Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

Tiffany Eberhard

Date

Systematic Review of Microplastics and Nanoplastics in Outdoor and Indoor air: Human Exposure Assessment

By

Tiffany Eberhard Master of Public Health

Global Environmental Health

Dr. Dana Barr Committee Chair

Systematic Review of Microplastics and Nanoplastics in Outdoor and Indoor air: Human Exposure Assessment

By

Tiffany Eberhard

B.S., University of Georgia, 2015 B.A., University of Georgia, 2015

Thesis Committee Chair: Dr. Dana Barr Ph.D., Georgia State University, 1994 B.S., Brenau University, 1987

An Abstract of a thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Global Environmental Health 2022

Abstract

Systematic Review of Microplastics and Nanoplastics in Outdoor and Indoor air: Human Exposure Assessment

By Tiffany Eberhard

Micro- and nanoplastic (MNP) exposure to humans is likely unavoidable with inhalation one of the main routes of exposure. To our knowledge, there is no comprehensive exposure assessment of Microplastics (MP) in indoor and outdoor air. The current paper provides a human exposure assessment of microplastics in the air using systematically reviewed literature of articles that provided dose or concentration of measured MNPs in indoor and/or outdoor air as well as doses used in animal and human toxicology studies of MNPs. Average inhalation exposure doses were calculated for different age groups ranging from 106 MPs/kg-BW/day for infants to 29.7 MPs/kg-BW/day for adults indoors, and 35.5 MPs/kg-BW/day for infants and 9.82 MPs/kg-BW/day for adults outdoors for active sampling methods. Pregnant women had higher MP inhalation exposure doses than adults and infants averaged the highest MP exposure doses from air compared to all other age groups. Average indoor inhalation exposure doses were higher that outdoor exposure doses for all ages. Passive sampling methods had higher averages for inhalation exposure doses with averages ranging between 1053 to 4555 MPs/kg-BW/day for all age categories for indoor samples. MNP doses used in animal and human in vitro studies averaged higher estimated inhalation exposure doses than exposure doses calculated from environmental MP samples. This study provides the first known exposure data of MP in air using systematically reviewed literature for MPs in indoor and outdoor air and provides inhalation exposure doses estimated from animal models or human exposure to MNPs and human in vitro toxicology studies.

Systematic Review of Microplastics and Nanoplastics in Outdoor and Indoor air: Human Exposure Assessment

By

Tiffany Eberhard

B.S., University of Georgia, 2015 B.A., University of Georgia, 2015

Thesis Committee Chair: Dr. Dana Barr Ph.D., Georgia State University, 1994 B.S., Brenau University, 1987

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Global Environmental Health 2022

Acknowledgments

I would like to extend my greatest appreciation to the many people who have contributed to the development of this thesis. Thank you to my thesis chair and mentor, Dr. Dana Barr, who has guided me throughout my time at Rollins School of Public Health and provided valuable knowledge during the research and writing of this thesis. A huge thank you to Dr. Gaston Casillas who has worked tirelessly with me from start to finish and whose optimism and insights propelled this project forward. Thank you to Greg Zarus for providing me the opportunity to work with this group and for your thoughtful contributions and to Yashu Gottigundala for your assistance with review analysis.

I am also indebted to my family, for their everlasting love and support. To my husband, who has been by my side since the beginning and whose encouragement and continual support has made this work possible as we raise two incredible boys. To my children for being flexible as I spend time researching and writing. I hope that I can be a light and role model for you both and I hope you know that my proudest achievement is being your Mother. To my Mom, who has gone above and beyond to guide me and be there as an ear to listen and lend her wisdom. To my sister, my best friend who is always willing to help and keeps me focused on the path ahead and my Dad whose thoughtful questions keep me open to life's possibilities. Thank you to my Mother- and Father-in-law, to my brothers- and sisters-in-law for being the most generous and supportive family I could have married into. I could not have completed this thesis without my family's love and support. To you all, I am eternally grateful.

Table of Contents

1.	Introduction	.1
2.	Methods	.2
	2.1 Literature Review	. 2
	2.2 Human Exposure Calculations	. 5
	2.3 Human and Animal Toxicology Studies	. 8
3.	Results	.9
	3.1 Literature Review	.9
	3.2 Human Exposure Calculations	10
	3.3 Human and Animal Toxicology Studies	13
4.	Discussion	14
5.	Conclusion and Recommendations	19
6.	References	20
7.	Tables and Figures	25
8.	Appendices	31

1. Introduction

Plastic is an essential material and has become globally ubiquitous. Once in the environment, plastics break down into smaller pieces, a process called fragmentation (Barnes et al., 2009). Broken-down plastics are categorized based on their size, with microplastics (MPs) measured at less than 5 millimeters in diameter and nanoplastics measured from 1 to 1000 nanometers in diameter (Barnes et al., 2009; Molenaar et al., 2021). Micro- and nanoplastics (MNPs) have been found in water and soil, and recent research is exposing the vast amount of MPs in ambient and indoor air (Zarus et al., 2021; Torres-Agullo et al., 2021). MP exposure to humans is likely unavoidable with inhalation as one of the main routes of exposure.

After inhalation, MNPs can be transported throughout the body depending on size and may end up in various organs (Wieland et al., 2022). Recent research provides evidence of MPs in human lung tissue from living people (Jenner et al., 2022). Animal models reveal potential health implications from inhaled MNPs such as MNP transport to the brain resulting in neurotoxic effects and increased pulmonary inflammation (Liu et al., 2022; Nemmar et al., 2003). In addition, toxic plastic additives that travel with microplastics may be disrupting human health (Campanale et al., 2020).

Microplastics have been found in ambient outdoor and indoor air; however, even with growing concern regarding MP exposure from air, no methodological standardization for measuring MPs in the air or evaluating human exposure are available. This lack of standardization makes it difficult to compare results and findings across studies. The challenge of standardizing MP research is partly due to the recent emergence of MPs in the environment, development of novel measurement techniques, and the difficulty in obtaining and analyzing samples without contamination. The evidence of human health outcomes from air exposure to MPs is also limited, but it is growing.

To our knowledge, there is no comprehensive exposure assessment of MNPs in indoor and outdoor air. The current paper provides a human exposure assessment of MNPs in the air via a systematic review of published research articles that have provided dose or concentrations of MNPs measured in indoor and/or outdoor air, human exposure to or detection of MNPs in laboratory studies, and animal model experiments of exposure to or detection of MNPs.

2. Methods

2.1 Literature Review

The initial literature search research questions were: 1) what evidence exists for human exposure to MPs in the air; 2) what are the health implications for inhaled MPs; and 3) what are the gaps in research on human exposure and health due to MPs in the air? Most of the recent MNP literature focuses on their presence in water, with little focus on MNPs in air. As such, search terms in this review were initially kept broad to capture as many articles as possible related to MNPs in the air due to the limited number of publications on the specific topic. To capture literature that may be relevant to MNPs in air but may not use the term "microplastic", search terms included common plastic polymers that are often the origin of MNPs in air. These polymers included

polyethylene, polyester, polyamide, polypropylene, and polystyrene. Literature that studied the aforenamed polymers with sizes < 5mm, the common size cutoff for MPs, and that fit the rest of the search criteria were included. Search terms included "Microplastic" or "Micro-plastic" or "Nanoplastic" or "Nano-plastic" OR "Microfiber" or "Micro-fiber" or "Polyethylene" or "Polyester" or "Polyamide" or "Polypropylene" or "Polystyrene" or "(plastic ADJ5 (particulate or particle or PM), and air" or "aerosol" or "atmosphere" or "indoor environment" and "respir*" or "lung" or "inhal*" or "breath" or "asthma" or "bronch*" or "health" or "exposure" or "toxic". There were initially no restrictions on the time of publication or language. The databases Medline (OVID), Embase (OVID), Global Health, CINAHL (EbscoHost), GreenFile (EbscoHost), Environmental Science Collection, and Scopus were searched on January 13, 2022. An additional identical literature search was completed on April 8, 2022 for the time period from January 13, 2022 to April 8, 2022.

All published peer-reviewed journal articles, non-published papers, and documents of the grey literature that focused on MNPs and their major polymer sources in indoor and outdoor air were included as well as those that focus on human exposure and routes of exposure to MNPs in air and those discussing the health effects of MNPs. The initial inclusion criteria for the abstract screen were literature that included information about MNPs in outdoor and/or indoor air (from now on referred to as *air*), human exposure to MNPs in air, pathways of human exposure to MNPs in air, health impacts/effects from exposure to MNPs in air, MNPs in human lung tissue and/or lung cells, respiration and/or inhalation of MNPs from air, fate and transport of MNPs in air, sampling and/or methods of measuring MNPs in air, occupational exposure and/or occupational health impacts of MNPs in air, mammal models for exposure and health outcomes from MNPs from air. The definition in this review of MNPs include polymers of plastic origin that are commonly found in microplastic air samples (I.e., polyethylene, polyester, polyamide, polypropylene, and polystyrene) that are < 5mm in diameter and only papers published in English were finally included. Literature describing PM2.5 and PM10 but with no mention of MNPs and articles discussing drug delivery and clinical usage of nano-and micro technologies in any manner were excluded. Conference presentations and conference abstracts were also excluded.

Additional exclusion criteria were incorporated for full text screening. In addition to the initial criteria, full text review inclusion criteria included only literature that defined specific dose or concentrations and size and length of MNPs in air, specific dose or concentration and size and length of MNPs exposed to human lung cells or animals or humans with measurable health outcomes. Literature with no primary MNPs exposure data and articles measuring only retention, clearance, or fate of MNPs in human or animal respiratory tract or lung were excluded during full text screening.

Specific data were defined for extraction of the final articles for inclusion for the review. Three broad categories emerged from the included papers: Environmental sampling, Human exposure, and Animal models. Ranges and averages for dose/concentration and size of MNPs as well as type and shape of plastic polymer used for exposure or detection was extracted for all papers when possible. Extracted data for literature in the environmental group included sampling methods and location of sampling. Extracted data for human exposure and animal model groups included study design and health effects from MNP exposure or detection.

2.2 Human Exposure Calculations

Multiple equations were used to determine inhalation exposure doses using data generated from the included literature. To determine exposure dose for active sampling that gave units in number of MPs/m³, the Exposure Factor Equation and Inhalation Exposure Equation were derived from ATSDR and were used to determine inhalation exposure dose from active sampling measurements (ATSDR, 2016b):

$$\mathsf{EF} = \frac{(\mathsf{F} \times \mathsf{ED})}{\mathsf{AT}}$$

where EF is the exposure factor, F is the frequency of exposure (days/year), ED is the exposure duration (years), AT is the averaging time (ED x 365 days/year).

$$\mathsf{D}_{\mathsf{inh}} = \frac{(\mathsf{C} \times \mathsf{IR} \times \mathsf{EF})}{\mathsf{BW}}$$

where D_{inh} is the exposure dose (number of MPs/kg/day), C is the contaminant concentration (MP/m³), IR is the intake rate (m³/day), and BW is the body weight (kg).

To determine inhalation exposure dose for passive deposition, a similar inhalation exposure dose equation was used for calculating daily inhalation exposure doses but with an added factor to convert area to volume (Kashfi et al., 2022; Soltani et al., 2021):

$$\mathsf{D}_{\mathsf{inh}} = \frac{(D_r \times \mathrm{IR} \times \mathrm{EF})}{\mathrm{V} \times \mathrm{BW}}$$

Where D_{inh} is inhalation exposure dose (number of MPs/kg/day), D_r is the deposition rate (MPs/m²/day), IR is the intake rate (m³/day), EF is the exposure factor (unitless and calculated in the previous equation), BW is the body weight (kg), and V represents the volume of air (m³) of a 1 m² sampling area. V was determined by subtracting the sampling height from the standard height of indoor places (2.4 m) (Kashfi et al., 2022; Soltani et al., 2021).

Inhalation exposure doses were calculated separately for six age groups: infant (birth to <1 year), preschooler (2 to <6 years), middle childhood (6 to <11 years), adolescent (11 to <16 years), pregnancy (second trimester), and (adult \ge 21 years). Variables for EF as well as IR and BW were derived from CDC for all age groups except pregnant women where EPA exposure standards were used for the second trimester (ATSDR, 2016a; ATSDR, 2020; ATSDR, 2016b; EPA, 2011a; EPA, 2011b). Calculations were done with all groups being exposed to the same levels of MPs per sampling location.

Ten location groups were established based on descriptions from included papers (residential, workplace, school, infrequent, indoor combined, outdoor urban, outdoor remote, roadside, occupational, and rooftop). Residential includes sampling done in any indoor living space from houses or apartments. Workplace sampling locations included any indoor work locations, offices, hallways, reception areas, and conference rooms. School locations include kindergarten through high school settings and university classrooms. Infrequent category includes samples taken inside a nail salon, hospital, and mosque. Indoor combined values represent daily exposure because they are the accumulation of multiple locations in one sampling average and include: residential, workplace, school, healthcare facilities, and public transit halls. Outdoor urban includes samples taken outside in urban areas such as town centers, shopping areas, and urban residential streets. Outdoor remote locations are samples taken outside in remote areas such as forests and farmland. Roadside sampling locations occurred along roads in urban and industrial areas. Occupational samples were taken in a waste transfer station and plastic recycling facility during injection molding steps and grinding of plastic. Rooftop samples were taken on the roof of buildings between 3 and 38 meters above ground level.

Residential EF was assumed to be 1 for all age groups (24hrs/day, 365 days/year) (ATSDR, 2020). Outdoor urban and roadsides EFs were also assumed to be 1 due to potential daily exposure. The average adult lifetime of 78 years was used to calculate adult ED of 57 years for all categories where lifetime exposure was assumed. The only location category where adult ED was less than 57 years was for workplace exposure duration which was calculated based on full retirement of age 67 years which equated to 46 years for adult workplace exposure (U.S. Bureau of Labor Statistics, 2019). Pregnancy ED was assumed for nine months total (0.75 years). For workplace frequency of exposure (F), full time exposure of 50 weeks/year was used (U.S. Bureau of Labor Statistics, 2019). The central tendency estimate (CTE) was used for values for infants at childcare facilities and preschoolers (school location category) which is 50 wks/year. CTE values for middle childhood and adolescent school times are 39 wks/year (ATSDR, 2016b). Frequency of exposure (F) for adolescent age group and younger were given a zero for workplace location. Adults and pregnant women were given a zero for frequency of exposure (F) for school location. Outdoor remote locations were assumed to have two days per month of exposure (F) and infrequent locations and rooftop sampling was assumed to have one day per week exposure (F).

2.3 Human and Animal Toxicology Studies

Human and animal exposure studies were analyzed for dose and concentration of MNPs to use for calculating estimated exposure doses in number of MNPs/kg-BW/day to compare with environmental exposure data. MNP exposure data from literature that provided mass per volume (mg/L or µg/L) units were used to calculate exposure doses in number of particles or fibers per volume (MNPs/m³) using the conversion equations from Leusch and Ziajahromi (2021):

$$x(\text{beads/L}) = \frac{y(\frac{\text{mg}}{\text{L}}) \times 10^{9} (\text{unit conversion factor})}{(\frac{\Pi}{6}) \times \text{density}(\frac{g}{cm^{3}}) \times [\text{diameter}(\mu m)]^{3}}$$
$$x(\text{fibres/L}) = \frac{y(\frac{\text{mg}}{\text{L}}) \times 10^{9} (\text{unit conversion factor})}{\Pi \times [\text{radius}(\mu m)]^{2} \times \text{length}(\mu m) \times \text{density}(\frac{g}{cm^{3}})}$$

The densities used for polystyrene, PET, and polyester were 1.05 g/cm³, 1.397 g/cm³, 1.37 g/cm³, respectively (Leusch & Ziajahromi, 2021; Guo et al., 2020).

The largest sized MNP and the minimum dose of MNPs for exposure in each study were used for calculations to determine the estimated exposure dose in number of MNPs/kg-BW/day for human and animal exposure studies.

3. Results

3.1 Literature Review

A total of 7587 articles were found in the initial search on January 13, 2022. After removing duplicates, 4863 articles were remaining for abstract screening. From the second literature search from January 13, 2022 to April 8, 2022, an additional 268 articles were found with 115 remaining after duplicates were removed totaling 4,978 abstracts screened. After screening at the abstract level, 258 articles were included for full text review. The scope of inclusion criteria for full text review was limited to papers that gave dose or concentration of MNPs in air. After screening full text literature, 63 papers were included for data extraction (Figure 1).

Environmental sampling papers were subdivided into active flow sampling (n=23 papers) and passive deposition (n=14 papers) sample collection methods with 2 papers having both active and passive sampling totaling 35 papers in the environmental sampling group. Environmental sampling papers were analyzed based on country of MP sampling with China publishing the most papers on MP in air captured in our systematic review (n=11 papers), following by the United Kingdom (n=4 papers), the United States (n=3 papers), Iran and Brazil (n=2 papers each), and the remaining countries publishing 1 paper (Figure 2).

Literature in the human exposure category included *in vitro* studies using human lung cells (n=12 papers), *ex vivo* articles measuring MNPs in human lung tissue (n=2 papers) and human exposure to MNPs (n=1 paper) totaling 15 papers in the human

exposure grouping. Literature defined in the animal exposure group was subdivided based on method of exposure and included instillation of MNPs either intratracheally (n=6 papers) or intranasally (n=2 papers), and ambient exposure (n=2 papers), noseonly exposure (n=2 papers), and oral pharyngeal aspiration (n=1 paper) of MNPs to animals totaling 13 papers in the animal exposure group (Figure 3).

3.2 Human Exposure Calculations

Data generated from included papers measuring environmental indoor and outdoor MNPs in air were in multiple units of measurement depending on the methods of sample collection and analysis. Active sampling of MPs using a flow sampler had units of measurement in number or unit of MP per volume of air (MP/m³) and were most often collected as particles, fibers, fragments, or a combination of different shapes of MPs. Passive sampling, often referred to as deposition of MPs, provided units in number of MPs per area (MPs/m²/day).

Locations of MP air sampling were categorized into nine location groups: residential (n=8), workplace (n=7), school (n=2), infrequent (n=3), indoor combined (n=3), outdoor urban (n=8), outdoor remote (n=4), roadsides (n=3), occupational (n=3) and rooftops (n=7) for a total of 48 sample locations. Of these, 13 sampling locations were removed prior to analysis due to incompatible measurement units (total fiber count, no specific MP values given, only ranges of concentrations, historically collected data, and high values skewing the data). For calculations of inhalation exposure dose, 29 sampling locations were used from active sampling which included residential (n=4), workplace

(n=2), infrequent (n=3), indoor combined (n=2), outdoor urban (n=7), outdoor remote (n=3), roadsides (n=1), occupational (n=3), and rooftops (n=4). Of these, 19 sampling values were collected via passive deposition (n=12 indoor & n=7 outdoor samples). Only indoor papers were used for passive deposition inhalation exposure dose calculations due to the conversion of area to volume and estimated indoor space volumes. A total of 10 sampling locations were used in final inhalation exposure dose calculations with 2 samples not reporting sampling height and therefore not used in exposure dose equations. The included samples for passive deposition were from these locations: indoor combined (n=1), residential (n=4), school (n=1), and workplace (n=4).

Infants had the highest inhalation exposure dose values for all locations followed by preschool age children, middle aged children, pregnant women, adolescents, and finally adults. Average inhalation exposure doses for active sampling can be found in Table 1. Roadsides had the highest exposure dose of airborne MPs using active sampling after indoor combined locations (Figure 4). Roadside exposure calculations were taken from one study by averaging sample values taken from roadsides with low, medium, and high traffic; results showed that larger numbers of MPs were found in roadsides with higher traffic volumes (Syafei et al., 2019). Outdoor urban average exposure doses followed the same trend for age groups at exposure levels similar to roadsides. For indoor sampling, residential locations had the highest MP exposure doses ranging from calculations for one sample at 0.21 MPs/kg-BW/day for adults to 43.35 MPs/kg-BW/day from one sample for infants. Workplace MP inhalation exposure doses were calculated from two studies with adult doses ranging between 1.17 to 3.61 MPs/kg-BW/day and

pregnant women ranging between 1.79 to 5.52 MPs/kg-BW/day (Xie et al., 2022; Uddin et al., 2022). Outdoor remote location exposure doses were under 5 MPs/kg-BW/day for all sampling locations in every age group, with the lowest exposure dose being 4.9 x 10^-5 for an adult at one outdoor remote location. Rooftop exposure doses were all under 1 MPs/kg-BW/day with the highest exposure dose at one sampling location estimated for an infant being the only inhalation dose above 1 at 1.02 MPs/kg-BW/day. Indoor combined MP inhalation exposure doses were the highest out of all sampling locations, which is understandable given that indoor combined included environmental MP samples averaged among various day-to-day locations which provide a good representation of daily exposure. Averages in this location group ranged from 151.9 MPs/kg-BW/day for an adult to 549.8 MPs/kg-BW/day for an infant.

Average inhalation doses for passive deposition sampling can be found in Table 2. As stated previously, only indoor sampling locations were used for calculated inhalation exposure doses (Figure 5). While the trend of age group differences between exposure doses may be similar, the inhalation exposure doses for passive deposition sampling are higher than for active sampling (Figure 6). The average Indoor Combined, residential, and workplace inhalation exposure doses for passive deposition from all age groups is 1053, 4555, and 1552 MPs/kg-BW/day, respectively. This is compared with active sampling in which the inhalation exposure doses for indoor combined, residential, and workplace is 315, 8.71, and 3.02 MPs/kg-BW/day, respectively.

Comparing indoor to outdoor MP inhalation exposure doses for active sampling, indoor average exposure doses are higher for all age groups compared with outdoor doses (Figure 7).

3.3 Human and Animal Toxicology Studies

Of the 15 human exposure studies included in data extraction, 24 concentrations of MNPs were identified as exposed to cells or detected in human lung tissue. Of these, 10 concentrations were removed because of incompatible units, detected MPs, or insufficient information for the calculations from mass per volume to number per volume of MNPs. A total of 14 MNP concentrations were calculated and converted to number of MNPs per m³ and subsequently to inhalation exposure dose of number of MPs/kg-BW/day.

The largest sized MNPs and the smallest dose of MNPs from each experiment were used for calculations to try to best mimic environmental sampling results. The average number of MNPs/m³ calculated from the human exposure studies was 2.45×10^{17} MNPs/m³ with ranges between 1.02×10^5 to 2.27×10^{18} and a median value of 5.84×10^{15} MNPs/m³. The adult average exposure dose calculated from the MNPs/m³ values is 6.55×10^{16} MNPs/kg-BW/day with a range from 2.73×10^4 to 6.08×10^{17} MNPs/kg-BW/day and median value of 1.56×10^{15} MNPs/kg-BW/day.

There were 13 papers and 13 different concentrations from the animal model exposure group. After removing doses in incompatible units or with insufficient information for

calculations, 7 papers remained for analysis. Out of the 7 papers, the number of $MNPs/m^3$ was calculated and averaged $1.94 \times 10^{16} MNPs/m^3$ with ranges from 6.8×10^6 to $7.58 \times 10^{16} MNPs/m^3$ and a median value of $9.09 \times 10^{13} MNPs/m^3$. The adult average MNP inhalation exposure dose was calculated from the MNPs/m³ values was an average of $5.18 \times 10^{15} MNPs/kg$ -BW/day ranging from 1.82×10^6 to $2.03 \times 10^{16} MNPs/kg$ -BW/day and median value of $2.43 \times 10^{13} MNPs/m^3$.

4. Discussion

Microplastic and nanoplastic research is still in its infancy so there are no set standards for MP research with most published papers having different sampling methods, quality control, and analyses. We did not exclude based on the afore mentioned differences which may have resulted in the inclusion of papers with differences in the quality of the data. The variables used for exposure calculations are based on US population averages which may not represent the global population. For example, Kashfi et al. estimated expose doses using lower body weight and inhalation rate for all age groups than this paper, most likely due to differences in population averages (2022). These differences may lead to different inhalation exposure dose calculations for papers using data from various countries.

Exposure values for rooftop samples were analyzed with the understanding that most people spend little time in this environment, however, rooftop samples may give us insight into MP atmospheric transport including deposition, contaminant transport over long distances, as well as possible exposure in high-rise apartments or buildings with windows open or on terraces. A recent study found that MP concentrations were positively associated with PM_{2.5} and polycyclic aromatic hydrocarbons (PAHs) on a three-meter-high building rooftop and were significantly higher on dusty days compared to normal days (Akhbarizadeh et al., 2021). In addition, airborne MPs have been found in remote areas such as on mountain tops, wetlands, and in the middle of the North Atlantic Ocean, (Liao et al., 2021; Kernchen et al., 2022; Trainic et al., 2020) suggesting distant MPs atmospheric transport and possible human exposure in areas where the MPs did not originate.

Pregnant women show higher inhalation dose exposure values compared to averages for adults. One possible explanation for the differences in exposure doses is due to higher inhalation rates during pregnancy. Another factor to consider when comparing pregnancy exposure data to adult data is that adult exposure dose is averaged for both males and females combined, with slightly higher variables for combined data than would be obtained for disaggregated data by sex. Even so, pregnant women and developing babies are more susceptible to toxins, especially long-term health complications from exposure *in utero* (Sripada et al., 2022). MPs have been detected in human placental tissue and meconium (Braun et al., 2021), suggesting maternal and fetal exposure to MPs. Animal models show inhaled MNP transport from mother to fetal liver, heart, lung, kidney, and brain as well as reduced fetal weight after maternal pulmonary exposure to nanoparticles (Fournier, 2020). During additional times of rapid development such as infancy and childhood, there may also be a greater risk for health impacts from exogenous toxins (Sripada et al., 2022). Our data suggest that school may

be a source for MP inhalation exposure, with MP exposure doses for infants, young children, and adolescents higher than for adults at the workplace (Figure 5).

The two main methods of sampling collection for MPs in indoor and outdoor air are active and passive deposition. Active sampling uses pumps to sample a known volume of air for a set time period with most studies providing units of measurement in number of MPs per m³ (Zhang et al., 2020). Passive deposition has been a common method of sampling atmospheric MPs and recently progress has been made to standardize collection using metallic or glass dishes with protocols designed by NILU (Norwegian Institute for Air Research) (Zhang et al., 2020). In the current review, papers measuring MPs using active sampling accounted for about 63% of included papers in the environmental sampling group and papers with methods using passive deposition were about 37%. When comparing inhalation exposure doses of MPs between active and passive sampling methods, passive sampling papers had higher levels for all comparable locations than active sampling. The length of sampling time differed between active and passive sampling as well. Most active sampling methods had pumps pulling air for under 24 hours with varying degrees of flow rates and volume of air sampled. Passive sampling methods varied between leaving deposition equipment open for 24 hours (n=2 papers), 1 to 4 weeks (n=8 papers), and 6 months or more (n=2 papers). It is possible that the length of sampling time and volume of air sampled impacted concentration of MPs in air.

Our results agree with previous studies showing that MPs have on average higher concentrations in indoor than outdoor air (Dris et al., 2017; Amato-Lourenço et al., 2022b; Liao et al., 2021; Fang et al., 2022). Indoor dust concentrations and low air circulation could be contributing factors for the disparity between indoor and outdoor MPs. One study identified MP accumulation on air conditioning filters and measured MPs released into indoor air when the AC was on, although it was only a small percentage of the total MP concentration (Chen et al., 2022). Another study found significantly higher airborne MP concentrations when the air conditioning unit was on for all lengths of time studied compared to when it was turned off (Zhang et al., 2020). The same study analyzed MPs in the air on weekdays versus weekends and found that in a university dormitory room, the MPs were threefold higher than on weekdays (Zhang et al., 2020). While our data show roadside exposure as the highest average inhalation exposure dose for all age groups, the outdoor remote and rooftop exposure doses are much lower than all other location groups bringing down outdoor exposure dose averages. In addition, more dense roadside traffic was found to increase the number of airborne MPs (Syafei et al., 2019) as well as urban air MP abundance being about 2x greater than rural areas in one study (Liao et al., 2021). Therefore, while average outdoor inhalation exposure doses are lower than the average exposure doses indoors, it seems to be highly dependent on specific locations and behavior patterns.

The size of MNPs effects health outcomes, with smaller sized particles and fibers depositing deeper in the lung and throughout the body (Wieland et al., 2022). Current sampling and analysis methods can only identify MPs in the micrometer range;

however, as MP size decreases in air, some studies find that concentration increases (Chen et al., 2022; Liao, 2021; Fang, 2022; Uddin et al., 2022). One study identified about three times higher concentrations of particles in the inhalable fraction than respirable fraction (Uddin et al., 2022). It is still unknown if and to what extent we are exposed to nanoplastics. With most toxicological studies using plastic particles in the nanoscale, it is important to determine our exposure to these smaller sized nanoplastics to inform policy and future research.

The doses of MNPs given to live animals or human *in vitro* cells from toxicology studies were converted to estimated inhalation exposure doses to enable a comparison of doses used in toxicology studies to MP doses found in air from this review. Our results suggest that MNP doses given to animals and *in vitro* are higher than MP doses measured in air. The lowest estimated MNP exposure dose calculated for an adult in this paper for *in vitro* human cell studies was 2.73 x 10⁴ MNPs/kg-BW/day and the lowest estimated MNP exposure dose for animal studies was 1.82 x 10⁶ MNPs/kg-BW/day. The highest exposure dose calculated from environmental samples from air for an adult was 3.14×10^3 MNPs/kg-BW/day for a passive sample, which is still lower than the lowest exposure doses used in toxicology studies. Most studies included in this review for toxicology exposure experiments (12 out 14 human in vitro studies and 6 out of 7 animal studies) are exposing cells and animals to nanoparticles. However, only microparticles have been identified in the environment so a direct comparison may not be feasible. In addition, since exposure dose units are in numbers of MNPs per weight, the values may be higher given nanoparticles are 1000x smaller than microparticles

which would give higher exposure doses when calculating number of particles from weight. However, these data could be beneficial for future work if sampling methods are able to measure nanoparticles in the environment.

5. Conclusion and Recommendations

While the question of whether humans are exposed to MPs in the air is mostly undebatable within the current literature, the extent of exposure and the human health implications are not clear. This systematic review searched the literature for publications measuring dose or concentration of MPs in air and MNPs used in human and animal toxicology studies. Using included articles, we calculated the inhalation exposure dose for MPs for varying age groups and different exposure locations. Results indicate that infants have the highest average exposure dose for airborne MPs followed by preschoolers, young children, pregnant women, adolescents, and adults. Indoor exposure to MPs in the air was calculated to be higher than outdoor exposure for all age groups. The exposure dose of MPs for passive deposition sampling could only be calculated for indoor samples due to the conversion from an area to known volume. Comparing indoor sampling locations, active sampling results showed much lower exposure doses compared to passive sampling.

This study did not analyze the various sized particles collected; however, it is important to understand the size ranges of MP exposure to estimate fate and transport within the body and health implications. The concentrations of MPs used for exposure dose calculations in this study are from points-in-time and may not represent daily exposure. As with other inhalation exposure methods, determining personal exposure in real time is challenging but should be a focus for future MP air exposure studies. The extent of toxicological effects of MNPs is still being debated, especially as new research on human and animal health from MNP exposure is published frequently. It is beneficial to see effects of MNPs on health, and it may be valuable at the present time to study longterm and lower dose exposures to represent environmental exposures.

6. References

Akhbarizadeh, R.; Dobaradaran, S.; Amouei Torkmahalleh, M.; Saeedi, R.; Aibaghi, R.; Faraji Ghasemi, F. (2022). Suspended fine particulate matter (PM_{2.5}), microplastics (MPs), and polycyclic aromatic hydrocarbons (PAHs) in air: Their possible relationships and health implications. Environmental Research 192:110339. https://doi-org.proxy.library.emory.edu/10.1016/j.envres.2020.110339

Amato-Lourenço, L.F., Galvão, L., Wiebeck, H., Carvalho-Oliveira, R., Mauad, T. (2022). Atmospheric microplastic fallout in outdoor and indoor environments in São Paulo megacity. Science of the Total Environment. 821: 153450 <u>https://doi-org.proxy.library.emory.edu/10.1016/j.scitotenv.2022.153450</u>

[ATSDR] Agency for Toxic Substances and Disease Registry. (2016a). Exposure Dose Guidance for Body Weight. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, October 26. <u>https://www.atsdr.cdc.gov/pha-guidance/resources/ATSDR-EDG-Body-Weight-508.pdf</u>

[ATSDR] Agency for Toxic Substances and Disease Registry. (2020). Guidance for Inhalation Exposures. Atlanta, Ga: U.S. Department of Health and Human Services, Public Health Service, December 1. <u>https://www.atsdr.cdc.gov/pha-</u> <u>guidance/resources/ATSDR-EDG-Inhalation-508.pdf</u>

[ATSDR] Agency for Toxic Substances and Disease Registry. (2016b). Exposure Dose Guidance for Determining Life Expectancy and Exposure Factor. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, Oct 26. https://www.atsdr.cdc.gov/pha-guidance/resources/ATSDR-EDG-Life-Expectancy-Exposure-Factor-508.pdf Barnes D.K.A., Galgani F., Thompson R.C., & Barlaz M. (2009). Accumulation and Fragmentation of Plastic Debris in Global Environments. Phil. Trans. R. Soc. B, 364, 1985–1998. http://doi.org/10.1098/rstb.2008.0205

Braun T, Ehrlich L, Henrich W, Koeppel S, Lomako I, Schwabl P, Liebmann B. (2021). Detection of Microplastic in Human Placenta and Meconium in a Clinical Setting. Pharmaceutics. Jun 22;13(7):921. doi: 10.3390/pharmaceutics13070921. PMID: 34206212; PMCID: PMC8308544.

Campanale, C., Massarelli, C., Savino, I., Locaputo, V., & Uricchio, V.F. (2020). A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health. Int. J. Environ. Res. Public Health, 17(4), 1212. https://doi.org/10.3390/ijerph17041212

Chen, E. Y.; Lin, K. T.; Jung, C. C.; Chang, C. L.; Chen, C. Y. Characteristics and influencing factors of airborne microplastics in nail salons. (2022). Science of the Total Environment. 806: 151472. https://doiorg.proxy.library.emory.edu/10.1016/j.scitotenv.2021.151472

Dris, R.; Gasperi, J.; Mirande, C.; Mandin, C.; Guerrouache, M.; Langlois, V.; Tassin, B. (2017). A first overview of textile fibers, including microplastics, in indoor and outdoor environments. Environmental Pollution. 221: Pages 453-458. <u>https://doi-org.proxy.library.emory.edu/10.1016/j.envpol.2016.12.013</u>

[EPA] Environmental Protection Agency. (2011a). Exposure Factors Handbook. Chapter 8—Body Weight Studies. October 3. <u>https://www.epa.gov/sites/default/files/2015-09/documents/efh-chapter08.pdf</u>

[EPA] Environmental Protection Agency. (2011b). Exposure Factors Handbook. Chapter 6—Inhalation Rates. October 3. <u>https://www.epa.gov/sites/default/files/2015-</u>09/documents/efh-chapter06.pdf

Fang, M.; Liao, Z.; Ji, X.; Zhu, X.; Wang, Z.; Lu, C.; Shi, C.; Chen, Z.; Ge, L.; Zhang, M.; Dahlgren, R. A.; Shang, X. (2022). Microplastic ingestion from atmospheric deposition during dining/drinking activities. 432: 128674. <u>https://doi-org.proxy.library.emory.edu/10.1016/j.jhazmat.2022.128674</u>

Fournier, S. B.; D'Errico, J. N.; Adler, D. S.; Kollontzi, S.; Goedken, M. J.; Fabris, L.; Yurkow, E. J.; Stapleton, P. A. (2020). Nanopolystyrene translocation and fetal deposition after acute lung exposure during late-stage pregnancy. Part Fibre Toxicol 17, 55. https://doi.org/10.1186/s12989-020-00385-9

Guo, S.-L., Chen, B.-L., Durrani, S.A. (2020) Chapter 3 – Solid-state nuclear track detectors. Handbook of Radioactivity Analysis (fourth Edition). Volume 1: Radiation Physics and Detectors. Pgs 307-407. https://www.sciencedirect.com/topics/chemistry/polyethylene-terephthalate

Jenner, L. C.; Rotchell, J. M.; Bennett, R. T.; Cowen, M.; Tentzeris, V.; Sadofsky, L. R. (2022) Detection of microplastics in human lung tissue using muFTIR spectroscopy. Science of the Total Environment 831:154907. <u>https://doi-org.proxy.library.emory.edu/10.1016/j.scitotenv.2022.154907</u>

Kashfi, F.S., Ramavandi, B., Arfaeinia, H., Mohammadi, A., Saeedi, R., De-la-Torre, G.E., Dobaradaran, S. (2022). Occurrence and exposure assessment of microplastics in indoor dusts of buildings with different applications in Bushehr and Shiraz cities, Iran. Science of the Total Environment. 829: 154651. <u>https://doi-org.proxy.library.emory.edu/10.1016/j.scitotenv.2022.154651</u>

Kernchen, S., Löder, M.G.J., Fischer, F., Fischer, D., Moses, S.R., Christoph Georgi, C., Nölscher, A.C., Held, A., Laforsch, C. Airborne microplastic concentrations and deposition across the Weser River catchment. Science of the Total Environmental. 818: 151812. <u>https://doi-org.proxy.library.emory.edu/10.1016/j.scitotenv.2021.151812</u>

Liu, X.; Zhao, Y.; Dou, J.; Hou, Q.; Cheng, J.; Jiang, X. (2022). Bioeffects of Inhaled Nanoplastics on Neurons and Alteration of Animal Behaviors through Deposition in the Brain. Nano Letter. Vol.22 (3), p.1091-1099. <u>https://doi-org.proxy.library.emory.edu/10.1021/acs.nanolett.1c04184</u>

Leusch, F.D.L. & Ziajahromi, S., (2021) Converting mg/L to Particles/L: Reconciling the Occurrence and Toxicity Literature on Microplastics. <u>https://doi-org.proxy.library.emory.edu/10.1021/acs.est.1c04093</u>

Liao, Z.; Ji, X.; Ma, Y.; Lv, B.; Huang, W.; Zhu, X.; Fang, M.; Wang, Q.; Wang, X.; Dahlgren, R.; Shang, X. (2021). Airborne microplastics in indoor and outdoor environments of a coastal city in Eastern China. Journal of Hazardous Materials. 17: 126007. https://doi-org.proxy.library.emory.edu/10.1016/j.jhazmat.2021.126007

Nemmar, A.; Hoylaerts, M. F.; Hoet, P. H.; Vermylen, J.; Nemery, B. (2003). Size effect of intratracheally instilled particles on pulmonary inflammation and vascular thrombosis.

Toxicology and Applied Pharmacology. 186: 38-45. <u>https://doi-org.proxy.library.emory.edu/10.1016/S0041-008X(02)00024-8</u>

Molenaar, R., Chatterjee, S., Kamphuis, B., Segers-Nolten, I.M.J., Mireille, M.A.E., & Claessens, E., & Blum, C., (2021). Nanoplastic sizes and numbers: quantification by single particle tracking. Environ. Sci.: Nano, 8,723-730. https://doi.org/10.1039/D0EN00951B

Syafei, A.D., Nurasrin, N.R., Assomadi, A.F., Rachmat, B. (2019). Microplastic Pollution in the Ambient Air of Surabaya, Indonesia. Current World Environment. 14(2):290-298. http://dx.doi.org/10.12944/CWE.14.2.13

Soltani, N.S., Taylor, M.P., Wilson, S.P. (2021). Quantification and exposure assessment of microplastics in Australian indoor house dust. Environ. Pollut. 283, 117064. <u>https://doi-org.proxy.library.emory.edu/10.1016/j.envpol.2021.117064</u>

Sripada, K., Wierzbicka, A., Abass, K., Grimalt, J. O., Erbe, A., Röllin, H.,B., Wagner, M. (2022). A Children's health perspective on nano- and microplastics.*Environmental Health Perspectives (Online), 130*(1) doi:https://doi.org/10.1289/EHP9086

Torres-Agullo, A., Karanasiou, A., Moreno, T., & Lacorte, S. (2021). Overview on the occurrence of microplastics in air and implications from the use of face masks during the COVID-19 pandemic. Sci Total Environ, 800(149555). 10.1016/j.scitotenv.2021.149555

Trainic, M., Flores, J.M., Pinkas, I. et al. (2020). Airborne microplastic particles detected in the remote marine atmosphere. Commun Earth Environ 1, 64. <u>https://doi.org/10.1038/s43247-020-00061-y</u>

Uddin, S.; Fowler, S. W.; Habibi, N.; Sajid, S.; Dupont, S.; Behbehani, M. (2022). A Preliminary Assessment of Size-Fractionated Microplastics in Indoor Aerosol-Kuwait's Baseline. Toxins. 10, 71. https://doi.org/10.3390/toxics10020071

U.S. Bureau of Labor Statistics. (June 2019). U.S. Department of Labor, American Time Use Survey, weekday work hours. https://www.bls.gov/news.release/archives/atus_06192019.htm

Wieland, S., Balmes, A., Bender, J., Kitzinger, J., Meyer, F., Ramsperger, A.F., Roeder, F., Tengelmann, C., Wimmer, B.H., Laforsch, C., Kress, H. (2022). From properties to

toxicity: Comparing microplastics to other airborne microparticles. Journal of Hazardous Materials. 428,128151. https://doi.org/10.1016/j.jhazmat.2021.128151.

Xie, Y.; Li, Y.; Feng, Y.; Cheng, W.; Wang, Y. (2022). Inhalable microplastics prevails in air: Exploring the size detection limit. Environment International. (162):107151 <u>https://doi-org.proxy.library.emory.edu/10.1016/j.envint.2022.107151</u>

Zarus, G.M., Muianga, C., Hunter, C.M., & Pappas, R.S. (2021). A review of data for quantifying human exposures to micro and nanoplastics and potential health risks. Science of the Total Environment 756 (144010). https://doi.org/10.1016/j.scitotenv.2020.144010

Zhang, Q., Zhao, Y., Du, F., Cai, H., Wang, G., Shi, H., (2020). Microplastic fallout in different indoor environments. Environment Science Technology. 4, 11, 6530–6539. https://doi-org.proxy.library.emory.edu/10.1021/acs.est.0c00087

7. Tables and Figures



Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) diagram of review process. (n) represents the number of studies.



Figure 2: World Map of countries included in this systematic review with published papers measuring MPs in Air.





Table 1: Average MP exposure doses from active sampling for different locations by age

groups (MPs/kg-BW/day)

Average MP Exposure Doses from Active Sampling (MPs/kg-BW/day)	Adults	Pregnant Women	Adolescents	Young Children	Preschoolers	Infants
Indoor Combined	152	232	213	300	447	550
Residential	4.19	6.41	5.86	8.27	12.3	15.2
Workplace	2.39	3.66	0	0	0	0
Rooftop	0.094	0.143	0.131	0.184	0.275	0.338
Outdoor Urban	19.0	29.1	26.6	37.6	56.1	68.9
Outdoor Remote	0.742	1.14	1.04	1.46	2.19	2.69
Roadsides	20.9	32.0	29.3	41.3	61.6	75.7
Infrequent	0.585	0.896	0.819	1.15	1.72	2.12



Figure 4: Active sampling average inhalation exposure doses for age categories and locations of sampling for indoor and outdoor.

Table 2: Average MP exposure doses from passive sampling for different locations (indoors) by age groups (MPs/kg-BW/day)

Average MP Exposure Doses from Indoors from Passive Sampling (MPs/kg- BW/day)	Adults	Pregnant Women	Adolescents	Young Children	Preschoolers	Infants
Indoor Combined	507	775	709	1000	1493	1835
Residential	2192	3354	3068	4326	6456	7936
School	0	0	1477	2083	3986	4900
Workplace	1227	1877	0	0	0	0



Figure 5: Passive deposition sampling average inhalation exposure doses for age categories and locations of sampling for indoor environments.



Figure 6: Comparison of average inhalation exposure doses between active sampling and passive deposition of MPs at three indoor locations.



Figure 7: Comparison of Indoor and Outdoor MP inhalation exposure doses from active sampling among different age groups.

8. Appendices