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$PM_{2.5}$ and NO_2 exposure errors using proxy measures, including derived personal exposure from outdoor sources: A systematic review and meta-analysis

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ABSTRACT

Background: The use of proxy exposure estimates for $PM_{2.5}$ and NO_2 in air pollution studies instead of personal exposures, introduces measurement error, which can produce biased epidemiological effect estimates. Most studies consider total personal exposure as the gold standard. However, when studying the effects of ambient air pollution, personal exposure from outdoor sources is the exposure of interest.

Objectives: We assessed the magnitude and variability of exposure measurement error by conducting a systematic review of the differences between personal exposures from outdoor sources and the corresponding measurements for ambient concentrations in order to increase understanding of the measurement error structures of the pollutants.

Data sources and eligibility criteria: We reviewed the literature (ISI Web of Science, Medline, 2000–2016) for English language studies (in any age group in any location (NO_2) or Europe and North America ($PM_{2.5}$)) that reported repeated measurements over time both for personal and ambient $PM_{2.5}$ or NO_2 concentrations. Only a few studies reported personal exposure from outdoor sources. We also collected data for infiltration factors and time-activity patterns of the individuals in order to estimate personal exposures from outdoor sources in every study.

Study appraisal and synthesis methods: Studies using modelled rather than monitored exposures were excluded. Type of personal exposure monitor was assessed. Random effects meta-analysis was conducted to quantify exposure error as the mean difference between "true" and proxy measures.

Results: Thirty-two papers for $PM_{2.5}$ and 24 for NO_2 were identified. Outdoor sources were found to contribute 44% (range: 33–55%) of total personal exposure to $PM_{2.5}$ and 74% (range: 57–88%) to NO_2. Overall estimates of personal exposure (24-hour averages) from outdoor sources were 9.3 $\mu g/m^3$ and 12.0 ppb for $PM_{2.5}$ and NO_2 respectively, while the corresponding difference between these exposures and the ambient concentrations (i.e. the measurement error) was 5.72 $\mu g/m^3$ and 7.17 ppb. Our findings indicated also higher error variability for NO_2 than $PM_{2.5}$. Large heterogeneity was observed which was not explained sufficiently by geographical location or age group of the study sample.

Limitations, conclusions and implications of key findings: Relying only on information available in published studies led to some limitations: the contribution of outdoor sources to total personal exposure for NO_2 had to be inferred, individual variation in exposure misclassification was unavailable and instrument error could not be addressed. The larger magnitude and variability of errors for NO_2 compared with $PM_{2.5}$ has implications for biases in the health effect estimates of multi-pollutant epidemiological models. Results suggest that further research is needed regarding personal exposure studies and measurement error bias in epidemiological models.

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1. Introduction

Air pollution exposure is a major public health concern worldwide (Cohen et al., 2017). There is strong evidence from epidemiologic studies that exposure, mainly to particulate matter but also gaseous pollutants, is associated with several health outcomes (Thurston et al., 2017). The concentration-response functions estimated in epidemiological investigations are often applied in health impact assessments, where an association is implicitly treated as causal (Williams et al., 2018; Walton et al., 2019). The choice of functions, however, is not straightforward as biases may occur due to exposure measurement error (Armstrong, 1998; Zeger et al., 2000).

Epidemiological studies often use ambient concentrations of pollutants, either measured at fixed monitoring stations or modelled, as their exposure metric. However, this is only a proxy of the actual exposure of interest, namely personal exposure to pollutants from outdoor sources. The question arises whether ambient concentrations can be considered as a good surrogate for personal exposures (Sarnat et al., 2006; Janssen et al., 1999; Sarnat et al., 2001; Mage et al., 1999; Koutrakis et al., 2005). In general, using proxy exposure estimates, introduces measurement error, which can produce biased estimates in observational studies (Zeger et al., 2000; Dionisio et al., 2014; Schwartz et al., 2007). This can cause problems in attributing health impacts correctly to different pollutants as the biases in the associations between exposures and health outcomes can differ by exposure (World Health Organization, 2013; COMEAP, 2015).

In measurement error theory, one typically contrasts a hypothetical error-free exposure and one (or more) error-prone exposure measures. In air pollution time-series studies, the most commonly used error-prone exposure is measured ambient concentrations from fixed monitors (*C*). These measurements account for neither the different time activities of the individuals nor the spatial heterogeneity of the pollutants and are subject to a mixture of classical and Berkson error (Zeger et al., 2000; Deffner et al., 2018). The contribution of each type of error to the observed measurements may differ by pollutant, for example because $PM_{2.5}$ is more spatially homogeneous than NO_2. Taking the above into consideration, we propose the use of personal exposure originating from outdoor sources (*A*), as the corresponding error-free exposure for the individuals.

Personal exposure to air pollution of ambient origin is important for policy-making and for policy evaluations of the impact of reductions in the air quality limits/concentrations, which do not influence pollution from indoor sources. In this context, it is useful to study exposures from outdoor and indoor sources separately. While these issues can be addressed in many specific locations, as a first step we took the pragmatic approach of examining the overall literature where personal exposure from outdoor sources is rarely directly addressed. It may be extremely difficult to measure this exposure, but it can be approximated based on specific assumptions. Most exposure studies measure total personal exposure which includes exposure to pollutants generated both from outdoor and indoor sources, as well as the “personal cloud”, i.e. localised generation of particulate matter as a consequence of human activity (Harrison et al., 2002; Brown et al., 2009); and consider this exposure as the main exposure of interest. However, there are some studies that have performed the partition for $PM_{2.5}$ by estimating the amount of total personal exposure that comes only from outdoor sources (Schwartz et al., 2007; Wilson and Brauer, 2006; Strand et al., 2006; Wallace and Williams, 2005; Cohen et al., 2009; Noullett et al., 2010). In particular, they approximated the exposure of interest by estimating home-specific infiltration factors for each participant assuming the home infiltration efficiency is representative of all the indoor micro-environments in which people spent time. Sulphate was used as a tracer, due to the similar spatial homogeneity to $PM_{2.5}$ and its negligible non-ambient sources, while Noullett et al. (2010) also checked elemental carbon. A review paper has summarised different methods of calculating the infiltration efficiency, with the surrogate method for infiltration estimates of determining the indoor/outdoor sulphur/sulphate ratio being the most commonly used approach (Diapouli et al., 2013).

In addition, previous studies do not generally discuss their results in the context of error structures, i.e. the magnitude and variability of exposure measurement error, or the impact of error on effect estimates from epidemiological models. For the latter, bias either away or, more often, towards the null can be observed with observed underestimations for the health effect estimates up to 60% under certain situations (Butland et al., 2013), and also loss of statistical power to detect exposure-response associations (Armstrong, 1998). However, it is not well-addressed in the literature that the magnitude and direction of bias, especially in multi-pollutant models, are highly dependent on the error structures of the pollutants (Dionisio et al., 2014).

Previous reviews and meta-analyses concerning exposure measurement error in PM2.5 (Avery et al., 2010; Kioumourtzoglou et al., 2014;13(1):) and NO2 (Meng et al., 2012) have studied the association between total personal exposure and ambient measurements, by pooling their correlations or estimating calibration coefficients for the health effect estimates of air pollution as the slope from a regression of total personal exposure on the ambient measures.

Objectives and PECO statement: In this paper we present a systematic review of studies which reported repeated measures of personal exposures over time using personal monitors, and the corresponding ambient concentrations, measured either at fixed monitoring sites or outside residences, in order to increase understanding of the measurement error structures leading to bias in epidemiological studies. Participants: Studies reviewed included those in any age group. Locations were any for NO_2 and Europe/North America for $PM_{2.5}$. Exposures: We focus on personal exposure to NO_2 and $PM_{2.5}$ originating from outdoor sources only. A few of these studies did attempt to separate exposure from outdoor vs other sources (Schwartz et al., 2007; Wilson and Brauer, 2006; Strand et al., 2006; Wallace and Williams, 2005; Cohen et al., 2009; Noullett et al., 2010), however, to increase the number of studies considered, we introduce a method for estimating exposure from outdoor sources only based on total personal exposure measurements. It depends on specific assumptions, so it can be regarded as an approximation rather than a truly measured exposure. Study design/comparisons and outcomes: We conduct a meta-analysis of the differences between personal exposure from outdoor sources and the proxy measures used for exposure to $PM_{2.5}$ and NO_2, looking at the magnitude of measurement error in the context of time varying exposures. Moreover, we assess error variability, i.e. a measure that has a strong influence on the bias in multi-pollutant models (Dionisio et al., 2014), by pooling the standard deviation of the difference between ambient concentrations and personal exposures from outdoor sources. The implications of the results for interpretation of epidemiological associations regarding the effects of short-term exposures are then discussed.

2. Methods

2.1. Notation

We use the same notation as described by Wilson and Brauer (2006). The terms outdoor and ambient are used interchangeably both for the measurements and the sources (or origins) of the pollutants. Non-ambient sources contributing to total personal exposures are dominated by the home indoor exposures due to the large amount of time individuals spend in residence compared to other micro-environments, such as work/school, in-transportation, etc. The time individuals spend in their residences is taken into account in the derivation of personal exposure from outdoor sources where only infiltration factors of residences were used. Thus, we use the term indoor and non-ambient interchangeably. For both pollutants, we hypothesized the following mass balance equation previously described elsewhere (Wilson and

Table 1
Study characteristics extracted from each paper.

Key study factors	Possible sources of heterogeneity	Other factors
Ambient concentrations C (Mean, SD)	Study period (season and duration) and temperature	Sample size
Total personal exposures T (Mean, SD)	Age group of participants	Journal of publication
Personal exposures from ambient sources A (Mean, SD)	Location of the study	Year of publication
Correlation between concentrations and errors	Location of outdoor measurement (residence or fixed site)	Instruments used

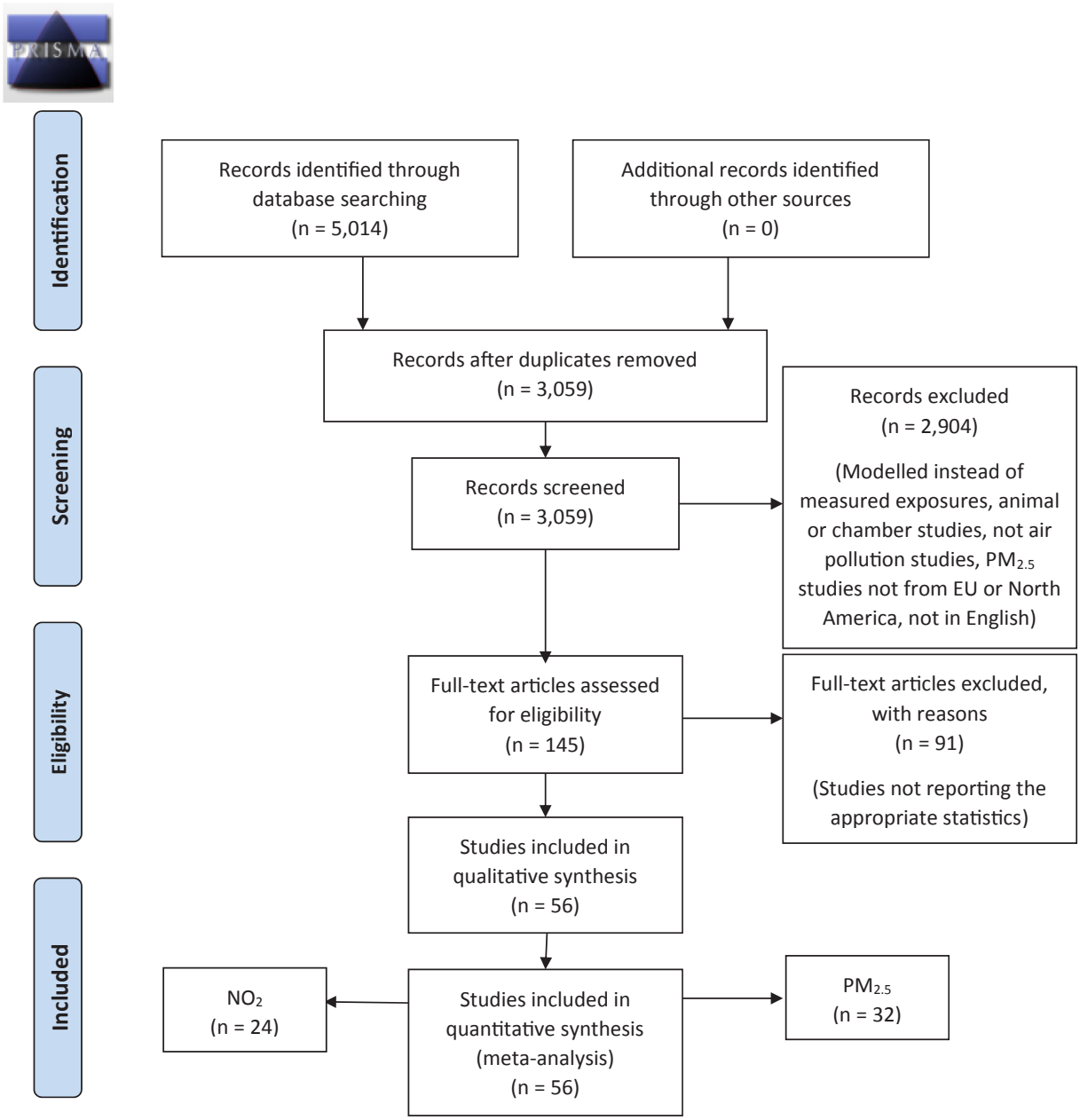

Fig. 1. PRISMA 2009 flow diagram of the review on the quantification of measurement error when using proxy exposure measures.

Brauer, 2006; Ott et al., 2000):

$$T = A + N = \alpha C + N = yC + (1 - y)F_{inf}C + N \quad (1)$$

where

C: Ambient concentrations measured at fixed sites or outside residences of the participants.
T: Total personal exposure measured using portable monitors carried by the individuals. It is the sum of personal exposure from ambient and non-ambient sources, $T = A + N$.
A: Personal exposure from ambient origins, derived using *T* and by making assumptions about the infiltration of the pollutants and the time-activity patterns of the individuals. A* was used for concentrations reported in studies that provided specific estimates of personal exposure from ambient origins.
N: Personal exposure from non-ambient origins, i.e. indoor- and personally-generated air pollution, measured as the difference *T-A*.
α: "Attenuation factor" (Ott et al., 2000), equals to A/*C*.

y: Percentage of time spent outdoors.
F_{inf}: Infiltration factor which multiplied by *C*, gives the amount of the pollutant that has infiltrated indoors and remains suspended (equation S1, Supplementary material).
C and *T* are available in the papers identified in the literature search described below. We describe the method to derive A later in the methods section.

Measurement error was defined as the difference between C and A. The parameters of interest in understanding measurement error structures and correcting bias in multi-pollutant model estimates are (i) the variance in the difference between C and A, (ii) the correlation between the errors of the different pollutants, i.e. $PM_{2.5}$ and NO_2, and (iii) the correlation between the pollutants (for both C and A) (Dionisio et al., 2014). The papers identified were examined for information on (i) and (ii), while (iii) is not discussed further here as, in general, it is widely reported in the literature.

2.2. Search strategy

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009). We searched the *ISI Web of Science* and *Medline* electronic databases for all document types in English from 2000 to 2016 that reported summary measures of both personal (*T*) and outdoor/ambient (*C*) $PM_{2.5}$ ($\mu g/m^3$) and/or NO_2 (ppb) concentrations (see "*Search string*" in Supplementary Material). *A* was derived from these measures.

If both residential outdoor and ambient concentrations from fixed stations were reported, we kept the former. While using fixed site monitoring stations would be the natural comparator to use in the context of time-series studies that use them as the exposure metric, there were far more studies using residential outdoor measurements. We therefore chose to use the average of all the participants' residential outdoor measurements in each study as the comparator. We considered that due to the averaging across many different residential locations, this would be a similar approximation of the general area background as the average of fixed site monitors in a city, but we also checked this assumption in sensitivity analysis by type of outdoor measurement.

2.3. Inclusion-exclusion criteria

The key outputs extracted (by DE) were those that inform analyses of the effect of measurement error on epidemiological associations, i.e. summary measures (means, variances and correlations) of *C*, *T* and *A* for each pollutant. These outputs, along with variables that could act as possible sources of heterogeneity (e.g. season and area of the study, age of the participants) and other study characteristics (sample size, instruments used, journal and year of publication) were extracted and are summarised in Table 1.

Animal or chamber studies or studies using predicted exposures from dispersion or land-use regression models were excluded (Fig. 1). Due to the large number of studies on $PM_{2.5}$ and the large heterogeneity of the concentrations worldwide, we restricted our search to studies from Europe and North America (US and Canada).

Air pollution measurements for both pollutants were reported as, or assumed to approximate, 24 h averages. We further classified the retrieved studies based on the mean daily temperature during the study period as studies performed in areas with: hot climate (> 15 °C), cold climate (≤ 15 °C) and mixed climate (conducted in periods with temperatures both higher and lower than 15 °C).

Some papers reported data separately for different time periods and/or different groups of subjects. We treated the resulting summary data as being from separate sub-studies. A database was built using an electronic reference manager (Endnote X7, Thomson Reuters) and summary data were collected in an *Excel* spreadsheet (*Microsoft Office 2016*).

2.4. Estimation of personal exposure from outdoor origin (A)

Personal exposure from outdoor origin is defined in this work as the error-free exposure to air pollution, but it cannot easily be measured directly (reported in only a limited number of studies included in this review). The measurements from the fixed sites are, usually, used as surrogates of the true exposure. However, the true personal exposure will differ to varying degrees from the fixed site measurements, mainly due to different amounts of time spent indoors by different individuals. Panel or cohort studies sometimes obtain personal measurements using individual monitoring devices (Tables S2 and S3), but the resulting measurements reflect total personal exposure which includes outdoor, indoor and personally-generated pollution such as smoking. A few papers have proposed different methods for the partition of total personal exposure into exposure from indoor and outdoor sources (Schwartz et al., 2007; Wilson and Brauer, 2006; Strand et al., 2006; Wallace and Williams, 2005; Cohen et al., 2009; Noullett et al., 2010).

We made some assumptions regarding the variables that are crucial for this partition. Time-activity patterns of the participants provide important variables; for example, in the US, individuals spend approximately 87% of their time indoors (averaged across the age distribution of the general population and including home, work, in-vehicle or other locations) (Klepeis et al., 2001). The infiltration factor (F_{inf}) for each pollutant, indicating the equilibrium fraction of ambient air pollution that penetrates indoor and remains suspended (Wilson and Suh, 1997), measured as a proportion, is another driving factor. $PM_{2.5}$ infiltration factors in the US vary around 0.5 based on the area and season of the study (Chen and Zhao, 2011). The main assumptions in our methodology for deriving an estimate of our true exposure of interest (*A*), based on data on total personal exposure (*T*) and ambient concentrations (*C*) of the two pollutants of interest, are described below.

2.4.1. $PM_{2.5}$

In order to estimate *A* for each study included in the meta-analysis (that reported only *T*), we used data for time-activity patterns of the population, *C* and F_{inf}. For the latter, there are numerous studies that have tried to estimate F_{inf} and most of them use sulphate (SO_4^{2-}), because of its similar spatial homogeneity to $PM_{2.5}$ and the negligible indoor sources. Chen and Zhao (2011) summarized the studies that reported infiltration factors (Chen and Zhao, 2011), including 21 large scale studies (more than 20 homes each), and reported that F_{inf} ranges between 0.30 and 0.82 for $PM_{2.5}$. This is in close agreement with the mean infiltration factor of 0.62 reported by Allen and his colleagues in the context of the MESA Air study conducted in six metropolitan areas in the US (Allen et al., 2012). In this context, we followed the procedure below to assign an infiltration factor to each study included in this review:

- we based our calculations on the F_{inf} published in the same study, if reported;
- otherwise, we reviewed the literature for other studies from the same city that reported infiltration factors (Table S4).
- If no such study was identified, we used the averages from review papers from Europe (based on the study area, i.e. Northern, Central and Southern Europe) (Hänninen et al., 2017) and the US and Canada (Chen and Zhao, 2011) (Table S4).

Also, for every study, a range for F_{inf} was constructed, generating a minimum and maximum plausible value (± 30% of the average informed by the F_{inf} range reported by Chen and Zhao (2011)). This allowed us to investigate whether the value of F_{inf} strongly affected our estimations for the personal exposure from outdoor origins as a sensitivity analysis.

For the time-activity patterns, we followed a similar approach to Hänninen et al. (2017), calculating fractional exposures for indoor and outdoor activities. Briefly, we included four activity profiles: (i) typical adult working age with most of the time spent indoors (home, work, etc.) ≈88% time-use, (ii) schoolchildren spending less time indoors than the adults ≈80%, (iii) sedentary elderly with almost all time spent indoors ≈98% and (iv) mixed panel with an average ≈90% of their time spent outdoors. Finally, ambient or residential outdoor concentrations, *C*, are reported in the included studies.

2.4.2. NO_2

NO_2, as a gaseous pollutant, penetrates more easily into buildings. However, there are no studies to the best of our knowledge that have reviewed infiltration factors of NO_2. As a result, we couldn't follow the approach used for $PM_{2.5}$. Thus, in order to estimate *A* from the studies that report only *T*, we made the following assumptions.

First, we know that the main indoor sources of NO_2 are cooking or heating systems (wood, natural gas, etc.) and tobacco use (World Health Organization, 2010). Assuming no indoor sources, and due to the fact that the infiltration factor of the pollutant is not well reported in the literature, we approximated it using the indoor/outdoor ratio, which is widely used for the relationship between indoor and outdoor pollution.

In this context, we used the probabilistic INDAIR model that, combined with the EXPAIR model, provides predictions of the personal exposure frequency distribution (PEFD) across a city (Dimitroulopoulou et al., 2006; Dimitroulopoulou et al., 2017). We used the average indoor/outdoor ratios in their no indoor sources scenario to approximate the NO_2 infiltration factors (Dimitroulopoulou et al., 2017). They provided summer and winter estimates, so we applied each calculated infiltration factor in every study according to the corresponding season of study. If a study was conducted both in cold and hot temperatures, we used the average of the winter and summer factors.

Similar time-activity patterns to the $PM_{2.5}$ approach were used and personal exposure from outdoor origins was calculated based again on Eq. (1). Unlike for $PM_{2.5}$, for which no measure of the F_{inf} uncertainty was reported in most studies, we constructed a 95% confidence interval (CI) for F_{inf}, using the standard errors reported. Our minimum and maximum scenarios for F_{inf} were based on the lower and upper limit of the CI respectively and we checked whether F_{inf} is a driving factor for the quantification of measurement error.

Hence for both pollutants, we estimated personal exposure from outdoor origin as a percentage of the total personal exposure, along with the differences between ambient concentrations and either total personal or personal from outdoor sources exposure. These differences (and their variability) were the variables that were meta-analysed for the quantification of the measurement error of the pollutants.

2.5. Statistical analysis

We applied a random effects meta-analysis as we observed large between-studies heterogeneity for the mean difference between *C* and *A*, i.e. *E*(*C-A*). Since personal exposure from outdoor sources was approximated in most studies, the difference between C and total personal exposure, T, was also assessed. Unstandardized mean differences were used for both pollutants. The between-study variance was estimated using the DerSimonian and Laird (1986) method. Heterogeneity was assessed by the Q-test and the I^2 and τ^2 measures of heterogeneity (Higgins et al., 2003).

Within each study we calculated the variance of the exposure differences (*Var(C-A)*), using the variances and correlations of C and A that were reported in each paper (equation S2, Supplementary material). Where the correlation coefficient between exposures was not reported, we assigned the average correlation coefficient from the studies that reported it. This imputation provided an enhancement in our database and allowed more studies to be added to our meta-analysis.

The standard deviation of the difference between ambient measurements and personal exposure from outdoor sources was also meta-analysed as a measure of the error variability. Under the assumption that $PM_{2.5}$ and NO_2 measurement error is (approximately) normally distributed, we constructed measures for the uncertainty of the error variability, i.e. 95% confidence intervals, and calculated pooled estimates ("*Meta-analysis of variance*" in Supplementary material).

We assessed publication bias by funnel plots, the Duval and Tweedie nonparametric "trim and fill" method and Egger's test (Duval and Tweedie, 2000; Egger et al., 1997). However, as our measure of interest is the difference between two exposures, we did not expect publication bias to be a concern, as it is a measure that is not usually discussed and is not in the primary research questions of the air pollution studies.

2.6. Sensitivity analysis

Subgroup analyses stratified by assumed *a priori* key variables (Table 1) were conducted to assess the consistency and robustness of our findings, in terms of the pooled estimates for measurement error. The age of the participants, the climate, and the location of the study were investigated. Also, we assessed whether infiltration rates for both pollutants contributed to the magnitude of measurement error by using the minimum and maximum F_{inf} value (calculated differently for the two pollutants) rather than its mean. Finally, we assessed the possible differences that might occur when measurements from fixed sites or residential outdoor measurements were used as proxies for the true exposures of the individuals. Especially for NO_2, the amount of error due to spatial heterogeneity could be much different depending on which type of outdoor measurement one is using, but if the number of participants in the studies is large and the monitoring system is quite dense, these two metrics might be very similar.

All statistical analyses were conducted using STATA 12 (Stata, 2011).

3. Results

145 studies met our inclusion criteria (Fig. 1). After excluding studies that did not report descriptive statistics, the final sample included a total of 82 studies or sub-studies from 56 articles: 32 for $PM_{2.5}$ (reporting measures for 50 sub-studies) and 24 for NO_2 (reporting for 32 sub-studies). There were no studies reporting summaries of the measurement error, defined as the difference between C and either A or T. Only six $PM_{2.5}$ articles reported summary measures for A. Tables 2 and 3 for $PM_{2.5}$ and NO_2 respectively summarise the main characteristics of the included studies.

For $PM_{2.5}$, eight studies were from Europe (10 sub-studies) and 24 from USA and Canada (40 sub-studies). Of the 50 populations, 14 were children, nine were elderly, 16 were adults and 11 were mixed panels. Nine sub-studies were performed in temperatures ≤15 °C, 16 in temperatures > 15 °C, and 25 in mixed climate. Mean ambient concentrations (*C*) ranged across studies from 4.8 to 32 μg/m^3 with a mean value of 15.2 μg/m^3 (SD: 8.9 μg/m^3). The corresponding mean total personal exposures (*T*) ranged between 6.5 and 88.0 μg/m^3 with a mean of 20.8 μg/m^3 (SD: 15.9 μg/m^3). In the majority of studies, *T* was higher than *C*, probably due to indoor sources and the personal cloud of the individuals. The reported correlation coefficient between C and T had a mean value of 0.42 (range: 0.04–0.81).

For NO_2, seven studies were from Europe (nine sub-studies) but one was excluded as an outlier due to the relatively large mean ambient concentrations of 47 ppb (almost three times higher than the overall average), probably due to local sources near the monitoring stations (Delgado-Saborit, 2012). Ten studies were conducted in North America (16 sub-studies) and seven in other regions. Regarding the age of the participants, nine sub-studies included children, two were on older people, 16 on adults and five on mixed panels. Seventeen out of 32 studies were performed in mixed climates, three in cold (≤15 °C) and

Table 2
Characteristics of studies included in the review of the differences between ambient and either total personal or estimated personal exposure only from outdoor sources to $PM_{2.5}$.

Study	Sub-study	Area	Climate	Panel	Mean Ambient C ($\mu g/m^3$)	Mean Total Personal T ($\mu g/m^3$)	Mean Personal from out A ($\mu g/m^3$)
(Adgate et al., 2003)		Minneapolis, USA	Mixed	32 Adults	10.1	26.4	3.9
(Arhami et al., 2009)	1	San Gabriel Valley, USA	Hot	49 Elderly	24.5	14.5	11.5
	2		Hot		20.1	13.8	10.1
	3	Riverside, USA	Hot	18 Elderly	22.1	11.8	11.0
	4		Hot		11.6	6.5	4.9
(Branis and Kolomaznikova, 2010)		Prague, Czech Republic	Mixed	1 Adult	13.5	14.9	9.1
(Brauer et al., 2000)	1	BanskaBystrica, Slovakia	Hot	49 Mixed	22.0	88.0	14.7
	2		Cold		32.0	69.0	21.3
(Brown et al., 2008)	1	Boston, USA	Cold	25 Adults	8.6	12.0	6.3
	2		Hot		12.5	10.0	9.2
(Cohen et al., 2009)		Six metropolitan areas, USA	Mixed	90 Mixed	13.8	11.8	9.1
(Crist et al., 2008)	1	Athens, Ohio, USA	Mixed	30 Children	13.7	17.6	10.2
	2	Koebel, Ohio, USA		30 Children	13.9	14.6	10.3
	3	New Albany, Ohio, USA		30 Children	12.7	13.9	9.5
(Delfino et al., 2008)	1	Riverside, USA	Hot	13 Children	27.0	32.8	17.1
	2	Whittier, USA	Hot	32 Children	19.3	36.2	12.2
(Delfino et al., 2004)		Alpine, USA	Hot	19 Children	11.0	37.9	7.0
(Evans et al., 2000)	1	Fresno, California, USA	Hot	5 Adults	20.5	13.3	12.2
	2		Hot	16 Adults	10.1	11.1	6.0
(Hampel et al., 2014)		Augsburg, Germany	Cold	5 Adults	10.5	13.2	7.1
(Hänninen et al., 2003)		Helsinki, Finland	Mixed	201 Adults	9.6	15.4	6.1
(Janssen et al., 2000)	1	Amsterdam, Netherlands	Cold	41 Mixed	20.6	24.3	13.7
	2	Helsinki, Finland	Cold	48 Mixed	12.6	10.8	7.6
(Johannesson et al., 2007)		Gothenburg, Sweden	Mixed	30 Adults	7.8	11.0	4.8
(Kim et al., 2006)		Toronto, Canada	Mixed	28 Mixed	11.0	22.0	6.2
(Kinney et al., 2002)	1	Harlem, New York, USA	Cold	46 Children	11.9	17.0	8.0
	2		Hot		13.6	18.5	9.1
(Liu et al., 2003)	1	Seattle, USA	Mixed	28 Elderly	9.0	9.3	5.9
	2			27 Elderly	12.8	10.8	8.4
	3			34 Elderly	9.2	10.5	6.0
	4			19 Children	11.3	13.3	8.1
(Nethery et al., 2008)		Vancouver, Canada	Mixed	62 Adults	4.8	11.3	3.1
(Noullett et al., 2010)		British Columbia, Canada	Cold	15 Children	18.1	20.8	11.3
(Oglesby et al., 2000)		Basel, Switzerland	Cold	50 Adults	19.0	23.7	12.8
(Rodes et al., 2010)		Detroit, USA	Mixed	137 Adults	16.4	20.3	6.3
(Rojas-Bracho et al., 2004)	1	Boston, USA	Cold	18 Mixed	10.9	21.6	8.0
	2		Hot	16 Mixed	16.4	21.5	12.0
(Sarnat et al., 2006)	1	Steubenville, USA	Hot	5 Elderly	20.1	19.9	14.8
	2		Mixed		19.3	20.1	12.3
(Schembari et al., 2013)		Barcelona, Spain	Mixed	54 Adults	19.8	26.2	14.0
(Schwartz et al., 2007)		Baltimore, USA	Mixed	56 Mixed	21.2	20.9	8.8
(Sloan et al., 2016)		Utah, USA	Hot	10 Adults	8.3	8.5	5.3
(Spira-Cohen et al., 2010)		South Bronx, New York, USA	Mixed	40 Children	14.3	24.1	9.6
(Wallace et al., 2006)		North Carolina, USA	Mixed	37 Mixed	19.3	23.0	9.7
(Weisel, 2005)	1	California, Texas, New	Mixed	309 Adults	18.1	36.3	9.5
	2	Jersey, USA		118 Children	18.1	51.5	10.3
(Wheeler et al., 2011)	1	Windsor, Canada	Mixed	48 Children	14.3	10.4	6.7
	2		Mixed		12.5	7.8	5.2
(Williams et al., 2012)		North Carolina, USA	Mixed	16 Adults	16.6	21.0	9.3
(Wilson and Brauer, 2006)		Vancouver, Canada	Hot	16 Mixed	11.4	18.5	8.5

12 in warm (> 15 °C) climates. Mean ambient concentrations were greater than the corresponding mean total personal exposures in most of the studies, with mean values of 20.5 ppb (SD: 7.9 ppb, range: 7.9–47) and 16.7 ppb (SD: 9.1 ppb, range: 5.8–45) respectively. The mean correlation coefficient between ambient concentrations and total personal exposure was 0.32 (range: −0.41–0.73).

3.1. Estimation of personal exposure from outdoor origin

Exposure measures for both pollutants are summarised in Table 4. For comparison, we also show the results from studies identified in the systematic review that reported $PM_{2.5}$ exposure from outdoor origin (no such NO_2 study was identified). Only small differences were observed between the reported exposures of interest (A*) and our approximations for the same studies (A), ranging from 0.4 to 1.7 $\mu g/m^3$. We, also, estimated that approximately 44% of the total $PM_{2.5}$ personal exposure originates from outdoor sources, ranging from 33.3 to 54.8%. The mean concentration was 9.3 $\mu g/m^3$ (SD: 3.6 $\mu g/m^3$). Regarding NO_2, the percentage of the total personal exposure that originates from outdoor sources is greater than for $PM_{2.5}$ (mean: 74.1%, range: 57.4–88.3%). We estimated that the average personal exposure only from outdoor origin was 12.0 ppb ranging from 9.3 to 14.3 ppb.

3.2. Meta-analysis

The overall pooled mean difference between ambient (*C*) and personal exposure from outdoor origin (*A*) for $PM_{2.5}$ was 5.72 $\mu g/m^3$ (95% CI: (4.98, 6.46)). In the studies conducted during the cold season, we observed smaller differences (pooled value 4.83 $\mu g/m^3$ (3.76, 5.89)) compared to the ones in hot temperatures (6.36 $\mu g/m^3$ (4.90, 7.82), Fig. 2). There was no evidence that the mean difference differed across the various locations (Fig. S1). In Eastern and Western US and Canada

Table 3
Characteristics of studies included in the review of the differences between ambient and either total personal or estimated personal exposure only from outdoor sources to NO_2.

Study	Sub-study	Area	Climate	Panel	Mean Ambient C (ppb)	Mean Total Personal T (ppb)	Mean Personal from out A (ppb)
(Bellander et al., 2012)		Stockholm, Sweden	Mixed	247 Adults	10.8	7.8	6.6
(Brown et al., 2009)	1	Boston, USA	Cold	25 Mixed	26.8	12.9	15.0
	2		Hot		22.8	17.4	14.9
(Chao and Law, 2000)		Hong Kong	Hot	60 Adults	38.2	24.5	25.2
(Delfino et al., 2006)	1	Riverside, USA	Hot	13 Children	27.2	24.3	18.8
	2	Whittier, USA		32 Children	28.0	30.9	19.4
(Delgado-Saborit, 2012)		Birmingham, UK	Mixed	16 Adults	47.0	23.0	28.9
(Demirel et al., 2014)		Eskisehir, Turkey	Cold	65 Children	16.4	22.8	10.0
(Kim et al., 2006)		Toronto, Canada	Mixed	28 Mixed	23.0	14.0	13.9
(Kousa et al., 2001)	1	Helsinki, Finland	Mixed	201 Adults	12.7	13.3	7.9
	2	Basel, Switzerland	Mixed	50 Adults	19.1	16.0	11.8
	3	Prague, Czech Republic	Mixed	35 Adults	32.4	22.9	20.0
(Lee et al., 2000)		Brisbane, Australia	Hot	57 Adults	14.5	15.0	9.6
(Moelter et al., 2012)		Manchester, UK	Mixed	71 Children	15.2	10.9	9.9
(Nethery et al., 2008)		Vancouver, Canada	Mixed	62 Adults	19.6	18.7	12.1
(Ouidir et al., 2015)		Grenoble, France	Mixed	40 Adults	12.8	12.7	7.9
(Physick et al., 2011)		Melbourne, Australia	Hot	24 Adults	18.7	12.1	12.3
(Rodes et al., 2010)		Detroit, USA	Mixed	137 Adults	24.0	27.6	14.8
(Rojas-Bracho et al., 2002)		Santiago, Chile	Hot	18 Children	36.9	25.9	25.5
(Sarnat et al., 2006)	1	Steubenville, USA	Hot	5 Elderly	9.5	9.9	5.9
	2		Mixed		11.3	12.1	6.5
(Schembari et al., 2013)		Barcelona, Spain	Hot	54 Adults	19.4	18.6	12.8
(Schwartz et al., 2007)		Baltimore, USA	Mixed	56 Mixed	21.8	11.1	13.2
(St Helen et al., 2015)		Trujillo, Peru	Hot	106 Adults	7.9	10.4	5.2
(Van Roosbroeck et al., 2008)		Utrecht, Netherlands	Mixed	67 Children	19.9	12.6	12.9
(Weichenthal et al., 2015)	1	Windsor, Canada	Mixed	47 Children	11.8	7.3	7.7
	2				20.9	13.0	13.6
	3			48 Adults	13.9	10.5	8.6
	4				19.4	10.6	11.9
(Williams et al., 2012)		North Carolina, USA	Hot	16 Adults	8.3	5.8	5.5
(Cho et al., 2006)		Seoul, Korea	Cold	42 Children	31.0	45.0	18.9
(Zipprich et al., 2002)		Richmond, USA	Hot	54 Mixed	15.0	15.0	9.8

the mean difference was very similar (5.68 μg/m^3 (4.18, 7.18) and 5.61 μg/m^3 (4.49, 6.73) respectively) while in Europe it was slightly lower (5.17 μg/m^3 (4.18, 6.15)). Additionally, studies on older participants were found to have the highest overall mean difference (6.92 μg/m^3 (4.98, 8.85)). Mean exposure differences for adults and children were 5.00 μg/m^3 (3.45, 6.56) and 5.11 μg/m^3 (4.11, 6.12) respectively (Table 5).

Mean total personal exposure (*T*) was 4.36 μg/m^3 (2.73, 5.99) higher than the corresponding ambient concentrations in the original analysis (pooled difference). When we used studies with imputed correlations as well, the corresponding difference went up to 3.96 μg/m^3 (2.56, 5.37). The highest mean difference across age groups was observed in children (6.72 μg/m^3 (2.64, 10.80)). For elderly participants, ambient $PM_{2.5}$ measurements were higher than total personal exposure by 3.39 μg/m^3 (0.79, 5.99). Using both *T* and *A* as the error-free exposure, we observed increased mean differences when higher ambient concentrations were reported.

For NO_2, we found that *C* is on average 7.17 ppb (6.25, 8.10) higher than *A*. The lowest difference by region of study was observed in Europe with a pooled value of 6.21 ppb (5.02, 7.40), while in North America and in studies from the rest of the world it was 7.29 ppb (6.09, 8.48) and 8.14 ppb (5.15, 11.14) respectively (Fig. 3). Studies on mixed panels and children were found to have the greatest pooled exposure differences (9.38 ppb (7.36, 11.41) and 8.08 ppb (6.58, 9.59) respectively), while adults' pooled difference was 6.35 ppb (5.28, 7.42) (Table 5). Finally, unlike $PM_{2.5}$, studies conducted in hot temperatures were found to have smaller differences (6.55 ppb (5.01, 8.09)) compared to the ones in cold temperature (12.27 ppb (10.69, 13.85) – only 3 studies). Studies on mixed climate had similar results as the overall pooled value (7.03 ppb (5.86, 8.20)) (Fig. S2). When we compared *C* and *T*, we found that outdoor concentrations were greater than total personal exposure in almost every stratum of the analysis, with an average value around 3.23 ppb (1.74, 4.72) (Table S1). In North American studies we observed the greatest discrepancies (3.85 ppb (1.53, 6.18)). Error variance was larger when *T* was used as the "error-free" exposure instead of *A*.

Moreover, we tested whether the magnitude of error (C-A) differs according to the levels of air pollution. As expected, based on the definition of A, which is linearly associated with C (Eq. (1)), the absolute error increased as the outdoor concentration increased for both pollutants (Fig. 4). However, when we checked the error as a proportion of the ambient concentrations, using a relative difference plot (Pollock et al., 1992), we found no association between it and the outdoor levels of both pollutants (lower panels Fig. 4). A different colour was used for each age group showing no patterns for the errors by age.

Table 5 presents sensitivity analysis results for the effect of the infiltration factor. We found substantially different pooled values between the minimum, mean and maximum scenarios. When the minimum F_{inf} was used, the overall exposure differences increased to 7.94 μg/m^3 (7.06, 8.81) and 10.00 ppb (8.76, 11.25) for $PM_{2.5}$ and NO_2 respectively, while the use of the maximum resulted in 3.54 μg/m^3 (2.82, 4.27) and 4.95 ppb (3.95, 5.95).

The estimation of measurement error, i.e. E(*C-A*), when only residential outdoor measurements were included in the meta-analysis was 5.72 μg/m^3 (4.98, 6.46) for $PM_{2.5}$ and 7.63 ppb (6.48, 8.77) for NO_2, whilst using the fixed site measurements it was 5.47 μg/m^3 (4.38, 6.57) and 6.69 ppb (5.26, 8.13) respectively.

Finally, we assessed the impact of the imputation of the correlation coefficient (*Corr(C,A)*) in a subsample of studies (25 in total) on our findings. We compared the pooled differences before and after the imputation for every sub-group analysis and found that it yielded fairly consistent results (Table 5, Fig. S3-4). More specifically, we added 20 sub-studies for $PM_{2.5}$ and only 5 for NO_2. For $PM_{2.5}$, the overall difference between ambient concentrations and personal exposure only

Table 4
Examples from studies that report mean personal $PM_{2.5}$ exposures from outdoor sources (A*) and the average of the studies for which we did the partition (A) for both $PM_{2.5}$ ($\mu g/m^3$) and NO_2 (ppb). C: ambient concentrations, T: total personal exposure.

	Reference	Area	Panel	Mean C	Mean T	Mean A*	Mean A	100·A*/T	100·A/T
Studies that reported C, T and A* ($PM_{2.5}$ only)	Cohen (2009)	Six metropolitan areas, USA	90 persons free of clinical CVD	13.8	11.8	7.6	9.1	64.4	77.1
	Noullett (2010)	British Columbia, Canada	15 elementary school students	18.1	20.8	9.6	11.3	46.2	54.3
	Schwartz (2007)	Baltimore, USA	20 healthy senior adults, 15 adults with COPD, 21 children	21.2	20.9	10.9	8.8	52.2	42.1
	Strand (2006)	Denver, USA	50 asthmatic children	12.7	[a]	6.4	[b]	NA	NA
	Wallace (2006)	North Carolina, USA	29 persons with hypertension, 8 with implanted cardiac defibrillators	19.5	23.0	10.9	9.7	47.4	42.2
	Wilson and Brauer (2006)	Vancouver, Canada	16 COPD patients	11.4	18.5	8.1	8.5	43.8	45.9
Studies that reported only C and T	**$PM_{2.5}$ (# of studies = 45)**	**Europe, USA & Canada**	**Various**	**15.0**	**21.0**	–	**9.3**	–	**44.3**
						–	**Range: (7.0–11.5)**	–	**Range: (33.3–54.8)**
	NO_2 (# of studies = 32)	**Worldwide**	**Various**	**19.3**	**16.2**	–	**12.0**	–	**74.1**
						–	Range: (9.3–14.3)	–	Range: (57.4–88.3)

a: Not reported in the study.
b: Not included in the meta-analysis.

from outdoor sources was 5.08 $\mu g/m^3$ (4.19, 5.98) before the imputation and 5.72 $\mu g/m^3$ after (+12.2%). For NO_2, we calculated a pooled value of 7.34 ppb (6.33, 8.36) before the imputation and 7.17 ppb after (−2.3%).

3.3. Heterogeneity and Small study effect (publication bias)

There was large heterogeneity in the pooled differences both for $PM_{2.5}$ and NO_2 (I^2 = 97.5% and 95.5% respectively), that was not explained by the sensitivity analyses by location, climate, or age group of the study sample. However, the I^2 statistic can be problematic because its value increases when the number of studies included in the meta-analysis increases. Thus, the corresponding values of τ^2, (a measure of the effect size variation that is not sensitive to a large number of studies) was 6.18 $\mu g/m^3$ and 5.89 ppb for $PM_{2.5}$ and NO_2 respectively.

Funnel plots (Fig. S5) and associated statistical tests (Egger's p = 0.070 for $PM_{2.5}$ and 0.004 for NO_2) also reflected the high heterogeneity and possible publication bias and small studies effects. Adjusting for the asymmetry by trim-and-fill decreased the pooled differences by 30% for both pollutants (Table 5 and Fig. S6).

3.4. Meta-analysis of error variability

Finally, after the exclusion of one study for PM2.5 (Branis and Kolomaznikova, 2010) and three for NO2 (Schwartz et al., 2007; Delgado-Saborit, 2012; Demirel et al., 2014) due to their extremely high values of estimated error variability, we assessed the error variability (*SD(C-A)*) which is a main driving factor for bias in epidemiological model estimates. The pooled $PM_{2.5}$ error standard deviation was 6.85 $\mu g/m^3$ (5.76, 7.94) when no imputed data were used, which decreased to 5.92 $\mu g/m^3$ (4.88, 7.18) when the "trim and fill" method was performed (Table 6). The corresponding value for NO_2 was higher, i.e. 7.63 ppb (no studies were filled). These findings indicate that the health effect estimates of NO_2 in epidemiological models might be more biased, compared to $PM_{2.5}$ due to the higher error variability.

4. Discussion

We conducted a systematic review and meta-analysis of 81 studies that reported total personal $PM_{2.5}$ and NO_2 exposure and the corresponding ambient concentrations. Of these, only six provided estimates of personal exposure from outdoor sources for $PM_{2.5}$. We enhanced the database by estimating personal exposure from outdoor sources in the remaining 76 studies by partitioning the total personal exposure into exposure only from indoor and outdoor sources. We calculated the mean difference between personal exposure from outdoor sources and ambient concentrations to estimate the pollutant-specific pooled measurement error.

Outdoor sources contributed 44.3% of total personal exposure to $PM_{2.5}$ and 74.1% to NO_2 (Table 4). Overall estimates of personal exposure from outdoor sources were 9.3 $\mu g/m^3$ and 12.0 ppb for $PM_{2.5}$ and NO_2 respectively. Summary estimates of the concentration differences, i.e. the measurement error, ranged between 3.54 $\mu g/m^3$ and 7.94 $\mu g/m^3$ for $PM_{2.5}$ and 4.95 ppb and 10.00 ppb for NO_2, depending on the assumptions made for the infiltration factor of each pollutant. In our subgroup analyses, increased errors were observed in studies with older participants and temperatures above 15 °C for $PM_{2.5}$. For NO_2, the difference was higher among studies in children or mixed age group populations, in cold climates and in western North America. Our findings are in agreement with previous studies which showed that ambient concentrations are a good proxy of neither personal exposure from outdoor origins nor total personal exposure (Wallace et al., 2006; Janssen et al., 1999; Sarnat et al., 2001; Mage et al., 1999). Interestingly, for both pollutants, the estimated measurement error was slightly larger when residential outdoor measurements were used compared to fixed sites. This finding indicates that the measurements from the

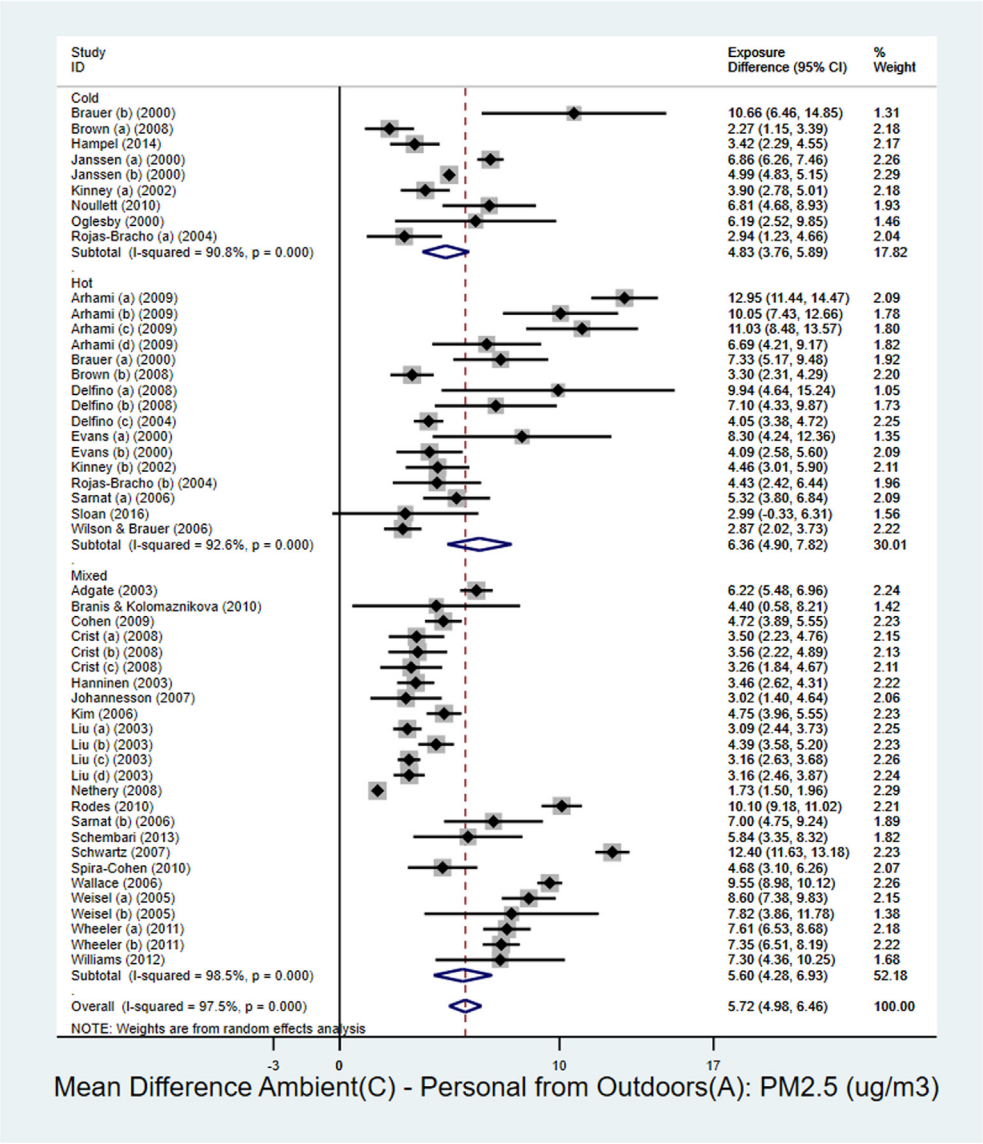

Fig. 2. Random effects meta-analysis forest plot for the mean difference between average ambient concentrations of $PM_{2.5}$ (C) and the corresponding personal exposure only from outdoor sources (A) stratified by temperature at the time of the study.

monitoring networks may underestimate the true ambient concentrations, probably due to preferential sampling (Shaddick and Zidek, 2014), or that people tend to travel to locations away from home that have higher average concentrations than outside their residence.

We found that measurement error for NO_2 was greater and more variable than for $PM_{2.5}$. This may hold because $PM_{2.5}$ is more spatially homogeneous (around two-thirds of $PM_{2.5}$ is due to regional sources) compared to NO_2, which is a traffic-pollution indicator. Also, even though NO_2 is a gaseous pollutant and penetrates into buildings more easily which would suggest less measurement error during time periods indoors, it reacts and decays more quickly compared with $PM_{2.5}$. As a result, the association between NO_2 and a health outcome could be underestimated in a multi-pollutant model containing both NO_2 and $PM_{2.5}$. Though with systematic error and correlation between pollutants which ranges across studies due to varying sources of air pollution, the biases could go in either direction. Taking our results and heterogeneity into account, the pooled differences for $PM_{2.5}$ and NO_2 could be used by researchers to inform regression calibration procedures for correcting effect estimates of epidemiological studies.

For assessing bias in the health effect estimates, the correlation between the exposure variables, the variance of the exposure errors and the correlation between the errors are some variables that should be taken into consideration. Studies often provide information on the correlation between the pollutants. Relationships between ambient concentrations and personal exposure are also studied but rarely expressed in terms of personal exposure of ambient origin. The variance of the measurement error is mentioned in some studies (Butland et al., 2013) but usually in respect of the variance in the difference between ambient concentrations and total personal exposure. Correlations between the errors in different pollutants were not reported despite this being an important variable in assessing bias in multi-pollutant models. Exposure or epidemiological studies that measure personal exposure and ambient concentrations should be encouraged to publish information on these types of parameters. Moreover, the use of highly spatially-resolved models instead of lower spatial resolution data, without incorporating data on time-activity patterns of the individuals, can introduce more bias in the health effect estimates (Sellier et al., 2014). In addition, as Weisskopf and Webster (2017) conclude, more personalised exposure assessment may not be the panacea for epidemiological study design (Weisskopf and Webster, 2017). It can eliminate exposure measurement error bias but, on the other hand, there may be a trade-off between this and (i) potential confounding, which can be increased

Table 5
Summary table of the core and subgroup meta-analyses conducted. Pooled estimates of the mean difference between ambient concentrations and personal exposure to the relevant pollutant from ambient origin E(C-A) and their 95% confidence intervals are presented.

	$PM_{2.5}$ Error ($\mu g/m^3$)			NO_2 Error (ppb)		
Infiltration factor (F_{inf}) used	**Minimum Scenario**	**Mean Scenario**	**Maximum Scenario**	**Minimum Scenario**	**Mean Scenario**	**Maximum Scenario**
	7.94 (7.06, 8.81)	**5.72 (4.98, 6.46)**	3.54 (2.82, 4.27)	10.00 (8.76, 11.25)	**7.17 (6.25, 8.10)**	4.95 (3.95, 5.95)
Overall, No imputation & Trim 'n' Fill	**Overall**	**No Imputation**	**Trim 'n' Fill**	**Overall**	**No Imputation**	**Trim 'n' Fill**
	5.72 (4.98, 6.46)	5.08 (4.19, 5.98)	4.20 (3.41, 5.00)	7.17 (6.25, 8.10)	7.34 (6.33, 8.36)	4.98 (3.97, 5.98)
By climate	**Hot**	**Cold**	**Mixed**	**Hot**	**Cold**	**Mixed**
	6.36 (4.90, 7.82)	4.83 (3.76, 5.89)	5.60 (4.28, 6.93)	6.55 (5.01, 8.09)	12.27 (10.69, 13.85)	7.03 (5.86, 8.20)
By age	**Children**	**Elderly**	**Mixed**	**Children**	**Elderly**	**Mixed**
	5.11 (4.11, 6.12)	6.91 (4.98, 8.85)	5.00 (3.45, 6.56)	6.39 (4.98, 8.04)	8.08 (6.58, 9.59)	4.36 (3.17, 5.55)	**Adults**	6.35 (5.28, 7.42)	9.38 (7.36, 11.41)
By area	**Eastern North America**	**Western North America**	**North America**	**Europe**	**Eastern North America**	**Western North America**	**Europe**	**Other**
	5.68 (4.18, 7.18)	5.61 (4.49, 6.73)	6.63 (4.87, 8.38)	5.17 (4.19, 6.15)	7.58 (5.14, 10.02)	8.60 (8.02, 9.17)	6.64 (5.14, 8.14)	6.21 (5.02, 7.40)	8.15 (5.15, 11.14)
By location of outdoor monitor	**Residential Outdoor**		**Fixed Sites**		**Residential Outdoor**		**Fixed Sites**		
	5.72 (4.98, 6.46)		5.47 (4.38, 6.57)		7.63 (6.48, 8.77)		6.69 (5.26, 8.13)		

with personal data, and (ii) reverse causation. Thus, the identification of the most appropriate study design to answer a research question may not be straightforward. We are currently working on methods to overcome the problem of the lack of information on, for example, correlation of errors, and in combination with inputs from this review provide corrected health effect estimates when using proxy exposures. This will enhance the interpretation of multi-pollutant model results.

In terms of the error type, we expect that the error as defined in this work, i.e. *C-A* would have two parts; a systematic and a random one. Systematic error can be easily minimized with better exposure assessment and by measuring the appropriate exposures, e.g. *A*, instead of using other proxies, e.g. *C*, but needs careful consideration when correcting epidemiological models (Keogh and White, 2014). Random error in air pollution measurements combines both Berkson and classical components (Zeger et al., 2000; Deffner et al., 2018). Most studies measure personal exposures of the participants for short periods. In this context, we expect a Berkson component due to use of aggregated and not individual data (Zeger et al., 2000). More specifically, we compiled data using exposures across individuals from different studies and assumed that these averaged exposures are representative of the true exposure of the participants. On the other hand, we, also, expect a classical component due to the temporal and spatial misalignment of the proxy exposures (Gryparis et al., 2009), i.e. the measurements of the monitoring stations or outside participants' homes. In each study included in the meta-analysis, data were collected from specific locations. The density of these specific locations, particularly for monitoring network sites might be sparse and measurements at residential locations might be over relatively short time periods which might not be representative for longer periods of time. Instrument error is another possible source of classical error, but mostly for personal monitors, as it is not expected to be substantial for fixed site monitors.

Furthermore, to the best of our knowledge no previous study has reported pooled estimates for the difference between the "error-prone" measurement *C* and the "error-free" (either *T* or *A)* for $PM_{2.5}$ and NO_2. Previous review papers have meta-analysed the correlation between the two concentrations or have estimated calibration coefficients for their associations (Avery et al., 2010; Kioumourtzoglou et al., 2014; Meng et al., 2012). Regarding the partition that we applied, it is important for policy makers to separate the effects of indoor and outdoor generated air pollution, as the reduction policies are completely different in each case. This paper has concentrated on the latter, but the approach can also be applied to the former. It should be noted that concentrations of pollutants from indoor sources, e.g. NO_2 during gas cooking, can be higher indoors but whether this leads to a higher contribution to total personal exposure is likely to depend on circumstance, e.g. frequency and duration of cooking; type of housing; ventilation, etc.

The current study has some limitations. First, while there are a limited number of studies that estimated the contribution of outdoor sources to total personal exposure for $PM_{2.5}$ using measurement techniques, we could not identify any such previous studies for NO_2. Thus, our findings for NO_2 could not be extensively discussed. However, similar to our approximation, in the context of the DEARS study (Meng et al., 2012), researchers used questionnaires for the cooking type, heating fuel and smoking to estimate personal exposure to NO_2 from outdoor sources by eliminating homes with indoor sources. They estimated that personal exposure from outdoor sources is around 57–83% of total personal exposure depending on the season, which is in close agreement to our findings (57–88%).

In addition, for both pollutants the partition of total personal exposure introduced another source of uncertainty, which was only partly considered with the varying infiltration factors across the studies. This partition was based on various assumptions, such as the use of home-specific infiltration efficiency as an average for all the different microenvironment in which people spend time and the hypothesized time spent outdoors across the various age groups. The estimated infiltration factors were collected either from the original studies as summaries

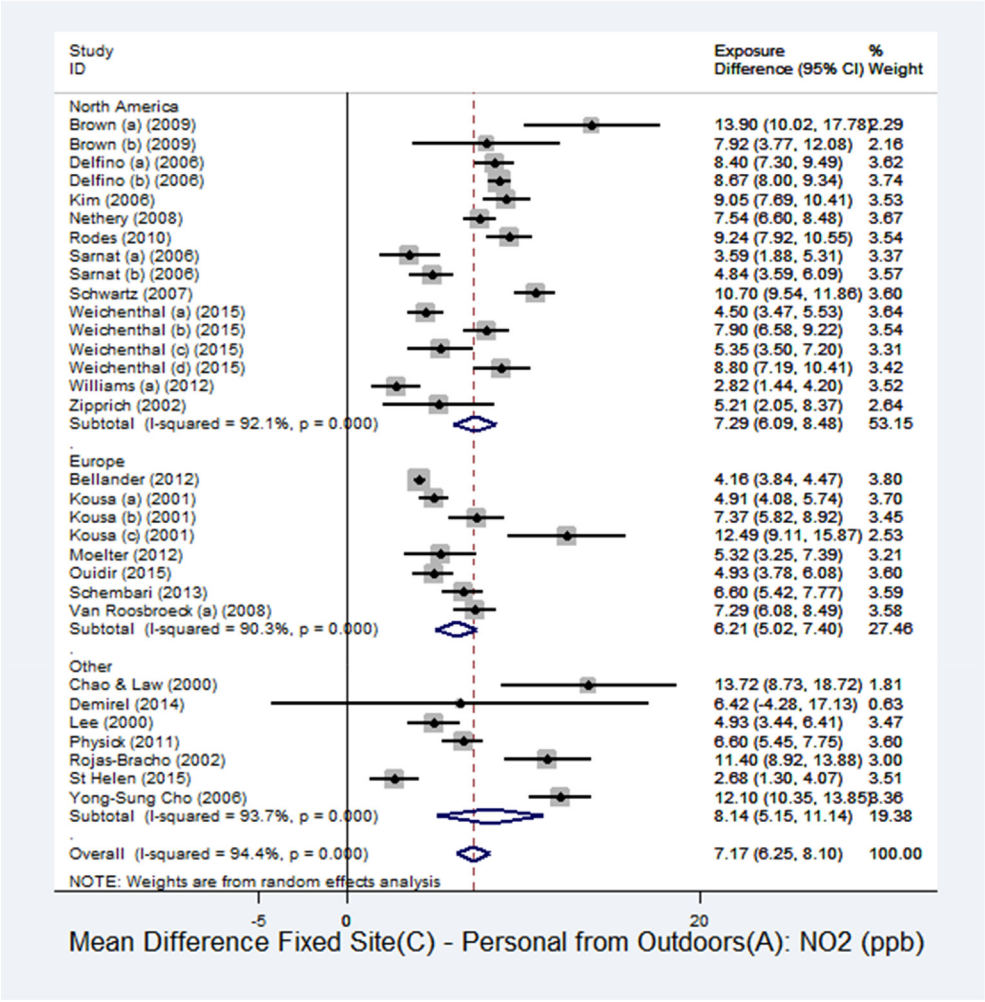

Fig. 3. Random effects meta-analysis forest plot for the mean difference between average ambient concentrations of NO_2 (C) and the corresponding personal exposure only from outdoor sources (A) stratified by study location.

between participants or from previous reviews and most of them used sulphate as a tracer of $PM_{2.5}$. Thus, our findings may be regarded as approximations of the true pollutant errors. An accurate method for estimating personal exposure to $PM_{2.5}$ and NO_2 from outdoor sources would provide better exposure estimates and more relevant estimates of the truly measured exposure errors. Using outdoor measurements to derive the contribution of outdoor sources to personal exposure and then calculating the difference between these outdoor measurements and the personal exposure from outdoor sources, seems a rather circular procedure, and more independent methods need to be established in exposure assessment studies. Among others (Diapouli et al., 2013), one such method is the use of sulphates, but this information is not often available. Additionally, the imputation of the correlation coefficient for some studies and the small sample sizes of other studies may have influenced our results. However, our sensitivity analyses indicated that the results were rather stable and not largely driven by these factors.

We chose to use residential outdoor measurements as our main ambient concentration metric rather than fixed site concentrations as there were more studies available with this metric. Sensitivity analysis suggested that this choice did not have a major influence on the results i.e. our findings are informative in terms of the measurement error parameters relevant to time-series studies using fixed-site monitors.

Moreover, in this meta-analysis we used between-subject summary statistics, as individual variation was not provided. Thus, we could not address the within-subject variability of the exposure misclassification. In fact, the concepts described in this study were based primarily on arguments about variations of time-averaged differences between personal exposures and ambient concentrations. We are not informed about day-to-day variability in exposure misclassification and its temporal component may have been underestimated due to the lack of raw, daily data. As a result, we assumed that the error is on average the same across different days. A study that incorporates individual exposure and location data and assesses within-subject day to day error variability would add new insight. These data can also increase understanding on the within-subject variation of the factors used to estimate measurement error in this review work. We are working on previously established cohorts to explore these issues, especially the sources of spatial and temporal variations and the degree to which estimation of errors from one relates to or can inform the other. Furthermore, the use of sulphate as a tracer assumes that SO_4^{2-} acts as an appropriate surrogate for the infiltration of $PM_{2.5}$. Some components of $PM_{2.5}$ may be smaller in size than SO_4^{2-} particles and/or of a different physical form. Nonetheless, SO_4^{2-} itself usually forms a significant part of ambient $PM_{2.5}$.

Finally, this study does not consider measurement error related to the performance of the pollutant measurement devices. While this error is generally low in fixed site reference monitors, it is often much larger in residential and personal monitoring devices due to their portable specifications and necessity for deployment in larger numbers. While all studies in this analysis provided details of the types of monitors used (Tables S2-S3), measurement uncertainty calculations were not provided.

Fig. 4. Scatter plots of ambient concentrations against either absolute error (upper graphs) or relative error (lower graphs). Left: $PM_{2.5}$, Right: NO_2, coloured by age group.

5. Conclusions

This study adds new perspectives to measurement error implications for the interpretation of air pollution epidemiological associations. In addition to a quantitative review of the personal exposure literature, we estimated personal exposure to air pollution from outdoor origin. In brief our study shows that:

(i). Outdoor sources contribute around 44% (range 33–55%) to total personal exposure to $PM_{2.5}$ and 74% (range 57–88%) for NO_2.
(ii). The overall estimate of the mean difference between personal exposure from outdoor sources and the ambient concentrations (i.e. measurement error) was 5.72 μg/m^3 for $PM_{2.5}$ and 7.17 ppb for NO_2.
(iii). The mean difference was greater and more variable for NO_2 than for $PM_{2.5}$, while the correlations between these differences, i.e. correlation between measurement errors, were not reported in any study.
(iv). Large heterogeneity makes interpretation difficult especially as it was not described sufficiently by geographical location or age group of the study sample. It is nevertheless expected considering the large variability of sources and air pollution mixtures between cities in the same large region (e.g. Europe) or even within the same country.

Our findings enrich understanding of the structure of pollutant measurement errors, including their size and variance. These findings can be used in epidemiological studies, by applying measurement error corrections, e.g. regression calibration or simulation extrapolation (Keogh and White, 2014), to quantify the impact of measurement error on estimates of epidemiological associations that becomes of greater importance when considering multi-pollutant models. While this paper discusses the implications from a time-series or panel study perspective (short-term effects), an analogous approach could be taken to inform the influence of measurement error on estimates from cohort studies (long-term effects) (Sheppard et al., 2012).

We propose that future personal exposure and epidemiological studies present information relevant to interpreting the effects of measurement error on epidemiological associations including regression of *A* on *C*, which is needed for regression calibration. More work is needed regarding personal exposure studies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to

Table 6
Standard deviation of the measurement error of $PM_{2.5}$ and NO_2 (derived from random effects meta-analysis). Results before and after the "trim and fill" method, N: number of studies included in each meta-analysis for $PM_{2.5}$/NO_2.

Pollutant	Error Standard Deviation (95% CI)			
	Original Data (N = 30/25)	Imputed Data (N = 49/29)	Original Data, Publication Bias Corrected (N = 30/-)	Imputed Data, Publication Bias Corrected (N = -/-)
$PM_{2.5}$ *(μg/m^3)	6.85 (5.76, 7.94)	7.64 (6.70, 8.60)	5.92. (4.88, 7.18)	No trim and fill performed
NO_2*(ppb)	7.63 (6.42, 8.84)	7.39 (6.31, 8.46)	No trim and fill performed	No trim and fill performed

* Results reported are after the exclusion of some outlier values for the standard deviation of the error, i.e. SD(C-A), which were found > 20 units.

influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.105500.

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