



Low levels of air pollution induce changes of lung function in a panel of schoolchildren

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ABSTRACT: In search of sensitive screening parameters for assessing acute effects of ambient air pollutants in young schoolchildren, the impact of 8-h average air pollution before lung function testing was investigated by oscillatory measurements of resistance and spirometry with flow-volume loops.

At a central elementary school in Linz, the capital of Upper Austria, 163 children aged 7–10 yrs underwent repeated examinations at the same time of day during 1 school year, yielding a total of 11–12 lung function tests per child. Associations to mass concentrations of particulate matter and nitrogen dioxide (NO₂) measured continuously at a nearby monitoring station were tested, applying the Generalised Estimating Equations model.

Reductions per 10 µg·m⁻³ (both for particles and for NO₂) were in the magnitude of 1% for most lung function parameters. The most sensitive indicator for acute effects of combustion-related pollutants was a change in maximal expiratory flow in small airways. NO₂ at concentrations below current standards reduced (in the multipollutant model) the forced expiratory volume in one second by 1.01%, maximal instantaneous forced flow when 50% of the forced vital capacity remains to be exhaled (MEF_{50%}) by 1.99% and MEF_{25%} by 1.96%. Peripheral resistance increased by 1.03% per 10 µg·m⁻³ of particulate matter with a 50% cut-off aerodynamic diameter of 2.5 µm (PM_{2.5}). Resistance is less influenced by the child's cooperation and should be utilised more often in environmental epidemiology when screening for early signs of small airway dysfunction from urban air pollution, but cannot replace the measurement of MEF_{50%} and MEF_{25%}. In the basic model, the reduction of these parameters per 10 µg·m⁻³ was highest for NO₂, followed by PM₁, PM_{2.5} and PM₁₀, while exposure to coarse dust (PM₁₀–PM_{2.5}) did not change end-expiratory flow significantly.

All acute effects of urban air pollution found on the lung function of healthy pupils were evident at levels below current European limit values for nitrogen dioxide. Thus, planned reduction of nitrogen dioxide emission (Euro 5; vehicles that comply with the emission limits as defined in Directive 99/96/EC) of 20% in 2010 would seem to be insufficient.

KEYWORDS: Lung function, nitrogen dioxide, particulate matter, resistance, schoolchildren

Suspended particles have recently received much interest because of increasing epidemiological and experimental evidence of their health impact. Notwithstanding the fact that the exact biological mechanisms are not entirely clear, both mass and number of very fine particles have been shown to correlate with acute health effects and measurable functional changes in the cardiovascular and respiratory system [1–4]. Numerous panel studies investigating short-term changes in lung function in children have been performed. Meta-analyses indicated adverse effects of ozone [5] and particulate matter [6] on lung function. However, most have focused on daily mean levels of air pollution [7] and, if investigating effect on lung function at all, have

concentrated on parameters such as peak expiratory flow (PEF) that are easily collected in children.

Fine particles of different origin and chemical composition are supposed to differ in their health impact. Nitrogen dioxide (NO₂) serves as an indicator of a whole range of pollutants (including very fine particles) originating from incineration sources. Previous studies [8] on the total population of schoolchildren from Linz, the capital of Upper Austria, have shown the good predictive value of NO₂ especially for maximal instantaneous forced flow when 50% of the forced vital capacity remains to be exhaled (MEF_{50%}) and MEF_{50%} in children's lung function testing.

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The present authors had the opportunity to monitor various measures of particulate matter over the course of a joint Austrian project (Austrian Project on Health Effects of Particulates (AUPHEP)) [9] in the school year 2000–2001 at the central air monitoring site in Linz, Upper Austria. In this town of 200,000 inhabitants, with steel industry and heavy motor traffic, chronic respiratory health effects on children have been found [8] and improvements in lung function were related to improvements in air quality [10]. Current levels of particulate matter with a 50% cut-off aerodynamic diameter of 10 μm (PM₁₀) and NO₂ are in a range typical for Middle European urban areas. It was hypothesised that acute respiratory effects could still be observed on days with elevated concentrations. Therefore, the present authors chose the elementary school next to the AUPHEP monitoring station for repeated lung function testing throughout the school year. The aim of this time series study was to quantify short-term effects of air pollutants on lung functions measured by spirometry and forced oscillation technique. It was expected that peak levels of air pollution shortly before lung function testing would have the strongest impact [11, 12]. Although respirable particulate air pollution in general is known to affect lung function, previous findings [10] indicate that particulate matter from combustion (for which NO₂ is a good proxy) is of prime importance.

This study had the following three aims. 1) To investigate short-term effects of air pollution on lung function (by choosing 8-h mean values instead of daily mean values for this panel study). 2) To find lung function parameters that are both sensitive to the acute impact of air pollution and suitable for screening of young schoolchildren. 3) To study these associations in an environmental setting that is typical for the current air pollution situation in many European towns.

MATERIAL AND METHODS

Air monitoring

The air of the city of Linz (located north of the Alps on the river Danube) is predominantly affected by industrial emissions (steel plant) and motor traffic (a high proportion of diesel trucks and cars) which can lead to a build up of elevated concentrations during stagnant conditions. The monitoring site, situated within a central living area, was operated between September 2000 and August 2001. The PM concentration at this site reflects the typical PM-burden in urban Linz and lies within the upper third of nine monitoring sites in and around the city. Details of the air monitoring project have been described by HAUCK *et al.* [9]. For this study, the half-hour mean values of PM₁, PM_{2.5}, PM₁₀ (measured by Tapered Element Oscillating Microbalance) and NO₂ (measured by chemoluminescence) were chosen to calculate the 8-h mean values between 00:00 h and 08:00 h on all days before lung function testing was conducted.

Lung function

At the school adjacent to the monitoring station, every second day (on Monday, Tuesday, Wednesday and Friday) ~20 of 164 children (aged 7–10 yrs) underwent lung function tests, so that each of the 69 female and 95 male children had spirometry approximately every fortnight at around the same time of day from September to May. Forced vital capacity (FVC), forced

expiratory volume in one second (FEV₁), FEV_{0.5}, mean forced expiratory flow at 25% (FEF_{25%}), FEF_{50%}, FEF_{75%} and PEF were obtained following the protocol of the American Thoracic Society [13], except for the minimum exhalation time of 6 s, which is not feasible for children. The lung function tests were conducted between 08:30 h and 10:30 h in a fixed sequence.

Before performing routine spirometry (in the standing position), the respiratory resistance was measured (in the sitting position) using the impulse oscillation system (IOS; Erich Jaeger, Hoechberg, Germany). IOS was applied according to the producer's specifications and the resistance at oscillation frequencies between 4 and 30 Hz were registered [14]. To collapse these 27 data points per examination into one meaningful number, the calculated hypothetical resistance at frequency=0 ($R(0,c)$) was calculated as the point where a line cut the ordinate, serving as a proxy for peripheral airway resistance [15]. This line was calculated by linear regression from all data points between the frequency of 4 and the frequency with the lowest resistance.

It was planned to test each child 11–12 times. Each child was assigned to a fixed day of the week to minimise bias from weekly cycles; however, due to holidays, sick leave or other organisational problems, most of the children on 1–3 occasions had to be tested on another day of the week. Due to longer sick leave, one child could only be tested 10 times. Two children who changed school during the school year could only be tested three and six times, respectively.

Statistical analysis

Lung function values were log-transformed because multiplicative effects were expected. Sex and the logs of age, height and weight were also entered into the models as explanatory variables. The health impact of air pollution was studied applying the Generalised Estimating Equations model assuming an auto-correlation structure with lag 1. In order to visualise the association between air pollutants and lung function, the same model was calculated without air pollution data and the residuals (of the logs of the lung function parameters) were plotted against the pollutant's concentration.

RESULTS

The 8-h mean values from 00:00–08:00 h included both the low concentrations of the night and the high concentrations of morning rush hour. Thus, on average, the 8-h mean levels were comparable to the daily mean levels (table 1). Annual average concentrations were mostly within current European Union (EU) and US limit values. Only PM_{2.5} exceeded the US limit value of 15 $\mu\text{g}\cdot\text{m}^{-3}$ for the annual mean, but not the cap of 25 $\mu\text{g}\cdot\text{m}^{-3}$ proposed by the European Commission in its Thematic Strategy on Air Pollution, 2005 [16]. (There is no legal limit value for PM_{2.5} in Europe yet.) The European PM₁₀ limit value for the daily average (50 $\mu\text{g}\cdot\text{m}^{-3}$) was exceeded on 46 days. At the time of the study, only 35 excess days were legally permitted. This noncompliance with the permitted excess days for PM₁₀ is a problem Linz shares with most European urban areas.

The indicators of air pollution under investigation were positively and significantly correlated with each other

TABLE 1 Concentrations of particulate matter and nitrogen dioxide (NO₂) in Linz during the study period

Percentiles	PM ₁₀	PM _{2.5}	PM ₁	NO ₂
24 h mean 25%	16.54	10.46	8.92	13.75
24 h mean 50%	25.73	15.79	13.20	17.50
24 h mean 75%	37.08	23.07	19.07	21.48
Maximum 24 h mean	127.44	76.39	58.20	40.73
US EPA NAAQS	150	65		
EU limit values	50			
8 h mean 25%	14.39	8.64	6.90	11.57
8 h mean 50%	24.85	15.70	12.30	15.49
8 h mean 75%	38.82	24.46	17.82	21.97
8 h mean-IQR	24.43	25.82	10.92	10.40
Annual average	30.28	19.06	15.03	18.07
US EPA NAAQS	50	15		100
EU limit values	40	(25)		40

PM_x: particulate matter with a 50% cut-off aerodynamic diameter of x µm; US EPA NAAQS: United States Environmental Protection Agency National Ambient Air Quality Standards; EU: European Union; IQR: interquartile range.

(table 2). Because of the high correlation between PM₁ and PM_{2.5}, only PM_{2.5} was entered into the multipollutant model.

All pollutants studied in the single pollutant models had adverse effects on most of the lung function parameters. The only exceptions were FVC for the particle parameters and PEF, for which the effect estimate for NO₂ did not reach significance. Overall effects were rather small. After re-transforming the log values of the lung function, the changes per 10 µg·m⁻³ or per interquartile range (IQR) were in the magnitude of 1% only. The strongest changes per IQR were seen for NO₂ as a pollution indicator and, after particle exposure, for R(0,c) as an outcome variable (table 3). (Contrary to the other lung function parameters, a positive association with the resistance indicates an adverse effect.) Dose-response relationships for NO₂ are shown in figure 1, using residuals of log FEV₁ (fig. 1a), MEF_{25%} (fig. 1b) and R(0,c) (fig. 1c).

Coarse particles (calculated as the difference between PM₁₀ and PM_{2.5}) were only weakly associated with all lung function outcomes (data not shown). In the multipollutant model, together with PM_{2.5} and NO₂, coarse particles did not exhibit any significant effect and were therefore not further investigated. Thus the multipollutant model focused on PM_{2.5}

TABLE 2 Correlation of ambient air pollution indicators in Linz during the study period

Pearson's r of 8 h means	NO ₂	PM ₁	PM _{2.5}
PM ₁	0.53		
PM _{2.5}	0.54	0.95	
PM ₁₀	0.62	0.91	0.93

NO₂: nitrogen dioxide; PM_x: particulate matter with a 50% cut-off aerodynamic diameter of x µm. All p<0.001.

TABLE 3 Lung function changes with three indicators of ambient air pollution

	PM ₁			PM _{2.5}			PM ₁₀			NO ₂		
	p-value	% change per 10 µg·m ⁻³	IQR	p-value	% change per 10 µg·m ⁻³	IQR	p-value	% change per 10 µg·m ⁻³	IQR	p-value	% change per 10 µg·m ⁻³	IQR
FEV ₁	0.006	-0.38	-0.41	0.019	-0.23	-0.59	0.049	-0.11	-0.27	<0.001	-0.89	-0.92
FVC	0.276 [#]	-0.14 [#]	-0.15 [#]	0.383 [#]	-0.08 [#]	-0.2 [#]	0.577 [#]	-0.03 [#]	-0.07 [#]	0.001	-0.59	-0.62
FEV _{0.5}	0.003	-0.50	-0.54	0.006	-0.33	-0.85	0.005	-0.19	-0.47	<0.001	-1.10	-1.14
MEF _{75%}	0.003	-0.85	-0.93	0.021	-0.49	-1.25	0.012	-0.30	-0.74	0.005	-1.14	-1.18
MEF _{50%}	0.005	-0.82	-0.89	0.007	-0.58	-1.48	0.004	-0.36	-0.86	<0.001	-1.96	-2.03
MEF _{25%}	0.006	-1.17	-1.27	0.008	-0.83	-2.14	0.027	-0.41	-0.98	<0.001	-2.17	-2.26
PEF	0.015	-0.63	-0.68	0.027	-0.41	-1.06	0.038	-0.22	-0.54	0.062 [†]	-0.67 [†]	-0.70 [†]
R(0,c)	<0.001	1.43	1.56	<0.001	1.45	3.78	0.001	0.91	2.24	0.002	2.11	2.20

PM_x: particulate matter with a 50% cut-off aerodynamic diameter of x µm; NO₂: nitrogen dioxide; IQR: interquartile range; FEV_x: forced expiratory volume in x number of seconds; FVC: forced vital capacity; MEF_x: maximal instantaneous forced flow when x percentage of the forced vital capacity remains to be exhaled; PEF: peak expiratory flow; R(0,c): hypothetical resistance at frequency=0. [#]: no association; [†]: trend only.

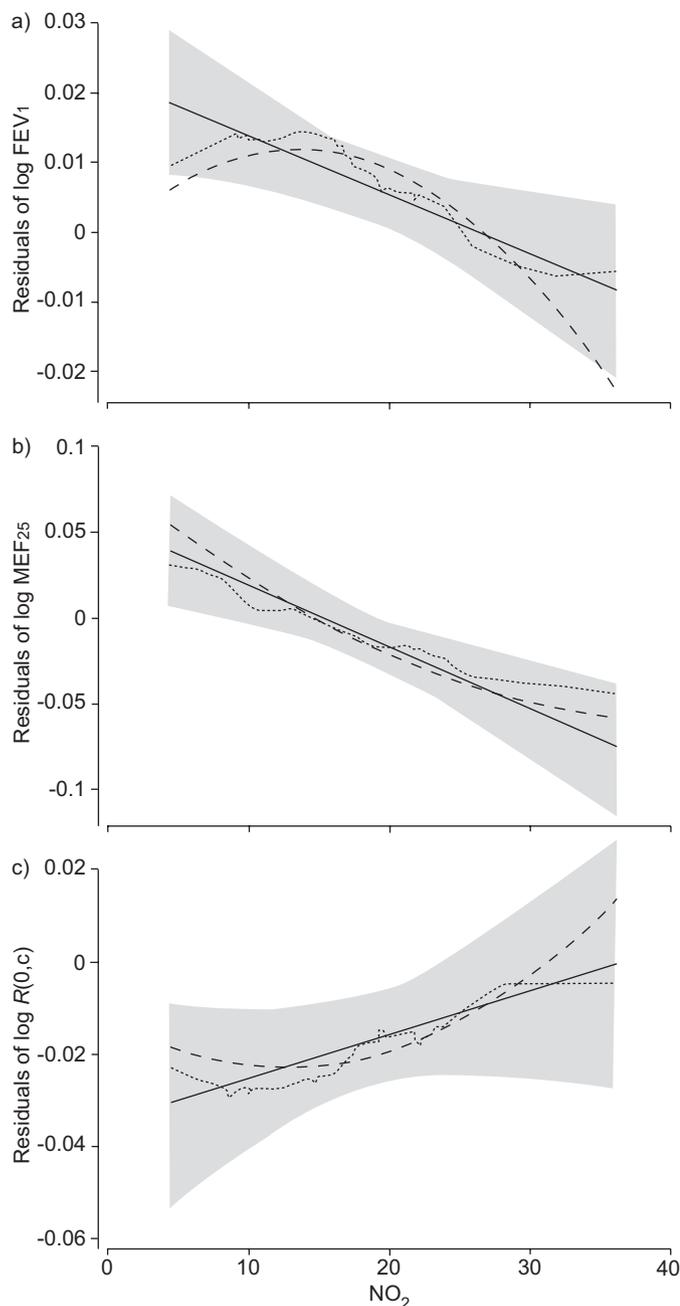


FIGURE 1. Selected outcomes for nitrogen dioxide (NO_2). Linear (—) and quadratic fit (---) and LOWESS plot (.....) on the residuals of the logs of forced expiratory volume in one second (FEV_1), maximal instantaneous forced flow at 25% of the forced vital capacity remaining to be exhaled ($\text{MEF}_{25\%}$) and hypothetical resistance at frequency=0 ($R(0,c)$).

and NO_2 (table 4). Most effect estimates for NO_2 remained significant and some even grew larger after controlling for $\text{PM}_{2.5}$. Only the effect of NO_2 on PEF and $R(0,c)$ was reduced and no longer significant. Resistance $R(0,c)$, however, was influenced by $\text{PM}_{2.5}$ but this was the only association with $\text{PM}_{2.5}$ that remained significant after controlling for NO_2 .

In contrast to the morning values, the 8-h mean values (NO_2 , PM) of the previous evening (16.00–24.00 h) were not associated with the lung function results (data not shown).

DISCUSSION

This study examined short-term effects of urban air pollution in morning hours on schoolchildren and could therefore disregard fluctuations in ozone concentrations. Earlier studies in Linz [8, 10] have shown relatively low ambient ozone during school years and no possibility of examining elementary schoolchildren in the afternoon and during summer vacation when ozone was higher, but children less localisable. From morning tests of lung functions during the school year, no negative associations with ozone had been found (and some positive ones were spurious and caused by the inverse relationship between ozone and NO_2). Mean daily oxygen concentrations ranged $0.3\text{--}30.5\ \mu\text{g}\cdot\text{m}^{-3}$ (median $4\ \mu\text{g}\cdot\text{m}^{-3}$). From earlier results at higher concentrations [8], the present sulphur dioxide exposure was considered to be negligible for changes in function of small airways.

The strong correlation between the three measures of particle mass and NO_2 made it difficult to separate the impact of each exposure metrically. However, in the multipollutant model, only NO_2 remained consistently associated with adverse health effects. This is noteworthy because, in previous studies, NO_2 was only inconsistently associated with lung function decrements [17]. This is true both for NO_2 measured outdoors (where it often serves as an indicator of exposure to road traffic pollutants) and indoors (where gas cooking and unvented heaters are relevant sources). This led to the conclusion that it is not NO_2 itself that causes the adverse effects, but that in many (but not all) settings it serves as a good proxy for the relevant pollution mixture. Other good proxies might be some volatile organic compounds [18, 19] or carbon monoxide. In the same environmental setting of Linz, NO_2 also proved to be a valuable predictor of long-term lung function growth [10].

Selection bias is unlikely to play an important role in this study, which attempted to examine all children who were healthy enough to come to school. Pupils on sick leave or with a respiratory infection on the day scheduled for spirometry were tested at a later date, and all children were tested repeatedly. If children with asthma stayed at home on days with high pollution, this would lead to an underestimation of the effect on lung function.

Effects of particulate matter and NO_2 on lung function decrements were in the same magnitude as reported by other studies [20]. Both LOWESS and quadratic fit (fig. 1) for FEV_1 and resistance suggest a levelling off of the effect at low concentrations (at $\sim 15\ \mu\text{g}\cdot\text{m}^{-3}$) which could indicate a threshold. No such threshold is evident for $\text{MEF}_{25\%}$. Small average changes on the population level can result in a relevant increase in the number of children with clinically poor lung function. Small changes are difficult to assess with spirometry in young children, because the results depend heavily on the children's cooperation. Respiratory resistance (measured with an impulse oscillation system at different frequencies) is less influenced by that. It was therefore expected to be a better indicator of small lung function changes than routine spirometric data. This expectation was met (in the single pollutant model for most parameters and in the multipollutant model for changes induced by $\text{PM}_{2.5}$), and therefore it is suggested that the oscillation technique be used more frequently in future

TABLE 4 Lung function changes in the multiple pollutants' model

	PM _{2.5}			NO ₂		
	p-value	% change per 10 µg·m ⁻³	% change per IQR	p-value	% change per 10 µg·m ⁻³	% change per IQR
FEV ₁	0.401 [#]	0.10 [#]	0.27 [#]	<0.001	-1.01	-1.05
FVC	0.064 [†]	0.21 [†]	0.54 [†]	<0.001	-0.85	-0.88
FEV _{0.5}	0.706 [#]	0.06 [#]	0.15 [#]	<0.001	-1.16	-1.20
MEF _{75%}	0.571 [#]	-0.15 [#]	-0.39 [#]	0.057 [†]	-0.97 [†]	-1.01 [†]
MEF _{50%}	0.868 [#]	0.04 [#]	0.11 [#]	<0.001	-1.99	-2.07
MEF _{25%}	0.596 [#]	-0.21 [#]	-0.54 [#]	0.01	-1.96	-2.04
PEF	0.434 [#]	-0.18 [#]	-0.47 [#]	0.328 [#]	-0.44 [#]	-0.46 [#]
R(0,e)	0.004	1.03	2.69	0.161 [#]	0.97 [#]	1.00 [#]

PM_{2.5}: particulate matter with a 50% cut-off aerodynamic diameter of 2.5 µm; NO₂: nitrogen dioxide; IQR: interquartile range; FEV_x: forced expiratory volume in x number of seconds; FVC: forced vital capacity; MEF_x: maximal instantaneous forced flow when x percentage of the forced vital capacity remaining to be exhaled; PEF: peak expiratory flow; R(0,c): hypothetical resistance at frequency=0. #: no association; †: trend only.

environmental studies on children's respiratory health, particularly to assess short-term effects of PM_{2.5}.

With regard to indicators of ambient urban air pollution as assessed at monitoring stations, the results of this study indicate that PM_{2.5} and NO₂ predict early decrements of lung function in children better than PM₁₀. Because of lower taxes for diesel compared with petrol in Austria, the number of diesel cars increased from 2.7% in 1980 to 49.2% in 2004. Stricter emission standards and the introduction of catalysts has been counterbalanced by an increase in motor traffic and, at kerbside monitoring stations in Linz and other Austrian towns, a slight increase of NO₂ has been seen in recent years. It seems unlikely that the foreseen reduction of emission concentration of only 20% in 2010 (Euro 5; vehicles that comply with the emission limits as defined in Directive 99/96/EC [21]) will solve this problem. The findings of this study suggest that exposure levels below EU standards have a health effect and that more stringent limitations of ambient peak NO₂ concentrations are necessary to prevent lung function impairment in children. Traffic-related NO₂ concentrations were also associated with wheezing and asthma medication of children [22] and with long-term effects, increasing respiratory mortality by 16 (6–26)% per 10 µg·m⁻³ of NO_x (where NO_x is any oxide of nitrogen) [23]. These findings contribute to the evidence for the serious health effects of urban air pollution indicated by NO₂ and the necessity to lower it.

The results of this lung function study also question the cap of 25 µg·m⁻³ for concentrations of ambient particulate matter with a 50% cut-off aerodynamic diameter of 2.5 µm, which is proposed as annual mean by the European Commission in its Thematic Strategy on Air Pollution, 2005. In the absence of an indication for a threshold, adverse effects of urban air pollution should be reduced as much as possible by minimising emissions of primary and secondary fine particulates, especially from combustion.

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