
Yasuaki Hayashino, MD, 1 Shunichi Fukuhara, MD, 1 Tomonori Okamura, MD, 2 Hiroshi Yamato, MD, 3 Hideo Tanaka, MD, 4 Taichiro Tanaka, MD, 5 Takashi Kadowaki, MD, and 2 Hirotsugu Ueshima, MD, 2 for the HIPOP-OHP Research Group*

1. Kyoto University Graduate School of Medicine, Japan
2. Shiga University of Medical Science, Japan
3. University of Occupational and Environmental Health, Japan
4. Osaka Medical Center for Cancer and Cardiovascular Diseases, Japan
5. University of Yamanashi, Japan

* Members of HIPOP-OHP Research Group members are listed in the Appendix.

Corresponding Author:
Yasuaki Hayashino, MD, MPH
Department of Epidemiology and Healthcare Research
Kyoto University Graduate School of Medicine
Konoe-cho, Yoshida, Sakyo-ku, Kyoto 606-8501
hayasino-y@umin.net

Received for publication 30 September 2007 and accepted in revised form 19 January 2008.
ABSTRACT

OBJECTIVE: We investigated the impact of active smoking and exposure to passive smoke on the risk of developing diabetes.

RESEARCH DESIGN AND METHODS: Data were analyzed from a cohort of participants in the High-risk and Population Strategy for Occupational Health Promotion Study (HIPOP-OHP) conducted in Japan from 1999 to 2004. Active and passive smoking status in the workplace was evaluated at baseline.

RESULTS: Of 6,498 participants (20.9% women), a total of 229 diabetes cases were reported over a median 3.4 years of follow-up. In the workplace, compared with zero exposure subjects, the multivariable-adjusted hazard ratios of developing diabetes were 1.81 (95%CI, 1.06-3.08: p=0.028) for present passive subjects and 1.99 (95%CI, 1.29-3.04: p=0.002) for present active smokers.

CONCLUSIONS: In this cohort, exposure to passive smoke in the workplace was associated with an increased risk of diabetes after adjustment for a large number of possible confounders.
A positive association between active smoking and the incidence of diabetes has been identified (1-3). Only one study has shown a significant association between passive smoke and impaired glucose tolerance (4), and the association between exposure to passive smoke and the risk of developing diabetes has not been fully investigated. Here, the relationship between exposure to passive smoke in the workplace or at home and the risk of developing diabetes in a large sample from a non-randomized health promotion intervention study conducted at workplaces in Japan.

**METHODS**

Analyses were performed using baseline and annual follow-up data from the High-risk and Population Strategy for Occupational Health Promotion Study (HIPOP-OHP) conducted between 1999 and 2004 at 12 large-scale companies, excluding prevalent diabetes cases or those who did not report active or passive smoking status at baseline. Full-time employees at the worksites were enrolled and then the worksites were non-randomly assigned to either the intervention or control groups (13-20).

All participants underwent an annual health check including blood testing at baseline and thereafter. A history of diabetes as well as lifestyle variables such as daily alcohol intake, smoking habits, were evaluated using a self-administered questionnaire (5-7).

We constructed the following four categories by combining active smoking status and passive smoking status at workplace or at home as follows: 1) “zero exposure” included those who never smoked and were not currently exposed to passive smoke, 2) “past active only” included those who had smoked in the past but did not currently smoke and were not currently exposed to passive smoke, 3) “present passive”, which included those currently exposed to passive smoke but who did not actively smoke, irrespective of past smoking, and 4) “present active”, which included those who currently smoke irrespective of exposure to passive smoke.

A subject was considered diabetes if at least one of the following parameters was met: 1) fasting blood glucose level of 126 mg/dL or greater (≥7.0 mmol/L); 2) random plasma glucose level of at least 200 mg/dl (11.1 mmol/L); and 3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agent). A self-reported history of diabetes was also accepted since self-reported diagnosis of diabetes is reliable (8), and has been used in many cohort studies (9, 10).

**Statistical Analyses.** We used the Cox-proportional hazards model to analyze the association between passive smoking, and incident diabetes cases. Person-time was calculated from the return of the baseline questionnaire until the date of the annual health-check at which the diagnosis of diabetes was confirmed, or the end of the follow-up, whichever occurred first.
We evaluated the effect of active smoking and exposure to passive smoke on the risk of developing diabetes in a multivariable-adjusted model, adjusting for all variables in Table 1. Likelihood ratio tests were used to test statistical interactions between passive smoking status and gender, BMI or assigned intervention.

RESULTS

Of the 6,498 participants (20.9% women), 44.6% of participants were current smokers (average of 19.6 cigarettes smoked per day), while 12.6% reported exposure to passive smoke in the workplace. About 32% of participants dropped out during the follow-up.

Age-adjusted baseline characteristics of the study participants are summarized in Table 1 by active smoking and exposure to passive smoke at workplace. In the workplace, compared with zero exposure subjects, the multivariable-adjusted hazard ratios for past active only subjects, present passive subjects and present active smokers were 1.15 (95%CI, 0.66-2.03: p=0.62), 1.81 (95%CI, 1.06-3.19: p=0.028) and 1.99 (95%CI, 1.29-3.04: p=0.002), respectively, in the analysis including all subjects; in the control group, 1.23 (95%CI, 0.56-2.73: p=0.60), 2.76 (95%CI, 1.38-5.50: p=0.004) and 2.09 (95%CI, 1.14-3.82: p=0.017), respectively: in the intervention group, 1.19 (95%CI, 0.23-2.71: p=0.84), 0.70 (95%CI, 0.25-1.92: p=0.50) and 1.99 (95%CI, 1.07-3.70: p=0.03), respectively. We did not observe statistically significant interactions between exposure to passive smoke and gender (p=0.74, 1df, χ²=0.60), obesity (p=0.77, 1df, χ²=0.08) or health promotion intervention (p=0.087, 1df, χ²=0.60). At home, the multivariable-adjusted hazard ratios for past active only subjects, present passive subjects and present active smokers were 0.97 (95%CI, 0.59-1.60: p=0.92), 0.80 (95%CI, 0.46-1.40: p=0.44) and 1.42 (95%CI, 0.98-2.04: p=0.062), respectively.

DISCUSSION

In this 4-year prospective study conducted in the workplace, self-reported exposure to environmental tobacco smoke in the workplace and current active smoking at baseline were positively associated with an increased risk of developing diabetes, even after adjustment for a large number of possible confounders. To our knowledge, only one study has explored the association between exposure to passive smoke and subsequent risk of diabetes, which yielded similar results to our study, although not statistically significant (4). Limitation of our study might be that our results might be underestimated by time-dependent confounding by smoking status; in fact, exposure to passive smoke in the workplace was not associated with the risk of diabetes in the intervention group, possibly due to lowered exposure to passive smoke by intervention. These findings add new evidence to support the need for measures to lessen environmental tobacco smoke in the workplace, especially in Asian populations, in which both the genetic susceptibility to diabetes (11, 12) and smoking rate is generally high (13).
ACKNOWLEDGEMENTS


We thank Toshimi Yoshida, Department of Health Sciences, Shiga University of Medical Science, for her excellent clerical support in this research.

APPENDIX

HIPOP-OHP Research group:
Chairman: Hirotsugu Ueshima (Department of Health Science, Shiga University of Medical Science, Otsu, Shiga).

Participants: Akira Okayama (Department of Preventive Cardiology, National Cardiovascular Center, Osaka); Kiyomi Sakata and Keiko Tsuji (Department of Hygiene and Public Health, Iwate Medical University, School of Medicine, Iwate); Katsushi Yoshita (Department of National Nutrition Survey and Health Informatics, National Institute of Health and Nutrition); Toru Takebayashi and Yuriko Kikuchi (Department of Preventive Medicine and Public Health, School of Medicine, Keio University); Hideaki Nakagawa and Katsuyuki Miura (Department of Epidemiology and Public Health, Kanazawa Medical University); Hiroshi Yamato (Institute of Industrial Ecological Science, University of Occupational and Environmental Health); Nagako Chiba (Department of Human-Life, Tsukuba International Junior College); Masahiko Yanagita (Department of Nursing Science, Fukui Prefectural University); Kazunori Kodama, Fumiyoshi Kasagi and Nobuo Nishi (Department of Epidemiology, Radiation Effects Research Foundation), Yukinori Kusaka (Department of Environmental Health, Faculty of Medical Sciences, University of Fukui); Shigeyuki Saitoh (Second Department of Internal Medicine School of Medicine, Sapporo Medical University); Hideo Tanaka (Department of Cancer Control and Statistics, Osaka Medical Center for Cancer and Cardiovascular Diseases); Masakazu Nakamura (Cholesterol Reference Method Laboratory Network at Osaka Medical Center for Health Science and Promotion); Masakazu Nakamura and Yoshihiko Naito (Osaka Medical Center for Health Science and Promotion); Yasuyuki Nakamura (Cardiovascular Epidemiology, Faculty of Home Economics, Kyoto Women’s University); Makoto Watanabe and Yoshikazu Nakamura (Department of Public Health, Jichi Medical School); Akira Babazono (Institute of Health Science, Kyushu University), Unai Tamura, Junko Minai, Zentaro Yamagata (Department of
Health Sciences, School of Medicine, University of Yamanashi; Sumio Urano (Matsushita Health Care Center), Fujihisa Kinoshita (Wakayama Wellness Foundation); Isao Saitoh (Department of Public Health, Nara Medical University); Shinichi Tanihara (Department of Public Health, School of Medicine, Shimane University, Japan); Junko Tamaki (Department of Public Health, Kinki University School of Medicine); Osamu Tochikubo (Department of Public Health, Yokohama City University School of Medicine); Takeo Nakayama (Department of Medical System Informatics, Graduate School of Medicine and Faculty of Medicine, Kyoto University); Shunichi Fukuhara (Department of Epidemiology and HealthCare Research, Graduate School of Medicine and Faculty of Medicine Kyoto University), Yoshiharu Fujieda (Department of Health and Sport Sciences, Tokyo Gakugei University); Mariko Naito (Department of Preventive Medicine/Biostatistics and Medical Decision Making, Nagoya University Graduate School of Medicine); Shunsaku Mizushima (Department of Human Resources Development, National Institute of Public Health); Yuji Miyoshi (Tokyo central Clinic, Health Insurance Society of Meiji Yasuda Life Insurance Company); Takayo Tada (Department of Food Science, Faculty of Human Life Science, Mimasaka University); Taichiro Tanaka, Takashi Kadowaki, Toshimi Yoshida, Mami Ide and Tomonori Okamura (Department of Health Science, Shiga University of Medical Science, Otsu, Shiga).
REFERENCES


<table>
<thead>
<tr>
<th></th>
<th>Zero exposure</th>
<th>Past active only</th>
<th>Present passive</th>
<th>Present active</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants, n</td>
<td>2129</td>
<td>779</td>
<td>690</td>
<td>2900</td>
</tr>
<tr>
<td>Age, y</td>
<td>36.9</td>
<td>41.7</td>
<td>39.3</td>
<td>37.9</td>
</tr>
<tr>
<td>Female, %</td>
<td>45.5</td>
<td>6.4</td>
<td>30.6</td>
<td>4.5</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>22.3</td>
<td>22.7</td>
<td>22.7</td>
<td>22.9</td>
</tr>
<tr>
<td>Physical activity, MET-h/wk †</td>
<td>4.8</td>
<td>6.7</td>
<td>6.3</td>
<td>4.6</td>
</tr>
<tr>
<td>Alcohol, g/d</td>
<td>11.2</td>
<td>22.7</td>
<td>15.7</td>
<td>26.9</td>
</tr>
<tr>
<td>Family history of diabetes, %</td>
<td>20.1</td>
<td>16.1</td>
<td>18.5</td>
<td>18</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>10.3</td>
<td>19.8</td>
<td>11.3</td>
<td>12.3</td>
</tr>
<tr>
<td>Health promotion intervention, %</td>
<td>46.0</td>
<td>41.6</td>
<td>46.7</td>
<td>44</td>
</tr>
<tr>
<td>Frequency of sweetened beverages intake &gt;= 1/day, %</td>
<td>20.5</td>
<td>17.6</td>
<td>19.0</td>
<td>19.7</td>
</tr>
<tr>
<td>Frequency of vegetable intake &lt; 1/week, %</td>
<td>47.3</td>
<td>45.9</td>
<td>46.7</td>
<td>47.2</td>
</tr>
<tr>
<td>Do not care about eating too much fat at all, %</td>
<td>18.2</td>
<td>16.4</td>
<td>17.3</td>
<td>17.8</td>
</tr>
</tbody>
</table>

* BMI, body-mass index; † MET, metabolic equivalent hours