Abstract. – OBJECTIVE: Environmental tobacco smoke exposure is a well-recognized risk factor for asthma development and poor asthma control in children. However, the relationship between changes in parental smoking habits over time and the prevalence of childhood asthma remains largely unknown. Our objective was to investigate the trends of parental smoking behaviors in relation to childhood wheeze/asthma rates over a 20-year period.

SUBJECTS AND METHODS: A standardized questionnaire on household overall smoking and household indoor tobacco smoking (HITS) habits was distributed to 8-9-years-old school children in the context of five cross-sectional surveys conducted in 1998 (n=3,076), 2003 (n=2,725), 2008 (n=2,688), 2013 (n=2,554) and 2018 (n=2,648).

RESULTS: The parental overall smoking and HITS rates have substantially decreased during the study period (p-for-trend<0.001). However, while HITS declined among the fathers of asthmatic and non-asthmatic children as well as among the mothers of non-asthmatic ones (p-for-trend<0.001), it remained unchanged in the case of the mothers of asthmatic participants (p-for-trend 0.283). The mothers of asthmatic children consistently reported more HITS than those of non-asthmatic participants, while prevalence changes of current wheeze/asthma over the surveillance period were in complete agreement with changes in maternal HITS (cross-correlation coefficient 0.916 at zero-year lag) but not with paternal smoking behaviors.

CONCLUSIONS: Overall and indoor smoking rates of school children’s adult family members declined substantially during the 1998-2018 period in Greece. However, no such trend was noted among mothers of asthmatic children, while temporal changes in maternal indoor smoking rates occurred in parallel with those of childhood asthma prevalence.

Introduction

Ample evidence shows that smoking is detrimental to human health. In an excellent series of systematic reviews in late 1990’s, evidence that related parental smoking to lower respiratory symptoms, allergic sensitization, bronchial reactivity, and asthma in children was highlighted. Further systematic reviews and meta-analyses have rendered support to these earlier observations. Until recently, Greece has maintained one of the highest prevalence rates of tobacco smoking globally, and an astonishingly high first-and second-hand smoke exposure rate.

In the context of Patras’ epidemiological study of asthma and allergies, five cross-sectional surveys were conducted in 1998, 2003, 2008, 2013 and 2018, based on a parental questionnaire which also included questions on overall household and indoor adult tobacco smoking (HITS). We hypothesized that, due to the increasing public awareness and the smoke-free legislation introduced by the Greek parliament in 2008, smoking would have decreased in the 20-year survey period, and that the changes in smoking behaviors would have positively affected the prevalence of childhood wheeze/asthma.

Subjects and Methods

Study Questionnaire and Definitions

A standardized parental questionnaire was distributed to 3rd and 4th-grade school children (eight...
and nine years of age; target population) of public schools in the city of Patras, Greece, every five years from 1998 to 2018. In all surveys, the three private schools within the municipality of Patras were not approached, and schools for children with special needs were excluded. The questionnaire consisted of simple questions on current (i.e., in the last two years) physician-diagnosed wheeze/asthma, the overall and indoor smoking habits of parents and other family members, and the educational level of the parents (Supplementary File 1). The exact wording of the questions remained unchanged in the five cross-sectional surveys18. Wheeze/asthma was considered and analyzed as a single group, since the ‘Patras Asthma and Allergies Epidemiological Study’18-22, includes 8- to 9-year-old children and, therefore, recurrent wheezing in the last two years most likely represents undiagnosed asthma. The term ‘overall tobacco smoking’ refers to the household members who were smokers (outdoors and/or indoors), while the term ‘household indoors tobacco smoking’ (HITS) refers to the subgroup of smokers who were smoking at home (indoors). A household smoker, other than the parents, was termed ‘other smoker’, while the presence of at least one adult smoker in the family was termed ‘any smoker’.

The method of distribution and collection of the questionnaires and the process of the confirmation of the responses have been described previously18.

Ethics

Formal approval was obtained for all five surveys from the Ethics Committee of the University Hospital of Patras and the Regional Directorate of Primary Education (Memorandum of Collaboration with the University of Patras, 23.9.2016). Parental written consent forms (Supplementary File 2) were distributed with the questionnaire sheets.

Statistical Analysis

The prevalence of smoking and wheeze/asthma was calculated as the ratio of respective cases to total number of responders. Prevalence differences between groups as well as overall prevalence trends were calculated by the Chi-square test. HITS was also assessed by means of ‘packs per year’ and compared between asthmatic and non-asthmatic children using the Mann-Whitney U test. The effect of parental educational level on parental smoking habits was assessed by logistic regression models.

Cross-correlation analysis was used to explore the relationship between the prevalence trends of childhood asthma and the trends of parental smoking habits over the survey period. Annual prevalence rates were estimated by fitting a third-order polynomial to prevalence data from 1998, 2003, 2008, 2013, and 2018, and cross-correlation coefficients were calculated for lags of ±5 years. The higher cross-correlation coefficient represents the year of best fit between the two series, while the year lag in which the higher coefficient is observed refers to how far the series are offset. For example, when the maximum cross-correlation coefficient occurs at a lag of zero years, the time series are in complete agreement, i.e., the prevalence changes in the two series have occurred in parallel.

Statistical analyses were performed using the IBM SPSS version 28 (IBM Corp., Armonk, NY, USA). A p-value <0.05 was considered statistically significant.

Results

In all five surveys18-22, the surveyed population exceeded 80% of the target population and the response rate ranged from 91.3% to 96.7%. The paternal age ranged from 29 to 67 years and the maternal age from 27 to 53 years.

The overall rate of smoking fathers, smoking mothers, other smoker, and any smoker, and their distribution according to the asthma status of their children are presented in Table I. There is a decreasing trend in smoking rates in all smoking groups throughout the survey period when all children are considered (p-for-trend<0.001). The fathers showed a significant decline in smoking rates both in asthmatic and non-asthmatic children (p-for-trend<0.001) (Table I). On the other hand, the mothers, despite the significant declining trend in smoking rates in non-asthmatic children (p-for-trend<0.001), exhibited no such trend in the wheeze/asthma subgroup (p-for-trend 0.283). The overall father-mother difference in smoking rates within the surveys is significant (p<0.001); this is particularly true for the non-asthmatic group of children, whereas in the wheeze/asthma group the difference noted in the 1998 and 2003 surveys ceased to exist thereafter (Table I).

Table II presents the rates of HITS exposure by smoking group and according to the wheeze/asthma status of children. Again, there is a decreasing trend in HITS in all smoking groups throughout the survey period when all children or only the non-asthmatic group are considered (p-for-trend<0.001). In children with current wheeze/
asthma, however, only the paternal HITS rates declined ($p$-for-trend$<0.001), while the maternal rates did not ($p$-for-trend 0.056) (Table II). The overall difference in HITS rates between fathers and mothers was significant up to the 2008 survey but ceased to exist thereafter; this is also true for the non-asthmatic group of children, while in the wheeze/asthma group, the difference was significant only in the 1998 survey (Table II).

Figure 1 presents HITS exposure of children with and without wheeze/asthma by means of packs per year smoked indoors by adult members of their

### Table I. Overall tobacco smoking of adult members of families of schoolchildren in Patras, Greece, between 1998 and 2018.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total surveyed</th>
<th>Current wheeze/asthma</th>
<th>Father smoker</th>
<th>Mother smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>3,076</td>
<td>184 (6.0)</td>
<td>1,645 (53.5)*</td>
<td>1,096 (35.6)*</td>
</tr>
<tr>
<td>2003</td>
<td>2,725</td>
<td>189 (6.9)</td>
<td>1,451 (53.2)*</td>
<td>986 (36.2)*</td>
</tr>
<tr>
<td>2008</td>
<td>2,688</td>
<td>185 (6.9)</td>
<td>1,233 (45.9)*</td>
<td>910 (33.9)*</td>
</tr>
<tr>
<td>2013</td>
<td>2,554</td>
<td>134 (5.2)</td>
<td>86 (46.5)</td>
<td>69 (37.3)</td>
</tr>
<tr>
<td>2018</td>
<td>2,648</td>
<td>114 (4.3)</td>
<td>926 (38.3)*</td>
<td>841 (33.6)*</td>
</tr>
</tbody>
</table>

Values are number of cases (%). Difference between current and no current wheeze/asthma: *$p<0.05$. Difference between fathers and mothers for the respective outcome (same survey): *$p<0.001$, †$p<0.01$. 

### Table II. Indoors tobacco smoking of adult members of families of schoolchildren in Patras, Greece, between 1998 and 2018.

<table>
<thead>
<tr>
<th>Year</th>
<th>Total surveyed</th>
<th>Current wheeze/asthma</th>
<th>Father smoking at home</th>
<th>Mother smoking at home</th>
<th>Other smoking at home</th>
<th>Any smoking at home</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>3,076</td>
<td>184 (6.0)</td>
<td>1,395 (45.4)*</td>
<td>964 (31.3)*</td>
<td>97 (3.2)</td>
<td>1,748 (56.8)</td>
</tr>
<tr>
<td>2003</td>
<td>2,725</td>
<td>189 (6.9)</td>
<td>1,098 (30.4)*</td>
<td>763 (28.0)*</td>
<td>127 (4.7)</td>
<td>1,439 (52.8)</td>
</tr>
<tr>
<td>2008</td>
<td>2,688</td>
<td>185 (6.9)</td>
<td>879 (32.7)*</td>
<td>668 (24.9)*</td>
<td>55 (2)</td>
<td>1,152 (42.9)</td>
</tr>
<tr>
<td>2013</td>
<td>2,554</td>
<td>134 (5.2)</td>
<td>583 (22.8)</td>
<td>488 (20.0)</td>
<td>74 (2.9)</td>
<td>828 (32.4)</td>
</tr>
<tr>
<td>2018</td>
<td>2,648</td>
<td>114 (4.3)</td>
<td>343 (13.0)</td>
<td>270 (10.2)</td>
<td>40 (1.5)</td>
<td>477 (18.0)</td>
</tr>
</tbody>
</table>

Values are number of cases (%). Difference between current and no current wheeze/asthma: *$p<0.01$, †$p<0.001$. Difference between fathers and mothers for the respective outcome (same survey): *$p<0.001$, †$p<0.01$. 

Figure 1 presents HITS exposure of children with and without wheeze/asthma by means of packs per year smoked indoors by adult members of their
family. It demonstrates that the HITS exposure (in packs per year) was not different between the asthmatic and non-asthmatic groups, neither within nor between surveys. In addition, the number of years of parental (paternal or/and maternal) smoking was not associated with current wheeze/asthma (ORs 1.00-1.03 among surveys; data not shown).

Cross-correlation analysis (Figure 2) revealed complete agreement between prevalence trends of current wheeze/asthma and maternal or ‘any smoker’ HITS rates during the surveillance period. Maternal and ‘any smoker’ HITS showed the highest cross-correlation coefficient (0.918 and 0.885, respectively) at a lag of zero years, while paternal HITS presented its maximum correlation coefficient (0.712) with an offset of three years (Figure 2, Supplementary Table I).

The educational level did not differ between fathers and mothers, neither within nor among surveys (Figure 3). The risk of being a smoker (either overall or indoors) was lower among fathers with higher educational levels in the 2013 survey, and lower among both fathers and mothers with higher educational levels in the 2018 survey (Table III). Nevertheless, the educational level of parents did not influence the risk of childhood wheeze/asthma in any survey (Table IV).

**Discussion**

The results of our study suggest that the overall and indoors smoking rates of schoolchildren’s adult family members declined substantially during the 1998-2018 period in Greece. These declining trends were more prominent in the case of fathers of both asthmatic and non-asthmatic children, and of the mothers of non-asthmatic

<table>
<thead>
<tr>
<th>Risk according to educational level</th>
<th>1998</th>
<th>2003</th>
<th>2008</th>
<th>2013</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paternal overall smoking</td>
<td>1.00 (0.92-1.09)</td>
<td>0.98 (0.90-1.07)</td>
<td>1.02 (0.95-1.08)</td>
<td>0.92 (0.85-0.98)</td>
<td>0.73 (0.68-0.79)</td>
</tr>
<tr>
<td>Paternal HITS</td>
<td>1.01 (0.93-1.10)</td>
<td>0.98 (0.89-1.07)</td>
<td>1.03 (0.96-1.10)</td>
<td>0.90 (0.83-0.98)</td>
<td>0.63 (0.57-0.71)</td>
</tr>
<tr>
<td>Maternal overall smoking</td>
<td>1.04 (0.95-1.13)</td>
<td>0.96 (0.88-1.06)</td>
<td>1.02 (0.95-1.10)</td>
<td>0.97 (0.90-1.05)</td>
<td>0.80 (0.74-0.87)</td>
</tr>
<tr>
<td>Maternal HITS</td>
<td>1.03 (0.94-1.13)</td>
<td>0.96 (0.87-1.05)</td>
<td>1.06 (0.98-1.14)</td>
<td>0.95 (0.87-1.04)</td>
<td>0.63 (0.55-0.72)</td>
</tr>
</tbody>
</table>

Data are OR with 95% CI as calculated by logistic regression analysis. HITS: household indoors tobacco smoking.
children. Surprisingly, no such trends were noted for the mothers of asthmatic children. Cross correlation analysis revealed that the changes in maternal HITS rates occurred in parallel with those of childhood asthma rates during the surveillance period; this, however, was not the case with the changes in paternal HITS rates, which were less strongly correlated and in temporal disagreement with those of asthma prevalence in children. The probability of less educated parents being smokers (outdoors and/or indoors) was significant only in the 2013 and 2018 surveys, although neither parental education nor the number of cigarette packs smoked indoors per year seemed to directly relate to the risk of childhood wheeze/asthma.

Tobacco smoke exposure has a detrimental effect on lung health in adults, while secondhand smoking is an important risk factor for respiratory morbidity in children. Adult smoking has been shown to be influenced by various socio-demographic factors such as gender, age group, marital status, and work status, depending on the cultural milieu. In addition, cognitive (visuospatial and attention skills) and emotional processes (depression and anxiety) impact the ability to quit smoking. Parental smoking at home is the most important means of tobacco smoke exposure in preadolescent children, although the presence of a child at home has been associated with restricted indoor smoking. Nevertheless, although an overwhelming body of evidence supports the association between childhood asthma and secondhand smoking, large studies such as the PIAMA birth cohort have failed to prove a causal relationship.

It has long been established that normal lung function is attained by the age of 20-25 years, followed by a gradual decline. At the end of 1990s, the meta-analyses of Cook and Strachan concluded that the epidemiological evidence for the association of environmental tobacco exposure and asthma and/or respiratory symptoms was so strong that no further prevalence investigations were justified; they suggested that further research should focus on ‘time-widows’ during which such exposure is most critical. Since then, prospective studies have advanced over time, and cohorts have been followed into their sixth decade of life. The picture which emerges from this body of evidence is that factors involved in abnormal lung growth or accelerated decline are most likely responsible for what is currently labeled as ‘chronic obstructive pulmonary disease’, the proverbial ‘COPD’. Factors involved in retarded lung/airway growth include: a) preconception transgenerational epigenetic influence

![Figure 2. Cross correlation analysis of the prevalence of current wheeze/asthma and household indoors smoke exposure (father smoker, mother smoker, any smoker) between 1998 and 2018. The graph shows cross correlation coefficients (bars) with the limit of significance (red dotted line). The lag (years) refers to how far the series are offset. The most dominant cross correlation (grey bar) represents the best fit between the two series. Raw data are available in Supplementary Table II. CCF: cross correlation function.](image-url)
stress – tobacco smoking and/or pollution may affect a number of these); c) early compromise of postnatal lung function of any etiology (viral lower respiratory tract infections, atopic sensitization, childhood obesity, pollution – also refer to antenatal exposures). The accelerated decline of lung function appears to be mostly affected by genetic predisposition (maternal and paternal asthma) and factors operating during childhood (i.e., maternal smoking, lower respiratory tract infections) and antenatally. In the above context, it appears that adult smoking is not the major factor in the personal accelerated decline of lung function. However, the abolishment of environmental tobacco exposure is perhaps the most easily accessible of the few manipulable preventive measures, which can currently help promote lung health ‘from womb to tomb’ at a population level.

Although the cross-sectional design of our surveys does not allow for etiologic conclusions, the strong temporal agreement between maternal HITS rates and the prevalence of childhood asthma, in combination with the persistence of high maternal HITS rates only in families of asthmatic children, suggest that maternal smoking behaviors should be of concern in case of children with troublesome or persistent respiratory symptoms. The finding of decreasing paternal but persistent maternal HITS rates, especially when an asthmatic child lives at home, most probably echoes the findings of a recent study showing that smoking-attributable mortality among women in 29 European countries has already or will soon become higher than that among men.

Our results discourage invoking a lower educational level as a contributing factor to parental smoking behaviors; it is possible that improvements in the educational level and a broader osmosis between sexes in social behaviors in the last decades may have contributed to a more ‘aggressive’ adoption of tobacco smoking by women, especially those at a socially and economically productive age.

Table IV. Risk of childhood wheeze/asthma according to parental educational level.

<table>
<thead>
<tr>
<th>Year</th>
<th>Paternal education level</th>
<th>Maternal education level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>0.98 (0.82-1.17)</td>
<td>0.96 (0.79-1.14)</td>
</tr>
<tr>
<td>2003</td>
<td>1.00 (0.84-1.19)</td>
<td>0.95 (0.80-1.13)</td>
</tr>
<tr>
<td>2008</td>
<td>0.90 (0.79-1.02)</td>
<td>0.92 (0.80-1.05)</td>
</tr>
<tr>
<td>2013</td>
<td>1.12 (0.95-1.36)</td>
<td>1.17 (0.98-1.41)</td>
</tr>
<tr>
<td>2018</td>
<td>1.05 (0.88-1.25)</td>
<td>1.07 (0.89-1.30)</td>
</tr>
</tbody>
</table>

Data are OR with 95% CI calculated by logistic regression analysis.
The need for effective measures to contain the use of tobacco smoke continues to be widely discussed. Although tobacco product labeling is considered an important tool, its implementation by the EU Directive 2001/37/EC was greeted differently by the EU counties; Greek male smokers – over 50% of the male population at that time – considered this measure as ‘annoying’ and ‘invasive’. In addition, despite ample evidence that relevant legislation may reduce secondhand smoke exposure, the implementation of the 2008 smoke-free law in Greece was disappointing. A 2011 survey reported that 45% of participants had noticed smoking in their workplace, while approximately 30% of smokers admitted having smoked in indoors establishments (coffeehouses, bars, nightclubs). Thus, it is not surprising that the primary and/or secondary exposure of the Greek population to tobacco smoke is estimated to approximate 90%.

However, the increase in tobacco taxation during the years of financial crisis has been shown to effectively improve tobacco control; adult smoking declined by 10.6% from 2008 to 2011, while the Hellenic Statistical Authority reported a 14% decrease in the number of daily smokers from 2009 to 2014. These data are in line with the significant deceleration of adult smoking rates observed during the last 20 years in our study.

Our approach to the smoking habits of the adult population was through questionnaires distributed to 8- and 9-years-old school children. Therefore, the age range of the adult responders is skewed, which may explain the differences in smoking prevalence from other Greek studies. Nevertheless, the gradual decline of smoking prevalence in our cohort resembles that of the above-mentioned reports.

Limitations

Apart from its cross-sectional design and the skewed age range of adult smokers already discussed, our study has other limitations. The most important is the lack of an objective measure of tobacco smoke exposure. Although the validity of information based on self-reported smoking behaviors may be questioned, self-reported exposure remains the most broadly used tool in large population samples. Specific questionnaire instruments have been developed to assess smoking prevalence in particular populations (e.g., secondhand smoke exposure in never smokers), but there is a lack of consensus regarding their use. Cotinine and other biomarkers of nicotine exposure in specimens such as serum, urine, saliva, hair, toenail, and meconium have also been utilized. It has also been shown that – due to the high specificity of self-reported smoking – the addition of self-reporting to serum or urine cotinine measurement increases the sensitivity of these methods. Second, we did not address non-residential (e.g., cars, cafeterias, private and public places) and thirdhand smoking exposure. Studies have shown that these sources and third-hand exposure may constitute a substantial part of total tobacco smoke exposure in the population. Our study is based on a concise set of questions incorporated into a standardized questionnaire for asthma and allergies; we chose to maintain the exact wording of the questionnaire since 1998 and keep it simple to maximize the response rate. Third, for the same reasons as above, we also elected not to specifically inquire about e-cigarette smoking; thus, we do not know whether parents have included this type of smoking behavior in their responses. E-cigarettes started becoming popular in Greece after 2010, particularly among youth, ex-, and current (‘dual users’) smokers. A recent observational study revealed no difference in harm reduction between tobacco and electronic cigarette smokers after six years of follow-up. The effects of e-smoking on childhood exposure and long-term respiratory health are still poorly understood.

Conclusions

We investigated the smoking behaviors of adult family members of 8- and 9-year-old school children in Patras, Greece, using data from five methodologically identical cross-sectional surveys conducted between 1998 and 2018. Overall and indoor smoking rates declined substantially among the parents of non-asthmatic children, as well as among the fathers of those with asthma. However, no such trend was noted in mothers of asthmatic children. In addition, temporal changes in maternal indoor smoking rates occurred in parallel with those of childhood asthma prevalence during the surveillance period, thus suggesting that maternal smoking behaviors should be of concern in children with troublesome or persistent respiratory symptoms and should be carefully sought by pediatric health professionals when obtaining an environmental and family history. Our findings may facilitate policymakers and state authorities to better target new health strategies for asthma control in countries with high smoking prevalence, such as Greece.
Acknowledgments
We wish to thank the children, their parents, and the school teachers for their enthusiasm in participating in Patras Asthma and Allergies Epidemiological study.

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None.

Authors’ Contributions
Study conception and design were performed by Kostas N. Priftis, Sotirios Fouzas and Michael B. Anthracopoulos. Material preparation, data collection and analysis were performed by Panagiotis Lampropoulos, Alexandros Ntzounas, Aris Berzouanis, Styliani Malliori, and Maria Triga. The first draft of the manuscript was written by Panagiotis Lampropoulos, Sotirios Fouzas and Michael B. Anthracopoulos, and all authors commented on previous versions of the manuscript. All authors read and approved the version of the article to be published.

Conflicts of Interest
The authors state that they have no conflict of interest to declare.

Data Availability
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval
The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Scientific Board of the University Hospital of Patras (act No. 3136/6.12.2017) and the Regional Directorate of Primary Education (Memorandum of Collaboration with the University of Patras, 23.9.2016).

Informed Consent
Written informed consent was obtained from the parents of the participants before enrollment.

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