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

H. Moshammer[1], H.-P. Hutter[1], H. Hauck[2], M. Neuberger[1,2]

[1]Institute of Environmental Health, Medical University of Vienna, Austria
[2]Austrian Academy of Sciences—Clean Air Commission, Postgasse 7-9, Vienna, Austria

Address correspondence to

Manfred Neuberger

Institute of Environmental Health

Kinderspitalgasse 15

A-1095 Vienna, Austria.

Telephone: ++43-1-4277-64711

Fax: ++43-1-4277-64799

e-mail: Manfred.neuberger@meduniwien.ac.at

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Abbreviations:

AUPHEP	Austrian Project on Health Effects of Particulates
FVC	Forced vital capacity
FEV_1, $FEV_{0.5}$	Forced expiratory volume in the first second, first 0.5 seconds
MEF75, MEF50, MEF25	Maximal expiratory flow at 75/50/25% of FVC left
PEF	Peak expiratory flow
R(0,c)	oscillatory resistance at 0 Hz, calculated

Abstract

In search of sensitive screening parameters for assessing acute effects of ambient air pollutants in young school children the impact of 8-hour 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 the capital of Upper Austria 163 children aged 7-10 years underwent repeated examinations at the same time of day during one school year, yielding a total of 11 to 12 lung function tests per child. Associations to mass concentrations of particulate matter and nitrogen dioxide measured continuously at a nearby monitoring station were tested, applying the Generalized Estimating Equations model.

Reductions per 10 µg/m³ (both for particles and for NO_2) were in the magnitude of one percent 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. NO_2 at concentrations below current standards reduced (in the multi-pollutant model) FEV_1 by 1.01%, MEF50 by 1.99% and MEF25 by 1.96%. Peripheral resistance increased by 1.03% per 10µg/m³ of $PM_{2.5}$. Resistance is less influenced by the child's cooperation, should be utilized more often in environmental epidemiology when screening for early signs of small airway dysfunction from urban air pollution, but cannot replace the measurement of MEF50 and MEF25. In the basic model the reduction of these parameters per 10µg/m³ was highest for NO_2, followed by PM_1, $PM_{2.5}$ and PM_{10} while exposure to coarse dust ($PM_{10} – PM_{2.5}$) did not change endexpiratory 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 NO_2. Planned reduction of NO_2 emission (Euro V) of 20% in 2010 seems to be insufficient.

Introduction

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. But most have focused on daily mean levels of air pollution [7] and – if investigating effect on lung function at all – have concentrated on parameters that are easily collected in children like PEF.

Fine particles of different origin and chemical composition are supposed to differ in their health impact. Nitrogen dioxide (NO_2) 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 school children from Linz, the capital of Upper Austria, have shown the good predictive value of NO_2 especially for MEF25 and MEF50 in children's lung function testing.

We had the opportunity to monitor various measures of particulate matter in the course of a joint Austrian project (AUPHEP) [9] in the school-year 2000-2001 at the central air monitoring site in Linz. In this town of 200 000 inhabitants with steel industry and heavy motor traffic chronic respiratory health effects on children had been found [8] and improvements in lung function were related to improvements of air quality [10]. Current levels of particulate matter (PM10) and nitrogen dioxide (NO_2) are in a range typical for Middle European urban areas. We hypothesised that acute respiratory effects could still be observed on days with elevated concentrations. Therefore we 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. We expected that peak levels of air pollution shortly before the 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 NO_2 is a good proxy) is of prime importance.

This study aimed at three targets: To investigate short term effects of air pollution on lung function (by choosing 8 hour mean values instead of daily mean values for this panel study), to find lung function parameters which are both sensitive to the acute impact of air pollution and suitable for screening of young school children, and 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 Danube) is predominantly affected by industrial emissions (steel plant) and motor traffic (high proportion of diesel trucks and cars) which can build up 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 9 monitoring sites in and around the city. Details of the air monitoring project have been described by Hauck et al. [9]. For this study we chose the half hour mean values of PM_1, $PM_{2.5}$, PM_{10} (measured by Tapered Element Oscillating Microbalance

- TEOM), and NO_2 (measured by chemoluminiscence) to calculate the 8-hour means between 0:00 and 8:00 o'clock 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) about 20 of 164 children (age 7-10 years) underwent lung function tests, so that each of the 69 girls and 95 boys had spirometry about every fortnight at about the same time of day from September to May. FVC, FEV_1, $FEV_{0.5}$, 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 sec which is not feasible for children. The lung function tests were conducted between 8:30 and 10:30 a.m. in a fixed sequence.

Before performing routine spirometry (in standing position) the respiratory resistance was measured (in 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 hypothetical resistance at frequency = 0 was calculated R(0,c) 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 to 12 times. Each child was assigned to a fixed day of the week to minimise bias from weekly cycles. But due to holidays, sick leaves or other organisational problems most of the children on 1 to 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 3 respectively 6 times.

Statistical analysis:

Statistical analysis was performed with STATA 8.2. Lung function values were log-transformed because multiplicative effects were expected. Also gender and the logs of age, height, and weight were entered into the models as explanatory variables. The health impact of air pollution was studied applying the Generalized Estimating Equations model GEE 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-hour mean values from 0:00 till 8:00 o'clock included both the low concentrations of the night and the high concentrations of morning rush hour. So on average the 8-hour mean levels were comparable to the daily mean levels (table 1). Annual average concentrations were mostly within current European and US limit values. Only $PM_{2.5}$ exceeded the US limit value of 15µg/m³ for the annual mean, but not the cap of 25 µg/m³ proposed by the European Commission in its Thematic Strategy on Air Pollution, 2005. (There is no legal limit value for $PM_{2.5}$ in Europe yet). The European PM_{10} limit value for the daily average (50 µg/m³) was exceeded on 46 days. At the time of the study only 35 excess days were legally permitted. This non-compliance with the allowable excess days for PM_{10} is a problem Linz shares with most of the European urban areas.

Table 1: Concentrations of particulate matter and NO_2 in Linz during the study period

percentiles	PM_{10}	$PM_{2.5}$	PM_1	NO_2
24h mean 25%	16.54	10.46	8.92	13.75
24h mean 50%	**25.73**	**15.79**	**13.20**	**17.50**
24h mean 75%	37.08	23.07	19.07	21.48
Max. 24 mean	127.44	76.39	58.20	40.73
US EPA NAAQS	150	65	-	-
EU limit values	50	-	-	-
8h mean 25%	14.39	8.64	6.90	11.57
8h mean 50%	**24.85**	**15.70**	**12.30**	**15.49**
8h mean 75%	38.82	24.46	17.82	21.97
IQR (8h mean)	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

The indicators of air pollution under investigation were positively and significantly correlated with each other (table 2). Because of the high correlation between PM_1 and $PM_{2.5}$ only $PM_{2.5}$ was entered into the multi-pollutant model.

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

Pearson's r of 8h 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

(all $p < 0.001$)

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 NO_2 did not reach significance. Overall effects were rather small. After re-transforming the log values of the lung function the changes per 10 µg/m³ or per inter-quartile range (IQR) were in the magnitude of 1 percent only. The strongest changes per IQR were seen for NO_2 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

NO_2 are shown in figure 1, using residuals of log FEV1 (fig. 1a), MEF25 (fig. 1b) and R(0,c) (fig. 1c).

Table 3: Lung function changes with 3 indicators of ambient air pollution

	PM_1			$PM_{2.5}$			PM_{10}			NO_2		
	p	% change per 10 µg/m³	% change per IQR	p	% change per 10 µg/m³	% change per IQR	p	% change per 10 µg/m³	% change per IQR	p	% change per 10 µg/m³	% change per 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

Cursive: trend only
Grey: no association

Coarse particles (calculated as the difference between PM_{10} and $PM_{2.5}$) were only weakly associated with all lung function outcomes (data not shown). In the multi-pollutant model together with $PM_{2.5}$ and NO_2 coarse particles did not exhibit any significant effect and were therefore not further investigated. Thus the multi-pollutant model focused on $PM_{2.5}$ and NO_2 (table 4). Most effect estimates for NO_2 remained significant and some even grew larger after controlling for $PM_{2.5}$. Only the effect of NO_2 on PEF and R(0,c) was reduced and no longer significant. Resistance R(0,c) on the other hand was influenced by $PM_{2.5}$ but this was the only association with $PM_{2.5}$ that remained significant after controlling for NO_2.

Table 4: Lung function changes in the multiple pollutants' model

	$PM_{2.5}$			NO_2		
	p	% change per 10µg/m³	% change per IQR	p	% change per 10µg/m³	% 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

Cursive: trend only
Grey: no association

Figure 1: selected outcomes for NO_2: Linear and quadratic fit and LOWESS plot on the residuals of the logs of FEV_1, MEF25, and R(0,c)

[figure1a.tiff; figure1b.tiff; figure1c.tiff]

In contrast to the morning values the 8-hour mean values (NO2, PM) of the previous evening (4 p.m. till midnight) 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 school children and could therefore disregard fluctuations in ozone concentrations. Earlier studies in Linz [8, 10] had shown relatively low ambient O_3 during school years and no possibility to examine elementary school children in the afternoon and during summer vacation when O_3 was higher, but children less localizable. From morning tests of lung functions during the school year no negative associations with O_3 had been found (and some positive ones were spurious and caused by the inverse relationship between O_3 and NO_2). Mean daily concentrations of SO_2 ranged from 0.3 to 30.5 µg/m³ (median 4 µg/m³). From earlier results at higher concentrations [8] we consider the present SO_2 exposure to be negligible for changes in function of small airways.

The strong correlation between the 3 measures of particle mass and also with NO_2 made it difficult to separate the impact of each exposure metric. But in the multi-pollutant 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 [16]. This is true both for NO2 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 [17, 18] 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 (e.g. [19]). 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 multi-pollutant model for changes induced by $PM_{2.5}$) and therefore it is suggested to use the oscillation technique more frequently in future 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 NO_2 predict early decrements of lung function in

children better than PM_{10}. Because of lower taxes for diesel compared to gasoline in Austria diesel cars increased from 2.7% in 1980 to 49.2% in 2004. Stricter emission standards and the introduction of catalysts was counterbalanced by increase of motor traffic and at kerbside monitoring stations in Linz and other Austrian towns a slight increase of NO_2 was seen in recent years. It seems unlikely that the foreseen reduction of emission concentration of only 20% in 2010 (Euro V) will solve that problem. Our findings suggest that exposure levels below EU standards have a health effect and that more stringent limitations of ambient peak NO_2 concentrations are necessary to prevent lung function impairment in children. Traffic-related NO_2 concentrations were also associated with wheezing and asthma medication of children [20] and with long term effects, increasing respiratory mortality by 16 (6-26)% per 10μg/m³ of NO_x [21]. These findings contribute to the evidence for serious health effects of urban air pollution indicated by NO_2 and the necessity to lower it.

The results of this lung function study also questions the cap for ambient $PM_{2.5}$ concentrations of 25 μg/m³ proposed as annual mean by the European Commission in its Thematic Strategy on Air Pollution, 2005. In lack of an indication for a threshold, adverse effects of urban air pollution should be reduced as much as possible by minimizing emissions of primary and secondary fine particulates, especially from combustion.

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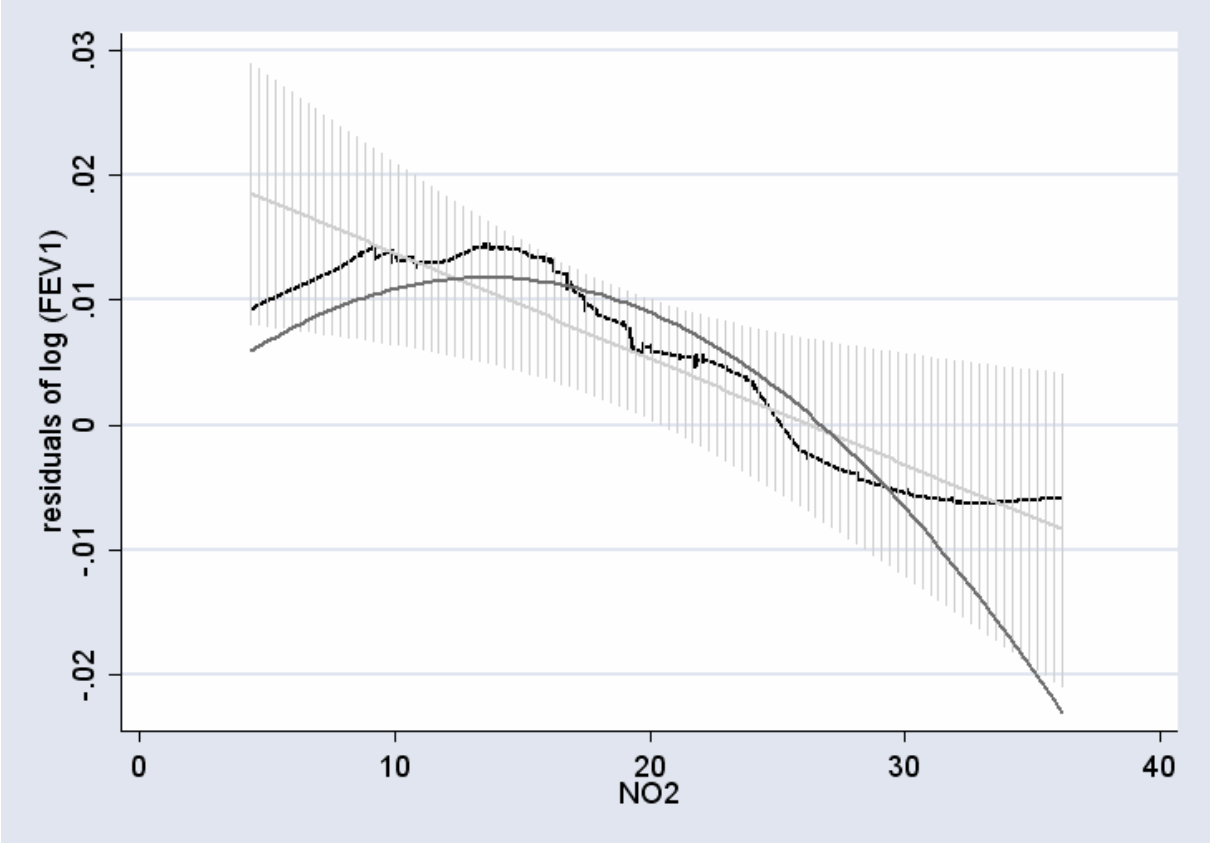

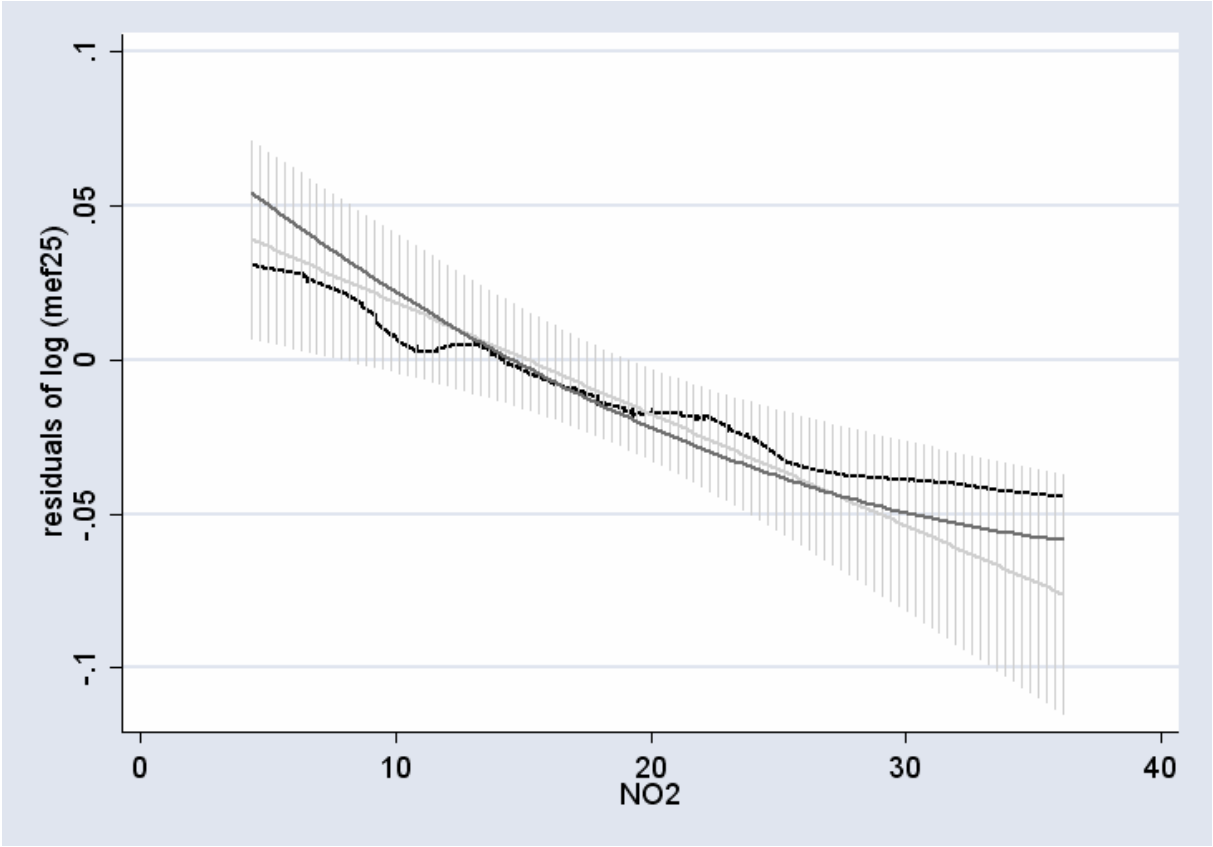
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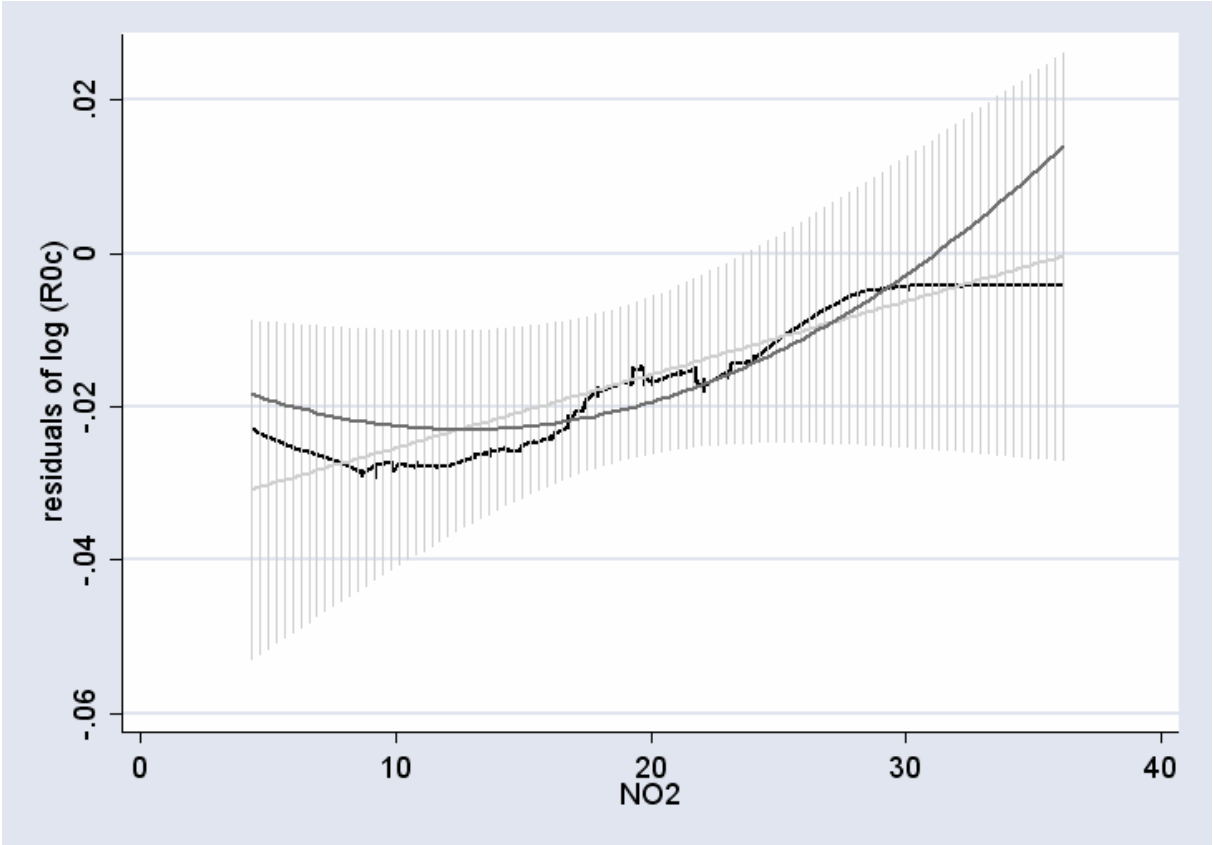
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