Changing prevalence of asthma in Taiwanese adolescents: two surveys 6 years apart


This study compared the prevalence of asthma among Taiwanese adolescents with individual-level risk factors and municipal-level air pollution and meteorology data to determine whether changes in these factors could explain the observed change in prevalence. We conducted two national surveys of respiratory illness and symptoms in Taiwanese middle-school students in 1995–96 and 2001. The effects of personal and environmental factors were assessed and temporal changes of outdoor monitoring data were also compared with asthma prevalence difference. A total of 44,104 children from the 1995–96 survey and 11,048 children from the 2001 survey attended schools located within 1 km of 22 monitoring stations. Lifetime prevalences of physician-diagnosed and questionnaire-determined asthma increased during this period. After adjustment for potential risk factors, the prevalence differences were statistically unchanged. Although parental education level contributed most, changes in investigated personal and environmental factors might not explain the observed changes in asthma prevalence. Municipalities with higher temperature increase were significantly associated with prevalence difference in questionnaire-determined asthma. We concluded that correlates of the investigated individual-level factors, which have changed over time, still underlie changes in asthma prevalence. Increasing temperature might be the main reason for the rising trends of asthma in Taiwanese adolescents.

The prevalence of asthma, the single most common chronic childhood disease in developed nations (1, 2), has recently been reported as increasing in many countries (3, 4). The changing pattern has not been fully explained, in part because of an incomplete understanding of the pathogenesis of asthma. Some researchers, however, have indicated that the increase has slowed or ceased (5, 6), and some have even reported prevalence as decreasing (7). In Taiwan, the prevalence of childhood asthma has also increased in recent years. Hsieh and Shen (8) reported that asthma prevalence was 1.34% and 5.04% in 1974 and 1985, respectively, in schoolchildren 7–15-yr-old. Although similar methodology was applied, the questionnaire used in their second survey was a revised version of the one used in the first, and neither was standardized. In addition, theirs was a local study with a population restricted to schoolchildren only in Taipei City. To the best of our knowledge, there is no other study that compares trends of asthma prevalence throughout Taiwan.

Many personal and environmental factors contribute to asthma attacks and their prevalence (5, 9–12). There were also possibly changes over time in the proportions of these factors between asthmatics. The widespread acceptance that asthma is indeed increasing has created considerable concern about what kinds of factors might be responsible. To date, however, population studies exploring the effects of these variables remained limited.

The data for this study comes from the standardized ‘International Study of Asthma and Allergies in Childhood’ – Chinese version (ISAAC-C) questionnaire used in two national surveys in 1995–96 and 2001. The first aim of the study was to determine whether the lifetime prevalence of asthma in adolescents actually
increased during this period. The second was to investigate whether changes in selected individual-level risk factors between two surveys could explain any observed change in prevalence. The third was to compare changes in air pollution and meteorology data with changes in asthma prevalence in order to assess their relationship.

Subjects and methods
Study design

Between November 1995 and March 1996, a nationwide mass screening survey was conducted for respiratory diseases and symptoms in middle-school students. A total of 800 middle schools and more than 1 million students were investigated. The study protocol has been described previously (9, 13), and was replicated in the 2001 survey. Briefly, the identical standardized ISAAC-C questionnaire was taken home by students and answered by parents. Classroom incentives but not individual incentives were used to encourage participation.

In order to compare outdoor air pollution and meteorology data with questionnaire results, we investigated schools within 1-km catchment areas of monitoring stations of the Taiwan Environmental Protection Agency (EPA) (Fig. 1). A total of 22 middle schools in Taiwan’s 22 counties were randomly chosen in 2001 survey, and student sampling was stratified by grade in each school. Participants in both surveys were mostly between the ages of 12–15. Data from the 2001 survey and data from the identical 22 middle schools in 1995–96 survey were combined for further analysis.

Definition of diseases by questionnaire

Two indicators of asthma were considered. Physician-diagnosed asthma was defined by parental reports, ‘Has your index child ever being diagnosed as having asthma by a physician?’. The symptoms of asthma were asked, ‘Has your index child ever had wheezing or whistling in the chest at any time in the past when you did not have a cold or the flu?’. Questionnaire-determined asthma was defined by either a report of physician-diagnosed asthma or symptoms of asthma. Atopic eczema was defined as the presence of itching skin eruptions at cubital, posterior popliteal, neck, periauricle, and eyebrow areas for 6 months or longer, and the diagnosis of atopic eczema by a physician in the participant’s history. Information on lifetime prevalences of asthma and atopic eczema were obtained using these definitions.

Covariates

Many individual-level predictors have been identified for childhood asthma. We also collected data on social and environmental factors including parental education level, active smoking habit, daily cigarette consumption in family, exercise habit, and incense burning at home in both surveys. Some personal data, such as active smoking habits, were reported by students themselves.

Air pollution and meteorology data

Complete monitoring data for the air pollutants 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, were available from EPA monitoring stations beginning in 1995. Concentrations of each pollutant were measured continuously and reported hourly – CO by non-dispersive infrared absorption, NOx by chemiluminescence, O3 by ultraviolet absorption, and PM10 by beta-gauge. Hourly and daily data were combined to calculate the monthly average. We used regression model to assess the slopes of the monthly average of temperature, relative humidity, and air pollutants from 1995 to 2000, and estimated the change of each between the study period of two surveys in every municipality.

Statistical analysis

Prevalences were directly standardized for age and sex. Bivariate analyses were conducted to determine the relative effectiveness of each potential risk factor on asthma. In order to investigate whether changes in the distributions of these factors between two surveys could explain the observed change in prevalence, the prevalence differences (2001 survey – 1995–96 survey) for physician-diagnosed and questionnaire-determined asthma were shown and attributable risks were calculated by comparing prevalence differences before and after adjustment for risk factors.

Previously reported analyses of municipal outcomes have demonstrated a larger inter-city variation than would be predicted by inter-individual variation (9, 13, 14). We used two-stage methods not only to derive more precise estimates of site-specific parameters and site-level effects, but also to correct for any excess between-site variability and adjust for multiple comparisons. In the first step, a logistic regression model was used to estimate the adjusted prevalences of asthma among students in each of the 22 schools, controlling for the individual-level covariates. The goodness-of-fit was also accessed with likelihood ratio tests to determine whether a variable contributed significantly to the model. Then we calculated the adjusted prevalence change for each school. In the second step, these community-specific asthma prevalence changes were regressed against the estimated changes in temperature, relative humidity, and air pollutants between two surveys, using weights proportional to the inverse variance \((1/\text{s.e.}^2)\) of the adjusted prevalence rates.

### Results

Between February and June 2001, a total of 11,738 students and their parents from 22 middle schools were investigated. The response rate was 94.1%. There were 44,104 data (response rate 89.3%) selected from the identical schools in 1995–96 survey. In both surveys, the response rates were independent and mutually exclusive of the reported diseases or symptoms. Compared with 1995–96 survey, children in 2001 survey seem to be a little older (13.6 yr vs. 13.3 yr) and have higher proportion of female (50.8% vs. 49.6%). Table 1 shows the changes in standardized prevalences of asthma during two surveys. Physician-diagnosed asthma increased from 4.54% in 1995–96 to 6.05% in 2001 (adjusted prevalence ratio 1.35, 95% CI: 1.23–1.47). Questionnaire-determined asthma also increased from 9.50% in 1995–96 to 11.80% in 2001. After adjustment for all covariates which might lead to differential responses, prevalence ratios of physician-diagnosed and questionnaire-determined asthma decreased but were statistically unchanged (Table 1).

In Table 2, the basic tabulation of unweighted prevalences by risk factors is presented for each survey. Male, younger subjects, higher parental education levels, greater daily cigarette consumption in the family, no exercise habit, no incense burning at home, and a positive history of atopic eczema were found to be associated with the occurrence of childhood asthma. For both physician-diagnosed and questionnaire-determined asthma, we detected no significant differences in associations between two surveys. There were also no significant survey and risk factor interactions (data not shown).

<table>
<thead>
<tr>
<th></th>
<th>1995–96</th>
<th>2001</th>
<th>PR adjusted for age, sex, and season of investigation (95% CI)</th>
<th>PR adjusted for all covariates† (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician-diagnosed asthma</td>
<td>4.54</td>
<td>6.05</td>
<td>(1.10–1.25)</td>
<td>(1.13–1.35)</td>
</tr>
<tr>
<td>Questionnaire-determined asthma</td>
<td>9.50</td>
<td>11.80</td>
<td>(1.17–1.33)</td>
<td>(1.10–1.25)</td>
</tr>
</tbody>
</table>

PR indicates prevalence ratio and CI indicates confidence interval.

*Standardized for age and sex.
†Age, sex, season of investigation, parental education, smoking habit, exercise habit, daily cigarette consumption in family, incense burning at home, atopic eczema, and municipality.
asthma (Table 3). Changes for most of the risk factors examined were small, the largest being parental education level. After adjustment for all potential risk factors, the prevalence differences were statistically unchanged at 1.08% (0.90–1.25%) for physician-diagnosed asthma and 1.57% (1.31–1.82%) for questionnaire-determined asthma. Thus, after allowing for the change in asthma prevalences that may be attributed to changes in any of these factors, there were unexplained increases of approximately 1.08% in physician-diagnosed asthma and 1.57% in questionnaire-determined asthma.

In Table 3, we could observe changes between two surveys in exercise habit, parental education level, daily cigarette consumption in the family, and history of eczema: all were associated with slight increases in prevalence differences of both asthma definitions. Among these risk factors, the largest was parental education level, which seemed to explain 23.6% of the increase in prevalence rates of physician-diagnosed asthma and 20.5% of questionnaire-determined asthma. Taken together, changes in the distributions of all the risk factors we concerned could explain 31.5% of the increase in physician-diagnosed asthma and 30.9% in questionnaire-determined asthma. However, the prevalence differences remained statistically unchanged and we could not attribute the increasing prevalences to any risk factor.
Prevalence differences of asthma were regressed against the estimated changes in temperature, relative humidity, and air pollutants by multi-pollutant model (Table 4). After controlling for all air pollution and meteorology data, municipalities with a higher temperature increase were related with a higher prevalence change in questionnaire-determined asthma but not reached statistical significance in physician-diagnosed asthma. In average of the 22 stations, from 1995–96 to 2001, it was estimated 1.31°C elevation in temperature (data not shown), which indicated 1.65% prevalence change in physician-diagnosed asthma and 4.85% in questionnaire-determined asthma.

### Discussion

Our most important finding was that lifetime prevalences of physician-diagnosed and questionnaire-determined asthma of Taiwanese adolescents have significantly increased during recent years. The increase was largely unexplained by changing distributions of risk factors including exercise habit, parental education level, active smoking habit, daily cigarette consumption in the family, incense burning at home, or a history of eczema. We also found a higher increasing trend in asthma prevalence for children growing up in areas with a higher temperature increase between two surveys.

Separate studies using different methodologies have rendered the comparison of prevalence difficult. In such cases, there has been some dispute about whether the upward trend truly reflects underlying morbidity (15). In order to minimize technical bias, we analyzed data from the same schools and used standardized procedures for data collection. The ISAAC questionnaire we used has been validated and used throughout the world (16). As the identical questionnaires were applied to students with the similar age, it is most unlikely that the differences in our findings are attributable to any changes of methodology (17). A valid estimate of the time trend was also allowed. However, owing to the lack of objective data, the increasing trend in our repeated cross-sectional studies should be interpreted with caution (4).

In children with a physician’s diagnosis of asthma, 77.3% in 1995–96 and 80.2% in 2001 were reported as having typical symptoms, whereas in those without such a diagnosis, only 5.2% and 5.9%, respectively, reported such symptoms (both p < 0.001). Of 4188 children with questionnaire-determined asthma in 1995–96, a diagnosis of asthma was known in 2001 instances (47.8%). In contrast, a diagnosis of asthma was known in 52.1% of children with

### Table 3. Prevalence difference (PD) and attributable risk (AR) for asthma between 1995–96 and 2001 surveys in Taiwanese adolescents, adjusted for potential risk factors

<table>
<thead>
<tr>
<th>Levels of factors</th>
<th>Physician-diagnosed asthma</th>
<th>Questionnaire-determined asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PD (%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>Sex + age + season of investigation + municipality</td>
<td>1.57</td>
<td>1.40–1.75</td>
</tr>
<tr>
<td>Smoking habit*</td>
<td>2</td>
<td>1.59</td>
</tr>
<tr>
<td>Exercise habit</td>
<td>2</td>
<td>1.52</td>
</tr>
<tr>
<td>Parental education</td>
<td>4</td>
<td>1.20</td>
</tr>
<tr>
<td>Daily cigarettes consumption in family</td>
<td>4</td>
<td>1.51</td>
</tr>
<tr>
<td>Incense burning at home</td>
<td>2</td>
<td>1.60</td>
</tr>
<tr>
<td>Atopic eczema</td>
<td>2</td>
<td>1.44</td>
</tr>
<tr>
<td>All of above</td>
<td>1.08</td>
<td>0.90–1.26</td>
</tr>
</tbody>
</table>

All prevalence differences are adjusted for sex, age, season of investigation, municipality, and the index risk factor.


*Responded to by the children themselves.

### Table 4. Relationship between prevalence differences (%) of asthma and temporal changes of temperature, relative humidity, and air pollutants in 22 middle schools in Taiwan

<table>
<thead>
<tr>
<th></th>
<th>Physician-diagnosed asthma</th>
<th>Questionnaire-determined asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>95% CI</td>
</tr>
<tr>
<td>Temperature [°C]</td>
<td>1.26</td>
<td>−0.95 to 3.46</td>
</tr>
<tr>
<td>Relative humidity (%)</td>
<td>0.08</td>
<td>−0.19 to 0.36</td>
</tr>
<tr>
<td>CO (p.p.b.)</td>
<td>−0.09</td>
<td>−0.25 to 0.07</td>
</tr>
<tr>
<td>O₃ (p.p.b.)</td>
<td>0.07</td>
<td>−0.36 to 0.51</td>
</tr>
<tr>
<td>PM₁₀ (µg/m³)</td>
<td>−0.09</td>
<td>−0.22 to 0.05</td>
</tr>
<tr>
<td>NOx (p.p.b.)</td>
<td>−0.09</td>
<td>−0.48 to 0.29</td>
</tr>
</tbody>
</table>

Prevalence is adjusted for sex, age, season of investigation, parental education, daily cigarette consumption in family, and atopic eczema.

Prevalence differences are calculated as (2001 survey – 1995–96 survey) in each school.

* p < 0.05.
questionnaire-determined asthma in 2001. This does not necessarily mean that the increase is attributable to the increase in parental recognition and awareness of symptoms. The adjusted prevalence ratio of non-asthmatic wheeze was 1.15 (95% CI: 1.04–1.26) between two surveys. Although the trends may be due in part to changes in the reporting and consulting behavior of parents and in the labeling of the disease by general practitioners (18, 19), it does mean that some of these increases are real. As the prevalence of non-asthmatic wheeze still increased, the rise in lifetime prevalence of asthma could not be attributed solely to a change in diagnostic terminology or public awareness.

It was widely known that younger subjects and males had a higher rate of asthma (5, 9, 12). We also found parental education level was associated with childhood asthma (Table 2). Parents with a higher education level were more anxious about their children's health conditions; therefore, these children would be more likely to be diagnosed as asthmatics or recognized as wheezers (9, 12). Exposure to cigarette smoke in early life may increase a child's susceptibility to the development of atopic diseases and to a more severe expression of atopy in the child (10). Active smoking in adolescence may also be associated with the onset of respiratory symptoms (11). However, our findings suggested a negative or relative weak relationship between an active smoking habit and asthma. The protective effect of incense burning at home on asthma was also noted. These reflected smoking cessation or avoidance effects by individuals with sensitive airways, as in other cross-sectional studies (12, 20, 21). In the present study, prevalence of atopic eczema had increased significantly from 1.57% in 1995–96 to 2.79% in 2001, in keeping with another study by Ng Man Kwong et al. (22). The apparent increase of wheeze in adolescence may be related to an increased tendency for atopy development (23), or to an increased susceptibility to wheeze as an expression of atopy (24). In our design, the past history of atopic eczema was used only as a surrogate of individual atopic characteristics.

Because the main outcome measurements are lifetime prevalences of asthma, season of investigation would not be a major confounder in our design. In fact, although study periods of two surveys were not identical, season of investigation did not show significant differences in association with asthma (Table 2). Current symptoms occurred in the past 12 months were also included in our ISAAC questionnaire surveys. However, prevalences of current symptoms were not all increasing during recent years (data not shown). Despite some studies showed that asthmatic episodes gradually decreased since 1993–94 (7), the reason concerning the inconsistent findings was beyond the scope in this report. Improvement in therapeutic compliance and accessibility of primary care over time might in part explain the circumstance.

In our results, the prevalence differences were statistically unchanged after controlling for potential confounders (Table 3). Although no investigated risk factors could be found to attribute to the increasing prevalences of physician-diagnosed and questionnaire-determined asthma, we believed that changes in genetic susceptibility to atopy, or to wheeze as a response of atopy, are unlikely to have occurred between 1995–96 and 2001. A more probable explanation of the increasing prevalence is that the trend is because of a change in exposure to undefined environmental determinants of asthma, or to other factors that promote wheeze in susceptible children. Increased awareness of asthma among the population and health care personnel could also explain the increasing prevalence over time.

The comparison from our two surveys showed a 1.35-fold increase in the lifetime prevalence of physician-diagnosed asthma and a 1.25-fold increase in questionnaire-determined asthma, which suggested 5.7% and 4.2% increases per year on average, respectively. Similar increases in prevalence have been reported all around the world (3, 4, 23, 25, 26).

Meteorological factors, especially non-summer temperature and winter humidity, were associated with the prevalence of childhood asthma in our previous Taiwanese study (9). In European Community Respiratory Health Survey during 1991–93, the prevalence of respiratory symptoms was directly related to temperature in the coldest month (27). A report from New Zealand showed that an increase of 1°C in annual average temperature was associated with a 1% increase in long-term asthma prevalence (28). There may indeed be some indoor factors, such as dust mites, endotoxins, or other humidity-sensitive allergens affected by outdoor climate. In our analysis, a municipality with an increase of 1°C in temperature change was estimated to have a 3.70% increase in the prevalence of questionnaire-determined asthma, but a relatively weak and non-significant association was noted in physician-diagnosed asthma (Table 4). The lack of power because of relatively small sample size was of major concern, but the reason why precise diagnosis by doctors had less effect than reported
symptoms from questionnaires still warrants additional investigation.

It was found that a 1.65% prevalence increase in physician-diagnosed asthma and 4.85% in questionnaire-determined asthma could attribute to temperature elevation between two surveys. However, because many outdoor allergens and air pollutants were not investigated, the virtual increase in asthma prevalence would seem somehow reduced. We therefore suggested that the increasing temperature might be the main reason for the rising trends of asthma in Taiwanese adolescents.

Time-series approaches to analyze the association between short-term variations in ecological data and asthma provide relatively good control for confounding by individual factors. These studies are not suitable to investigate the effects of long-term exposures and chronic outcomes (29). Ecologic exposure assessment had many advantages in our study. Estimates of changes based on 22 different areas covering diverse parts of Taiwan were unlikely to be attributable to local changes in the composition of the population. The density of middle schools in Taiwan was very high and almost all the surveyed students attended schools within 1 km of their homes. Monitoring stations thus provided good indicators for both school and home exposure.

We do not think we have missed any important confounder in our analysis. Migrating from one community to another could lead to misclassification of ecological exposure. However, errors in exposure assessment were likely to be random, which would reduce the magnitude of association, but would not introduce a positive bias in the associations. Ecologic confounders like urbanization and socialization actually could exist and there might be incomplete adjustment and residual confounding. However, more complete personal risk factors were very difficult to obtain in such large-scale surveys. The exposure information obtained from monitoring stations was limited in 1995 and later years. We used air pollution and meteorology data from 1995 and estimated their changes between two surveys in each school as proxy of the differences in the past. Previous studies suspected that the cumulative exposure before the examination had a greater contribution to health than exposures within early infancy (30). So far, no data are available to point out clearly which specific effects are associated with exposures at a particular age.

In conclusion, the present study has suggested a substantial increase in the lifetime prevalence of physician-diagnosed and questionnaire-determined asthma in Taiwanese adolescents, and has established that several factors previously implicated were not major contributors to the observed increase. Future studies are required to investigate the contribution of changes over time in other potential etiological factors, including levels of indoor pollutant exposure, allergen exposure, and other personal risks such as diet and prenatal exposure.

Acknowledgments
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