Asthma in exercising children exposed to ozone: a cohort study


Summary

Background Little is known about the effect of exposure to air pollution during exercise or time spent outdoors on the development of asthma. We investigated the relation between newly-diagnosed asthma and team sports in a cohort of children exposed to different concentrations and mixtures of air pollutants.

Methods 3535 children with no history of asthma were recruited from schools in 12 communities in southern California and were followed up for up to 5 years. 265 children reported a new diagnosis of asthma during follow-up. We assessed risk of asthma in children playing team sports at study entry in six communities with high daytime ozone concentrations, six with lower concentrations, and in communities with high or low concentrations of nitrogen dioxide, particulate matter, and inorganic-acid vapour.

Findings In communities with high ozone concentrations, the relative risk of developing asthma in children playing three or more sports was 3.3 (95% CI 1.9–5.8), compared with children playing no sports. Sports had no effect in areas of low ozone concentration (0–2). Time spent outside was associated with a higher incidence of asthma in areas of high ozone (1.4–2.1), but not in areas of low ozone. Exposure to pollutants other than ozone did not alter the effect of team sports.

Interpretation Incidence of new diagnoses of asthma is associated with heavy exercise in communities with high concentrations of ozone, thus, air pollution and outdoor exercise could contribute to the development of asthma in children.

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Introduction

Asthma is the most common chronic disease of childhood; asthma prevalence and incidence have been increasing in children in developed countries during the past few decades.1,2 Causes for this epidemic are unknown, although changes in frequency and severity of early-life infections, diet, and exposure to indoor allergens and to indoor and outdoor air pollutants have all been linked with asthma.

Cross-sectional studies3–5 have shown that competitive athletes have a high prevalence of asthma and exercise-induced bronchospasm or bronchial hyper-reactivity. Possible mechanisms for this association include increased inhalation of cold air, allergens, or air pollutants, increased response to respiratory infections, and increased parasympathetic tone.6,7 Various mechanisms could be linked with sports-associated asthma. However, few epidemiological investigations have all been done, and there have been no prospective studies of asthma in competitive athletes or children playing team sports.5

Acute exposure to ozone and other outdoor air pollutants exacerbates asthma;8 the chronic effects of air pollution have been less studied, but combustion-related air pollution is not thought to cause asthma.9 However, this conclusion is based on studies in which personal exposure was measured with community air pollution monitors. The true dose of outdoor air pollutants to the lung depends on local pollutant concentrations, which may vary within a community, and on personal habits such as time spent outside and physical activity. People exercising outside should receive greater doses of outdoor pollutants to the lung than those who do not, and thus be more susceptible to any chronic effects of air pollution. Because the onset of asthma might cause athletes to reduce their levels of exercise, cross-sectional studies are not an appropriate way to measure the causal relations between exercise, air pollution, and asthma.

We postulated that children engaged in team sports in polluted communities might also be at high risk of asthma. Because the amount of time spent playing sports is an individual factor that affects exposure to ambient pollution, this approach avoids many biases of studies of air pollution that have relied on between-community comparisons of rates of asthma and other illnesses. We assessed the association of playing team sports with subsequent development of asthma during 5 years of follow-up of participants in the Southern California Children’s Health Study. Study communities were selected on the basis of concentrations of ambient ozone and other pollutants.10

Methods

Participants

We selected 12 communities in southern California for variability of concentrations of ozone, particles with aerodynamic diameter less than 10 μm (PM_{10}), and nitrogen dioxide (NO_{2}).11 In 1993, in each of the 12 communities, we recruited around 150 children aged 9–10 years, 75 aged 12–13 years, and 75 aged 15–16 years from schools in areas of the communities with stable, mainly middle-income populations. All children from targeted classrooms were invited to take part; participants completed a baseline questionnaire with help from their parents. In
early 1996, we recruited an additional cohort of around 175 children aged 9–10 years from every community. Children were followed up and interviewed yearly until 1998 (or until 1995, for children aged 15–16 years at entry).

Procedures
Children were excluded if they answered yes to “Has a doctor ever diagnosed this child as having asthma?” on the baseline questionnaire sent home to every child’s parents or if a child answered yes to the question “Has a doctor ever said you had asthma?” on a questionnaire administered by an interviewer in 1993 (or in 1996, for the 1996 cohort). We ascertained history of wheezing in the baseline questionnaire with the question “Has your child’s chest ever sounded wheezy or whistling, including times when he or she had a cold?” A study interviewer administered a questionnaire yearly to every child. Children were classed as having newly-diagnosed asthma in the year that they first answered yes to the question “Has a doctor ever said you had asthma?”

A question on the baseline questionnaire asked “Has your child been on any sports teams in the past 12 months?” and, if the answer was yes, “what teams?” Children were grouped into those who played no team sports, and those who played one, two, and three or more sports. The question had eight answer options, including sports with high metabolic indices, typically involving six or more times resting work expenditure (basketball, football, soccer, swimming, and tennis), low metabolic indices, typically involving less than six times resting work expenditure (baseball, softball, and volleyball), and other sports.15 For some analyses, children who played sports were grouped into those who played at least one high activity sport and children who played no high activity sports, but at least one low activity sport.

In the baseline questionnaire we also obtained information on children’s sex, age, race and ethnic origin (Hispanic, non-Hispanic white, Asian or Pacific Islander, African American, or other), history of allergies, reported time spent outdoors, current maternal smoking, history of asthma in either parent, membership of a health insurance plan, and family income. We split each cohort (1993 and 1996) into children playing more than the median time outdoors and those playing less. We classed families as having low socioeconomic status if their income was less than US$15 000 (or, if income was not reported, if the responding parent had not completed a secondary school education). We defined high socioeconomic status as family income of $100 000 or more (or, if income was not reported, by responding parent having received postgraduate training). We classified remaining families as having middle socioeconomic status. Body-mass index (BMI) was calculated from children’s heights and weights at the time of the first interview of the child, and was used to divide children into quartiles for analysis.

We established air pollution monitoring stations in all 12 communities, and measured pollutant concentrations from 1994 to 1998.16–21 Every station monitored hourly concentrations of ozone, PM$_{10}$ and NO$_2$. PM$_{2.5}$ (particulate mass less than 2.5 μm in diameter) and acid vapour were measured with 2-week integrated samplers. Yearly means were calculated from 24-h mean concentrations of ozone, PM$_{10}$ and NO$_2$; from 10:00 h to 18:00 h mean concentrations of ozone (ozon$c_{10}$); and from a daily maximum 1-h ozone concentration. We also calculated yearly means from 2-week mean concentrations of PM$_{2.5}$ and inorganic hydrochloric and nitric acid vapour. We calculated 4-year mean concentrations (1994–97) in every community for every pollutant. We used 4-year means to rank communities because between-year variation was small,1 and these means provided more stable estimates of exposure than yearly means. For every pollutant, we grouped the 12 communities into six with high 4-year mean concentrations and six with low concentrations. For some analyses, communities were stratified by tertiles of selected pollutants.

Statistical analyses
Before grouping into high and low pollution communities, Pearson correlation coefficients were calculated to measure the relation between different pollutants in the 12 communities. Relative risks (hazard ratios) of asthma for living in a high or low pollutant community, adjusted for ethnic origin, were evaluated for every pollutant with a multivariate proportional hazards model. We stratified baseline hazards by age and sex. We selected age groups to divide the 9–10-year-old cohort by median age at study entry, and for least overlap of this cohort with other cohorts. Age groups were: younger than 9–70 years, 70–11·49 years, and older than 11·49 years. To establish whether ozone had more effect than NO$_2$ (which was highly correlated with particulate pollutants and acid), the effect of team sports on the risk of new asthma was assessed in every pollution setting. To assess whether type of sport played...
was relevant, models containing indicator variables for each type of sport or a linear term for total number of sports played were compared with our final model with the Akaike Information Criterion (AIC) to see whether a model with information on specific sports was better than models without such information. We also assessed effects of community, history of allergy, family history of asthma, membership of a health insurance plan, BMI, current maternal smoking, and socioeconomic status. Analyses were done with the Statistical Analysis System (version 8.1) software package.

Role of the funding source
The California Air Resources Board helped establish the air pollution monitoring network and helped collect the air pollution data from this network for use in the study.

Results
5762 (79%) of eligible children completed baseline questionnaires. 479 children were excluded because they were not at school at the time of a questionnaire administered during the entry year by an interviewer, and an additional 883 were excluded for a history of asthma. We excluded 312 children because of missing or “not known” answers to questions on wheezing, and 26 for a history of cystic fibrosis, severe chest injury, or chest surgery. 527 additional children were excluded who did not have at least 1 year of follow-up. 3535 children were included who did not have a history of asthma and who were available for follow-up, 2752 (78%) of whom had no history of wheezing. At study entry, 65 children had missing information about the number of sports played. 1934 (67%) children played sports. Only 273 (8%) of 3470 children played three or more team sports. Several factors were associated with number of team sports played (table 1). Girls were much less likely to play team sports than boys, and children in the top quartile of BMI were slightly less likely to play sports than those in other quartiles. Hispanic and non-Hispanic white children were more likely to play three or more team sports. Although family history of asthma was not associated with team sports, a child’s history of allergy was associated. Children from families with low socioeconomic status and with the related characteristics of a mother who smoked and lack of health insurance, were less likely to play sports. Spending more time outside was also associated with playing sports.

Children with wheeze were not less likely to play sports.

We analysed the relation between newly-diagnosed asthma and number of sports played (table 2). 265 children developed asthma, 259 of whom had provided complete information on sports. Across all communities there was a 1-8-fold increased risk (95% CI 1.2–2.8) for asthma in children who had played three or more team sports in the previous year. There was a linear trend of increasing asthma for the total of eight possible team sports played (relative risk 1·1 per team sport played, 1·0–1·3).

Table 3 shows the profile of each pollutant in high and low pollution communities. Even communities with low \(\text{ozone}_{15-18}\) had high mean 4-year concentrations, up to 51 parts per billion. The high and low pollution communities were the same for \(\text{NO}_2\), \(\text{PM}_{10}\), \(\text{PM}_{2.5}\), and acid, which was not surprising as 4-year mean concentrations of these pollutants were highly correlated across communities: from \(r=0.65\) for \(\text{PM}_{10}\), to 0·96 for \(\text{PM}_{10}\), \(\text{Ozone}_{10-18}\), although highly correlated with mean daily 1-h maximum ozone concentration (0·98) and with 24-h mean ozone (0·72), was not strongly correlated with the other pollutants. The highest correlation of \(\text{ozone}_{15-18}\) with other pollutants was with acid (0·48).

Risk of developing asthma was not greater overall in children living in the six high pollution communities than children living in the six low pollution communities, after adjustment for stratified baseline hazards for age and sex, and for ethnic origin, irrespective of which pollutant was used to classify communities as high or low. The relative risks were 0·8 (0·6–1.0, \(p=0.08\)) for \(\text{ozone}_{15-18}\) 0·7 (0·6–0.9) for daily maximum ozone, and 1·1 (0·9–1·4) for 24-h ozone. For \(\text{NO}_2\), \(\text{PM}_{10}\), \(\text{PM}_{2.5}\), and acid, all of which shared the same high and low communities, the relative risk was 0·8 (0·6–1·0, \(p=0.08\)). Communities with high \(\text{NO}_2\) and associated pollutants, and communities with high \(\text{ozone}_{15-18}\) or daily maximum ozone were associated with a decreased risk of asthma; these associations were significant (\(p<0.05\)) only for daily maximum ozone.

The effect of team sports was similar in communities with high and low particulate matter (and associated pollutants; all of which gave the same high or low groupings of communities as did particulate matter). In both groups of communities there was a small increase in asthma among children playing team sports, which was largest among those playing three or more sports (table 4).

In high \(\text{ozone}_{15-18}\) communities, there was a 3.3-fold increased risk of asthma in children playing three or more sports; an increase that was not seen in low \(\text{ozone}_{15-18}\) communities (table 5). In high ozone communities there was a trend of increasing asthma with number of team sports played (relative risk 1·3 per sport, 1·1–1·6). There was a significant interaction between total number of sports played and ozone (\(p=0.004\)). In assessing interaction, we also tested models that used indicator variables for each sport or dummy variables for none, one, two, and three sports. The model that used total number of sports was found to give the best fit. In high ozone communities, risk of
compared the characteristics of the 20 children who played asthma, or time spent outside. However, when we team sports. There was no significant interaction of number communities (1·1, 0·8–1·6) in models that also included communities (1·4, 1·0–2·1), but not in low ozone outside was also associated with asthma in high ozone communities (5·2, 1·3–20·4), but power was limited for identifying the effect of specific sports.

The overall pattern of effects of sports on asthma risk was similar in models that also included socioeconomic status, history of allergy, family history of asthma, insurance, maternal smoking, and BMI at study entry. Time spent outside was also associated with asthma in high ozone communities (1·4, 1·0–2·1), but not in low ozone communities, the relative risk for high activity sports was 1·0 (0·7–1·4) and for low activity sports the risk was 0·9 (0·5–1·7). In models with individual sports entered as dummy variables, only tennis was significantly associated with asthma and only in high ozone communities (3·2, 1·0–9·6), but power was limited for identifying the effect of specific sports.

The effect of sports was similar in boys and girls, although the effect of playing three or more sports in high activity communities, was somewhat greater in girls (2·5, 1·1–5·4) than in boys (2·5, 1·1–5·4). Among children with no lifetime history of wheeze at study entry, the relative risk of new diagnosis of asthma in children playing three or more sports in high ozone communities, three of seven of those in low ozone communities (2·1, 0·8–5·6) had a family history of asthma, compared with none of 17 in high ozone communities (p=0·02, Fisher’s exact test). In these 29 children, no other demographic or personal characteristic differed significantly between low and high ozone communities.

The effect of sports was similar in boys and girls, although the effect of playing three or more sports in high ozone communities, compared with no sports in high ozone communities, was somewhat greater in girls (4·7, 2·1–10·5) than in boys (2·5, 1·1–5·4). Among children with no lifetime history of wheeze at study entry, the risk of new diagnosis of asthma in children playing three or more sports in a high ozone community was 4·4 (2·1–9·3). In children with a history of wheeze, the relative risk was 2·7 (1·1–6·4).

### Table 4: Effect of number of team sports played on the risk of new asthma diagnosis in high and low PM (and other pollutant) communities

<table>
<thead>
<tr>
<th>Number of sports played</th>
<th>Low PM communities</th>
<th>High PM communities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (incidence)* RR (95% CI)</td>
<td>N (incidence)* RR (95% CI)</td>
</tr>
<tr>
<td>0</td>
<td>49 (0·023) 1·0</td>
<td>55 (0·021) 1·0</td>
</tr>
<tr>
<td>1</td>
<td>51 (0·032) 1·5</td>
<td>36 (0·021) 1·1</td>
</tr>
<tr>
<td>2</td>
<td>22 (0·024) 1·2</td>
<td>14 (0·018) 0·9</td>
</tr>
<tr>
<td>3</td>
<td>13 (0·033) 1·7</td>
<td>16 (0·033) 2·0</td>
</tr>
</tbody>
</table>

PM=particulate matter; N=number of cases of asthma; RR-relative risk, adjusted for ethnic origin, and for stratified baseline hazards by sex and age group. *Denominator=person-years of follow-up.

### Table 5: Effect of number of team sports played on the risk of new asthma diagnosis in high and low ozone communities

<table>
<thead>
<tr>
<th>Number of sports played</th>
<th>Low ozone communities</th>
<th>High ozone communities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (incidence)* RR (95% CI)</td>
<td>N (incidence)* RR (95% CI)</td>
</tr>
<tr>
<td>0</td>
<td>58 (0·027) 1·0</td>
<td>46 (0·018) 1·0</td>
</tr>
<tr>
<td>1</td>
<td>50 (0·033) 1·3</td>
<td>40 (0·021) 1·3</td>
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<tr>
<td>2</td>
<td>20 (0·023) 0·8</td>
<td>16 (0·020) 1·3</td>
</tr>
<tr>
<td>3</td>
<td>9 (0·019) 0·8</td>
<td>20 (0·050) 3·3</td>
</tr>
</tbody>
</table>

N=number of cases of asthma; RR-relative risk, adjusted for ethnic origin, and for stratified baseline hazards by sex and age group. *Denominator=person-years of follow-up.

When ozone was used to divide communities into tertiles, playing three or more team sports was associated with asthma only in the upper tertile (3·1, 1·8–5·5). The range of exposure across the four communities in the upper tertile was 56·8–69·0 parts per billion. Playing three team sports was associated with a small, not significant decrease in relative risk of asthma in the lower tertile (0·7, 0·3–1·8) and in the middle tertile (0·9, 0·2–3·1). However, these estimates for the effect of team sports were based on few cases, and the models converged only if Asian, Black, and other races were combined into one category.

When the effect of sports was analysed in communities divided into combinations of high and low mean concentrations of other pollutants, there was no interaction between sports, ozone, and other pollutants. In communities with high ozone, and low levels of other pollutants, there was a 4·2-fold (1·6–10·7) increased risk of asthma in children playing three or more sports, compared with children who played no sports. In communities with a combination of high levels of ozone and other pollutants, there was a 3·3-fold (1·6–6·9) increased risk of asthma in children playing three or more sports. There was little effect of playing team sports in low ozone communities, irrespective of whether other pollutants were present.

### Discussion

Our results show that playing multiple team sports in a high ozone environment is associated with development of physician-diagnosed asthma. The results are consistent with a large increased risk both for new-onset asthma and for exacerbation of previously undiagnosed asthma, because playing multiple sports was associated with asthma in children with no lifetime history of wheezing at baseline and children with a previous history of wheezing. The larger effect of high activity sports than low activity sports, and an independent effect of time spent outdoors, also only in high ozone communities, strengthens the inference that exposure to ozone may modify the effect of sports on the development of asthma in some children. Exercise-induced asthma by itself is unlikely to have been the explanation for these results, because asthma onset was associated with exercise only in polluted communities.

The high prevalence of asthma in competitive figure skaters might be related to NO2 generated by ice grooming equipment.1 However, prevalence of asthma greater than 40% has been reported in competitive cross-country skiers,3 a group inhaling cold air, but who might not be heavily exposed to air pollution. Competitive long distance and speed runners and swimmers (especially atopic individuals) have high prevalence of asthma, bronchial hyper-responsiveness, or both, and these rates were higher in atopic individuals.4 However, the role of atopy in sports-induced asthma is unclear. Atopy did not modify the risk of asthma associated with nordic skiing.5 We saw no interaction between history of allergy and sports, but our indicator for allergy based on reported history might have resulted in misclassification of atopy, compared with skin testing. Our results suggest that asthmatic children playing three or more team sports were less likely to have a family history of asthma in high ozone communities than in low ozone communities. In as much as family history is suggestive of atopy, this result is in contrast with those of other studies. Although previous studies of sports and asthma have focused on competitive athletes, one other prospective population-based study has been done in Danish children.12 Information about physical activity and team sports were not provided, but physical fitness was associated with a lower risk of subsequent development of
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response, is good. Self-report, at least in adults, reflects what physicians actually said to patients, and physician assessment of asthma has been recommended as the epidemiological gold standard for this disease. Our list of sports did not include some high-activity sports such as running, which has been shown to be associated with asthma in cross-sectional studies of athletes, and bicycling, which has been shown in amateur cyclists exposed recreationally to low ambient levels of ozone to result in acute decreases in lung function and increases in symptoms. These exceptions might have resulted in some misclassification of team sports. However, the effect of misclassification would not have been likely to have differed with stratum of ozone exposure, and so would probably have resulted in an underestimate of a true effect of sports. Finally, variation in loss to follow-up between subgroups of children might have biased estimates of associations. However, in children aged 9–10 and 12–13 years available for follow-up at study entry, 78% were examined in either high or low ozone community, or wheeze at study entry.

We conclude that the incidence of new asthma diagnoses is associated with heavy exercise in communities with high levels of ambient ozone, and that in these conditions, air pollution and outdoor exercise might contribute to development of asthma in children.

Contributors
All authors participated in study design, analysis, interpretation, and in drafting the report.

Conflict of interest statement
None declared.

Disclaimer
The statements and conclusions in this report are those of the contractor and not necessarily those of the California Air Resources Board. The mention of commercial products, their source, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products.

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