The new WHO air quality guidelines for $PM_{2.5}$: predicament for small/medium cities

Gabriela Polezer[1]*, Sanja Potgieter-Vermaak[3,4], Andrea Oliveira[5], Leila D. Martins[6], Jéssica C. Santos-Silva[7], Camila A. B. Moreira[1], Theotonio Pauliquevis[8], Ana F. L. Godoi[1], Yara Tadano[9], Carlos I. Yamamoto[10], Ricardo H. M. Godoi[1]

1- Environmental Engineering Department, Federal University of Paraná, Curitiba, Paraná, Brazil;
2- Departament of Technology, State University of Maringá, Umuarama, Paraná, Brazil
3- Ecology & Environment Research Centre, Department of Natural Science, Manchester Metropolitan University, Manchester M1 5GD, United Kingdom;
4- Molecular Science Institute, University of the Witwatersrand, Johannesburg, South Africa;
5- Chemistry Department, Federal University of Paraná, Curitiba, Paraná, Brazil;
6- Chemistry Department, Federal University of Technology - Paraná, Londrina, Paraná, Brazil;
7- Water Resources and Environmental Engineering Department, Federal University of Paraná, Curitiba, Paraná, Brazil;
8- Department of Environmental Sciences, Federal University of São Paulo, Diadema, Brazil;
9- Mathematics Department, Federal University of Technology - Paraná, Ponta Grossa, Paraná, Brazil;
10- Chemical Engineering Department, Federal University of Paraná, Curitiba, Paraná, Brazil.

Correspondence to: Gabriela Polezer (gabipolezer@gmail.com)

ABSTRACT

The Global Burden of Disease estimated that approximately 7.1 million deaths worldwide were related to air pollution in 2016. However, only a limited number of small- and middle-sized cities have air quality monitoring networks. To date, air quality in terms of particulate matter is still mainly focused on mass concentration, with limited compositional monitoring even in mega cities, despite evidence indicating differential toxicity of particulate matter. As this evidence is far from conclusive, we conducted $PM_{2.5}$ bioaccessibility studies of potentially harmful elements (PHE) in a medium-sized city, Londrina-Brazil. The data was interpreted in terms of source apportionment, the health risk evaluation, and the bioaccessibility of inorganic contents in an artificial lysosomal fluid. The daily average concentration of $PM_{2.5}$ was below the WHO guideline, however, the chemical health assessment indicated a considerable health risk. The in vitro evaluation showed different potential mobility when compared to previous studies in large-sized cities, those with 1 million inhabitants or more (Curitiba and Manaus). The new WHO guideline for $PM_{2.5}$ mass concentration puts additional pressure on cities where air pollution monitoring is limited and/or neglected, because decision making is mainly revenue- and not socio-economical-driven. Given the further emerging evidence that PM chemical composition is as, or even more, important than mass concentration levels, the research reported in the paper could pave the way for the necessary inter- and intra-city collaborations that are needed to address this global health challenge.

Keywords: Fine particles; aerosol chemical composition; Bioaccessibility of heavy metals; Urban area.

1. INTRODUCTION

Air pollution has received attention in recent decades due to its adverse impact on eco-systems and human health. The global burden of disease (GBD) study estimated that approximately 7.1 million deaths worldwide were related to air pollution in 2016 (Landrigan et al., 2018; WHO, 2021), of which 543 000 (just shy of 8%) were that of children under five years of age, but less than 1% for the ages between 5 and 15 years. It is evident that the more vulnerable groups are at high-risk, even at low exposure levels (Chen et al., 2018; Klepac et al., 2018; Landrigan et al., 2018; WHO, 2018). In addition, 99% and 89% of deaths related to household and ambient air pollution, respectively, occurred in low-and middle-income countries in 2015 (Landrigan et al., 2018). Although air quality has improved in high-income countries, the contrary can be said for low- and middle-income countries, due to urbanisation and economic development.

Because of the growing evidence that burden of disease is strongly associated with ambient and household air pollution exposure, the World Health Organization (WHO) launched its latest latest Air Quality Guidelines (AQG) in September 2021, after a thorough evidence-based review. For $PM_{2.5}$ the former update (dated to 2005) was based mainly on two studies (Dockery et al., 1993; Pope et al., 2002), whereas the 2021 update was based on 25 studies (Chen & Hoek, 2020) which concluded that $PM_{2.5}$ exposure poses a moderate to strong health risk. The review concludes that the lowest level of long-term exposure associated with mortality, was between 3 and 6.7 μg m^{-3}, with a mean of 4.2 μg m^{-3} and a sensitivity analysis value of 4.9 μg m^{-3}, leading to the long-term AQG level of 5 μg m^{-3} annual mean concentration of $PM_{2.5}$ (WHO, 2021). Moreover, mortality due to circulatory, non-malignant respiratory diseases and lung cancer showed even higher relative risks than the all-cause of death, and there may be a higher relative risk in the lower levels of exposure (Chen & Hoek, 2020). With the 2005 WHO update, it was estimated that a reduction of air pollutant levels would avoid 3.4 million deaths (47.8%) (Evangelopoulos et al., 2020) where the new 2021 update (WHO, 2021) predicts a decrease of 5.6 million (79.5%).

Even so, scientific reports highlight that only a limited number of cities have $PM_{2.5}$ sources and components consistently measured (Lelieveld et al. 2015). In addition, the authors point out that most information about air pollution is related to megacities and/or capital cities due to their political relevance or industrial complexity. To estimate air quality in rural locations, towns and smaller cities, atmospheric chemistry and transport models are used (Lelieveld et al., 2015) by reason of a lack of monitoring data. Due to the complexity of $PM_{2.5}$ emissions and the impact of diverse local and long-rage transport sources on the levels and chemistry of these airborne particles, reliable monitoring should be carried out frequently and/or continuously across all areas (Martins et al., 2018).

However, the air quality guidelines (AQG) of the World Health Organization (WHO) is still based on the exposure-response functions that rely on $PM_{2.5}$ mass concentration, implicitly treating all fine particles as equally toxic without regard of their sources and/or chemical composition (Lelieveld et al., 2015).The main exposure route for $PM_{2.5}$ is through inhalation by which potentially toxic, carcinogenic, and genotoxic compounds in the aerosol can become partially or totally soluble in the lung fluid. This fraction, called the bioaccessible fraction, can then pass through the blood barrier and thus be taken up in the blood stream, causing systemic health effects such as increasing the relative risk to a stroke (Nascimento et al., 2012; Fisher et al., 2019). During the last decade researchers documented the importance of the chemical composition of $PM_{2.5}$ and identified compounds of specific health importance (Pope et al., 2009; Canova et al., 2012; Cao et al., 2012; Langrish et al., 2012; Sorensen et al., 2012; Wu et al., 2012). Specifically, metals have been associated with adverse effects, such as respiratory, neurological, reproductive and carcinogenic effects (Kurt-Karakus, 2012; Liu et al., 2015; Fang et al., 2018). Some metals such as Fe, Cu and Mn have the capacity to generate reactive oxygen species (ROS), which can cause damage to DNA and cellular functionality through the oxidation of proteins and lipids associated with oxidative stress (Angelé-

Martínez et al., 2014). To that end, the pulmonary bioaccessibility of these metals are of importance to establish exposure risk.

In vitro studies using artificial biological fluids have the advantage of producing rapid and inexpensive results compared to in vivo studies, in addition to the worldwide concern over animal cruelty and the difficulties associated with human studies. Artificial pulmonary fluids seek to mimic the lung environment, presence of macrophages and pulmonary surfactants. Artificial Lysosomal Fluid (ALF) currently presents the closest composition to the more acidic lung environment, simulating phagocytosis conditions when inflammatory conditions prevail (Midander et al., 2007).

The new WHO guidelines put all countries on the spot, asking them to take action, not only in monitoring levels but reducing the health risks associated with it. By means of an extensive characterization of fine particles in a medium sized middle-income city, the present paper aims to call into question why and how to guide efforts to reduce air pollution emissions to the new WHO guidelines levels, using Londrina, Brazil as a case study. To estimate the toxic and carcinogenic potential of potentially harmful elements (PHEs) present in inhaled PM, we conducted lung bioaccessibility tests using ALF. Although bioaccessibility data, using artificial lung fluids, are available in a limited number of papers, very few studies were conducted in medium size cities (those with 1 million inhabitants or less) all over the world (Mbengue et al., 2015; Coufalík et al., 2016; Hernández-Pellón et al., 2018; Expósito et al., 2021). To provide data on such a middle-sized city, we investigated the long-term trend of $PM_{2.5}$ in Londrina, Brazil. Londrina has a population of around 569,733 inhabitants (IBGE, 2019), similar to some important cities worldwide, as shown in Table 1. This research presents the results of almost 2 years of daily $PM_{2.5}$ monitoring. We report mass, black carbon and elemental concentrations (used for source apportionment). Using an in vitro approach, the pulmonary bioaccessibility in ALF simulated lung fluid, were determined and resident's health exposure risks estimated.

Table 1 - Worldwide cities population estimate in 2018.

Country	Region/City	Population	Ref.	Country	Region/City	Population	Ref.
USA	New Mexico/ Albuquerque	560.218	(USCB, 2019)	Italy	Genoa	580.097	(Istat, 2018)
USA	Maryland/ Baltimore	602.495	(USCB, 2019)	Spain	Málaga	571.026	(INEbase, 2018)
USA	Arizona/ Tucson	545.975	(USCB, 2019)	China	Mongolia/ Wuhai	532.900	(NBSPRC, 2019)
UK	Glasgow	615.070	(ONS-UK, 2017)	China	Tibet/ Lhasa	559.400	(NBSPRC, 2019)
Germany	Dortmund	585.813	(IT.NRW, 2013)	China	Yunnan/ Nujiang	534.000	(NBSPRC, 2019)

2. MATERIALS AND METHODS

2.1. SAMPLING SITE DESCRIPTION AND $PM_{2.5}$ SAMPLING PROCEDURES

The study site is located at the Historical Museum of Londrina, Paraná state, Brazil (Figure S1 - coordinates 23°18'29"S 51°09'35.1"W, and at 608 m asl). The museum is situated in the central part of the city where traffic density between 746 and 1,300 vehicles per hour are experienced during peak times. The Central Bus Station, which is responsible

for transporting approximately 45 million commuters per year, is in close vicinity. The 400 buses in the fleet are on average five years old and run on S500 and S10 diesel fuel (500 and 10 ppm of Sulphur) (CMTU, 2015; IPPUL, 2016).

Londrina area is about 1,652 km^2 with a population of 569,733 inhabitants registered in 2018 (IBGE, 2019). It has almost 400,000 vehicles of which 59% are light vehicles, 18% motorcycles, and 15% heavy duty vehicles (DENATRAN, 2019). The main Gross Domestic Product (GDP) of the metropolitan region of Londrina are mainly services (40%), agriculture and livestock (23%), industry (19%), and administration/education (18%) (IBGE, 2017). Londrina has a subtropical climate with temperature highs of 24ºC (December to March) and lows of 16 °C (May to August).

Twenty four-hour $PM_{2.5}$ continuous mass sampling was carried out from September 2014 to February 2015 and from June 2015 to July 2016, using an inertial low volume Harvard impactor sampler (Marple et al., 1987) operated at 10 L min^{-1} and collecting particulates on 37 mm polycarbonate filters. The impactor was positioned at 2 m height and field blanks were kept for both campaigns to reduce filter handling and transport errors.

$PM_{2.5}$ mass concentration was determined using gravimetry by determining weight differences before and after sampling, using a microbalance and an electrostatic charge eliminator. Black Carbon (BC) mass concentration was obtained using a transmissometer SootScan OT21 (Magee Scientific) at an 880 nm wavelength (infrared), the meteorological data of the city was obtained in the National Institute of Meteorology website database (INMET, 2016).

2.2. SOURCE APPORTIONMENT

In order to determine the sources of the pollutant over time and season, the elemental profile of each filter had to be determined. The elemental concentrations were obtained by non-destructive X-ray Fluorescence Spectrometry, using a Minipal-4 (PANalytical. Almelo. The Netherlands) equipped with a thermo-electrically cooled Silicon Drift Detector (SDD). The optimum tube voltage and current were determined based on reference standards (Micromatter. Seattle. WA. USA) and validated by the measurement of a certified reference material from NIST (2783 air particulate on filter media). The best spectra and calibration curves were obtained using a He-atmosphere with 600 s of acquisition time under two conditions: a tube voltage of 30 kV. and a current of 0.3 mA with the limit of detection in brackets in ng m^{-3} for Cr (0.39), Cu (0.32), Fe (0.69), Mn (0.35), Pb (0.81), Ti (0.35), K (1.3) and Zn (0.5); a tube voltage of 9 kV and a current of 1.0 mA for Al (0.53), Si (2.3), S (1.4), Ca (0.39), Cl (1.9), and Mg (9.0). The limit of detection (LOD) was calculated as three times the inverse of instrumental sensitivity multiplied by the square root of the background noise signal from the measure of ten blank filters divided by the measurement time.

In order to determine the $PM_{2.5}$ sources in the region of interest, two methods were applied, Firstly, enrichment factor analysis (EF), which enables the identification of anthropogenic elements, and secondly, principal component analysis (PCA), a receptor modelling method.

The EF analysis was applied as described in previous studies (Godoi et al., 2006, Polezer et al., 2018) using Equation 1 (Molnar et al., 1993; Hoornaert et al., 2004). Al is used as the crustal reference element, and average crustal elemental concentrations were obtained from literature (Mason, 1966). An element with an EF value close to one (below 10) is considered to be of natural origin and values higher than 10 is indicative of anthropogenic sources at play (Liu et al., 2003).

$$EF = \frac{\frac{X_{experimental}}{RE_{experimental}}}{\frac{X_{crustal}}{RE_{crustal}}} \qquad \text{Equation 1}$$

Where $X_{experimental}$ is the concentration of the element under assessment on the filter, $RE_{experimental}$ is the concentration of the chosen reference element (Al) on the filter, $X_{crustal}$ is the concentration established for the element under assessment in nature, and $RE_{crustal}$ is the concentration established for the RE nature. As described by Polezer et al. (2018), the PCA was performed with a Varimax rotation of the coordinates system, where the principal components were related to specific sources due to the high loadings of specific variables. This was followed by absolute principal component analysis (APCA). The combination of these two methods provides a quantitative chemical profile of sources instead of the known qualitative factor loading matrix as in PCA, a method previously applied successfully in aerosol studies (Echalar et al., 1998; Maenhaut and Cafmeuyer, 2002). The method was applied using the SPSS 16.0 software®. The variables data was composed of $PM_{2.5}$ mass, BC and elemental concentration.

2.3. HEALTH RISK EVALUATION

Ambient airborne particulates are complex chemical mixtures made up of primary and secondary particles, each of which is prone to further chemical ageing due to atmospheric processes such as adsorption and absorption. The resulting product is a polydisperse system with complex toxic and carcinogenic potential due to its diverse chemical and biochemical character. To assess the impact on health, two health risk assessment procedures were performed. Firstly, the toxic and carcinogenic risk was assessed using the elemental composition and the web-based Risk Assessment Information System (RAIS) (https://rais.ornl.gov). Secondly, in-vitro studies were performed to determine the pulmonary bioaccessibility.

2.3.1 Toxic and carcinogenic risk assessment

The elemental profile of the $PM_{2.5}$ samples was subjected to a chemical health risk assessment using the RAIS, which is based on a method created by the United States Environmental Protection Agency (USEPA, 1989; USEPA, 2009) as described by Godoi et al. (2013). The RAIS models the Carcinogenic Risk (CR) and non-carcinogenic risks (Hazardous Quotient - HQ) of adverse health effects that may occur through ingestion with the pollutant based on the equations 2 and 3 presented below. The input parameters used to model the CR and HQ risks are: C - Concentration of contaminant in air ($\mu g/m^3$); ET: Exposure Time (hours/day); EF: Exposure Frequency (days/year); ED: Exposure Duration (years); RfCi: Chronic Inhalation Reference Concentration (mg/m^3); IUR: Chronic Inhalation Unit Risk ($1\ (\mu g/m^3)^{-1}$); LT: Lifetime (years). CR is the probability of an individual to develop cancer over a lifetime in relation to the population exposed to the pollutants, where values in excess of 10^{-4} are considered a significant risk to develop cancer. An HQ< 1 indicates there is no significant risk of non-carcinogenic effects occurring, with a probability that tends to increase as the value of HQ increases (USEPA, 1989; Hu et al., 2011; USEPA, 2009).

$$HQ = \frac{\left(\frac{C \times ET \times EF \times ED}{24 \times 365 \times 1000 \times ED}\right)}{RFC_i} \qquad \text{Equation 2}$$

$$CR = IUR \times \left(\frac{C \times ET \times EF \times ED}{24 \times 365 \times LT}\right) \qquad \text{Equation 3}$$

For Cr (VI) exposure, 40% of the total Cr obtained was used (Swietlik et al., 2011). The other elemental concentrations were used as total elemental concentration. Other parameters for the calculation were: exposure duration of 40 years, exposure frequency of 350 days per year, exposure time of 24 hours per day (the average exposure of resident obtained in the chemical risk users guide (RAIS, 2020), and a lifetime of 76 years (IBGE, 2018). These values were deemed

representative of describing the exposure duration and frequency of the population of the urban area of the city under investigation.

2.3.2 Bioaccessibility analysis

The percentage bioaccessibility of each studied element (Cu, Pb, and Mn) in $PM_{2.5}$ was obtained by the element mass concentration solubilized in a simulated lung fluid, artificial lysosomal fluid (ALF) in relation to total mass concentration as determined by XRF. To simulate the inhalation of air pollution process, $PM_{2.5}$ collected on filters were subjected to an in vitro test (Colombo et al., 2008), whereby each filter was incubated at 37 °C with agitation at 40 cycles per minute for 1 hour in ALF with a solid:liquid ratio between 1/16,000 and 1/30,000 g mL^{-1}. There after the supernatant was analysed by graphite furnace atomic absorption spectrometer (GFAAS) (model AA 6800. Shimadzu. Japan).

A method blank was obtained by treating a field blank filter to the same procedure as the $PM_{2.5}$ filters. The instrumental settings and chemical modifiers employed were the same as those used in previous work and can be found in Polezer et al. (2020). The limits of detection obtained were 0.4, 2.9 and 0.3 μg L^{-1}; and the limits of quantification were 1.5, 9.8 and 1.2 μg L^{-1} for Cu, Pb, and Mn, respectively. The accuracy and repeatability of the analytical methods were evaluated by the analysis of the ALF previously spiked with known amounts of each element (Cu, Pb, and Mn) and the recovery tested. The recovery of the spiked ALF solution for different levels of the calibration curve was 91% to 109% for Cu, 82% to 108% for Pb and 84% to 104% to Mn. Likewise, the repeatability values of spiked samples were within the acceptable range, RSD <10% (European Commission, 2002).

3. RESULTS AND DISCUSSION

3.1. $PM_{2.5}$ MASS CONCENTRATION, BC AND ELEMENTAL CONTENT

The results obtained for $PM_{2.5}$ 24-hour mass concentrations (μg m^{-3}), BC concentration (μg m^{-3}), and elemental profiles (ng m^{-3}) during the two sampling campaigns are reported in Table 2. The chemical elements are ordered from the highest concentrations to the lowest. Three hundred and seven $PM_{2.5}$ samples were collected of which 268 were analysed for BC and 172 for elemental concentration. The sum of the average BC and total elemental concentrations constituted 37% of the $PM_{2.5}$ mass, corresponding to 16% and 21%, respectively.

The mean mass concentration of $PM_{2.5}$ of 4.4 μg m^{-3} was below either the former (WHO, 2006) and the new (WHO, 2021) World Health Organization (WHO) annual guidelines level, respectively 10 μg m^{-3} and 5 μg m^{-3} (the most restrictive current guideline). The 24-hour mean guideline was exceeded one day in the former WHO guideline (25 μg m^{-3}), whereas 6 days exceeded the new value (15 μg m^{-3}) within a year in 2015, that is more than the 99th percentile permitted exceedance of 3 days. The mean $PM_{2.5}$ mass concentration found is also below 12.9 μg m^{-3} (11.0 – 16.2 μg m^{-3}), the mean $PM_{2.5}$ in Brazil for the 1990 – 2016 period (Ritchie and Roser, 2019). Brazil is one of the most populated countries and it is among the most important emerging economies (Brazil, Russia, India, China – BRICs) and classified as a middle-income country (MIC). It is interesting to note that the mean $PM_{2.5}$ mass concentration in Brazil is well below the average of 48.9 μg m^{-3} (45.0 – 55.5 μg m^{-3}) observed for MICs during the same period (Ritchie and Roser, 2019).

The mean $PM_{2.5}$ mass concentrations reported here for Londrina were also lower than other medium-sized cities around the world. Ribeirão Preto, São José dos Campos, Piracicaba, Guaratinguetá, Taubaté, middle-size cities located in the São Paulo state of Brazil, presented annual averages from 10 to 15 μg m^{-3} (CETESB, 2019). In Denver (EUA), for example, the values found were between 5.7 and 6.5 μg m^{-3} (Clements et al., 2014), while in Genoa (Italy), 22.3 μg m^{-3} was reported

by Ariola et al. (2006). In several medium-sized cities in Southern Spain (with populations ranging from 250 000 to 700 000 inhabitants), $PM_{2.5}$ varied from 18 to 37 μg m^{-3} (Amato et al., 2014).

Table 2 - Average and standard deviation of $PM_{2.5}$ mass concentration (μg m^{-3}), BC (μg m^{-3}), and elemental concentration (ng m^{-3}), enrichment factor and chemical health risks (Hazard Quotient (HQ) and Carcinogenic Risk (CR) of samples obtained during the two sampling campaigns.

	Concentration			Enrichment factor	HQ	CR (10^{-5})
	Mean	**S.D.**	**Median**			
$PM_{2.5}$	4.4	3.8	3.5			
BC	0.7	0.7	0.5			
Mg	285	90	281	19		
S	227	157	188	920		
Si	151	98	119	1		
Fe	57	47	40	1		
Ca	56	19	54	2		
K	49	87	0.1	1		
Mn	26	11	23	40	0.50	
Al	25	28	13	0.2	0.005	
Cu	12	6.2	10	310		
Sr	7.0	2.3	7	33		
Co	4.9	1.7	4.6	319	0.24	2.3
Ti	4.1	4.5	2.7	1		
Pb	4.0	5.7	0.1	327		0.002
Cr	1.0	1.0	0.9	19	0.001	3.0
Zn	0.50	1.4	0.1	4		
Total risk					0.75	5.3

*Risk for Cr^{6+} was obtained assuming that it constitutes 40% of total Cr.

A previous study done in Londrina (Beal et al., 2017), measured $PM_{2.5}$ mass and BC concentrations during winter and summer periods (one month). These were conducted at the Federal University of Technology -Paraná (UTFPR), which is a semi-urbanized residential region with agricultural fields in close vicinity, light and heavy-duty traffic and is situated about 4 km from our sampling site. Beal et al. (2017) report average $PM_{2.5}$ and BC concentrations of 7.7 μg m^{-3} and 1.6 μg m^{-3} in September 2013, 4.4 μg m^{-3} and 0.9 μg m^{-3} in December 2013, and 10.3 μg m^{-3} and 1.8 μg m^{-3} in August 2014, respectively. For comparison purposes, our temporal data is also displayed in Figure S2, showing the monthly mean and variation for both BC and $PM_{2.5}$ mass concentrations across the two campaigns. Although the $PM_{2.5}$ mass concentrations (Beal et al., 2017) are mostly higher (41%) than the average value reported in our study, comparing on a month by month basis (even though different years) there seems to be a fair correlation for the September and December concentrations.

According to Ritchie and Roser (2019) there was a general decrease in $PM_{2.5}$ mass concentration in Brazil since the 1990s, however, from 2015 there seems to be an increase again (~10%). The data has been obtained from fixed monitoring stations (only 10 of the 27 states are monitored) of which none are close to the Parana State. In fact, the Brazilian Government only announced the launching of monitoring air pollution in the remaining states in June 2019. Even if it becomes a reality, when the data from these stations become available, it has to be said that it will not account for local hot spots and therefore the value of these local studies is obvious.

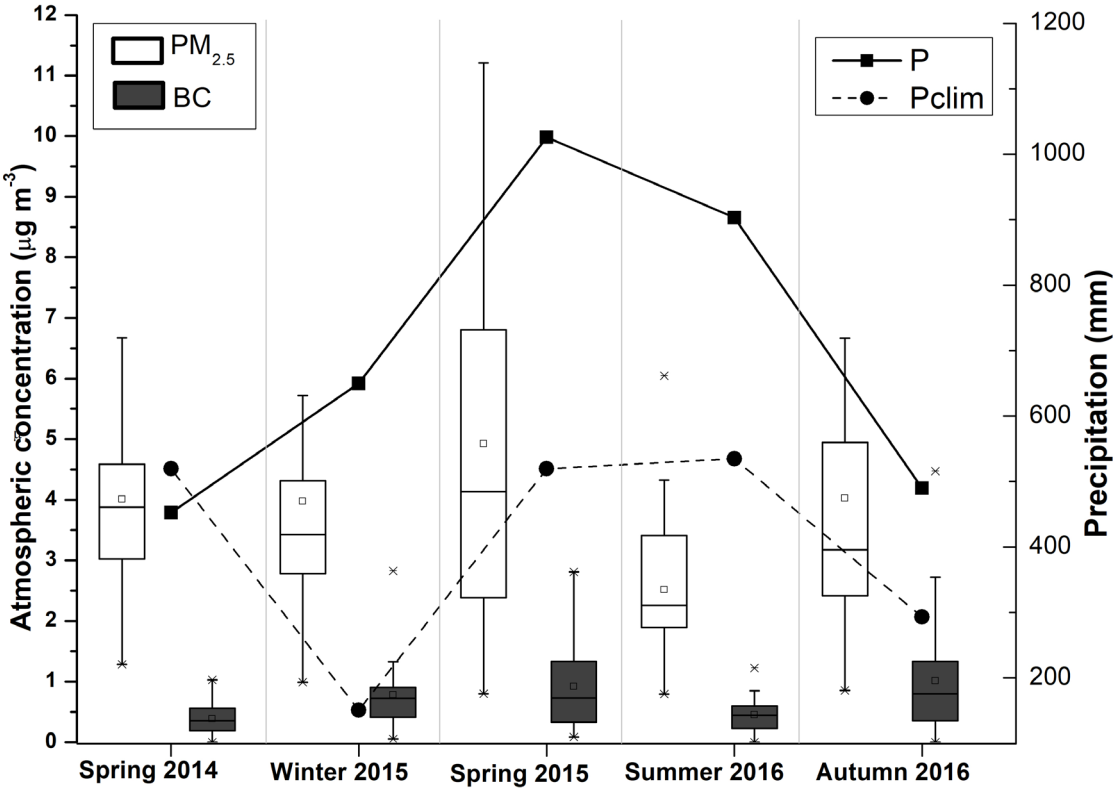

Figure 1. Boxplots of $PM_{2.5}$ and BC mass concentrations, precipitation of the sampling period (P) and historic precipitation (Pclim) in Londrina among seasons of the sampling campaign between October 2014 and February 2016. Boxplots show the median, 25th and 75th percentile, and average (□).

This tendency is not observed in this data, displaying a decrease on average compared to the Beal et al. (2017) study, albeit not directly comparable (Figure 1). One plausible explanation for this is the precipitation, the main natural process whereby airborne PM are removed from the atmosphere. The rainfall during the campaign was significantly higher than the historic rainfall data for the city, but it has to be noted that there is no direct correlation on a month-to-month basis, and one has to conclude that it cannot be the prime reason for the lower concentrations observed. The BC concentration in our study is also similar to background values (roof top measured) reported in Londrina (Krecl et al., 2018). Comparing the Beal et al. (2017) campaign with our study it is evident that location, and therefore different sources of pollution and meteorological conditions, seems to be the main reasons for the differences observed.

The elemental profiles and the corresponding enrichment factors (EFs) are displayed in Figure 2. It is seen that Mg, Ca, Sr, and Co do not vary significantly across the four seasons and crustal elements (Al, Fe, Si, Ca) seem to vary the most, generally speaking. The Beal et al. (2017) paper also report large variations in Al concentrations, but interestingly their concentrations were an order of magnitude higher in comparison with this study, pointing towards the different sources influencing the chemical character of the PM. In their case it may well be that the higher Al concentration is due to resuspension of dust due to the dryer weather.

Pb and Mn were similar to those found in Albuquerque, New Mexico (USA), and probably mostly associated with road dust (Kavouras et al., 2015). Beal et al. (2017), however, reported four times higher concentrations for Pb, both from the Londrina and Maringa (~100 km west to Londrina) sites. In Cuiaba (Brazil), an agricultural city with around 600,000 inhabitants (Santanna et al., 2016), and in the harbour city of Genoa (Italy) much lower values were found for Mn, although

Pb in Genoa presented similar concentrations (Bove et al., 2014). Similar Al and Fe concentrations are reported in Denver, EUA (Clements et al., 2014) and is probably associated with industrial and vehicular (abrasion and fuel consumption) emissions. While in Cuiaba and Genoa, Fe and Al concentrations were higher than in this study (Bove et al., 2014; Santanna et al., 2016).

Londrina presented higher Cr levels on the other hand than observed in Albuquerque (Kavouras et al., 2015) and at the Londrina site of the Beal et al. (2017) study, whilst in Cuiaba Cr levels where similar (Santanna et al., 2016). The Zn levels were higher than that reported in Denver, and lower than Cuiaba and Genoa (Bove et al., 2014). The relatively high (above 10) EFs for the PHEs (here referring to those with toxic/carcinogenic and/or reactive oxidative generating properties), Cu, Cr, Pb, Zn, and Co, not only informs on sources but predicts that significant health risks upon inhalation is plausible.

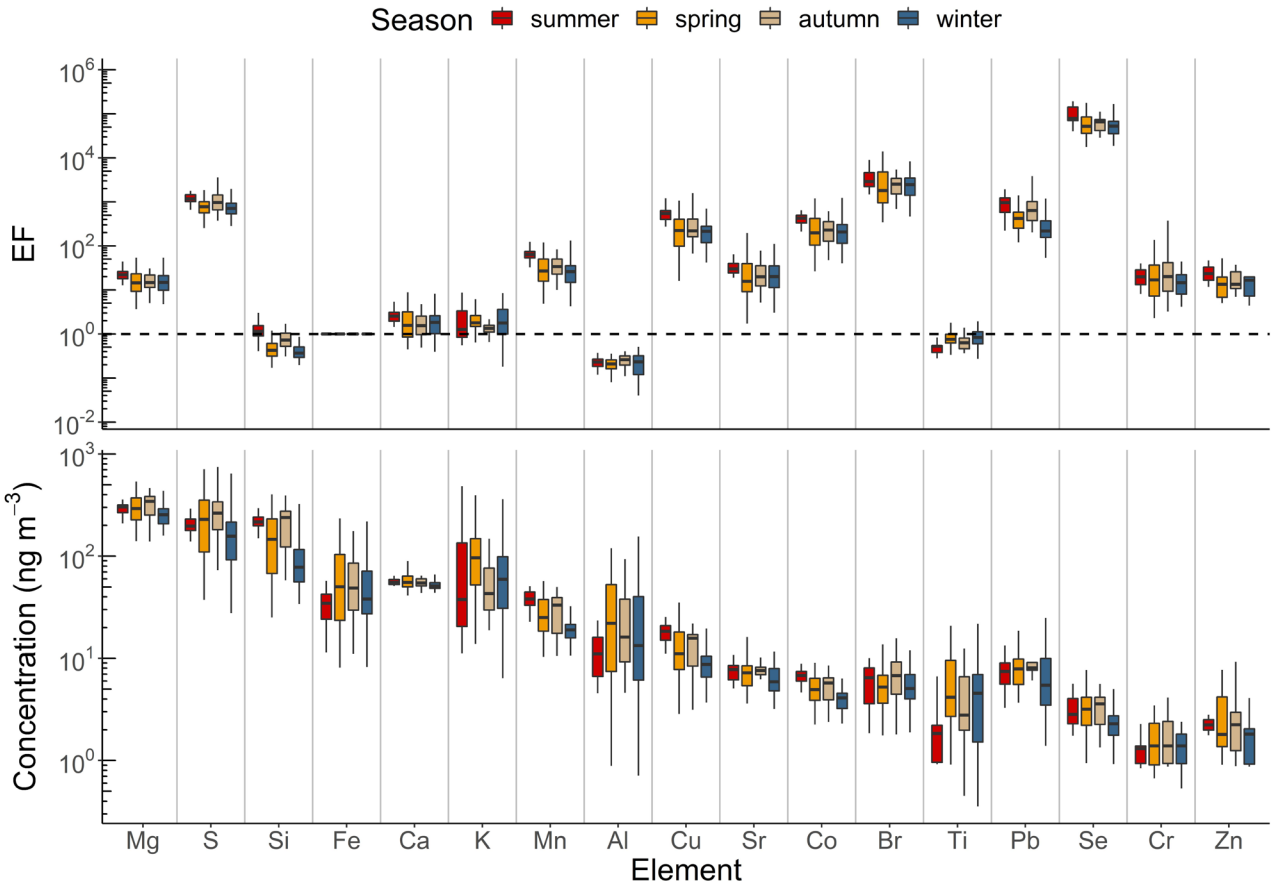

Figure 2 – Comparison of mean enrichment factors (top), and element concentrations (bottom) among different seasons. Boxplots show the median, 25th and 75th percentile. EF = 1 line is also shown as reference.

3.2. SOURCE APPORTIONMENT

The enrichment factor (EF) and absolute principal component analysis (APCA) of $PM_{2.5}$ and its contents were performed for Londrina in order to obtain the source apportionment. The EF results displayed in Table 2 and illustrated temporally in Figure 2 indicate that the elements Al, Si, Fe, Ca, K, Zn, and Ti (EF close to 1) could be ascribed to resuspension of soil as they are crustal related. The remaining chemical elements were enriched in relation to the crustal reference (i.e. EF > 10) (Liu et al., 2003), indicating that they probably were generated by anthropogenic sources. Pb and S had the highest EFs pointing to PM being highly enriched with these elements.

After the EF analysis, the data group consisting of $PM_{2.5}$ mass, BC and the elemental concentrations were subjected to APCA analysis, in which the variables and samples containing more than 30% of missing data (below the quantification limits) were excluded. Then the variables selected to compose the data group for APCA analysis were $PM_{2.5}$, BC, Mg, Al, Si, Cu, Pb, Fe, Ti, Mn, and S concentrations.

Table S1 contains the Pearson correlation of the data set selected for APCA analysis. As expected, the typical crustal correlations that both Al and Si displayed with Fe and Ti, were observed and is probably representative of the resuspended soil or road dust contribution. It is known that road dust could make up a substantial portion of airborne particulate matter and this also seems to corroborate with the correlation between $PM_{2.5}$ mass concentration and these four crustal elements. The slightly higher correlation between Fe and $PM_{2.5}$ mass could be the contribution from vehicle wear and tear (Srimuruganandam and Nagendra, 2012). $PM_{2.5}$ mass and BC were correlated to Al and Fe, indicating the contribution of fuel combustion and soil (Viana et al., 2008). For the S correlation one would not see the realistic correlation unless you take away the soluble sulphates, which will be correlated with Na, NH_4^+ and potentially K.

Applying APCA to the chosen variables, 12 principal components were initially identified, which were reduced to four after Varimax rotation, contributing 86% of the total cumulated variation (%CPC). The rotated principal components with the loadings of each variable are shown in Table S2. Loadings below 0.3 were ignored. The four principal components were assigned to four different $PM_{2.5}$ sources, based on the loadings of variables (BC, Mg, Al, Si, Cu, Pb, Fe, Ti, Mn, and S concentrations) and in concordance with published literature (Song et al., 2006).

The APCA was followed by a linear regression analysis between $PM_{2.5}$ mass concentration and the factor scores matrix of the four selected principal components. This enabled the prediction of the relative $PM_{2.5}$ mass concentration contribution of each sample for each principal component. The average mass concentration of $PM_{2.5}$ (%AVG $PM_{2.5}$ mass) attributed to each principal component could then be determined, allowing source apportionment. Both the %AVG $PM_{2.5}$ mass and absolute average concentrations for each principal component are presented in Table S2.

The first principal component (PC) presented the highest contribution (36%) to the data set variance, as well as the %AVG $PM_{2.5}$ mass. This component is associated with transport emissions, namely diesel vehicle, high loading of BC and low loading of S associated with diesel combustion (Brito et al., 2010, Herich et al., 2011; Andrade et al., 2012; Sharma et al., 2021), and resuspended road dust (high loadings of Al, Fe, Ti, and Si, corroborating with the low EF values indicative of natural sources such as sediments) (Viana et al., 2008; Srimuruganandam and Nagendra, 2012), as well as a high loading of Mg which had a high EF value, indicative of an anthropogenic source (Song et al., 2006). Brake lining dusts are associated with markers Mg, Fe, and to a lesser extent Al, Cr, Mn, Ca, and Na, indicating a possible source reason for Mg's presence in this PC (Srimuruganandam and Nagendra, 2012). The percentage AVG $PM_{2.5}$ mass associated with this PC suggests that 65% of the $PM_{2.5}$ mass can be apportioned to diesel vehicles and/or resuspended road dust.

The second component corresponding to a strong soil signature due to the high Al, Si, Fe, and Ti loadings (Srimuruganandam and Nagendra, 2012; Chow et al., 2015; Sharma et al., 2021), represent 5.3% of the $PM_{2.5}$ mass concentration. The third component showed high Cu and Mn loadings and could be attributed to industrial sources such as metallurgical activities (Yang et al., 2013; Qi et al., 2016; Sharma et al., 2021) which totalled 1.5% of $PM_{2.5}$ mass. The fourth component had a high loading of Pb and S, an industrial source, possibly smelting of metals, contributing to 1.2% of $PM_{2.5}$. Londrina has several recycling industries, for example battery recycling that could contribute to this component. Unfortunately, no specific source could be assigned to the remaining 24% of $PM_{2.5}$ mass concentration, using APCA analysis, suggesting that other sources different from that identified in the PC contributes either to $PM_{2.5}$ budget in Londrina.

The limited number of source apportionment studies of $PM_{2.5}$ in medium/small-sized cities worldwide makes comparison difficult (some results are summarized in the Table 3). Comparing the data from the studies listed in Table 3, it is noted that the $PM_{2.5}$ levels varied greatly (2 to 37 μg m^{-3}). This was mirrored by an equally wide variation in types of sources allocated, as well as the percentage contribution to the $PM_{2.5}$ budget. The major contributors were from road transport sources, such as emissions from vehicle exhausts, wear and tear, and road dust resuspension (4 – 68%) and crustal or soil sources (4 to 28%). The industrial sources presented in the studies, including our study, are of such diverse nature that a general comparison is not possible, suffice to say that it varied from as low as 1.5% to as high as 36%. Several other sources are reported, such as biomass and oil burning, maritime and sea salt emissions, and undetermined sources. This variance in source apportionment and contribution has also been reported for larger urban conurbations (Putaud et al., 2004, 2010; Hand et al., 2012; Snider et al., 2016; Hama et al., 2021), further emphasising the importance of monitoring at local level.

346 Table 3 – $PM_{2.5}$ mass concentration (μg m^{-3}) and estimated percentage of sources in brackets when available, for medium sized cities with source apportionment studies.

City	Pop. (1,000)	$PM_{2.5}$ (μg m^{-3})	Sources (% of $PM_{2.5}$)								Reference
Albuquerque (USA)	800		Automobile (4-12)			Road dust (5-15)	Biomass burning (32-43)	Sulphate (9-48)	Nitrate (7-34)		Kavouras et al., 2015
Cuiaba (Brazil)	600	2-20	Urban	Soil dust	Fire	Biogenic					Santanna et al., 2016
Spain	250-700	18-37	Vehicle /traffic (10-63)	Mineral (4-12)	Metallurgy (0-19)	Road dust (6-31)	Sulphate (4-34)	Nitrate (0-11)	Sea salt (0-31)	Oil (0-20)	Amato et al., 2014
Genoa (Italy)	580	12.6-14	Road transport (35-38)		Energy/ industry (33-36)	Others (14-18)	Maritime (14-16)				Bove et al., 2014
Denver (USA)	650	5.7-6.5	Vehicle (6-15)	Crustal/ road dust (13-28)		Road salt (7-8)	Sulphur (46-62)				Clements et al., 2014
São Jose do Rio Preto (Brazil)	450	10.88		Crustal	Industrial combustion	Biomass burning					Franzin et al., 2020
Londrina (Brazil)	**570**	**4.4**	**Diesel Vehicle /Road Dust (68)**	**Soil (5.3)**	**Industrial (1.5)**	**Battery recycling (1.2)**					**Present study**

3.3. HEALTH RISK EVALUATION

3.3.1. Chemical assessment

The results obtained from the elemental health risk assessment (RAIS) are presented in Table 2. The sum of the non-carcinogenic risks (HQ) observed for Mn, Co, Al and Cr (VI) was 0.75, with Mn and Co contributing to 50 % and 24 % of the risk, respectively. Although below unity, this is still important to consider. The total carcinogenic risk (CR = $5x10^{-5}$, meaning a 5 in 100,000 chance to develop cancer during lifetime) observed, indicates a moderate risk according to the US EPA. The maximum daily values found for HQ was 1.53 while for CR was $9.9x10^{-5}$ (almost 1 in 10,000 chance to develop cancer during lifetime), and 21.7% of the days investigated for non-carcinogenic risk were above the unit risk of health effects.

Moreira et al. (2018) present personal monitoring data, sampling fine particles and their trace elements during typical workdays (about 9 hours of sample collection during travel to and from work) to assess personal exposure of workers in Londrina. The hazard quotient (HQ) calculated, considering the reference dose, ranged from 0.15×10^{-03} to 1.38 for all volunteers, indicating potential non-carcinogenic effects. Moreira et al. (2018) found $PM_{2.5}$ average level of 12.3 μg m^{-3} (maximums of 20 μg m^{-3} and 100 μg m^{-3} during non-peak and peak-time hours respectively) during a working day trial including one bus ride commute. In our study, 24-hour samples were collected, resulting in an obvious lowering of the average due to lower night-time traffic density.

So, we can infer that although the 24-hour data indicates a non-carcinogenic risk below the dose reference of observed outcomes, the dose exposure during work/day activities and high pollution days may pose a significant risk. In addition, the great variability in the concentration of $PM_{2.5}$ composition throughout the exposure time indicates that a responsible and correct health risk evaluation should be performed with epidemiological studies that consider both concentrations and responses in health of the population.

3.3.2. Bioaccessibility

The bioaccessibility of Cu, Mn, and Pb in ALF was calculated as the ratio of the ALF-soluble concentration and the total sampled concentration of the elements in $PM_{2.5}$, expressed as a percentage. Boxplots, to provide insight on the distribution of the spread of data (the average is indicated by the square symbol), are presented in Figure S3.

Cu presented the highest bioaccessibility average (59%) and variability in the results (38 – 97%). A similar study developed in two large Brazilian capitals (about 2 million inhabitants) obtained averages of 56% in Curitiba associated with traffic source, and 31% in Manaus associated with Thermal Power Plants (TPP) sources (Polezer et al., 2019). Wiseman and Zereini (2014) reported Cu bioaccessibility after 24-hour ALF-incubation of 80% during a study performed in Frankfurt (730.000 inhabitants in the city and 2.3 million in the urban region). They indicated that the main source of Cu was vehicle traffic, probably originating from brake lining attrition and rubber tire degradation (Midander et al., 2007; Sysalová et al., 2012; Wiseman and Zereini, 2014). The lower bioaccessibility average of Cu in Londrina could indicate that the primary Cu source in Londrina is obviously different than that of Frankfurt. This finding was confirmed by the APCA, where we found a 96% correlation with industrial sources and no correlation with vehicular emissions, although Cu bioacessibility in Londrina was much more similar to Curitiba than Manaus. These results give rise to the hypothesis that source apportionment at local level is crucial to build air pollution inventories that could inform decision making and result in responsible and sustainable health interventions. Besides that, deleterious effects of Cu on human health are generally associated with the rare Wilson's disease, a hereditary disorder of the homeostasis regulation process of Cu leading to a high concentrations of Cu in body

tissues (WHO, 1998). It has been recently observed that anthropogenic Cu has the most potential of all of the transition metals to induce the formation of reactive oxygen species (ROS), generating oxidative stress in the body (Becker et al., 2005; Godoi et al., 2016, Charrier & Anastasio, 2015). Differential leaching is also observed in this study, where even though the Cu had a lower concentration than either Mn or Fe (both with concentrations two and five times higher), it had a much higher bioaccessibility than Mn (the latter three time lower). Indicating yet again the importance of Cu content and hazard health risk exposure.

The lowest average bioaccessibility in Londrina was observed for Mn (17%). Similar values were obtained in the Curitiba and Manaus study with an average of 15% for Mn bioacessibility with sources related to limestone/ceramic/cement kilns and TPP respectively (Polezer et al., 2019), while the study conducted in Frankfurt observed 52% of bioaccessibility for Mn (Wiseman and Zereini, 2014). It seems that the Mn traffic related emissions in Frankfurt had a higher soluble fraction in relation to the Mn from industrial processes in Londrina, Curitiba and Manaus. Mn is an essential nutrient with the level of its absorption controlled by the body homeostasis regulation system (firstly by metabolised in the liver and potentially excreted before entering the circulation system) (Mehvar, 2018). For example, generally, up to 95% of ingested Mn is retained in the liver, and 5% is absorbed into the circulatory system (WHO, 1999). However, the respiratory exposure route can deliver this element to the circulatory/systemic system before it passes through metabolisms and excretion, enabling a higher amount of Mn that could reach for instance the brain. Consequently, long-term respiratory exposure to high levels of Mn has been associated with a syndrome similar to Parkinson's disease, with progressive neurodegenerative damage (WHO, 1999; Chen et al., 2015). Crossgrove and Zheng (2004) reported that the neurotoxicity of Mn may be associated with its interaction with iron (Fe) homeostasis, leading to high Fe deposition in the brain, which generates cellular oxidative stress and neural damage. Then besides the low bioacessibility of Mn found in Londrina samples, the concentration of Mn (second highest between transition metals) and its possible interaction with Fe (highest concentration between transition metals) could produce health risks to the population upon exposure.

Pb is a toxic element and it has the ability to accumulate in the hard tissues (e.g., bones and teeth), with a half-life of about 20 years, and it can cause severe and sometimes irreversible damage in the nervous system from fetuses to adults (ATSDR, 2019). In the present study the Pb bioacessibility average was 42%, compared to an average of 57% in Curitiba (traffic source), 71% in Manaus (associated with the TPP's), and 84% in the Frankfurt study (related to traffic sources) (Wiseman and Zereini, 2014). A similar study developed in Nanjing (8 million inhabitants) indicated that the bioaccessibility of Pb is between 66% and 78%, when the metallurgic smelters are in operation together with coal combustion power plants; and 61% when only coal combustion power plants are in operation, showing that the emissions of metallurgical operations have a higher Pb bioaccessibility (Li et al., 2016).

These data suggest that population health in Londrina is at risk to be adversely affected by $PM_{2.5}$ inhalation, due to high elemental concentrations, as well as bioaccessible fractions of PHEs (Cu, Pb, Mn). The data further confirms the hypothesis that without local monitoring and analysis, an informed risk assessment in terms of population health cannot be made.

3.4. WORLD URBAN DEVELOPMENT AND AIR POLLUTION IN PERSPECTIVE

Sustainable and responsible urban development is co-dependent on air quality. At least two goals of the 2030 Agenda for Sustainable Development recognize the importance: SDG3 - Ensure healthy lives and promote wellbeing for all at all ages, and SDG11 - Make cities and human settlements inclusive, safe, resilient, and sustainable (UN, 2020). Clearly, air pollutant inventories, specifically of $PM_{2.5}$ (including its composition and levels), in small- and medium-sized cities of

middle/low-income countries, are greatly beneficial as a tool to formulate policies to improve the well-being and quality of life for those most at risk (Landrigan et al., 2018).

According to the report by the World Urbanization Prospects of the United Nations (UN, 2018) about 57%, 2.4 billion people, of the urban world population live in a city with less than 1 million inhabitants (Figure 3). Each agglomeration (city, metropolitan areas, conurbations, etc.) in the world was ranked by its population size (the number of inhabitants) and the number of people living in each category was summed to give the total number of populations by agglomeration size. For instance, in the most populated countries in the world, China, India, and USA, this percentage is 52.0%, 54.1%, and 43.5%, respectively (UN, 2018). The largest growing rate, 20 million residents per year in average, is predicted in cities with fewer than 300,000 inhabitants and those with more than 10 million (Fig. 3), followed by those with populations larger than 1 million inhabitants (19 million inhabitants per year in average).

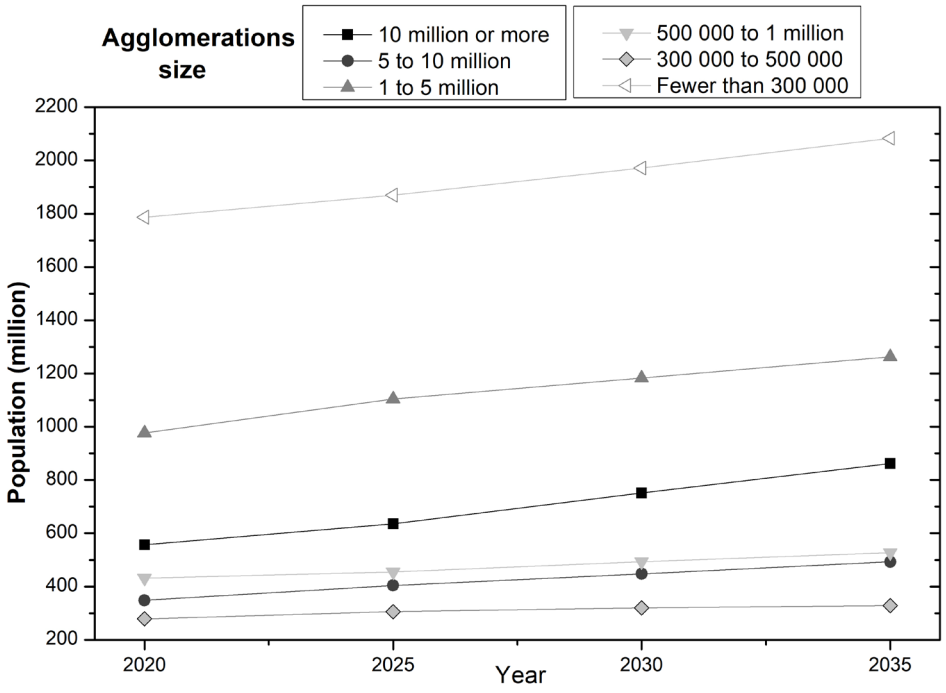

Figure 3: Sum of the world population that lives in each agglomeration size. (UN, 2018)

It is important and necessary to manage the air pollution health risk not only in large cities but also in medium- and small-sized cities, the most prevalent type of urban settlements in all the geographic regions of the world (Figure 4). This is especially of importance taking into account that in the next few years the number of small/medium size cities is expected to rise most in the Less Developed Regions, Middle-income, Lower-middle-income and Low-income countries (which are also the countries most at risk of the effects of climate change which goes hand in hand with air pollution) (USEPA, 2021; Manisalidis et al., 2020).

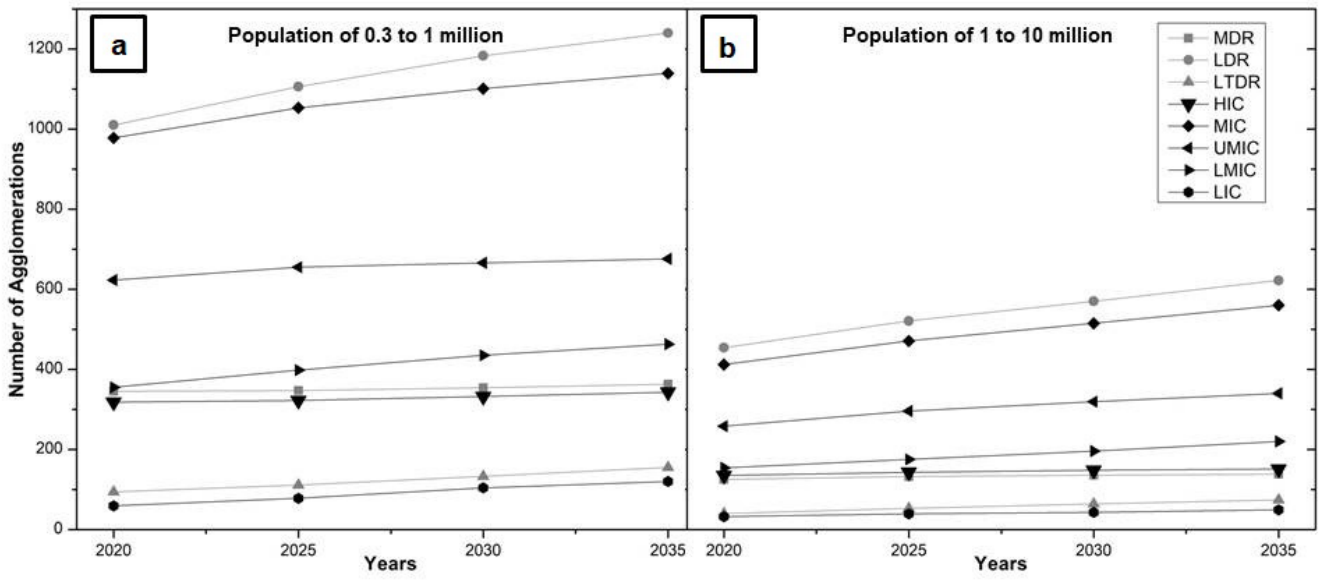

Figure 4: Number of agglomerations (cities proper, urban agglomeration, or metropolitan area) by population size (a- from 0.3 to 1 million inhabitants. b- from 1 to 10 million inhabitants) in the world. The used classifications are based on country development by the United Nations (MDR: more developed regions; LDR: less developed regions; LTDR: least developed regions; in gray) and the economic development by the Word Bank (HIC: high-income countries; MIC: middle-income countries; UMIC: upper-middle-income countries; LMIC: lower-middle-income countries; LIC: low-income countries; in black).

Therefore, as the world continues to grow and urbanize (Figure 5), the proportion of the population exposed to urban air pollution will increase, further exacerbated by the fact that urbanization is predicted to be 2 to 2.5 times higher in the low- and middle income countries, exactly were the air pollution management and control is more limited.

Although the growing role of technologies such as Satellite Observations and Chemical Transport Modeling to evaluate the global burden of $PM_{2.5}$ exposure, the ground and air-craft-based observations produce specific detailing in inventory information that are not noted from satellite (Snider et al., 2016). For instance, the chemical composition of $PM_{2.5}$ ranges more than one order of magnitude between populated sites (Polezer et al., 2019; Snider et al., 2016), being dependent on several local particularities such as social-economic development models (Gouveia et al., 2021; Polezer et al., 2019), and climate and geographic characteristics (Hand et al., 2012), and source contributions (Cepeda et al., 2017; Evans et al., 2021), that lead to specific and unique aerosol mixtures. Consequently, the improvement of the global health $PM_{2.5}$ risk factor, providing a better understanding of the role of the chemical components in this global health challenge to assess health effects, needs additional local observations of this pollutant all over the word, and more so in the low and medium size sites (Hand et al., 2012; Putaud et al., 2004, 2010; Lippman, 2014; Bell et al., 2007).

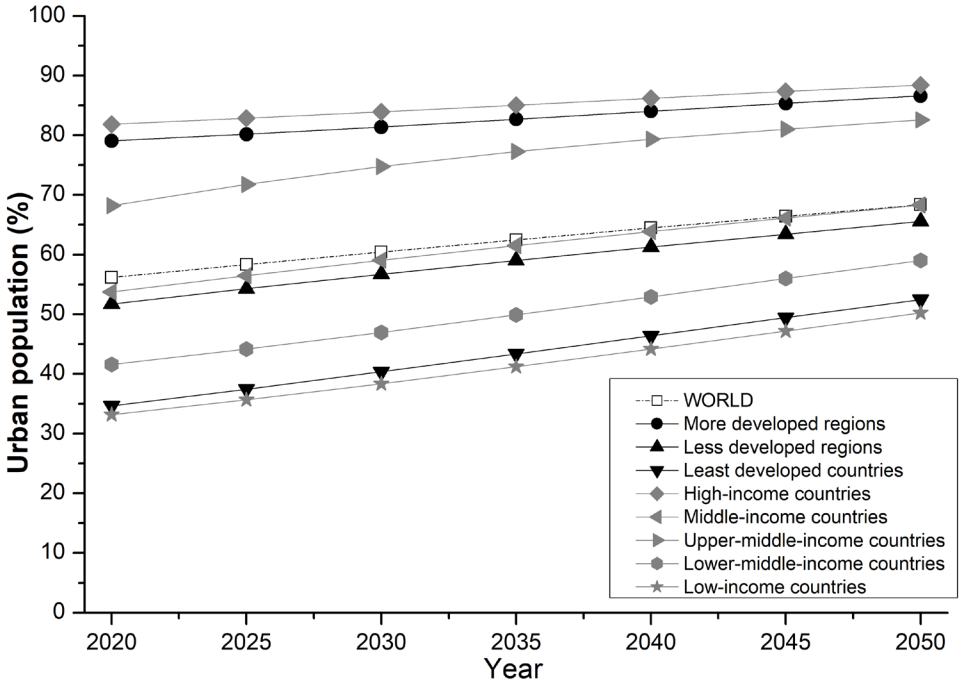

Figure 5: Proportion of population living in urban areas in the world and categorized by development regions and economic status of the countries.

Finally, beyond the need to determine the specific features of air pollution, it is also necessary to investigate the local population characteristics such as social conditions, access to medical care, genetics, age, sex, and behavior (Pope et al., 2020; West et al., 2016; Pope et al., 2009). A recent study by Shi et al. (2020), applying a longitudinal nationwide open cohort population-based study in the United States of America (all above 65 years from 2000 to 2016), investigated the annual mean $PM_{2.5}$ concentrations associated with zip codes and the first hospital admissions for Parkinson's disease, Alzheimer's disease, and Related Dementias. The health model adjustment considered, besides the usual possible confounds, also age, sex, race, zip code, medical eligibility (indicating level of socio-economic status), level of education, population density, previous smoking, median home value, owner-occupied housing, and median household income. It was possible to obtain Hazard Ratios relating the hospital admissions for both outcomes with 5 μg m^{-3} change, and strong evidence of linearity with $PM_{2.5}$ concentrations less than 16 μg m^{-3} was found. Moreover, it was found that subgroups of women, white people, and more urbanized populations were more susceptible for hospital admissions for Parkinson's and Alzheimer's diseases, and Related Dementias.

4. CONCLUSIONS

As in any city, air quality in Londrina is determined by the balance between pollutant emissions sources and the capacity to disperse and remove those air pollutants. We found that a substantial health risk is present even at pollutant concentrations below the new updated WHO AQGs, highlighting the general unspoken hypothesis that no level of $PM_{2.5}$ is safe. The important statement to be made is that high levels of anthropogenic metals, including Cu, Pb, and Mn, are critical factors compounding the health risk of the population of Londrina.

The differential bioaccessibility of the PHEs in $PM_{2.5}$ observed during this study is of particular importance, not only for the Londrina population, but also in the wider global context, as absolute concentrations did not reflect necessarily in the degree of mobility of the elements. As this differential behavior is chemistry dependent, which in turn is source

dependent, the true health risk can only be determined by performing local ground-based studies. It is therefore, not unrealistic to expect a wide spectrum of pathologies at different locations. The fact that the disease burden due to poor air quality is most prone in low- to middle-income countries and that the indiscriminate use of atmospheric chemistry and transport models to estimate the local/regional air quality of medium-sized cities underestimate the real impact of air pollution on the population, provides a basis for urgent global action to empower these countries to monitor effectively and widely. Lastly, in view of the predictions of increased urbanization, growth of small- and medium-sized cities, and increased numbers of agglomerations (especially in the Less Developed and Low Income Countries) in the near future, local authorities will need to take action urgently to protect their citizens from the additional burden on population health.

Declarations

Funding: The authors gratefully acknowledge for financial support to Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) (Finance Code 001), and Fundação Araucária de Apoio ao Desenvolvimento Científico e Tecnológico do Estado do Paraná / Research Program for SUS - PPSUS (Grant no. 435/2014).

Declaration of competing interest

The authors declare that they have no known competing financial interest or personal relationship that could have appeared to influence the work reported in this paper.

Availability of data and material

Data available within the article or its supplementary materials

CRediT authorship contribution statement

Gabriela Polezer: Methodology, Investigation, Data Curation, Writing - Original Draft, Writing - Review & Editing. **Sanja Potgieter-Vermaak:** Conceptualization, Data Curation, Writing - Review & Editing, Visualization. **Andrea Oliveira:** Validation, Investigation, Writing - Review & Editing. **Leila D. Martins:** Methodology, Investigation, Writing - Review & Editing. **Jéssica C. Santos-Silva:** Software, Writing - Review & Editing. **Camila A. B. Moreira:** Software, Writing - Review & Editing. **Theotonio Pauliquevis:** Formal analysis, Writing - Review & Editing. **Ana F. L. Godoi:** Resources, Writing - Review & Editing. Yara Tadano Resources, Writing - Review & Editing. **Carlos I. Yamamoto:** Resources, Writing - Review & Editing, Funding acquisition. **Ricardo H. M. Godoi:** Conceptualization, Writing - Review & Editing, Supervision, Project administration, Funding acquisition.

5. REFERENCES

Amato, F., Alastuey, A., Rosa, J., Castanedo, Y. G., de la Campa, A. M. S., Pandolfi, M., Lozano, A., González, J. C., Querol, X., (2014). Trends of road dust emissions contributions on ambient air particulate levels at rural, urban and industrial sites in southern Spain. *Atmospheric Chemistry and Physics*. 14, 3533–3544.

Andrade, M. D., de Miranda, R. M., Fornaro, A., Kerr, A., Oyama, B., de Andre, P. A., Saldiva, P., (2012). Vehicle emissions and $PM_{2.5}$ mass concentrations in six Brazilian cities. *Air Quality, Atmosphere & Health*. 5, 79–88.

Angelé-Martínez, C., Goodman, C., Brumaghim, J., (2014). Metal-mediated DNA damage and cell death: mechanisms, detection methods, and cellular consequences. *Metallomics*. 6,1358-81.

Ariola, V., D'Alessandro, A., Lucarelli, F., Marcazzan, G., Mazzei, F., Nava, S., Garcia-Orellana I., Prati, P., Valli, G., Vecchi, R., Zucchiatti, A., (2006). Elemental characterization of PM_{10}, $PM_{2.5}$ and PM_1 in the town of Genoa (Italy). *Chemosphere*. 62, 226-232.

ATSDR (2019*). Toxicological profile for lead*. In U.S. Department of Health and Human Services (Ed.): Agency for Toxic Substances and Disease Registry. https://www.atsdr.cdc.gov/toxprofiles/tp13.pdf. Acessed 23 December 2020.

Beal, A., Bufato, C. A., de Almeida, D. S., Squizzato, R., Zemiani, A., Vernilo, N., Batista, C. E., Salvador, G., Borges, D. L., Solci, M. C., da Silva, A. F., Martins, J. A., Martins, L. D., (2017). Inorganic Chemical Composition of Fine Particulates in Medium-Sized Urban Areas: A Case Study of Brazilian Cities. *Aerosol and Air Quality Research*. 17, 920-932.

Becker, S., Dailey, L. A., Soukup, J. M., Grambow, S. C., Devlin, R. B. & Huang, Y-C. T., (2005). Seasonal Variations in Air Pollution Particle-Induced Inflammatory Mediator Release and Oxidative Stress. *Environmental Health Perspectives*. 113, 1032-1038.

Bell, M. L., Dominici, F., Ebisu, K., Zeger, S. L., and Samet, J. M., (2007). Spatial and temporal variation in PM2:5 chemical composition in the United States for health effects studies. *Environmental Health Perspectives*. 115, 989–995.

Bove, M. C., Brotto, P., Cassola, F., Cuccia, E. Massabò, D., Mazzino, A., Piazzalunga, A., Prati, P., (2014). An Integrated PM2.5 Source Apportionment Study: Positive Matrix Factorisation Vs. The Chemical Transport Model Camx. *Atmospheric Environment.* 94, 274-286.

Brito, J. M., Belotti, L., Toledo, A. C., Antonangelo, L., Silva, F.S., Alvim, D.S., Andre, P. A., Saldiva, P. H. N., Rivero, D. H. R. F, (2010). Acute Cardiovascular and Inflammatory Toxicity Induced by Inhalation of Diesel and Biodiesel Exhaust Particles. *Toxicological Sciences*. 116, 67–78.

Canova, C., Dunster, C., Kelly, F. J., Minelli, C., Shah, P. L., Caneja, C., Tumilty, M. K., Burney, P., (2012). PM10-induced Hospital Admissions for Asthma and Chronic Obstructive Pulmonary Disease The Modifying Effect of Individual Characteristics. *Epidemiology.* 23, 607-615.

Cao, J. J., Xu, H. M., Xu, Q., Chen, B. H. & Kan, H. D., (2012). Fine Particulate Matter Constituents and Cardiopulmonary Mortality in a Heavily Polluted Chinese City. *Environmental Health Perspectives*. 120, 373-378.

Cepeda, M., Schoufour, J., Freak-Poli, R., Koolhaas, C. M., Dhana, K., Bramer, W. M., Franco O. H., (2017). Levels of ambient air pollution according to mode of transport: a systematic review. *Lancet Public Health.* 2, E23-E34.

CETESB (2019). *Air Quality in the São Paulo state* 2018. ISSN 0103-4103

Charrier, J. G. & Anastasio, C. (2015). Rates of hydroxyl radical production from transition metals and quinones in a surrogate lung fluid. *Environmental Science & Technology*. 49, 9317-9325.

Chen, G., Guo, Y., Abramson, M. J., Williams, G. & Li, S. (2018). Exposure to low concentrations of air pollutants and adverse birth outcomes in Brisbane, Australia, 2003–2013. *Science of the Total Environment*. 622, 721-726.

Chen, P., Chakraborty, S., Mukhopadhyay, S., Lee, E., Paoliello, M. M. B., Bowman, A. B., Aschner, M., (2015). Manganese homeostasis in the nervous system. *Journal of Neurochemistry*. 134-601-610.

Chen, J., Hoek, G., (2020). Long-term exposure to PM and all-cause and cause-specific mortality: a systematic review and meta-analysis. *Environment International.* 143:105974.

Clements, N., Eav, J., Xie, M., Hannigan, M. P., Miller, S. L., Navidi, W., Peel, J. L., Schauer, J. J., Shafer, M. M., Milford, J. B., (2014). Concentrations and source insights for trace elements in fine and coarse particulate matter. *Atmospheric Environment*. 89, 373-381.

CMTU (2015). *Transporte urbano*. Companhia Municipal de Trânsito e Urbanização. https://cmtu.londrina.pr.gov.br/index.php/transporte-urbano.html. Acessed 20 June 2016.

Colombo, C., Monhemius, A. J. & Plant, J. A., (2008). Platinum, palladium and rhodium release from vehicle exhaust catalysts and road dust exposed to simulated lung fluids. *Ecotoxicology and Environmental Safety*. 71, 722-730.

Coufalík, P., Mikuska, P., Matousek, T., Vecera, Z., (2016). Determination of the bioaccessible fraction of metals in urban aerosol using simulated lung fluids. *Atmospheric Environment.* 140, 469-475.

Crossgrove, J. and Zheng, W., (2004). Manganese toxicity upon overexposure. *NMR in Biomedicine*. 17, 544-553.

DENATRAN (2019). *Frota de Veículos - 2019: Frota por município e tipo.* National Department of Transit. https://www.denatran.gov.br/component/content/article/115-portal-denatran/8559-frota-de-veiculos-2019.html Acessed 22 December 2019.

Dockery, D. W., Pope, C. A. III, Xu, X., Spengler, J. D., Ware, J. H., Fay M. E., Ferris Jr, B. G., Speizer, F. E., (1993). An association between air pollution and mortality in six US cities. *The New England Journal of Medicine*. 329, 1753–1759.

Echalar, F., Artaxo, P., Martins, J. V., Yamasoe, M., Gerab, F., Maenhaut, W., and Holben, B., (1998). Long-term monitoring of atmospheric aerosols in the Amazon Basin: Source identification and apportionment, *Journal of Geophysical Research: Atmospheres.* 103, 31849–31864.

European Commission (2002). *Commission Decision 2002/657/EC* of 12 August 2002 implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results. Official journal of the European Communities, 221, 8-36.

Evangelopoulos, D., Perez-Velasco, R., Walton, H., Gumy, S., Williams, M., Kelly, F., Künzli**.,** **(**2020). The role of burden of disease assessment in tracking progress towards achieving WHO global air quality guidelines. *International Journal of Public Health*. 65:1455–65.

Evans, J.S., Rojas-Bracho, L., Hammitt, J.K. and Dockery, D.W., (2021). Mortality Benefits and Control Costs of Improving Air Quality in Mexico City: The Case of Heavy Duty Diesel Vehicles. *Risk Analysis*. 41, 661-677.

Expósito, A, Markiv, B. Ruiz-Azcona, L. Santibáñez, M. Fernández-Olmo. I. (2021). Personal inhalation exposure to manganese and other trace metals in an environmentally exposed population: Bioaccessibility in size-segregated particulate matter samples. *Atmospheric Pollution Research*.12, 101123.

Fang, G-C., Chen, Y-C., Lo, C-T., Cho, M-H., Zhuang, Y-J., Tsai, K-H., Huang, C.-Y., Xiao, Y.-F. (2018). Concentrations and analysis of health risks of ambient air metallic elements at Longjing site in central Taiwan. *Environmental Geochemistry and Health.* 40, 461-472.

Fisher, J. A., Puett, R. C., Laden, F., Wellenius, G. A., Sapkota, A., Liao, D., Yanosky, J. D., Carter-Pokras, O., He, X., Hart, J. E., (2019). Case-crossover analysis of short-term particulate matter exposures and stroke in the health professionals follow-up study. *Environment International*. 124, 153-160.

Franzin, B.T., Guizellini, F. C., Babos, D. V., Hojo, O., Pastre, I. A., Marchi, M. R. R., Fertonani, F. L., Oliveira, C. M. R. R.(2020). Characterization of atmospheric aerosol (PM10 and PM2.5) from a medium sized city in São Paulo state, Brazil. *Journal of Environmental Sciences*., 89, 238-251.

Godoi, R. H. M., Godoi, A. F. L., de Quadros, L. C., Polezer, G., Silva, T. O. B., Yamamoto, C. I., Van Grieken, R., Potgieter-Vermaak, S., (2013). Risk assessment and spatial chemical variability of PM collected at selected bus stations. *Air Quality, Atmosphere & Health*. 6, 725-735.

Godoi, R. H. M., Kontozova, V. & Van Grieken, R., (2006). The shielding effect of the protective glazing of historical stained glass windows from an atmospheric chemistry perspective: Case study Sainte Chapelle, Paris. *Atmospheric Environment*. 40, 1255-1265.

Godoi, R. H. M., Polezer, G., Borillo, G. C., Brown, A., Valebona, F. B., Silva, T. O. B., Ingberman, A. B. G., Nalin, M., Yamamoto, C. I., Potgieter-Vermaak, S., Penteado Neto, R. A., Marchi, M. R. R., Saldiva, P. H. N., Pauliquevis T., Godoi, A. F. L., (2016). Influence on the oxidative potential of a heavy-duty engine particle emission due to selective catalytic reduction system and biodiesel blend. *Science of the Total Environment*. 560, 179-185.

Gouveia, N., Kephart, J. L., Dronova, I., McClure, L., Granados, J. T., Betancourt, R. M., O'Ryan, A. C., Texcalac-Sangrador, J. L., Martinez-Folgar, K. Rodriguez, D., Diez-Roux, A. V., (2021). Ambient fine particulate matter in Latin American cities: Levels, population exposure, and associated urban factors. *Science of the Total Environment.* 772, 145035.

Hama, S., Kumar, P., Alam, M. S., Rooney, D. J., Bloss, W. J., Shi, Z., Harrison, R. M., Crilley R. L., Khare, M., Gupta, S. K., (2021). Chemical source profiles of fine particles for five different sources in Delhi. *Chemosphere*. 274, 129913.

Hand, J. L., Schichtel, B. A., Pitchford, M., Malm,W. C., and Frank, N. H. (2012). Seasonal composition of remote and urban fine particulate matter in the United States. *Journal of Geophysical Research*. 117.

Herich, H., Hueglin, C. & Buchmann, B., (2011). A 2.5 year's source apportionment study of black carbon from wood burning and fossil fuel combustion at urban and rural sites in Switzerland. *Atmospheric Measurement Techniques*. 4, 1409–1420.

Hernández-Pellón, A, Nischkauer, W, Limbeck, A, Fernández-Olmo, I. (2018). Metal(loid) bioaccessibility and inhalation risk assessment: A comparison between an urban and an industrial area, *Environmental Research*.165.

Hoornaert, S., Godoi, R. H. M. & Van Grieken, R., (2004). Elemental and single particle aerosol characterisation at a background station in Kazakhstan. *Journal of Atmospheric Chemistry*. 48, 301-315.

Hu, X., Zhang, Y., Luo, J., Wang, T. J., Lian, H. Z. & Ding, Z. H., (2011). Bioaccessibility and health risk of arsenic, mercury and other metals in urban street dusts from a mega-city, Nanjing, China. *Environmental Pollution*. 159, 1215-1221.

IBGE (2017). *Gross Domestic Product (GDP)*. Brazilian Institute of Geography and Statistics. https://www.ibge.gov.br/estatisticas-novoportal/economicas/contas-nacionais/9088-produto-interno-bruto-dos-municipios.html?=&t=resultados. Accessed 23 December 2019.

IBGE (2018).. *Mortality Table for Brazil in 2017.* Brazilian Institute of Geography and Statistics ftp://ftp.ibge.gov.br/Tabuas_Completas_de_Mortalidade/Tabuas_Completas_de_Mortalidade_2017/tabua_de_mortalidade_2017_analise.pdf. Accessed 23 December 2019.

IBGE (2019). *IBGE Cidades: Londrina.* Brazilian Institute of Geography and Statistics. https://cidades.ibge.gov.br/brasil/pr/londrina/panorama. Acessed 23 December 2019.

INMET, 2016. BDMEP - *Banco de Dados Meteorologicos para Ensino e Pesquisa*. National Institute of Meteorology.

INEbase (2018). *Official Population Figures referring to revision of Municipal Register* (2018). INEbase. Instituto Nacional de Estadística.

IPPUL (2016). *Contagens de Tráfego. Instituti de Pesquisa e Planejamento Urbano de Londrina.* https://ippul.londrina.pr.gov.br/index.php/contagens-de-trafego.html. Acessed 23 February 2020.

Istat (2018*). Bilancio Demografico della Popolazione Residente per Mes*e (2018). Instituto Nazionale di Statistica.

IT.NRW (2013). *Population figures based on the census of 9 May 2011* (2013). Information und Technik Nordrhein-Westfalen.

Kavouras, I. G., DuBois, D. W., Nikolich, G., & Etyemezian, V. (2015). Monitoring, source identification and health risks of air toxics in Albuquerque, New Mexico, USA. *Aerosol and Air Quality Research*. 15, 556-571.

Klepac, P., Locatelli, I., Korošec, S., Künzli, N. & Kukec, A. (2018). Ambient air pollution and pregnancy outcomes: A comprehensive review and identification of environmental public health challenges. *Environmental Research*. 167, 144-159.

Krecl, P., Targino, A. C., Landi, M. K. & Ketzel, M., (2018). Determination of black carbon, PM2.5, particle number and NOx emission factors from roadside measurements and their implications for emission inventory development, *Atmospheric Environment*. 186, 229-240.

Kurt-Karakus, P. B. (2012). Determination of heavy metals in indoor dust from Istanbul, Turkey: Estimation of the health risk. *Environment International.* 50, 47-55.

Landrigan, P. J., Fuller, R., Acosta, N. J. R., Adeyi, O., Arnold, R., Basu, N., et al., (2018). The Lancet Commission on pollution and health. *The Lancet*. 391, 10119.

Langrish, J. P., Li, X., Wang, S. F., Lee, M. M. V., Barnes, G. D., Miller, M. R., Cassee, F. R., Boon, N. A., Donaldson, K., Li, J., Li, L., Mills, N. L., Newby, D. E., Jiang, L., (2012). Reducing Personal Exposure to Particulate Air Pollution Improves Cardiovascular Health in Patients with Coronary Heart Disease. *Environmental Health Perspectives*. 120, 367-372.

Lelieveld, J., Evans, J. S., Fnais, M., Giannadaki, D. & Pozzer, A., (2015). The contribution of outdoor air pollution sources to premature mortality on a global scale. *Nature*. 525, 367-371.

Li, S.-W., Li, H.-B., Luo, J., Li, H.-M., Qian, X., Liu, M.-M., Bi, J., Cui, X.-Y., Ma, L. Q., (2016). Influence of pollution control on lead inhalation bioaccessibility in PM2.5: A case study of 2014 Youth Olympic Games in Nanjing. *Environment International.* 94, 69-75.

Liu, Q.-T., Diamond, M. L., Gingrich, S. E., Ondov, J. M., Maciejczyk, P. & Stern, G. A., (2003). Accumulation of metals, trace elements and semi-volatile organic compounds on exterior window surfaces in Baltimore. *Environmental Pollution*. 122, 51-61.

Liu, X., Zhai, Y., Zhu, Y., Liu, Y., Chen, H., Li, P., Peng, C., Xu, B., Li, C., Zeng, G., (2015). Mass concentration and health risk assessment of heavy metals in size-segregated airborne particulate matter in Changsha. *Science of the Total Environment*. 517, 215-221.

Maenhaut, W.; Cafmeuyer, H. (1987). Particle Induced X-Ray Emission Analysis And Multivariate Techniques: As Application To The Study Of Teh Sources Of Respirable Atmospheric Particles In Gent, Belgium. *J. Trace Microprobe* T. 5, 135-158.

Manisalidis, I., Stavropoulou, E., Stavropoulos, A., Bezirtzoglou, E., (2020). Environmental and Health Impacts of Air Pollution: A Review. *Frontiers in Public Health*. 8, 14.

Marple, V. A., Rubow, K. L., Turner, W. & Spengler, J. D. (1987). Low Flow Rate Sharp Cut Impactors for Indoor Air Sampling: Design and Calibration. *JAPCA*. 37, 1303-1307.

Martins, L.D., Hallak, R., Alves, R.C., de Almeida, D.S., Squizzato, R., Moreira, C.A., Beal A., da Silva, I., Rudke A., Martins J. A., (2018). Long-range Transport of Aerosols from Biomass Burning over Southeastern South America and their Implications on Air Quality. *Aerosol and Air Quality Research.* 18, 1734-1745.

Mason, B. (1966). *Principles of geochemistry*. John Willey and Sons. Inc., New York.

Mbengue, S., Alleman, L. Y., Flament, P. (2015). Bioaccessibility of trace elements in fine and ultrafine atmospheric particles in an industrial environment. *Environmental Geochemistry and Health*. 37, 875-889.

Mehvar, R. (2018). Clearance Concepts: Fundamentals and Application to Pharmacokinetic Behavior of Drugs. *Journal of Pharmaceutical Sciences.* 21, 88-102.

Midander, K., Pan, J., Wallinder, I. O. & Leygraf, C., (2007). Metal release from stainless steel particles in vitro-influence of particle size. *Journal of Environmental Monitoring*. 9, 74-81.

Molnar, A., Meszaros, E., Bozo, L., Borbelykiss, I., Koltay, E. & Szabo, G., (1993). Elemental composition of atmospheric aerosol-particles under different conditions in Hungary. *Atmospheric Environment. A-Gen*. 27, 2457-2461.

Moreira, C. A. B., Squizzato, R., Beal, A., Almeida, D. S., Rudke, A. P., Ribeiro, M., Andrade, M. F., Kumar, P., Martins, L. D. (2018). Natural variability in exposure to fine particles and their trace elements during typical workdays in an urban area. *Transportation Research Part D: Transport and Environment*. 63, 333-346.

Nascimento, L. F. C., Francisco, J. B., Patto, M. B. R. & Antunes, A. M., (2012). Environmental pollutants and stroke-related hospital admissions. *Cadernos de Saúde Pública*. 28.

NBSPRC (2019). *The total population at the end of 2018* (2019). National Bureau of Statistics of the People's Republic of China. https://baike.baidu.com/item/%E4%B8%AD%E5%9B%BD%E5%9F%8E%E5%B8%82%E4%BA%BA%E5%8F%A3%E6%8E%92%E5%90%8D%E8%A1%A8#reference-[3]-16614821-wrap. Acessed 23 December 2019.

ONS-UK (2017). *Population Estimates for UK, England and Wales, Scotland and Northern Ireland* (2017). Office for National Statistics.

Polezer, G., Tadano, Y. S., Siqueira, H. V., Godoi, A. F. L., Yamamoto, C. I., de André, P. A., Pauliquevis, T., Andrade, M. F., Oliveira, A., Saldiva, P. H. N., Taylor, P. E., Godoi, R. H. M. (2018). Assessing the impact of PM2.5 on respiratory disease using artificial neural networks. *Environmental Pollution*. 235, 394-403.

Polezer, G., Oliveira, A., Potgieter-Vermaak, S., Godoi, A. F. L., de Souza, R. A. F., Yamamoto, C. I., Andreoli, R. V., Medeiros, A. S., Machado, C. M. D., Santos, E. O., André, P. A., Pauliquevis, T., Saldiva, P. H. N., Martin, S. T., Godoi, R. H. M., (2019). The influence that different urban development models has on PM2.5 elemental and bioaccessible profiles. *Scientific Reports*. 9, 14846.

Polezer, G., Godoi, R. H. M., Potgieter-Vermaak, S., de Souza, R. A. F., Andreoli, R. V., Yamamoto, C. I., Oliveira, A., (2020). Atomic Absorption Spectrometry Methods to Access the Metal Solubility of Aerosols in Artificial Lung Fluid. *Applied Spectroscopy*. 74, 932-939.

Pope, C. A. III, Burnett, R. T., Thun, M. J., Calle, E. E., Krewski, D., Ito, K., Thurston, G. D., (2002). Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA*. 287,1132–41.

Pope, C. A., Ezzati, M. & Dockery, D. W. (2009). Fine-Particulate Air Pollution and Life Expectancy in the United States. *The New England Journal of Medicine*. 360, 376-386.

Pope, C. A. III, Coleman, N., Pond, Z. A., Burnett, R. T., (2020). Fine particulate air pollution and human mortality: 25+ years of cohort studies. *Environmental Research*. 183, 108924.

Putaud, J.-P., Raes, F., Van Dingenen, R., Brüggemann, E., Facchini, M.-C., Decesari, S. et al., (2004). A European aerosol phenomenology- 2: chemical characteristics of particulate matter at kerbside, urban, rural and background sites in Europe. *Atmospheric Environment*. 38, 2579-2595.

Putaud, J.-P., Van Dingenen, R., Alastuey, A., Bauer, H., Birmili, W., Cyrys, J. et al., (2010). A European aerosol phenomenology – 3: Physical and chemical characteristics of particulate matter from 60 rural, urban, and kerbside sites across Europe, *Atmospheric Environment*. 44, 1308-1320.

Qi, L., Chen, M., Ge, X., Zhang, Y., & Guo, B., (2016). Seasonal variations and sources of 17 aerosol metal elements in suburban Nanjing, China. *Atmosphere*. 7, 153.

RAIS (2020). *The Risk Assessment Information System*. http://rais.ornl.gov/.. Acessed 10 February 2021.

Ritchie, H., Roser, M., (2019). *Outdoor Air Pollution*. https://ourworldindata.org/outdoor-air-pollution. Acessed 25 February 2020.

Santanna, F. B., Almeida Filho, E. O., Vourlitis, G. L., Arruda, P. H. Z., Palácios, R. S., Nogueira, J. S., (2016). Elemental Composition Of PM_{10} And $PM_{2.5}$ For A Savanna (Cerrado) Region Of Southern Amazonia. *Química Nova*. 39, 1170-1176.

Sharma, S.K., Mukherjee, S., Choudhary, N., Rai, A., Ghosh, A., Chatterjee, A., Vijayan, N., Mandal, T. K., (2021). Seasonal variation and sources of carbonaceous species and elements in PM2.5 and PM10 over the eastern Himalaya. *Environmental Science and Pollution Research*. 28, 51642-51656.

Shi, L., Wu, X., Yazdi, M. D., Braun, D., Awad, Y. A., Wei, Y., Liu, P., Di, Q., Wang, Y., Schwartz, J., Dominici, F., Kioumourtzoglou, M.-A., (2020). Long-term effects of $PM_{2.5}$ on neurological disorders in the American Medicare population: a longitudinal cohort study, *The Lancet Planetary Health*. 4, E557-E565.

Snider, G., Weagle, C. L., Murdymootoo, K. K., Ring, A., Ritchie, Y., Stone, E., Walsh, A., Akoshile, C., Anh, N. X., Balasubramanian, R., Brook, J., Qonitan, F. D., Dong, J., Griffith, D., He, K., Holben, B. N., Kahn, R., Lagrosas, N., Lestari, P., Ma, Z., Misra, A., Norford, L. K., Quel, E. J., Salam, A., Schichtel, B., Segev, L., Tripathi, S., Wang, C., Yu, C., Zhang, Q,, Zhang, Y., Brauer, M., Cohen, A., Gibson, M. D., Liu, Y., Martins, J. V., Rudich, Y., Martin, R. V., (2016). Variation in global chemical composition of PM2.5: emerging results from SPARTAN, *Atmospheric Chemistry and Physics.* 16, 9629-9653.

Song, Y., Xie, S., Zhang, Y., Zeng, L., Salmon, L. G., Zheng, M., (2006). Source apportionment of PM2.5 in Beijing using principal component analysis/absolute principal component scores and UNMIX, *Science of the Total Environment.* 372, 278-286.

Sorensen, M., Hoffmann, B., Hvidberg, M., Ketzel, M., Jensen, S. S., Andersen, Z. J., Tjønneland, A., Overvad, K., Raaschou-Nielsen, O. (2012). Long-Term Exposure to Traffic-Related Air Pollution Associated with Blood Pressure and Self-Reported Hypertension in a Danish Cohort*. Environmental Health Perspectives*. 120, 418-424.

Srimuruganandam, B.; Nagendra, S. M. S. (2012). Source characterization of PM10 and PM2.5 mass using a chemical mass balance model at urban roadside. *Science of the Total Environment*. 433, 8-19.

Swietlik, R., Molik, A., Molendar, M., Trojanowska, M., Siwiec, J., (2011). Chromium(III/VI) speciation in urban aerosol. *Atmospheric Environment*. 45, 1364-1368.

Sysalová, J., Sýkorová, I., Havelcová, M., Száková, J., Trejtnarová, H., Kotlík, B., (2012). Toxicologically important trace elements and organic compounds investigated in size-fractionated urban particulate matter collected near the Prague highway. *Science of the Total Environmen*t. 15, 127-136.

UN (2018). *United Nations, Department of Economic and Social Affairs*, Population Division. World Urbanization Prospects: The 2018 Revision, Online Edition.

UN (2020). *United Nations. Department of Economic and Social Affairs*, Sustainable Development. Accessed 28/10/2020 https://sdgs.un.org/goals

USCB 2019. *United States Census Bereau* (2019). https://census.gov/. 11 November 2019.

USEPA (1989). *Risk Assessment Guidance for Superfund Volume I.* Human Health Evaluation Manual (Part A).

USEPA (2009). *Risk Assessment Guidance for Superfund (RAGS*), Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment).

USEPA (2021). *Air Quality and Climate Change Research*. https://www.epa.gov/air-research/air-quality-and-climate-change-research. Accessed. 23/11/2021.

Viana, M., Kuhlbusch, T. A. J., Querol, X., Alastuey, A., Harrison, R. M., Hopke, P. K., Winiwarter, W., Vallius, M., Szidat, S., Prévôt, A.S.H., Hueglin, C., Bloemen, H., Wåhlin, P., Vecchi, R., Miranda, A.I., Kasper-Giebl, A., Maenhaut, W., Hitzenbergerq, R., (2008). Source apportionment of particulate matter in Europe: A review of methods and results. *Journal of Aerosol Science*. 39, 827-849.

West, J. J.; Cohen, A.; Dentener, F.; Brunekreef, B.; Zhu, T.; Armstrong, B., Bell, M. L., Brauer, M., Carmichael, G., Costa, D. L., Dockery, D. W., Kleeman, M., Krzyzanowski, M., Künzli, N., Liousse, C., Lung, S.-C. C., Martin, R. V., Pöschl, U., Pope III, C. A., Roberts, J. M., Russell, A. G., Wiedinmyer, C., (2016). What we breathe impacts our health: improving understanding of the link between air pollution and health. *Environmental Science & Technology*. 50, 4895-4904.

WHO (1998*). Environmental health criteria, Copper*. International program on chemical safety. World Health Organization.

WHO (1999). *Manganese and its compounds. Concise international chemical assessment*. World Health Organization.

WHO (2006). *Air Quality Guidelines, Global Update 2005, Particulate matter, ozone, nitrogen dioxide and sulfur dioxide.* World Health Organization.

WHO (2018). *Air pollution and child health: prescribing clean air.* World Health Organization.

WHO (2021). *Global air quality guidelines*. *Particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide.* Geneva: World Health Organization.

Wiseman, C. L. S. & Zereini, F., (2014). Characterizing metal(loid) solubility in airborne PM10, PM2.5 and PM1 in Frankfurt, Germany using simulated lung fluids. *Atmospheric Environment*. 89, 282-289.

Wu, C. F., Li, Y. R., Kuo, I. C., Hsu, S. C., Lin, L. Y. & Su, T. C., (2012). Investigating the association of cardiovascular effects with personal exposure to particle components and sources. *Science of the Total Environment*. 431, 176-182.

Yang, L., Cheng, S., Wang, X., Nie, W., Xu, P., Gao, X., Yuan, C., Wang, W., (2013). Source identification and health impact of $PM_{2.5}$ in a heavily polluted urban atmosphere in China. *Atmospheric Environment*. 75, 265-269.