Environmental Research 170 (2019) 243–251

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Incidence and mortality for respiratory cancer and traffic-related air pollution in São Paulo, Brazil

Adeylson Guimarães Ribeiro[a,*,1], George Stanley Downward[b,*,1], Clarice Umbelino de Freitas[c,3], Francisco Chiaravalloti Neto[d], Maria Regina Alves Cardoso[d], Maria do Rosario Dias de Oliveira Latorre[d], Perry Hystad[e], Roel Vermeulen[b,2], Adelaide Cassia Nardocci[a,2]

[a] Department of Environmental Health, School of Public Health, University of São Paulo, Av. Dr. Arnaldo, 715, São Paulo, SP CEP 01246-904, Brazil
[b] Institute for Risk Assessment Sciences, Utrecht University, P.O. Box 80178, 3508 TD Utrecht, the Netherlands
[c] Center for Epidemiological Surveillance, State Department of Health, Av. Dr. Arnaldo, 351, São Paulo, SP CEP:01246-000, Brazil
[d] Department of Epidemiology, School of Public Health, University of São Paulo, Av. Dr. Arnaldo, 715, São Paulo, SP CEP 01246-904, Brazil
[e] College of Public Health and Human Sciences, Oregon State University, 20C Milam Hall, Corvallis, OR 97331, USA

ARTICLE INFO

Keywords:
Air pollution
Vehicle emissions
Respiratory cancer
Vulnerable population
Environmental justice

ABSTRACT

Background: Multiple lines of evidence have associated exposure to ambient air pollution with an increased risk of respiratory malignancies. However, there is a dearth of evidence from low-middle income countries, including those within South America, where the social inequalities are more marked.
Objectives: To quantify the association between exposures to traffic related air pollution and respiratory cancer incidence and mortality within São Paulo, Brazil. Further, we aim to investigate the role of socioeconomic status (SES) upon these outcomes.
Methods: Cancer incidence between 2002 and 2011 was derived from the population-based cancer registry. Mortality data (between 2002 and 2013) was derived from the Municipal Health Department. A traffic density database and an annual nitrogen dioxide (NO_2) land use regression model were used as markers of exposure. Age-adjusted Binomial Negative Regression models were developed, stratifying by SES and gender.
Results: We observed an increased rate of respiratory cancer incidence and mortality in association with increased traffic density and NO_2 concentrations, which was higher among those regions with the lowest SES. For cancer mortality and traffic exposure, those in the most deprived region, had an incidence rate ratio (IRR) of 2.19 (95% CI: 1.70, 2.82) when comparing the highest exposure centile (top 90%) to the lowest (lowest 25%). By contrast, in the least deprived area, the IRR for the same exposure contrast was.1.07 (95% CI: 0.95, 1.20). For NO_2 in the most deprived regions, the IRR for cancer mortality in the highest exposed group was 1.44 (95% CI: 1.10, 1.88) while in the least deprived area, the IRR for the highest exposed group was 1.11 (95% CI: 1.01, 1.23).
Conclusions: Traffic density and NO_2 were associated with an increased rate of respiratory cancer incidence and mortality in São Paulo. Residents from poor regions may suffer more from the impact of traffic air pollution.

1. Introduction

Ambient air pollution has been well established as a risk factor in the development of lung cancer, with the International Agency for Research on Cancer (IARC) classifying ambient air pollution and its associated particulate matter as a Group 1 carcinogen (IARC, 2013). Further, diesel engine exhaust or emissions are also classified as Group 1 carcinogens based on sufficient evidence of increased risk of lung cancer (IARC, 2012).

The bulk of the evidence investigating air pollution and lung cancer

* Corresponding author.
E-mail addresses: adeylsonribeiro@usp.br (A.G. Ribeiro), G.S.Downward@uu.nl (G.S. Downward), franciscochiara@usp.br (F. Chiaravalloti Neto), rcardoso@usp.br (M.R.A. Cardoso), mdrddola@usp.br (M.d.R.D.d.O. Latorre), perry.hystad@oregonstate.edu (P. Hystad), R.C.H.Vermeulen@uu.nl (R. Vermeulen), nardocci@usp.br (A.C. Nardocci).
[1] Co-first author.
[2] Co-senior author.
[3] In memorian.

https://doi.org/10.1016/j.envres.2018.12.034
Received 18 September 2018; Received in revised form 29 November 2018; Accepted 15 December 2018
Available online 18 December 2018
0013-9351/

risk has been derived from high-income countries, predominantly in North America and Europe (Beelen et al., 2008a; Hamra et al., 2014; Hystad et al., 2013; Olsson et al., 2011; Puett et al., 2014; Raaschou-Nielsen et al., 2016, 2013; Villeneuve et al., 2014; Yorifuji et al., 2016). With the exception of several studies conducted mainly in China (Li et al., 2018; Shao et al., 2019; Yue et al., 2017), there is a dearth of evidence from low and middle income countries (LMIC). Furthermore, a large number of recent studies only utilized mortality data and long-term exposure to conduct their risk analyses (Beelen et al., 2014; Bidoli et al., 2016; Carugno et al., 2016; Crouse et al., 2015; Fischer et al., 2015; Hansell et al., 2016; Lepeule et al., 2012; Yorifuji et al., 2013; Zhou et al., 2015) with relatively few studies using incidence data, with the notable exception of the ESCAPE study which analyzed air pollution and lung cancer incidence in European cohorts (Raaschou-Nielsen et al., 2013).

Previous studies have established that socioeconomic status (SES) can influence the exposure and effects of air pollution (Cesaroni et al., 2010; Deguen and Zmirou-Navier, 2010; Habermann et al., 2014; Havard et al., 2009; Pearce et al., 2006). In 2009, the Environmental Protection Agency (EPA) initiated activities to formalize and ensure that the development of regulations, in the context of environmental and health impacts, take into account environmental justice (Nweke et al., 2011). Thus, when evaluating the relationship between living near areas of high traffic density and exposure to air pollution, a socioeconomic analysis should be considered. According to Galobardes et al. (2007), socioeconomic measures on an area-level are specifically needed to investigate whether these aspects of the place where a person lives affects the person's health. Moreover, understanding the role of SES as an important factor of susceptibility to ambient air pollution is essential to the process of implementing air quality control programs (Samet and White, 2004).

To address the dearth of studies in LMICs and to evaluate the impact of a wider contrast in SES, we performed a study in São Paulo, where a broad contrast in SES exists, to quantify the association between incidence and mortality for respiratory cancers and traffic-related air pollution and its interaction with SES.

2. Methods

2.1. Study area

The municipality of São Paulo occupies an area of 1521.11 km^2 and has a population of approximately 12 million, making it the largest and most populous city in Brazil (Fig. 1). It is the capital of the state of São Paulo, which is considered the main national industrial center, with a Gross Domestic Product (GDP) per capita of approximately 16 thousand dollars in 2014 (IBGE, 2017). It has a fleet of approximately 8.6 million vehicles (of which approximately 16% are diesel operated) which circulate daily on its 18,000 km of routes (DETRAN, 2017). The distribution of traffic routes and volume is varied, with a high density both in the central region of the city, as well as extensive corridors and highways that cross the urban area.

2.2. Case ascertainment

The outcomes of interest to the present study were the incidence and mortality of respiratory malignancies among men and women above the age of 20. These outcomes were coded by the International Classification of Diseases (ICD-10) as follows: C32 - malignant neoplasm of the larynx, C33 - malignant neoplasm of the trachea, and C34 - malignant neoplasm of the bronchi and lungs.

The incidence of respiratory malignancies between 2002 and 2011 was acquired from the population-based cancer registry of São Paulo. The mortality rate of respiratory malignancies between 2002 and 2013 was acquired from the Mortality Information System (SIM) of the Municipal Health Department. The incidence registry was the result of active surveillance and the mortality registry passive surveillance. Together they covered all cases in the city of São Paulo.

A total of 15,411 incident cases (10,270 men, 5141 women) and 19,500 deaths attributable to respiratory cancers (12,826 men, 6674 women) were identified. The incident cases were geocoded by home address and the mortality cases by residential zip code using the centroid (home address information is unavailable for mortality cases – residential zip code contains equivalent geographic information for the purposes of exposure assignment). The software ArcGIS version 9.3 was used for the geocoding process.

2.3. Exposure assessment

Residential exposure to traffic-related emissions was estimated for 500 m × 500 m cells. Cell size was determined based on a review study which reported that an exposure zone within a range of 300–500 m from a major road represented the area most highly affected by traffic emissions (HEI Panel on the Health Effects of Traffic-Related air

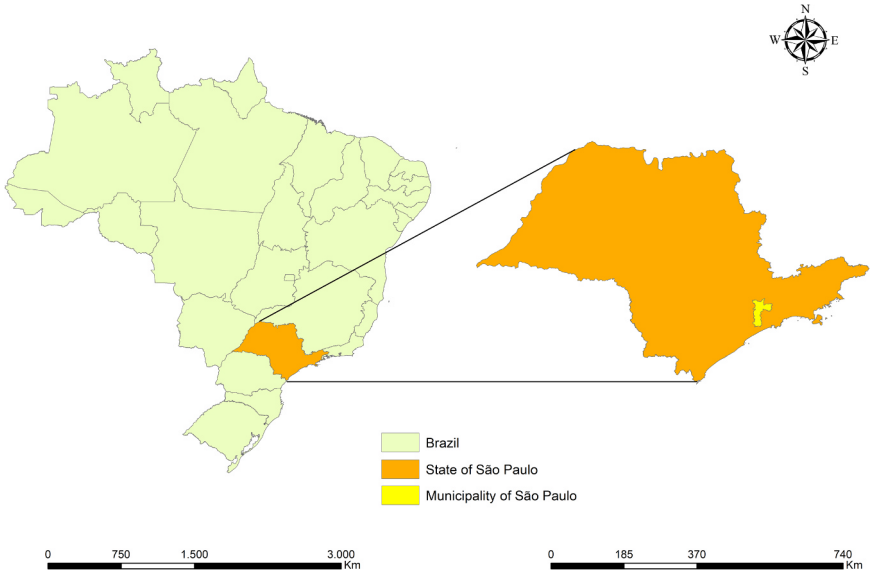

Fig. 1. Geographical location of the municipality of São Paulo, Brazil.

Pollution, 2010). Therefore, the definition of cell size considered both that the greatest exposure occurs at a distance of up to 500 m of high-traffic roads and that the cell could not be smaller than 100 m × 100 m (which is the usual size of the blocks).

The volume and density of traffic were assigned for the year 2008, and the annual estimates of nitrogen dioxide (NO_2) averaged between 1997 and 2011, at the home street of incident and mortality cases. The development of the traffic density dataset has been described elsewhere (Cardoso et al., 2010). Briefly, the Traffic Engineering Company of São Paulo (CET) conducts vehicular counts in streets throughout the city, which are classified according to their function in traffic distribution as: expressway, arterial-1, arterial-2, arterial-3, collector-1, collector-2, and local. These categories correlate well with their traffic volumes. The number of cars, motorcycles, buses and trucks were counted, from Monday to Friday, during the peak hours of the morning (7–10 a.m.) or afternoon (5–8 p.m.). The number of vehicles were counted in 15 min intervals and multiplied by four to convert into hourly volumes. Measurements were never performed near traffic lights nor when traffic was stagnant.

The current study complemented this routine data with additional traffic counts, performed using the same method used by the CET in additional streets which were evenly distributed throughout the city. In total, 681 streets were measured, corresponding to 21% of the total number of expressways; 16% of arterial-1; 21% of arterial-2; 14% of arterial-3; 9% of collector-1; 6% of collector-2; and 0.5% of the local streets of the city. The mean volume for each street category was attributed to the other streets of the same category without any measurement. All traffic information was entered into a geo-coded street database. The urban area was subsequently divided into a grid with 500 m x 500 m cells. The software ET Geowizards 9.9 for ArcGIS 9.2 was used for constructing the vectorial grid of the units of analysis. The traffic density was calculated for each cell by:

$$TD = \frac{\sum_{i=1}^{n} V_i L_i}{A}$$

Where TD is the traffic density of each cell (vehicles/hour/meter), V_i is the number of vehicles (vehicles/hour), L_i is the length of the i-th segment of the street (meters), A is the area (meters^2) of the cell (500 m x 500 m) and n is the number of segments of streets inside the cell. Using this approach, the total traffic density (TTD), the traffic density of vehicles powered by gasoline and ethanol (TDG) (cars + motorcycles)[4] and vehicles powered by diesel (buses + trucks) (TDD) were calculated. Traffic density was calculated using the software ArcGIS ArcInfo 9.3 (Environmental Systems Research Institute ESRI, 2008).

Annual estimates of NO_2 were obtained from a global NO_2 land use regression (LUR) model, which included satellite observations and geographic predictor variables. The detailed description of the NO_2 LUR model has been described elsewhere (Larkin et al., 2017). Briefly, 5220 ground-based monitors from 57 nations were used to develop the LUR model. Satellite estimates of NO_2, developed by combining tropospheric NO_2 column retrievals from the SCIAMACHY and GOME-2 satellites with output from the global GEOS-Chem model (from 1997 to 2011), captured regional NO_2 concentrations at a 10 × 10 km resolution. Multiple land use predictor variables (e.g. length of roads, population density, green spaces etc.) were included in the final LUR models (variable selection was performed via Lasso), which predicted NO_2 at a 100 × 100 m resolution, thus capturing fine-scale within-city variation in traffic related air pollutants. The final LUR predicted 54% of the global NO_2 variation with a mean absolute error of 3.7 ppb. We averaged NO_2 predictions to the 500 m x 500 m analytics cells, where each cell had a predicted annual NO_2 that was used to assign exposure to residential locations located within this area unit.

[4] 16% of the vehicles run only on ethanol and the others run on a mixture of 75% of gasoline and 25% of ethanol.

The Municipal Human Development Index (MHDI) was used as an indicator of SES. This indicator considered three dimensions: longevity, income and education grouped by a geometric mean, according to the methodology of the United Nations Development Programme (UNDP Brazil, 2013), which ranges on a scale from 0 to 1, by census tract. For longevity, the dimension used an average of mortality data from the years 2009, 2010 and 2011, which was obtained from the Municipal Health Department. The use of an average avoided an atypical mortality event in a single year producing a bias. For the income and education dimensions, data from the most recent Demographic Census, performed in 2010 by the Brazilian Institute of Geography and Statistics (which aggregated individual-level measures by census tract) were used (IBGE, 2010). The income dimension was measured by the per capita income, defined as the sum of the income of all residents, divided by the number of residents. In the calculation of the education dimension the educational level of adults and children were treated and weighted separately. The educational level of the adult population was measured by the percentage of people 18 years and older who had completed grade school. This metric was given a weighting of 1. For children, the percentages of children attending schools and completing specific years at school were given a weighting of 2. The education dimension was calculated as the geometric mean of these components. In these analyses, population data and MHDI were converted to grid cells. The values of the intercept census tract in each grid cell, weighted by the proportion of the area occupied by each of them, were summed to calculate populations and obtain an average to calculate the MHDI. This conversion was done with the software ArcGIS ArcInfo 9.3 (Environmental Systems Research Institute ESRI, 2008).

The population was categorized in five groups according to age: 21–40, 41–60, 61–70, 71–80 and ≥ 81 years old. The grid cells were classified by MHDI in four categories: low (quartile ≤ 25), medium (quartile 26–50), medium-high (quartile 51–75) and high (quartile > 75) (Table 1). The level of exposure was measured by traffic density and NO_2 measurements categorization into five centile groups: 0–25, 26–50, 51–75, 76–90 and > 90% (Fig. 2). Grid cells with a total population less than 20 inhabitants were excluded from analysis, (1876 cells out of a total of 6384 were excluded).

2.4. Statistical analyses

The effect of traffic density and NO_2 exposure on the rate of incidence and mortality from respiratory cancers was quantified by means of incidence rate ratios (IRRs) and corresponding 95% confidence intervals (CI), calculated using Binomial Negative Regression models. The dependent variable was the number of incident respiratory cancer cases and the number of deaths from all respiratory cancers, offset by population above the age of 20. All IRRs were adjusted for MHDI, age and gender. To further investigate the role of SES, models were also stratified by MHDI category. Further, the interaction between exposure and MHDI was also tested. In interaction analysis, MHDI was kept as a categorical variable and exposure as a continuous one. Analyses were performed using Stata version 12 (StataCorp, 2011).

3. Results

Of the incident cases, 21% were laryngeal malignancies (C32), 78% were bronchial and lung malignancies (C34) and less than 1% were tracheal malignancies (C33). Of the mortalities, 15% were related to laryngeal malignancies, 85% bronchial and lung malignancies, and less than 1% tracheal malignancies.

Fig. 2a and b show the traffic density and annual NO_2 estimates for São Paulo respectively. In general, traffic density and NO_2 were higher in the central regions than the peripheral regions and were moderately correlated with each other (correlation coefficient of 0.56), likely representing traffic-related generation of NO_2. Traffic density ranged from 0 to 163 m.vehicles.hour/m^2 (the number of vehicles for each

Table 1
Distribution of the study population[a] stratified by age group, gender and category of MHDI – 2010[b] (São Paulo, Brazil).

Total people in study population	7,846,441
Age group (%)	
21–40	50.2
41–60	34.1
61–70	8.6
71–0	4.9
≥ 80	2.2
Gender (%)	
Men	46.0
Women	54.0
MHDI category (%)	
1 (lowest)	19.7
2	28.6
3	25.8
4 (highest)	25.9

[a] Grid cells with a total population less than 20 inhabitants were excluded.
[b] MHDI – 2010: Municipal Human Development Index.

street segment within one hour divided by the area in square meters) and ambient NO_2 concentrations ranged from 3 to 32 μg/m^3. The geographic distribution of MHDI is shown in Fig. 2c. Areas with the highest index were typically concentrated in the central regions with the index declining towards the peripheral regions.

The IRRs for cancer incidence and mortality for all individuals, men, and women are shown in Table 2. Overall, the incidence of respiratory cancer showed a statistically significant exposure-response gradient for both traffic density (IRR: 1.03, 95% CI: 1.02, 1.05 per 10 m.vehicle-s.hour/m^2 increase) and NO_2 (IRR: 1.14, 95% CI: 1.11, 1.18 per 5 μg/m^3 increase). Individuals in the highest 2 centile groups for traffic density had approximately 2-fold increases in cancer incidence (IRR for highest vs. lowest centile (1.63, 95% CI: 1.46, 1.81). For NO_2 exposure, individuals in the highest centile had an IRR of 1.34 (95% CI: 1.22, 1.47) compared to the lowest centile. Similar incidence rates between men and women were observed in relation to traffic exposure while lower rates were observed for NO_2 in women.

For cancer mortality, a significant exposure-response gradient was seen for ambient NO_2 (IRR: 1.05, 95% CI: 1.02, 1.08 per 5 μg/m^3 increase). The rate of death was approximately 30% higher in NO_2 exposure groups higher than the reference centile (e.g. IRR among the highest centile: 1.18, 95% CI: 1.09, 1.29). When stratifying by gender, men generally had a higher rate of death, except for the highest exposed group where findings were equivalent – men had an IRR of 1.19 (95% CI: 1.07, 1.32) and women an IRR of 1.20 (95% CI: 1.04, 1.39). The IRR for mortality in relation to traffic density was generally higher for men than women. For example, in the highest centile men had an IRR of 1.56. (95% CI: 1.38, 1.76) and women an IRR of 1.27 (95% CI: 1.08, 1.49).

The IRRs of incidence and mortality in relation to traffic density, stratified by MHDI category are shown in Table 3. Overall, an excess in incidence and mortality rates within MHDI 1 (the lowest) is observed compared to the other MHDI categories. The exposure-response gradient between traffic density and both incidence and mortality is notably higher in the lowest MHDI strata (1.26, 95% CI: 1.14, 1.40 and

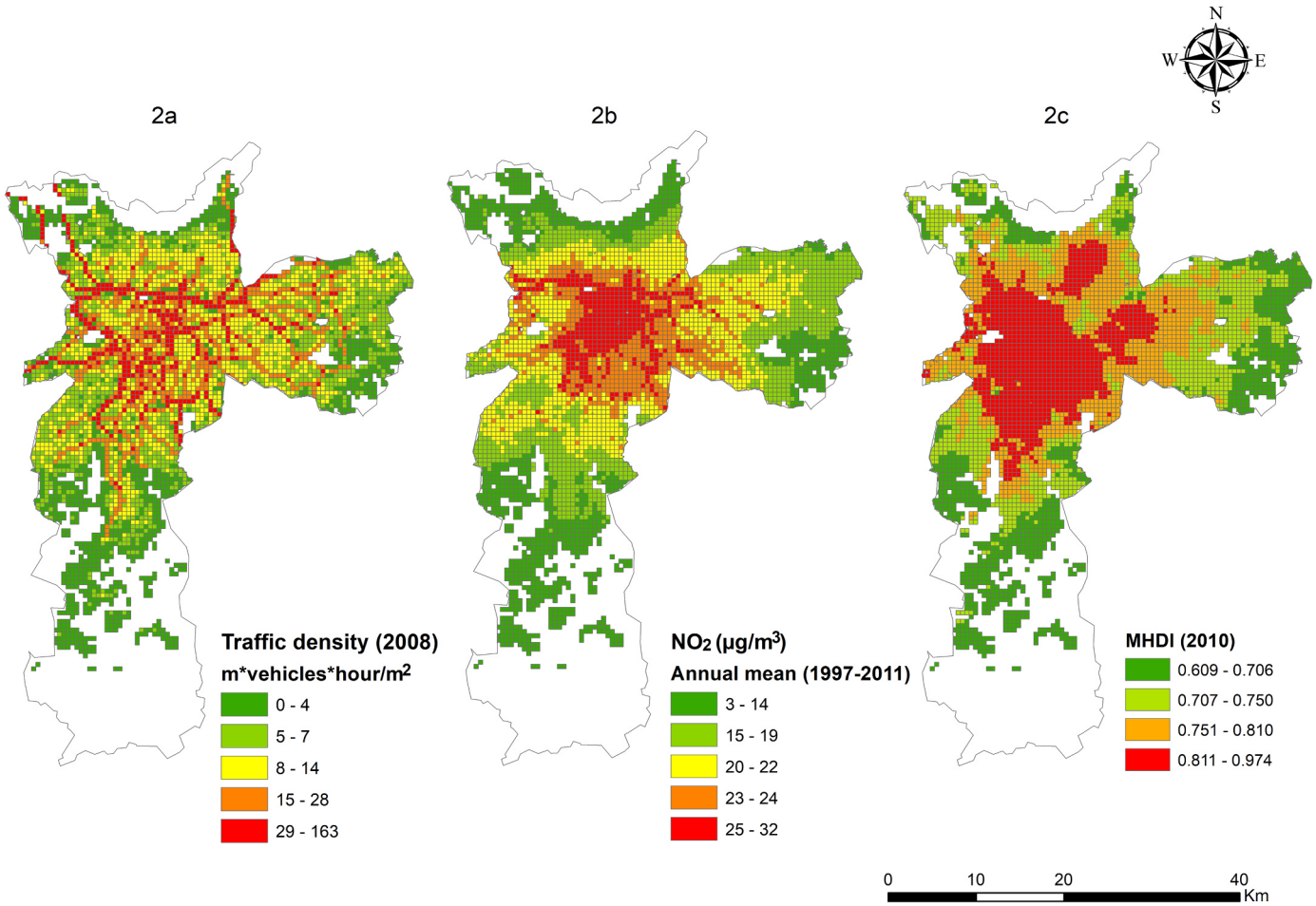

Fig. 2. (a) Total traffic density (2008), (b) mean annual NO_2 concentrations (1997–2011) and (c) Municipal Human Development Index (MHDI) − 2010, by grid cells (500 m × 500 m), in São Paulo, Brazil.

Table 2
Incidence rate ratio (IRR) (and 95% CI) for incidence and mortality for respiratory cancer by proximity to traffic density and NO_2 concentrations (São Paulo, Brazil).

	All		Men		Women	
	IRR[a]	(95% CI)	IRR[b]	(95% CI)	IRR[b]	(95% CI)
Incidence (2002–2011)						
Traffic Density (%)						
0–25	1		1		1	
26–50	1.36	(1.24–1.50)	1.41	(1.25–1.59)	1.46	(1.22–1.74)
51–75	1.58	(1.43–1.73)	1.66	(1.47–1.87)	1.62	(1.35–1.93)
76–90	1.69	(1.53–1.87)	1.76	(1.55–1.99)	1.78	(1.48–2.14)
> 90	1.63	(1.46–1.81)	1.75	(1.53–2.00)	1.65	(1.36–2.01)
10-unit increase	1.03	(1.02–1.05)	1.04	(1.03–1.06)	1.02	(1.00–1.05)
NO_2 (%)						
0 − 25	1		1		1	
26 − 50	0.98	(0.91–1.06)	0.99	(0.90–1.09)	0.97	(0.84–1.11)
51 − 75	1.07	(0.99–1.16)	1.13	(1.02–1.25)	0.98	(0.85–1.13)
76 − 90	1.13	(1.04–1.24)	1.21	(1.09–1.35)	1.00	(0.86–1.16)
> 90	1.34	(1.22–1.47)	1.40	(1.25–1.58)	1.24	(1.06–1.45)
5-μg/m^3 increase	1.14	(1.11–1.18)	1.16	(1.12–1.20)	1.12	(1.06–1.17)
Mortality (2002–2013)						
Traffic Density (%)						
0–25	1		1		1	
26–50	1.36	(1.25–1.47)	1.45	(1.30–1.61)	1.25	(1.08–1.43)
51–75	1.44	(1.32–1.56)	1.61	(1.45–1.79)	1.24	(1.07–1.43)
76–90	1.47	(1.35–1.61)	1.60	(1.43–1.80)	1.30	(1.12–1.51)
> 90	1.42	(1.29–1.56)	1.56	(1.38–1.76)	1.27	(1.08–1.49)
10-unit increase	1.00	(0.99–1.02)	1.01	(0.99–1.02)	1.00	(0.98–1.02)
NO_2 (%)						
0–25	1		1		1	
26–50	1.06	(0.99–1.13)	1.06	(0.97–1.15)	1.11	(0.99–1.25)
51–75	1.10	(1.02–1.18)	1.14	(1.04–1.25)	1.08	(0.95–1.22)
76–90	1.06	(0.98–1.15)	1.13	(1.02–1.24)	1.01	(0.88–1.16)
> 90	1.18	(1.09–1.29)	1.19	(1.07–1.32)	1.20	(1.04–1.39)
5-μg/m^3 increase	1.05	(1.02–1.08)	1.05	(1.01–1.08)	1.05	(1.00–1.10)

[a] Estimates from negative binomial regression models adjusted by Municipal Human Development Index – MHDI (2010), age and gender.
[b] Adjusted by MHDI 2010 and age.

1.21, 95% CI: 1.11, 1.32 per 10 units respectively) than the highest (1.04, 95% CI: 1.02, 1.05 and 1.01, 95% CI: 1.00, 1.03 per 10 units). Further, individuals in the lowest MHDI strata who experienced the highest traffic density centile had incidence and mortality IRRs up to 2 times higher than those experiencing similar density in the highest MHDI group (incidence IRR for lowest MHDI: 2.72, 95% CI: 1.98, 3.73 and for the highest: 1.30, 95% CI: 1.16, 1.46).

The excess incidence and mortality rates among the lowest MHDI is also seen when examining ambient NO_2 concentrations (Table 4). As with traffic density, those in the lowest MHDI category who experience the highest levels of ambient NO_2 have higher IRRs for both incidence (1.45, 95% CI: 1.04, 2.00) and mortality (1.44, 95% CI: 1.10, 1.88) than those in the highest MHDI category (IRR for incidence: 1.42, 95% CI: 1.29, 1.57; for mortality: 1.11, 95% CI: 1.01, 1.23). However, the

Table 3
Incidence rate ratio (IRR)[a] (and 95% CI) for incidence and mortality for respiratory cancer by proximity to traffic density, stratified by category of MHDI – 2010[b] (São Paulo, Brazil).

	Incidence (2002–2011)		Mortality (2002–2013)			Incidence (2002–2011)		Mortality (2002–2013)	
	IRR	(95% CI)	IRR	(95% CI)		IRR	(95% CI)	IRR	(95% CI)
MHDI 1 (lowest)					**MHDI 2**				
Traffic Density (%)					Traffic Density (%)				
0–25	1		1		0–25	1		1	
26–50	1.95	(1.39–2.73)	1.49	(1.13–1.96)	26–50	1.26	(1.08–1.47)	1.20	(1.05–1.38)
51–75	2.27	(1.67–3.10)	2.03	(1.58–2.60)	51–75	1.35	(1.16–1.57)	1.22	(1.07–1.40)
76–90	2.45	(1.80–3.34)	2.26	(1.77–2.88)	76–90	1.45	(1.23–1.70)	1.34	(1.16–1.55)
> 90	2.72	(1.98–3.73)	2.19	(1.70–2.82)	> 90	1.41	(1.17–1.69)	1.18	(1.00–1.40)
10-unit increase	1.26	(1.14–1.40)	1.21	(1.11–1.32)	10-unit increase	1.05	(1.01–1.08)	1.01	(0.98–1.05)
MHDI 3					**MHDI 4 (highest)**				
Traffic Density (%)					Traffic Density (%)				
0–25	1		1		0–25	1		1	
26–50	1.14	(1.03–1.26)	1.15	(1.05–1.26)	26–50	1.25	(1.15–1.36)	1.11	(1.02–1.20)
51–75	1.31	(1.19–1.45)	1.19	(1.09–1.30)	51–75	1.30	(1.19–1.41)	1.13	(1.04–1.23)
76–90	1.25	(1.12–1.41)	1.10	(0.99–1.22)	76–90	1.36	(1.23–1.50)	1.23	(1.12–1.35)
> 90	1.14	(0.97–1.33)	0.98	(0.85–1.13)	> 90	1.30	(1.16–1.46)	1.07	(0.95–1.20)
10-unit increase	1.02	(0.99–1.04)	0.98	(0.96–1.00)	10-unit increase	1.04	(1.02–1.05)	1.01	(1.00–1.03)

[a] Estimates from negative binomial regression models adjusted by age and gender.
[b] MHDI-2010: Municipal Human Development Index.

Table 4
Incidence rate ratio (IRR)[a] (and 95% CI) for incidence and mortality for respiratory cancer by NO_2 concentrations, stratified by category of MHDI – 2010[b] (São Paulo, Brazil).

	Incidence (2002–2011)		Mortality (2002–2013)			Incidence (2002–2011)		Mortality (2002–2013)	
	IRR	(95% CI)	IRR	(95% CI)		IRR	(95% CI)	IRR	(95% CI)
MHDI 1 (lowest)					**MHDI 2**				
NO_2 (%)					NO_2 (%)				
0–25	1		1		0–25	1		1	
26–50	1.50	(1.08–2.10)	1.19	(0.90–1.57)	26–50	0.99	(0.86–1.13)	0.96	(0.86–1.09)
51–75	1.45	(1.05–2.00)	1.48	(1.14–1.93)	51–75	1.09	(0.96–1.24)	1.02	(0.91–1.14)
76–90	1.45	(1.05–2.01)	1.41	(1.08–1.84)	76–90	1.12	(0.98–1.29)	0.99	(0.87–1.11)
> 90	1.45	(1.04–2.00)	1.44	(1.10–1.88)	> 90	1.24	(1.07–1.44)	1.06	(0.93–1.21)
5-μg/m^3 increase	1.06	(0.97–1.14)	1.12	(1.05–1.20)	5-μg/m^3 increase	1.13	(1.06–1.20)	1.05	(0.99–1.11)
MHDI 3					**MHDI 4 (highest)**				
NO_2 (%)					NO_2 (%)				
0–25	1		1		0–25	1		1	
26–50	1.01	(0.92–1.11)	1.03	(0.96–1.13)	26–50	1.10	(1.00–1.20)	1.03	(0.95–1.12)
51–75	1.05	(0.96–1.15)	1.00	(0.92–1.08)	51–75	1.14	(1.05–1.24)	1.00	(0.92–1.08)
76–90	1.18	(1.06–1.31)	1.01	(0.91–1.11)	76–90	1.25	(1.14–1.37)	1.17	(1.07–1.27)
> 90	1.23	(1.07–1.40)	0.93	(0.82–1.06)	> 90	1.42	(1.29–1.57)	1.11	(1.01–1.23)
5-μg/m^3 increase	1.09	(1.03–1.16)	0.96	(0.91–1.01)	5-μg/m^3 increase	1.23	(1.17–1.29)	1.09	(1.04–1.14)

[a] Estimates from negative binomial regression models adjusted by age and gender.
[b] MHDI-2010: Municipal Human Development Index.

exposure-response gradient between NO_2 and mortality is only slightly higher between the lowest MHDI strata (1.12, 95% CI: 1.05, 1.20 per 5 μg/m^3) and the highest (1.09, 95% CI: 1.04, 1.14 per 5 μg/m^3) and the difference was not statistically significant considering the overlap of CI values.

The interaction of MHDI as a categorical variable and exposure as a continuous variable was examined. This yielded similar results to the stratified results, finding differing IRRs for the varying MHDI categories. For example, the lung cancer mortality IRR for traffic density and MHDI category 1 was 1.22 (95% CI: 1.12, 1.33) while for MHDI category 4 it was 1.01 (95% CI: 1.00, 1.03). For NO_2 and cancer mortality, the IRR for MHDI category 1 was 1.13 (95% 1.05, 1.21) and for MHDI category 4 it was 1.09 (95% CI: 1.04, 1.15). Full results are available in the supplement.

4. Discussion

This study found an increased rate of respiratory cancer incidence and mortality in association with an increase in traffic density and NO_2 concentrations within São Paulo. Stratifying by categories of MHDI showed that the degree of this relationship was even more pronounced in the lowest, indicating that residents of these regions may suffer more from the effects of traffic-related air pollution.

Our results are generally consistent with previous work, although the larger IRRs observed here may reflect differences in tailpipe emissions since most studies have been conducted in North America and Europe which have more stringent emission controls. Chen et al. (2009) showed an increased risk of lung cancer in areas with high traffic density in the United States, reporting risks 136% and 68% higher for adenocarcinoma and squamous cells carcinomas, respectively, for the highest (937 motor vehicles per square mile) vs. lowest (one motor vehicle per square mile) exposed groups. Hystad et al. (2013), in a Canadian case-control study, found elevated risks for lung cancer incidence associated with living within 100 m of highways for a period of 10 years (OR: 1.10, 95% CI: 0.83, 1.46) and per 10 ppb increase for NO_2 (OR: 1.34; 95% CI: 1.07, 1.69). Another Canadian study, with a large national-level cohort, found positive associations (HR: 1.07; 95% CI: 1.05, 1.10) between trachea, bronchus, and lung cancer deaths and cumulative exposure to an increment of 8.1ppb for NO_2 (Crouse et al., 2015). Raaschou-Nielsen et al. (2011), in a Danish cohort study, reported an IRR for lung cancer of 1.30 (95% CI: 1.05, 1.61) when comparing the highest quartile of residential nitrogen oxides (> 29.7 μg/m^3), to the lowest concentrations (< 17.2 μg/m^3). Studies conducted in The Netherlands showed an association between exposure to NO_2 and an elevated risk of incident lung cancer (HR: 1.29, 95% CI: 1.08, 1.54, per 30 μg/m^3) and lung cancer mortality (HR: 1.10, 95% CI: 1.09, 1.11, per 10-μg/m^3 increase) (Fischer et al., 2015; Hart et al., 2015). A systematic review and meta-analysis found that a 10-μg/m^3 increase in exposure to NO_2 was associated with a meta-estimate for lung cancer of 1.04 (95% CI: 1.01, 1.08) (Hamra et al., 2015). In an Italian study, Bidoli et al. (2016) reported elevated of risks of death from lung cancer among those residing within 25 m of a major road, adjusting for urban and rural environments, in both men (1.10, 95% CI: 1.06, 1.14) and women (1.25, 95% CI: 1.10, 1.44). Long-term exposure to NO_2 was also associated with lung cancer mortality in Italy (HR: 1.04, 95% CI: 1.02, 1.07) and Japan (HR: 1.20, 95% CI: 1.03, 1.40), per 10 μg/m^3 increase (Cesaroni et al., 2013; Yorifuji et al., 2013). However, the ESCAPE study has not found any significant association between lung cancer and nitrogen oxides concentration or traffic intensity on the nearest street in Europe (Raaschou-Nielsen et al., 2013).

The present paper investigated the relationship between traffic densities, NO_2 concentrations, and cancer incidence/mortality in the context of MHDI categories. The traffic density and NO_2 concentrations in São Paulo were higher in the central regions, which was characterized by a better MHDI, indicating that the residents of these central regions are probably exposed to higher levels of air pollution than those who live in the most deprived regions. However, we found a higher rate of respiratory cancer mortality among residents from regions with the lowest MHDI, regardless of local traffic intensity and NO_2 concentrations, indicating that SES plays an important role in the relationship between air pollution and disease (however we note that this difference is less pronounced for disease incidence and ambient NO_2 as seen when comparing the exposure-response gradient between the lowest MHDI and the highest). These findings are consistent with a study conducted in South Carolina, USA, which found a strong association between SES metrics and estimated cancer risks associated with air pollutants, while also highlighting that on-road source risk was significantly related to all sociodemographic factors (Wilson et al., 2015). A partial explanation for this phenomenon may be that poorer people living in the peripheries of São Paulo have longer commuting hours, and thus using their residential address alone to assign traffic exposure may result in an underestimation of their true exposures. However, various vulnerability

factors, such as smoking prevalence and biological, nutritional, and educational status, the regular practice of physical activities and accessibility to health care services are also likely to have contributed to the increased rates in areas with the worst index. Differences in accessibility to health centers, health insurances, preventive care services and effective treatment options for population from regions with high MHDI in comparison those who live in peripheral regions are likely to impact disease prevention, treatment, and prognosis. Arcaya et al. (2015) affirms that an unequal distribution of physical health risks and resources across geographies and social groups contributes to social inequalities in health via material pathways.

The relationship between exposure to ambient air pollution and SES was discussed by Deguen and Zmirou-Navier (2010) who, in their analysis of European studies, concluded that deprived populations, although not always more exposed, suffer more from air pollution effects because of vulnerability factors. A comprehensive assessment of risk factor exposure and attributable burden of disease, from 1990 to 2016, estimated that air pollution was the second highest risk factor in terms of attributable disability-adjusted life-years (DALYs) in low Socio-demographic Index countries (Abajobir et al., 2017). This injustice in traffic-related air pollution exposure was discussed by Jerrett (2009) who stated that even in economically advanced countries air pollution and other environmental risks remain unequally distributed, disproportionately affecting disadvantaged populations.

Despite our findings, the current study has several limitations, including a lack of individual information. We assumed that all individuals within the 500 m x 500 m cells had the same exposure as it was not possible to assess the variation of individual exposures during daily movements within the city, potentially leading to exposure misclassification. Mortality cases were geocoded by the centroid of their residential zip code, which was less precise than the address level information available for incident cases. However, zip code information in São Paulo is highly detailed, and relative to the cell size we used in analysis, postal code remains a valid method of assigning residential location. Another consideration is that information on individual smoking habits was not available. Smoking is a well-known major risk factor for respiratory cancers, and historically was more prevalent in men. The population level smoking rates, by gender, reported in 2008, that women were more likely to report being never smokers (65%) than men (55%). Consequently, a lower proportion of women reported being current smokers (20% versus 24% for men) and ex-smokers (16% versus 21%) (São Paulo SP, 2010). However, despite these different smoking patterns, we observed comparable cancer rates for men and women by proximity to traffic density and exposure to higher ambient NO_2 concentrations, further strengthening our finding of an association between air pollution and respiratory cancers. To further investigate any potential bias by smoking, we accessed a periodic health survey, conducted by the Municipal Health Department and University of São Paulo, using a representative São Paulo sample for the years 2003, 2008 and 2015 (São Paulo SP, 2018). Using this information, we tested the associations between smoking status (never smoker, current smoker and ex-smoker) and per capita income ($\leq$ 2 and $>$ 2 minimum wages, being the smallest amount of money that employers are legally allowed to pay someone who works for them), finding no statistically significant results in 2003 ($p = 0.18$), 2008 ($p = 0.34$) and 2015 ($p = 0.93$). Smoking rates in the low income group were 19.61%, 19.46% and 16.48%, and in the high were 17.58%, 17.05% and 17.25%, in 2003, 2008 and 2015, respectively. Therefore, this slight (and non-statistically significant) difference in smoking rates between the two groups would not be sufficient to explain the disparity in IRRs. Moreover, previous western studies have found associations between air pollution and lung cancer in non-smoking groups (Beelen et al., 2008b; Hamra et al., 2014; Raaschou-Nielsen et al., 2011; Turner et al., 2011).

An additional limitation is that as respiratory cancers have long latency periods, and the specific exposures responsible for the measured outcomes likely occurred before the period in this study, requiring us to assume that the traffic-related exposures remained stable over preceding decades. There are some limitations to this assumption as while the number of cars in use was lower in previous years, the car fleet was less technologically advanced and the policies on the emissions of pollutants were less rigorous. Furthermore, the historical air quality data reported pollutants level higher in previous years in related to the year of the traffic density and estimates of NO_2 used in this study. For example, the PM_{10} and NO_2 concentrations decreased by around 60 $\mu g/m^3$ to 40 $\mu g/m^3$ and 80 $\mu g/m^3$ to 50 $\mu g/m^3$, respectively, from 1987 to 2008 (Andrade et al., 2017) meaning that the exposures assigned here likely under-estimate historical exposures.

Previous studies have investigated the impact of air pollution on the health of São Paulo's population (Marcilio and Gouveia, 2007; Pereira et al., 2005; Toledo and de, Nardocci, 2011; Yanagi et al., 2012) but no analyses to date were conducted to evaluate cancer risks in relation to residential proximity to traffic and exposure to NO_2 concentrations and its interaction with SES. São Paulo is characterized by great social inequalities and the use of small area units improved the SES evaluation. Although air quality reports have indicated a general improvement in air pollution rates in São Paulo over recent decades (Andrade et al., 2017), the population still coexists with high exposures to toxic pollutants. For example, PM_{10} in the metropolitan region, according the Environmental Company of the State of São Paulo (CETESB), presented an average concentration of 39 $\mu g/m^3$ over the last 17 years (CETESB - Companhia Ambiental do Estado de São Paulo, 2017), which is higher than the value recommended by the World Health Organization (WHO) of 20 $\mu g/m^3$ (WHO - World Health Organization, 2006). São Paulo has a pollutant monitoring network that includes 17 fixed stations with regular measurements for: PM_{10}, SO_2, NO_X, CO, O_3 and $PM_{2.5}$ but the number and geographical distribution of the stations are insufficient to measure exposures to these pollutants on a fine spatial scale. Furthermore, CETESB reported that the data from their monitoring networks are more representative of background pollution and do not have a good correlation with surrounding traffic. Therefore, despite the lack of other sources of air pollution data, a major strength of our study was the use of the global NO_2 land use regression model that allowed estimating NO_2 concentrations at a relatively fine spatial scale (100 m resolution). Other strengths include the use of a complete incidence and mortality database, the ability to estimate traffic density at a fine spatial scale, that might be used as a proxy for traffic exposure in São Paulo (Silva et al., 2006), and detailed information on socio-economic factors. Further, this study represents only one of a few studies investigating proxies of ambient air pollution on health within Latin American countries and represents the first time that the relationship between traffic density and NO_2 with respiratory cancers in Sao Paulo has been investigated.

5. Conclusions

The results of this study show that traffic density and ambient NO_2 concentrations were associated with an increased rate of incidence and death for respiratory cancers in São Paulo. This study also indicates that those with lower SES were more vulnerable to the development of respiratory cancers due to traffic pollution. While the reasons for this are not completely clear, it indicates an important at-risk group that warrants additional focus by policy makers and health providers.

Acknowledgments

We thank the National Council for Scientific and Technological Development (CNPq) – Process number 475362/2012-8, and the State of São Paulo Research Foundation (FAPESP) – FAPESP/PPP-SUS 2006/61616-5.

We also acknowledge the São Paulo Municipal Population-Based Cancer Registry and the São Paulo Municipal Health Department for the availability of the databases and the Institute for Risk Assessment

Sciences – IRAS, Utrecht University, The Netherlands, as an important partner in this work.

Funding

This work was supported by the Brazilian Ministry of Education – Coordination for the Improvement of Higher Education Personnel (CAPES), Adeylson G. Ribeiro/PDSE Program/Process number 88881.134281/2016-01.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2018.12.034.

References

Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., Abdulle, A.M., et al., 2017. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of disease study 2016. Lancet 390, 1345–1422. https://doi.org/10.1016/S0140-6736(17)32366-8.

Andrade, M., de, F., Kumar, P., de Freitas, E.D., Ynoue, R.Y., Martins, J., Martins, L.D., Nogueira, T., Perez-Martinez, P., de Miranda, R.M., Albuquerque, T., Gonçalves, F.L.T., Oyama, B., Zhang, Y., 2017. Air quality in the megacity of São Paulo: evolution over the last 30 years and future perspectives. Atmos. Environ. 159, 66–82. https://doi.org/10.1016/j.atmosenv.2017.03.051.

Arcaya, M.C., Arcaya, A.L., Subramanian, S.V., 2015. Inequalities in health: definitions, concepts, and theories. Glob. Health Action 8, 27106. https://doi.org/10.3402/gha.v8.27106.

Beelen, R., Hoek, G., van den Brandt, P.A., Goldbohm, R.A., Fischer, P., Schouten, L.J., Armstrong, B., Brunekreef, B., 2008a. Long-term exposure to traffic-related air pollution and lung cancer risk. Epidemiology 19, 702–710. https://doi.org/10.1097/EDE.0b013e318181b3ca.

Beelen, R., Hoek, G., van den Brandt, P.A., Goldbohm, R.A., Fischer, P., Schouten, L.J., Jerrett, M., Hughes, E., Armstrong, B., Brunekreef, B., 2008b. Long-term effects of traffic-related air pollution on mortality in a Dutch cohort (NLCS-AIR study). Environ. Heal. Perspect. 116, 196–202. https://doi.org/10.1289/ehp.10767.

Beelen, R., Raaschou-Nielsen, O., Stafoggia, M., Andersen, Z.J., Weinmayr, G., Hoffmann, B., et al., 2014. Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. Lancet 383, 785–795. https://doi.org/10.1016/S0140-6736(13)62158-3.

Bidoli, E., Pappagallo, M., Birri, S., Frova, L., Zanier, L., Serraino, D., 2016. Residential proximity to major roadways and lung cancer mortality. Italy, 1990–2010: an observational study. Int. J. Environ. Res. Public Health 13, 191. https://doi.org/10.3390/ijerph13020191.

Cardoso, M.R.A., Nardocci, A.C., Freitas, C.U., 2010. Estudo da relação entre doenças respiratórias e cardiovasculares e poluição veicular nas regiões metropolitanas do estado de São Paulo com a finalidade de subsidiar a estruturação das atividades do Programa de Vigilância em Saúde e Qualidade do Ar. São Paulo.

Carugno, M., Consonni, D., Randi, G., Catelan, D., Grisotto, L., Bertazzi, P.A., Biggeri, A., Baccini, M., 2016. Air pollution exposure, cause-specific deaths and hospitalizations in a highly polluted italian region. Environ. Res. 147, 415–424. https://doi.org/10.1016/j.envres.2016.03.003.

Cesaroni, G., Badaloni, C., Gariazzo, C., Stafoggia, M., Sozzi, R., Davoli, M., Forastiere, F., 2013. Long-term exposure to urban air pollution and mortality in a cohort of more than a million adults in Rome. Environ. Heal. Perspect. 121, 324–331. https://doi.org/10.1289/ehp.1205862.

Cesaroni, G., Badaloni, C., Romano, V., Donato, E., Perucci, C.A., Forastiere, F., 2010. Socioeconomic position and health status of people who live near busy roads: the Rome Longitudinal Study (RoLS). Environ. Heal. 9, 41. https://doi.org/10.1186/1476-069x-9-41.

CETESB - Companhia Ambiental do Estado de São Paulo, 2017. Qualidade do ar no estado de São Paulo 2016. São Paulo. URL ⟨https://cetesb.sp.gov.br/ar/wp-content/uploads/sites/28/2013/12/relatorio-ar-2016.pdf⟩ (accessed 30 October 2017).

Chen, F., Jackson, H., Bina, W.F., 2009. Lung adenocarcinoma incidence rates and their relation to motor vehicle density. Cancer Epidemiol. Biomark. Prev. 18. https://doi.org/10.1158/1055-9965.EPI-08-0741.

Crouse, D.L., Peters, P.A., Hystad, P., Brook, J.R., van Donkelaar, A., Martin, R.V., Villeneuve, P.J., Jerrett, M., Goldberg, M.S., Pope, C.A., Brauer, M., Brook, R.D., Robichaud, A., Menard, R., Burnett, R.T., 2015. Ambient PM2.5, O3, and NO2 exposures and associations with mortality over 16 years of follow-up in the Canadian Census Health and Environment Cohort (CanCHEC). Environ. Health Perspect. 123, 1180–1186. https://doi.org/10.1289/ehp.1409276.

Deguen, S., Zmirou-Navier, D., 2010. Social inequalities resulting from health risks related to ambient air quality–A European review. Eur. J. Public Health 20, 27–35. https://doi.org/10.1093/eurpub/ckp220.

DETRAN. Departamento Estadual de Trânsito de São Paulo, 2017. Frota de veículos em São Paulo. . URL ⟨https://www.detran.sp.gov.br/⟩ (accessed 13 July 2017).

Environmental Systems Research Institute (ESRI), 2008. ArcGis Release 9.3.

Fischer, P.H., Marra, M., Ameling, C.B., Hoek, G., Beelen, R., de Hoogh, K., Breugelmans, O., Kruize, H., Janssen, N.A.H., Houthuijs, D., 2015. Air Pollution and Mortality in Seven Million Adults: the Dutch Environmental Longitudinal Study (DUELS). Environ. Health Perspect. 123, 697–704. https://doi.org/10.1289/ehp.1408254.

Galobardes, B., Lynch, J., Smith, G.D., 2007. Measuring socioeconomic position in health research. Br. Med. Bull. 81–82, 21–37. https://doi.org/10.1093/bmb/ldm001.

Habermann, M., Souza, M., Prado, R., Gouveia, N., 2014. Socioeconomic inequalities and exposure to traffic-related air pollution in the city of Sao Paulo, Brazil. Cad Saude Publica 119–125.

Hamra, G.B., Guha, N., Cohen, A., Laden, F., Raaschou-Nielsen, O., Samet, J.M., Vineis, P., Forastiere, F., Saldiva, P., Yorifuji, T., Loomis, D., 2014. Outdoor particulate matter exposure and lung cancer: a systematic review and meta-analysis. Environ. Health Perspect. 122. https://doi.org/10.1289/ehp.1408092.

Hamra, G.B., Laden, F., Cohen, A.J., Raaschou-Nielsen, O., Brauer, M., Loomis, D., 2015. Lung cancer and exposure to nitrogen dioxide and traffic: a systematic review and meta-analysis. Environ. Health Perspect. 123, 1107–1112. https://doi.org/10.1289/ehp.1408882.

Hansell, A., Ghosh, R.E., Blangiardo, M., Perkins, C., Vienneau, D., Goffe, K., Briggs, D., Gulliver, J., 2016. Historic air pollution exposure and long-term mortality risks in England and Wales: prospective longitudinal cohort study. Thorax 71, 330–338. https://doi.org/10.1136/thoraxjnl-2015-207111.

Hart, J.E., Spiegelman, D., Beelen, R., Hoek, G., Brunekreef, B., Schouten, L.J., van den Brandt, P., 2015. Long-Term Ambient Residential Traffic-Related Exposures and Measurement Error-Adjusted Risk of Incident Lung Cancer in the Netherlands Cohort Study on Diet and Cancer. Environ. Health Perspect. 860, 860–866. https://doi.org/10.1289/ehp.1408762.

Havard, S., Deguen, S., Zmirou-Navier, D., Schillinger, C., Bard, D., 2009. Traffic-related air pollution and socioeconomic status: a spatial autocorrelation study to assess environmental equity on a small-area scale. Epidemiology 20, 223–230. https://doi.org/10.1097/EDE.0b013e31819464e1.

HEI Panel on the Health Effects of Traffic-Related air Pollution, 2010. Traffic-related air pollution: a critical review of the literature on emissions, exposure, and health effects. Health Effects Institute, Boston, Massachusetts. URL ⟨https://www.healtheffects.org/publication/traffic-related-air-pollution-critical-review-literature-emissions-exposure-and-health⟩ (accessed 16 March 2015).

Hystad, P., Demers, P.A., Johnson, K.C., Carpiano, R.M., Brauer, M., 2013. Long-term residential exposure to air pollution and lung cancer risk. Epidemiology 24, 762–772. https://doi.org/10.1097/EDE.0b013e3182949ae7.

IARC. International Agency for Research on Cancer, 2013. Outdoor Air Pollution a Leading Environmental Cause of Cancer Deaths. WHO. URL ⟨https://www.iarc.fr/en/media-centre/iarcnews/pdf/pr221_E.pdf⟩ (accessed 7 November 2017).

IARC. International Agency for Research on Cancer, 2012. Diesel Engine Exhaust Carcinogenic. WHO. URL ⟨http://www.iarc.fr/en/media-centre/pr/2012/pdfs/pr213_E.pdf⟩ (accessed 7 November 2017).

IBGE. Instituto Brasileiro de Geografia e Estatística, 2017. Brasil em Síntese. URL ⟨https://cidades.ibge.gov.br/brasil/sp/sao-paulo/panorama⟩ (accessed 30 October 2017).

IBGE. Instituto Brasileiro de Geografia e Estatística, 2010. Censo 2010. URL ⟨http://censo2010.ibge.gov.br/⟩ (accessed 27 September 2016).

Jerrett, M., 2009. Global geographies of injustice in traffic-related air pollution exposure. Epidemiology 20, 231–233. https://doi.org/10.1097/EDE.0b013e31819776a1.

Larkin, A., Geddes, J.A., Martin, R.V., Xiao, Q., Liu, Y., Marshall, J.D., Brauer, M., Hystad, P., 2017. Global land use regression model for nitrogen dioxide air pollution. Environ. Sci. Technol. 51, 6957–6964. https://doi.org/10.1021/acs.est.7b01148.

Lepeule, J., Laden, F., Dockery, D., Schwartz, J., 2012. Chronic exposure to fine particles and mortality: an extended follow-up of the Harvard Six Cities study from 1974 to 2009. Env. Heal. Perspect. 120, 965–970. https://doi.org/10.1289/ehp.1104660.

Li, J., Liu, H., Lv, Z., Zhao, R., Deng, F., Wang, C., Qin, A., Yang, X., 2018. Estimation of PM2.5 mortality burden in China with new exposure estimation and local concentration-response function. Environ. Pollut. 243, 1710–1718. https://doi.org/10.1016/j.envpol.2018.09.089.

Marcilio, I., Gouveia, N., 2007. Quantifying the impact of air pollution on the urban population of Brazil. Cad. Saude Publica 23 (Suppl 4), S529–S536.

Nweke, O.C., Payne-Sturges, D., Garcia, L., Lee, C., Zenick, H., Grevatt, P., Sanders, W.H., Case, H., Dankwa-Mullan, I., 2011. Symposium on integrating the science of environmental justice into decision-making at the Environmental Protection Agency: an overview. Am. J. Public Health 101, 19–26. https://doi.org/10.2105/AJPH.2011.300368.

Olsson, A.C., Gustavsson, P., Kromhout, H., Peters, S., Vermeulen, R., Brüske, I., et al., 2011. Exposure to diesel motor exhaust and lung cancer risk in a pooled analysis from case-control studies in Europe and Canada. Am. J. Respir. Crit. Care Med. 183, 941–948. https://doi.org/10.1164/rccm.201006-0940OC.

Pearce, J., Kingham, S., Zawar-Reza, P., 2006. Every breath you take? Environmental justice and air pollution in Christchurch, New Zealand. Environ. Plan. A 38, 919–938. https://doi.org/10.1068/a37446.

Pereira, F.A.C., de Assunção, J.V., Saldiva, P.H.N., Pereira, L.A.A., Mirra, A.P., Braga, A.L.F., 2005. Influence of air pollution on the incidence of respiratory tract neoplasm. J. Air Waste Manag. Assoc. 55, 83–87. https://doi.org/10.1080/10473289.2005.10464603.

Puett, R.C., Hart, J.E., Yanosky, J.D., Spiegelman, D., Wang, M., Fisher, J.A., Hong, B., Laden, F., 2014. Particulate matter air pollution exposure, distance to road, and incident lung cancer in the nurses' health study cohort. Environ. Health Perspect. 122, 926–932. https://doi.org/10.1289/ehp.1307490.

Raaschou-Nielsen, O., Andersen, Z.J., Beelen, R., Samoli, E., Stafoggia, M., Weinmayr, G., et al., 2013. Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects

(ESCAPE). Lancet Oncol. 14, 813–822. https://doi.org/10.1016/s1470-2045(13)70279-1.

Raaschou-Nielsen, O., Andersen, Z.J., Hvidberg, M., Jensen, S.S., Ketzel, M., Sorensen, M., Loft, S., Overvad, K., Tjonneland, A., 2011. Lung cancer incidence and long-term exposure to air pollution from traffic. Environ. Heal. Perspect. 119, 860–865. https://doi.org/10.1289/ehp.1002353.

Raaschou-Nielsen, O., Beelen, R., Wang, M., Hoek, G., Andersen, Z.J., Hoffmann, B., et al., 2016. Particulate matter air pollution components and risk for lung cancer. Environ. Int. 87, 66–73. https://doi.org/10.1016/j.envint.2015.11.007.

Samet, J.M., White, R.H., 2004. Urban air pollution, health, and equity. J. Epidemiol. Community Heal. 58, 3–5.

São Paulo (SP). Secretaria Municipal de Saúde, 2018. Inquérito de Saúde do Município de São Paulo - ISA Capital. . URL 〈http://www.prefeitura.sp.gov.br/cidade/secretarias/saude/epidemiologia_e_informacao/isacapitalsp/index.php?P=177260〉 (accessed 3 May 2018).

São Paulo (SP), 2010. Secretaria Municipal de Saúde. Boletim ISA - Capital 2008: Inquérito de Saúde/Primeiros Resultados. URL 〈https://www.prefeitura.sp.gov.br/cidade/secretarias/upload/saude/arquivos/publicacoes/PrimeirosResultados.pdf〉 (accessed 3 May 2018).

Shao, Y., Wang, Y., Yu, H., Zhang, Y., Xiang, F., Yang, Y., Yang, Y., Li, L., Dong, S., Yang, D., Cheng, W., Chen, Y., Jiang, Q., Xie, J., Sun, W., Zhou, Y., 2019. Geographical variation in lung cancer risk associated with road traffics in Jiading District, Shanghai. Sci. Total Environ. 652, 729–735. https://doi.org/10.1016/j.scitotenv.2018.10.266.

Silva, A.S., Cardoso, M.R., Meliefste, K., Brunekreef, B., 2006. Use of passive diffusion sampling method for defining NO_2 concentrations gradient in São Paulo, Brazil. Environ. Health 5, 19. https://doi.org/10.1186/1476-069X-5-19.

StataCorp, 2011. Stata Statistical Software: Release 12.

Toledo, G.I.F.M., de, Nardocci, A.C., 2011. Poluição veicular e saúde da população: uma revisão sobre o município de São Paulo (SP). Bras. Rev. Bras. Epidemiol. 14, 445–454.

Turner, M.C., Krewski, D., Pope, C.A., Chen, Y., Gapstur, S.M., Thun, M.J., 2011. Long-term ambient fine particulate matter air pollution and lung cancer in a large cohort of never-smokers. Am. J. Respir. Crit. Care Med. 184, 1374–1381. https://doi.org/10.1164/rccm.201106-1011OC.

UNDP Brazil. United Nations Development Program, 2013. Atlas of Human Development in Brazil. . URL 〈http://atlasbrasil.org.br/2013/en/o_atlas/idhm/〉 (accessed 6 January 2015).

Villeneuve, P.J., Jerrett, M., Brenner, D., Su, J., Chen, H., McLaughlin, J.R., 2014. A case-control study of long-term exposure to ambient volatile organic compounds and lung cancer in Toronto, Ontario, Canada. Am. J. Epidemiol. 179, 443–451. https://doi.org/10.1093/aje/kwt289.

WHO - World Health Organization, 2006. WHO Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide: global update 2005: summary of risk assessment. Genebra.

Wilson, S., Burwell-Naney, K., Jiang, C., Zhang, H., Samantapudi, A., Murray, R., Dalemarre, L., Rice, L.S., Williams, E., 2015. Assessment of sociodemographic and geographic disparities in cancer risk from air toxics in South Carolina. Environ. Res. 140, 562–568. https://doi.org/10.1016/j.envres.2015.05.016.

Yanagi, Y., Assunção, J.V., de, Barrozo, L.V., 2012. The impact of atmospheric particulate matter on cancer incidence and mortality in the city of São Paulo, Brazil. Cad Saude Publica 28, 1737–1748.

Yorifuji, T., Kashima, S., Doi, H., 2016. Fine-particulate air pollution from diesel emission control and mortality rates in Tokyo. Epidemiology 27, 769–778. https://doi.org/10.1097/EDE.0000000000000546.

Yorifuji, T., Kashima, S., Tsuda, T., Ishikawa-Takata, K., Ohta, T., Tsuruta, K., Doi, H., 2013. Long-term exposure to traffic-related air pollution and the risk of death from hemorrhagic stroke and lung cancer in Shizuoka, Japan. Sci. Total Environ. 443, 397–402. https://doi.org/10.1016/j.scitotenv.2012.10.088.

Yue, S., Wang, Y., Wang, J., Chen, J., 2017. Relationships between lung cancer incidences and air pollutants. Technol. Heal. Care 25, S411–S422. https://doi.org/10.3233/THC-171344.

Zhou, M., He, G., Liu, Y., Yin, P., Li, Y., Kan, H., Fan, M., Xue, A., Fan, M., 2015. The associations between ambient air pollution and adult respiratory mortality in 32 major Chinese cities, 2006–2010. Environ. Res. 137, 278–286. https://doi.org/10.1016/j.envres.2014.12.016.