Respiratory Diseases and Allergies in Two Polluted Areas in East Germany

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This cross-sectional epidemiological study collected health data for 2,470 school children between 5 and 14 years of age (89% of eligible children) who had lived most of their lives in either one of two counties strongly impacted by industrial pollution (Bitterfeld and Hettstedt) or in a neighboring county without any sources of industrial pollution (Zerbst). The objective of the study was to examine whether regional differences—with respect to the occurrence of childhood respiratory diseases and symptoms or allergies—exist and, if such differences are found, whether they persist when we adjust for the effects of known risk factors such as medical and sociodemographic factors or factors related to the indoor environment. Controlling for medical, sociodemographic, and indoor factors, according to parental reports, children residing in Hettstedt have about a 50% increased lifetime prevalence for physician-diagnosed allergies, eczema, and bronchitis compared to children from Zerbst and about twice the number of respiratory symptoms such as wheeze, shortness of breath, and cough without cold. Sensitization to common aeroallergens according to skin prick tests [odds ratio (OR) = 1.38; 95% confidence interval (CI), 1.02–1.86] and specific IgE levels (OR = 1.75; CI, 1.31–2.33) was more common for children from Hettstedt than children from the nonpolluted county. Bitterfeld children, on the other hand, more often received a diagnosis of asthma and eczema than children residing in Zerbst and also showed slightly increased sensitization rates. In conclusion, industrial pollution related to mining and smelting operations in the county of Hettstedt were associated with a higher lifetime prevalence of respiratory disorders and an increased rate of allergic sensitization in children between the ages of 5 and 14 years. Further studies are needed to determine what role the high dust content of heavy metals plays in Hettstedt. *Key words:* allergy, bronchial reactivity, children, eastern Germany, IgE, industrial pollution, respiratory health, skin prick test.
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In industrialized countries of the Northern Hemisphere, the prevalence of atopic diseases such as asthma, atopic dermatitis, and allergic rhinitis appear to have increased during the last decades (*1–4*). Possible explanations for this increase are changes of diagnostic criteria, lifestyle factors, and environmental factors such as indoor and outdoor air pollution. Ambient air pollution has previously been associated with adverse chronic health effects such as diseases of the airways, including chronic bronchitis and dry cough (*5–11*) and a decrease of lung function (*12–13*). However, it is not clear what role ambient air pollution or other environmental factors might play in the development of atopic diseases, or if they are even involved in this process.

Epidemiologic studies examining the long-term effects of ambient air pollution on the occurrence of asthma and allergies have not been unequivocal. In most cross-sectional studies, asthma prevalence was not related to higher levels of sulfur dioxide or total suspended particulates (*5,8,14–15*). Some of these studies did not adequately control for potential confounding factors such as indoor air pollution or individual risk factors. One U.S. study found an association of asthma with increases in traffic-dependent pollutants (*16*). Two studies conducted in West Germany showed increased prevalences of hay fever (*17*) and allergic sensitization (*18*) depending on proximity of residence to streets with heavy traffic, while another study found no such association (*19*).

Recent publications reported higher rates of atopy among children (*3,20–22*) and young adults (*23,24*) living in western compared to eastern Germany. In the late 1980s and the early 1990s, air pollution levels in eastern Germany exceeded western levels by an order of magnitude, especially with regard to sulfur dioxide and total suspended particles. This observation further adds to the controversy about the impact of environmental factors on atopic diseases. It is not clear, however, whether the east–west comparison adequately controlled for many potential risk factors that might be differentially distributed between these two distinct German populations.

The goal of the present study was to determine whether regional differences exist for the occurrence of respiratory and atopic diseases and symptoms in school-age children who exclusively live in eastern Germany. Furthermore, we examined whether known or suspected medical and sociodemographic risk factors or factors related to the indoor environment could explain regional differences. In general, region provided a proxy measure for long-term environmental pollution, specifically air pollution, because the populations of the three counties included in this study have been exposed to air pollution to different degrees. Prior to 1992, air-monitoring measurements were not documented in a manner comprehensive enough to allow sophisticated air-pollution effect analyses such as time–series analyses. However, the available data were useful for general characterization of the air quality experienced by residents of each county.

Methods

Study area. The study was conducted in the state of Sachsen-Anhalt [formerly German Democratic Republic (GDR)]. The data presented in this paper were collected between September 1992 and July 1993. The results are based on the first of three subsequent surveys embedded in a cohort study investigating the effects of environmental factors on respiratory health.

The Bitterfeld study area includes the towns of Bitterfeld and Wolfen and four adjoining villages located in a mountainless region of Sachsen-Anhalt. The population of the county of Bitterfeld consisted of

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Table 1. Annual means of SO_2, particulates, and heavy metals in dust fall at the three ambient monitoring stations in Zerbst (control), Bitterfeld (polluted), and Hettstedt (polluted), 1984–1994

Pollutant	Zerbst	Bitterfeld	Hettstedt
Emission			
SO_2 (tons/km²/year)			
1984	NA	272.7[a]	30.1[a]
1990	4.7[a]	155.1[a]	15.4[a]
1993	NA	NA	NA
Dust (tons/km²/year)			
1984	NA	112.4	8.8
1990	2.7[a]	51.6[a]	7[a]
1993	NA	NA	NA
NO_x (tons/km²/year)			
1985			
1990	1[a]	15.2[a]	1.9[a]
1993	NA	NA	NA
Lead (tons/km²/year)			
1984	NA	NA	0.34[b]
1989	NA	NA	0.22[b]
Arsenic (kg/km²/year)			
1984	NA	NA	15.2[b]
1989	NA	NA	13.9[b]
Ambient concentration			
SO_2 (passive sampling) (µg/m³)			
1988	NA	229[a]	123[a]
1990	NA	181[a]	81[a]
1992	NA	73[c]	61[c]
SO_2 (active measurement) (µg/m³)			
1988	NA	NA	NA
1991	50[d,e]	130[e]	84[e]
1994	29[f]	44[f]	38[f]
NO_2 (active measurement) (µg/m³)			
1988	NA	NA	NA
1991	NA	NA	NA
1993	21[c]	21[c,g]	23[c]
1994	22[f]	22[f]	19[f]
Dust fall (g/m²/day)			
1988	NA	0.96–1.40[a]	0.37–0.40[a]
1990	0.21[a,d]	0.83–1.07[a]	0.31–0.38[a]
1994	0.08[f]	0.13–0.16[f]	0.12–0.14[f]
TSP (µg/m³) 1993	44[c]	48[c,g]	65[c]
PM_{10} (µg/m³)			
October 1993–March 1994	33	NA	40
Black smoke (µg/m³)			
October 1993–March 1994	26[h]	NA	42[h]
Heavy metals in dust fall			
Lead (µg/m²/day)			
1985	NA	NA	NA
1992	18.0[d,e]	18.0–41.2[e]	147.6–367.1[e]
1994	16.2[f]	19.4–26.1[f]	47.0–280.2[f]
Cadmium (µg/m²/day)			
1985	NA	NA	NA
1992	1.2[d,e]	1.6–2.6[e]	3.5–4.7[e]
1994	0.3[f]	0.4–0.5[f]	0.8–3.5[f]
Chromium (µg/m²/day)			
1985	NA	NA	NA
1992	5.1[d,e]	5.8[e]	7.7–21.9[e]
1994	1.9[f]	2.9–4.4[f]	1.1–2.3[f]
Nickel (µg/m²/day)			
1985	NA	NA	NA
1992	8.0[d,e]	3.7–5.7[e]	14.4–25.8[e]
1994	1.6[f]	2.5–3.8[f]	3.8–18.0
Arsenic (µg/m²/day)			
1985	NA	NA	NA
1992	NA	NA	NA
1994	2.4[f]	1.6–2.6[f]	2.3–6.8[f]

Abbreviations: TSP, total suspended particulate matter; PM_{10}, particulate matter <10 µm in diameter; NA, not available.
[a]Data from Ministerium für Umwelt und Naturschutz des Landes Sachsen-Anhalt (*26*).
[b]Data from TÜV-Bayern (*27*).
[c]Data from Landesamt für Umweltschutz Sachsen-Anhalt (*28*).
[d]Data for Zerbst are not available; data presented were measured at a station in Stendal located in close proximity to Zerbst.
[e]Data from Landesamt für Umweltschutz Sachsen-Anhalt (*29*).
[f]Data from Landesamt für Umweltschutz Sachsen-Anhalt (*30*).
[g]Data for Bitterfeld are not available; data presented were measured at a station in Greppin located in close proximity to Bitterfeld.
[h]Data from Beyer et al. (*31*).

approximately 117,400 people in 1992 (*25*). Ambient air pollution in Bitterfeld county was caused by emissions from chemical and power plants.

Factories formerly operated in Bitterfeld produced cyclic hydrocarbons such as DDT and γ-hexachlorocyclohexane (HCH), and large amounts of these products and their waste products α- and β-HCH, polychlorinated biphenyls, and polychlorinated dibenzodioxins and dibenzofurans (PCDDs/PCDFs) were emitted into the local environment due to leaks and insufficiant air filters. Furthermore, power plants used to burn local brown coal, which has a sulfur content up to 4%.

The predominant airborne pollutants were sulfur dioxide, particulates, nitrogen oxides, and halogenated hydrocarbons.

The second county included in this study and plagued by environmental pollution is situated approximately 100 km west of Bitterfeld; Hettstedt includes the towns of Hettstedt and Mansfeld and two other villages, with a population of approximately 52,000 inhabitants in 1992. Before 1990, Hettstedt was the center for mining and smelting operations of nonferrous metals, primarily copper, dating as far back as the 12th century. The study area is situated in a valley along a small river and is surrounded by hills of less than 70 m altitude. Air pollution in Hettstedt is due to heavy metal-containing dust emissions from the smelters and domestic burning of brown coal.

The county of Zerbst, including the two towns of Zerbst and Loburg and four villages, was selected as the control area with approximately 36,800 inhabitants. The town of Zerbst is the agricultural and administrative center of the county and is located approximately 60 km north of Bitterfeld. Emissions in this county are minimal, and ambient air pollution is limited to combustion products from domestic heating with brown coal. Because Zerbst is a mountainless county, any pollutants emitted from theses domestic sources are widely distributed.

Table 1 shows large differences between the three counties with respect to emissions of SO_2, dusts, and NO_x. The emissions of SO_2 and NO_x were estimated by inclusion of industrial, traffic, and domestic heating sources. However, the dust emissions were estimated without traffic-related sources, and the metal emissions reflect only industrial sources.

Thus, all three counties experienced air pollution to some degree from domestic burning of brown coal. They also share similar climatic conditions. Although the prevailing wind direction is west and southwest, air quality in the control county of Zerbst could be influenced

by air pollutant transport from the other two polluted regions. Yet, the transported pollutants should have been measured by the monitoring systems we used, no matter what the sources were for the pollutants. Table 1 shows selected annual mean concentrations of air pollutants measured at the three study sites during the period 1984–1994 (*26–31*). Sulfur dioxide was measured using an Ansyco model AF 21 M pulsed fluorescence analyzer (Environnement, Poissy, France). Nitrogen dioxide was measured using the Ansyco model AC 30 M chemiluminescence analyzer (Environnement) in Hettstedt and Zerbst and the Horiba APNA 350 E chemiluminescence analyzer (Horiba Europe GmbH, Steinbach, Germany) in Bitterfeld. Total suspended particulate (TSP) was measured using the FH 62 IN β ray absorption monitor (FAG Kugelfischer, Schweinfurt, Germany). For the continuous measurements of black smoke (BS), we used the Euroglas 01K21425 critical orifice (Euroglas, Delft, The Netherlands). The measurements of particulate matter <10 μm in diameter (PM_{10}) were performed with the Harvard Impactor (Air Diagnostics and Engineering Inc., Naples, ME).

Missing values in the table are due to incomplete air monitoring in the former GDR. Comparisons of the two polluted regions with Zerbst show that the Bitterfeld area had the highest annual mean concentration of SO_2 in the past (*26*). After the German reunification in 1989, mean SO_2 and particulate levels decreased in the two polluted areas by a factor of approximately 2–3. A similar trend was observed for particulates in Hettstedt and Bitterfeld.

Dust contents for lead and cadmium were higher in Hettstedt, most likely as a result of pollution from the former metal processing industries. We found that the metal concentration in the dust actually depended on the distance of the monitoring station from the primary source of the emission (*32*). The lead and cadmium concentrations in dust decreased between 1992 and 1994, but were still higher than in the other polluted county (Bitterfeld) and the reference county of Zerbst.

Subjects and settings. We invited all first-, third-, and sixth-grade school children who were residents of Zerbst and Hettstedt and a subgroup of children from Bitterfeld county from selected schools to participate in our study. Schools in the Bitterfeld area were selected to represent all resident school-age children. All participants were white. Parents of 2,470 children between 5 and 14 years of age completed a questionnaire (response rate 89.1%) (Table 2). Thus the study population consisted of three groups of school children: 769 children were school entrants (5–7 years of age), 796 were third graders (8–10 years of age), and 905 were sixth graders (11–14 years of age). The response rates differed only slightly by location. Furthermore, we excluded children from the analysis if they had lived in their current home for less than 2 years or if the previous home was located more than 2 km from the current residency (n = 135; see Table 2). Data for 2,335 children contributed to most of the analyses. Children living in the three counties were quite comparable with regard to sex and parental educational attainment, but children from Bitterfeld were slightly younger (Table 2). Approval of the study protocol was granted by the University of Rostock Ethics Committee. Informed consent was obtained from the parents of all participating children.

Questionnaire. Teachers distributed letters explaining the study goals and the questionnaires to the children's parents and collected completed ones a week later. Parents of 89.1% of all children returned the questionnaires. The questionnaire contained 78 items and was previously used and tested in several national and international studies (*33*), and was further adapted to address East German living and housing conditions. It addressed socioeconomic factors, medical history of the child and the parents (including respiratory and allergic diseases and symptoms), breast feeding history, attendance of day-care centers, housing characteristics, nutrition, indoor environmental exposures such as environmental tobacco smoke and contact to pets, and outdoor environmental exposures measured as proximity of the home to an industrial complex and location close to busy streets. The questions regarding diagnoses and symptoms, translated into English, are shown below.

- Did a physician ever mention that your child suffers from one of following diseases? 1) Asthma, asthmalike bronchitis, obstructive bronchitis, bronchitis, none of these; or 2) bronchitis, any allergy, eczema.
- Did you ever notice wheezing or whistling sounds in your child's chest? No, once, more than once, do not know.
- Did your child ever experience attacks of shortness of breath?
- Does your child cough frequently in the morning or during the day without having a cold?

Information on birth weight was abstracted from the child's health record.

Dermatological examination. A trained dermatologist performed a complete skin examination for all study subjects using a standardized examination protocol that focused on the detection of atopic dermatitis. All study subjects were examined by the same dermatologist.

Pulmonary function tests. Detailed information concerning the measurement of lung function and bronchial reactivity has been previously published elsewhere (*34*). Briefly, medical technicians were trained at the beginning of the study and examined the children from September 1992 through July 1993. Each child was asked about current respiratory symptoms. Pulmonary function tests were performed from 0800 hr to 1400 hr using randomly either an electronic spirometer or a body plethysmograph (both from Jaeger, Wuerzburg, Germany) mounted on a bus.

Table 2. Response rates, mobility, and sociodemographic characteristics of the study population in Zerbst, Bitterfeld, and Hettstedt, Germany

	Zerbst		Bitterfeld		Hettstedt		Total	
Population	Percent	Frequency	Percent	Frequency	Percent	Frequency	Percent	Frequency
Target population	100.0	971/971	100.0	918/918	100.0	884/884	100.0	2,773/2,773
Responders (questionnaire)	88.3	857/971	87.0	799/918	92.1	814/884	89.1	2,470/2,773
Excluded from the comparison[a]	4.6	39/971	7.8	62/918	4.2	34/884	5.5	135/2,773
Considered in analysis	84.2	818/971	80.3	737/918	88.2	780/884	84.2	2,335/2,773
Characteristics of participants								
Age 5–7 years	27.5	225/818	35.7	263/737	30.5	238/780	31.1	726/2,335
Age 8–10 years	32.5	266/818	30.9	228/737	32.7	255/780	32.1	749/2,335
Age 11–14 years	40.0	327/818	33.4	246/737	36.8	287/780	36.8	860/2,335
Male	50.9	416/818	51.2	377/737	50.0	390/780	50.7	1,183/2,335
Higher parental education[b]	41.1	328/799	42.7	303/710	42.9	327/763	42.2	958/2,272

[a]Children were excluded if they had lived <2 years in their current homes and their previous homes were >2 km away.
[b]Education of father or mother was at least 12 years.

Subjects performed forced expiration in a sitting position while using a nose-clip. The forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV_1), and forced peak expiratory flow (PEF) were recorded and followed by a complete body plethysmography. Forced flow volume tests were performed until three reproducible loops were achieved. Data of the maneuvers with the highest sum of FEV_1 and FVC according to criteria of the American Thoracic Society was used for the analysis. The body was calibrated each 2 hr. Cold air challenge with -15°C air was carried out using a respiratory heat exchange system (Jaeger, Wuerzburg, Germany). The children hyperventilated cold air supplemented with 5% carbon dioxide for 4 min at 75% of their maximum ventilation rate per minute. Pulmonary function testing was then repeated within 5 min following the exposure to cold air.

All data presented in this paper are based on measurements taken with the body plethysmograph since only children assigned to this instrument participated in the cold air-challenge test (n = 1,028). Children suffering from infectious disease during the previous 2 weeks were excluded from analysis; children who did not perform the repeated lung function measurement according to the ATS criteria or did not follow the cold air challenge test were also exluded. Bronchial reactivity was defined as a 9% drop in FEV_1 after a cold air challenge.

Skin prick testing. Sensitivity to 12 common allergens (house dust mite allergens *Der p1* and *Der f1*, *Aspergillus fumigatus*, *Alternaria alternata*, cat epithelium, mixed local grasses, mugwort, hazel, birch, plantain, milk, egg) were assessed by skin prick tests (SPT) according to a standardized application protocol. Commercially available purified and immunochemically characterized allergens produced by Allergopharma (Reinbek, Germany) were applied to the child's forearm using an uncoated lancet for each allergen. A 1:1000 titer of histamine provided the positive control and a 0.9% saline solution was the negative control. The size of the wheal was documented according to the protocol of the European Community Respiratory Health Survey [ECRHS; see Nowak et al. (*24*)]. After 15 min, the wheals were outlined with a ballpoint pen and the markings transferred to data sheets with transparent tape. Wheal diameters were read at the widest diameter. Skin tests were repeated if the wheal diameter of the histamine chloride was less than <2 mm or the wheal diameter of the saline was greater than 3 mm. Wheals ≥3 mm in diameter were considered positive, provided that the control solution produced no reaction and there was a positive reaction to histamine. A skin test was considered positive if a positive reaction to at least one allergen was documented.

IgE measurement. Blood collection, centrifugation of the blood, and serum storage followed the protocol of the ECRHS (*24*). The serum samples were stored until the end of the study at temperatures of -20°C. Specific IgE to *Dermatophagoides pteronyssinus* (d1), *Cladosporium* (m2), cat (e1), mixed grasses (g6), and birch (t3) were measured. All frozen serum samples were analyzed by the CAP-FEIA method for specific IgEs by the same laboratory (Pharmacia Diagnostics, Freiburg, Germany) using identical batches of all reagents for all assays (*35*). The intraassay and interassay coefficient of variation was 7% (*36*). The measurement range was 0.35–100 kU/l, with a detection limit >0.35 kU/l. Duplicate standard curves were set up, and all samples were assayed in a single determination.

Quality control. Study personnel collecting clinical data attended a training course prior to its beginning. During this pilot phase, we checked all procedures to be used later in the study. Procedures that depend on investigators' skills, such as lung function measurement and skin testing, were performed by the same trained personnel at all three study sites. The same equipment was used at all three locations as well. Instead of conducting parallel exams in all three counties, we rotated personnel and equipment between regions in a biweekly pattern. This approach allowed the same personnel to perform all examinations and also avoided possible problems due to seasonal influences on disease patterns for each region.

Statistical methods. We calculated crude region-specific prevalence rates for all binary outcome variables. Multiple logistic regression analyses (*37*) allowed us to estimate regional effects on respiratory and allergic diseases adjusted for a fixed set of potential confounding variables. Children living in Zerbst served as the reference group in all analyses. We used a complete-subset approach to deal with missing covariate values (i.e., only children for whom all covariate data were available were included in the analyses). This procedure leads to a fluctuating number of subjects [e.g., the bronchial reactivity test was performed on a

Table 3. Crude prevalence rates of physician's diagnoses, self-reported symptoms, bronchial reactivity, sensitization and findings of the inspection of the skin in children 5–14 years of age from the polluted areas (Bitterfeld and Hettstedt) and the control area (Zerbst)

	Zerbst		Bitterfeld		Hettstedt	
Health characteristics	Prevalence	Frequency[a]	Prevalence	Frequency[a]	Prevalence	Frequency[a]
Self-reported physician's diagnoses (%)						
Asthma[b]	1.6	(13/816)	4.4	(32/728)	2.1	(16/775)
Bronchitis[b]	49.8	(406/816)	51.5	(375/728)	61.7	(478/775)
Allergy[b]	11.9	(96/809)	11.8	(86/727)	17.3	(134/776)
Eczema[b]	8.2	(67/815)	11.7	(86/736)	11.1	(86/776)
Self-reported respiratory symptoms (%)						
Wheezing[b]	20.9	(163/781)	26.8	(186/693)	30.9	(226/731)
Shortness of breath[b]	9.4	(73/773)	11.1	(77/693)	17.2	(128/744)
Cough without cold	4.7	(37/788)	7.3	(52/716)	8.3	(63/760)
Lung function tests (%)						
Bronchial reactivity[c]	13.9	(35/252)	19.4	(43/222)	16.7	(49/293)
Skin prick test (%)						
One or more positive[d]	18.2	(133/731)	21.5	(142/659)	23.1	(158/684)
Pollen[e]	12.2	(89/731)	15.5	(102/659)	15.6	(107/684)
Mites (*D. pteronyssinus*, *D.* farinae)	7.0	(51/731)	8.3	(55/659)	8.0	(55/685)
Fungi (*Aspergillus*, *Alternaria*)	5.6	(41/731)	7.0	(46/660)	6.6	(45/685)
Cat	3.3	(24/731)	2.1	(14/660)	4.1	(28/685)
Food (eggs, milk)	0.3	(2/731)	0.3	(2/660)	0.4	(3/685)
Specific IgE (%)						
One or more increased[f]	29.8	(216/726)	32.2	(132/410)	37.2	(182/489)
Pollen IgE (grass, birch) increased[f]	22.3	(162/726)	24.4	(109/447)	27.4	(145/529)
Mite IgE (*der p1*) increased[f]	14.1	(103/732)	14.4	(90/624)	16.7	(110/660)
Fungi IgE (*Cladosporium*) increased[f]	4.1	(30/729)	7.0	(32/458)	3.7	(20/534)
Cat IgE increased[f]	6.0	(44/732)	6.2	(37/596)	9.2	(60/649)
Physical examination (%)						
Atopic dermatitis	1.8	(13/733)	2.7	(18/664)	3.2	(22/691)

[a]The variation in total subjects is a result of missing data.
[b]Lifetime.
[c]Fall in forced expiratory flow in 1 sec >9% from baseline after the cold air challenge test.
[d]Wheal diameter ≥3 mm.
[e]Grasses, birch, hazel, mugwort, plantain.
[f]>0.35 kU/l.

small subgroup of children (n = 585) for which we were able to obtain complete data]. We examined potential effect modification for each of the selected covariates including interaction terms with region in our models. We did not find any effect modification and, thus, excluded these terms from our final regression models. We report adjusted odds ratios (ORs) and 95% confidence intervals (CIs). All computations were performed using SAS Version 6.09 (SAS Institute, Cary, NC) in a Unix environment.

Results

Descriptive analyses. Table 3 displays crude prevalences of parent-reported diagnoses and symptoms, bronchial reactivity in our cold air-challenge test, signs of atopic disease noted by the study dermatologist, and the sensitization rate for major aeroallergens by study region. Parents of children living in Hettstedt county reported the highest proportion of lifetime diagnoses of atopic diseases and asthmoid respiratory symptoms. Asthma diagnosed by a physician ("ever asthma bronchiale" or "wheezy bronchitis") was reportedly more frequent for Bitterfeld (4.4%) and Hettstedt (2.1%) youths than for children living in the comparison region of Zerbst (1.6%).

The parental reports of higher proportions of asthmoid symptoms experienced by children residing in Hettstedt and Bitterfeld were substantiated by the results from the cold air challenge test performed during this survey. The same trend as for asthma diagnosis was found for increased bronchial reactivity: children from Bitterfeld most often responded positively (19.4%), followed by children from Hettstedt (16.7%) and Zerbst (13.9%). Yet, we did not find regional differences for other lung function tests (FEV_1, etc; results not shown).

We also observed slightly higher allergic sensitization rates among children from Hettstedt and Bitterfeld, according to both methods employed (the skin prick test and IgE measurements). Most of the sensitized children showed a skin reaction to pollen allergens. Sensitization to food allergens, eggs, and milk were negligible (0.3% of all tested children). Specific IgE increases were found for the common antigens pollen and mites. Cat-specific IgE and IgE against fungi were less frequent.

Finally, children from Zerbst (1.8%) suffered less from atopic dermatitis than children from Bitterfeld (2.7%) or Hettstedt (3.2%), according to the assessment of our study dermatologist. A small trend was found for parental reports of previously diagnosed eczema (8.2–11.7%). A greater proportion of parents reported childhood tonsillitis in Hettstedt than in Zerbst (70.0% vs. 63.6%); this was paralleled by a higher proportion of abnormal or removed tonsils diagnosed in our physical examinations (data not shown).

Table 4. Prevalence rates of potential predictors of health outcomes in 5–14-year-old children of two polluted areas (Bitterfeld and Hettstedt) in comparison with the control area (Zerbst)

	Zerbst		Bitterfeld		Hettstedt	
Predictors	Prevalence	Frequency[a]	Prevalence	Frequency[a]	Prevalence	Frequency[a]
Medical history						
Low birth weight (<2,500 g)	6.9	(54/779)	6.9	(49/708)	5.7	(43/753)
No breast-feeding	22.1	(179/811)	14.6	(107/735)	23.9	(185/775)
Parental atopy[b]	24.9	(204/818)	28.4	(209/737)	26.5	(207/780)
Housing characteristics						
House was built before 1960	49.8	(395/793)	52.1	(366/702)	45.8	(349/762)
House made of concrete	38.1	(302/792)	41.9	(298/712)	40.6	(301/741)
Dwelling on ground floor	46.1	(367/796)	31.8	(230/724)	45.9	(351/764)
Habitable surface per person >20 m^2	49.8	(377/757)	39.2	(267/681)	41.7	(300/720)
Child shared bedroom	44.8	(360/804)	52.9	(384/726)	49.2	(377/767)
Dampness or visible molds	20.2	(163/808)	19.0	(139/730)	17.6	(136/774)
District or central heating	50.3	(410/815)	55.0	(404/734)	46.7	(364/779)
Heating with coke/ coal/briquettes	35.8	(285/797)	37.8	(274/724)	36.8	(281/763)
Heating with gas	8.7	(69/797)	4.0	(29/724)	8.1	(62/763
Child's room						
Child's room near main street/industry	22.7	(183/807)	22.0	(157/715)	22.3	(172/772)
Wall-to-wall carpet in child's room	67.0	(547/816)	57.4	(421/734)	67.9	(529/779)
Environmental tobacco smoke						
Current or prior exposure at home	53.2	(431/810)	61.5	(448/728)	59.0	(457/774)
Mother smoked during pregnancy	6.4	(51/797)	6.2	(45/731)	3.5	(27/767)
Contact with pet						
Contact to cats	39.0	(313/803)	23.3	(169/726)	34.8	(268/771)
Other						
Child ever attended day-care center	87.1	(705/809)	91.4	(672/735)	89.0	(685/770)

[a]The variation in total subjects is a result of missing data.
[b]Atopic diseases (asthma, hay fever, eczema, other allergy) in at least one parent.

Potential predictors of health outcomes. Table 4 presents the distribution of factors potentially related to the health outcomes of interest by region. Most of these possible risk factors were quite homogenously distributed throughout the three counties. Slightly more parents from Bitterfeld and Hettstedt reported suffering from atopic diseases (28.4% and 26.5%, respectively) than parents living in Zerbst (24.9%). Bitterfeld children more often lived in houses built before 1960 and in houses made out of concrete. Because these structures were usually multilevel complexes, dwelling on the ground floor was less common in Bitterfeld (31.8%) compared to Zerbst (46.1%) and Hettstedt (45.9%). Bitterfeld children were also more likely to share their bedrooms than their peers living in Zerbst or Hettstedt. Consequently, Bitterfeld residents also reported less living space per person.

Of all homes, 18.9% were described as damp or showed visible mold. Approximately half of the homes were heated by a long-distance steam pipeline or a central heating system. Homes in Bitterfeld used gas furnaces less often for heat. Parents reported wall-to-wall carpeting in the child's room and the use of mattresses made of horsehair, curtains, chipboards, and upholstered furniture in similar proportions. Currently, as well as throughout their lives, a higher proportion of Bitterfeld and Hettstedt children had lived with a household member who smoked tobacco, and mothers of children from Bitterfeld and Zerbst more often reported smoking during pregnancy. Children from Zerbst had more contact to pets.

Multivariate analyses. Logistic regression modeling allowed us to adjust for the influence of potential confounders while examining the effect of the study region on each of the health outcome measures of interest separately. Tables 5–7 show crude and adjusted (i.e., adjusted for all of the above mentioned variables) ORs for residing in Bitterfeld or Hettstedt versus Zerbst (reference county).

We found 1.5–2 times more parents in Hettstedt who reported that physicians had diagnosed their children with asthma (adjusted OR = 1.97), allergies (adjusted OR = 1.69), eczema (adjusted OR = 1.52), or bronchitis (adjusted OR = 1.52). On the

Table 5. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for lifetime prevalence of self-reported physician's diagnoses

	Asthma or wheezy bronchitis (*n* = 1,773)		Bronchitis (*n* = 1,773)		Allergy (*n* = 1,768)		Eczema (*n* = 1,780)	
Potential predictors	Adj OR	CI	Adj OR	CI	Adj OR	CI	Adj OR	CI
Age 8–10 years (vs. 5–7 years)	1.16	(0.55–2.43)	0.97	(0.76–1.24)	1.44*	(0.99–2.09)	0.93	(0.62–1.39)
Age 11–14 years (vs. 5–7 years)	1.13	(0.54–2.38)	1.07	(0.84–1.37)	1.64**	(1.14–2.36)	1.08	(0.73–1.60)
Male vs. female	1.43	(0.79–2.61)	1.18*	(0.98–1.44)	1.27*	(0.96–1.68)	0.91	(0.67–1.25)
Higher parental education[a]	1.99*	(1.06–3.74)	1.54#	(1.26–1.90)	1.27	(0.95–1.70)	1.32*	(0.95–1.83)
Low birth weight (<2,500 g)	2.47	(0.77–7.93)	0.91	(0.60–1.39)	0.70	(0.35–1.41)	0.27*	(0.08–0.89)
No breast-feeding	0.24*	(0.07–0.82)	0.78*	(0.60–1.02)	0.95	(0.66–1.38)	0.82	(0.52–1.29)
Parental atopy[b]	1.04	(0.55–1.95)	1.17	(0.94–1.46)	1.37*	(1.02–1.84)	1.49*	(1.08–2.08)
House was built before 1960	2.01	(0.57–7.09)	1.07	(0.79–1.47)	0.88	(0.57–1.38)	0.83	(0.51–1.34)
House made of concrete	3.76*	(1.03–13.7)	1.48*	(1.06–2.08)	1.04	(0.65–1.68)	0.81	(0.48–1.38)
Dwelling on ground floor	1.92*	(0.96–3.84)	0.94	(0.75–1.17)	1.12	(0.82–1.54)	1.33	(0.93–1.89)
Habitable surface per person >20 m^2	0.52*	(0.24–1.10)	0.87	(0.69–1.10)	0.93	(0.67–1.31)	0.85	(0.58–1.25)
Child shared bedroom	0.69	(0.36–1.30)	0.97	(0.78–1.20)	0.78	(0.58–1.06)	0.85	(0.60–1.20)
Dampness or visible mold	1.28	(0.60–2.76)	1.42**	(1.09–1.84)	1.19	(0.83–1.70)	1.23	(0.82–1.84)
District or central heating	0.62	(0.13–2.96)	0.94	(0.55–1.58)	0.57*	(0.31–1.07)	1.04	(0.45–2.41)
Heating with coke/coal/briquettes	0.54	(0.11–2.58)	0.89	(0.53–1.50)	0.44*	(0.24–0.84)	0.94	(0.41–2.20)
Heating with gas	1.30	(0.22–7.69)	1.10	(0.60–2.02)	0.61	(0.29–1.29)	0.90	(0.33–2.43)
Child's room near main street/industry	1.09	(0.50–2.40)	0.85	(0.67–1.08)	1.35*	(0.97–1.88)	0.88	(0.58–1.32)
Wall-to-wall carpet in child's room	0.78	(0.42–1.46)	0.91	(0.74–1.12)	1.08	(0.80–1.46)	1.01	(0.72–1.41)
Current or prior ETS exposure at home	0.68	(0.37–1.27)	1.14	(0.93–1.40)	0.99	(0.74–1.32)	1.06	(0.77–1.48)
Mother smoked during pregnancy	1.48	(0.33–6.78)	1.41	(0.86–2.31)	0.87	(0.40–1.89)	0.70	(0.27–1.80)
Contact with cats	0.66	(0.30–1.46)	0.88	(0.71–1.10)	1.06	(0.77–1.45)	1.02	(0.71–1.46)
Child ever attended day-care center	0.97	(0.33–2.86)	1.58**	(1.13–2.19)	0.98	(0.62–1.56)	1.15	(0.66–2.00)
Geographic area								
Bitterfeld vs. Zerbst, adjusted[c]	4.40#	(1.84–10.5)	0.95	(0.75–1.22)	1.15	(0.79–1.67)	1.42*	(0.94–2.15)
Bitterfeld vs. Zerbst, crude	4.51#	(1.95–10.4)	1.08	(0.86–1.36)	1.11	(0.77–1.59)	1.39	(0.93–2.06)
Hettstedt vs. Zerbst, adjusted[c]	1.97	(0.78–4.99)	1.52#	(1.20–1.92)	1.69**	(1.21–2.36)	1.52*	(1.03–2.24)
Hettstedt vs. Zerbst, crude	2.04	(0.82–5.08)	1.56#	(1.24–1.96)	1.73**	(1.25–2.39)	1.54*	(1.05–2.26)

ETS, environmental tobacco smoke.

[a]Education of father or mother was at least 12 years.

[b]Atopic diseases (asthma, hay fever, eczema, other allergy) in at least one parent.

[c]Adjusted for potential predictors.

*$p<0.05$; **$p<0.01$; #$p<0.001$.

other hand, we observed higher rates of physician-diagnosed asthma (OR = 4.40) and eczema (OR = 1.42) for children from Bitterfeld. Adjusting for other risk factors did not change the fact that Hettstedt children had suffered from more symptoms of wheezing (OR = 1.79), shortness of breath (OR = 2.36), and coughing without having a cold (OR = 1.72) throughout their lifetime. Bitterfeld children did not report such an increased lifetime prevalence of asthmoid respiratory symptoms. The pulmonary function test suggested a slightly increased reactivity of the airways to cold air for children living in the polluted areas (Table 7).

Children from Hettstedt were more often sensitized to common aeroallergens, as assessed by skin prick tests (OR = 1.38) and specific IgE measurements (OR = 1.75), and suffered slightly more from atopic dermatitis (OR = 1.89) as diagnosed by the study's dermatologist. Specific IgE to pollen, mites, and cats were higher in children from Hettstedt. Neither skin test reactivity, IgE elevation, nor atopic dermatitis were found to be increased in Bitterfeld.

Overall, adjustment for individual covariates did not substantially influence the association between health outcomes and study area.

Table 6. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for lifetime prevalence rates of parent-reported symptoms

	Wheezing (*n* = 1,712)		Shortness of breath (*n* = 1,711)		Cough without cold (*n* = 1,738))	
Potential predictors	Adj OR	CI	Adj OR	CI	Adj OR	CI
Age 8–10 years (vs. 5–7 years)	0.88	(0.67–1.16)	1.13	(0.78–1.64)	1.09	(0.68–1.74)
Age 11–14 years (vs. 5–7 years)	0.79*	(0.60–1.04)	1.19	(0.82–1.72)	0.71	(0.43–1.17)
Male vs. female	1.29*	(1.03–1.60)	1.36*	(1.01–1.82)	0.97	(0.66–1.43)
Higher parental education[a]	1.22*	(0.97–1.54)	1.46*	(1.08–1.99)	0.93	(0.61–1.40)
Low birth weight (<2,500 g)	1.21	(0.75–1.96)	1.05	(0.54–2.04)	2.03*	(1.01–4.11)
No breast-feeding	0.66*	(0.48–0.91)	0.85	(0.57–1.27)	1.25	(0.75–2.07)
Parental atopy[b]	1.38**	(1.09–1.75)	1.49*	(1.09–2.02)	1.53*	(1.02–2.31)
House was built before 1960	1.04	(0.73–1.49)	1.08	(0.67–1.75)	1.48	(0.72–3.08)
House made of concrete	1.12	(0.76–1.63)	1.03	(0.62–1.70)	1.86	(0.87–3.97)
Dwelling on ground floor	1.15	(0.89–1.48)	1.19	(0.85–1.66)	0.94	(0.60–1.46)
Habitable surface per person >20 m^2	0.69**	(0.53–0.91)	0.76	(0.53–1.10)	1.07	(0.67–1.72)
Child shared bedroom	1.01	(0.79–1.28)	1.11	(0.81–1.53)	0.86	(0.56–1.32)
Dampness or visible mold	1.18	(0.89–1.57)	1.27	(0.87–1.85)	1.46	(0.91–2.36)
District or central heating	2.40*	(1.16–4.93)	1.64	(0.73–3.67)	1.36	(0.44–4.18)
Heating with coke/coal/briquettes	2.02*	(0.99–4.14)	1.06	(0.47–2.37)	1.26	(0.42–3.80)
Heating with gas	1.86	(0.83–4.18)	0.85	(0.32–2.28)	0.80	(0.20–3.20)
Child's room near main street/industry	1.17	(0.90–1.53)	1.29	(0.91–1.85)	1.70*	(1.09–2.63)
Wall-to-wall carpet in child's room	1.21	(0.96–1.54)	1.53*	(1.10–2.13)	0.93	(0.61–1.40)
Current or prior ETS exposure at home	1.19	(0.94–1.50)	0.94	(0.70–1.28)	1.00	(0.66–1.51)
Mother smoked during pregnancy	1.04	(0.59–1.82)	0.93	(0.41–2.12)	2.22*	(1.02–4.82)
Contact with cats	0.99	(0.77–1.28)	0.97	(0.69–1.36)	0.86	(0.54–1.37)
Child ever attended day care center	1.31	(0.87–1.96)	0.77	(0.48–1.25)	0.96	(0.48–1.90)
Geographic area						
Bitterfeld vs. Zerbst, adjusted[c]	1.22	(0.92–1.63)	1.21	(0.80–1.82)	1.36	(0.81–2.28)
Bitterfeld vs. Zerbst, crude	1.34*	(1.02–1.77)	1.23	(0.83–1.83)	1.43	(0.87–2.36)
Hettstedt vs. Zerbst, adjusted[c]	1.79#	(1.37–2.34)	2.36#	(1.65–3.38)	1.72*	(1.05–2.81)
Hettstedt vs. Zerbst, crude	1.81#	(1.40–2.34)	2.34#	(1.65–3.32)	1.66*	(1.03–2.67)

ETS, environmental tobacco smoke.

[a]Education of father or mother was at least 12 years.

[b]Atopic diseases (asthma, hay fever, eczema, other allergy) in at least one parent.

[c]Adjusted for potential predictors.

*$p<0.05$; **$p<0.01$; #$p<0.001$.

Table 7. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for physical examinations

	Bronchial reactivity[a] (*n* = 585)		One or more skin prick test positive[b] (*n* = 1,581)		One or more specific IgE increased[c] (*n* = 1,236)		Atopic dermatitis (*n* = 1,595)	
Confounders	Adj OR	CI	Adj OR	CI	Adj OR	CI	Adj OR	CI
Age 8–10 years (vs. 5–7 years)	0.90	(0.50–1.61)	1.42*	(1.04–1.94)	1.59**	(1.16–2.19)	1.49	(0.65–3.42)
Age 11–14 years (vs. 5–7 years)	1.02	(0.59–1.79)	1.07	(0.78–1.48)	1.74#	(1.27–2.39)	1.44	(0.63–3.29)
Male vs. female	0.94	(0.61–1.46)	2.02#	(1.57–2.60)	1.84#	(1.44–2.36)	0.85	(0.45–1.60)
Higher parental education[d]	1.28	(0.81–2.02)	0.98	(0.76–1.27)	1.23	(0.95–1.60)	0.64	(0.32–1.25)
Low birth weight (<2,500 g)	0.95	(0.40–2.27)	0.97	(0.55–1.71)	0.83	(0.49–1.40)	0.45	(0.06–3.54)
No breast-feeding	1.20	(0.68–2.12)	0.94	(0.67–1.32)	1.05	(0.76–1.46)	0.59	(0.22–1.57)
Parental atopy[e]	1.08	(0.66–1.76)	1.47**	(1.13–1.91)	1.14	(0.87–1.49)	1.33	(0.68–2.62)
House was built before 1960	0.92	(0.45–1.85)	0.97	(0.65–1.43)	1.06	(0.71–1.58)	0.59	(0.22–1.53)
House made of concrete	0.94	(0.45–1.99)	0.93	(0.61–1.42)	1.19	(0.76–1.85)	0.90	(0.33–2.41)
Dwelling on ground floor	1.09	(0.66–1.78)	1.17	(0.88–1.55)	1.16	(0.88–1.54)	1.09	(0.53–2.27)
Habitable surface per person >20 m^2	1.16	(0.68–1.99)	0.97	(0.72–1.31)	1.09	(0.80–1.47)	0.84	(0.39–1.81)
Child shared bedroom	0.98	(0.61–1.56)	1.10	(0.84–1.44)	1.15	(0.88–1.52)	0.60	(0.30–1.21)
Dampness or visible molds	0.83	(0.45–1.51)	1.07	(0.77–1.47)	0.98	(0.71–1.34)	0.98	(0.43–2.25)
District or central heating	0.78	(0.23–2.58)	1.47	(0.73–2.97)	2.22*	(1.08–4.59)	0.28*	(0.09–0.95)
Heating with coke/coal/briquettes	1.17	(0.36–3.86)	1.11	(0.55–2.25)	2.17*	(1.05–4.49)	0.35*	(0.11–1.16)
Heating with gas	1.04	(0.26–4.19)	1.15	(0.51–2.60)	1.63	(0.72–3.69)	0.13*	(0.01–1.21)
Child's room near main street/industry	1.26	(0.74–2.15)	0.83	(0.60–1.13)	0.88	(0.65–1.20)	1.18	(0.55–2.53)
Wall-to-wall carpet in child's room	0.80	(0.50–1.26)	1.23	(0.94–1.62)	1.21	(0.93–1.58)	1.21	(0.59–2.49)
Current or prior ETS exposure at home	0.65*	(0.41–1.03)	0.86	(0.67–1.12)	0.87	(0.67–1.12)	0.89	(0.46–1.72)
Mother smoked during pregnancy	0.29	(0.04–2.21)	0.52*	(0.24–1.13)	0.68	(0.34–1.34)		
Contact with cats	0.96	(0.57–1.61)	0.83	(0.62–1.11)	1.06	(0.80–1.40)	0.63	(0.28–1.40)
Child ever attended day-care center	0.86	(0.40–1.83)	0.82	(0.54–1.23)	1.00	(0.66–1.51)	2.67	(0.62–11.5)
Area								
Bitterfeld vs. Zerbst, adjusted[f]	1.69*	(0.93–3.07)	1.25	(0.91–1.72)	1.31	(0.95–1.81)	1.29	(0.54–3.09)
Bitterfeld vs. Zerbst, crude	1.56	(0.90–2.71)	1.31*	(0.97–1.77)	1.27	(0.94–1.72)	1.37	(0.59–3.20)
Hettstedt vs. Zerbst, adjusted[f]	1.40	(0.80–2.43)	1.38*	(1.02–1.86)	1.75#	(1.31–2.33)	1.89	(0.86–4.15)
Hettstedt vs. Zerbst, crude	1.31	(0.77–2.22)	1.39*	(1.04–1.87)	1.61#	(1.22–2.13)	2.00*	(0.92–4.34)

ETS, environmental tobacco smoke.

[a]Fall of 9% in forced expiratory volume in 1 sec after a cold air challenge test.

[b]Wheal diameter ≥3 mm.

[c]>0.35 kU/l.

[d]Education of father or mother was at least 12 years.

[e]Atopic diseases (asthma, hay fever, eczema, other allergy) in at least one parent.

[f]Adjusted for potential confounding factors.

*$p<0.05$; **$p<0.01$; #$p<0.001$.

Discussion

Our study found higher prevalences of respiratory diseases and symptoms, higher sensitization rates to most common aeroallergens, and more signs of atopic skin disorders in children aged 5–14 years of age who had lived most of their lives in Hettstedt and Bitterfeld, compared to children who lived in Zerbst. These three counties, although located geographically in close proximity to each other in eastern Germany, differ extensively with respect to environmental pollution, with Hettstedt and Bitterfeld having been centers of industrial and mining operations until the early 1990s and Zerbst being a purely agricultural region. Parental reports of physician's diagnoses of asthma, bronchitis, allergy, and eczema and symptoms of wheezing, shortness of breath, and cough experienced by the children clearly indicated an increased disease burden in the polluted regions. Our survey's tests and medical examinations confirmed these parental reports: responsiveness to pulmonary cold air challenge, sensitization to aeroallergens assessed with the help of skin prick tests and specific IgE measurements, and dermatological findings of atopic signs were found more often among children residing in the polluted areas. Children living in Hettstedt showed the most consistent adverse pattern for all health outcomes taken together, (i.e., they were of poorer respiratory health and were sensitized at a higher rate). Asthma diagnosis, however, was more common among children from Bitterfeld. Adjustment for many potential risk factors did not appreciably change the ORs for the effect of area of residence on allergies. About 80% of all families enrolled had two or fewer children, and almost 90% of the children attended a day care center before 3 years of age. Thus, we used the variable "bedroom sharing (with a sibling)" and "having attended a day care center" to adjust for the effects of "family size" and "early childhood infections" on allergies (*38*). Although discussions about the possible role of nutrition as a potential risk factor for allergies are widespread (*39,40*), we do not believe that major differences in nutritional behavior existed for the residents of the three study areas.

The data shown in Table 1 indicated large differences in the emitted amounts of air pollutants, specifically particulates and sulfur dioxide emitted during the 1980s and even the 1990s, in industrial regions of Hettstedt and Bitterfeld as compared with Zerbst. Due to the closure of most industries in the two former counties after German unification, emissions decreased considerably in the early 1990s. All of the children included in this study were born between 1970 and the mid-1980s, and thus have been exposed to high levels of air pollutants for a large part of their lives.

We are lacking data concerning pollutants stemming from the production of organochlorine chemicals in Bitterfeld and the smelting of plastic-insulated copper materials in Hettstedt. SO_2 and TSP are the only compounds recorded that reflect pollution from industrial combustion processes. Yet, these two substances must be interpreted as indicators for a great mixture of nonmeasured pollutants. The increased lead content found in dust around Hettstedt can be considered an indicator for general pollution from all emissions caused by the smelting operations.

Figure 1. Map of Germany showing the three study locations (Zerbst, Bitterfeld, and Hettstedt). Hettstedt is 100 km from Bitterfeld.

The place of residence was used as a proxy measure of long-term exposure of the children to environmental pollutants, i.e., mostly air pollutants. A cross-sectional study design does not lend itself easily to the causal interpretation of associations observed between environmental pollutant exposures and health outcomes. A major concern is that the locations being compared might differ with respect to risk factors for health outcomes other than pollution levels such as poverty status, access to health care, different nutritional behaviors, or smoking rates.

However, our study compares three unique eastern German regions located in relative proximity to each other, two of which were highly polluted by heavy metals and/or organochlorine compounds, while the third area historically has not been impacted by pollution due to industrial production. Not only is the ethnic composition in all three communities virtually the same but also these communities can be regarded as homogenous with respect to general social and lifestyle factors and access to medical care.

This region represents all environmental factors impacting a child's health (i.e., it is nonspecific and potentially confounded by migration processes). To reduce bias due to migration out of or into the study regions, we excluded children who had moved farther than 2 km from their current residence within the last 2 years. The overall mobility of the study population was extremely low. As many as 73.3% of the children had lived for more than half of their lives at the current address, or at least nearby. We believe that the low mobility of this eastern German population helped to reduce the potential for bias due to migration in this cross-sectional study.

Our results are in agreement with previous studies that examined the effect of air pollution on nonasthmatic respiratory symptoms and diseases. A recently published review of studies from central and eastern European countries reported positive associations between traditional air pollutants such as SO_2 and TSP and the prevalence of respiratory symptoms and diseases and reduced lung function in children (*10*). According to Pope et al. (*7*), studies from the United States using the most sophisticated analyses approaches showed clear adverse health effects for long-term exposure to particulate matter and to a lesser degree to NO_2 and O_3 (*12*). The U.S. 24-cities study examined the health effects of a large range of air pollutants: particulate matter (PM_{10} and $PM_{2.5}$), sulfate, particle strong acidity, ozone, sulfur dioxide, ammonia, and nitrous acid (*41*). A comparison of the respiratory health profiles of 13,000 children (8–12 years of age) residing in these 24 communities showed that children living in communities with the highest particle strong acidity more often reported at least one episode of bronchitis in the past year (OR = 1.66). In addition, fine particulate sulfate was associated with higher reporting of bronchitis (OR = 1.65). No other respiratory symptoms were found to be associated with the air pollutants measured in these cities.

Recently published results of the Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution (SCARPOL) (*5*) provide further evidence that rates of respiratory illness and symptoms, but not allergies, are associated with increasing but moderate levels of air pollution. A recently published Polish cross-sectional study of 1,129 children who were 9 years of age reported an association between outdoor air pollutants and chronic phlegm (OR = 4.2) and hay fever (OR = 1.43) (*42*). The authors postulated either that allergy is predisposing to respiratory reactivity or that ambient pollution is a cofactor in the process of allergization experienced by preadolescent children.

Although the source of the pollutants—and thus their mixtures and levels—differed considerably between studies, most authors reported increases in respiratory symptoms such as wheeze and dry cough, respiratory diseases (including bronchitis and chest illness), and small decrements in lung function measured by FVC, FEV_1, and PEF (*5,8–16*). We were not able to detect lung function differences (FVC, FEV_1, PEF) by study region, but children from the polluted regions responded positively more often to the cold air challenge.

Several epidemiologic studies compared the prevalence of asthma and allergy in areas with different air pollution levels. Some comparisons are restricted to developed countries, and others attempt intercountry comparisons, particularly of the east–west type. East–west studies compare locations with great heterogeneity in many aspects, such as ethnicity, social factors, health care system, etc. Interpreting the regional differences in disease prevalence in such studies as indicators of the effects of long-term exposure to ambient pollutants is limited due to the insufficient ability to control for such risk factors (*43*). The second National Health and Nutrition Examination Survey (NHANES II) covered a large group of randomly selected households within the United States. In whites, the sensitization assessed by skin prick test was higher among urban than rural residents (*12*). Several other studies also reported higher rates of atopy among urban populations (*3,44–46*). It was suggested that differences in lifestyle may lead to higher exposure to indoor allergens in cities (*43*). Others attribute these differences to effects of pollutants such as nitrogen dioxide, ozone, and diesel exhaust particulates that are more prevalent in urban environments. None of the previous studies reporting such regional differences was able to distinguish between the effect of urban lifestyle and the effect of exposure to higher levels of traffic related air pollutants.

The association between increased air pollution and allergic disorder has not been unequivocally described in epidemiologic studies. Our results with respect to increased allergic symptoms are comparable to results from an Italian cross-sectional study (*45*) and two German studies that found higher rates of self-reported allergic rhinitis (*17*) and increased SPT positivity (*18*) among children residing near busy streets. These traffic-related studies focused on pollutants such as nitrogen dioxide and fine particles rather than on sulfur dioxide and larger particles. Neither the Swiss SCARPOL study (*5*) nor the U.S. Six Cities Study (*15*) found positive associations between prevalence of allergic rhinitis and increased levels of either sulfur dioxide, particulate matter, nitrogen dioxide, or ozone. One reason for these differences might be that the health effects caused by pollutants such as TSP depend on the chemical composition of the particles or the size distribution, all of which can be quite different for each region studied.

Air quality in Bitterfeld was diminished primarily by two measured criteria air pollutants, SO_2 and suspended particulates, while the Hettstedt environment was impacted more heavily by lead and cadmium in dust and soil. This is paralleled by higher rates of respiratory diseases and allergies found in children from Hettstedt. Yet, no plausible explanation, particularly for the higher sensitization rate in Hettstedt, can be given. There is no known biological mechanism that links exposure to heavy metals to respiratory symptoms and disease. Lead exposure that leads to increased sensitization with respect to aeroallergens has not been previously described. Because the sources of air pollution differed between Hettstedt and Bitterfeld, the measured ambient pollutants may be surrogates for other unknown or unmeasured pollutants in both areas. Furthermore, differences in prevalence rates for certain health outcomes could be due to bias (i.e., differential reporting or diagnosis due to higher awareness in the public and diagnostic preferences of local physicians). Indeed, the ORs of Hettstedt versus Zerbst for self-reported symptoms and diagnoses tend to be somewhat higher compared to the ORs derived from the findings of the medical examination. On the other hand, objective data such as SPT results, specific IgE analyses, and our cold air challenge test mostly confirmed the reported diagnoses and symptoms.

Obviously, differences in respiratory health do exist between the two polluted areas and the reference county. On the other hand, controlling for information concerning previous habits might be limited when this information was obtained retrospectively: such information might be subject to reporting bias, and lifestyle changes might have been adopted in response to disease occurrence such as allergen avoidance. However, such lifestyle changes and reporting biases would most likely be the same in all three areas.

The same standardized methods were used in all of the three study regions. The populations in these three regions were comparable. Regional differences remained even after controlling for many individual and indoor risk factors.

A cross-sectional study is limited in the generalizibility of its results, mostly because of the difficulty in attributing observed regional differences in health outcomes to environmental pollution alone. Although we attempted to control for a broad range of potential confounding risk factors, confounder control might still have been insufficient because we had to rely on retrospective and possibly biased information. This limits any attempt to causally interprete our results concerning pollution-related risk factors for allergy.

Overall, the observed regional differences in respiratory health and allergic sensitization may reflect the impact of long-term exposure to ambient pollutants. Because comprehensive air-pollution measurements are not available for the lifetimes of the studied children, we cannot attempt to single out any one pollutant that might be responsible for poorer respiratory health in Hettstedt or Bitterfeld. During the time of investigation (between 1992 and 1993), the levels of air pollution differed only marginally (see Table 1). Thus, the observed health differences are either attributable to past exposures that are known to have differed considerably or by unmeasured pollutants not associated with the ones measured between 1992 and 1993. The latter argument is less convincing because all major industry had been closed down in the polluted areas. A cohort study currently being conducted in the same population will allow us to follow the children included in this first survey and observe whether changes in their health status occur and to examine whether children born in times of diminished air pollution have different respiratory and health profiles. Thus, the data collected in the next phase of our study may help us to evaluate whether respiratory and allergic disorders are reversible and/or preventable via pollution reduction such as the one that took place in these East German counties due to industry shutdowns.

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