

Long-Term Effects of Ambient Air Pollution on Lung Function

A Review

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Abstract: Lung function is an important measure of respiratory health and a predictor of cardiorespiratory morbidity and mortality. Over the past 2 decades, more than 50 publications have investigated long-term effects of ambient air pollution on lung function with most finding adverse effects. Several studies have also suggested effects from traffic-related air pollution. There is strong support for air pollution effects on the development of lung function in children and adolescents. It remains unclear whether subjects with slower development of lung function compensate by prolonging the growth phase, or whether they end their development at a lower plateau, thus entering the decline phase with a reduced lung function. In adults, the evidence for long-term air pollution effects is mostly based on cross-sectional comparisons. One recent longitudinal study observed that decreasing pollution attenuated the decline of lung function in adults. Earlier inconclusive cohort studies were based on limited data. There is great diversity in study designs, markers of air pollution, approaches to the measurement of exposure, and choices in lung function measures. These limit the comparability of studies and impede quantitative summaries. New studies should use individual-level exposure assessment to clarify the role of traffic and to preclude potential community-level confounding. Further research is needed on the relevance of specific pollution sources, particularly with regard to susceptible populations and relevant exposure periods throughout life.

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Air pollution has been associated with numerous adverse health outcomes.^{1–4} There are acute effects causing respiratory symptoms, cardiovascular events, hospital admissions, and mortality. Short-term effects on lung function—mainly effects of gases such as ozone and sulfur dioxide—are well documented in animal models and human chamber studies,⁵ and in observational studies of daily air pollution levels and pollution episodes.^{6,7} Long-term exposures to air pollution have been associated with chronic bronchitis, markers of atherosclerosis, lung cancer, and mortality. In long-term studies, lung function is of interest as an objective measure of respiratory health and an early predictor of cardiorespiratory morbidity and mortality.⁸

Air pollution studies use spirometric measures obtained from forced expiration maneuvers. Forced vital capacity (FVC) measures the total volume exhaled after a maximum inspiration. Forced expiratory volume within 1 second (FEV1) is a marker of airway obstruction, measuring the maximum volume that can be exhaled within 1 second. Other commonly used measures are peak expiratory flow (PEF) and forced expiratory flow between the 25th and 75th percentile of FVC (FEF_{25–75}), also known as maximum midexpiratory flow (MMEF). Flow measures are markers of small-airway function,⁹ which is particularly sensitive to ozone exposure^{10,11} and to early exposures to tobacco smoke.^{12,13} Lung function steadily increases from birth until early adulthood, culminates in a so-called plateau phase in the mid-twenties, and thereafter decreases with age.

This review attempts to include all studies on long-term effects of air pollution on lung function published in the past 20 years. As will be shown, the diversity of the studies is substantial; this precludes a quantitative summary of the results. Instead, a descriptive summary of the studies is followed by a discussion of the most relevant aspects of their comparability and validity. The review concludes with a qualitative summary of the current knowledge and an outlook for future studies.

SEARCH METHODS

We searched the OVID MedLine and PubMed databases for papers on lung function, using the terms “lung function,” “pulmonary function,” “FEV1,” and “FVC.” The search terms

TABLE 1. Cross-Sectional Studies of Long-Term Effects of Air Pollution on Lung Function Comparing 4 or More Communities or Comparing Individuals Within Communities

Publication	Country	N	Age (yrs)	Lung Function Measures				Exposure Contrast		
				FVC, FEV1	FEV1/FVC	PEF, MMEF, FEF()	<0.7/0.8 Predicted	Among Communities (No. Communities)	Within Community	Among Individuals
Children and adolescent										
Brunekreef ¹⁴	Netherlands	877	7–12	x		x		6	13	
Dockery ¹⁵	United States	5422	10–12	x		x		6		
Fritz ¹⁶	Germany	235	3–7	x	x				x	
Frye ¹⁷	Germany	2493	11–14	x	x			t		
Galizia ¹⁸	United States	520	17–21	x		x				x
Hirsch ¹⁹	Germany	1137	9–11	x		x				x
Hogervorst ²⁰	Netherlands	429	8–13	x		x			6	
Janssen ²¹	Netherlands	1726	7–12	x			x	24	(w)	
Kuenzli ²²	United States	130	16–19	x		x				x
Nicolai ²³	Germany	904	9–11	x				(3)	x	x
Oftedal ²⁴	Norway	2307	9–10	x		x				x
Peters ²⁵	United States	3293	9–16	x		x		12		
Raizenne ²⁶	United States/ Canada	10251	8–12	x				22		
Schwartz ²⁷	United States	3922	6–24	x		x		44		
Sugiri ²⁸	Germany	2574	5–7	TL		R		13	(w)	
Tager ²⁹	United States	255	16–19	x		x				x
Wjst ³⁰	Germany	4320	9–11	x		x			x	
Adults										
Abbey ³¹	United States	1510	25+	x	x	x				x
Ackermann ³²	Switzerland	9651	18–61	x				8		
Chestnut ³³	USA	6913	25–75	x	x	x	x	49		
Kan ³⁴	United States	15792	~54	x	x					x
Schikowski ³⁵	Germany	4757	52–56	x	x		x	7		x
Schindler ³⁶	Switzerland	7656	18–60	x				8	<13	

FEF() indicates forced expiratory flow (various cutoffs); TL, total lung capacity; R, airway resistance; t, temporal exposure contrast; (w), consider within community contrasts in some way; EC, elemental carbon; H+, acidity; (c), PM10 calculated from TSP; VOC, volatile organic compounds; ROS, radical oxygen species; bz, benzene.

“air pollution,” “particulate matter” (PM), “PM_{2.5},” and “PM₁₀” (PM of aerodynamic diameter smaller than 2.5 and 10 μm, respectively), “NO₂” (nitrogen dioxide), “SO₂” (sulfur dioxide),

and “O₃” (ozone) were used to identify publications on air pollution. We selected the relevant publications manually by reviewing titles, abstracts, and reference lists.

TABLE 1. (Continued)

TSP	Air Pollutants					Other Exposures				Main Results
	PM ₁₀ , PM _{2.5}	EC, Black Smoke, Soot	NO ₂	O ₃	SO ₂	Others	Model- Based Exposures	In/Out Conc., Residential History	Traffic (Proximity, Density, etc.)	
	x	x	x						x	Effect for truck traffic on lung function; stronger effects in girls.
x	x		x	x						Null findings.
x	x		x	x	x	VOC				Lower lung function in areas with traffic-related pollution profiles.
x					x					Negative association with lung function and air pollution over time, significant for FVC.
				x						Lower lung function in male subjects from high O ₃ counties.
x	x		x	x	x	x	ROS	x		Null findings.
	x	x	x						x	Effect of ROS per PM mass, positive association for ROS per m ³ air, PM mass.
	x		x						x	Null findings for lung function, but effect on respiratory symptoms.
	x		x	x					x	Effect of O ₃ on FEF, no associations for lung volumes, PM ₁₀ .
		x	x			bz	x		x	Null findings for lung function, but associations for respiratory symptoms.
	x		x					x		Effects of early and lifetime modeled PM _{2.5} , PM ₁₀ , NO ₂ on flow measures.
	x		x	x		H+				Effect in females, stronger in subjects spending time outdoors.
	x			x			x			Effect of PM, acidity, O ₃ on FEV1, FVC, FEF.
x			x	x	x					Effect on FVC, FEV1, PEF, threshold at 100 µg/m ³ TSP.
x									x	Better lung function with lower TSP, but not for children living near traffic.
	x		x	x					x	Effect for O ₃ on FEF among subjects with low FEF ₂₅₋₇₅ /FVC.
									x	Effect between FEF and car counts.
	x			x	x	x			x	Effect for SO ₄ in men, PM ₁₀ , O ₃ , in men with parental history of respiratory disorder.
x	x		x	x	x					Effect on FVC (all pollutants), FEV1 (SO ₂ , NO ₂ , O ₃).
x										Effect on FVC, FEV1, threshold at 60 µg/m ³ TSP.
	x		x	x					x	Effect and trend of traffic on FEV1, FVC in women, not significant in men.
x	(c)		x						x	Effect on FEV1, FVC, FEV1/FVC, COPD of PM10(TSP), near major road.
			x							Effect on lung function of NO ₂ within and across centers.

RESULTS

Overall, we reviewed 58 publications. Forty-one were cross-sectional and 17 were longitudinal. A total of 37 studies

investigated children. Air pollution measurements were predominantly made at the community level, using centrally located monitors that usually sampled several pollutants. We

TABLE 2. Longitudinal Studies of Long-Term Effects of Air Pollution on Lung Function Comparing 4 or More Communities or Comparing Individuals Within Communities

Publication	Country	No. Individuals	Age (yrs)	Lung Function Measures			No. Measurements	Years of Follow-Up	Exposure Contrast		
				FVC, FEV1	PEF, MMEF, <0.7;0.8 Predicted	FEF0			Among Communities (No. Communities)	Within Community	Among Individuals
Children and adolescents											
Avol ³⁷	United States	110	10–15	x	x		2+	5			x
Gauderman ^{38–40}	United States	1759	10–18	x	x	x	8	8	12		
Gauderman ⁴¹	United States	3677	10–18	x	x	x	8	8	12	x	
Horak ⁴²	Austria	975	6–9	x	x		6	3	8		
Ihorst ⁴³	Austria	2153	6–10	x			7	3.5	15;3		
Kopp ⁴⁴	Austria	797	6–9	x	x		4	2	10;3		
Neuberger ⁴⁵	Austria	3451	ES	x	x		2–8	5		(2)	
Rojas-Martinez ⁴⁶	Mexico	3170	8–12	x	x			3		10	
Adults											
Downs ⁴⁷	Switzerland	8047	18–60	x	x		2	11	(8)		x
Goss ⁴⁸	United States	11484	6~40	x			8	2			x
Nakai ⁴⁹	Japan	444	30–59	x			10	2.5	2	2	
Sekine ⁵⁰	Japan	406	30–59	x			8	8		3	

ES indicates elementary school children; 15;3, 10;3, communities divided into 3 exposure categories; (8), individual level analysis with community random effects; (x), not used in analysis.

provide results for multiple pollutants where those may be surrogates for different types of air pollution.

Studies comparing lung function across only 2 or 3 communities were not included. Spatial comparisons across so few exposure clusters are susceptible to distortions because of errors in exposure measurements and confounding by community-level factors. Information on studies with more than 3 communities or that are based on individually assigned exposure can be found in Tables 1 and 2, for cross-sectional and longitudinal studies, respectively. Tables listing studies of fewer communities can be found in the online version of this article (eTables 1 and 2). Main findings from studies in children and adolescents, in adults, and on traffic are also shown in Figures 1 to 3.

Cross-Sectional Studies in Children and Adolescents

Oftedal et al²⁴ modeled residential outdoor air pollution over the lifetimes of 2307 9- and 10-year-old children who had lived in Oslo, Norway since birth. The dispersion model took into account emissions, meteorology, topography, and

background air pollution concentrations. Complete residential history for each subject was available from the Norwegian Population Register. Early and lifetime exposures to PM_{2.5}, PM₁₀, and NO₂ were associated with reduced forced expiratory flows (especially in girls), but not with forced expiratory volumes.

The University of California Berkeley Ozone Studies^{22,29} investigated 2 convenience samples of 130 and 255 college freshmen aged 17 to 21. “Effective lifetime exposure” was assessed by combining central monitor data, residential history, and information on time-activity from questionnaires and population-based surveys. The pilot study by Kunzli et al²² observed significant negative effects for O₃ on flow measures, but not on FEV1 or FVC. PM₁₀ and NO₂ had no effects on lung function. The main study by Tager et al²⁹ found significant negative associations between flows and O₃ in subjects with a low ratio of FEF_{25–75}/FVC, a marker of narrower small airways. In a similarly designed study, Galizia and Kinney¹⁸ observed significantly lower lung function among male Yale freshmen who grew up in counties with

TABLE 2. (Continued)

TSP	Air Pollutants						Other Exposures		Main Results
	PM ₁₀ , PM _{2.5}	EC, Black Smoke, Soot	NO ₂	O ₃	SO ₂	Others	Residential History	Traffic (Proximity, Density, etc.)	
	x		x	x			x		Lung function growth lowered by moving to high pollution area, up when moved to low air pollution area
	x	x	x	x		H+			Reduced lung function growth in children from higher polluted communities
	x	x	x	x				x	Lung function growth independently associated with freeway distance and regional pollution
	x		x	x	x				Reduced lung function growth in summer in children from higher polluted communities
x	x		x	x					O ₃ decreased lung function growth in summer, opposite pattern in winter
	(x)		(x)	x					O ₃ decreased lung function growth in summer, opposite pattern in winter
x			x	x	x				Faster growth in MMEF in districts with declining NO ₂
	x		x	x	x				Reduced lung function growth in children from areas with higher PM ₁₀ , NO ₂ , O ₃
	x						x		Association of decrease in modeled home outdoors PM ₁₀ and lung function decline
	x		x	x	x				Pulmonary exacerbation associated with PM, O ₃ ; FEV1 decline associated with PM _{2.5}
x			x					x	No significant differences in lung function level or change between 3 exposure zones, incl. one in proximity to traffic
	x		x					x	Indication of faster lung function decline in proximity to traffic

high long-term O₃ levels, as compared with those who grew up in low ozone counties. No differences were observed in women.

Several studies investigated traffic-related exposure contrasts within communities. Nicolai et al²³ used a model based on traffic counts within 50 m of residence and stop-and-go traffic characteristics to predict exposure for 2019 children aged 9 to 11. They found no associations between traffic and lung function (spirometric measures not specified), despite significant adverse effects on respiratory symptoms. In contrast, Wjst et al³⁰ showed significant associations between traffic density in school districts and measures of expiratory flow in 4320 children aged 9 to 11 years. Hirsch et al¹⁹ used extensive measurements of SO₂, NO₂, CO, benzene, and O₃ on a 1-km grid and estimated residential exposure of 1256 9- to 11-year-old children. They found associations with respiratory symptoms, but none with lung function. Fritz and Herbarth¹⁶ reported on a descriptive study of lung function among 5-year-old preschoolers. The effect of air pollution resulting from traffic was stronger than that from pollution from heating with coal, but the exposure assignment was

crude. Brunekreef et al¹⁴ studied 877 schoolchildren who lived within 1000 m of motorways in 6 areas of the Netherlands. They found negative effects of truck traffic density on various lung function indicators (FEV1, PEF, FEF₂₅₋₇₅) ranging between 2.5% and 8% per 10,000 trucks. Black smoke, NO₂, and car traffic density tended to have negative effects as well. In a second study of the same design that included 24 schools, the Dutch group could not reproduce the earlier findings on lung function, although associations between symptoms and traffic indicators prevailed.²¹

In a novel approach, Hogervorst et al²⁰ used oxygen-radical formation by particles as a marker for their potential to cause oxidative stress.⁵¹ They studied children from 6 schools located at varying distances from traffic. Long-term exposure estimates were based on measurements on 4 days only. They found some significant negative effects of radical formation per particle mass, but less so for radical formation per volume of air; unexpectedly, particle mass itself showed statistically significant positive associations with both FEV1 and FVC.

Two papers reported on repeated cross-sectional assessments after the German reunification. This was a period of

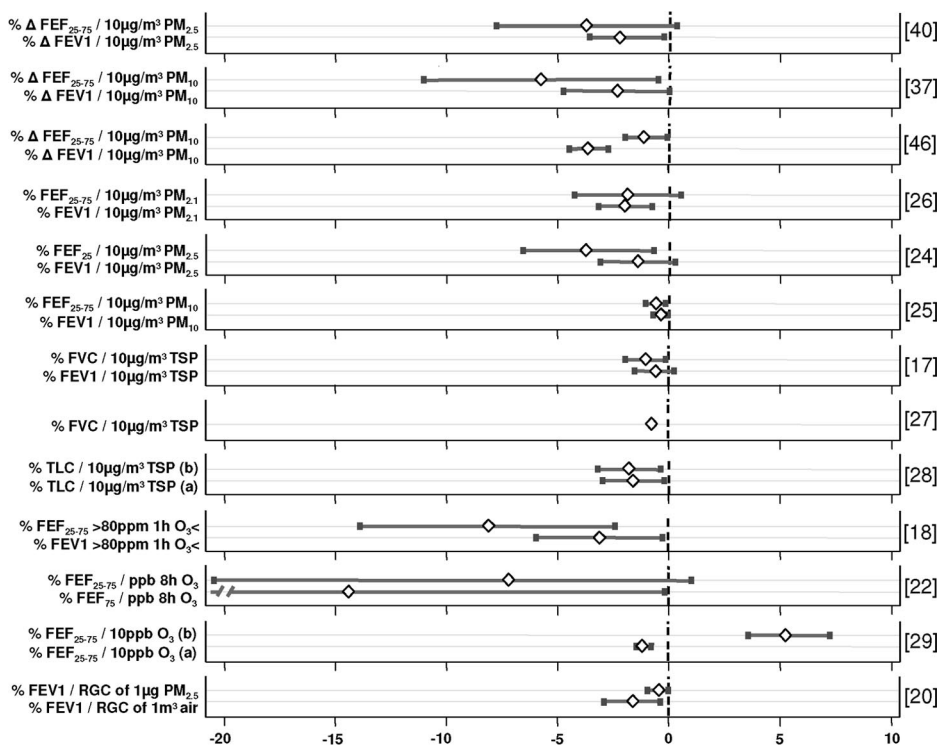


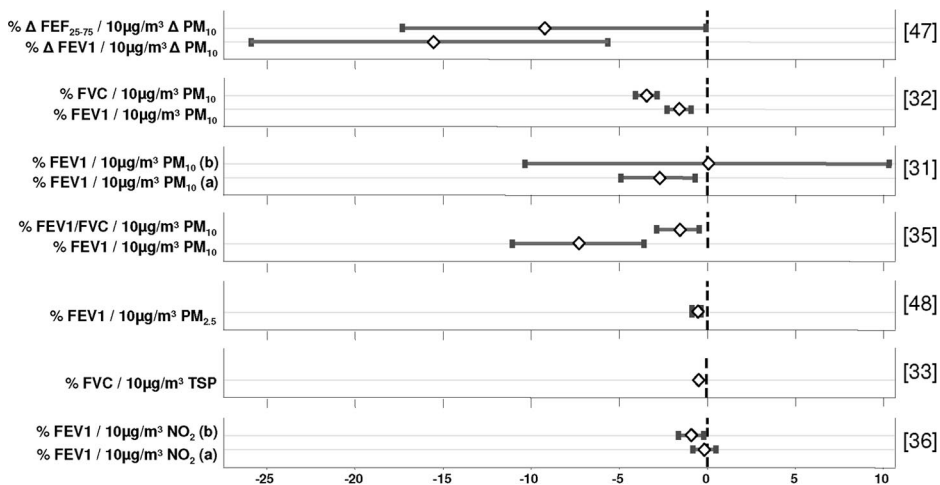
FIGURE 1. Effect estimates from studies of long-term effects of air pollution on lung function in children. For Gauderman et al,⁴⁰ percent effect estimates averaged over boys and girls, based on common linear effect estimate. For Rojas-Martinez et al,⁴⁶ effect estimates for girls (similar findings for boys). For Schwartz,²⁷ nonlinear effect, displayed above threshold of 100 μg/m³ TSP. Effect size estimated from graph. Confidence interval not available. Sugiri et al,²⁸: (a) East German sample; (b) West German sample. Galizia and Kinney,¹⁸ adj. mean difference between high exposure (4+ years in counties with 10 years 1hO₃ summer average >80 ppm) and low exposure. Kunzli et al,²² upper limit of confidence interval for FEF₇₅ cropped; actual value 28.3%. Tager et al,²⁹ (a) estimates for boys at (a) 25th percentile of FEF₂₅₋₇₅ and (b) 75th percentile of FEF₂₅₋₇₅. Hogervorst et al,²⁰ RGC indicates radical-generating capacity of PM_{2.5}. For Figures 1 to 3, diamonds indicate effect estimates and horizontal lines indicate confidence intervals. All studies of 4 or more centers or based on within-community exposure contrasts were considered for inclusion. Effect estimates were selected based on their relevance for the study; where feasible, a measure of lung volume (preferably FEV1) and a measure of flow (preferably midexpiratory flow, FEF₂₅₋₇₅) are provided. Where necessary, reported effect estimates have been converted to percent estimates, based on the sample mean. Units and interpretation of effect estimates are not directly comparable across studies and are shown here only for the purpose of qualitative comparisons. Dashed lines indicate null effect. For exact interpretation of effect estimates, refer to the text or original publications. The following studies could not be included in the graphs: Dockery et al,¹⁵ Nicolai et al²³ (no effect estimates reported, null findings), Hirsch et al,¹⁹ Neuberger et al⁴⁵ (effect estimates not quantified), Janssen et al²¹ (reported odds ratios for lung function smaller than 85% predicted, not statistically different from 1), Ihorst et al⁴³ (reported seasonal effects, but not estimates for long term null findings), and Sekine et al⁵³ (reported change in FEV1 was -20 mL/y in proximity to traffic and -9 mL/y away from traffic based on highly varying year-to-year trends).

dramatic change, not only in air pollution levels but in many aspects of life as well. Sugiri et al²⁸ observed an improvement in lung function with decreasing levels of total suspended particles (TSP) and SO₂ among 2574 east German 6-year-old children, catching up with their western counterparts by the time of the third survey, 8 years after the reunification. The improvement was weaker in children living within 50 m of a busy street—a finding that was attributed to the 50% to 75% increase in motor vehicles during this period in eastern Germany. Frye et al¹⁷ reported improvements of FEV1 and FVC over 3 consecutive cross-sectional surveys (1992–1997) of 2493 11- to 14-year-old children in 3 east German com-

munities. FVC increased by 4.7% for a 50-μg/m³ decrease of TSP and 4.9% for a 100-μg/m³ decrease of SO₂, whereas effects for FEV1 were smaller.

Schwartz²⁷ found highly significant associations of TSP, NO₂, and O₃ with lung function in a large cross-sectional study that included 4300 6- to 24-year-old subjects from 44 US cities (TSP 10%–90%: 43–95 μg/m³). The National Health and Nutrition Examination Survey (NHANES) is the only study that suggested threshold effects, namely at 100 μg/m³ TSP, 0.04 ppm O₃, and less clearly at 0.04 ppm NO₂. Most of the communities above the threshold were in California.

FIGURE 2. Effect estimates from studies of long-term effects of air pollution on lung function in adults. For Abbey et al,³¹ (a) PM₁₀ effect in men with parental history of asthma, bronchitis, emphysema, or hay fever. Main effect of such history = +1.6%. (b) PM₁₀ effect in men without such history. Goss et al,⁴⁸ in cystic fibrosis patients. Chestnut et al,³³ nonlinear effect, displayed at mean pollution level (87 μg/m³ TSP). Confidence interval not available. Schindler et al,³⁶ (a) home outdoor NO₂ averaged over zones of residence within communities; (b) home outdoor NO₂ averaged over communities.



In a comparison across 24 American and Canadian cities, Raizenne et al²⁶ found significant associations between air pollution levels (O₃, NO₂, PM) and lung function (FEV1, FVC, FEV0.75, FEF₂₅₋₇₅, PEFR, <85%) in 10,251 8- to 12-year-old children. The observed effects were strongest and most consistent for particle acidity, a marker of very small particles.

Peters et al²⁵ reported significant associations between various air pollutants (PM₁₀, PM_{2.5}, acid vapor, NO₂, O₃) and several measures of lung function (FVC, FEV1, MMEF, PEF) in the cross-sectional baseline investigation of the Southern Californian Children’s Health Study (CHS) across 12 communities. Cross-sectional correlations were predominantly observed among girls of this cohort of 3293 children (age 9–16), and were more pronounced in subjects who spent more time outdoors. (Results from the follow-up analysis are described below, under longitudinal studies.^{37–41})

In the Harvard 6-Cities Study, one of the early air pollution studies, Dockery et al¹⁵ did not find significant associations between air pollution and lung function mea-

asures in a cross-sectional cross-community comparison of preadolescent children enrolled in 1974–1979. They investigated a sample of 5422 10- to 12-year-old children across 6 cities using FEV1, FVC, and flow measures (MMEF) and various particle measures (TSP, PM₁₅; PM_{2.5}, range: 12–37 μg/m³). Their null findings are consistent with a previous analysis of lung function from the same study, whereas investigations of respiratory symptoms did reveal significant associations with air pollution.¹⁵

Cross-Sectional Studies in Adults

Abbey et al³¹ provide a cross-sectional analysis of adults enrolled in a large cohort study in 1977 (Adventist Health Study of Smog). Participants were tested for lung function in 1993. Life time exposure to PM₁₀, O₃, SO₄, and SO₂ was calculated based on subjects’ residential history back to 1973. Significant negative effects on FEV1 were found only after using a particular exposure metric—the number of days with PM₁₀ exceeding 100 μg/m³—and then only in men with a parental history of obstructive airway disease.

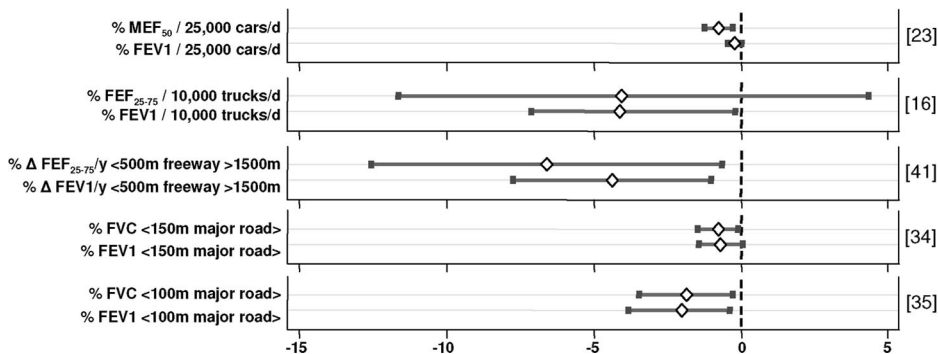


FIGURE 3. Effect estimates from studies of long-term effects of traffic on lung function. Wjst et al,³⁰ traffic density per school district. Brunekreef et al,¹⁴ among children living within 300 m of a motorway. Gauderman et al,⁴¹ percent effect estimates averaged over boys and girls, based on common linear effect estimate. Kan et al,³⁴ associations in women only. Similar findings with quartiles of traffic density. MEF₅₀ indicates maximum expiratory flow at 50% FVC.

Women in the Atherosclerosis Risk in Communities (ARIC) study had significantly decreased FEV1 and FVC with increased density of and proximity to traffic. No effects were observed in men. Although this study did conduct follow-up measurements 3 years after the baseline examination, the follow-up period was considered too short to detect effects on lung function change. Cross-sectional analyses of the follow-up data provided results similar to the baseline analysis.

Chestnut et al³³ reported significant associations between TSP and lung function in the adult sample (25–75-year-old, $n = 6913$) of the NHANES I survey. The association was nonlinear, suggesting a threshold at $60 \mu\text{g}/\text{m}^3$ TSP, similar to the findings for the younger participants of the study.²⁷

The Swiss Study on Air Pollution and Lung Disease in Adults (SAPALDIA)³² found significant associations between air pollution (PM_{10} , NO_2 , SO_2 , O_3) and FVC and FEV1 in 9651 subjects across 8 study communities. The predicted effect of $10\text{-}\mu\text{g}/\text{m}^3$ increase in annual mean concentration of PM_{10} was a 3.4% decrease in FVC and a 1.6% decrease in FEV1. Schindler et al³⁶ used a SAPALDIA subsample ($n = 560$) with NO_2 measured at home outdoors. The within-community comparison revealed consistently negative, despite statistically nonsignificant associations between home outdoor NO_2 and lung function.

In the German study on the Influence of Air Pollution on Lung Function, Inflammation, and Aging (SALIA), Schikowski et al³⁵ included proximity to the nearest busy road ($>10,000$ vehicles/d) in a cross-community analysis that was otherwise based on central monitors. They found an increased risk for COPD ($\text{FEV1}/\text{FVC} < 0.7$) among women in their mid-fifties living closer than 100 m to a busy road ($\text{OR} = 1.33$ [95% CI 1.03–1.72]). FEV1 and FVC were also lower in proximity to the nearest road (-1.3% and -1.7% , respectively). Their analysis across 7 communities showed significant negative associations of NO_2 and PM_{10} (calculated from TSP) with FEV1, FVC, and FEV1/FVC ratio (-4.7% , -3.4% , and -1.1% per $10\text{-}\mu\text{g}$ PM_{10} , respectively).

Goss et al⁴⁸ observed significant negative associations of $\text{PM}_{2.5}$ and PM_{10} with FEV1 in a cross-sectional analysis of longitudinal data from cystic fibrosis patients.

Longitudinal Studies in Children and Adolescents

In the CHS, Gauderman et al^{38–40} followed up 1759 children aged 10 to 18 in 12 communities ($n = 747$ at last follow-up). Over 8 years, children living in the most polluted community had a growth deficit in FEV1 of approximately 100 mL ($\sim 7\%$ for girls, $\sim 4\%$ for boys), as compared with those living in the cleanest community (exposure range 4–38-ppb NO_2 , findings were similar for black carbon, PM, and acid vapor, whereas there was no association with O_3). The proportion of children with clinically low lung function at age 18 ($\text{FEV1} < 80\%$) was estimated to be 5 times larger in the most polluted community compared with the cleanest com-

munity ($29 \mu\text{g}/\text{m}^3$ vs. $6 \mu\text{g}/\text{m}^3$ $\text{PM}_{2.5}$). In an analysis of a subsample of 110 children from the same study who moved away after their initial examination, Avol et al³⁷ observed an improvement in lung function growth among those who moved to areas with lower PM_{10} , and slower lung function growth in those who moved to more polluted areas. In a more recent analysis, Gauderman et al⁴¹ found that children living within 500 m of a freeway had significant deficits in 8-year growth of FEV1 (-81 mL) and MMEF (-127 mL/s), compared with children living at least 1500 m from a freeway, independent of the effects of background pollution.

Rojas-Martinez et al⁴⁶ followed up schoolchildren from 10 schools in Mexico City over 3 years. PM_{10} , NO_2 , and O_3 levels were based on monitors in close proximity (< 2 km) to the children's schools. All 3 pollutants were associated with significant deficits in lung function growth. Effects for annual growth in FEV1 per interquartile range of exposure ranged from -16 mL for O_3 in boys to -32 mL for NO_2 in girls, with estimates for FVC and FEF_{25-75} , and estimates from multipollutant models showing effects of similar magnitude.

In a series of publications on lung function growth in Austrian schoolchildren, Ihorst et al,⁴³ Horak et al,⁴² Kopp et al,⁴⁴ and Frischer et al,⁵² reported on seasonal and long-term effects of O_3 and PM_{10} . Negative effects of O_3 and to a lesser degree for PM_{10} during summer were compensated for during the winter seasons. Over the study period of 3.5 years, they did not detect deficits in lung growth among children in more highly polluted areas.

In a smaller Austrian cohort study of 200 children drawn from a larger cross-sectional sample, Neuberger et al⁴⁵ attributed small improvements of lung function to the decrease in NO_2 levels over 5 years.

Longitudinal Studies in Adults

Researchers with the SAPALDIA study recently reported results after 11 years of follow-up.⁴⁷ PM_{10} concentrations were modeled for each residence for the entire follow-up period. On average, pollution decreased during follow-up. Improvements in air quality were associated with attenuated declines of FEV1, FEV1/FVC, and FEF_{25-75} . After adjustment for PM_{10} at baseline, a reduction of $10 \mu\text{g}/\text{m}^3$ PM_{10} over 11 years of follow-up slowed the decline in FEV1 by 9%. This is so far the only study investigating the effect of changes in air pollution on lung function.

Sekine et al⁵³ provided a cohort study in Tokyo women that categorized exposure based on traffic proximity, NO_2 , and particle measurements. Cross-sectional annual means of lung function for 3 exposure groups varied considerably over the 8 study years, with somewhat stronger declines in FEV1 for women in the higher exposure groups.

Nakai et al⁴⁹ compared lung function measurements of 444 30- to 59-year-old women who lived in 3 different zones of Tokyo, 2 of which were defined by their proximity to a busy road. Women had up to 10 spirometric tests over a

period of 2 1/2 years. The sparse presentation of data precludes a detailed assessment, but authors reported no differences in lung function level or decline across the 3 exposure groups.

DISCUSSION

Most (50 of 58) of the reviewed publications reported some statistically significant adverse effects of air pollution on lung function. The first and biologically most relevant pattern emerges from the analyses of the CHS. This study found reduced lung growth in children exposed to higher levels of air pollution, both regionally^{38–40} and in proximity to traffic.⁴¹ The study further showed that an “exposure intervention,” such as moving to a community with different pollution levels, modifies the lung growth pattern. This suggests that improvements in air quality may allow children’s lungs to recover from previously experienced adverse effects.³⁷ The main findings from the CHS have recently been confirmed by a study in Mexico City.⁴⁶

A second pattern shows that lung function levels in adults correlate with air pollution exposure, as findings from larger studies such as NHANES,³³ SAPALDIA,³² and SALIA³⁵ suggest. SAPALDIA also associated air pollution with lung function decline, suggesting that cross-sectional differences in adults are due not only to growth deficits obtained during childhood or adolescence but also to acceleration of lung aging by air pollution. However, the SAPALDIA findings on lung function decline need to be confirmed.

Apart from these general patterns, comparisons across studies are difficult, and we refrain from providing quantitative summary measures. Where present, differences between exposed and unexposed groups are mostly within the range of a few percent. The magnitude of effects seems plausible and similar to that reported for environmental tobacco smoke exposures,^{54–56} whereas active smoking results in stronger effects on lung function.⁵⁷ Studies in children and adults need to be distinguished because the nature of air pollution effects on lung function growth, levels, or decline may differ. The same may be said for cross-sectional and longitudinal designs. Further, several methodological and design-related aspects limit a quantitative summary of the reported effects; studies vary on lung function and pollution measures, units of effect measures, exposure categorization, subgroup analyses, and on adjustment for potential confounders. We discuss below those aspects of most relevance for the interpretation of the reviewed studies.

Variations in Exposure Assessment

There are notable differences in exposure assessment. Methods include community-level (ecological) exposure assignment, various more powerful approaches to assign exposure individually,^{18,22,24,31,36,47} and the use of traffic as a specific source of pollution.^{14,35,41,58}

Community-level exposures have been applied by most studies. Central monitors allow continuous measurements of multiple pollutants. However, despite suggestive results from some studies,^{22,26,40} identifying specific causal agents among the pollutants remains difficult because of correlations among long-term concentrations of many measured (and unmeasured) pollutants.

Several studies used individual-level exposure assignment.^{18,22,23,29,31,35–37,41} Actual measurements of individual exposure to pollutants was only done by 1 study.³⁶ A few studies combined pollution data from central site monitors with individuals’ mobility or residential history.³¹

Several studies considered traffic, without measuring actual pollutants.^{21,23,30,34,53} The overall picture seems somewhat less clear for the few lung function studies than for respiratory symptoms and other outcomes.^{21,23,59–65} Recently, however, the findings of the Children’s Health Study,⁴¹ SALIA,³⁵ and ARIC³⁴ strongly suggest that proximity to traffic reduces lung function in children and adults.

Specificity of Lung Function Parameters

All of the major air pollution studies comply with the guidelines of the American Thoracic Society⁶⁶ or the European Respiratory Society.⁶⁷ Most of the reviewed studies either measured lung volumes alone (FEV1, FVC) or measured both volume and flow measures finding consistent effects on the two. Only a few studies, all of children or adolescents, observed associations for flow measures but not for volumes.^{22,24,29,30,45} These findings suggest stronger or earlier effects of air pollution on smaller airways, which presumably receive the highest tissue doses,^{11,68} and would therefore undergo preclinical structural changes before the larger airways (and thus FEV1 or FVC) are affected. However, these studies do not provide enough evidence to relate effects of air pollution conclusively to one or the other specific spirometric measure.

Confounding

Most studies adjusted for common confounders on the individual level, such as age, height, and smoking. The effects of such adjustments on the main results, however, are rarely discussed.^{15,32,40} A formal assessment of community-level confounding is impossible, as most of the larger multicity studies rely on community-level factors to be distributed randomly across communities, without quantitatively verifying this assumption. A few use hierarchical regression models to adjust for contextual confounders,^{24,38–40} or they control community-level confounding through assignment of exposure on an individual or within-community basis. Nonetheless, full control of socioeconomic and other contextual factors remains challenging in within-city comparisons of proximity to traffic.^{69,70}

Effect Modifiers

Several studies report stronger effects for various subgroups, such as women,^{24,25,34,71} men,^{18,31,72–74} or subjects with smaller airways²⁹ or a family history of respiratory diseases.³¹ However, these findings are not consistent. Several studies stratified their samples by smoking status, with no differences in air pollution effects between smokers and nonsmokers.^{23,26,32,33,35,47} Some studies did not include smokers to avoid confounding.^{29,31} No study investigated interaction of the effects of air pollution with genetic factors or prescription drug use. The latter may be of particular relevance among older adults. Effects of smoking on lung function can be modified by genetic polymorphisms⁷⁵ and by anti-inflammatory treatments, mainly statins.⁷⁶ Stratified analyses have also been used to exclude the possibility of (residual) confounding and to reduce random misclassification by limiting analyses to subjects (such as long-term residents) with more precise exposure estimates.^{26,32,35,77}

Selection and Measurement Bias

Subjects in air pollution studies are generally unaware of their precise level of exposure, and lung function is an objective end point; thus bias because of selective participation may be of limited concern.⁷⁸ Some cross-community studies may be more susceptible to misclassification of community estimates than others, both for exposure and outcome. For example, the timing of spirometry,^{21,71} the need for extrapolation of exposure data for selected communities,³⁵ or the location of central monitors may lead to biased community estimates, and thereby to biased overall health effect estimates. The larger the number of communities, the lower the likelihood for such biases. Although occurrence of non-random misclassification cannot be excluded entirely, it is unlikely to explain the overall evidence across all studies.

Publication Bias

The heterogeneity across studies precludes a formal assessment of publication bias using funnel plots or other techniques. The strongest evidence for long-term effects of air pollution on lung function is provided by a few large studies specifically designed to investigate effects of air pollution on lung function. Publication bias is unlikely among these studies.

Nonetheless it is noteworthy that many of the reported significant findings are small effects and are often singled out from several nonsignificant analyses of various pollutants or outcomes. One would therefore expect some studies to observe no significant associations at all. One indication of selective publication is that, among the 8 studies that reported no significant associations between air pollution and lung function, 4 reported significant associations for other outcomes within the same publication.^{19,21,23,79} In addition, 2 publications^{15,77} are from the large 6-cities study that reported important results for other outcomes (ie, mortality).⁸⁰

Exclusively null findings are provided only by Devereux et al⁸¹ in a small qualitative comparison across 2 regions in England, and by Nakai et al⁴⁹ in a relatively basic longitudinal analysis. It must therefore be assumed that publication bias is likely to be present among the smaller studies (eTables 1 and 2).

CONCLUSIONS

Because of the diversity of the reviewed studies, formal quantitative comparisons of their findings are difficult and the magnitude of the effect of air pollution on lung function cannot be generalized. Support is strong for concluding that there are adverse long-term effects of air pollution on lung function growth in children, resulting in deficits of lung function at the end of adolescence. No study has, however, followed up adolescents until they reached the plateau phase of early adulthood. It therefore is not known whether growth deficits will be compensated by a prolonged growth phase, or whether these subjects will enter the lung-function decline phase of later adulthood with a reduced lung function.

In adults, the strongest evidence for adverse long-term effects of air pollution on lung function comes from cross-sectional investigations. Although these cross-sectional associations may reflect growth deficits experienced during childhood, the only sufficiently large long-term follow-up study among adults indicates a role of air pollution in accelerating lung function decline.

Based on the published literature it can be concluded that, although many studies suggest adverse effects of long-term exposure to air pollution on lung function, important questions regarding the most relevant age period and exposure windows remain unresolved. Moreover, the role of specific pollutants or pollution sources needs to be clarified. Findings of several recent studies emphasize the importance of traffic-related air pollution. Endogenous or exogenous susceptibility factors modifying adverse effects of air pollution on lung function are barely understood and need further investigation. Future studies should implement state-of-the-art exposure assessment technologies aiming at individual level exposures to capture relevant exposures and limit confounding simultaneously.

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