, hazard ratio.

*Controlled for age at baseline.

*p < .05; **p < .01; ***p < .001.

the higher end of the scale among the PHC participants, whereas the distribution was flatter among the non-participants. The scores were distributed more symmetrically between the two groups in women.

3.3 Cox-proportional hazard model analysis

Then, we estimated three types of Cox-proportional hazards models for each health outcome. As an illustrative example, Table 4 compares the results of the three models for the onset of inpatient care for diabetes in men. Model 1, which was adjusted only for age, indicated the negative impact of PHCs (HR, 0.69, 95% CI: 0.54–0.88).

Model 2 found that PHCs had no impact on the risk of diabetes after controlling for SES and health behavior. Self-employment, not working, lower educational attainment, smoking, and, to a lesser extent, lower household spending were positively associated with the risk of diabetes. The result remained largely intact in Model 3, which used the propensity score-matched sample, and this model reported the non-significant impact of PHCs.

We repeated a similar regression for other health outcomes. Table 5 compares the estimated HRs for each outcome across the three models for both men and women. In men, Model 1 showed that PHCs were negatively associated with diabetes, stroke, hypertension, poor SRH, and ADL problems. However, PHCs were negatively related only to stroke and poor SRH in Model 2. Using the PSM method, Model 3 showed that PHCs reduced only the risk of hypertension (HR: 0.56; 95% CI: 0.36–0.85). In women, no impact of PHCs was observed. Model 1 indicated the preventive impact of PHCs on poor SRH and ADL problems, but no association was observed in any other combination of the model and health outcomes.

To check the robustness of the estimation results, we examined how the results would change if we redefined PHC participants as those who underwent health check-ups at least once over the first three waves. Table S1 in the Supporting Information summarizes the key results, which remained generally intact from those in Table 5, except that PHCs had a preventive impact on dyslipidemia and hypertension in men in Model 3.

Finally, we examined sex differences using the entire sample. Table S2 in the Supporting Information shows the estimated HRs of PHC, women, and their interaction in each model for each health outcome. Of the seven health outcomes, the HR of women was below one in Models 1 and 2, indicating lower risks of poor health, but this effect disappeared in Model 3, except for heart disease. The HR of the interaction term between women and PHC was non-significant in most model specifications, suggesting no substantial sex differences in the sensitivity of health outcomes to PHC.

4 DISCUSSION

In this study, we examined the long-term impact of PHCs on health outcomes among middle-aged adults. To the best of our knowledge, this is the only study to investigate the preventive impact of PHCs on the onset of inpatient care for NCDs among middle-aged adults.

Based on these observations, we can argue that the benefits of PHCs are generally limited in terms of their preventive impact on the risk of NCDs, deterioration in general health conditions or health-related quality of life.
Before controlling for SES and health behavior, PHCs were found to postpone the onset of three types of NCDs (diabetes, heart disease, and hypertension) in men; PHCs were also found to reduce the risk of deterioration in SRH and ADL for both men and women. However, these associations largely disappeared, except for hypertension in men, after controlling for SES and health behavior, or using the PSM method.

These observations were largely consistent with the general results of a recent research survey, \(^{1,28}\) that reviewed randomized controlled trials and provided a negative view of the beneficial effects of PHCs on health. The limited benefits of PHCs can be largely explained by the fact that participation in PHCs is closely associated with an individual’s SES, as reported in previous studies.\(^{8,9,13}\) As indicated in Table 2, regular employees and individuals with higher SES (i.e., higher educational attainment and housing spending) were more likely to participate in PHCs for both men and women, resulting in higher propensity scores in terms of PHC participation. Moreover, the finding that participation in PHCs did not affect health outcomes after controlling for SES may suggest that PHCs did not mediate the impact of SES on health outcomes.

We also noticed asymmetric results between men and women. The preventive impact of PHCs was not observed for any NCD in women, even before controlling for SES in Model 1, unlike in men. As illustrated in Figure 1, the propensity scores were more symmetrically distributed between PHC participants and non-participants in women than in men. This finding suggests that participation in PHCs was more independent of SES in women than in men. For example, married women with higher educational attainment or higher household income often work as part-time employees or a full-time homemaker, which may reduce their chances of participating in PHCs. Hence, health outcomes were not significantly correlated with PHCs even before controlling for SES, underscoring the limited benefit of PHCs in women compared with men. However, the results of the supplementary analysis suggested that differences in the sensitivity of health outcomes to PHCs between men and women are generally limited.

These results, which are largely not in favor of the benefit of PHCs, were not consistent with the observation in a previous study in Japan,\(^{5}\) which reported that the PHC participants had lower mortality rates using the PSM method. This study used a sample of the Japanese National Health Insurance beneficiaries, consisting of self-employed workers, farmers, pensioners, and their dependents in one local municipality, focusing on the effect of their one-time participation in municipality-managed PHCs in 1995. Hence, it is difficult to compare the results,
which may significantly depend on the heterogeneity of the sample. Another previous study, which used French data, observed a lower mortality rate in PHC participants. When the PSM method was applied, however, this study observed a favorable impact of PHCs only in men and found that the impact became more limited, even in men. These findings are largely in line with our results.

This study had several limitations. First, we should be cautious about the reliability of self-reported information about health outcomes and participation in PHCs obtained from the survey. We focused on the onset of inpatient care rather than the initial diagnosis and the onset of outpatient care, the latter two of which may represent detection of illness or a start of medical intervention induced by the reported PHC. However, we cannot exclude the possibility that the detection of illness by PHC may lead to inpatient care, especially in the case of hyperlipidemia, hypertension, and diabetes. Although the findings in this study were not indicative of any clear causation from PHC to the onset of inpatient care, more detailed medical information is needed to identify their association more precisely. Second, randomized controlled trials should be conducted to precisely identify the preventive effects of SES. Although we controlled for SES and health behavior and used the PSM method, the estimation results may have been affected by the choice of SES variables and specific PSM method. Third, we did not discuss the mechanisms linking PHC and health outcomes. It is theoretically reasonable to suspect that PHCs may enable the early detection of risk factors, early medical intervention, and/or favorable changes.

| TABLE 4 | Estimation results of Cox-proportional hazards models to explain the hazards of the onset of the inpatient care for diabetes for men (N = 8796) |
|---|---|---|
| **Model 1** | **Model 2** | **Model 3** |
| **HR (95% CI)** | **HR (95% CI)** | **HR (95% CI)** |
| PHCs | 0.69** (0.54, 0.88) | 0.93 (0.72, 1.20) | 1.25 (0.68, 2.27) |
| **Job status** | | | |
| Regular employee | 1 | 1 | |
| Manager | 0.97 (0.59, 1.61) | 1.14 (0.50, 2.60) | |
| Non-regular employee | 0.79 (0.51, 1.25) | 0.94 (0.42, 2.10) | |
| Self-employed | 1.74** (1.27, 2.38) | 2.40** (1.39, 4.15) | |
| Other job | 1.66 (0.87, 3.17) | 1.84 (0.82, 4.12) | |
| Not working | 1.57*** (1.06, 2.31) | 1.48 (0.75, 2.94) | |
| **Educational attainment** | | | |
| College or above | 1 | 1 | |
| Junior high school | 1.55*** (1.04, 2.31) | 1.39 (0.63, 3.06) | |
| High school | 1.42*** (1.05, 1.93) | 0.92 (0.43, 1.94) | |
| Junior college | 1.13 (0.52, 2.47) | 0.56 (0.17, 1.81) | |
| Other | 0.79 (0.19, 3.31) | 0.67 (0.14, 3.27) | |
| **Household income** | | | |
| 4th quartile [highest] | 1 | 1 | |
| 1st quartile | 1.39* (0.98, 1.98) | 2.03*** (1.14, 3.62) | |
| 2nd quartile | 1.11 (0.78, 1.57) | 1.34 (0.79, 2.28) | |
| 3rd quartile | 1.24 (0.87, 1.75) | 1.89 (0.84, 4.25) | |
| Unanswered | 1.52* (0.93, 2.47) | 1.32 (0.62, 2.82) | |
| **Health behavior** | | | |
| Smoking | 1.77* (1.39, 2.26) | 1.85** (1.20, 2.85) | |
| Alcoholic consumption | 0.60* (0.47, 0.76) | 0.52** (0.33, 0.80) | |
| No physical activity | 0.86 (0.46, 1.57) | 0.68 (0.33, 1.38) | |

Abbreviations: CI, confidence interval; HR, hazard ratio.

aControlled for age at baseline.
bControlled for socioeconomic status, health behavior, and age at baseline.
cAfter propensity score matching.
dPeriodic health checkups.

*p < .1
*p < .05; **p < .01; ***p < .001.
in health behavior, which in turn will improve health outcomes. It is also interesting to examine the determinants of seeking medical care among workers after receiving PHCs in the workplace.29–31 Fourth, more detailed information about the relevance of each item in PHCs may be necessary, which may likely differ by NCD type.

Despite these limitations, the results of this study suggest that caution should be exercised when arguing the favorable effect of PHCs on health outcomes. We should carefully control for differences in SES between PHC participants and non-participants to examine the preventive impact of PHCs.

However, this conclusion does not exclude the possibility of enhancing the effectiveness of PHCs as policy measures for health promotion. As regular employees are usually obliged to participate in PHCs, while other individuals are left to decide whether to participate in PHC or not, the rate of PHC participation may largely reflect the differences in SES between the two groups. We should consider policy measures to encourage precarious employees and individuals with lower SES to participate in PHCs, to offset any SES-related health disparity, which is likely to widen among middle-aged adults.

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**DISCLOSURE**

Approval of the research protocol: In this study, we used data obtained from a nationwide fourteen-wave panel survey, “The Longitudinal Survey of Middle-Aged and Elderly Persons,” conducted by the Japanese Ministry of Health, Labour and Welfare (MHLW) each year from 2005 to 2018. Japan’s Statistics Law required the survey to be reviewed from statistical, legal, ethical, and other viewpoints. We obtained survey data from the MHLW with official permission. Furthermore, this study was not subject to the Ethical Guidelines for Medical and Biological Research Involving Human Subjects (enacted as of March 23, 2013), because this study utilized the information obtained from the MHLW survey, which (1) has an already-established academic value and is widely used for academic purposes and is open to the public and (2) contains only anonymous information to avoid any identification of individuals. Therefore, ethical approval was not required in this study. Informed consent:

| TABLE 5 Estimated hazard ratios of periodic health checkups for the onset of each health outcome |

|          | Model 1<sup>a</sup> | Model 2<sup>b</sup> | Model 3<sup>b,c</sup> |
|----------|---------------------|---------------------|----------------------|
|          | HR (95% CI)         | HR (95% CI)         | HR (95% CI)          |
| **Men**  |                     |                     |                      |
| Diabetes | 0.69** (0.54, 0.88) | 0.93 (0.72, 1.20)   | 1.25 (0.68, 2.27)    |
| Heart disease | 0.84 (0.68, 1.02) | 0.94 (0.75, 1.18)   | 0.74 (0.47, 1.17)    |
| Stroke   | 0.59* (0.46, 0.77)  | 0.72** (0.53, 0.97) | 0.61 (0.36, 1.04)    |
| Hypertension | 0.69** (0.55, 0.88) | 0.80 (0.60, 1.05)  | 0.56** (0.36, 0.85)  |
| Dyslipidemia | 1.49 (0.84, 2.65) | 1.46 (0.80, 2.65)   | 0.89 (0.29, 2.70)    |
| Poor SRH<sup>d</sup> | 0.74 (0.68, 0.83) | 0.86** (0.78, 0.96) | 0.92 (0.74, 1.14)    |
| ADL<sup>e</sup> problems | 0.81*** (0.68, 0.97) | 1.02 (0.84, 1.25)  | 1.32 (0.93, 1.87)    |
| **Women**|                     |                     |                      |
| Diabetes | 0.73 (0.52, 1.03)   | 0.81 (0.58, 1.15)   | 0.86 (0.27, 2.68)    |
| Heart disease | 0.90 (0.62, 1.29) | 0.94 (0.64, 1.39)   | 1.76 (0.42, 7.33)    |
| Stroke   | 0.90 (0.62, 1.32)   | 1.00 (0.68, 1.49)   | 0.65 (0.20, 2.04)    |
| Hypertension | 0.86 (0.64, 1.15) | 1.01 (0.74, 1.37)   | 0.98 (0.28, 3.39)    |
| Dyslipidemia | 1.15 (0.71, 1.87) | 1.04 (0.62, 1.76)   | 0.67 (0.19, 2.27)    |
| Poor SRH<sup>d</sup> | 0.91*** (0.82, 1.00) | 0.96 (0.87, 1.06)  | 1.00 (0.74, 1.36)    |
| ADL<sup>e</sup> problems | 0.84*** (0.72, 0.98) | 0.97 (0.83, 1.13)  | 0.96 (0.62, 1.50)    |

Abbreviations: CI, confidence interval; HR, hazard ratio.

*Controlled for age at baseline.
*Controlled for socioeconomic status, health behavior, and age at baseline.
*After propensity score matching.
*Self-rated health.
*Activities of daily living

*<sup>p</sup> < .05; **<sup>p</sup> < .01; ***<sup>p</sup> < .001.
N/A. Registry and the registration no. of the study/trial: N/A. Animal studies: N/A. Conflict of interest: The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS
Takashi Oshio: Conceptualization (lead); writing—original draft (lead); formal analysis (lead); writing—review and editing (lead). Akizumi Tsutsumi: Writing—review and editing (support). Akiomi Inoue: Writing—review and editing (support).

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the Japanese Ministry of Health, Labour and Welfare (MHLW). Restrictions apply to the availability of these data, which were used under license for this study. Data are available with the permission of the MHLW.

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**SUPPORTING INFORMATION**

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