NO2 and PM2.5 Exposures and Lung Function in Swiss Adults: Estimated Effects of Short-Term Exposures and Long-Term Exposures with and without Adjustment for Short-Term Deviations

Strassmann, Alexandra; de Hoogh, Kees; Röösli, Martin; Haile, Sarah R; Turk, Alexander; Bopp, Matthias; Puhan, Milo A

Abstract: Background: The impact of nitrogen dioxide (NO2) and particulate matter with an aerodynamic diameter of less than or equal to 2.5 microns (PM2.5) exposures on lung function has been investigated mainly in children and less in adults. Furthermore, it is unclear whether short-term deviations of air pollutant concentration need to be considered in long-term exposure models. Objectives: The aims of this study were to investigate the association between short-term air pollution exposure and lung function and to assess whether short-term deviations of air pollutant concentration should be integrated into long-term exposure models. Methods: Short-term (daily averages 0–7 d prior) and long-term (1- and 4-y means) NO2 and PM2.5 concentrations were modeled using satellite, land use, and meteorological data calibrated on ground measurements. Forced expiratory volume within the first second (FEV1) of forced exhalation and forced vital capacity (FVC) were measured during a LuftiBus assessment (2003–2012) and linked to exposure information from the Swiss National Cohort for 36,085 adults (ages 18–95 y). We used multiple linear regression to estimate adjusted associations, and additionally adjusted models of long-term exposures for short-term deviations in air pollutant concentrations. Results: A 10 g/m3 increase in NO2 and PM2.5 on the day of the pulmonary function test was associated with lower FEV1 and FVC (NO2: FEV1 −8.0 ml [95% confidence interval: −13.4, −2.7], FVC −16.7 ml [−23.4, −10.0]; PM2.5: FEV1 −15.3 ml [−21.9, −8.7], FVC −18.5 ml [−26.5, −10.5]). A 10 g/m3 increase in 1-y mean NO2 was also associated with lower FEV1 (−7.7 ml; −15.9, 0.5) and FVC (−21.6 ml; −31.9, −11.4), as was a 10 g/m3 increase in 1-y mean PM2.5 (FEV1: −42.2 ml; −56.9, −27.5; FVC: −82.0 ml; −100.1, −63.9). These associations were robust to adjustment for short-term deviations in the concentration of each air pollutant. Conclusions: Short- and long-term air pollution exposures were negatively associated with lung function, in particular long-term PM2.5 exposure with FVC. Our findings contribute substantially to the evidence of adverse associations between air pollution and lung function in adults.

https://doi.org/10.1289/EHP7529

DOI: https://doi.org/10.1289/ehp7529

Posted at the Zurich Open Repository and Archive, University of Zurich
ZORA URL: https://doi.org/10.5167/uzh-198265
Journal Article
Published Version

Originally published at:
Strassmann, Alexandra; de Hoogh, Kees; Röösli, Martin; Haile, Sarah R; Turk, Alexander; Bopp, Matthias; Puhan, Milo A (2021). NO2 and PM2.5 Exposures and Lung Function in Swiss Adults:
Estimated Effects of Short-Term Exposures and Long-Term Exposures with and without Adjustment for Short-Term Deviations. Environmental Health Perspectives, 129(1):017009.
DOI: https://doi.org/10.1289/ehp7529
NO₂ and PM$_{2.5}$ Exposures and Lung Function in Swiss Adults: Estimated Effects of Short-Term Exposures and Long-Term Exposures with and without Adjustment for Short-Term Deviations

Alexandra Strassmann,$^1$ Kees de Hoogh,$^{2,3}$ Martin Röösli,$^{2,3}$ Sarah R. Haile,$^1$ Alexander Turk,$^4$ Matthias Bopp,$^4$ and Milo A. Puhan$^4$ for the Swiss National Cohort Study Group

$^1$Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland
$^2$Swiss Tropical and Public Health Institute, Basel, Switzerland
$^3$University of Basel, Basel, Switzerland
$^4$See-Spital Horgen, Horgen, Switzerland

BACKGROUND: The impact of nitrogen dioxide (NO₂) and particulate matter with an aerodynamic diameter of less than or equal to 2.5 microns (PM$_{2.5}$) exposures on lung function has been investigated mainly in children and less in adults. Furthermore, it is unclear whether short-term deviations of air pollutant concentration need to be considered in long-term exposure models.

OBJECTIVES: The aims of this study were to investigate the association between short-term air pollution exposure and lung function and to assess whether short-term deviations of air pollutant concentration should be integrated into long-term exposure models.

METHODS: Short-term (daily averages 0–7 d prior) and long-term (1- and 4-y means) NO₂ and PM$_{2.5}$ concentrations were modeled using satellite, land use, and meteorological data calibrated on ground measurements. Forced expiratory volume within the first second (FEV1) of forced exhalation and forced vital capacity (FVC) were measured during a LuftpBus assessment (2003–2012) and linked to exposure information from the Swiss National Cohort for 36,085 adults (ages 18–95 y). We used multiple linear regression to estimate adjusted associations, and additionally adjusted models of long-term exposures for short-term deviations in air pollutant concentrations.

RESULTS: A 10 μg/m³ increase in NO₂ and PM$_{2.5}$ on the day of the pulmonary function test was associated with lower FEV1 and FVC (NO₂: FEV1 = −8.0 ml [95% confidence interval: −13.4, −2.7], FVC = −16.7 ml [−23.4, −10.0]; PM$_{2.5}$: FEV1 = −15.3 ml [−21.9, −8.7], FVC = −18.5 ml [−26.5, −10.5]). A 10 μg/m³ increase in 1-y mean NO₂ was also associated with lower FEV1 (−7.7 ml; −15.9, 0.5) and FVC (−21.6 ml; −31.9, −11.4), and was a 10 μg/m³ increase in 1-y mean PM$_{2.5}$ (FEV1: −42.2 ml; −56.9, −27.5; FVC: −82.0 ml; −100.1, −63.9). These associations were robust to adjustment for short-term deviations in the concentration of each air pollutant.

CONCLUSIONS: Short- and long-term air pollution exposures were negatively associated with lung function, in particular long-term PM$_{2.5}$ exposure with FVC. Our findings contribute substantially to the evidence of adverse associations between air pollution and lung function in adults. https://doi.org/10.1289/EHP7529

Introduction

Outdoor air pollution is one of the most important risk factors for respiratory and other chronic diseases, and was estimated to contribute to 3.3 million premature deaths worldwide in 2010 (Lelieveld et al. 2015; Sun and Zhu 2019). Monitoring and reducing the key sources of outdoor air pollution is a high priority for the World Health Organization (WHO 2016). Nitrogen dioxide (NO₂) and fine particulate matter (PM$_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 microns) has been identified as an important pollutant that can penetrate into the lungs and trigger an inflammatory response (Dauchet et al. 2018; Weinmayer et al. 2010; WHO 2016).

Studies investigating the impact of outdoor air pollution on lung function have focused mainly on the effect of short-term exposures, for example, air pollutant concentrations up to 7 days prior to a pulmonary function test (PFT) (Dauchet et al. 2018; Panis et al. 2017; Rice et al. 2013; Schindler et al. 2001), or on long-term exposures, such as annual mean concentrations (Ackermann-Liebrich et al. 1997; Adam et al. 2015). Although the evidence for adverse long-term effects of air pollution on lung function is strong in children and adolescents, evidence is still weak for the adult general population (Götschi et al. 2008). Evidence from observational studies suggests negative associations between lung function in adults and short- and long-term air pollutant exposures (Ackermann-Liebrich et al. 1997; Adam et al. 2015; Dauchet et al. 2018; Edginton et al. 2019; Götschi et al. 2008; Panis et al. 2017; Rice et al. 2015, 2013; Schindler et al. 2001). Most of these studies have estimated associations with particulate matter with aerodynamic diameter less than or equal to 10 μm (PM$_{10}$), rather than with PM$_{2.5}$, but finer particles of PM$_{2.5}$ can enter more deeply into the lungs than PM$_{10}$ and may represent a greater health risk (Ackermann-Liebrich et al. 1997; Dauchet et al. 2018; Panis et al. 2017). Furthermore, few previous studies have simultaneously estimated and compared associations with short- and long-term exposures.

Recent high-resolution spatiotemporal air pollution models suggest that PM$_{2.5}$ and NO₂ concentrations may vary substantially within a few days (de Hoogh et al. 2018, 2019). For example, the average value of daily mean NO₂ concentrations measured across Switzerland on 8–14 February 2005 ranged from 11 to 60 μg/m³ (de Hoogh et al. 2019). If lung function measures are influenced by recent air pollutant concentrations, daily variation in air pollution may distort estimated effects of long-term exposures. For example, the association between lung function and long-term air pollutant concentration may be underestimated if individuals who live in areas with low long-term air pollution complete a PFT in a place where there is high air pollution. We are aware of only two studies that have considered the potential influence of adjusting models of long-term air pollution exposures and lung function for recent air pollution exposures.
Rice et al. 2015
Egger et al. 2018
Miller et al. 2005

Data were enriched with individual data from the Swiss National Organization (the Zurich Lung Association (Switzerland), a not-for-profit health organization). LuftiBus is a health promotion campaign conducted by the Zurich Lung Association (Switzerland), a not-for-profit health organization (Zurich Lung Association 2020). The campaign included a bus that traveled throughout Switzerland (and all Swiss cantons) between 2002 and 2012 providing health information and offering free spirometry to the general population. Additionally, information on smoking and self-reported height and weight was collected during the LuftiBus assessment. These data were enriched with individual data from the Swiss National Cohort (SNC), and residential NO2 and PM2.5 data.

The SNC is a nationwide census-based cohort (covering all residents of Switzerland) that combines anonymized individual data from the 1990 and 2000 federal population censuses and yearly registry censuses since 2010 (Bopp et al. 2009; Egger et al. 2018). The SNC provides information on education, occupation, housing, and other sociodemographic characteristics on an individual level. Education was classified according to the International Standard Classification of Education 1997 (ISCED-97) as low/medium (ISCED levels 0–3) or high (ISCED levels 4–6) (UNESCO 1997).

An area-based index of socioeconomic position (SEP) in Switzerland was derived from the 2000 census based on education, occupation, and housing conditions for ~50 of the nearest households, and—as a proxy for household income—median rent per square meter of the 50 nearest rented flats, mapped to a scale ranging from 0 (lowest SEP) to 100 (highest SEP) (Panczak et al. 2012).

The LuftiBus data set and the SNC database contain information on date of birth, residential postcode, and sex. Due to unavailability of a unique person identifier, we used this set of identifiers to deterministically link the respective SNC records to LuftiBus participants and approved this study (BASEC-Nr. 2017–01804).

Methods

Study Design and Population

This observational study is based on data from the “LuftiBus” cohort. LuftiBus is a health promotion campaign conducted by the Zurich Lung Association (Switzerland), a not-for-profit health organization (Zurich Lung Association 2020). The campaign included a bus that traveled throughout Switzerland (and all Swiss cantons) between 2002 and 2012 providing health information and offering free spirometry to the general population. Additionally, information on smoking and self-reported height and weight was collected during the LuftiBus assessment. These data were enriched with individual data from the Swiss National Cohort (SNC), and residential NO2 and PM2.5 data.

The LuftiBus data set and the SNC database contain information on date of birth, residential postcode, and sex. Due to unavailability of a unique person identifier, we used this set of identifiers to deterministically link the respective SNC records to LuftiBus participants and approved this study (BASEC-Nr. 2017–01804).

Environmental Health Perspectives 017009-2 129(1) January 2021

Residential NO2 and PM2.5 Estimates

Residential NO2 and PM2.5 concentrations were estimated from fine scale prediction models with NO2 data from 2005 to 2016 and PM2.5 data from 2003 to 2013 in Switzerland (de Hoogh et al. 2018, 2019). The NO2 model integrates NO2 measurements from 67 to 108 monitoring sites depending on the year, with a minimum of 30 measurements per day and site. The PM2.5 model integrates data obtained from 10 PM2.5 measurement sites between 2003 and 2013 and PM10 measurements from 89 monitoring sites that were converted to PM2.5 concentrations using empirically derived conversion factors. In both models, satellite data, land use, and meteorological parameters were considered in a geostatistical framework. The final prediction models provide estimated daily averages of NO2 and PM2.5 concentrations (in micrograms per cubic meter) at a spatial resolution of 100 × 100 m. Validation of the NO2 and PM2.5 models was performed using a 10-fold cross-validation by dividing the monitoring data randomly into 10 groups of equal size. For each of the 10 validations, in turn, the model was trained on 90% of the data and predicted NO2 and PM2.5 on the 10% left out. The predicted NO2 and PM2.5 concentrations of all the test data were then regressed against the measured NO2 and PM2.5 concentrations. The 10-fold cross-validations of the NO2 and PM2.5 models were robust, predicting 57% (NO2) and 73% (PM2.5) of the variation in measured NO2 and PM2.5 concentrations at the 1 × 1 km level and another 73% (NO2) and 89% (PM2.5) of the variation in the residuals at a 100 × 100 m resolution (de Hoogh et al. 2018, 2019). Finally, residential coordinate information in the SNC was used to derive daily NO2 and PM2.5 concentrations for each individual in the LuftiBus–SNC cohort.

Pulmonary Function Test

During the LuftiBus assessment, participants completed a spirometry test using a computerized pneumotachograph (SensorMedics® Vmax Legacy 20c spirometer run by Vision 7-2b software; VIASYS) without prior use of bronchodilator. LuftiBus technicians calibrated the device daily and were trained at least twice a year. After receiving oral instructions from the technicians, participants performed the test while sitting with a straight back and with their neck in a neutral position, without use of a nose clip, according to ATS/European Respiratory Society guidelines (American Thoracic Society 1991; Miller et al. 2005). A minimum of two acceptable tests out of a maximum of eight performed tests was required. For the analyses, we used the highest FEV1 and FVC from the two acceptable tests. FEV1 measures how much air a person can exhale within the first second of forced exhalation, and FVC measures the total amount of exhaled air during the same test.

Statistical Analysis

Our analysis was divided into two steps. In the first step, we estimated the impact of short-term NO2 and PM2.5 exposure on lung function. We defined “short-term” exposure as the daily mean air pollutant concentration on the day of the PFT (day 0) and each of the 7 d preceding the PFT. We estimated FEV1 and FVC values per 10 μg/m3 increment of NO2 and PM2.5 using multiple linear regression models with and without adjustment for potential confounders identified using a directed acyclic graph (Figure S2), specifically, sex, age, height, weight, smoking status (never smoker/passive smoker, former smoker, current smoker), education (low vs. high), SEP index (continuous, as a measure of neighborhood socioeconomic status); the year, season (fall, winter, spring, summer), and time of the PFT (continuous); and relative humidity and temperature at the location and day of the PFT.
We performed a sensitivity analysis excluding current smokers to determine whether associations were affected by smoking status.

In the second step, we examined the influence of additionally adjusting for short-term deviations in air pollutant concentrations when estimating associations between lung function and long-term air pollution exposures, including 1- and 4-y means based on daily concentrations during the preceding 12 and 48 months, respectively. Short-term air pollution deviations were defined for each individual as the absolute difference between the air pollutant concentration on the day of PFT and their 1- or 4-y mean concentrations, respectively. For example, the short-term deviation in NO₂ for models of 1-y mean NO₂ was:

\[ \text{Short-term deviation = NO₂ concentration on day of PFT - 1-y mean NO₂ concentration} \]

Long-term NO₂ and PM₂.₅ data were limited to certain years. Therefore, LuftiBus participants were included in the long-term analyses if they completed the study assessment in 2006–2012 for 1-y mean NO₂, 2004–2012 for 1-y mean PM₂.₅, 2009–2012 for 4-y mean NO₂, and 2007–2012 for 4-y mean PM₂.₅. Missing values were present for smoking status \((n = 108, 0.3\%)\), education \((n = 3,282, 9.1\%)\), SEP index \((n = 679, 1.9\%)\), NO₂ concentration \((n = 1,056 \text{ participants}, 3.5\%)\), PM₂.₅ concentration \((n = 1,626, 2.9\%)\), temperature and relative humidity \((n = 6,609 \text{ for each variable due to missing information on the location of the PFT})\. Therefore, we performed multiple imputation with 25 imputations, using all covariates and the outcomes as predictors in the imputation model (White et al. 2011), to impute missing covariate and exposure data. All analyses were conducted in R (version 3.6.1; R Development Core Team), and the “mice” package in R was used for multiple imputation (van Buuren and Groothuis-Oudshoorn 2011).

## Results

### Study Population

The mean age of the study population was 53 y old (maximum 95 y), and 51.6% were female (Table 1). Just over half of the participants were never smokers (56%), 24% were ex-smokers, and 20% were current smokers. The educational level was high, with 29% having completed higher education (ISCED levels 4–6). Most visits were in fall (40%); the number of visits in spring (28%) and summer (25%) were similar. The visits mainly took place between 1000 hours and 1600 hours (10 A.M. and 4 P.M.) (73%), with a peak time between 1000–1200 (26%) and 1400–1600 (28%). The mean FEV₁ was 3.1 L (± 0.9, range 0.4–7.0 L), and mean FVC was 4.1 L (± 1.1, range 0.6–9.0 L).

### Air Pollution Exposure

The mean residential NO₂ concentration on the day of PFT was 19.9 ± 12.1 μg/m³ (range 0–86.1 μg/m³), and the PM₂.₅ concentration was 18.0 ± 9.2 μg/m³ (range 0–89.9 μg/m³) (Table 2). The 1- and 4-y mean NO₂ concentrations were 21.4 ± 7.7 μg/m³ and 21.3 ± 7.7 μg/m³, respectively, and 1- and 4-y mean PM₂.₅ concentrations were 18.5 ± 4.1 μg/m³ and 18.0 ± 3.0 μg/m³, respectively. There were strong correlations between NO₂ on the day of PFT and the 1- and 4-y mean concentrations (0.69 and 0.70, respectively) and weak to moderate correlations between PM₂.₅ on the day of PFT and the 1- and 4-y mean concentrations (0.29 and 0.35, respectively).

### Short-Term NO₂ Exposure and Lung Function

After adjustment for confounders, short-term NO₂ concentrations were negatively associated with FEV₁ and FVC (Figure 1; Tables S1 and S2). A 10 μg/m³ increment in daily mean NO₂ on the third day before the PFT (−3 d preceding) was associated with a 3.0 mL [95% confidence interval (CI): −8.3, 2.3] lower FEV₁, whereas a 10 μg/m³ increment of NO₂ on the day of the PFT (0 d) was associated with a 9.0 mL (95% CI: −13.4, −2.7) lower FEV₁. Adjusted associations between a 10 μg/m³ increase in short-term NO₂ and FVC ranged from 7.8 mL (95% CI: −14.4, 1.1) lower FVC for daily mean NO₂ 3 d before the PFT to a 16.7 mL (95% CI: −23.4, −10.0) lower FVC for NO₂ on the day of PFT. The associations in the unadjusted models are less consistent and partially reverse in comparison with the associations in the adjusted models (Tables S1 and S2). The direction of the associations in the complete case analyses are similar but less negative (closer to zero) in comparison with the results using multiple imputation. The adjusted associations between short-term NO₂ exposure and lung function did not change greatly in the sensitivity analysis with only nonsmokers.

### Short-Term PM₂.₅ Exposure and Lung Function

Associations between recent PM₂.₅ concentrations and lung function were all negative (Figure 2). A 10 μg/m³ increment of PM₂.₅ 3 d before the PFT was associated with a 0.5 mL (95% CI: −6.7, 5.6) lower FEV₁, and a 10 μg/m³ increment on the day of the PFT (0 d) was associated with a 15.3 mL (95% CI: −21.9, −8.7) lower FEV₁. Associations between FVC and PM₂.₅ ranged from −4.3 mL (95% CI: −11.9, 3.2) for PM₂.₅ 3 d before the PFT to −18.5 mL (95% CI: −26.5, −10.5) for PM₂.₅ on the day of the PFT. The unadjusted results were all negative and with one exception stronger than the adjusted results (Tables S1 and S2). The estimates were again less negative when including only the complete cases. The adjusted associations in the sensitivity analysis with only nonsmokers were consistent with the primary model estimates.

### Long-Term NO₂ and PM₂.₅ Exposure and Lung Function

A 10 μg/m³ increment in 1-y mean NO₂ concentration was associated with a 7.7 mL (95% CI: −15.9, 0.5) lower FEV₁ and a 21.6 mL (95% CI: −31.9, −11.4) lower FVC (Table 3, primary model). The 4-y mean NO₂ concentration was associated with a 0.7 mL (95% CI: −11.6, 10.1) lower FEV₁ and a 13.5 mL (95% CI: −23.4, 23.4) lower FVC. Negative associations were also found for PM₂.₅. The 4-y mean PM₂.₅ concentration was associated with a 3.0 mL (95% CI: −10.0, 10.0) lower FEV₁ and a 6.0 mL (95% CI: −12.4, 2.4) lower FVC.
CI: $-27.2, 0.1$ lower FVC. For PM$_{2.5}$, the 1-y mean concentration was associated with a 42.2 mL (95% CI: $-56.9, -27.5$) lower FEV1 and a 82.0 mL (95% CI: $-100.1, -63.9$) lower FVC. The 4-y mean PM$_{2.5}$ concentration was associated with a 29.7 mL (95% CI: $-54.6, -5.1$) lower FEV1 and a 66.4 mL (95% CI: $-97.5, -35.3$) lower FVC. Unadjusted associations

Note: Day from 0 to $-7$ represents the number of days preceding the pulmonary function test (0 = day of pulmonary function test, $-1$ = one day preceding the pulmonary function test, etc.). NO$_2$, nitrogen dioxide; PM$_{2.5}$, particulate matter with an aerodynamic diameter of $\leq 2.5$ microns; SD, standard deviation.

Figure 1. Multiple linear regression models estimating FEV1 and FVC values per 10 mg/m$^3$ increase in short-term NO$_2$ exposure of the preceding days (0 = day of pulmonary function test) and the corresponding confidence interval in the Swiss population between 2005 and 2012 ($n = 30,371$). The models are adjusted for sex, age, height, weight, smoking status, education, socioeconomic position (SEP index), year, season, time, humidity, and temperature. Multiple imputation was used to deal with missing values in any variables of the analysis model. Note: CI, confidence interval; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; PFT, pulmonary function test.
were more negative except for FEV1 and FVC of the 4-yr mean PM2.5 concentration (Tables S1 and S2). The estimates in the complete-case analyses were inconsistent, showing partially more and less strong associations in comparison with the analysis with multiple imputation. The adjusted associations among nonsmokers were similar to estimates for the entire study population.

Short-Term Deviation in Long-Term Exposure Models

There was little change in effect estimates for long-term air pollutant exposures after adjustment for short-term deviations, i.e., the absolute difference between the air pollutant concentration on the day of the PFT and its 1- or 4-yr mean concentration (Table 3). For example, the estimated difference in FEV1 with a 10 μg/m³ increase in short-term PM2.5 exposure of the preceding days (0 = day of pulmonary function test) and the corresponding confidence interval in the Swiss population between 2003 and 2012 (N = 36,085). The models are adjusted for sex, age, height, weight, smoking status, education, socioeconomic position (SEP index), year, season, time, humidity, and temperature. Multiple imputation was used to deal with missing values in any variables of the analysis model. Note: CI, confidence interval; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; PFT, pulmonary function test.

Table 3. Associations between lung function and long-term NO2 and PM2.5 exposure and the estimated impact of short-term deviations in the Swiss study population (estimated effects per 10 μg/m³ increment).

|                | n    | FEV1 in mL (95% CI) | p-Value | FVC in mL (95% CI) | p-Value |
|----------------|------|---------------------|---------|-------------------|---------|
| NO2: 1-yr mean|      |                     |         |                   |         |
| Primary model  | 25,528| −7.7 (−15.9, 0.5)   | 0.07    | −21.6 (−31.9, −11.4) | <0.001  |
| +short-term dev. |      | −7.7 (−15.9, 0.5)   | 0.07    | −21.5 (−31.8, −11.3) | <0.001  |
| NO2: 4-yr mean|      |                     |         |                   |         |
| Primary model  | 13,964| −0.7 (−11.6, 10.1)  | 0.89    | −13.5 (−27.2, 0.1)  | 0.05    |
| +short-term dev. |      | −1.3 (−12.1, 9.6)   | 0.82    | −14.0 (−27.7, −0.4) | 0.04    |
| PM2.5: 1-year mean |      |                     |         |                   |         |
| Primary model  | 32,826| −42.2 (−56.9, −27.5) | <0.001  | −82.0 (−100.1, −63.9) | <0.001  |
| +short-term dev. |      | −42.4 (−57.1, −27.7) | <0.001  | −82.0 (−100.2, −63.9) | <0.001  |
| PM2.5: 4-year mean |      |                     |         |                   |         |
| Primary model  | 21,058| −29.7 (−54.6, −5.1) | 0.02    | −66.4 (−97.5, −35.3) | <0.001  |
| +short-term dev. |      | −29.0 (−53.6, −4.5) | 0.02    | −65.2 (−96.3, −34.0) | <0.001  |

Note: This table represents the association between lung function (FEV1, FVC) and long-term NO2 and PM2.5 exposure with and without considering short-term deviations in air pollutant concentrations using multiple linear regression. The short-term deviation is defined by the absolute difference between the air pollutant concentration on the day of pulmonary function test and the long-term concentration. All models are adjusted for sex, age, height, weight, smoking status, education, socioeconomic position (SEP index), year, season, time, humidity, and temperature. Multiple imputation was used to deal with missing values in any variables of the analysis model. CI, confidence interval; dev., deviation; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; NO2, nitrogen dioxide; PM2.5, particulate matter with an aerodynamic diameter of ≤2.5 microns.
increase in 4-y mean PM$_{2.5}$ concentration was $-29.7 \text{ mL}$ (95% CI: $-54.6, -5.1$) based on the primary model, compared with $-29.0 \text{ mL}$ (95% CI: $-53.6, -4.5$) after adjustment for short-term deviation in PM$_{2.5}$.

**Discussion**

In Swiss adults who participated in the LuftiBus health campaign, higher short- and long-term exposures to NO$_2$ and PM$_{2.5}$ were associated with lower FEV$_1$ and FVC, with stronger associations for FVC than for FEV$_1$. Associations between PM$_{2.5}$ and lung function were stronger for 1- and 4-y mean concentrations compared with concentrations on the same day or up to 7 d before lung function was measured, whereas associations with long- and short-term NO$_2$ concentrations were similar in magnitude. Adjusting for short-term deviations in air pollutant concentrations had little effect on estimated associations with long-term exposures.

We made two important observations in our study. First, long-term PM$_{2.5}$ exposure was more strongly associated with lower FEV$_1$ and FVC, with stronger associations for long- and short-term NO$_2$ concentrations. Second, we estimated stronger associations with FVC than with FEV$_1$ for long- and short-term exposures to both pollutants. In the meta-analysis of the multicenter European Study of Cohorts for Air Pollution Effects (ESCAPE) with 7,613 participants, associations between lung function and 10 $\mu$g/m$^3$ increments in 1-y PM$_{2.5}$ exposure were similar in magnitude to our estimates (FEV$_1$ $-4.22 \text{ mL}$; 95% CI: $-112.8, 28.2$; FVC $-72.8 \text{ mL}$; 95% CI: $-166.6, 21.0$) (Adam et al. 2015).

Second, we estimated stronger associations with FVC than with FEV$_1$ for long- and short-term exposures to both pollutants. Studies providing lung function changes in percentage instead of with FEV$_1$ for long- and short-term exposures to both pollutants. In the meta-analysis of the multicenter European Study of Cohorts for Air Pollution Effects (ESCAPE) with 7,613 participants, associations between lung function and 10 $\mu$g/m$^3$ increments in 1-y PM$_{2.5}$ exposure were similar in magnitude to our estimates (FEV$_1$ $-4.22 \text{ mL}$; 95% CI: $-112.8, 28.2$; FVC $-72.8 \text{ mL}$; 95% CI: $-166.6, 21.0$) (Adam et al. 2015).

To our knowledge, adjustment for recent air pollutant concentrations has been considered by only two studies of long-term air pollution exposures and lung function (Adar et al. 2015; Rice et al. 2015). In a prospective cohort study with 2,222 participants, a 2 $\mu$g/m$^3$ increase in long-term PM$_{2.5}$ exposure was associated with a 13.5 mL lower FEV$_1$ (95% CI: $-26.2, -0.3$) (Rice et al. 2015). After additionally adjusting for the previous-day PM$_{2.5}$ concentration, the association increased to $-17.6 \text{ mL}$ (95% CI: $-31.0, -4.1$). The Multi-Ethnic Study of Atherosclerosis (MESA), with 3,791 participants ages 45–84 y, reported only that negative associations between lung function (FEV$_1$, FVC) and 1-y average PM$_{10}$, PM$_{2.5}$, and NO$_2$ concentrations were robust to adjustment for 1-d average PM$_{2.5}$ concentrations (Adar et al. 2015). We adjusted for short-term deviations in NO$_2$ and PM$_{2.5}$ concentrations instead of previous- or same-day concentrations and found that adjusting for short-term deviation did not influence or alter conclusions about potential associations between lung function and long-term air pollution exposures. This finding suggests that it may not be necessary to adjust for short-term deviations in air pollution when estimating effects of long-term ambient air pollution exposures on lung function.

The Swiss federal government has introduced limits for annual and daily NO$_2$ and PM$_{2.5}$ concentrations to protect public health (Federal Office for the Environment 2019b). In our study population, 16.2% of the annual NO$_2$ concentrations in 2011 exceeded the statutory annual limit of 30 $\mu$g/m$^3$, and one of the 4,349 estimated daily NO$_2$ concentrations exceeded the daily NO$_2$ limit of 80 $\mu$g/m$^3$. In contrast, annual PM$_{2.5}$ concentrations in 2011 were above the statutory limit of 10 $\mu$g/m$^3$ for all participants. The government has not defined a daily limit for PM$_{2.5}$. Hence, whereas air quality in Switzerland has improved substantially since 1990, air pollutant concentrations in our study population frequently exceeded statutory limits, particularly for PM$_{2.5}$ (Federal Office for the Environment 2019a). At first glance, the estimated effect sizes for short-term exposures seem small, but given recent evidence that NO$_2$ concentrations in Switzerland can vary up to 60 $\mu$g/m$^3$ within a 7-d period, the small estimated differences in lung function with a 10 $\mu$g/m$^3$ increase in exposure may indicate a nonnegligible public health impact.

Nevertheless, we acknowledge some limitations to our study. First, our study population may differ from the general Swiss population by being sicker or healthier (Bopp et al. 2014). Therefore, generalizability of the study results may be limited. Because the Zurich Lung Association is located in the city of Zurich, the health promotion campaign called LuftiBus was most active in the canton of Zurich (62% participants). Hence, measurements from the French-speaking parts of Switzerland are less represented. Second, we enhanced the LuftiBus data set by external data using deterministic record linkage. We cannot completely rule out that there may have been exposure misclassifications for some individuals and that some participants may have moved in the years preceding the PFT. Third, we could not account for exposures at locations other than residence, including exposure to ambient air pollution at workplaces. Because people spend a lot of time at work, it would be appropriate to take into account the air pollutant concentration at the workplace. The fact that we could not consider air pollution exposure at the workplace may have led to an under- or overestimation of the associations. Fourth, we cannot distinguish between various pollutant types; therefore, it may be that pollutants other than NO$_2$ or PM$_{2.5}$ may have caused reduced lung function. If so, NO$_2$ is more likely to represent primary air pollution close to combustion sources like road traffic and cement plants, whereas PM$_{2.5}$ is a surrogate for the spatial distribution of secondary background air pollutants (Manisalidis et al. 2020).

This study benefits from a long exposure time, the linkage with air pollutant concentrations based on fine scale prediction models, a large number of observations, and participants from the general population. Furthermore, we were able to adjust for smoking status, as well as relative humidity and temperature at the day of PFT, which may be important confounders for association with short-term exposures. In conclusion, our findings contribute to the evidence of adverse associations between residential short- and long-term NO$_2$ and PM$_{2.5}$ exposure and lung function in adults. We also provide evidence that short-term deviation of air pollutant concentration does not have significant impact in long-term exposure models. Our findings indicate that controlling air pollution emission is of great importance to protect public health, especially in regard to the lungs.

**Acknowledgments**

This study was funded by the Swiss National Science Foundation and by a Zurich Lung Association grant. The authors thank the Swiss Federal Statistical Office for providing mortality and census data and for the support, which made the SNC and this study possible. The SNC was supported by the Swiss National Science Foundation (grants 3347CO-108806, 33CS30_134273, and 33CS30_148415). The members of the Swiss National Cohort Study Group are M. Egger (Chairman of the Executive Board), A. Spoerri, and M. Zwahlen (all Bern); M.
References

Ackermann-Liebrich U, Leuenberger P, Schwartz J, Schindler C, Monn C, Bolognini G, et al. 1997. Lung function and long-term exposure to air pollutants in Switzerland. Am J Respir Crit Care Med 155(1):122–129, PMID: 9001300, https://doi.org/10.1164/ajrccm.155.1.9001300.

Adam M, Schikowski T, Carsin AE, Cai Y, Jacquemin B, Sanchez M, et al. 2015. Adult lung function and long-term air pollution exposure. ESCAPE: a multi-centre cohort study and meta-analysis. Eur Respir J 45(1):38–50, PMID: 25193394, https://doi.org/10.1183/09031936.0000114.

Adar SD, Kaufman JD, Diez-Roux AV, Hoffman EA, Soutza J, Stokovsky K, et al. 2015. Air pollution and percent emphysema identified by computed tomography in the Multi-Ethnic study of Atherosclerosis. Environ Health Perspect 123(2):144–151, PMID: 25302408, https://doi.org/10.1289/ehp.1307951.

American Thoracic Society. 1991. Lung function testing: selection of reference values and interpretative strategies. Am Rev Respir Dis 144:1202–1218, PMID: 1952453, https://doi.org/10.1164/ajrccm.144.5.1202.

Bopp M, Braun J, Faeh D, Swiss National Cohort Study Group. 2014. Variation in mortality patterns among the general population, study participants, and different types of nonparticipants: evidence from 25 years of follow-up. Am J Epidemiol 180(10):1028–1035, PMID: 25344268, https://doi.org/10.1093/aje/kwu226.

Bopp M, Spoerri A, Zwahlen M, Gutzwiller F, Paccaud F, Braun-Fahrlander C, et al. 2009. Cohort profile: the Swiss National Cohort—a longitudinal study of 8.8 million people. Int J Epidemiol 38(2):379–384, PMID: 18328512, https://doi.org/10.1093/ije/dyn042.

Dauchet L, Hulo S, Cherot-Kornobis N, Matran R, Amouyel P, Edmé J-L, et al. 2018. Short-term exposure to air pollution: associations with lung function and inflammatory markers in non-smoking, healthy adults. Environ Int 121:610–619, PMID: 30312964, https://doi.org/10.1016/j.envint.2018.09.036.

de Hoogh K, Héritier H, Stafoggia M, Künzli N, Kloo J. 2018. Modelling daily PM2.5 concentrations at high spatio-temporal resolution across Switzerland. Environ Pollut 233:1147–1154, PMID: 29037492, https://doi.org/10.1016/j.envpol.2017.11.005.

de Hoogh K, Saucy A, Stein N, Schwartz J, West EA, Strassmann A, et al. 2019. Predicting fine-scale daily NO2 for 2005–2016 incorporating OMI satellite data across Switzerland. Environ Sci Technol 53(17):10279–10287, PMID: 31415154, https://doi.org/10.1021/acs.est.9b03107.

Edginton S, D’Sullivan DE, King W, Lougheed MD. 2019. Effect of outdoor particulate air pollution on FEV1 in healthy adults: a systematic review and meta-analysis. Occup Environ Med 76(8):583–591, PMID: 31188964, https://doi.org/10.1136/semed-2018-105420.

Egger M, Spoerri A, Zwahlen M. 2018. The Swiss National Cohort. [https://www.swissnationalcohort.ch] (accessed 25 May 2020).

Federal Office for the Environment. 2019a. Grafiken Jahresarwerte NABEL. Federal Office for the Environment. 2019b. Luftqualität 2018. Messresultate des Nationalen Beobachtungsinstitutes und NABEL. Bern, Switzerland: BAFU.

Göttschi T, Heinrich J, Suryer J, Künzli N. 2008. Long-term effects of ambient air pollution on lung function: a review. Epidemiology 19(5):690–701, PMID: 18703932, https://doi.org/10.1097/EDE.0b013e318181650f.

Guo C, Zhang Z, Lau AKH, Lin CO, Chuang YC, Chan J, et al. 2018. Effect of long-term exposure to fine particulate matter on lung function decline and risk of chronic obstructive pulmonary disease in Taiwan: a longitudinal, cohort study. Lancet Planet Health 2(3):e114–e125, PMID: 29615226, https://doi.org/10.1016/S2542-5196(18)30008-7.

Leevelev J, Evans JS, Fnais M, Giannadaki D, Pozzer A. 2015. The contribution of outdoor air pollution sources to premature mortality on a global scale. Nature 525(7598):367–371, PMID: 26381985, https://doi.org/10.1038/nature15371.

Manalisid I, Stavropoulou E, Stavropoulos A, Bezirtzoglou E. 2020. Environmental and health impacts of air pollution: a review. Front Public Health 8:1–13, PMID: 32154200, https://doi.org/10.3389/fpubh.2020.00001.

Miller MR, Hankinson J, Brusasco V, Burgess F, Casaburi R, Coates A, et al. 2005. Standardisation of spirometry. Eur Respir J 26(2):319–338, PMID: 16055882, https://doi.org/10.1183/09031936.05.0003405.

Panczak R, Galobardes B, Voorpostel M, Spoerri A, Zwahlen M, Egger M, et al. 2012. A Swiss neighbourhood index of socioeconomic position: development and association with mortality. J Epidemiol Community Health 66(12):1129–1136, PMID: 22717282, https://doi.org/10.1136/jech-2011-200699.

Panić L, Provest EB, Cox B, et al. 2017. Short-term air pollution exposure decreases lung function: a repeated measures study in healthy adults. Environ Health 16:60, PMID: 28615020, https://doi.org/10.1186/s12940-017-0271-z.

Rice MB, Ljungman PL, Wilker EH, Gold DR, Schwartz JD, Koutrakis P, et al. 2013. Short-term exposure to air pollution and lung function in the Framingham Heart Study. Am J Respir Crit Care Med 188(11):1351–1357, PMID: 24200465, https://doi.org/10.1164/ajrccm.201308-1414OC.

Rice MB, Ljungman PL, Wilker EH, Dorans KS, Gold DR, Schwartz JD, et al. 2015. Long-term exposure to traffic emissions and fine particulate matter and lung function decline in the Framingham Heart Study. Am J Respir Crit Care Med 191(6):656–664, PMID: 25596321, https://doi.org/10.1164/rrc.201410-1575OC.

Schindler C, Künnzli N, Bongard JP, Leuenberger P, Karrer W, Rapp R, et al. 2001. Short-term variation in air pollution and in average lung function among never-smokers: the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA). Am J Respir Crit Care Med 163(2):356–361, PMID: 11179106, https://doi.org/10.1164/ajrccm.163.2.9911116.

Sun Z, Zhu D. 2019. Exposure to outdoor air pollution and its human health outcomes: a scoping review. PLoS One 14(10):e0216550, PMID: 31955992, https://doi.org/10.1371/journal.pone.0216550.

UNESCO (United Nations Educational, Scientific and Cultural Organization). 1997. International Standard Classification of Education - ISCED 1997. Paris, France: UNESCO.

van Buuren S, Groothuis-Oudshoorn K. 2011. mice: multivariate imputation by chained equations in R. J Stat Softw 45(1):44–67, https://doi.org/10.18637/jss.v045.i03.

Weimayr G, Romeo E, Sario MD, Weiland SK, Forastiere F. 2010. Short-term effects of PM2.5 and NO2 on respiratory health among children with asthma or asthma-like symptoms: a systematic review. Environ Health Perspect 118(6):449–457, PMID: 20064765, https://doi.org/10.1289/ehp.990844.

White IR, Royston P, Wood AM. 2011. Multiple imputation using chained equations. Stat Med 30(4):377–399, PMID: 21225900, https://doi.org/10.1002/sim.4067.

WHO (World Health Organization). 2016. Ambient air pollution: a global assessment of exposure and burden of disease. Clean Air J 26(2), https://doi.org/10.17159/2410-972X/2016/v26n2a4.

Zurich Lung Association. 2020. LuftiBus. [https://www.lunge-zuerich.ch/de/projekte/luftibus] (accessed 25 May 2020).