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Abbreviations
Total suspended particulate (TSP); Particulate matter (PM); particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$); Light detection and ranging (LIDAR)

Keywords
Asian dust; *Kosa*; Chronic cough; Daily cough symptom; $PM_{2.5}$

ABSTRACT

Asian dust, known as *kosa* in Japanese, is a major public health concern. In this panel study, we evaluated the effects of exposure to *kosa* on daily cough occurrence. The study subjects were 86 patients being treated for asthma, cough variant asthma, or atopic cough in Kanazawa University Hospital from January 2011 to June 2011. Daily mean concentrations of *kosa* and spherical particles were obtained from light detection and ranging (LIDAR) measurements, and were categorized from Grade 1 (0 μg/m^3) to 5 (over 100 μg/m^3). The association between *kosa* and cough was analyzed by logistic regression with a generalized estimating equation. *Kosa* effects on cough were seen for all Grades with potential time lag effect. Particularly at Lag 0 (the day of exposure), a dose-response relationship was observed: the odds ratios for Grades 2, 3, 4, and 5 above the referent (Grade 1) were 1.111 (95% confidence interval (CI): 0.995–1.239), 1.171 (95% CI: 1.006–1.363), 1.357 (95% CI: 1.029–1.788), and 1.414 (95% CI: 0.983–2.036), respectively. Among the patients without asthma, the association was higher: the odds ratios for Grades 2, 3, 4 and 5 were 1.223 (95% CI: 0.999–1.497), 1.309 (95% CI: 0.987–1.737), 1.738 (95% CI: 1.029–2.935) and 2.403 (95% CI: 1.158–4.985), respectively. These associations remained after adjusting for the concentration of spherical particles or particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$). Our findings demonstrate that *kosa* is an environmental factor which induces cough in a dose-response relationship.

1. Introduction

The desert dust storms are major contributors to the atmospheric particulate matter (PM) with an aerodynamic diameter of less than 10 μm (PM_{10}). The adverse health effects of desert dust are demonstrated in many reports; The desert dust have relation with cardiac and respiratory mortality (Barnett et al., 2012; Jimenez et al., 2010; Mallone et al., 2011; Perez et al., 2012) and daily hospitalization (Alessandrini et al., 2013). Asian dust, known as *kosa* in Japanese, originates from the Taklamakan and Gobi deserts and the Loess plateau of interior China. The dust is then blown eastwards by the westerly winds to countries such as Korea, Taiwan and Japan (Iwasaka et al., 2003; Minoura et al., 1998). Epidemiological studies show that *kosa* decreases peak expiratory flow values in patients with asthma (Park et al., 2005), and increases the number of hospitalizations and emergency visits through exacerbation of asthma (Kanatani et al., 2010; Yang et al., 2005). These findings are supported by experimental studies in which *kosa* inhalation enhanced allergen-induced airway inflammation in mouse models (Hiyoshi et al., 2005; Ichinose et al., 2008; Lei et al., 2004).

Asthma is a chronic inflammatory airway condition characterized by repetitive coughing, wheezing, dyspnea, reversible airway narrowing, and airway hyperresponsiveness (Ohta et al., 2011). The prevalence of asthma amongst Japanese adults has increased over the past decade (Fukutomi et al., 2010), and the number of patient suffering from chronic cough without wheezing or dyspnea has also increased in recent years. In Japan, most patients in the latter group are diagnosed with either cough variant asthma or atopic cough (Fujimura et al., 2005). Cough variant asthma is a precursor of asthma (Corrao et al., 1979; Irwin et al., 1997), whereas atopic cough is defined as a non-asthmatic bronchodilator-resistant chronic cough associated with atopy (Fujimura et al., 1992).

Chronic cough can result from hypersensitivity to environmental factors such as chemicals, cold air, and smoke (Matsumoto et al., 2012; Ternesten-Hasseus et al., 2011). Our preliminary data indicate that there are significantly more cough-positive patients during *kosa* period than non-*kosa* period among the adult patients with asthma, cough variant asthma, or atopic cough (Higashi et al., in press). In the present study, we assessed the relationship between exposure to *kosa* and cough occurrence among the same subjects by a panel study.

2. Methods

2.1 Subjects

We enrolled adult patients with physician-diagnosed at least one of asthma, cough variant asthma, or atopic cough between January 2011 and June 2011 at the Kanazawa University Hospital, Ishikawa Prefecture, Japan. This study was approved by the Medical Ethics Committee of Kanazawa University. All patients gave informed consent before participating in the study.

Asthma was diagnosed on the basis of the Japan Asthma Prevention and Management Guidelines 2011 (Ohta et al., 2011). Cough variant asthma was diagnosed using the criteria of the Japanese Cough Research Society (Kohno et al., 2006). Atopic cough was diagnosed according to previously reported criteria (Fujimura et al., 1992), which are based on bronchodilator-resistant cough and the resolution of the cough with the use of histamine H1 antagonists and/or inhaled corticosteroids (ICS).

Patients continued to take their usual medications, according to the standard medical treatment of each disease during the study period. Patients with asthma and cough variant

asthma took medications such as bronchodilator and/or ICS, and patients with atopic cough took medications such as histamine H1 antagonists and/or ICS. No patient experienced symptoms suggestive of chronic obstructive pulmonary diseases or other potentially confounding cardiorespiratory disorders.

2.2 Surveys

At the first consultation day during the study period, each patient was required to record his/her symptoms in a cough diary every day. The time period of study for each patient was from his/her first consultation day to the end of the study, June 30 for all. To prevent patients dropout based on lack of recording, we asked the patients to show their diary to the doctor when they visited the hospital during the study period. We used the data regarding the presence or absence of cough for analyzing the effects of *kosa* on coughing.

2.3 Measurements

The daily mean concentrations of *kosa* and spherical particles were estimated as described previously (Onishi et al., 2012). Briefly, we used the dust extinction coefficient and the sphere extinction coefficient derived from light detection and ranging (LIDAR) system with a polarization analyzer which distinguishes mineral dust particles that are non-spherical, including *kosa*, from spherical particles by identifying the differences in the shape of the particles (Iwasaka et al., 2004; Shimizu et al., 2004; Sugimoto et al., 2011). We used the data at the Toyama monitoring station (Imizu City, Toyama Prefecture, Japan) which is the nearest,

approximately 40 km east, from Kanazawa City. To obtain the daily near-surface extinction coefficients, the 6 h median values in 120- 1000 m height areas were averaged over 24 h. The concentrations of *kosa* and spherical particles were calculated by conversion factors from the dust extinction coefficient and the sphere extinction coefficient, respectively (Shimizu et al., 2011; Sugimoto et al., 2013).

The concentrations of particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) were monitored at a Mattou monitoring station (Hakusan City, Ishikawa Prefecture, Japan) which is the nearest, approximately 15.5 km west, from Kanazawa City. The temperature and rainfall were measured continuously at a Kodatsuno monitoring station in Kanazawa City.

2.4 Data Analysis

To evaluate the effects of *kosa* on cough, we used logistic regression with a generalized estimating equation which is suitable for correlated data in individuals (Janes et al., 2008; Jennrich and Schluchter, 1986; Liang and Zeger, 1986), according to previous reports (Cesaroni et al., 2008; Gehring et al., 2010; Ma et al., 2008). Briefly, in the model of,

$$\text{logit } P\,(Y_{it} = 1/X_{it}) = \beta_0 + \beta^{M} X_{it},$$

Y_{it} represent the binary outcome, population average occurrence of cough, for subject *i* at time *t*, and X_{it} represent *kosa* level at time *t*. In a marginal model, $P(Y_{it} = 1/X_{it})$ represent the occurrence of cough as a function of the *kosa* level (Janes et al., 2008; Leisenring et al., 1997; Martus et al., 2004). The marginal parameter, β^{M}, was estimated using generalized estimating equation with independent working correlation and robust standard errors. We categorized the *kosa* concentration into five grades as follows: Grade 1, equated to 0 μg/m^3; Grade 2, 0–10 μg/m^3; Grade 3, 10–30 μg/m^3; Grade 4, 30–100 μg/m^3; and Grade 5, over 100 μg/m^3. It was

reported that the standard threshold of the dust concentration for an Asian dust day was 100 μg/m^3 (Sugimoto et al., 2003). Besides these days, the typical *kosa* days were identified as increase in the LIDAR signal of more than 30μg/m^3 in this study period. We used these values for setting up the grades of *kosa* concentration. The odds ratios (ORs) with 95% confidence intervals (CIs) were calculated relative to the referent level (Grade 1) after adjustment for sex, age, body mass index (BMI), temperature, and rain. In addition, seasonality was included in the model as categorical variables: winter (January and February) and spring (from March to June). The concentration of spherical particles and $PM_{2.5}$ were categorized into quartiles and the ORs with 95% (CIs) were calculated above the referent (first quartile). The time lag from the exposure to cough occurrence was taken into consideration (Lag 0 – Lag 3). Two-pollutant model included sex, age, body mass index (BMI), temperature, rain, seasonality, *kosa*, and spherical particles or $PM_{2.5}$. All statistical analyses were performed using the SPSS® 19.0 software (SPSS Inc., Chicago, IL, USA).

3. Results

3.1 Descriptive Statistics

Of 104 patients aged 23–84 years who gave informed consent, 90 (86.5%) completed the cough diary, and were enrolled in our study. However, we excluded four patients because they were current smokers. Therefore, we studied 86 adults (28 males and 58 females) with a mean ± standard deviation (SD) age of 64.0 ± 12.7 years and a physician- diagnosis of at least one of the following conditions: asthma, cough variant asthma, or atopic cough (Table 1). We compared the subgroups of subjects with and without a diagnosis of asthma. Subgroups with

asthma consisted of 49 patients with asthma and 4 patients with asthma and atopic cough. Of 33 subjects without asthma, eight, 15, and 10 patients were diagnosed with cough variant asthma, atopic cough, and cough variant asthma and atopic cough, respectively. The age distribution, gender ratio and BMI were not different between two subgroups. The prevalence of cough was significantly different between two subgroups with medians of 7.8 (interquartile range (IQR), 32.2) and 66.7 (IQR, 72.7) in subjects with and without asthma, respectively ($p< 0.001$, Table 1). Throughout the study period, the daily prevalence of cough was higher in subjects without asthma than with asthma, as shown in Figure 1A.

The daily concentrations of dust (*kosa*) particles, spherical particles and $PM_{2.5}$ during the study period are shown in Figure 1B. Typical large-scale *kosa* events were identified on May 2, 3 and 13 as remarkable increase in the LIDAR signal (>100μg/m^3; Grade 5) as shown in Figure 1B. Increases in the dust concentration (30-100 μg/m^3; Grade 4) were also observed 12 days such as April 10 to 15 and May 14 to 16. Weak increases in the dust concentration (10 -30 μg/m^3; Grade 3) were recorded for 46 days. In these days of Grade 5, 4, and 3, 91.5%, 93.2% and 86.1% of the subjects recorded their diaries, respectively. The concentration of dust (*kosa*) particles correlated with the concentration of spherical particles and $PM_{2.5}$ with Pearson's correlation coefficients of 0.252 ($p< 0.001$, Figure 2A) and 0.519 ($p< 0.001$, Figure 2B), respectively. At the extremely high *kosa* days (>100μg/m^3; Grade 5), the concentration of $PM_{2.5}$ correlated with the dust (*kosa*) particles, although spherical particles had no correlation (Figure 2).

3.2. Cough and Exposure to Particulate Matters

To analyze the relationship between *kosa* levels and cough occurrence, the

concentrations of *kosa* were categorized into five grades. The adjusted ORs with 95% CIs of cough occurrence, as calculated relative to the lowest level (Grade 1) of *kosa* concentration using single-pollutant models adjusted for sex, age (years), BMI, temperature, rain, and seasonality were shown in Table 2. *Kosa* concentrations were significantly associated with cough occurrence on the day of exposure (Lag 0) in total subjects following a dose-response manner, with ORs for Grade 2, 3, 4, and 5 of 1.111 (95% CI: 0.995–1.239), 1.171 (95% CI: 1.006–1.363), 1.357 (95% CI: 1.029–1.788), and 1.414 (95% CI: 0.983–2.036), respectively. The ORs in subjects without asthma were higher than in total subjects; the ORs for Grade 2, 3, 4 and 5 were 1.223 (95% CI: 0.999–1.497), 1.309 (95% CI: 0.987–1.737), 1.738 (95% CI: 1.029–2.935) and 2.403 (95% CI: 1.158–4.985), respectively. On the other hand, association was not observed between *kosa* and cough symptoms among subjects with asthma. The time lag effect from *kosa* exposure to cough occurrence was observed for one day following exposure (Lag 1) and up to three days following exposure (to Lag 3), although the ORs for Lag 1-3 were lower than for Lag 0 in total subjects and subjects without asthma (Table2).

Similarly, the relationship between spherical particle level and cough occurrence were analyzed. Subjects without asthma were more likely to have association with cough from Lag 0 to Lag 2 (Table 3), whereas the values of ORs were lower than ORs for *kosa* exposure. Subjects with asthma characteristically exhibited association with cough at Lag 3; the ORs for 2nd, 3rd and 4th compared to reference (1st) were 1.023 (95% CI: 0.912–1.148), 1.193 (95% CI: 1.004–1.418) and 1.245 (95% CI: 1.020–1.519), respectively (Table 3). When we analyzed the relationship between $PM_{2.5}$ and cough, the association was evidently observed among subjects without asthma at Lag 0 with statistically significant interaction; the ORs for 2nd, 3rd and 4th were 1.271 (95% CI: 1.043–1.548), 1.267 (95% CI: 1.019–1.574) and 1.411 (95% CI: 1.101–1.808), respectively (Table 4).

Then, we investigated whether cough occurrence was dependent on the quantity of *kosa* or other spherical particles and $PM_{2.5}$. The effects of *kosa* on cough on the day of exposure (Lag 0) were similar in two-pollutant models adjusting for presence of spherical particles (Figure 3A): ORs of subjects without asthma for Grade 2, 3, 4, and 5 were 1.196 (95% CI: 0.898–1.594), 1.260 (95% CI: 0.909–1.747), 1.738 (95% CI: 0.981–3.081) and, 2.260 (95% CI: 1.032–4.953), respectively. And, while somewhat attenuated, the effects of *kosa* on cough were also suggestive in two-pollutant models adjusting for $PM_{2.5}$ (Figure 3B): ORs of subjects without asthma for Grade 2, 3, 4, and 5 were 1.208 (95% CI: 0.989–1.476), 1. 272 (95% CI: 0.978–1.653), 1.631 (95% CI: 0.984–2.7041), and 2.198 (95% CI: 1.079–4.479), respectively. These results indicate that adversely *kosa* effect on cough was independent of other spherical particles or $PM_{2.5}$.

4. Discussion

The main aim of this study was to evaluate the relationship between exposure to *kosa* and cough occurrence in adult patients suffering from at least one of the following: asthma, cough variant asthma, or atopic cough. We demonstrated a significant association between *kosa* and cough in patients with chronic cough. This association was particularly high among subjects without asthma, whereas no association was found in subjects with asthma. With respect to patients with asthma, our findings were consistent with a previous panel study which reported no association between *kosa* and cough among patients with asthma in Korea (Park et al., 2005). In this study, the subjects without asthma consisted of patients with cough variant asthma and/or atopic cough. As far as we know, this is the first study to demonstrate the dose-response relation between *kosa* exposure and cough occurrence in patient with cough variant asthma and/or atopic

cough. A cross-sectional study showed that more than 60% of patients with chronic unexplained cough reported that coughing was induced by environmental factors and that this had a negative impact on health status and daily life (Ternesten-Hasseus et al., 2011). These factors included chemicals, scents, exercise, and cold air. Our findings showed that in addition to these, *kosa* is an environmental factor that can induce cough among patients with chronic cough.

In our assessment of the health effects of dust, data were measured with the LIDAR system, which distinguishes mineral dust particles from spherical particles by identifying the differences in the shape of the particles (Shimizu et al., 2011; Sugimoto et al., 2013). Thus, it can specifically estimate each concentration of *kosa* and spherical particles (Shimizu et al., 2011; Sugimoto et al., 2013). Because spherical particles and $PM_{2.5}$ adversely affect respiratory diseases (Brunekreef et al., 1995; Dockery et al., 1993; Peng et al., 2008; Pope et al., 1995), it remains unclear whether adverse effects in Asian dust days are dependent on the quantity of *kosa* or other particles. In this study, we clearly demonstrated that *kosa* effect on cough was independent of other particles in two-pollutant model adjusting for spherical particles or $PM_{2.5}$, whereas association between cough and spherical particles or $PM_{2.5}$ was observed in single-pollutant model. However, there is a limitation of the assessment of exposure. Because observation stations of LIDAR and $PM_{2.5}$ were limited, we used the data at the nearest stations from Kanazawa city. There was possibility that data at the observation station was not always reflective of the concentration of study area and the individual exposures.

Time series analyses have shown that *kosa* is associated with the mortality of circulatory and respiratory diseases (Kashima et al., 2012), hospitalization for cerebrovascular disease (Bell et al., 2008), and the variability of peak expiratory flow values in patients with asthma (Park et al., 2005) in a dose-response manner. However, an association has not been established regarding cough. We have shown that *kosa* also affects cough among patients with

chronic cough in a dose-response manner. The Japan Meteorological Agency defines a *kosa* day—the occurrence of a *kosa* event—as a day when visibility is <10 km in a Japanese city. The standard threshold of dust concentrations for a *kosa* day is approximately 100 μg/m^3. We demonstrated that adverse respiratory symptoms increased at levels of exposure as low as 10–30 μg/m^3, which are not detectable by visible observation. This represents an important, and potentially manageable, public health issue.

A time lag occurs when surveying patients who visit the hospital because most patients visit the hospital the day after exposure, when the majority of severe symptoms are relieved. However, we were able to eliminate this effect in the present study by using cough diaries that were recorded on the day of exposure. The data obtained from these diaries clarified that exposure to *kosa* induces cough on the same day of exposure (Lag 0). In addition, the cough remained association with *kosa* for up to three lag days, indicating prolonged effects of *kosa*.

In this study, patients had different comorbidities and continued to take their usual medications, according to the standard medical treatment of each disease. The severity of disease status and medication use may have effects on the cough symptoms and act as confounders. Our study subjects included the patients who had no cough symptoms throughout the study period, implying the possibility that there are missing covariate data which ignores subjects with incomplete information. It may be necessary to approach in other models including missing covariates (Janssen et al., 2010; Lipsitz et al., 1999). Moreover, confirmation of whether symptoms vary with asthma, cough variant asthma, and atopic cough, and the determination of additional environmental factors that adversely affect these respiratory diseases, including chemical factors, metals, pollens, and microorganism, (Maki et al., 2010; Onishi et al., 2012) are required. Further studies with larger sample sizes will help address these issues.

5. Conclusions

A dose-response relationship between *kosa* and daily cough occurrence and potential lag effects were observed in this study. Adversely *kosa* effect on cough was independent of other spherical particles or $PM_{2.5}$. Our findings demonstrated that *kosa* is an environmental factor which induces cough in patients with chronic cough, especially with cough variant asthma and/or atopic cough.

Conflict of interest

The authors declare that they have no conflicts of interest.

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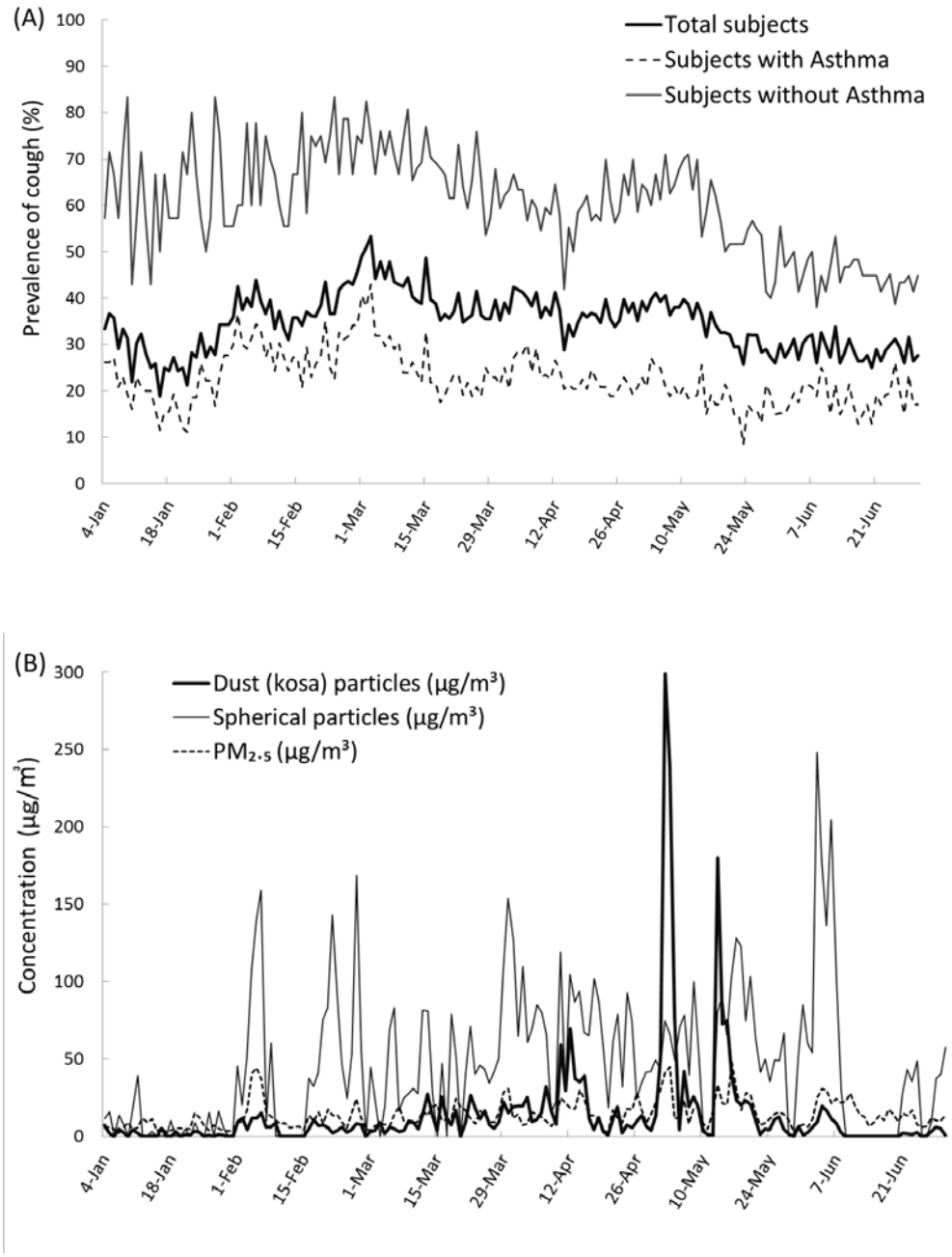
Figure legends

Figure 1. The daily cough prevalence among total subjects, subjects with and without a diagnosis of asthma (A) and daily concentrations of airborne particulate matter during the study period (B).

Figure 2. Scatter plots of Dust (*kosa*) particles and Spherical particles (A) and $PM_{2.5}$ (B). *: $p < 0.001$, Pearson's correlation coefficient

Figure 3. Adjusted odds ratios (ORs) for relationship between cough symptoms and concentration of Dust (*kosa*) particles on the day of exposure (Lag 0) in the two-pollutant model with spherical particles (A) and $PM_{2.5}$ (B). The model includes sex, age, BMI, temperature, rain, seasonality, *kosa* and spherical particles (A) and $PM_{2.5}$ (B). ORs are estimated by using generalized estimating equations with independent working correlation. Error bars represent 95% confidence intervals.



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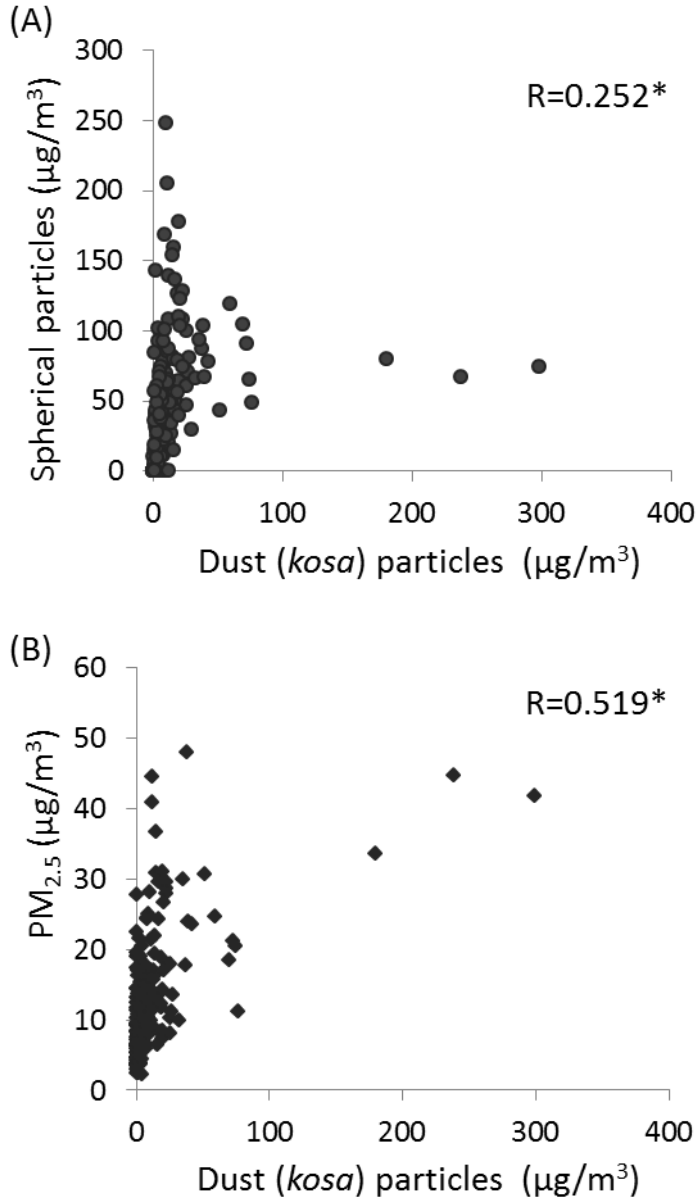

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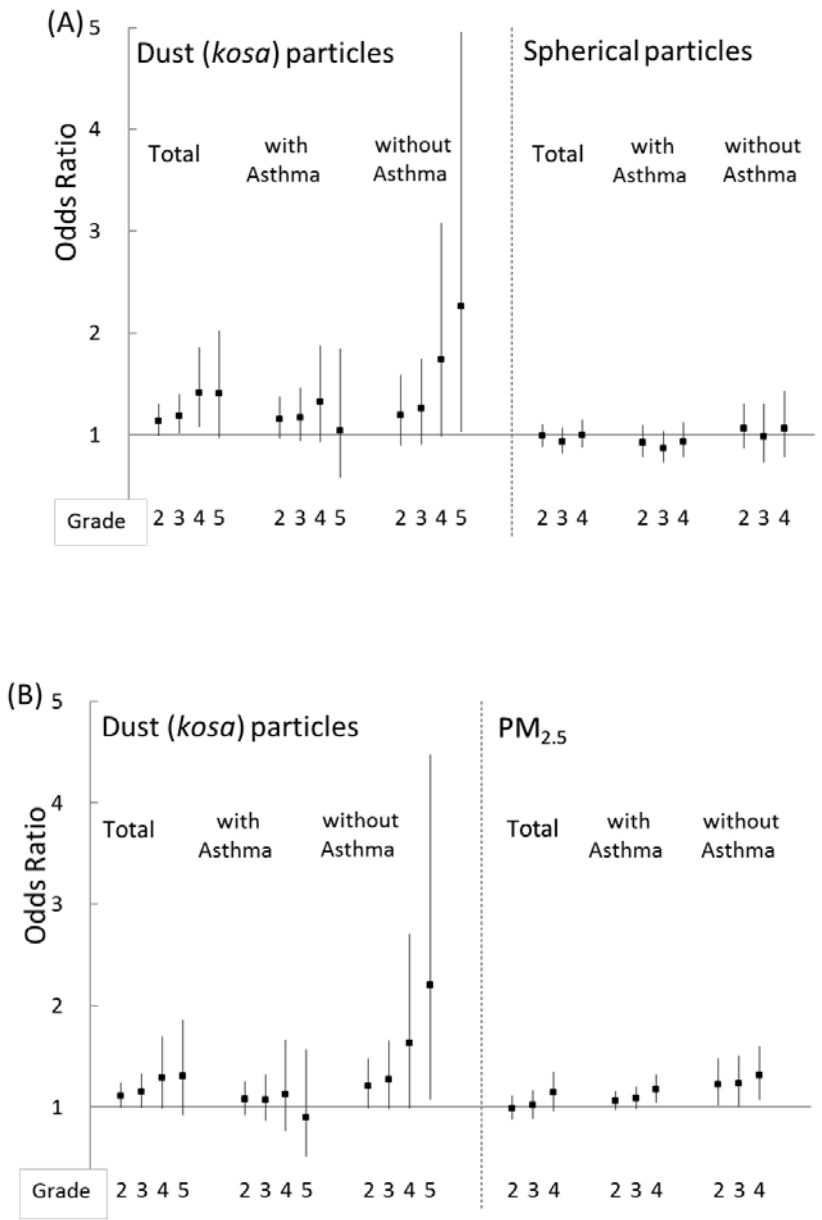

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Table1. Characteristics of the study subjects

	Total subjects (n = 86)	Subjects with Asthma (n = 53)	Subjects without Asthma (n = 33)
Age (years)	64.0 ± 12.7	65.7 ± 12.0	61.1 ± 13.4
Gender			
Male	28 (32.6)	19 (35.8)	9 (27.3)
Female	58 (67.4)	34 (64.2)	24 (72.7)
BMI (kg/m^2)	22.8 ± 3.3	22.7 ± 2.8	22.9 ± 4.0
Disease			
Asthma	49 (57.0)	49 (92.5)	-
CVA	8 (9.3)	-	8 (24.2)
AC	15 (17.4)	-	15 (45.5)
Asthma and AC	4 (4.7)	4 (7.5)	-
CVA and AC	10 (11.6)	-	10 (30.3)
Disease duration (years)	15.6 ± 9.4	17.9 ± 9.8	12.1 ± 7.6
Smoking status			
non-smoker	60（69.8)	32（60.4)	28（84.8)
ex-smoker	26 (30.2)	21 (39.6)	5 (15.2)
Number of recorded days	124.9 ± 51.0	142.5 ± 39.5	96.7 ± 55.0
Prevalence of cough (%)*			
Mean ± SD	35.9 ± 36.9	22.6 ± 30.8	57.2 ± 36.3
Median (IQR, range)†	20.3 (65.3, 0-100)	7.8 (32.2, 0-100)	66.7 (72.7, 0-100)
Time period of study (day)**	134.9 ± 22.2	142.4 ± 17.7	122.8 ± 23.7

Data are presented as the no (%) or mean ± SD.

CVA, cough variant asthma; AC, atopic cough

* (Number of days with cough)/ (Number of recorded days)

** From the entry (the first consultation day during study period for each subject) to the end of study (30 June for all)

†: $p < 0.001$, with Asthma vs. without Asthma, by Mann-Whitney's U test

Table 2. **Adjusted odds ratios and 95% confidence intervals for cough symptoms associated with Dust (*kosa*) concentration at various exposure lags in the single-pollutant model**

	number of days	Total subjects (n = 86) OR†	95% CI			Subjects with Asthma (n=53) OR†	95% CI			Subjects without Asthma (n=33)† OR†	95% CI		
Lag 0													
Dust (μg/m^3)													
Grade 5: 100 -	3	1.414	0.983	2.036		0.981	0.547	1.759		2.403	1.158	4.985	*
Grade 4: 30 -100	12	1.357	1.029	1.788	*	1.186	0.811	1.735		1.738	1.029	2.935	*
Grade 3: 10 -30	46	1.171	1.006	1.363	*	1.084	0.875	1.344		1.309	0.987	1.737	
Grade 2: -10	84	1.111	0.995	1.239		1.062	0.914	1.236		1.223	0.999	1.497	
Grade 1: 0	33	1				1				1			
Lag 1													
Dust (μg/m^3)													
Grade 5: 100 -	3	1.261	0.853	1.864		1.366	0.797	2.343		1.139	0.565	2.295	
Grade 4: 30 -100	12	1.284	0.977	1.688		1.128	0.788	1.614		1.567	0.931	2.638	
Grade 3: 10 -30	46	1.209	1.043	1.402	*	1.034	0.846	1.262		1.511	1.159	1.971	*
Grade 2: -10	84	1.145	1.020	1.284	*	1.086	0.923	1.277		1.250	1.023	1.527	*
Grade 1: 0	33	1	.	.		1	.	.		1	.	.	
Lag 2													
Dust (μg/m^3)													
Grade 5: 100 -	3	0.986	0.675	1.439		0.712	0.399	1.270		1.261	0.591	2.691	
Grade 4: 30 -100	12	1.239	0.950	1.617		1.165	0.819	1.657		1.346	0.797	2.273	
Grade 3: 10 -30	46	1.155	0.995	1.342		1.065	0.872	1.300		1.264	0.926	1.725	
Grade 2: -10	84	1.066	0.950	1.197		1.091	0.916	1.301		0.988	0.809	1.208	
Grade 1: 0	33	1	.	.		1	.	.		1	.	.	
Lag 3													
Dust (μg/m^3)													
Grade 5: 100 -	3	1.267	0.917	1.749		1.029	0.592	1.787		1.655	0.939	2.916	
Grade 4: 30 -100	12	1.333	1.025	1.733	*	1.338	0.973	1.840		1.369	0.796	2.352	
Grade 3: 10 -30	46	1.132	0.973	1.318		1.125	0.913	1.386		1.115	0.821	1.513	
Grade 2: -10	84	1.077	0.977	1.188		1.101	0.956	1.268		1.032	0.856	1.245	
Grade 1: 0	33	1	.	.		1	.	.		1	.	.	

†: Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for cough symptoms relative to the concentration of dust (*kosa*), adjusted for sex, age, BMI, temperature, rain and seasonality.

* : $p < 0.05$

Table 3. Adjusted odds ratios and 95% confidence intervals for cough symptoms associated with concentration of spherical particles (Sphere) at various exposure lags in the single-pollutant model

	Total subjects (n = 86)				Subjects with Asthma (n=53)				Subjects without Asthma (n=33)†			
	OR†	95% CI			OR†	95% CI			OR†	95% CI		
Lag 0												
Sphere (quartiles, μg/m^3)												
4th: 70.5 -248.2	1.135	0.987	1.304		1.033	0.855	1.248		1.293	0.979	1.707	
3rd: 40.3 -70.5	1.045	0.928	1.177		0.965	0.805	1.157		1.152	0.933	1.421	
2nd: 1.3 -40.3	1.078	0.978	1.190		1.014	0.884	1.163		1.205	0.998	1.455	
1st: 0.0 -1.3	1	.	.		1	.	.		1	.	.	
Lag 1												
Sphere (quartiles, μg/m^3)												
4th: 70.5 -248.2	1.197	1.036	1.382	*	1.131	0.928	1.378		1.299	0.993	1.699	
3rd: 40.3 -70.5	1.167	1.043	1.306	*	1.146	0.958	1.371		1.219	1.020	1.458	*
2nd: 1.3 -40.3	1.156	1.042	1.281	*	1.096	0.957	1.255		1.270	1.024	1.575	*
1st: 0.0 -1.3	1	.	.		1	.	.		1	.	.	
Lag 2												
Sphere (quartiles, μg/m^3)												
4th: 70.5 -248.2	1.154	1.010	1.319	*	1.141	0.947	1.375		1.173	0.900	1.529	
3rd: 40.3 -70.5	1.098	0.985	1.225		1.129	0.941	1.354		1.050	0.892	1.235	
2nd: 1.3 -40.3	1.050	0.971	1.136		1.025	0.928	1.133		1.066	0.891	1.275	
1st: 0.0 -1.3	1	.	.		1	.	.		1	.	.	
Lag 3												
Sphere (quartiles, μg/m^3)												
4th: 70.5 -248.2	1.200	1.043	1.380	*	1.245	1.020	1.519	*	1.174	0.903	1.527	
3rd: 40.3 -70.5	1.141	1.022	1.272	*	1.193	1.004	1.418	*	1.065	0.886	1.280	
2nd: 1.3 -40.3	1.090	0.995	1.194		1.023	0.912	1.148		1.186	0.972	1.447	
1st: 0.0 -1.3	1	.	.		1	.	.		1	.	.	

†: Adjusted odds ratios(ORs) and 95% confidence intervals (CIs) for cough symptoms relative to the concentration of spherical particles, adjusted for, sex, age, BMI, temperature, rain and seasonality.

* : $p < 0.05$

Table 4. **Adjusted odds ratios and 95% confidence intervals for cough symptoms associated with $PM_{2.5}$ concentration at various lags of exposure in the single-pollutant model**

		Total subjects (n = 86)				Subjects with Asthma (n=53)				Subjects without Asthma (n=33)†			
		OR†	95% CI			OR†	95% CI			OR†	95% CI		
Lag 0													
$PM_{2.5}$ (quartiles, μg/m^3)													
4th: 17.3	-48.0	1.218	1.067	1.392	*	1.147	0.962	1.368		1.411	1.101	1.808	*
3rd: 11.9	-17.3	1.105	0.992	1.231		1.035	0.898	1.193		1.267	1.019	1.574	*
2nd: 7.8	-11.9	1.082	0.987	1.187		0.998	0.890	1.118		1.271	1.043	1.548	*
1st: 2.2	-7.8	1	.	.		1	.	.		1	.	.	
Lag 1													
$PM_{2.5}$ (quartiles, μg/m^3)													
4th: 17.3	-48.0	1.147	0.990	1.328		1.092	0.904	1.319		1.249	0.927	1.683	
3rd: 11.9	-17.3	1.112	0.990	1.248		1.047	0.909	1.206		1.246	0.970	1.602	
2nd: 7.8	-11.9	1.030	0.939	1.130		0.992	0.882	1.115		1.080	0.876	1.331	
1st: 2.2	-7.8	1	.	.		1	.	.		1	.	.	
Lag 2													
$PM_{2.5}$ (quartiles, μg/m^3)													
4th: 17.3	-48.0	1.144	0.991	1.322		1.079	0.874	1.332		1.300	1.019	1.659	*
3rd: 11.9	-17.3	1.081	0.959	1.220		1.099	0.915	1.319		1.085	0.897	1.312	
2nd: 7.8	-11.9	0.965	0.871	1.070		0.933	0.794	1.096		0.988	0.836	1.167	
1st: 2.2	-7.8	1	.	.		1	.	.		1	.	.	
Lag 3													
$PM_{2.5}$ (quartiles, μg/m^3)													
4th: 17.3	-48.0	1.175	1.035	1.334	*	1.143	0.962	1.358		1.345	1.057	1.712	*
3rd: 11.9	-17.3	1.108	0.984	1.247		1.170	0.992	1.380		1.076	0.864	1.340	
2nd: 7.8	-11.9	1.018	0.926	1.119		0.937	0.802	1.094		1.163	0.988	1.369	
1st: 2.2	-7.8	1	.	.		1	.	.		1	.	.	

†: Adjusted odds ratios(ORs) and 95% confidence intervals (CIs) for cough symptoms relative to the concentration of $PM_{2.5}$, adjusted for sex, age, BMI, temperature, rain and seasonality.

* : $p < 0.05$