The impact of second-hand smoke on nitrogen oxides concentrations in a small interior

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Nitrogen oxides (NOx), especially nitrogen dioxide (NO2), are among the most hazardous forms of air pollution. Tobacco smoke is a main indoor source of NOx, but little information is available about their concentrations in second-hand smoke (SHS), particularly in small indoors. This study presents data of NOx and its main components nitric oxide (NO) and NO2 in SHS emitted by ten different cigarette brands measured in a closed test chamber with a volume of 2.88 m3, similar to the volume of vehicle cabins. The results show substantial increases in NOx concentrations when smoking only one cigarette. The NO2 mean concentrations ranged between 105 and 293 µg/m3, the NO2 peak concentrations between 126 and 357 µg/m3. That means the one-hour mean guideline of 200 µg/m3 for NO2 of the World Health Organization was exceeded up to 47%, respectively 79%. The measured NO2 values show positive correlations with the values for tar, nicotine, and carbon monoxide stated by the cigarette manufacturers. This study provides NO2 concentrations in SHS at health hazard levels. These data give rise to the necessity of health authorities’ measures to inform about and caution against NOx exposure by smoking in indoor rooms.

Air pollution is potentially the greatest environmental risk factor for health worldwide. The World Health Organization (WHO) estimates 4.2 million premature deaths per year caused by ambient (outdoor) air pollution and 3.8 million premature deaths caused by indoor air pollution1. Since the sulfur dioxide concentrations in the atmosphere decreased in the last decades, the focus is set more and more on particulate matter (PM), ozone, and nitrogen dioxide (NO2) as the most hazardous air pollutions2.

Nitrogen oxides (NOx), mainly nitric oxide (NO), and, at a lower level, NO2, are gases formed by combustion processes at high temperatures3. The main anthropogenic outdoor sources are the combustion of fossil and green fuels in vehicles and power plants. Important indoor sources are oil-, gas-, kerosene-, coal-, and wood-burning ovens, heaters or open fireplaces, and tobacco smoke4. In the last years, NOx emissions caused by road traffic and diesel vehicles, in particular, came into the focus of the public and policy. Emission limit values of engines were discussed and tightened. The aim was not to exceed the determined limit values of NO2 in ambient air too often, particularly in metropolitan areas. The air quality standards of the European Union for NO2 in ambient air are currently 200 µg/m3 (1 h mean, should not exceed more than 18 times each year) and an annual mean of 40 µg/m3 5. Therewith, they followed the recommendations of the WHO air quality guidelines from 20056. As indoor air pollution came more and more into the focus, the WHO published in 2010 guidelines for indoor air quality, whereby the NO2 limit values are consistent with the values for ambient air4.

NO2, in particular, is associated with a lot of adverse health effects on several organ systems7. Long-term exposure to NO2 besides PM, is an important risk factor for cardiopulmonary mortality7. Moreover, the NO2 concentration is positively associated with a variety of harmful effects, the mortality of respiratory and cardiovascular diseases, and lung cancer8.

NO is largely considered a toxic pollutant. The exposure can cause, among others, irritation to the skin, eyes, and respiratory system, but also unconsciousness and methemoglobinemia10. Albeit, NO may be hazardous to the health of humans not until relatively high doses11. For workplace atmospheres, the U.S. National Institute for Occupational Safety and Health gives an NO exposure limit value (8 h time-weighted-average) of 25 ppm (30 mg/m3)10. Under environmental conditions, NO will be quickly oxidized to NO2 by, e.g., ozone or oxygen. This oxidation process is, however, much slower under indoor conditions4,12.

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Several studies investigated indoor air pollution, including NOx, respectively NOx concentrations, caused by ovens (primarily gas stoves) or fireplaces for heating or cooking. Some studies focused on tobacco smoke reporting a relatively lower influence on NOx concentrations by burning tobacco products in normal-sized rooms or houses. The impact of second-hand smoke (SHS) on NOx burden in very small indoors like smoking cabins, telephone cells, or cabins of vehicles, for example, remains widely unclear. This study presents the results of the NO, NO2, and NOx investigations in SHS of ten different cigarette brands with different strengths, additives, and origin in a 2.88 m3 measuring chamber. The measurements were realized as part of the Tobacco Smoke Particles and Indoor Air Quality (ToPIQ) studies at two PM investigations. The PM-related results of these studies are already described and published.

### Material and methods

**Tobacco products.** The concentrations of NO, NOx, and NOy in SHS were measured of nine commercial cigarette brands (named cigarette A to I) and the 3R4F reference cigarette (Kentucky Tobacco Research and Development Center, University of Kentucky, USA). As the measurements took place during two PM investigations, the reference cigarettes (RC) were termed RC1 and RC2. The cigarette brands A, C, and E were bought at the International Airport of Dubai, United Arab Emirates (UAE), while the brands B, D, and F were from the International Airport of Frankfurt, Germany. Additionally, three mentholated cigarette brands (G, H, I) were tested, purchased at the central station, Frankfurt, Germany. The brand names of the cigarettes are given in Table 1. The cigarette brands differ in amounts of tar, nicotine, carbon monoxide (CO), and PM10 (Table 1). Further information on the cigarettes from Germany is available from the tobacco additives database of the Federal Ministry of Food and Agriculture of Germany.

### Test chamber. All measurements took place in a test chamber with an internal volume of 2.88 m3. During the experiments, the vents for the supply and exhaust air were closed to minimize air exchange. The test chamber is placed in a laboratory room of the Institute of Occupational Medicine, Social Medicine and Environmental Medicine, Goethe University Frankfurt. The institute is located in an urban area but not near a traffic road. That avoided high NOx concentrations in ambient air by road traffic (see baseline evaluation).

### Ambient nitrogen oxide monitor (NOx monitor). To ascertain the NO, NOy, and NOx (NO + NOx) concentrations of SHS, the ambient nitrogen oxide monitor APNA-370 of HORIBA, Ltd. (Kyoto, Japan) was applied. By using a cross-flow modulated semi-decompression chemiluminescence method, NOx concentrations were internally calculated from those of NO and NOy. All measurement values were recorded in the unit ppm (parts per million) every three minutes. The not mixed sample air was collected at a point 40 cm above the burning tobacco product and 170 cm above the floor of the test chamber.

### Automatic environmental tobacco smoke emitter. SHS was generated in the closed test chamber by an Automatic Environmental Tobacco Smoke Emitter (AETSE), developed and constructed by Schimpf Ing. (Trondheim, Norway). This programmable microprocessor-controlled smoke pump imitated the smoker by moving a 200 ml glass syringe connected with the mouthpiece of the tobacco product via a polyamide tube. Moving the syringe led to puffing the tobacco product. Two valves controlled the air stream and pressed the

| Brand Tested cigarettes (n) | Tar (mg) | Nicotine (mg) | Carbon monoxide (mg) | Particulate matter PM10 (µg/m3) | Format and attribute |
|-----------------------------|---------|---------------|----------------------|-------------------------------|---------------------|
| Reference Cigarette 3R4F (RC1, RC2) | 41 (RC1 = 21, RC2 = 20) | 9.4 | 0.73 | 12 | 1147 | KS Filter |
| Cigarette A Marlboro Gold UAE | 20 | 6 | 0.5 | 7 | 1163 | KS Filter |
| Cigarette B Marlboro Gold GER | 20 | 6 | 0.5 | 7 | 874 | KS Filter |
| Cigarette C Winston Red UAE | 20 | 7 | 0.6 | 7 | 1016 | KS Filter |
| Cigarette D Winston Classic GER | 18 | 10 | 0.8 | 10 | 778 | KS Filter |
| Cigarette E Parliament Platinum UAE | 24 | 1 | 0.1 | 1 | 1099 | KS Filter |
| Cigarette F Parliament Night Blue GER | 24 | 10 | 0.8 | 10 | 1071 | 100 s Filter |
| Cigarette G Pall Mall Menthol Blast | 15 | 10 | 0.8 | 10 | 1103 | KS Filter, mentholated |
| Cigarette H Winston Menthol | 22 | 10 | 0.8 | 10 | 1182 | KS Filter, mentholated |
| Cigarette I Eliry Menthol | 21 | 10 | 0.8 | 10 | 1186 | KS Filter, mentholated |
mainstream smoke after each puff into the closed chamber. Between the puffs, the tobacco product smoldered and produced side-stream smoke. In doing so, no person was exposed to the generated SHS.

**Smoking protocol.** The number (n) of investigated cigarettes of each brand varied between 15 and 41 (Table 1). According to the ToPIQ studies23–25, all cigarettes were smoked following a modified protocol. Puff volume was 40 ml, and the flow rate was 13 ml/s. After two ignition puffs, each cigarette was smoked in the combustion phase with seven puffs and a frequency of two puffs/min. Subsequently, the post-combustion phase followed after the extinguishing of the cigarette. After ten minutes in total, the chamber was ventilated with outdoor air by an industrial radial fan for at least five minutes to clean the air.

**Baseline evaluation.** As the NOx monitor detected data permanently, continuous measuring data of 61 h between the two measuring campaigns without SHS generation were chosen to determine the baseline values of NO, NO2, and NOx.

**Data processing.** The NOx monitor provided every three minutes measuring data. Therefore, in the 10-min combustion and post-combustion phase, three values of NO, NO2, and NOx, respectively, per investigated cigarette could be taken into account for the following data processing. The mean concentrations (Cmean) of these three measuring values of NO, NO2, and NOx were calculated. Additionally, the highest values of NO, NO2, and NO were considered as peak values (Cpeak) for each cigarette. For the statistical analysis, all Cmean and Cpeak values were tested for outliers (Grubbs' test). Sixteen outliers were detected and subsequently excluded from further statistical tests. All data were normally distributed. To compare the data of all investigated cigarettes, a one-way analysis of variance (ANOVA) including Tukey's multiple comparison test was performed.

The associations of the Cmean values of NO, NO2, and NOx with concentrations of tar, nicotine, CO, and PM10 were examined by using correlation analysis (Spearman) and linear regression. PM10 is classified by the US Environmental Protection Agency (EPA) as inhalable particles ≤ 10 µm and includes the fraction of the fine inhalable particles ≤ 2.5 µm (PM2.5).36 The measured PM10 Cmean values of RC1 were lower than those of RC2. Therefore, it was necessary to adjust the PM10 data of RC1 and the associated cigarette brands G, H, and I on the PM10 data of RC2 by statistical data transformation (Y = K°Y) using the factor K = 1.47.

**Software**. The statistical analyses were performed using GraphPad Prism software (version 8 for Windows, GraphPad Software, La Jolla California USA, www.graphpad.com).

**Data conversion.** For the comparison of the in this study measured values with common used limit values or guidelines, the data of NO and NO2 were converted in µg/m3 using the formula31:

\[
c [\text{µg/m}^3] = 0.0409 \times c [\text{ppb}] \times MW [\text{g/mol}] \times 1013.25 \text{ mbar and 25 °C}
\]

where c concentration, ppb parts per billion, MW molecular weight, MW NO = 30.01 g/mol, MW NO2 = 46.01 g/mol.

As the NOx monitor display the data in ppm, all values were multiplied by 1000 to convert to the unit ppb (parts per billion).

**Results**. Table 2 and Fig. 1 present the NO, NO2, and NOx results of Cmean and Cpeak of all investigated cigarette brands.

Regarding NO, the range of the Cmean values was from 132 to 422 ppb (equal to 162 µg/m3 to 518 µg/m3 at 1013.25 mbar and 25 °C). For NO2, the Cmean values ranged from 56 to 156 ppb (equal to 105 µg/m3 to 293 µg/m3 at 1013.25 mbar and 25 °C). Looking at the Cmean data of NOx, the values ranged from 247 to 499 ppb. The ranges of the ascertainment peak values (Cpeak) were as followed: NO: 207 ppb to 584 ppb (equal to 254 µg/m3 to 716 µg/m3 at 1013.25 mbar and 25 °C). NO2: 67 ppb to 190 ppb (equal to 126 µg/m3 to 357 µg/m3 at 1013.25 mbar and 25 °C). NOx: 349 ppb to 661 ppb.

To compare the measured NOx values in SHS with the usually NOx concentration in indoor air at the study location, we took continuous data of 61 h where no investigation was done into account recorded between the two measurement campaigns. The mean of the thus collected data resulted in the baselines for NO = 0.072 ppb (equal to 0.1 µg/m3 at 1013.25 mbar and 25 °C), NO2 = 5.08 ppb (equal to 9.6 µg/m3 at 1013.25 mbar and 25 °C) and NOx = 5.15 ppb.

A detailed overview of associations of the Cmean Values of NO, NO2, and NOx with concentrations of tar, nicotine, CO, and PM10 shows Table 3. Additionally, Fig. 2 presents the correlations between NO, NO2, and NOx and the stated amounts of tar (A), nicotine (B), CO (C), and the measured values of PM10 (D). The measured NO data are negatively correlated with the concentrations of tar, nicotine, and CO as specified by the cigarette manufacturers. The concentrations of NOx correlates positively with the stated values of tar, nicotine, and CO. NOx correlated negatively with the concentrations of tar, nicotine, and CO, but in the case of CO without significance. The measured PM10 values show no correlations with the concentrations of NO, NO2, and NOx.

**Discussion**. The measured indoor baseline concentration revealed for NO2 a mean value of 9.6 µg/m3 (5.08 ppb). That is in line with previous studies on NO2 indoor concentrations35. Our findings show remarkable rises of NO2 in small indoors by the smoke of only one cigarette. Of all ten tested cigarette brands, the measured Cmean values of five brands exceeded the WHO one-hour mean guideline of 200 µg/m3 for NO2 by 9% to 47%. The remaining five brands showed between 1.5% and 47% lower NO2 values compared to the WHO guideline. The measured NO2 Cmean Value of all examined cigarettes was 215 µg/m3 (119 ppb) and, therefore, exceeded the WHO guideline by
8%. Regarding the detected C_{peak} values of NO\textsubscript{2}, six brands exceeded the WHO guideline even in a range from 12 to 79%. Four brands were 12% to 37% below the guideline. The NO\textsubscript{2} C_{peak} mean value of all cigarettes was 264 µg/m\textsuperscript{3} (140 ppb) and consequently 32% higher than the WHO guideline value. The WHO state unambiguously "that NO\textsubscript{2}—at short-term concentrations exceeding 200 µg/m\textsuperscript{3}—is a toxic gas with significant health effects"\textsuperscript{6}. It should be borne in mind that the WHO annual mean guideline for NO\textsubscript{2} is with 40 µg/m\textsuperscript{3} even stricter\textsuperscript{4}. There are other guidelines often following the WHO indoor and ambient guidelines for NO\textsubscript{2}, but some differ\textsuperscript{32}. At Health Canada, for example, there is an indoor short-term limit value of 170 µg/m\textsuperscript{3} and a long-term limit value of 20 µg/m\textsuperscript{3} based on toxicological data\textsuperscript{35}.

Several former studies dealt with NO\textsubscript{x} emitted by tobacco products in normal-sized indoor rooms. Cyrys et al.\textsuperscript{20} reported NO\textsubscript{2} mean concentrations in living rooms in Hamburg and Erfurt (both Germany) of 17 µg/m\textsuperscript{3}.

Table 2. Mean concentrations (C_{mean}) and peak concentrations (C_{peak}) of nitric oxide (NO), nitrogen dioxide (NO\textsubscript{2}), and nitrogen oxides (NO\textsubscript{x}) of the measured baseline (BL), reference cigarette 3R4F (RC1, RC2), and the cigarette brands A (Marlboro Gold UAE), B (Marlboro Gold GER), C (Winston Red UAE), D (Winston Classic GER), E (Parliament Platinum UAE), F (Parliament Night Blue GER), G (Pall Mall Menthol Blast), H (Winston Menthol), and I (Elixyr Menthol). UAE United Arab Emirates, GER Germany. The given concentrations in the unit µg/m\textsuperscript{3} were calculated using the formula \(c (\mu g/m^3) = 0.0409 \times c (ppb) \times MW (g/mol)\) (at 1013.25 mbar and 25° C, c = concentration, ppb = parts per billion, MW = molecular weight, MW NO = 30.01 g/mol, MW NO\textsubscript{2} = 46.01 g/mol). Standard deviations are stated in brackets. n/a = not available.

|   | C_{mean} NO (ppb) | C_{peak} NO (µg/m\textsuperscript{3}) | C_{peak} NO (ppb) | C_{mean} NO\textsubscript{2} (ppb) | C_{mean} NO\textsubscript{2} (µg/m\textsuperscript{3}) | C_{peak} NO\textsubscript{2} (ppb) | C_{peak} NO\textsubscript{2} (µg/m\textsuperscript{3}) | C_{mean} NO\textsubscript{x} (ppb) | C_{mean} NO\textsubscript{x} (µg/m\textsuperscript{3}) | C_{peak} NO\textsubscript{x} (ppb) | C_{peak} NO\textsubscript{x} (µg/m\textsuperscript{3}) |
|---|------------------|----------------------------------|------------------|----------------------------------|----------------------------------|------------------|----------------------------------|----------------------------------|----------------------------------|------------------|----------------------------------|
| BL | 0.11 (0.15) | 0.1 | n/a | 5.08 (2.14) | 9.6 | n/a | 5.15 (2.21) | n/a |
| RC1 | 226 (57) | 277 | 319 (64) | 391 | 155 (15) | 292 | 190 (28) | 357 |
| RC2 | 209 (29) | 256 | 307 (48) | 377 | 152 (16) | 286 | 180 (21) | 339 |
| A | 394 (36) | 483 | 563 (70) | 691 | 80 (7) | 150 | 94 (8) | 177 |
| B | 300 (65) | 368 | 405 (79) | 497 | 105 (8) | 197 | 119 (7) | 224 |
| C | 367 (70) | 450 | 532 (105) | 653 | 56 (15) | 105 | 67 (18) | 126 |
| D | 132 (35) | 162 | 207 (51) | 254 | 116 (18) | 218 | 137 (23) | 258 |
| E | 422 (35) | 518 | 584 (70) | 716 | 79 (4) | 149 | 91 (4) | 171 |
| F | 227 (63) | 278 | 316 (80) | 388 | 125 (17) | 125 | 144 (20) | 271 |
| G | 153 (42) | 188 | 245 (72) | 301 | 151 (24) | 284 | 175 (26) | 329 |
| H | 188 (25) | 231 | 269 (46) | 330 | 139 (11) | 261 | 162 (11) | 305 |
| I | 164 (30) | 201 | 232 (52) | 285 | 156 (21) | 293 | 184 (28) | 346 | 317 (40) | 397 (48) |

Figure 1. Mean and peak concentrations (ppb) of nitric oxide (NO), nitrogen dioxide (NO\textsubscript{2}), and nitrogen oxides (NO\textsubscript{x}) of the reference cigarette 3R4F (RC1, RC2) and the cigarette brands A to I. Baseline (BL) only given at mean concentrations.
and 15 µg/m³, respectively, an increase of 18% in smokers' homes, and an increase of 41% in households using gas for cooking, the main indoor source of NO₂. Additionally, the authors found that outdoor sources can influence indoor NO₂ levels more than indoor sources depending on the location and season of year. However, they differentiated between smoking and non-smoking in the living room (including the use or non-use of gas in the household) and reported on their influence on indoor NO₂ levels in general. They did not report on the influence of one single combustion event (burning cigarette or gas cooking, e.g.) and how this can boost NO₂ concentration in the indoor air temporarily. Slightly lower NO₂ mean concentrations (2–3 weeks averaged) were found

Table 3. Spearman correlations of the C_mean values of NO, NO₂, and NOₓ with concentrations of tar, nicotine, CO (as specified by the cigarette manufacturers), and PM₁₀. P values show the significance of the correlations. ns = not significant (P ≥ 0.05). * = significant (P = 0.01 to 0.05). ** = very significant (P = 0.001 to 0.01). *** = very significant (P < 0.001).

|                     | Spearman r | 95% Confidence Interval | R squared | P value (two-tailed) | P value summery | Significant? (P<0.05) |
|---------------------|------------|--------------------------|-----------|---------------------|-----------------|----------------------|
| NO versus Tar       | −0.87      | −0.9664 to −0.543        | 0.75      | 0.001               | **              | Yes                  |
| NO versus Nicotine  | −0.87      | −0.9664 to −0.543        | 0.75      | 0.001               | **              | Yes                  |
| NO versus CO        | −0.67      | −0.9098 to −0.099         | 0.45      | 0.027               | *               | Yes                  |
| NO versus PM        | 0.10       | −0.6743 to 0.542         | 0.11      | 0.760               | ns              | No                   |
| NO, versus Tar      | 0.62       | 0.0163 to 0.8943         | 0.39      | 0.046               | *               | Yes                  |
| NO, versus Nicotine | 0.62       | 0.0163 to 0.8943         | 0.39      | 0.046               | *               | Yes                  |
| NO₂ versus CO       | 0.85       | 0.5075 to 0.9630         | 0.73      | 0.001               | **              | Yes                  |
| NO₂ versus PM       | 0.57       | −0.0666 to 0.8764        | 0.32      | 0.071               | ns              | No                   |
| NO₂, versus Tar     | −0.93      | −0.9838 to −0.7521       | 0.87      | <0.001              | ***             | Yes                  |
| NO₂, versus Nicotine| −0.93      | −0.9838 to −0.7521       | 0.87      | <0.001              | ***             | Yes                  |
| NO₂, versus CO      | −0.60      | −0.8879 to 0.0148        | 0.36      | 0.053               | ns              | No                   |
| NO₂, versus PM      | −0.84      | −0.6378 to 0.5866        | <0.01     | 0.909               | ns              | No                   |

Figure 2. Association between nitric oxide (NO), nitrogen dioxide (NO₂), and nitrogen oxides (NOₓ) concentrations and concentrations of tar (A), nicotine (B), carbon monoxide (CO) (C), and particulate matter (PM₁₀) (D). Coefficients of determination (R²) of linear regression: NO-tar: 0.779; NO-nicotine: 0.753; NO-CO: 0.684; NO-PM₁₀: 0.007; NO₂-tar: 0.526; NO₂-nicotine: 0.462; NO₂-CO: 0.592; NO₂-PM₁₀: 0.105; NOₓ-tar: 0.718; NOₓ-nicotine: 0.724; NOₓ-CO: 0.5; NOₓ-PM₁₀: 0.079.
in Scottish and Irish homes: 12.8 µg/m² (6.82 ppb) in smokers’ homes and 16.9 µg/m³ (9.01 ppb) in households where gas was used for cooking²². In a 20 m² room with a volume of 57 m³, water pipes were smoked in four-hour sessions, and NO and NO₂ concentrations were measured²¹. The authors reported for the smoking sessions a NO mean concentration of 100 ppb and a NO₂ mean concentration of 60 ppb, meaning 123 µg/m³ and 113 µg/m³, respectively. That indicates that smoking significantly increases NO₂ concentrations also in normal-sized indoor rooms. Our study found remarkable mean values (up to 518 µg/m³ for NO and 293 µg/m³ for NO₂) and peak values (up to 716 µg/m³ for NO and 357 µg/m³ for NO₂) caused by smoking of only one cigarette. Admittedly, the measuring chamber with an indoor volume of 2.88 m³ corresponds more to vehicle indoor volumes than indoor volumes of living rooms. However, it can be assumed that chain-smoking or simultaneously smoking of several cigarettes (by several smokers) will increase NOx concentrations also in larger rooms in a similar way. Therefore, this should be in focus for future studies.

The present findings show statistically significant correlations between the strength of a cigarette brand (amount of tar, nicotine, and CO as stated by the manufacturers) and the measured data of NO, NO₂, and NOₓ. Interestingly, the lower the tar, nicotine, and CO values, the higher were the measured NO and NO₂ levels, while the measured NO₂ levels correlated positively with the cigarette strength but with lower significance. The higher the combustion temperature, the more NO₂ will be generated. Also, the content of bound nitrogen in the tobacco product in the form of nitrate or nitrosamine compounds, e.g., could influence the NOₐ amount in tobacco smoke²³,²⁴. Possibly, “lighter” cigarettes burn at smoking with higher combustion temperatures or contain more bound nitrogen. Further investigations on more numerous cigarette brands with various strengths should also examine the burning temperature and the nitrogen amount in the tobacco product. It was reported that NO and NO₂ concentrations in the mainstream smoke of cigarettes correlated positively with their strength³⁶, whereby generation of mainstream smoke took place in a smoking machine following ISO machine-smoking conditions with an as short as possible distance to the NOₓ analyzer³⁷. This set-up is rather comparable to a smokers’ NOₓ exposure inhaling mainstream smoke. In opposite to this, we simulated the situation of a person exposed to SHS near a burning cigarette. Other studies focusing on NOₓ in mainstream smoke detected mainly NO but almost no NO₂. Among others, it was assumed that the reducing conditions near the glowing zone of the cigarette favored the formation of NO as the lower oxide of nitrogen or that reactive volatile organic compounds (VOCs) in the tobacco smoke react with NO₂. Some NO₂ was detected in the mainstream smoke from the initial puff, but not from the following puffs, while NO was detected continuously in the side-stream smoke⁴⁰. Only when using a Cambridge filter pad between the cigarette and the analyzer NO₂ was observed for each puff. The on the pad sampled smoke of the previous puffs could have interacted with NO in the smoke forming NO₂. As the pad also acted as a barrier between the cigarette and the analyzer, the smoke could age, and, consequently, NO₂ values could increase⁴⁰. That indicates that the more toxic NO₂ is mainly detectable in side-stream smoke and aged smoke but less in mainstream smoke and during a prompt measurement. Since SHS is mainly composed of side-stream smoke (85%)⁴¹, the detection of NO₂ in SHS is plausible. In addition, the smoke generated in this study had time to age.

A strength of the present study was that the used measuring set-up in the test chamber allowed to create and investigate SHS in a reproducible way without the exposition of any person to tobacco smoke. A methodological limitation was the low frequency of only three measurements per cigarette by the NOₓ monitor used. Therefore, the real peak values of NO, NO₂, and NOₓ could not be detected in all investigated cigarettes. That resulted possibly in slightly too low C_mean and C_peak measurement values.

Conclusion
In the last years, the discussion about NO and especially NOₓ generated by diesel vehicles in urban areas has made massive waves. To name is the so-called Dieselgate scandal commenced in September 2015³². The focus was set on ambient NOₓ formation, certainly, influencing also indoor burden by NOₓ. But, smoking is a not neglecting source of NOₓ in indoor rooms. The present study provides NOₓ concentrations in SHS generated by smoking cigarettes in small indoors at levels known to be a health hazard. Keeping in mind that the used test chamber (2.88 m³) has a similar volume to vehicle cabins³⁵, smoking in cars can lead to a hazardous increase of NOₓ concentration. This risk multiples accordingly if more than one cigarette is smoked (e.g., chain smoking), there is more than one smoker in the car, or the car is driven with closed windows without sufficient ventilation. Therefore, health authorities’ measures are useful and required to inform about and caution against NOₓ exposure by smoking in cars and other indoor rooms.

Data availability
Datasets of this study are available from the corresponding author upon request.

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Author contributions
M.B., D.K., R.M., and D.A.G. contributed significantly to the conception and design of the study. Moreover, they prepared the experiments, which were performed by M.B. M.B. analyzed the data. The manuscript was written by M.B. and critically reviewed by all authors. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors have read and approved the final manuscript.

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Additional information
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