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Association between exposure to secondhand aerosol from heated tobacco products and respiratory symptoms among current non-smokers in Japan: a cross-sectional study

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ABSTRACT

Objectives To investigate the association between secondhand-aerosol exposure from heated tobacco products (HTPs) and respiratory symptoms among current non-smokers.

Design Cross-sectional study.

Setting Internet survey conducted between 8 and 26 February 2021 in Japan.

Participants Non-smoking respondents at the survey aged 15–80 years.

Exposure Self-reported secondhand-aerosol exposure.

Primary and secondary outcomes We defined asthma/asthma-like symptoms as a primary outcome and persistent cough as a secondary outcome. We examined the association between secondhand-aerosol exposure from HTPs and respiratory symptoms (asthma attacks/asthma-like symptoms and persistent cough). The prevalence ratio (PR) and 95% CI were calculated by using weighted, multivariable 'modified' Poisson regression models.

Results Of the 18 839 current non-smokers, 9.8% (95% CI 8.2% to 11.7%) and 16.7% (95% CI 14.8% to 18.9%) of those who were exposed to secondhand aerosols reported asthma attacks/asthma-like symptoms and persistent cough, whereas 4.5% (95% CI 3.9% to 5.2%) and 9.6% (95% CI 8.4% to 11.0%) of those who were not, respectively. Secondhand-aerosol exposure was associated with respiratory symptoms (asthma attacks/asthma-like symptoms: PR 1.49, 95% CI 1.21 to 1.85; persistent cough: PR 1.44, 95% CI 1.21 to 1.72) after adjusting for covariates.

Conclusion Secondhand-aerosol exposure from HTPs was associated with both asthma attacks/asthma-like symptoms and persistent cough. These results provide policymakers with meaningful information in the regulation of HTP use for the protection of current non-smokers.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study used large-scale internet survey data with sampling weights from a nationally representative survey in Japan.
⇒ This study focused on current non-smokers that are the most important population for tobacco control policy but are currently underexamined.
⇒ There may be some differences between respondents and the general population.
⇒ There may also be measurement errors because all variables were based on self-reported questionnaires.

INTRODUCTION

It is widely known that secondhand smoke (SHS) from combustible cigarettes has a harmful effect on health.[1] The detrimental effects of SHS vary, including: ear and respiratory infections, and respiratory symptoms such as asthma attacks among children; and heart disease, stroke and lung cancer among adults.[1] SHS exposure is also associated with death among all age groups due to the diseases mentioned above. The estimated global deaths associated with SHS exposure increased from 848 702 in 2006 to 883 930 in 2016.[2] Notably, SHS exposure is harmful to current non-smokers; therefore, the Centers for Disease Control and Prevention in the USA clearly emphasise that complete protection of non-smokers from SHS is essential for a comprehensive smoke-free policy.[1] Such a policy may reduce smoking prevalence and associated harms.[3] Taken together, the protection of non-smokers from SHS is a relevant and established issue for healthcare professionals, public health researchers and policymakers.

As new tobacco products, such as electronic cigarettes (e-cigarettes) and heated tobacco products (HTPs), were introduced in and spread rapidly since the early 2010s,[4 5] secondhand aerosols from such products are emerging as another public health interest

associated with SHS. Secondhand aerosols from e-cigarettes are prevalent in the USA and European countries.[6 7] In the USA, middle and high school students have been exposed to secondhand aerosols from e-cigarettes, with an increasing trend (approximately 25% in 2015 and 33.2% in 2018).[7–9] In the TackSHS survey that included nationally representative samples aged 15 years in 12 European countries, 16.0% of respondents experienced secondhand aerosols from e-cigarettes.[6] Secondhand aerosols from HTPs have also been prevalent, especially in Japan, which has the most fertile market for HTPs.[5]

In recent studies, associations of secondhand aerosol from e-cigarettes with negative respiratory outcomes were observed. For example, there was a cross-sectional association between secondhand aerosol from e-cigarettes and asthma symptoms in youth aged 11–17 years in Florida, the USA.[10] Outside the USA, a similar cross-sectional study was conducted in Kuwait and the same association was observed.[11] In addition, a recent study showed that exposure to secondhand aerosol from e-cigarettes was longitudinally associated with bronchitic symptoms among young adults.[12] Compared with secondhand aerosol from e-cigarettes, evidence regarding negative respiratory outcomes by secondhand aerosols from HTPs is scarce. To our knowledge, only one study in Japan examined the association between exposure to secondhand aerosol from HTPs and respiratory symptoms immediately after inhalation.[13]

Despite the current evidence, it remains unclear whether exposure to secondhand aerosol from HTPs is associated with chronic to subacute respiratory symptoms. Moreover, it is also unclear whether such an association is observed among current non-smokers in whom the smoke-free policy is really interested.[1]

Given the above evidence, in this study, we aimed to investigate the cross-sectional association of secondhand-aerosol exposure from HTPs with the presence of respiratory symptoms among current non-smokers by using large-scale, internet-based survey data.

METHODS

Data sources, design and setting

In this cross-sectional study, we used data from the 2021 Japan 'Society and New Tobacco' Internet Survey (JASTIS). The JASTIS is a longitudinal cohort study in which a series of annual internet surveys have been performed since 2015. The survey is used to collect information about the use of tobacco products, including new tobacco products (such as HTPs and e-cigarettes) and combustible cigarettes, as well as participant demographics and socioeconomic status.[14] The online questionnaire was designed such that respondents had to answer each question before they could proceed to the next, ensuring that all questions were answered before submission. Participants of the JASTIS were recruited via a survey panel provided by a major internet research group in Japan (Rakuten Insight).[15] The research group houses information of about 2.3 million panellists, including socioeconomic information such as education level, household income and marital status. The survey panel consisted of those who were initially recruited by the research group. In the 2021 JASTIS, 26 000 participants were recruited from the Japan 'COVID-19 and Society' Internet Survey (JACSIS), a sister survey of JASTIS. The participants of the 2021 JASTIS were obtained between the 8 and 26 of February 2021. Among the 2021 JASTIS participants, 87.8% (22 840/26 000) came from the 2020 JACSIS. To achieve the targeted response number in the 2021 JASTIS, we additionally recruited 3160 participants from all respondents who previously participated in the 2015–2020 JASTISs. Detailed information regarding the JASTIS is described in the study profile.[14]

Inclusion and exclusion criteria

In this study, we included data from all the 2021 survey respondents who were current non-smokers, determined by using the following question: 'Do you currently use any of the following tobacco products? (Cigarettes, roll-your-own cigarettes, Ploom Tech, Ploom Tech plus, Ploom S, IQOS, glo, glo hyper, glo sens, PULZE, electronic cigarettes containing nicotine, electronic cigarettes without nicotine, electronic cigarettes with unknown nicotine content, cigars, little cigars, pipes, chewing tobacco, snuffing tobacco, and hookahs)'. The response options were 'never', 'several times in the past', 'habitually in the past', 'occasionally' and 'almost every day'. In this study, we defined current non-smokers as those who selected one of the first three options. We excluded surveys as straightlining responses if the respondents chose the same number in answer to all questions in a set of questions. We also excluded responses in which respondents reported an amount of tobacco product use but had indicated that they had never used or were only former users of tobacco products. In addition to these exclusion criteria, we performed an attention check with the following question: 'Please choose the answer second from the bottom'. With this attention check, we excluded respondents who selected responses other than the second answer from the bottom.

Measurement of exposure variables

The exposure variable that we examined was the exposure to secondhand aerosols from HTPs over the past year. Hence, in the questionnaire, respondents were asked, 'During the past 12 months, have you knowingly inhaled aerosols from HTPs when someone used HTPs in your presence?' The response options were 'never', 'rarely', 'sometimes' and 'frequently'. In this study, we defined those who were exposed to secondhand aerosols from HTPs as those who selected the latter three options

Main outcomes and measures

In this study, we defined self-reported respiratory symptoms as outcomes. As a primary outcome, we selected asthma attacks/asthma-like symptoms, which previous

studies indicated were associated with aerosols from HTPs.[13 16] As a secondary outcome, we selected non-specific persistent cough, for which a previous study indicated a possible association with e-cigarette use.[17] The JASTIS included the question, 'During the past 12 months, have you experienced any of the following conditions: asthma attacks/asthma-like symptoms or persistent cough?' The response options were 'never', 'rarely', 'sometimes' and 'frequently'. We defined the presence of each respiratory symptom as a selection of any of the latter three options.

Covariates

As evidence for a relationship between secondhand aerosols and respiratory symptoms is limited, we selected the following 12 variables as potential confounding factors: age groups based on the definition from a previous study (15–29, 30–44, 45–59 or 60–80 years),[18] sex (male or female), education status ('high school or less' or 'college or more'), marital status (married, never married or widowed/divorced), household size (living alone or living with others), equivalent household income (first quartile, second quartile, third quartile, fourth quartile or unknown/declined to answer), combustible cigarette use, HTP use, other tobacco-product use, SHS exposure over the past month and two respiratory comorbidities: asthma and bronchitis/pneumonia. Out of these confounding factors, age, sex, income, past combustible cigarette, HTP or other tobacco product use, SHS exposure, respiratory comorbidities were selected from previous studies regarding secondhand aerosols from e-cigarettes.[10 11] The others, for example, education and marital status, were also defined as confounding factors, based on a previous study regarding secondhand aerosols from HTPs and socioeconomic inequality.[19]

Statistical analysis

First, we calculated the frequency of each variable as baseline characteristics. Second, we stratified the experience of respiratory symptoms over the past year by exposure to secondhand aerosols. Third, we conducted multivariable, 'modified' Poisson regression analysis with a robust estimator to estimate the prevalence ratio (PR) and CI for the prevalence of each respiratory symptom. The exposure variable (exposure to secondhand aerosols from HTPs) was dichotomised, as previously noted, or included as a categorical variable (with 'never' as a reference, and 'rarely', 'sometimes' and 'frequently'). The equivalence of outcome prevalence in each category was tested by assigning a linear score by treating secondhand-aerosol frequencies as an ordinal variable. In addition, to examine the multicollinearity of variables in the multivariable models, we evaluated the variance inflation factors in all analyses.

We also conducted a sensitivity analysis using a parsimonious model. We constructed a weighted multivariable 'modified' Poisson model to examine the consistency of the results for our main analysis. In the model, we selected all the confounding factors with a minimal set of classifications from previous studies.[10 11] The selected variables are as follows: age (15–29 or 30–80), sex (male or female), education ('high school or less' or 'college or more'), income (lower half or upper half or unknown/declined to answer), past combustible cigarette use (never or past), past HTP use (never or past), SHS (absent or present) and asthma (absent or present).

To account for the differences between the sociodemographic status of respondents from the survey panel and that of the Japanese general public, we used inverse probability weighting for all analyses.[14 20] The sampling weights, which were scaled such that the total amounted to 26 000 (original number of respondents), were predicted from a logistic model in which we adjusted for area of residence, marital status, education status, home-ownership status, self-rated health and smoking status in individuals aged 20–80 years; and area of residence, education status, home-ownership status and self-rated health (omitting marital and smoking status) in individuals aged 15–19 years. In this way, we adjusted for the difference between respondents in the current internet survey and the 2016 Comprehensive Survey of Living Conditions, a nationally representative survey in Japan.[21] All CIs and p values were based on the robust variance estimator to account for the inverse probability weighting. Statistical significance was set at $p<0.05$. The data were analysed using 'svy: tabulate' and 'svy: glm' commands in Stata V.16.1 (StataCorp, College Station, Texas, USA).

Patient and public involvement

No patients or the public were involved in this study. We did not invite any patients to comment on the study design, interpretation of the results or the readability or accuracy of the manuscript.

RESULTS

Of the 26 000 respondents, 18 839 current non-smokers were included for analyses (online supplemental figure 1). With inverse probability weighting, 36.6% (95% CI 34.2% to 39.1%) of participants were aged 60–80, 55.7% (95% CI 53.8% to 57.6%) were women, 53.8% (95% CI 51.6% to 55.9%) were high-school graduates or had less education and 66.0% (95% CI 64.0% to 67.8%) were married. Regarding smoking and SHS status, 34.0% (95% CI 32.1% to 36.0%) were past combustible-cigarette users, 4.1% (95% CI 3.7% to 4.6%) were past HTP users and 9.5% (95% CI 8.7% to 10.4%) were past users of other tobacco products. In particular, 80.3% (95% CI 79.0% to 81.6%) of participants had been exposed to SHS in the past month (table 1).

Of the 18 839 respondents, 4402 (23.4%) were exposed to secondhand aerosols from HTPs. With inverse probability weighting, 9.8% (95% CI 8.2% to 11.7%) and 16.7% (95% CI 14.8% to 18.9%) of those who were exposed to secondhand aerosols reported asthma attacks/asthma-like symptoms and persistent cough, whereas 4.5% (95%

Table 1 Demographics of study participants

Characteristics	N=18 839	n	%	Weighted %*	95% CI
Age	15–29	3024	16.1	15.5	14.5 to 16.6
	30–44	4205	22.3	20.4	19.3 to 21.5
	45–59	4967	26.4	27.5	26.1 to 28.9
	60–80	6643	35.3	36.6	34.2 to 39.1
Sex	Male	8598	45.6	44.3	42.4 to 46.2
	Female	10 241	54.4	55.7	53.8 to 57.6
Education status	High school or less	5789	30.7	53.8	51.6 to 55.9
	College or more	13 050	69.3	46.2	44.1 to 48.4
Marital status	Married	11 431	60.7	66.0	64.0 to 67.8
	Not married	5670	30.1	25.1	23.6 to 26.7
	Widowed/divorced	1738	9.2	8.9	7.5 to 10.7
Household size	Living alone	15 266	81.0	84.9	82.8 to 86.8
	Living with others	3573	19.0	15.1	13.3 to 17.2
Equivalent household income	First quartile	3816	20.3	23.0	21.5 to 24.6
	Second quartile	3874	20.6	21.5	19.7 to 23.5
	Third quartile	3716	19.7	18.4	16.9 to 20.1
	Fourth quartile	3403	18.1	13.1	12.1 to 14.2
	Unknown/declined to answer	4030	21.4	23.9	22.0 to 25.8
Combustible cigarette use	Never	12 822	68.1	66.0	64.1 to 67.9
	Past	6017	31.9	34.0	32.1 to 36
HTP use	Never	18 008	95.6	95.9	95.4 to 96.3
	Past	831	4.4	4.1	3.7 to 4.6
Other tobacco product use	Never	17 035	90.4	90.5	89.6 to 91.3
	Past	1804	9.6	9.5	8.7 to 10.4
Exposure to secondhand smoke over the past month	Absent	3663	19.4	19.7	18.4 to 21.0
	Present	15 176	80.6	80.3	79.0 to 81.6
Asthma	Absent	18 271	97.0	96.3	95.2 to 97.1
	Present	568	3.0	3.7	2.9 to 4.8
Bronchitis or pneumonia	Absent	18 624	98.9	98.4	97.9 to 98.8
	Present	215	1.1	1.6	1.2 to 2.1
Exposure to secondhand aerosol from HTPs over the past 12 months	Absent	14 437	76.6	77.4	75.9 to 78.9
	Present	4402	23.4	22.6	21.1 to 24.1

*The sampling weights, which were scaled such that the total amounted to 26 000 (the original number of respondents), were predicted from a logistic model in which we adjusted for area of residence, marital status, education status, home-ownership status, self-rated health and smoking status in individuals aged 20–80 years; and area of residence, education status, home-ownership status and self-rated health (omitting marital and smoking status) in individuals aged 15–19 years, to adjust for the difference in respondents between the current internet survey and the 2016 Comprehensive Survey of Living Conditions in Japan. All CIs were based on the Wald-type test on the probability scale, which was accompanied by the robust variance estimator of the weighted proportions accounting for the inverse probability weighting ('svy: tabulate' command in Stata).
HTP, heated tobacco product.

CI 3.9% to 5.2%) and 9.6% (95% CI 8.4% to 11.0%) of those who were not, respectively, (table 2).

In the multivariable analysis, exposure to secondhand aerosols was associated with both primary and secondary outcomes after adjusting for covariates using 'modified' Poisson regression models (asthma attacks/asthma-like symptoms: PR 1.49, 95% CI 1.21 to 1.85, p<0.001; persistent cough: PR 1.44, 95% CI 1.21 to 1.72, p<0.001) (table 3).

When examining the association of ordinal exposure variables with the outcomes, the same associations were observed (figure 1, online supplemental table 1). Notably, all outcomes exhibited a nearly monotonic relationship with the frequency of exposure to secondhand aerosols

Table 2 Respiratory symptoms over the past year among non-smokers classified into the experience of secondhand aerosols

Symptoms	Frequency	Secondhand aerosol (–) n=14 437 n	%	Weighted % *	95% CI	Secondhand aerosol (+) N=4402 n	%	Weighted % *	95% CI
Asthma attacks/asthma-like symptoms	Never	13 772	95.4	95.5	94.8 to 96.1	4043	91.8	90.2	88.3 to 91.8
	Rarely	424	2.9	2.7	2.3 to 3.2	211	4.8	5.6	4.5 to 6.8
	Sometimes	205	1.4	1.6	1.2 to 2.1	124	2.8	3.3	2.3 to 4.8
	Frequently	36	0.2	0.2	0.1 to 0.3	24	0.5	0.9	0.5 to 1.6
Persistent cough	Never	13 163	91.2	90.4	89.0 to 91.6	3787	86.0	83.3	81.1 to 85.4
	Rarely	697	4.8	4.9	4.3 to 5.7	346	7.9	8.2	6.9 to 9.7
	Sometimes	446	3.1	3.9	2.9 to 5.2	224	5.1	7.1	5.6 to 8.9
	Frequently	131	0.9	0.8	0.6 to 1.1	45	1.0	1.4	0.9 to 2.1

*The sampling weights, which were scaled such that the total amounted to 26 000 (the original number of respondents), were predicted from a logistic model in which we adjusted for area of residence, marital status, education status, home-ownership status, self-rated health and smoking status in individuals aged 20–80 years; and area of residence, education, home-ownership status and self-rated health (omitting marital and smoking status) in individuals aged 15–19 years, to adjust for the difference in respondents between the current internet survey and the 2016 Comprehensive Survey of Living Conditions in Japan. All CIs were based on the Wald-type test on the probability scale, which was accompanied by the robust variance estimator of the weighted proportions accounting for the inverse probability weighting ('svy: tabulate' command in Stata).

(both p<0.001 with the linear trend test). The maximum variance inflation factor was 2.01, suggesting that there was no problematic multicollinearity in the regression models (online supplemental table 2).

The results of the sensitivity analysis were shown in table 4. Consistent associations between exposure to secondhand aerosols from HTPs and two outcomes were observed (asthma attacks/asthma-like symptoms, PR 1.64, 95% CI 1.31 to 2.04, p<0.001; persistent cough, PR 1.48, 95% CI 1.22 to 1.79, p<0.001).

DISCUSSION

Using data from a large-scale, nationwide survey conducted in February 2021 in Japan, we discovered a cross-sectional association between secondhand-aerosol exposure and two respiratory symptoms (asthma attacks/asthma-like symptoms and persistent cough) after adjusting for 12 potential confounding factors. The PRs of respiratory symptoms increased as the frequency of exposure to secondhand aerosols from HTPs increased. Furthermore, the weighted prevalence of secondhand-aerosol exposure over the past month was approximately 20%, and, similar to those of SHS from combustible cigarettes and secondhand aerosols from e-cigarettes.[1 6] Given these findings, many current non-smokers in Japan may be exposed to secondhand aerosols from HTPs, which may have detrimental effects on their respiratory systems.

There are several potential mechanisms by which secondhand aerosols may cause respiratory symptoms. First, in the biochemical context, aerosols from HTPs contain substantial amounts of chemical compounds such as carbonyl compounds and polycyclic aromatic hydrocarbons.[22] These chemicals damage human bronchial epithelial cells,[23] inducing asthma attacks or asthma-like symptoms. Second, in the physiological context, inhalation of the chemical compounds in aerosols from HTPs impairs respiratory function (forced expiratory volume in 1 s, both absolute and as a percentage of the predicted value),[24] resulting in respiratory symptoms. Finally, in the indoor environmental context, secondhand aerosols contain concentrations of harmful chemical compounds, such as nicotine and fine particulate matter, greater than the upper limits of the range of tolerable concentrations.[25] Consequently, even current non-smokers may experience asthma attacks/asthma-like symptoms or persistent cough via the above-mentioned biochemical and physiological mechanisms after inhalation of secondhand aerosols emitted by others, especially indoors.

Secondhand aerosols from e-cigarettes have already been an emerging public health threat. A study by Bayly *et al* presented a cross-sectional association between exposure to secondhand aerosol from e-cigarettes and asthma attacks in youth aged 11–17 years (n=11 830) in the USA.[10] In the study, both secondhand aerosol from e-cigarettes and SHS were associated with asthma attacks in the multivariable logistic regression model; however, the estimated OR in SHS was smaller than that in secondhand aerosols (SHS, OR 1.19, 95% CI 1.05 to 1.35; and secondhand aerosol from e-cigarettes, OR 1.27, 95% CI 1.11 to 1.47). Although the study adjusted for numerous confounding factors including various patterns of tobacco product use, there was an important limitation regarding inconsistent time frames of the measurements, that is, the time frame of the exposure was past 30 days and that of the outcome was 12 months. Such an inconsistent time frame may imply an increased risk of the reverse relationship between exposure to secondhand aerosol from e-cigarettes and asthma attacks. Another study by Alnajem *et al* also showed a cross-sectional

Table 3 Multivariable weighted Poisson regression analysis for respiratory symptoms among non-smokers

		Asthma attacks/asthma-like symptoms			Persistent cough		
Characteristics	**N=18 839**	**PR**	**95% CI**	**P value**	**PR**	**95% CI**	**P value**
Exposure to secondhand aerosols	**Absent**	**Reference**			**Reference**		
	Present	1.49	1.21 to 1.85	<0.001	1.44	1.21 to 1.72	<0.001
Age	15–29	1.35	1.01 to 1.79	0.04	1.02	0.79 to 1.31	0.87
	30–44	1.14	0.89 to 1.46	0.30	1.15	0.96 to 1.38	0.14
	45–59	Reference			Reference		
	60–80	0.85	0.64 to 1.14	0.27	1.13	0.91 to 1.39	0.27
Sex	Male	Reference			Reference		
	Female	0.92	0.74 to 1.15	0.45	1.12	0.93 to 1.36	0.24
Education status	High school or less	Reference			Reference		
	College or more	1.04	0.86 to 1.26	0.69	0.92	0.74 to 1.15	0.47
Marital status	Married	Reference			Reference		
	Not married	1.02	0.81 to 1.29	0.87	0.97	0.77 to 1.22	0.78
	Widowed/divorced	1.60	1.03 to 2.46	0.04	1.39	0.93 to 2.08	0.11
Household size	Living alone	Reference			Reference		
	Living with others	0.85	0.61 to 1.19	0.34	1.14	0.8 to 1.61	0.47
Equivalent household income	First quartile	Reference			Reference		
	Second quartile	0.81	0.61 to 1.07	0.14	0.90	0.67 to 1.21	0.49
	Third quartile	0.88	0.62 to 1.24	0.47	0.77	0.56 to 1.06	0.11
	Fourth quartile	0.87	0.65 to 1.17	0.35	0.92	0.69 to 1.23	0.58
	Unknown/declined to answer	0.72	0.53 to 0.97	0.03	0.81	0.6 to 1.09	0.16
Combustible cigarette use	Never	Reference			Reference		
	Past	0.93	0.71 to 1.22	0.60	1.17	0.88 to 1.55	0.28
HTP use	Never	Reference			Reference		
	Past	1.71	1.19 to 2.44	0.003	1.34	1.05 to 1.72	0.02
Other tobacco product use	Never	Reference			Reference		
	Past	1.35	0.96 to 1.90	0.09	1.42	1.09 to 1.85	0.01
Exposure to secondhand smoke over the past month	Absent	Reference			Reference		
	Present	0.86	0.67 to 1.11	0.26	0.97	0.78 to 1.21	0.80
Asthma	Absent	Reference			Reference		
	Present	12.39	9.75 to 15.75	<0.001	4.12	3.13 to 5.42	<0.001
Bronchitis or pneumonia	Absent	Reference			Reference		
	Present	1.68	1.20 to 2.35	0.003	2.04	1.46 to 2.85	<0.001

The sampling weights, which were scaled such that the total amounted to 26 000 (the original number of respondents), were predicted from a logistic model in which we adjusted for area of residence, marital status, education status, home-ownership status, self-rated health and smoking status in individuals aged 20–80 years; and area of residence, education status, home-ownership status and self-rated health (omitting marital and smoking status) in individuals aged 15–19 years, to adjust for the difference in respondents between the current internet survey and the 2016 Comprehensive Survey of Living Conditions in Japan. All CIs and p values were based on the robust variance estimator to account for the inverse probability weighting.
HTP, heated tobacco product; PR, prevalence ratio.

association between secondhand-aerosol exposure from e-cigarettes in the past 7 days and respiratory symptoms in the past 12 months among schoolchildren aged 16–19 years in Kuwait.[11] In that study, frequent secondhand-aerosol exposure was associated with an increased risk of wheeze (PR 1.30, 95% CI 1.04 to 1.59), asthma (PR 1.56, 95% CI 1.13 to 2.16) and uncontrolled asthma symptoms (PR 1.88, 95% CI 1.35 to 2.62). However, like the study by Bayly *et al*, the same limitation for time frame was observed (7 days for the exposure and 12 months for the outcome). A. recent study by Islam *et al* showed the longitudinal association between exposure to e-cigarette

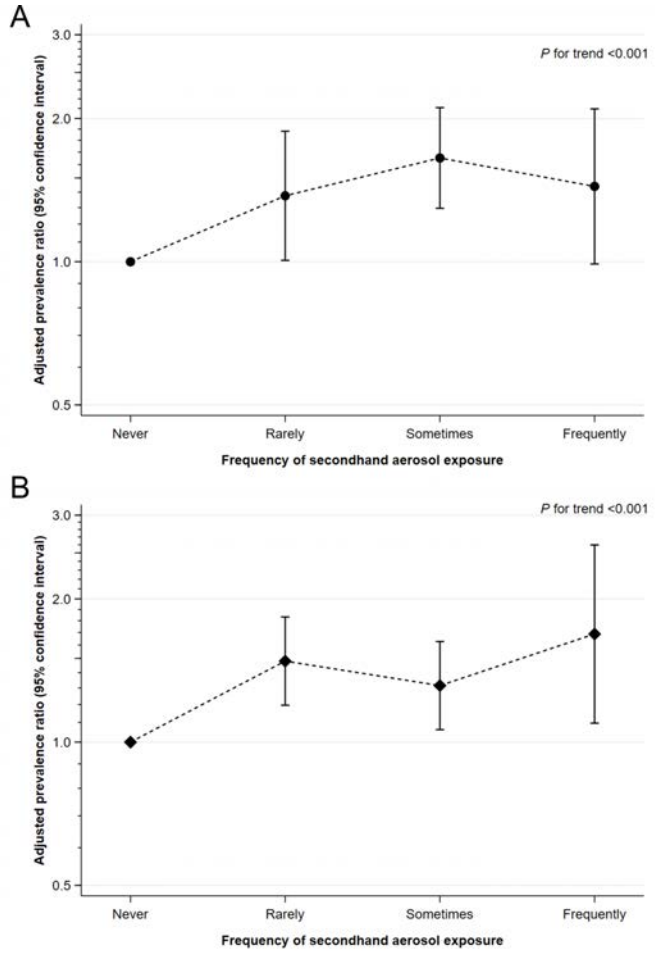

Figure 1 Prevalence ratios of ordinal exposure variables for the outcomes. (A) asthma attacks/asthma-like symptoms, (B) persistent cough.

secondhand aerosols and bronchitic symptoms (OR 1.40, 95% CI 1.06 to 1.84) and shortness of breath (OR 1.53, 95% CI 1.06 to 2.21) among young adults (average age, 17.3 years; n=2090) in the USA.[12] Although these studies are informative, they commonly focus on e-cigarettes and a specific population (adolescents and young adults). There have been few studies on the association of exposure to secondhand aerosol from HTPs with respiratory outcomes. To date, we could find only one study by Imura and Tabuchi, via an internet survey conducted in 2019, which examined the cross-sectional association between exposure to secondhand aerosols and symptoms directly induced by such exposure.[13] They revealed that asthma-like attacks and chest pain were more prevalent in those who were exposed to secondhand aerosols from HTPs than to SHS from combustible cigarettes. Although this study is informative, evaluation of its association with subacute to chronic respiratory symptoms remains limited. Thus, we examined the association between exposure to secondhand aerosols from HTPs and asthma attacks/asthma-like symptoms and persistent cough. When designing this study, we used the same frame for the measurement of the exposure and outcomes (past 12 months) to compensate for the previous cross-sectional studies. The associations were mostly consistent with the previous studies regarding secondhand aerosols from e-cigarettes. However, there were some inconsistent estimates, for example, the association between SHS and respiratory outcomes was not observed. Nevertheless, as noted above, a previous study showed that the OR of SHS for asthma was smaller than that of secondhand aerosols from e-cigarettes.[10] The phenomenon that the ORs or PRs in SHS were lower than those in secondhand aerosols from HTPs might be induced by the different time frames of measurements for SHS (30 days) and outcomes (12 months) both in this study and a previous study. Moreover, when stratified by exposure to SHS, the associations of exposure to secondhand aerosol from HTPs with both asthma attacks/asthma-like symptoms and persistent cough were consistently observed among the exposure to SHS group in our data (asthma attacks/asthma-like symptoms, PR 1.53, 95% CI 1.21 to 1.93; persistent cough, PR 1.44, 95% CI 1.19 to 1.74). Therefore, we believe that our results were not discrepant from the previous studies. Notably, the strength of this study is that we focused on current non-smokers whom most policymakers have interested,[1] and used consistent time frames for the measurements of the exposure and outcomes. To our knowledge, this is the first study in which the environments in which people were exposed to secondhand aerosols from HTPs were clarified and the association between such exposure and respiratory symptoms was evaluated among current non-smokers, by using nationally representative, large-scale survey data. As the number of HTP users is growing in Europe and the USA,[26 27] as well as in Japan, the threat to current non-smokers' health due to secondhand-aerosol exposure from HTPs will increase globally. Thus, our findings provide policymakers with meaningful information in regulating HTP use for the protection of current non-smokers. In addition, we believe our results will contribute to longitudinal epidemiological studies, biological studies for the relationship between respiratory systems and toxic effects of aerosols from HTPs, environmental studies that examined the chemical pounds from HTP aerosols and so on.

Our study has several limitations. First, because of this study's cross-sectional design, the temporal relationship between secondhand-aerosol exposure and respiratory symptoms was unclear, and our results cannot be used to infer causality. However, the results from this study implied a nearly monotonic relationship between the frequency of exposure to secondhand aerosols and the PR for each respiratory symptom under assessment, which is a key component in explaining causality.[28] Second, this study was based on self-report questionnaires and not all variables were measured with validated questionnaires; therefore, measurement errors may exist. However, we developed an algorithm for exclusion of responses that were unreliable or invalid, and excluded such respondents a priori. Moreover, our questionnaire for exposure variables clearly assumed that someone used HTPs

Table 4 Multivariable Poisson regression analysis based on a parsimonious model

Characteristics	N=18 839	Asthma attacks/asthma-like symptoms			Persistent cough		
		PR	(95% CI)	P value	PR	(95% CI)	P value
Exposure to secondhand aerosols from HTPs	Absent	Reference			Reference		
	Present	1.64	(1.31 to 2.04)	<0.001	1.48	(1.22 to 1.79)	<0.001
Age	15–29	1.30	(1.04 to 1.64)	0.02	0.89	(0.74 to 1.08)	0.23
	30–80	Reference			Reference		
Sex	Male	Reference			Reference		
	Female	0.88	(0.70 to 1.11)	0.29	1.06	(0.84 to 1.34)	0.60
Education status	High school or less	Reference			Reference		
	College or more	0.99	(0.81 to 1.22)	0.96	0.89	(0.71 to 1.12)	0.33
Equivalent household income	Lower half	Reference			Reference		
	Upper half	0.93	(0.72 to 1.19)	0.56	0.81	(0.64 to 1.03)	0.09
	Unknown/declined to answer	0.76	(0.58 to 0.99)	0.04	0.80	(0.62 to 1.03)	0.08
Combustible cigarette use	Never	Reference			Reference		
	Past	0.94	(0.71 to 1.26)	0.69	1.26	(0.93 to 1.71)	0.13
HTP use	Never	Reference			Reference		
	Past	2.05	(1.48 to 2.84)	<0.001	1.54	(1.17 to 2.02)	<0.001
Exposure to secondhand smoke over the past month	Absent	Reference			Reference		
	Present	0.84	(0.64 to 1.11)	0.22	0.99	(0.79 to 1.24)	0.92
Asthma	Absent	Reference			Reference		
	Present	14.64	(11.63 to 18.42)	<0.001	5.23	(4.05 to 6.76)	<0.001

The sampling weights, which were scaled such that the total amounted to 26 000 (the original number of respondents), were predicted from a logistic model in which we adjusted for area of residence, marital status, education status, home-ownership status, self-rated health and smoking status in individuals aged 20–80 years; and area of residence, education status, home-ownership status and self-rated health (omitting marital and smoking status) in individuals aged 15–19 years, to adjust for the difference in respondents between the current internet survey and the 2016 Comprehensive Survey of Living Conditions in Japan. All CIs and p values were based on the robust variance estimator to account for the inverse probability weighting.
HTP, heated tobacco product; PR,prevalence ratio.

in the respondents' presence. In combination with the high prevalence of HTP use in 2020 Japan,[29] we believe that our questionnaire for exposure had substantial sensitivity. Third, this study is based on an internet survey; the composition of study participants may have differed from that of the general Japanese public. However, to minimise such differences, we adjusted for demographic, socioeconomic and health-related differences between respondents in the present study and the Japanese general public by using nationally representative survey data. Finally, this study was conducted in Japan, where HTPs are more popular than in other countries[30]; therefore, our findings may not be generalisable to other countries.

In conclusion, by using data from a nationally representative survey, this study revealed that exposure to secondhand aerosols from HTPs were prevalent in 2021 in Japan. This study clarified the association between such exposure and asthma attacks/asthma-like symptoms and persistent cough among current non-smokers. Our results will provide policymakers with meaningful information for a smoke-free policy. Also, we can provide good evidence to make progress in future research in relation to respiratory diseases induced by secondhand aerosol from HTPs.

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Contributors TY, TS, AH, KN, SO and TT contributed to the conceptualisation of this study. TY and TT collected data, and TY, TS and TT developed the plan for analysis. TY analysed the data. TY wrote the original manuscript, and TS, AH, KN, SO and TT reviewed, interpreted, critically appraised and revised the original manuscript. TY, TS, AH, KN, SO and TT reviewed the final version of the manuscript and approved its submission. TY takes full responsibility for the whole content of the manuscript including the data and analysis as guarantor, has access to the data, and controlled the decision to publish.

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Patient consent for publication Consent obtained directly from patient(s).

Ethics approval All procedures were conducted according to the ethical standards of the Declaration of Helsinki. We obtained web-based informed consent from all the respondents for use of their data from the Japan 'Society and New Tobacco' Internet Survey study in our research. A credit point known as 'Epoints', which could be used for internet shopping and cash conversion, was provided to the participants as an incentive. This study was approved by the Institutional Review Board of Osaka International Cancer Institute (Number: 20084). The internet research group fully respected the Act on the Protection of Personal Information in Japan. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cross-sectional studies.

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Data availability statement No data are available. The data used in this study are not available in a public repository because they contain personally identifiable or potentially sensitive participants' information. Based on the regulations for ethical guidelines in Japan, the Institutional Review Board of the Osaka International Cancer Institute has imposed restrictions on the dissemination of the data collected in this study. All data inquiries will be channelled through Takahiro Tabuchi (tabuchitak@gmail.com) to Osaka Cancer Institute Institutional Ethics Committee.

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