Traffic related air pollution as a determinant of asthma among Taiwanese school children

B-F Hwang, Y-L Lee, Y-C Lin, J J K Jaakkola, Y L Guo

Background: There is evidence that long term exposure to ambient air pollution increases the risk of childhood asthma, but the role of different sources and components needs further elaboration. To assess the effect of air pollutants on the risk of asthma among school children, a nationwide cross sectional study of 32 672 Taiwanese school children was conducted in 2001.

Methods: Routine air pollution monitoring data for sulphur dioxide (SO\(_2\)), nitrogen oxides (NO\(_x\)), ozone (O\(_3\)), carbon monoxide (CO), and particles with an aerodynamic diameter of 10 \(\mu\)m or less (PM\(_{10}\)) were used. Information on individual characteristics and indoor environments was from a parent administered questionnaire (response rate 93%). The exposure parameters were calculated using the mean of the 2000 monthly averages. The effect estimates were presented as odds ratios (ORs) per 10 ppb changes for SO\(_2\), NO\(_x\), and O\(_3\), 100 ppb changes for CO, and 10 \(\mu\)g/m\(^3\) changes for PM\(_{10}\).

Results: In a two stage hierarchical model adjusting for confounding, the risk of childhood asthma was positively associated with O\(_3\) (adjusted OR 1.138, 95% confidence interval (CI) 1.001 to 1.293), CO (adjusted OR 1.045, 95% CI 1.017 to 1.074), and NO\(_x\) (adjusted OR 1.005, 95% CI 0.954 to 1.117). Against our prior hypothesis, the risk of childhood asthma was weakly or not related to SO\(_2\) (adjusted OR 0.874, 95% CI 0.729 to 1.054) and PM\(_{10}\) (adjusted OR 0.934, 95% CI 0.909 to 0.960).

Conclusions: The results are consistent with the hypothesis that long term exposure to traffic related outdoor air pollutants such as NO\(_x\), CO, and O\(_3\) increases the risk of asthma in children.

There is a large worldwide variation in the prevalence of asthma in children and there is also evidence that the prevalence has been increasing.\(^1\) Both genetic and environmental factors play important roles in the aetiology of childhood asthma, and there is probably also genetic susceptibility to the effects of air pollution.\(^2\) Short term changes in the occurrence of asthma are more likely to be influenced by changes in the environment, diet, and lifestyle than by changes in the genetic pool. From a preventive perspective, information on environmental, dietary, and behavioural factors is crucial.\(^3\) Identification of indicators of genetic susceptibility to environmental exposures could be useful from the preventative point of view. There is evidence that long term exposure to ambient air pollution increases the risk of childhood asthma, but the role of different sources and components needs further elaboration.\(^4\)\(^-\)\(^12\)

In a nationwide cross sectional study in Taiwan, Guo et al found an association between traffic related air pollution concentrations and the risk of asthma in school children.\(^13\) This study did not adjust for parental atopy or indoor exposures which are potential sources of confounding and effect modification. In 2001 we conducted a new nationwide cross sectional study in which we also collected information on these important potential determinants of allergic disease in children.

In the present study we have elaborated the relation between exposure to urban air pollution and the risk of asthma in school children, focusing on predominantly traffic related pollutants such as nitrogen oxides (NO\(_x\)), ozone (O\(_3\)), and carbon monoxide (CO). We also assessed the role of air pollutants, mainly from other fossil fuel combustion sources such as sulphur dioxide (SO\(_2\)), and particles with an aerodynamic diameter of 10 \(\mu\)m or less (PM\(_{10}\)). Furthermore, we studied the joint effects of parental atopy and outdoor air pollution on the risk of asthma. Parental asthma, allergic rhinitis, and allergic atopic eczema were used as surrogates of the genes that are responsible for susceptibility to the effects of air pollutants on asthma. We applied a two stage hierarchical model to adjust for confounding and to elaborate effect modification at the individual level and to assess the effects of air pollution at the municipal level.\(^14\)\(^-\)\(^15\)

METHODS

Data collection and study population

A nationwide cross sectional study was conducted in Taiwan in 2001 where a modified Chinese version of the International Study of Asthma and Allergies in Childhood (ISAAC-C) questionnaire was used to collect information on children's health, environmental exposures, and other relevant factors.\(^16\) The study population was recruited from elementary and middle schools in 22 municipalities within 1 km from Taiwan Environmental Protection Agency (EPA) air monitoring stations. The questionnaire was taken home by students and answered by parents. A total of 35 036 children aged 6–15 years were approached. The response rate was 93.2%. 2364 children were excluded because of an incomplete questionnaire, leaving a final study population of 32 672 schoolchildren.

The study protocol was approved by the Respiratory Health Screening Steering Committee of the Taiwan Department of Health and the Institutional Review Board of National Cheng Kung University Hospital, and it complied with the principles outlined in the Helsinki Declaration.\(^17\)

Health outcome

The outcome of interest was childhood asthma, which was defined on the basis of the answer to the question: "Has a physician ever diagnosed your child as having asthma?".

Abbreviations: CO, carbon monoxide; NO\(_x\), nitrogen oxides; O\(_3\), ozone; PM\(_{10}\), particles with aerodynamic diameter 10 \(\mu\)m or less; SO\(_2\), sulphur dioxide.
Exposure assessment
Complete monitoring data for the air pollutants including sulphur dioxide (SO₂), nitrogen oxides (NOx), ozone (O₃), carbon monoxide (CO), and particles with an aerodynamic diameter of 10 μm or less (PM₁₀), as well as daily temperature and relative humidity, are available from 1994 for 22 EPA monitoring stations on Taiwan’s main island (fig 1). Concentrations of each pollutant are measured continuously and reported hourly—CO by non-dispersive infrared absorption, NOx by chemiluminescence, O₃ by ultraviolet absorption, SO₂ by ultraviolet fluorescence, and PM₁₀ by beta-gauge. Exposure parameters in the present study were annual average concentrations, calculated from the monthly averages of the year 2000. Forty four schools in Taiwan’s 22 municipalities were investigated. Stratified sampling by grade was applied in each school.¹⁸

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The 22 municipalities with selected air pollution monitoring
stations in this study in Taiwan 2001. Circles indicate 1 km catchment
area.

Figure 1 The 22 municipalities with selected air pollution monitoring
stations in this study in Taiwan 2001. Circles indicate 1 km catchment
area.

Covariates
Information on potential confounders was obtained from the
parent administered questionnaire. The covariates in the
present analyses included age, sex, parental atopy, parental
education, maternal smoking history during pregnancy,
environmental tobacco smoke (ETS), and visible mould
(table 1). Parental atopy was a measure of genetic predis-
position to asthma and it was defined as the father or mother
of the index child ever having been diagnosed as having
asthma, allergic rhinitis, or atopic eczema.

Statistical methods
The odds ratio (OR) was used as a measure of the relation
between exposure to air pollution and the risk of childhood
asthma. Adjusted ORs were estimated in a two stage
hierarchical model using logistic and linear regression
analyses. The models assume two sources of variation—the
variation among subjects in the first stage, part of which
could be explained by the individual characteristics, and the
variation among municipalities in the second stage, part of
which could be explained by variables measured at the
municipal level. In the analyses we assumed that (1) the
outcome variable follows Bernoulli distribution; (2) intercept
terms are random at the municipal level; and (3) all the
explanatory variables are fixed effects. A logistic regression
model was fitted in the first stage for the risk of childhood
asthma as a function of site-specific intercepts j, where
\[ \logit \{\text{prevalence rate} = j\} = \alpha_j + \beta_j \text{exposure} \]
and personal covariates. The adjusted site-specific
intercepts and prevalence rates are related by
\[ \text{prevalence rate} = e^{\alpha_j} \]
In the second stage these intercept terms representing
the logit of the site-specific prevalence rates (\( \text{prevalence rate} = j \mid \text{exposure} \)), adjusted for personal covariates, were regressed on each
site-specific ambient pollutant level by using a linear
“ecologic” regression—that is, logit \( \alpha_j = \beta_j \text{pollutant} + U_j \text{random deviation} \)
where \( U_j \) denotes the random departure from the general prevalence
\( \text{prevalence rate} \) on the logit scale for site j and \( Z_j \) denotes the ambient
pollution level for site j. Thus, \( \beta \) can be interpreted as the log
OR (per unit change) for each pollutant, adjusted for
personal characteristics. The results from the models are
presented as ORs, along with their 95% confidence intervals
(CIs).

The goodness of fit was assessed with likelihood ratio tests
(LR) to determine whether a variable contributed signifi-
cantly to the model. Firstly, we fitted a full model with a
complete set of covariates. To study further the sources of
confounding we fitted models with different combinations of
covariates and compared the effect from models with and
without the covariate of interest. If the adjusted OR differed
from the crude OR by more than 10%, that covariate was be
included in the final model. We first fitted one pollutant
models and then considered two-pollutant models by fitting
one traffic related and one stationary fossil fuel combustion
related pollutant. Finally, we fitted two-pollutant models
with \( O_3 \) and another pollutant. The two-pollutant models
provide estimates of the independent effects of \( CO, \ NOx, \SO_2, \ PM_{10}, \) and \( O_3 \) on childhood asthma, controlling for the
second pollutant in the model. We also considered three-
pollutant models with one traffic related, one stationary fossil
fuel combustion related pollutant, and \( O_3 \). The effect of each
pollutant on the risk of childhood asthma was presented as
ORs per 10 ppb changes for \( SO_2, \ NOx, \) and \( O_3 \), 100 ppb
changes for \( CO, \) and 10 μg/m³ changes for \( PM_{10} \) along with
their 95% CIs. We assessed potential effect modification by
parental atopy by comparing crude and adjusted effect
estimates for children with and without atopic parents.
The two-stage hierarchical model was used not only to derive
more precise estimates of site specific parameters and site
level effects, but also to adjust for multiple comparisons.¹⁹

RESULTS
Study population and occurrence of childhood asthma
The characteristics of the study population and the pre-
valence of childhood asthma according to the covariates are
shown in table 1. The prevalence of asthma was 6.86% (95%
CI 6.59 to 7.13). The prevalence of childhood asthma was
related to young age, high level of parental education, male
sex, parental atopy, maternal smoking during pregnancy and
the presence of cockroaches and visible mould in the home.
The prevalence of asthma was lower in children exposed to
environmental tobacco smoke (ETS) than in those not
exposed.

Air pollution
The distributions of the annual mean air pollutant concen-
trations, temperature, and relative humidity in the 22
monitoring stations in the year 2000 are presented in table 2
and the correlations between different pollutants are shown
in table 3. The correlation between NOx and \( CO \) concentra-
tions was high (0.88), which reflects the common source of
traffic related and \( O_3 \). The effect of each
pollutant on the risk of childhood asthma was presented as
ORs per 10 ppb changes for \( SO_2, \ NOx, \) and \( O_3 \), 100 ppb
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The two-stage hierarchical model was used not only to derive
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also highly correlated (0.58), indicating a common source of stationary fuel combustion, although SO2 concentrations were also correlated with both traffic related pollutants. The concentration of O3 was negatively correlated with the mainly traffic related pollutants but positively correlated with PM10 and SO2, and it was only weakly correlated with that of traffic related and stationary fossil fuel combustion related air pollutants.

**Air pollution and childhood asthma**

In the one-pollutant model, the risk of asthma was not related to NOx levels (adjusted OR 1.005 per 10 ppb change (95% CI 0.945 to 1.060)). Addition of either SO2 (adjusted OR 1.048 (95% CI 0.983 to 1.117)) or PM10 (adjusted OR 1.065 (95% CI 1.009 to 1.123)) increased the effect estimate for NOx substantially, and addition of O3 (adjusted OR 1.029 (95% CI 0.973 to 1.089)) slightly (table 4). In the three-pollutant model the estimates for NOx were 1.113 (95% CI 1.038 to 1.194) and 1.152 (95% CI 1.082 to 1.227), respectively, when (SO2 and O3) or (PM10 and O3) were added and showed statistical significances (table 5). The adjusted OR for 100 ppb change in CO was 1.045 (95% CI 1.017 to 1.074) and the estimates changed little when a second or third pollutant was added. The adjusted OR for a

| Table 1 | Number of asthma cases, prevalence of asthma, and odds ratios (ORs) of asthma with 95% confidence interval (95% CI) by age, parental education, parental atopy, environmental tobacco smoke, maternal smoking during pregnancy, cockroaches, water damage, and visible mould in Taiwan 2001 |

<table>
<thead>
<tr>
<th>Determinant</th>
<th>No of children</th>
<th>No with physician diagnosed asthma</th>
<th>Prevalence (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>32672</td>
<td>2241</td>
<td>6.86</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7</td>
<td>4692</td>
<td>349</td>
<td>7.44</td>
<td>1.34 (1.09 to 1.64)</td>
</tr>
<tr>
<td>8</td>
<td>3559</td>
<td>251</td>
<td>7.05</td>
<td>1.26 (1.02 to 1.57)</td>
</tr>
<tr>
<td>9</td>
<td>3582</td>
<td>268</td>
<td>7.48</td>
<td>1.35 (1.09 to 1.67)</td>
</tr>
<tr>
<td>10</td>
<td>3760</td>
<td>290</td>
<td>7.71</td>
<td>1.39 (1.13 to 1.72)</td>
</tr>
<tr>
<td>11</td>
<td>3539</td>
<td>238</td>
<td>6.73</td>
<td>1.20 (0.97 to 1.49)</td>
</tr>
<tr>
<td>12</td>
<td>3809</td>
<td>273</td>
<td>7.17</td>
<td>1.29 (1.04 to 1.59)</td>
</tr>
<tr>
<td>13</td>
<td>3730</td>
<td>240</td>
<td>6.43</td>
<td>1.15 (0.92 to 1.42)</td>
</tr>
<tr>
<td>14</td>
<td>3634</td>
<td>198</td>
<td>5.45</td>
<td>0.96 (0.77 to 1.20)</td>
</tr>
<tr>
<td>15</td>
<td>2367</td>
<td>134</td>
<td>5.66</td>
<td>1.00</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16540</td>
<td>1340</td>
<td>8.10</td>
<td>1.49 (1.37 to 1.63)</td>
</tr>
<tr>
<td>Female</td>
<td>16132</td>
<td>901</td>
<td>5.59</td>
<td>1.00</td>
</tr>
<tr>
<td>Parental education (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6</td>
<td>1831</td>
<td>74</td>
<td>4.04</td>
<td>1.00</td>
</tr>
<tr>
<td>6–8</td>
<td>5725</td>
<td>269</td>
<td>4.70</td>
<td>1.17 (0.90 to 1.52)</td>
</tr>
<tr>
<td>9–11</td>
<td>14749</td>
<td>937</td>
<td>6.35</td>
<td>1.61 (1.26 to 2.05)</td>
</tr>
<tr>
<td>≥12</td>
<td>10367</td>
<td>961</td>
<td>9.27</td>
<td>2.43 (1.90 to 3.09)</td>
</tr>
<tr>
<td>Parental atopy*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>22761</td>
<td>1083</td>
<td>4.76</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>9208</td>
<td>1103</td>
<td>11.98</td>
<td>2.72 (2.50 to 2.97)</td>
</tr>
<tr>
<td>Environmental tobacco smoke*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13212</td>
<td>990</td>
<td>7.49</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>19229</td>
<td>1232</td>
<td>6.41</td>
<td>0.85 (0.78 to 0.92)</td>
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<tr>
<td>Maternal smoking during pregnancy*</td>
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<tr>
<td>No</td>
<td>31791</td>
<td>2168</td>
<td>6.82</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>706</td>
<td>56</td>
<td>7.93</td>
<td>1.18 (0.89 to 1.56)</td>
</tr>
<tr>
<td>Cockroaches noted monthly*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>6663</td>
<td>410</td>
<td>6.15</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>25507</td>
<td>1796</td>
<td>7.04</td>
<td>1.15 (1.03 to 1.29)</td>
</tr>
<tr>
<td>Water damage*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29845</td>
<td>2055</td>
<td>6.89</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>2667</td>
<td>176</td>
<td>6.60</td>
<td>0.96 (0.81 to 1.12)</td>
</tr>
<tr>
<td>Visible mould*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>24308</td>
<td>1581</td>
<td>6.50</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>7573</td>
<td>616</td>
<td>8.13</td>
<td>1.27 (1.16 to 1.40)</td>
</tr>
</tbody>
</table>

*Numbers of subjects do not add up to total N because of missing data.

| Table 2 | Mean and distribution of 2000 annual air pollution and meteorology data from 22 monitoring stations in Taiwan |

<table>
<thead>
<tr>
<th>Determinant</th>
<th>Mean (SD)</th>
<th>Minimum</th>
<th>25th percentile</th>
<th>Median</th>
<th>75th percentile</th>
<th>Interquartile range*</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO (ppb)</td>
<td>664 (153)</td>
<td>416</td>
<td>540</td>
<td>647</td>
<td>752</td>
<td>212</td>
<td>964</td>
</tr>
<tr>
<td>NOX (ppb)</td>
<td>27.64 (8.38)</td>
<td>10.88</td>
<td>21.47</td>
<td>33.07</td>
<td>29.58</td>
<td>11.60</td>
<td>43.98</td>
</tr>
<tr>
<td>O3 (ppb)</td>
<td>23.14 (3.25)</td>
<td>18.65</td>
<td>20.34</td>
<td>25.20</td>
<td>22.69</td>
<td>4.86</td>
<td>31.17</td>
</tr>
<tr>
<td>PM10 (µg/m³)</td>
<td>55.58 (16.57)</td>
<td>29.36</td>
<td>42.96</td>
<td>53.81</td>
<td>70.37</td>
<td>27.41</td>
<td>99.58</td>
</tr>
<tr>
<td>SO2 (ppb)</td>
<td>3.53 (2.00)</td>
<td>0.35</td>
<td>1.96</td>
<td>3.34</td>
<td>4.84</td>
<td>2.88</td>
<td>10.12</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>23.65 (0.75)</td>
<td>22.36</td>
<td>23.20</td>
<td>23.50</td>
<td>24.17</td>
<td>1.17</td>
<td>25.27</td>
</tr>
<tr>
<td>Relative humidity (%)</td>
<td>74.0 (3.0)</td>
<td>69.0</td>
<td>72.2</td>
<td>74.1</td>
<td>76.5</td>
<td>4.3</td>
<td>80.0</td>
</tr>
</tbody>
</table>

*Range from 25th to 75th percentile of site specific concentrations.
In cross sectional studies, selection bias is a potential threat to validity. A plausible mechanism of selection is that parents of children with asthma move to residential areas with lower levels of air pollution which will lead to underestimation of the relation between exposure and outcome. Any random migration is likely to result in underestimation of the air pollution effects but would not introduce a positive bias in the associations. Information on residential history in a cross sectional study could be used to reduce the possibility of selection bias, whereas a longitudinal study would provide a stronger design for minimising this problem. We did not have sufficient information on children’s residential history to formally assess the lifetime exposure to air pollution, so current exposure was used as the proxy of previous exposure. Most of the studies to date on the relationship between exposure to air pollutants and risk of asthma in children have been cross sectional.10–12

In our statistical analyses we controlled for a number of potential individual level confounders such as parental education and indoor environmental exposures. In stratified analyses on different levels of covariates, we studied the possibility of residual confounding. Parental education had a positive association with concentrations of traffic related pollutants. The prevalence of childhood asthma was also positively associated with the level of parental education, which could be explained by both the influence of air pollution and better access to health care.

Assessment of the independent effects of different pollutants is difficult because urban air pollution constitutes a complex mixture of several compounds. Although all the measured pollutants have several sources, NOx and CO are predominantly from vehicle emissions while SO2 and PM10 are mainly from stationary fossil combustion processes.21 22 In the present study, NOx and CO concentrations were highly correlated, indicating the common source of motor vehicle traffic emissions. SO2 and PM10 concentrations were also correlated, their common sources being stationary fossil fuel combustion. In the modelling, we were able to control for one stationary fossil fuel pollutant at a time as a potential confounder when assessing the effect of one of the traffic related pollutants and vice versa. Due to collinearity problems, it was not possible to separate the impact of traffic related pollutants (NOx and CO) from each other.

### Synthesis with previous knowledge

The results of the present study are in line with several previous studies from Seattle, Illinois, Los Angeles, Austria, the Netherlands, Czech Republic and Poland, Germany, Japan, and China indicating that exposure to outdoor air pollutants increases the risk of asthma. All available studies suggest an increased risk for traffic related air pollutants (CO and NOx)4–9 11–12 and O3, but the findings are inconsistent for stationary fossil fuel combustion related air pollutants (SO2 and PM10).2 10–12

A panel study conducted in Seattle showed no association between exposure to CO and the occurrence of asthma related symptoms.9 In a cross sectional study carried out in Illinois, increased morning and evening asthma symptom
Table 4

<table>
<thead>
<tr>
<th>Pollutant Combination</th>
<th>Single-pollutant OR (95% CI)</th>
<th>Two-pollutant model 1 (NOx + SO2)</th>
<th>Two-pollutant model 2 (NOx + PM10)</th>
<th>Two-pollutant model 3 (NOx + O3)</th>
<th>Two-pollutant model 4 (CO + SO2)</th>
<th>Two-pollutant model 5 (CO + PM10)</th>
<th>Two-pollutant model 6 (CO + O3)</th>
<th>Two-pollutant model 7 (SO2 + PM10)</th>
<th>Two-pollutant model 8 (PM10 + O3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOx (10 ppb)</td>
<td>1.063 (1.100 to 1.474)</td>
<td>1.048 (0.983 to 1.117)</td>
<td>1.065 (1.009 to 1.112)</td>
<td>0.987 to 1.048</td>
<td>1.034 to 1.099</td>
<td>0.939 to 1.009</td>
<td>1.007 to 1.048</td>
<td>1.007 to 1.048</td>
<td>0.999 to 1.009</td>
</tr>
<tr>
<td>CO (100 ppb)</td>
<td>1.029 (0.973 to 1.089)</td>
<td>1.053 (1.001 to 1.109)</td>
<td>1.060 (1.001 to 1.122)</td>
<td>1.059 to 1.101</td>
<td>1.029 to 1.099</td>
<td>1.007 to 1.048</td>
<td>1.007 to 1.048</td>
<td>1.007 to 1.048</td>
<td>0.999 to 1.009</td>
</tr>
<tr>
<td>SO2 (10 ppb)</td>
<td>1.029 (0.973 to 1.089)</td>
<td>1.053 (1.001 to 1.109)</td>
<td>1.060 (1.001 to 1.122)</td>
<td>1.059 to 1.101</td>
<td>1.029 to 1.099</td>
<td>1.007 to 1.048</td>
<td>1.007 to 1.048</td>
<td>1.007 to 1.048</td>
<td>0.999 to 1.009</td>
</tr>
<tr>
<td>PM2.5 (10 mg/m3)</td>
<td>0.724 (0.679 to 0.779)</td>
<td>0.724 (0.679 to 0.779)</td>
<td>0.724 (0.679 to 0.779)</td>
<td>0.724 (0.679 to 0.779)</td>
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<td>0.724 (0.679 to 0.779)</td>
<td>0.724 (0.679 to 0.779)</td>
</tr>
<tr>
<td>O3 (10 ppb)</td>
<td>1.166 (1.022 to 1.331)</td>
<td>1.166 (1.022 to 1.331)</td>
<td>1.166 (1.022 to 1.331)</td>
<td>1.166 (1.022 to 1.331)</td>
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<td>1.166 (1.022 to 1.331)</td>
<td>1.166 (1.022 to 1.331)</td>
</tr>
</tbody>
</table>

Conclusion

The present study provides additional evidence that exposure to outdoor air pollutants increases the risk of childhood asthma in school children. The observed relations between the risk of childhood asthma and NOx and CO levels suggests that emissions from motor vehicles play an important role. In
addition, the relationship with O3 levels indicates that photochemical air pollution contributes to adverse health effects.

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Table 5  Adjusted odds ratios (ORs) and 95% confidence interval (CIs) of physician-diagnosed asthma in three-pollutant models

<table>
<thead>
<tr>
<th></th>
<th>Three-pollutant model 1 (NOx×SO2×O3)</th>
<th>Three-pollutant model 2 (NOx×PM10×O3)</th>
<th>Three-pollutant model 3 (CO×SO2×O3)</th>
<th>Three-pollutant model 4 (CO×PM10×O3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOx (10 ppb)</td>
<td>1.113 (1.038 to 1.194)</td>
<td>1.152 (1.082 to 1.227)</td>
<td>1.111 (1.074 to 1.150)</td>
<td>1.119 (1.084 to 1.155)</td>
</tr>
<tr>
<td>CO (100 ppb)</td>
<td>0.585 (0.433 to 0.791)</td>
<td>0.888 (0.858 to 0.918)</td>
<td>0.528 (0.405 to 0.688)</td>
<td>0.886 (0.859 to 0.914)</td>
</tr>
<tr>
<td>SO2 (10 ppb)</td>
<td>1.360 (1.152 to 1.604)</td>
<td>1.501 (1.274 to 1.768)</td>
<td>1.500 (1.273 to 1.767)</td>
<td>1.587 (1.351 to 1.865)</td>
</tr>
</tbody>
</table>

*Two-stage hierarchical analysis adjusting for age, sex, parental education, parental atopy, environmental tobacco smoke (ETS), and visible mould.

Table 6  Crude and adjusted odds ratios (ORs) with 95% confidence interval (CIs) of physician-diagnosed asthma stratified by parental atopy in the relation between childhood asthma and air pollutants

<table>
<thead>
<tr>
<th>Parental atopy</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOx (10 ppb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.00 (0.93 to 1.08)</td>
<td>0.99 (0.92 to 1.07)</td>
</tr>
<tr>
<td>No</td>
<td>1.04 (0.97 to 1.13)</td>
<td>1.02 (0.95 to 1.09)</td>
</tr>
<tr>
<td>CO (100 ppb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.07 (1.01 to 1.09)</td>
<td>1.04 (1.00 to 1.08)</td>
</tr>
<tr>
<td>No</td>
<td>1.08 (1.04 to 1.12)</td>
<td>1.06 (1.02 to 1.10)</td>
</tr>
<tr>
<td>SO2 (10 ppb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.76 (0.55 to 1.06)</td>
<td>0.86 (0.62 to 1.21)</td>
</tr>
<tr>
<td>No</td>
<td>0.70 (0.51 to 0.95)</td>
<td>0.77 (0.56 to 1.07)</td>
</tr>
<tr>
<td>PM10 (10 μg/m3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.93 (0.89 to 0.96)</td>
<td>0.94 (0.90 to 0.98)</td>
</tr>
<tr>
<td>No</td>
<td>0.90 (0.87 to 0.94)</td>
<td>0.92 (0.89 to 0.96)</td>
</tr>
<tr>
<td>O3 (10 ppb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.09 (0.89 to 1.33)</td>
<td>1.15 (0.93 to 1.42)</td>
</tr>
<tr>
<td>No</td>
<td>1.08 (0.90 to 1.30)</td>
<td>1.20 (1.00 to 1.47)</td>
</tr>
</tbody>
</table>

*Two-stage hierarchical analysis adjusting for age, sex, parental education, environmental tobacco smoke (ETS), and visible mould.

REFERENCES
22. Cyrys J, Pitz M, Bischof W, et al. Relationship between outdoor and indoor levels of fine particles mass, particle number concentrations and black smoke.
Further evidence on the dangers of exposure to second hand tobacco smoke

Vineis et al report a prospective case-control study examining 123 479 “healthy” never smokers or former smokers. Over 7 years of follow up, cases were defined as deaths from COPD. Controls were well matched. Information about tobacco smoke exposure and a thorough list of confounders was obtained by questionnaire at recruitment. This strengthens the study by cutting out recall bias. Follow up data were from multiple sources. A subset of subjects and controls were tested for the presence of genetic polymorphisms implicated in carcinogenesis.

Exposure to tobacco smoke was associated with increased risk of death from respiratory cancers/COPD (hazard ratio (HR) 1.30, 95% CI 0.87 to 1.95) and lung cancer alone (HR 1.34, 0.85 to 2.13). The effect was significantly greater for exposure at work (HR for lung cancer 1.65, 1.04 to 2.63) than at home (HR 1.03, 0.60 to 1.76) and for former smokers than for never smokers. Work exposure may have been higher than at home but exposure was not quantified and only measured at one point in time. The authors postulate that the greater effect in former smokers may be due to genetic mutations already accrued. The case for causality is strengthened as genetic polymorphisms increase the susceptibility to smoke: odds ratio (OR) for lung cancer increased from 1.33 to 2.86 between the presence of one or two versus three or more risk polymorphisms. Self-reported exposure to smoke in childhood showed a clear dose-response effect in never smokers. Daily exposure for many hours as a child increased the HR for lung cancer in adulthood from 1.0 to 3.63 (1.19 to 11.11).

McGhee et al report a retrospective case-control study. Cases were identified from all deaths reported amongst never smokers, and those reporting the death completed a questionnaire about the deceased. Second hand smoke exposure was classified by the number of smokers who lived with the deceased (0, 1, 2 or more). There was no attempt to further quantify exposure. This retrospective nature risks recall bias and the only confounder controlled for was education, a proxy of social class. There was a 34% increase in all cause mortality with any exposure to second hand smoke. Importantly, there was a significant dose-dependent association between second hand smoke and mortality from lung cancer (OR 1.74, 1.06 to 2.86 comparing no exposure to living with >2 smokers). There was a similar association between exposure and mortality from COPD (OR 2.51, 1.22 to 5.18), stroke (OR 2.08, 1.33 to 3.25) and ischaemic heart disease (OR 1.68, 1.05 to 2.68).

These studies add impetus to the demand for restrictions on smoking in public places. In the Hong Kong study deaths from poisoning were also analysed, as a control measure, and showed no relation to tobacco smoke exposure. Perhaps now there is an argument for reclassifying some of the other environmental tobacco related deaths as “poisoning”?

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