Soz.- Präventivmed. 45 (2000) 208–217
0303-8408/00/050208-10 $ 1.50 + 0.20/0

Nino Künzli [1], Joel Schwartz [2], Elisabeth Zemp Stutz [1],
Ursula Ackermann-Liebrich [1], Philippe Leuenberger [3]
on behalf of the SAPALDIA-Team [4]

[1] *Institute for Social and Preventive Medicine, University Basle*
[2] *Harvard School of Public Health, Boston*
[3] *Division of Pulmonology, CHUV, Lausanne*
[4] *Swiss Study on Air Pollution and Lung Diseases in Adults*

Association of environmental tobacco smoke at work and forced expiratory lung function among never smoking asthmatics and non-asthmatics

Abstract

Inconsistencies across studies on the association of environmental tobacco smoke (ETS) and pulmonary function may be clarified addressing potentially susceptible subgroups. We determined the association of ETS exposure at work with FVC, FEV1, and FEF25-75% in life-time never smokers (N = 3534) of the SAPALDIA random population sample (age 18–60). We considered sex, bronchial reactivity, and asthma status as a priori indicators to identify susceptible riskgroups. The multivariate regression models adjusted for height, age, education, dust/aerosol exposure, region, and ETS at home. Overall, ETS was not significantly associated with FVC (0.7%; −0.4 to +1.8), FEV1 (−0.1%, 95% CI: −1.3 to +1.1) or FEF25-75% (−1.9%; −4.2 to +0.5). Effects were observed among asthmatics (n = 325), FEV1 (−4.8%; 0 to −9.2), FEF25–75% (−12.4%; −3.7 to −20.4), FVC: (−1.7%; +2.1 to −5.5), particularly in asthmatic women (n = 183), FVC −4.4% (−9.6 to +1.1), FEV1: −8.7% (−14.5 to −2.5), FEF25–75%: −20.8% (−32 to −7.6), where duration of ETS exposure at work was associated with lung function (FEV1 −6% per hour of ETS exposure at work (p = 0.01), FEF25–75%: −3.4%/h (p<0.05). In non-asthmatic women (n = 1963) and in men no significant effect was observed. The size of the observed effect among susceptible subgroups has to be considered clinically relevant. However, due to inherent limitations of this cross-sectional analysis, selection or information biases may not be fully controlled. For example, asthmatic women reported higher ETS exposure at work than asthmatic men. Given the public health importance to identify susceptible subgroups, these results ought to be replicated.

Studies on long-term effects of exposure to environmental tobacco smoke (ETS) on pulmonary function show impaired lung function in children but inconsistent results among adults [1–4]. The contradictory findings among adults may indicate that ETS has no or very little effect on lung function. Other explanations relate to methodological issues such as differences in the level of exposure, incomparable selection and measurement procedures across studies, or uncontrolled cumulative burden of other respiratory insults among adults [2]. Furthermore, epidemiologic studies on ETS might be affected by self-selection bias, if subjects prevent ETS exposure for health reasons. This bias will be particularly strong assessing the impact of ETS exposure *at home* which is easier to influence than ETS exposure at work or elsewhere.

Apart from biases, disparate results may also be expected if susceptibility to ETS were heterogeneous within populations. If ETS affects subgroups only, the average effect in the general population may be diluted, depending on the proportion of susceptible. An adequate approach to deal with this problem would be to focus investigations on susceptible subjects. Increased susceptibility has been suggested for asthmatics [5]. However, epidemiological studies on chronic effects of ETS often excluded asthmatics [6–8] or did not report on this group specifically [9–12]. Jindal et al. reported increased morbidity and lower lung function values among ETS exposed asthmatics as compared to non-exposed asthmatics [13]. A similar marker of susceptibility may be hyperreactive air ways [14,15]. No other markers of

susceptibility for ETS have been identified, although suggestions have been made that the impact of ETS may differ depending on the ethnic background or across sex[16].
In a first report from the large random population of the Swiss Study on Air Pollution and Lung Disease in Adults (SAPALDIA) we showed significant associations of ETS with the prevalence of respiratory symptoms[17]. The purpose of this analysis is to assess the association of ETS exposure with pulmonary function. We will particularly address whether the association of ETS with pulmonary function varies by asthma status and/or sex as suggested markers of susceptibility. To limit biases and to improve the efficiency of this study we follow three strategies. First, we restrict on life-time never smokers. Second, we exclusively focus on ETS exposure *at work* rather than at home, given ETS at home to be more likely to be subject to uncontrolled self-selection. This might be particularly the case among ETS susceptible asthmatics. Third, we do not only use measures of lung volume (FVC and FEV1) as health endpoints but include mid-expiratory flow measures (FEF25–75%) which are more specific for changes in the small airways, where the earliest effects may occur[18–20].

Materials and methods

Study population

This analysis is based on life-time never smoking participants of SAPALDIA with acceptable and reproducible forced expiratory lung function assessment[21]. SAPALDIA is a multi-centre study to evaluate the relationship between environmental factors and respiratory symptoms and disease. Eight areas in Switzerland were chosen to represent a range of urbanization, altitude, air pollution, and meteorology[22]. Random samples of adults (N = 17300), aged 18–60 years, were drawn from the registries of residents in each location. Successfully recruited subjects (59%) were asked on respiratory health and symptoms, active and passive smoking exposure, and spirometric examinations and allergy tests were performed. A total of 9651 subjects completed the questionnaire interview and spirometry. Of them, 3534 yielded both acceptable pulmonary function tests and a negative history of smoking at any time in life. Sampled persons who refused to participate were asked a shorter questionnaire. Over 70% of the non-participants provided this information[23].

Pulmonary function test

Pulmonary function was measured according to published guidelines[21] with a computerized equipment (SENSORMEDICS 2200). At least three and up to eight manoeuvres were required in sitting position with nose clip. Spirometry quality control training and studies were conducted to evaluate systematic area specific errors and improve standardized assessment across teams and technicians[24].
Bronchial reactivity was measured by the dosimeter method, using MEFAR nebulizers. The standardized procedure, identical to the short protocol of the European Community Respiratory Health Survey[25], consisted in one to five inhalation steps up to a cumulative dose of 2 mg methacholine or until FEV1 decreased at least 20% compared to baseline (PD20). Throughout this text, subjects with a PD20 up to 2 mg were defined as having "reactive airways". Participants with an FEV1 baseline measure below 70% predicted or an FEV1/FVC ratio below 80% predicted were excluded from the metchacholine challenge.

Working definitions

Those who had never smoked or smoked less than 20 packs of cigarettes or less than 360 gram of tobacco in their entire life were defined as "never smokers". Exposure to other peoples smoke was first asked for the last 12 months. We asked about the number of smokers exposed to at home, whether or not other people regularly smoked at work, and total hours of ETS exposure per day, irrespective of location. The next set of questions addressed long-term history of ETS exposure, asking about the total number of both years of ETS exposure and the persons exposed. A last question assessed the subjective disturbance due to ETS exposure, shown on a scale from 0 ("not at all") to 10 (extremely disturbed).
There is no single epidemiological definition of asthma[26]. In the present analyses, "asthma" included those with a positive response to both questions: "Have you ever had asthma?" and "Was this confirmed by a doctor?" or with a positive answer to both questions: "Have you had wheezing or whistling in your chest at any time in the last 12 months?" and "Have you had this when you did not have a cold?". Major reasons to define this broader group were that asthma – a wheezing disease – not being uniquely defined, and considering "history of wheezing without cold in the last 12 months" to be a likely predictor for undiagnosed asthma in adults. The questionnaire covered recent use of medication for asthma and other respiratory diseases.
We will use the dichotomous result of the Phadiatop® test as measured in a blood sample to define atopic hypersensitivity (IgE mediated sensitization).
Information on highest educational level achieved was used to define four categories of socio-economic status.

Analysis

Forced expiratory pulmonary function measures were used as dependent variables. Apart from the forced vital capacity, FVC, and the volume expired in the first second, FEV1, we particularly included mid-expiratory flow rates, FEF25–75%, as they also reflect changes in the peripheral airways, where the first tobacco smoke related structural changes may occur. Models were chosen such to not violate linear model assumptions regarding the distribution of residuals. To reduce heteroscedasticity of residuals across age, log-transformed lung function values were used. Inclusion of "age squared", in addition to age, improved the fit of the model, given the age dependent plateau of pulmonary function values in the third decade[27,28]. ETS at work was used as binary variable. We adjusted on geographic area, a surrogate for factors not included in the model but potentially related to lung function and ETS such as environmental air pollution, climate, or technical factors in lung function assessment[22,24].

ETS exposure at home, gas/dust/fume exposure at work, cooking with gas, educational level, reported mould at home within the last 12 months, atopic status based on Phadiatop®, history of respiratory infection in childhood, ETS exposure *in utero* and during childhood from mother and/or father and subjective annoyance levels due to ETS were considered potential confounders, i.e. risk factors – or proxy measures for risk – of lung function decrement and possibly being associated with our exposure variable.

Analyses were performed with SAS/STAT software on a main frame. The General Linear Model (GLM) procedure was used for the regressions. The non-parametric data summary (Figure 1) was based on median smoothing lines with the software package STATA.

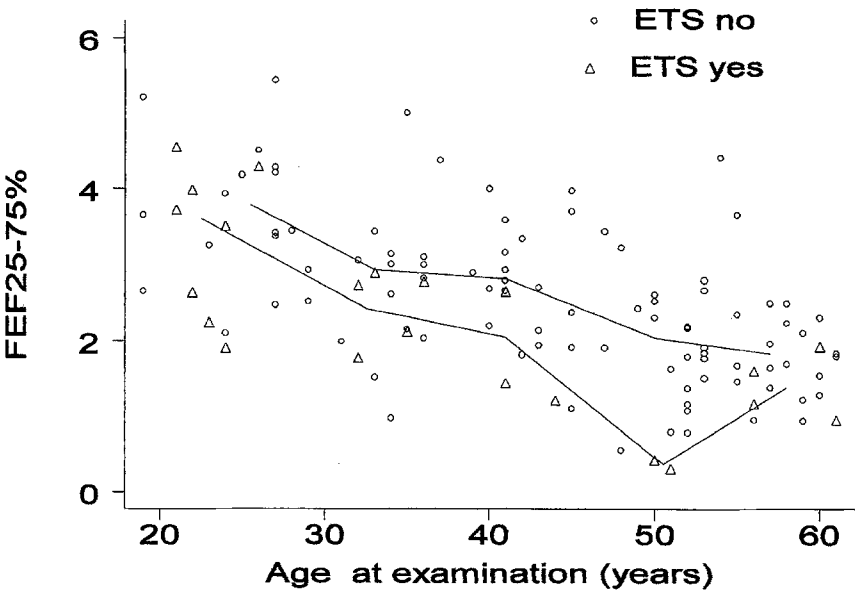

Figure 1. *Observed FEF25–75% by age, among asthmatic women with bronchial reactivity or no participation in methacholine challenge; with (△) and without (○) ETS at work. (Definitions see text). (Overlaid are non-parametric smoothing lines by ETS group, based on five median bands).*

Results

Table 1 summarizes characteristics of the SAPALDIA participants, non-participants, and the non-smoking subgroup selected for these analyses. There was little difference in age across these samples. Non-participants were more likely to be female, but less likely to be wheezers than participants. Females were over-represented in our subsample due to their lower smoking prevalence.

Table 2 summarizes univariate distributions of major characteristics in the selected population, by gender and asthma status. In women, 15% reported ETS exposure at work and 18% at home. Males who were more likely to hold a full time job, had higher prevalence of ETS at work (22%) but lower prevalence at home (12%). Asthmatic

Variable	Participants (N = 9651)	Non-participants (N ≤ 7749)[a]	Selected sample (N = 3534)[b]
Age (years)	41.1	42.1	39.7
Female (%)	50.8%	55.0%	61.0%
Currently smoking (%)	33.7%	32.2%	0.0%
Wheeze apart from colds (%)	7.7%	5.5%	4.4%

[a] Total N varies across variables due to different data sources.
[b] Never-smoking population with acceptable spirometry as used in this analysis.

Table 1. *Mean age and prevalence of characteristics among participants and non-participants of SAPALDIA and the sample as selected for this presentation*[a].

Variable	Male		Female	
	no asthma (N = 1246)	asthma/ wheezing[a] (N = 142)	no asthma (N = 1963)	asthma/ wheezing[a] (N = 183)
Age (years)	36.6 (12.1)	37.4 (13.2)	41.5 (12)	42.2 (12)[c]
Height (cm)	176.2 (6.8)	176.2 (6.8)	163.3 (6.5)	163.1 (7.0)[c]
Forced expiratory lung function:				
FVC (ml)	5352 (791)	5129 (895)[b]	3775 (634)	3674 (644)[b,c]
FEV1 (ml)	4281 (671)	3923 (876)[b]	3059 (551)	2873 (597)[b,c]
FEF25-75 % (liters/sec)	4.18 (1.3)	3.51 (1.4)[b]	3.14 (1.0)	2.73 (1.1)[b,c]
ETS annoyance score (0 = no at all, 10 = intolerable)	4.8 (3.6)	5.2 (3.5)	5.1 (3.7)	5.6 (3.8)[b]
Atopy (= positive Phadiatop® test result)	406 (33 %)	93 (65 %)[b]	437 (22 %)	90 (49 %)[b,c]
Environmental tobacco smoke at work	262 (21 %)	37 (26 %)	290 (15 %)	36 (20 %)
Environmental tobacco smoke at home	148 (12 %)	23 (16 %)	339 (17 %)	37 (20 %)
Bronchial reactivity, methacholine (BR):				
BR = no	1007 (81 %)	66 (48 %)	1283 (65 %)	66 (36 %)
BR = yes	92 (7 %)	37 (26 %)	277 (14 %)	60 (33 %)
BR = not measured	147 (12 %)	39 (27 %)[b]	403 (21 %)	57 (31 %)[b]

[a] Doctors diagnosed asthma and/or wheezing without cold.
[b] $p \leq 0.05$ for t-test or X^2, respectively, comparing asthmatic/wheezing versus non-asthmatic, within gender.
[c] $p \leq 0.05$ for t-test or X^2, respectively, comparing female versus male among asthmatic/wheezing only.

Table 2. *Univariate distributions of population characteristics, asthmatic versus non-asthmatic subjects, by gender. SAPALDIA never smokers 1991. Mean values (and standard deviation) or number of subjects (and percent), respectively.*

men and women had lower lung function, increased prevalence of atopy and higher annoyance scores for ETS.

Table 3 presents the percent change in lung function associated with ETS exposure at work. The main model indicated slightly lower FEV1 (–0.1 %) and FEF25–75 % (–1.9 %) among those with ETS exposure at work. The coefficients were, however, not statistically significant nor was FVC associated with ETS (+0.7 %). Interaction terms of ETS with asthma status and sex were strongly significant, indicating the need for stratified analyses. Among asthmatics, the main model indicated a significant decrease of both FEV1 (–4.8 %) and FEF25–75 % (–12.4 %) whereas the reduced FVC was not statistically significant (–1.7 %). The interaction of ETS with sex remained again significant. In the stratified analyses, one can see that the aforementioned association with ETS was mostly due to the impact of ETS among asthmatic women, where FEV1 and FEF25–75 % were significantly lower among those exposed to ETS at work. In non-asthmatic women and in men with or without asthma, ETS was not associated with pulmonary function.

Given the limitations of a questionnaire based definition of "asthma", we used bronchial reactivity status for a more specific definition of asthma. As expected, significantly independent effects of ETS at work on FEV1 and FEF25–75 % were most pronounced among asthmatics with hyperreactive airways and non-participants of the bronchial challenge (Table 4). Non-participation in the methacholine challenge, among asthmatics, was mostly due to obstructive pre-test conditions. In "asthmatics" with no reaction to methacholine, the coefficients for ETS at work were not statistically significant. Again, among men, the coefficients were close to zero in all subgroups considered in Table 4.

The impact of ETS among the most susceptible women (asthmatic with hyperreactive airways) is presented in Figure 1, showing the decline of FEF25–75 % with age for both exposure groups.

To test the sensitivity of the effects to the statistical modeling, we included a large set of potentially

Forced expiratory lung function	all subjects	asthmatics	Male		Female	
			no asthma	asthma/ wheezing[a]	no asthma	asthma/ wheezing[a]
	(N = 3'534)	(N = 325)	(N = 1246)	(N = 142)	(N = 1963)	(N = 183)
FVC	0.7 (– 0.4 to + 1.8)	– 1.7 (– 5.5 to + 2.1)	1.1 (– 0.5 to + 2.7)	1.4 (– 4.0 to + 7.1)	1.0 (– 0.7 to + 2.7)	– 4.4 (– 9.6 to + 1.1)
FEV1	– 0.1 (– 1.3 to + 1.1)	– 4.8 (– 9.2 to 0)	0.5 (– 1.3 to + 2.3)	0.5 (– 7.9 to + 9.6	0.4 (– 1.3 to + 2.1)	– 8.7 (– 14.5 to – 2.5)
FEF25–75%	– 1.9 (– 4.2 to + 0.5)	– 12.4 (– 20.4 to – 3.7)	– 0.2 (– 4.7 to + 3.8)	– 1.4 (– 18.0 to + 18.5)	0.1 (– 3.4 to + 3.7)	– 20.8 (– 32.0 to – 7.6)

[a] Doctors diagnosed asthma and/or wheezing without cold.
[b] Main model: log(lung function), adjusted on log(age), log(age) squared, log(height), ETS at home, occupational gas/dust/smoke, area of residency.

Table 3. *Percent change (and 95% confidence intervals) in lung function measures associated with environmental tobacco smoke exposure at work. Main model for asthmatic[a] versus non-asthmatic, by gender. SAPALDIA never smokers 1991[b].*

Bronchial reactivity status (BR)[c]	N	FEV1		FEF25-75%	
		mean, ml (SD)	% change	mean, l/s (SD)	% change
All asthmatics[a]	183	2873 (597)	– 8.7 (– 14.5 to – 2.5)	2.73 (1.1)	– 20.8 (– 32.0 to -7.6)
BR = no	66	3072 (547)	– 1.7 (– 9.4 to + 6.7)	3.14 (0.9)	– 4.7 (– 19.4 to + 12.6)
BR = yes[c]	60	2857 (458)	– 8.7 (– 18.0 to + 1.8)	2.6 (0.9)	– 21.5 (– 37.2 to – 1.9)
BR = not measured	57	2660 (705)	– 19.1 (– 31.4 to – 4.6)	2.4 (1.2)	– 44.0 (– 62.7 to – 15.7)
BR = yes or not measured	117	2761 (597	– 12.3 (– 19.9 to -3.9)	2.5 (1.1)	– 30.6 (– 43.4 to – 14.8)

[a] Doctors diagnosed asthma and/or wheezing without cold.
[b] Main model: log(lung function), adjusted on log(age), log(age) squared, log(height), ETS at home, occupational gas/dust/smoke, area of residency with main model r^2 ranging 0.47–0.60 for FEV1 and 0.35–0.56 for FEF25-75%.
[c] Hyperreactivity defined as PD20 FEV1 ≤ 2 mg methacholine.

Table 4. *Percent change (and 95% confidence intervals) in FEV1 and FEF25–75% associated with environmental tobacco smoke exposure at work. Main model for asthmatic women[a], by bronchial reactivity status. SAPALDIA never smokers 1991[b].*

confounding covariates (see methods). The coefficients of ETS on pulmonary function showed very little increase or decrease in this sensitivity analysis.

Dose-response

Our questionnaire included quantitative ETS measures, such as "hours per day exposed to ETS" (referring to the last 12 months) and total number of years. These questions, however, were not specifically limited to ETS *at work*, compromising a direct dose-response assessment for ETS *at work*. Thus, we restricted the analyses on subjects with no ETS exposure at home, among which quantitative ETS measures are likely to reflect primarily ETS at work. Both, hours per day and number of years exposed to ETS were significantly related to decreased FEF25–75% and FEV1 in asthmatic women but not in men and other groups. FEF25–75% decreased by −3.4% per hour/day ($p < 0.05$) and −1% per year ($p = 0.02$). Results for FEV1 were −6%/hour ($p = 0.01$) and −1% per year (not significant), respectively. Among those exposed, 43% reported up to two hours per day; 35% indicated five or more hours of daily exposure.

Discussion

Our cross-sectional population-based study revealed significantly impaired lung function among asthmatic women reporting ETS exposure at work as compared to non-exposed. The impact was particularly strong on FEF25–75% and FEV1 whereas for FVC the effect was small and did not reach statistical significance.

The major strength of this study is its focus on susceptible subgroups. The analyses indicated that ETS exposure at work was associated with lower pulmonary function among asthmatics only. The independent effect of ETS was not confounded by any available and potentially relevant covariate, including ETS exposure at home. Convincingly, the association was strongest in hyperreactive asthmatics and those not participating in the bronchial challenge. Inclusion of bronchial reactivity status can be considered an efficient approach to improve the specificity of our asthma working definition[26,29]. In fact, our data showed non-reactive asthmatics to be three to four times less likely to report recent use of beta mimetica than the other asthmatics (data not shown) and their lung function mean values were similar to those among non-asthmatic (Table 2, Table 4). The additional independent decrement that was associated with ETS at work has to be considered relevant in a subgroup with already limited lung function. Our results are consistent with findings, comparing ETS exposed and unexposed asthmatics, age 15 to 50[13]. The exposed group had higher morbidity indices and a 15% and 28% significantly lower FEV1 and FEF25–75%, respectively. Furthermore, a recent chamber study confirmed acute effects of ETS on FEV1 among asthmatics but not in non-asthmatics[30].

The further focus on sex specific effects showed, however, that the effect observed among asthmatics was clearly driven by the effect in women with asthma, whereas among men, ETS was not associated with lower lung function values. Thus, the question arises whether female sex is a marker for susceptibility to ETS. The literature gives no consistent evidence for female being at higher risk of ETS effects, although one may argue that smaller lungs and airways may partially explain differential susceptibility[31]. In our study, however, no significant interaction between ETS and lung size could be observed (not shown). Recently, Corbo et al. reported smoking and ETS to be more strongly related to COPD in women than in men, with particularly strong effects in atopic women[32]. Furthermore, if one may compare ETS with smoking, it is to emphasize that several studies conclude that the deleterious effects of smoking are stronger in female, given the same amount smoked[33–35].

Apart from the fact the statistical power was lower in men where sample sizes were 35% smaller than in female subgroups, the apparent sex difference of ETS effects may be explained by reporting bias or by differences in the level of ETS exposure across gender.

In the cross-sectional design, questionnaire-based exposure assessment may be biased. Asthmatic women with hyperreactive airways were more likely to report ETS exposure at work then non-asthmatic ($p = 0.05$); no such difference was observed in male subgroups. In addition, hyperreactive asthmatic women without ETS at home reported higher number of hours of ETS exposure per day then the male comparison group (7.4 h/d versus 4.3, $p = 0.09$; data not shown). We cannot directly assess whether this reflects higher ETS exposure, over reporting among hyperreactive female asthmatics, or limited awareness of ETS in male asthmatics and non-asthmatic subjects. Within strata of asthma history, the subjective annoyance score, asked for ETS in general, was slightly but not significantly higher in women (see Table 2). Furthermore, ETS was not much in public debate in Switzerland (1991) nor a specific focus of SAPALDIA which limits the problem of differential reporting bias. Thus, the higher reporting of ETS exposure may reflect true differences in exposure rather than reporting bias. Asthmatic women held jobs of lower status, on average, compared to men and might have been prone to increased ETS at work and crowding, combined with limited options to avoid ETS.

Unfortunately, the study did not include an objective measure of long-term ETS exposure to confirm our interpretation. However, the observed dose-response relationship for ETS at work ("hours per day") among those not exposed to ETS at home strongly supports the notion of a true ETS effect in asthmatic.

We conclude that differences in the level of exposure may be the main reason for the observed sex pattern in our study whereas both, the lack of focus on susceptible subgroups and exposure differences may explain discrepancies across other studies on ETS and lung function.

White et al. reported significant 13–14% lower FEF25–75% among women and men exposed to ETS at work[6]. Inconsistencies between French and Dutch results on one side, confirming lower FEF25–75% among women aged 40 or older[11,12] and the negative US results[36] compared to the strongly positive study from China[37] were explained with potentially different life-style and housing conditions which may modify exposure. Hole et al., in a population cohort, reported a significant 3.2% lower FEV1 when a cohabitee smoked >15 cigarettes per day[38]. Other studies with positive findings[7,9] or negative or unclear results[8,10] are based on not further specified volunteers, prone to uncontrolled selection bias. In a recent publication on the Seventh Day Adventist cohort, Abbey et al. observed lower lung function among ETS exposed men but not among women[39]. The authors highlight that in their cohort, ETS exposure among women was lower than in men. In the future, molecular biomarkers may improve the power to establish effects of ETS on those truly susceptible. A recent presentation of von Ehrenstein showed that the association of ETS impaired lung function among children was driven by the subgroup with low levels of alpha1-Antitrypsin[40].

In a cross-sectional design we cannot assess whether ETS exposure induced increased unspecific bronchial reactivity or whether subjects with reactive airways are prone to ETS induced obstruction. Experimental studies are neither conclusive on this issue. In an experiment undertaken by Danuser et al. comparing ten hyperreactive patients with ten healthy controls, reactivity to side stream smoke and methacholine provocation were highly correlated[14]. Knight reported that ETS might trigger attacks in asthmatics and that histamine reactivity was increased four hours after the passive smoke challenge[15]. Other experiments did not specifically address the impact of bronchial reactivity status[41,42].

It is to emphasize that our decision to focus the analyses on susceptible subgroups based on asthma status and sex, although suitable to address our question, has to be considered a subgroup analysis, which showed an effect in a rather small subgroup. Thus, from a statistical point of view, the probability of a significant result does not correspond to the nominal p-value. Results among asthmatic women, however, were significant at a p-value of 0.01 (FEV1) and 0.008 (FEF25–75%) hence even under a very conservative adjustment for multiple testing, the findings among asthmatic women are unlikely to be due to chance.

In contrast to the negative results among non-asthmatics, a previous analysis based on the SAPALDIA population[17] showed significant associations of total ETS exposure and prevalence of respiratory symptoms, suggesting symptoms to be a more sensitive measure than lung function. Although our results among non-asthmatics can not exclude that ETS exposure might induce small lung function decrements in healthy subjects[1], the impact of ETS at work, might be difficult to detect with epidemiological methods, unless exposure may be very strong.

In summary, our study suggests that asthmatics are particularly susceptible for adverse effects of ETS exposure. However, the inherent methodologic limitations requires cautious interpretation. Further research should focus on susceptible subgroups, based on biologic measures of susceptibility. Objective measures of ETS exposure profiles will allow to disentangle true and perceived exposure. This will lead to an adequate characterization of the impact of ETS among those at highest risk.

Zusammenfassung

Zusammenhang zwischen Passivrauchbelastung am Arbeitsplatz und forcierter expiratorischer Lungenfunktion bei Nichtrauchenden mit und ohne Asthma

Resultate betreffend den Zusammenhang zwischen Passivrauchexposition (ETS) und spirometrischen Lungenfunktionswerten sind bei Erwachsenen inkonsistent. Wir untersuchten, ob sich ein allfälliger Zusammenhang nur bei bisher nicht berücksichtigten Risikogruppen beobachten lässt. Wir verwendeten die Spirometriedaten (FVC, FEV1, und FEF25–75%) aller Nichtraucher (18- bis 60-jährig) der SAPALDIA-Querschnittstudie (N = 3534). Die Beziehung zwischen ETS-Belastung am Arbeitsplatz (Fragebogen) und Lungenfunktion (Spirometrie) wurde analysiert. Die Faktoren Geschlecht, Asthmastatus und bronchiale Reaktivität wurden als potentielle Indikatoren der ETS-Sensitivität verwendet. In den multivariaten Regressionsmodellen kontrollierten wir für Körpergrösse, Alter, Ausbildungsstand, Staubexposition am Arbeitsplatz, Studienregion sowie ETS zu Hause. Bei Asthmatikern (n = 325), nicht jedoch im Gesamtkollektiv, zeigte sich ein Zusammenhang zwischen ETS am Arbeitsplatz und schlechteren Lungenfunktionswerten (FEV1: –4,8% (0 bis –9,2); FEF25–75%: –12,4% (–3,7 bis –20,4); FVC: –1,7% (+2,1 bis –5,5)). Bei asthmatischen Frauen (n = 183) war dies besonders deutlich (FVC: –4,4% (–9,6 bis +1,1); FEV1: –8,7% (–14,5 bis –2,5); FEF25–75%: –20,8% (–32 bis –7,6)). Verzerrungen infolge Selektion oder der subjektiven Angaben betreffend ETS-Belastung können in dieser Querschnittanalyse nicht ausgeschlossen werden. Aus Public Health Sicht bleibt die Identifikation von sensitiven Risikogruppen vordringlich.

Résumé

Association entre exposition à la fumée passive au travail et paramètres fonctionnels de l'expiration forcée chez les non-fumeurs avec et sans asthme

L'inconsistance de l'association entre exposition passive à la fumée de tabac (ETS) et fonction pulmonaire chez l'adulte pourrait être la conséquence de susceptibilités variables entre sous-groupes. L'association entre ETS au travail et fonction pulmonaire a été étudiée en utilisant les données spirométriques (FVC, FEV1 et FEF 25–75%) des non-fumeurs (âge 18–60 ans) de l'étude transversale de SAPALDIA (n = 3534). Les facteurs sexe, asthme et réactivité bronchique étaient considérés comme facteurs de risque pour une sensibilité accrue à l'ETS. Des modèles multivariés sont contrôlés pour la taille, l'âge, le niveau de formation professionnelle, l'exposition à la place de travail, la région de l'étude et l'exposition domestique à l'ETS. Chez les asthmatiques, mais pas dans le collectif global, une association entre ETS au travail et diminution de la fonction pulmonaire a été démontrée (n = 325) (FEV1: –4.8% (0 à –9.2); FEF 25–75%: –12.4% (–3.7 à –20.4); FVC: –1.7% (+2.1 à –5.5)). Les effets étaient particulièrement marqués chez les femmes asthmatiques (n = 183) (FVC: –4.4% (–9.6 à +1.1); FEV1 –8.7% (–14.5 à –2.5); FEF 25–75%: –20.8% (–32 à –7.6)). Le design transversal de l'étude ne permet pas d'exclure des biais de sélection ou d'information sur l'exposition à l'ETS. L'identification des groupes à risque constitue un but important de la recherche en santé publique.

References

1 U.S. Environmental Protection Agency. Respiratory health effects of passive smoking: lung cancer and other disorders. Washington, DC: Office of Health and Environmental Assessment, 1992.

2 National Research Council, Committee on passive smoking board on environmental studies and toxicology. Environmental tobacco smoke: measuring exposures and assessing health effects. Washington, DC: National Academy Press, 1986.

3 *Jaakkola M, Jaakkola J, Becklake M, Ernst P.* Effect of passive smoking on the development of respiratory symptoms in young adults: an 8-year longitudinal study. J Clin Epidemiol 1996; *49*: 581–6.

4 *Corbo G, Agabiti N, Forastiere F,* et al. Lung function in children and adolescents with occasional exposure to environmental tobacco smoke. Am J Respir Crit Care 1996; *154*: 695–700.

5 *Menon P, Stankus R, Rando R, Salvaggio JE, Lehrer S.* Asthmatic response to passive cigarette smoke: persistence of reactivity and effect of medications. J Allergy Clin Immunol 1991; *88*: 861–9.

6 *White J, Froeb H.* Small-airways dysfunction in nonsmokers chronically exposed to tobacco smoke. N Engl J Med 1980; *302*: 720–3.

7 *Masjedi M, Kazemi H, Johnson D.* Effects of passive smoking on the pulmonary function of adults. Thorax 1990; *45*: 27–31.

8 *Kentner M, Triebig G, Weltle D.* The influence of passive smoking on pulmonary function - a study of 1,351 office workers. Prev Med 1984; *13*: 656–9.

9 *Masi M, Hanley J, Ernst P, Becklake M.* Environmental exposure to tobacco smoke and lung function in young adults. Am Rev Respir Dis 1988; *138*: 296–9.

10 *Comstock G, Meyer M, Helsing K, Tockman M.* Respiratory effects of household exposures to tobacco

smoke and gas cooking. Am Rev Respir Dis 1981; *124*: 143–8.

11 *Kauffmann F, Tessier J, Oriol P.* Adult passive smoking in the home environment: a risk factor for chronic airflow limitation. Am J Epidemiol 1983; *117*: 269-80.

12 *Brunekreef B, Fischer P, Remijn B, Van der Lende R, Schouten J, Quanjer P.* Indoor air pollution and its effect on pulmonary function of adult non-smoking women: III. Passive smoking and pulmonary function. Int J Epidemiol 1985; *14*: 227–30.

13 *Jindal S, Gupta D, Singh A.* Indices of morbidity and control of asthma in adult patients exposed to environmental tobacco smoke. Chest 1994; *106*: 746–9.

14 *Danuser B, Weber B, Hartmann A, Krueger H.* Effects of a bronchoprovocation challenge test with cigarette sidestream smoke on sensitive and healthy adults. Chest 1993; *103*: 353–8.

15 *Knight A, Breslin B.* Passive cigarette smoking and patients with asthma. Med J Aust 1985; *142*: 194–5.

16 *Cunningham J, Dockery DW, Gold D, Speizer F.* Racial differences in the association between maternal smoking during pregnancy and lung function in children. Am J Respir Crit Care Med 1995; *152*: 565–9.

17 *Leuenberger P, Schwartz J, Ackermann-Liebrich U,* et al. Passive smoking exposure in adults and chronic respiratory symptoms (SAPALDIA Study). Am J Respir Crit Care Med 1994; *150*: 1221–8.

18 *Tager I, Weiss S, Rosner B, Speizer F.* Effect of parental cigarette smoking on the pulmonary function of children. Am J Epidemiol 1979; *110*: 15–26.

19 *Bates DV.* Detection of chronic respiratory bronchiolitis in oxidant-exposed populations: analogy to tobacco smoke exposure. Environ Health Perspect 1993; *101* Suppl. 4: 217–8.

20 *Künzli N, Lurman F, Segal M, Ngo L, Balmes J, Tager I.* Association between lifetime ambient ozone exposure and pulmonary function in college freshman – results of a pilot study. Environ Res 1997; *72*: 8–23.

21 American Thoracic Society. Standardization of spirometry – 1987 update. Am Rev Respir Dis 1987; *136*: 1285–98.

22 *Ackermann-Liebrich U, Leuenberger P, Schwartz J,* et al. Lung function and long-term exposure to air pollutants in Switzerland. Am J Respir Crit Care Med 1997; *155*: 122–9.

23 *Martin BW, Ackermann-Liebrich U, Leuenberger P,* et al. SAPALDIA – methods and participation in the cross-sectional part of the Swiss Study on Air Pollution and Lung Disease in Adults (SAPALDIA). Soz Praventivmed 1997; *42*: 67–84.

24 *Künzli N, Ackermann-Liebrich U, Keller R, Perruchoud AP, Schindler C.* Variability of FVC and FEV1 due to technician, team, device and subject in an eight centre study: three quality control studies in SAPALDIA. Swiss Study on Air Pollution and Lung Disease in Adults. Eur Respir J 1995; *8*: 371–6.

25 *Burney P, Luczynska C, Chinn S, Jarvis D.* The European Community Respiratory Health Survey. Eur Respir J 1994; *7*: 954–60.

26 *Bates D.* Respiratory function in disease. Philadelphia: W.B. Saunders 1989.

27 *Brändli O, Schindler C, Künzli N, Keller R, Perruchoud AP.* Lung function in healthy never smoking adults. Reference values and lower limits of normal of a Swiss population. Thorax 1996; *51*: 277–83.

28 *Knudson R, Lebowitz M, Holberg C, Burrows B.* Changes in the normal maximal expiratory flow-volume curve with growth and aging. Am Rev Respir Dis 1983; *127*: 725–34.

29 *Siersted H.* Constructing a "Bronze Standard" for asthma in epidemiology – a pragmatic approach to the diagnostic dilemma. Am J Respir Crit Care Med 1994; *149*(4): A 918 (abstract).

30 *Lehrer S, Menon P, Simlote P,* et al. The acute effect of environmental tobacco smoke exposure on asthmatics: studies with a dynamic challenge chamber. Indoor Air 1997; *7*: 269–77.

31 *Bourbeau J, Delfino R, Ernst P.* Tracheal size is a determinant of the bronchoconstriction response to inhaled methacholine. Eur Respir J 1993; *6*: 991–5.

32 *Corbo G, Forastiere F, Agabiti N.* Risk factors for chronic obstructive pulmonary disease (COPD) among adults in Italy. Eur Respir J 1999; *14* Suppl. 30: s213 abstract 1460.

33 *Xu X, Weiss S, Rijcken B, Schouten J.* Smoking, changes in smoking habits, and rate of decline in FEV1: new insight into gender differences. Eur Repir J 1994; *7*: 1056–61.

34 *Gold D, Wang X, Wypij D, Speizer F, Ware J, Dockery DW.* Effects of cigarette smoking on lung function in adolescent boys and girls. N Engl J Med 1996; *335*: 931–7.

35 *Prescott E, Bjerg A, Andersen P, Lange P, Vestbo J.* Gender difference in smoking effects on lung function and risk of hospitalization for COPD: results from a Danish longitudinal population study. Eur Respir J 1997; *10*: 822–7.

36 *Kauffmann F, Dockery DW, Speizer F, Ferris BJ.* Respiratory symptoms and lung function in relation to passive smoking: a comparative study of American and French women. Int J Epidemiol 1989; *18*: 334–44.

37 *Xu X, Lee B, Wang L.* Exposure-response relationship between passive smoking and adult pulmonary function. Am J Respir Crit Care Med 1995; *151*: 41–6.

38 *Hole D, Watt G, Davey-Smith G, Hart C, Gillis C, Hawthorne V.* Impaired lung function and mortality risk in men and women: findings from the Renfrew and Paisley prospective population. Brit Med J 1996; *313*: 711–5.

39 *Abbey D, Burchette R, Knutsen S, McDonnel W, Lebowitz M, Enright P.* Long-term particulate and other pollutants and lung function in non-

smokers. Am J Respir Crit Care Med 1998; *158*: 289–98.

40 *Von Ehrenstein O, Schaal W, Maier E*, et al. Children with A1-antitrypsin deficiency and exposure to environmental tobacco smoke (ETS) have diminished lung function. Epidemiology 1999; 10(4): S149 abstract 447.

41 *Jörres R, Magnussen H.* Influence of short-term passive smoking on symptoms, lung mechanics and airway responsiveness in asthmatic subjects and healthy controls. Eur Respir J 1992; *5*: 936–44.

42 *Stankus R, Menon P, Rando R, Glindmeyer H, Salvaggio JE, Lehrer S.* Cigarette smoke-sensitive asthma: challenge studies. J Allergy Clin Immunol 1988; *82*: 331–8.

Acknowledgement

Study director: *Leuenberger Ph (p)*; **Programme director:** *Ackermann-Liebrich U.*, Alean P (am), Blaser K (a), Bolognini G (p), Bongard JP(p), Brändli O (p), Braun P (p), Defila C (m), Domenighetti G (p), Elsasser S (l), Grizé L (s), Karrer W (p), Keller-Wossidlo H (o), Keller R (p), Künzli N (e), Martin BW (l), Medici T (p), Monn Ch (am), Peeters AG (pa), Perruchoud AP (p), Schindler Ch (s), Schwartz J (s), Solari G (p), Schöni M (p), Tschopp JM (p), Villiger B (p), Wüthrich B (a), Zellweger JP (p), Zemp E (e).
(a) allergology, (am) air pollution monitoring, (e) epidemiology, (l) local assistant MD, (m) meteorology, (o) occupational medecine, (p) pneumology, (pa) palynology, (s) biostatistic

Financial support

SAPALDIA, a project of the Swiss National Science Foundation, is part of the National Research Program NFP/PNR 26 (Grant 4026-028099). The first author is a recipient of a National Science Foundation Advanced Scientist Fellowship (#3233-048922.96/1). No conflict of interest.

Address for correspondence

Dr. med. Nino Künzli
Institut für Sozial- und Präventivmedizin Basel
Steinengraben 49
CH-4051 Basel
Tel.: +41 61 267 60 66
Fax: +41 61 267 61 90
Nino.Kuenzli@unibas.ch