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Cross-sectional study of asthma and rhinitis symptoms in the context of exposure to air pollution in Nepal

To the Editor:

Asthma is common in children worldwide, although its prevalence varies substantially by location. The prevalence of wheeze over a 12-month period ranged from 2.1% to 32.2% in the older age group (13–14 years) and 4.1% to 32.1% in the younger age group (6–7 years) [1]. There is a positive association between current symptoms of asthma in younger and older children with gross national income [2], and it is generally slightly less common in girls than boys in the younger group [1–3]. Exposure to air pollution is associated with asthma exacerbations. Odds ratios for wheeze in the past year and the use of solely an open fire for cooking were 2.17 (95% CI 1.64–2.87) for children aged 6–7 years and 1.35 (95% CI 1.11–1.64) for children aged 13–14 years [4]. Nepalese children are exposed to high levels of indoor air pollution from the burning of biomass fuels [5]. This study aimed to estimate their prevalence of asthma, and to investigate the association of air pollution and risk of wheeze and rhinitis symptoms using personal exposure estimates of air pollution.

The study was included in a larger follow-up of a double-blind randomised controlled trial of antenatal multiple micronutrient (MMN) supplementation, in which participating children were seen at 7–9 years of age [6, 7]. At a mean age of 8.5 years, there was no effect of antenatal MMN on child growth or lung function. Nepali and Maithili versions of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaires were administered to their parents after informed consent. The ISAAC questionnaires were developed to detect the prevalence of asthma, rhinitis and eczema. The study was not part of the ISAAC collaboration. The main outcomes were wheeze, dry cough and runny nose in the last 12 months.

The method of air pollution measurement has been described in detail elsewhere [5]. Briefly, air pollution exposure was assessed by estimating microenvironment respirable particle mass (particulate matter with an aerodynamic diameter $\leqslant 4$ µm (PM_4)) using both gravimetric and photometric sampling (in the bedroom, in the kitchen during and between cooking, outdoors, at school, and on the verandah) in a subsample of children three times over a year. Time activity data were collected from all children using a structured questionnaire, dividing the day in 30-min time slots, and a 24-h time-weighted-average was calculated for an average school day for each child.

A directed acyclic graph based on *a priori* knowledge was constructed, from which potential confounding factors were selected for inclusion in multivariable logistic regression models, for boys and girls separately. Socioeconomic circumstances, maternal education, household tobacco smoke exposure, and urban *versus* rural residence were controlled for and, to account for the initial trial, a covariate for original allocation to multiple micronutrient supplements was included in the model. A socioeconomic score was derived from principal component analysis of variables including household assets and house structure. To explore the association between air pollution and dry cough, we used the same statistical methods as above with the exposure variable divided into tertiles (the numbers were too small to investigate wheeze and sneezing in this way) as an ordered categorical variable. Statistical analysis was carried out using Excel (Microsoft Corp., Redmond, WA, USA) and Stata (Stata Corp., College Station, TX, USA).

The study was approved by the University College London research ethics board and the Nepal Health Research Council. Informed consent was obtained from all participants in their native language.

Questionnaire data were obtained from all available children in the follow-up study (n=848) at a mean age of 8.5 years. 14 children were excluded from the analysis as they were from outside the region (where we did not have air pollution estimates). While 12.8% (n=52) of girls and 16.3% (n=70) of boys had a history of wheezing or whistling "ever", there was a very low prevalence of recent wheeze (2.2% of girls and 1.6% of boys in the last 12 months). A further six children who were not detected by the ISAAC questionnaire had a doctor diagnosis of asthma. In contrast, dry cough at night was very common, being reported for 22.2% of girls and 25.2% of boys in the last year. 10.4% of girls and 10.3% of boys had "a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu" in the last 12 months, and these were slightly more common during winter.

In total, 247 exposure measurements were collected from 55 households (6.6% of the cohort), eight representative outdoor locations and eight schools, amounting to 2649 h of pollution monitoring. The mean±SD 24-h time-weighted average was 168±25.9 $\mu g \cdot m^{-3}$, with no sex difference. 63% of exposure occurred in the home, 16% at school and the remainder outside.

The association of air pollution with wheeze, dry cough and sneezing, and runny or blocked nose is shown in table 1. In girls, there was no association with any of the outcomes investigated in univariable or multivariable regression models. In boys, there was an association with dry cough at night: odds ratio 1.14 (95% CI 1.04–1.25) for a 10-$\mu g \cdot m^{-3}$ increase in air pollution. There was no association with sneezing, or runny or blocked nose. In comparison with the lowest tertile of air pollution, the odds ratio in boys for dry cough at night was 1.45 (95% CI 0.81–2.59) for the middle tertile and 2.14 (95% CI 1.21–3.77) for the upper.

Using standard data collection methods, we documented a low prevalence of wheeze overall and severe symptoms were rare. The prevalence of wheeze was low compared with worldwide figures, but was in keeping with a review of studies from Nepal that showed a prevalence of 6% [8] and a review from India that found a median prevalence of 4.8%, with some studies reporting <1% [9]. The only common symptom was dry cough at night, reported in the last year by ∼25% of the sample. This may reflect high local air pollution levels and the dusty nature of the region outside the rainy season. In keeping with our results, a review of the evidence showed an association of air pollution with cough alone [10].

We believe that ours was the first study to use personal exposure estimates for air pollution. Overall, we did not find an association between PM_4 and symptoms of asthma or rhinitis, except for dry cough and wheeze in the last 12 months among boys. While air pollution is known to be associated with exacerbations of asthma, the evidence of it playing a role in primary causation of asthma is mixed and is based mostly on data from high-income countries [2]. Data from Nepal suggest there are increased odds of asthma or wheeze associated with biomass fuels [8, 11] but worldwide estimates have shown no association between PM_{10} and current wheeze [12], and a large multicentre comparison of asthma prevalence showed an inverse association overall, but the results were inconsistent [2].

At the age of our study subjects, exposure to air pollution was similar in boys and girls, as the children were generally not involved in cooking. It is possible that the sex difference in association with cough was related to boys having a narrower airway calibre before puberty [13].

The lack of association with most outcomes in our study may be a true phenomenon. Other possibilities derive from the limited inferences of a cross-sectional design, the fact that particle mass estimates were based on modelled data and might not account for all airborne toxins, and that the public hospital sample did not include the very richest and poorest tails of the socioeconomic distribution. It is also possible that potential associations between air pollution and respiratory illness were masked by the children in our study being exposed to much higher average concentrations of air pollution than experienced by most children in high-income countries.

TABLE 1 Associations between air pollution and International Study of Asthma and Allergies in Childhood outcomes for 834 children in southern Nepal in 2012

	Univariable regression		Multivariable regression#	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Wheeze in the last 12 months				
Girls	0.93 (0.69–1.25)	0.620	1.10 (0.80–1.53)	0.551
Boys	1.41 (0.96–2.08)	0.078	1.52 (0.98–2.36)	0.062
Dry cough at night in the last 12 months				
Girls	0.99 (0.91–1.08)	0.864	1.00 (0.92–1.10)	0.930
Boys	1.16 (1.06–1.27)	0.001	1.14 (1.04–1.25)	0.004
Sneezing/runny, or blocked nose in last 12 months				
Girls	0.96 (0.69–1.35)	0.830	0.83 (0.50–1.37)	0.459
Boys	1.19 (0.89–1.60)	0.235	1.19 (0.86–1.65)	0.295

The odds ratios indicate the increased risk of a 10-$\mu g \cdot m^{-3}$ increase in particulate matter with an aerodynamic diameter ⩽4 μm (24-h time-weighted average). #: adjusted for socioeconomic circumstances, maternal education, presence of a smoker in the household and urban or rural residence.

In summary, participants described a low prevalence of asthma and rhinitis symptoms, consistent with other studies from South Asia. Air pollution levels were high in general but a specific association was seen only with cough at night in boys.

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Amongst children in rural Nepal, an association of dry cough with air pollution was seen only in boys http://ow.ly/MOa5u

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