Why is the potential for ultrafine particles (PM0.1) to damage human health greater than fine particles (PM2.5)?

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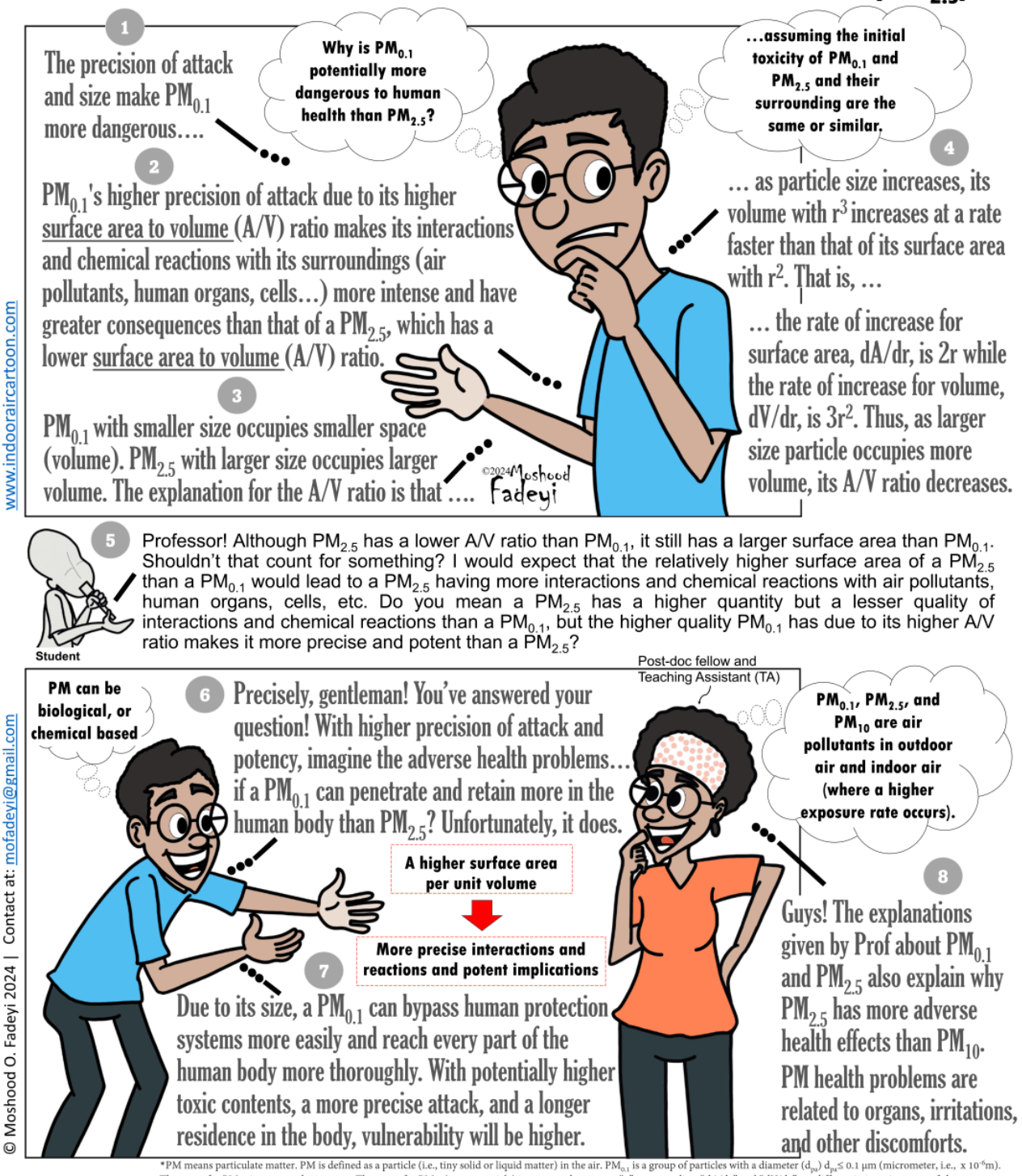
Artistic-Educational Research

WHY IS THE POTENTIAL FOR ULTRAFINE PARTICLES ($PM_{0.1}$) TO DAMAGE HUMAN HEALTH GREATER THAN FINE PARTICLES ($PM_{2.5}$)?



*PM means particulate matter. PM is defined as a particle (i.e., tiny solid or liquid matter) in the air. $PM_{0.1}$ is a group of particles with a diameter (d_{pa}) $d_{pa} \leq 0.1$ µm (micrometer, i.e., x 10^{-6}m). The range for $PM_{2.5}$ is 0.1 µm $< d_{pa} \leq$ 2.5 µm. The range for PM_{10} (coarse particle) is 2.5 µm $< d_{pa} \leq$ 10 µm. "r" means radius. "dA/dr" and "dV/dr" are differentiations, i.e., rates of change.

REFERENCES

Afshari, A., Matson, U., and Ekberg, L. E. (2005). Indoor Air, 15(2).
Madureira, J., Slezakova, K., Costa, C., Pereira, M. C., and Teixeira, J. P. (2020). Environmental Pollution, 264, 114746.
Schraufnagel, D. E. (2020). Experimental & Molecular Medicine, 52(3), 311-317.

Fictional Case Story (Audio – available online) – Part 1

Fictional Case Story (Audio – available online) – Part 2

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Autism spectrum disorder is a complex neurodevelopmental condition characterised by challenges in social interaction, communication, and repetitive behaviours. While genetics contributes significantly to autism spectrum disorder susceptibility, environmental factors, including exposure to pollutants, are increasingly recognised as potential contributors to the disorder's development. During critical periods of prenatal and early postnatal development, the brain is highly vulnerable to environmental insults. Exposure to air pollutants, tiny enough to bypass human protection systems, can cause serious harm to human brains and several organs in the human body. An example of such air pollutants is ultrafine particles on a nanometre scale. Ultrafine particles during these sensitive windows may disrupt normal neurodevelopmental processes even more than fine particles, which are rightfully receiving attention, leading to alterations in brain structure and function that manifest as autism spectrum disorder symptoms. The concern and lack of evidence on the impact of ultrafine particles set up the academic journey of a young man living with autism to provide the needed evidence and develop and recommend solutions for reducing exposure to ultrafine particles. At that time, there was a high prevalence of autism spectrum disorder and indoor and outdoor environmental pollution globally. The journey of the man, from his youth to later years, filled with lessons on the importance of turning one's weakness into strength and the goodness of the human heart, is the focus of this short fiction story.

1…….

Mr. and Mrs. Afonso had been married for 6 years without a child. They tried their best to have one, but to no avail. They moved from doctor to doctor and consulted several religious priests with no success. Mrs. Afonso could not conceive. However, doctors certified Mr. and Mrs. Afonso as healthy and capable of having their own child.

Eight years into the marriage, Mrs. Afonso finally became pregnant. The couple were overjoyed and looked forward to becoming parents. Unfortunately, Mrs. Afonso lost the pregnancy two months in. They were both devastated! As they usually did, they were there for each other and motivated themselves. Mrs. Afonso did not become pregnant again for several years.

Seven years later, after losing the pregnancy, Mrs. Afonso became pregnant at the age of 39. Both were very happy but cautioned themselves not to be overly joyous. The couple visited Mrs. Afonso's gynaecologist regularly to monitor and ensure the healthiness of the pregnancy.

Nine months and two weeks into the pregnancy, Mrs. Afonso's labour pains began around 2 am. While enduring the pain, she tapped her husband with all her power to wake him up. "Finally!" Mr. Afonso said while packing the baby's clothes. He gently walked his wife to their car. He drove his wife straight to the emergency.

By the time they got to the hospital, the baby was on the edge of being born. Mrs. Afonso, who was in serious pain at this time, was rushed straight to the delivery room. At the adamant request of Mrs. Afonso, Mr. Afonso was allowed to enter the delivery room.

Mr. Afonso held his wife's hand tightly, his eyes filled with anticipation and excitement as they prepared to welcome their first child into the world. But as the hours stretched into eternity, the joyous occasion turned tragic.

Complications arose during childbirth. At this point, the doctors had to tell Mr. Afonso to step out. Despite the frantic efforts of the medical team, Mrs. Afonso's life slipped away, leaving behind a shattered husband and a newborn son who would never know the loving embrace of his mother.

In the extremely quiet and tranquil delivery room, Mr. Afonso cradled his son in his arms, his heart heavy with grief and disbelief. He had dreamed of starting a family with Mrs. Afonso, of watching their child grow and flourish, but now those dreams lay shattered at his feet. He named his son Alonso.

As the days turned into weeks, Mr. Afonso struggled to come to terms with the devastating loss of his beloved wife. Every corner of their home echoed with memories of Mrs. Afonso: her laughter, warmth, and love. And yet, amidst the darkness of his grief, there was a flicker of hope – a tiny, fragile life that depended on him for survival.

But fate was not finished with its cruel hand. Just four months after Alonso's birth, tragedy struck once again. Mr. Alonso, a devoted father and dedicated employee, never made it to work that fateful morning. A reckless driver, blinded by the glare of the rising sun, veered into his lane, colliding head-on with Mr. Afonso's car and robbing baby Alonso of his last remaining parent.

With no family to turn to, Alonso was placed in the care of the state, a helpless infant adrift in a sea of uncertainty. The orphanage, with its sterile walls and impersonal caregivers, became his new reality, a world devoid of love, warmth, and affection.

As Alonso approached his fourth birthday, the staff at the orphanage began to notice certain behaviours and traits that set him apart from the other children. Unlike his peers, Alonso struggled to engage in social interactions, often preferring solitary activities and showing little interest in playing with others. He also exhibited repetitive behaviours, such as rocking back and forth or lining up his toys in precise patterns, which seemed to soothe him in times of stress or uncertainty.

Concerned about Alonso's development, the orphanage caregivers consulted with a child psychologist who specialised in developmental disorders. Through a series of observations, assessments, and evaluations, the psychologist identified a pattern of behaviours consistent with an autism spectrum disorder.

As Alonso navigated his way through the corridors of the bustling school, he could not shake the feeling of dread that accompanied him every day. His classmates, oblivious to his struggles, made no effort to conceal their disdain for his differences. They mocked his awkward way of walking and peculiar mannerisms, their laughter ringing in his ears like a constant taunt.

During lunch breaks, Alonso would find himself sitting alone in a corner of the cafeteria, his untouched meal a stark reminder of his isolation. The other children would cast sneaky glances in his direction, whispering among themselves as if discussing some forbidden secret. Occasionally, their curiosity would give way to open hostility as they hurled hurtful insults and cruel taunts in his direction.

Even in the classroom, Alonso was not spared from the relentless onslaught of ridicule and scorn. His summed-up courageous attempts to participate in group activities were met with mockery; his contributions were dismissed with disdain. The teachers, though well-meaning, seemed oblivious to the suffering unfolding before their eyes, their attention consumed by the demands of the curriculum.

Alonso's sense of despair only deepened as the days turned into weeks and the weeks into months. Each morning brought with it a fresh wave of anxiety, and each afternoon, a crushing sense of defeat. He longed for acceptance, friendship, and the chance to be seen as more than just the sum of his differences.

But amidst the quiet and calm atmosphere of the school corridors, Alonso's silent cries for help went unheard, drowned out by the clamour of a world that refused to understand. Unfortunately for Alonso, there were no parents to turn to for solace. As a child in primary school, he felt alone in this world.

Alonso's struggles with autism became more pronounced as he transitioned into secondary school. The demands of academic life and the social pressures of adolescence proved overwhelming for him. He found it difficult to keep pace with his classmates.

As Alonso fell behind in his studies, his insecurity and frustration began to surface in unruly behaviour. He would often act out in class, disrupting lessons and challenging his teachers' authority. His outbursts were met with reprimands and punishments, further exacerbating his feelings of alienation and isolation.

Despite the efforts of his teachers and counsellors to support him, Alonso's behaviour continued to deteriorate as he progressed through secondary school. He struggled to form meaningful connections with his peers, feeling like an outsider in a world that seemed to move too fast for him to keep up.

By the time Alonso reached his final year of secondary school, his behaviour had reached a breaking point. Five months before his Secondary School Leaving Examination (SSLE), he was suspended from school for two months due to a particularly grievous act that contravened the school rules and regulations. He was found smoking cigarettes in the school and selling them to classmates. Alonso was happy to receive the suspension as he did not want to be in school either and did not care about the forthcoming SSLE.

2…….

During his suspension from school, Alonso found himself seeking solace from the turmoil of his thoughts. It was at that time he encountered Mr. Ramirez, a retired teacher known for his kindness and generosity towards the community. Mr. Ramirez, a 75-year-old, decided to volunteer at the orphanage home where Alonso was residing.

Mr. Ramirez decided to volunteer at the orphanage home when his wife of 38 years died. He did this partly to keep his mind sharp and not feel bored, which staying home alone could cause. Mr. Ramirez's two daughters were grown up and married with children.

Mr. Ramirez was considered a valuable asset by the administrator of the orphanage home. Mr. Ramirez spent decades in the education industry, dedicated to helping students reach their full potential. Despite being retired, his passion for teaching and mentoring had not waned.

One day, Alonso sat closer to a place where Mr. Ramirez was talking to three teenagers. He was drawn to how Mr. Ramirez talked to the teenagers calmly and empathetically. Alonso initially hesitated to approach Mr. Ramirez, but something about the older man's warm smile and gentle demeanor drew him in. Over time, Alonso began to open up to Mr. Ramirez, sharing his struggles with autism and his frustrations with school.

Moved by Alonso's story, Mr. Ramirez offered to help him with his studies, knowing firsthand the transformative power of education and the struggle one of his children also went through. In addition to his bachelor's and master's degrees in STEM Education and decades of teaching in secondary school and pre-university level schools (A-level), Mr. Ramirez also had a post-graduate diploma in special needs education.

With patience, empathy, and a deep understanding of diverse learning styles, Mr. Ramirez tailored his teaching approach to meet Alonso's specific needs. He broke down complex concepts into manageable chunks and provided hands-on guidance and support.

With his experience and expertise, Mr. Ramirez was able to identify and develop certain unique skills and characteristics in Alonso that even Alonso himself did not know he possessed. After several interactions, Mr. Ramirez identified Alonso's attention to detail and focus on what he is interested in, as well as his strong visual thinking, logical thinking, pattern recognition, and demonstration of high memorisation skills for what interests him.

Alonso also demonstrated persistence, problem-solving abilities, creativity, and innovative abilities in areas of interest to him. To develop these undiscovered talents in Alonso, Mr. Ramirez first ensured that Alonso understood the reasons for taking his studies seriously and being interested.

As they spent hours together, Mr. Ramirez tutored Alonso in subjects ranging from mathematics and physics to chemistry and English. Alonso's confidence and interest in academic studies grew with each session, fuelled by Mr. Ramirez's encouragement and belief in his abilities.

The tutoring began during Alonso's suspension period and continued until the Secondary School Leaving Examination (SSLE) period. After several interactions with Mr. Ramirez, Alonso found a new sense of purpose in life, where he had always felt alone with no real family.

When Alonso returned to school after his suspension, he was a changed young man. Armed with the knowledge and skills he gained with the support of Mr. Ramirez, he tackled his studies with renewed vigour and determination, no longer hindered by the limitations of his autism.

Everyone who knew Alonso before the suspension was very surprised to see a "new" Alonso. Alonso's changed attitude towards his studies and coping skills with the challenges posed by his autism also had positive impacts on other subjects he was taking, but Mr. Ramirez did not teach him.

And when the day of the Secondary School Leaving Examination arrived, Alonso was ready. With Mr. Ramirez's guidance echoing in his mind, he approached each question with confidence and poise, knowing that he had the support of a mentor who believed in him every step of the way.

When the results were announced, Alonso's hard work and dedication had paid off—he had not only passed the examination but had excelled beyond his wildest dreams. He scored Bs in all nine subjects he took in the SSLE. Alonso's teachers and principal were very surprised about his result but very happy for him.

As he stood on the threshold of a new chapter in his life, Alonso knew that he owed his success to Mr. Ramirez – the mentor who had seen his potential when no one else did and who had ignited a passion for learning that would stay with him forever.

Alonso subsequently went on to do his A-level studies and performed well enough to gain admission to the university to pursue a bachelor's degree in sustainable building engineering (mechanical option) at the National University of Banada. Alonso's interest in sustainable building engineering was first ignited by his experience at the orphanage home.

Alonso witnessed firsthand the struggles of living in a living space with outdated infrastructure and inefficient systems. He dreamt of a day when he could use his knowledge to design buildings that provided shelter and improved the health and comfort of occupants in the environment. His interest in sustainability was deepened during his A-level studies.

Throughout his undergraduate studies at the National University of Banada, Alonso faced unique challenges due to his autism. Social interactions and sensory sensitivities often posed hurdles along his academic journey. However, Alonso's autism also gave him a remarkable advantage in his sustainable building engineering programme.

His autism fuelled an unparalleled focus and attention to detail, qualities that proved invaluable in the meticulous work of sustainable building engineering. Alonso's ability to hyperfocus allowed him to dive deep into complex subjects, dissecting them with precision and thoroughness that set him apart from his peers. His interest in the programme and his training from Mr. Ramirez enabled him to take advantage of the benefits his autism provided.

While navigating the complexity of group projects and collaborative assignments presented challenges, Alonso's determination and resilience propelled him forward. He found solace in the structured environment of his studies, where equations and blueprints provided a sense of order and clarity amidst the chaos of the world around him.

During his third year, Alonso's interest in indoor air quality blossomed. In an environmental engineering course, he was introduced to the critical role that indoor air quality plays in the health and well-being of building occupants. As he delved deeper into the subject, Alonso's keen attention to detail allowed him to uncover insights that eluded others, propelling him to the forefront of his class.

Driven by a passion for making a difference, Alonso immersed himself in research projects as a research assistant for professors in his department, leveraging his unique perspective to uncover innovative solutions to complex problems. His autism, far from being a hindrance, became a source of strength, allowing him to approach challenges with clarity of thought and depth of analysis that left his professors in awe.

As Alonso approached graduation, his journey was not just one of academic achievement but of personal triumph. Despite the obstacles he faced, he persevered, emerging stronger and more determined than ever before. When he received his degree, Alonso stood tall, a testament to the power of passion, perseverance, and unwavering belief in oneself.

With distinction, Alonso graduated with first-class honours, and his accomplishments are a testament to his extraordinary talent and unwavering dedication inspired by Mr. Ramirez. Alonso was particularly happy that Mr. Ramirez was able to attend his graduation. He felt indebted to Mr. Ramirez because of the transformation he had made in his life.

Mr. Ramirez died a few months after Alonso's Bachelor's degree graduation. Alonso held Mr. Ramirez in high regard throughout his life. Mr. Ramirez was the father he never had. He was also close to Mr. Ramirez's children.

After graduating with first-class honours, Alonso received a prestigious PhD scholarship to pursue advanced studies at the Makelele Institute of Technology (MIT) in the United States of Arabambi. The scholarship was a testament to Alonso's exceptional academic achievements despite his challenges.

At MIT, Alonso's passion for improving indoor air quality and health took center stage as he delved into his PhD studies. Guided by his experiences and driven by a desire to make a meaningful impact, Alonso decided to focus his research on the impact of ultrafine and fine particles on the risk of autism spectrum disorder in foetuses.

Alonso's decision to pursue this topic was first ignited by a documentary he watched during his undergraduate studies. The title of the documentary was "Prevalence of neurodevelopmental disorders in a polluted and unsustainable world." Alonso could relate to the documentary because he has autism.

As Alonso delved deeper into the literature, he noticed a gap in research regarding the specific impact of ultrafine particles on human neurodevelopmental disorders, particularly during critical stages of foetal development. He observed that many of the research studies on particulate matter focused on several organs in the human body, with little research on the human brain.

While few studies were conducted on the impact of fine particles ($PM_{2.5}$) on human neurodevelopmental disorders, after months of intense search, he could not find any studies addressing the impact of ultrafine particles ($PM_{0.1}$) on human neurodevelopmental disorders. Even the research efforts on the impact of fine particles on human neurodevelopmental disorders were at an early stage.

Alonso's curiosity led him to explore the lesser-studied area of ultrafine particles (PM0.1), which he learnt during his undergraduate studies to have unique properties that may pose greater risks to human health.

Alonso learnt during his undergraduate studies that PM stands for particulate matter. Particulate matter is defined as a particle (i.e., tiny solid or liquid matter) in the air. $PM_{0.1}$ is a group of particles with a diameter (d_{pa}) of ≤ 0.1 μm (micrometre, i.e., x 10^{-6}m). The range for $PM_{2.5}$ is 0.1 μm < d_{pa} ≤ 2.5 μm.

He also learned about another category called PM_{10}, which is another major indoor air quality concern because of its adverse impact on human health and comfort. The range for PM_{10} (coarse particles) is 2.5 μm < d_{pa} ≤ 10 μm. Particulate matters are generated from chemical, biological, and physical processes.

This gap intrigued Alonso, sparking his interest in investigating whether exposure to ultrafine particles could be a major contributing factor to the rising prevalence of neurodevelopmental disorders, which include autism spectrum disorder.

At that time, when Alonso was contemplating a research area for his PhD studies, there had been news in the media reporting the increasing cases of autism spectrum disorder globally. Additionally, reports in the media on the increase in outdoor air and indoor air pollution and their sources due to unsustainable human practices were also gaining traction.

Alonso's personal experiences as an individual with autism fuelled his desire to better understand the potential impact of indoor air pollution on neurodevelopmental outcomes. Alonso was concerned because of the struggle he went through as a person with autism and how people treated him unfairly because of it.

Alonso's PhD supervisor was Professor Esther Jacob, a world-renowned Professor of Environmental Health Sciences at MIT. She specialised in indoor air quality, exposure assessment, toxicology, epidemiology, and environmental engineering, conducting research to understand the mechanisms underlying the health effects of indoor air pollutants on human health. Professor Jacob provided valuable guidance to Alonso.

The aim of Alonso's PhD research study was to bridge the gap in understanding the potential causal relationship between particulate matter exposure, including ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) and autism spectrum disorder.

The practical implication of his research is the potential effects ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) could have on humans. However, due to the challenges of using humans for this study, the duration required to complete PhD studies, and to have control over parameters involved in the research, mice were used instead of humans. Alonso asked four research questions in an attempt to achieve the aim of his PhD studies.

The overarching research questions were: (i) How does prenatal exposure to ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) correlate with the risk of autism spectrum disorder-related development in foetuses? (ii) How does exposure to ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) during the mother's pregnancy affect the risk of autism spectrum disorder-related development in young offspring? (iii) What is the relationship between early-life exposure to ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) and the risk of autism spectrum-related disorder development in young offspring? (iv) How do exposure to different concentrations of ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) correlate with the risk of autism spectrum-related disorder development in foetuses?

The research questions informed the research objectives for the PhD studies. The objectives were: (i) To examine the impact of prenatal exposure to ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) on the risk of autism spectrum disorder-related development in foetuses. (ii) To examine the impact of exposure to ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) during the mother's pregnancy on the risk of autism spectrum disorder-related development in young offspring. (iii) To examine the impact of early-life exposure to ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) on the risk of autism spectrum disorder-related development in young offspring, and (iv) To examine the impact of different concentrations of ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) exposures on the risk of autism spectrum disorder-related development in foetuses.

Summaries of Alonso's PhD research methods and results are provided below.

3.…….

Research Methods: Pregnant mice were obtained from a controlled breeding colony to ensure genetic homogeneity and minimise variability in maternal care. Random assignment of pregnant mice to experimental groups was conducted to mitigate potential confounding factors. Twelve pregnant mice were randomly assigned to each of the following experimental groups: (i) Control group, (ii) Fine particle ($PM_{2.5}$) exposure group, and (iii) Ultrafine particle ($PM_{0.1}$) exposure group. There are three experimental chambers, one for each group housing 12 pregnant mice assigned to the group.

In the control group, pregnant mice were housed in experimental chambers devoid of any exposure to particulate matter. This chamber maintained similar environmental conditions to those of the exposure groups but with no introduction of any particulate matter, serving as a baseline comparison for assessing the effects of particulate matter exposure.

In the fine particle ($PM_{2.5}$) exposure group, pregnant mice were exposed to controlled levels of fine particles generated from controlled cigarette combustion. Cigarette smoke was injected into the chamber using a cigarette combustion machine at a rate typically considered not dangerous to the health of the pregnant mice and their foetuses. The exposure protocol involved exposing pregnant mice to a constant steady-state concentration of fine particles throughout pregnancy (19-21 days).

In the ultrafine particle ($PM_{0.1}$) exposure group, pregnant mice were exposed to controlled levels of ultrafine particles at the same steady-state concentration as fine particles. The exposure duration and frequency for the ultrafine particle exposure group mirrored that of the fine particle dose group.

Tabletop transparent acrylic boxes were experimental chambers to house pregnant mice during particulate matter exposure or exposure to no particulate matter. These chambers were designed to accommodate 12 pregnant mice comfortably while allowing for visual monitoring of their behaviour and well-being. The use of transparent materials enabled observation of the mice without disturbing their natural behaviour.

An automated tracking and video recording system was integrated into each of the environmental chambers to document pregnant mice's behaviour and well-being. Measures were also taken to monitor any adverse effects on pregnancy outcomes, such as litter size (i.e., number of offspring reproduced) or neonatal viability (i.e., survival of newborn), which were recorded and analysed.

The experimental chambers were equipped with a controlled cigarette combustion machine designed to generate particulate matter into the chamber environment. This system ensured precise control over the needed constant injection rate and particulate matter delivery to pregnant mice in experimental groups where pregnant mice were exposed to particulate matter.

The generated cigarette smoke contained both fine and ultrafine particles. Thus, a particle size fractionation system was utilised to separate ultrafine particles ($PM_{0.1}$) from fine particles ($PM_{2.5}$) based on size. The smoke from the cigarette combustion was not injected directly into the experimental chambers.

The smoke was injected into the particle size fractionation system integrated into the transparent acrylic box used as the environmental chamber to separate particulate matter depending on the particulate matter exposure group, i.e., fine or ultrafine exposure group.

For the fine particle exposure group, ultrafine particles and any other particulate matter sizes were removed from the smoke to ensure only fine particles were injected into the chamber. For the ultrafine particle exposure group, fine particles and any other particulate matter sizes were removed from the smoke to ensure only ultrafine particles were injected into the chamber.

Controlling the injected particulate matter ensured that each group was exposed to particles of a specific size range, allowing for the isolation of the effects of ultrafine particles versus fine particles on foetuses' autism spectrum disorder.

Throughout the exposure period, particulate matter concentrations within the experimental chambers were continuously monitored to ensure consistency and accuracy of exposure conditions. Environmental parameters such as temperature, humidity, and airflow were monitored to maintain stable experimental conditions.

Airflow within the chambers was regulated to ensure a uniform distribution of particulate matter and to prevent the buildup of stagnant air pockets. The chamber operated under air recirculation mode. The air that leaves the experimental chamber was transported to another particle size fractionation system to remove any particulate matter sizes not meant to be recirculated into the environmental chamber.

It is important to put the air leaving the room through the fractionation system before it is recirculated into the chamber because phenomena such as coagulation, fragmentation, nucleation, condensation, evaporation, agglomeration, etc., may change particle sizes.

An innovative prenatal imaging system called the NeuroMouse Scan system, specifically designed for research laboratories conducting studies on foetal development in pregnant mice, was adopted to monitor potential autism spectrum disorder-related abnormalities of the foetuses.

The NeuroMouse Scan's advanced neuroimaging techniques, combined with its user-friendly features, made it easy to collect and document crucial insights into foetal brain structure, function, and connectivity. This aids in the early detection or risk of potential autism spectrum disorder-related abnormalities. The NeuroMouse Scan is very sensitive even to a slight change in the risk of autism spectrum disorder-related abnormalities.

The NeuroMouse Scan produced a high amount of imaging with ease. Equipped with ultrasound and MRI (Magnetic Resonance Imaging) capabilities, it enabled non-invasive assessment of foetal brain development in real-time, aiding in detecting subtle autism spectrum disorder-related abnormalities. AI (artificial intelligence) – powered analysis tools of the NeuroMouse Scan have enhanced data processing and interpretation, accelerating potential scientific discovery.

The NeuroMouse Scan was easily integrated with the transparent acrylic box. This setup allowed for easy and user-friendly prenatal imaging studies without removing the pregnant mice from the chamber, minimising their stress and disturbance.

By seamlessly integrating the NeuroMouse Scan with the experimental chamber, the process of prenatal imaging and gathering valuable data on foetal brain development and autism spectrum disorder-related abnormalities were streamlined for more efficient and ethical prenatal imaging.

During the postnatal period, the newborn mice were put in new transparent acrylic boxes similar to those used for prenatal studies. As each pregnant mouse gave birth to multiple mice, and the chamber was designed to comfortably accommodate only 12 mice, one offspring mouse was taken as a representative of offspring reproduced by a pregnant mouse for postnatal studies.

The newborn mice were separated into the new three environmental chambers that were not used for the prenatal experiments based on their mother's grouping. In the post-natal studies, there was no particle injection into any of the environmental chambers for the first 3 months.

Depending on the exposure group, there was an ultrafine or fine particle injection for the next 3 months. That is, each of the offspring spent a total of 6 months in their environmental chamber during the post-natal stage. The injection rate was the same as the prenatal stage.

The NeuroMouse Scan system attached to each of the environmental chambers provided postnatal monitoring of autism spectrum disorder-related behaviours and neurobiological changes in newborn mice till they were 6 months old. Changes in brain structure, function, and connectivity suggesting risk of autism spectrum disorder-related development were monitored for 6 months.

The NeuroMouse Scan prioritises the ethical treatment of research animals, ensuring minimal stress and discomfort for pregnant mice and offspring during imaging and assessment procedures. Gentle handling techniques and non-invasive imaging modalities minimise the impact on maternal health, foetal development, and offspring development, ensuring the welfare of experimental subjects.

An automated tracking and video recording system was also integrated into each of the environmental chambers used during the postnatal experimental studies, as it was during the prenatal experimental studies.

The above prenatal and postnatal research procedures were repeated for two additional ultrafine and fine particle injection rates. That is, there were three ultrafine and fine particle injection rates, where applicable, in the whole research. The injection rate for the above experimental procedures was considered the "medium" injection rate.

Additional two sets of research studies were conducted when injection rates were "low" and "high." The impacts of prenatal exposures on post-natal and exposure to particulate matter during offspring development were also conducted for these two additional research sets, like in the case of the first set of research described above.

All experimental procedures adhered to ethical guidelines for animal research, prioritising the welfare and humane treatment of pregnant mice and their offspring. Measures were taken to minimise stress and discomfort for pregnant mice during particulate matter exposure, and appropriate veterinary care was provided as needed.

4.……

Research Findings: In the control group, which was not exposed to any particulate matter, typical foetal brain development with no indications of autism spectrum disorder-related abnormalities was observed. Neuroimaging studies conducted on foetuses of the pregnant mice in this group revealed normal brain morphology and connectivity patterns, providing a baseline comparison for assessing the effects of particulate matter exposure on autism spectrum disorder risk.

In contrast, foetuses exposed to ultrafine particles ($PM_{0.1}$) during pregnancy exhibited alterations in brain structure and function, indicative of a risk of autism spectrum disorder-related abnormalities. Utilising advanced neuroimaging techniques with the NeuroMouse Scan, disruptions in synaptic connectivity, neuronal migration, and neurotransmitter signalling pathways in foetuses exposed to ultrafine particles were observed.

These neurobiological changes were more pronounced compared to the control group, highlighting the specific impact of ultrafine particle exposure on foetal brain health and autism spectrum disorder risk.

Similarly, foetuses exposed to fine particles ($PM_{2.5}$) during pregnancy demonstrated alterations in brain structure and function associated with a risk of autism spectrum disorder-related abnormalities, albeit to a lesser extent compared to the ultrafine particle exposure group. Neuroimaging studies revealed disruptions in brain morphology and connectivity patterns in foetuses exposed to fine particles, indicating a moderate impact on foetal neurodevelopment and autism spectrum disorder risk.

In essence, both ultrafine particles ($PM_{0.1}$) and fine particles ($PM_{2.5}$) demonstrated a clear association with an increased risk of autism spectrum disorder-related development in foetuses. The observation in the ultrafine particle exposure group is significantly ($p < 0.001$) higher than in the control group.

The observation in the fine particle group is also significantly ($p < 0.05$) higher than in the control group for the three injection rates. The ultrafine particles exposure group is observed to be significantly ($p < 0.05$) higher than the fine particle exposure group for the injection rates.

The findings underscore the detrimental effects of prenatal exposure to particulate matter on foetal brain health and highlight the need for mitigating strategies to reduce environmental pollutant exposure during pregnancy. The specific impact of ultrafine particles on autism spectrum disorder risk emphasises the importance of targeted interventions to safeguard foetal neurodevelopment and reduce autism spectrum disorder risk in young offspring.

Young offspring from the ultrafine particle-exposed group demonstrated a highly elevated ($p < 0.001$) range of autism spectrum disorder-like behaviours compared to the control group. These behaviours include reduced social sniffing, decreased social grooming, avoidance behaviour, lack of interest in social exploration, aggressive behaviour, and repetitive behaviours.

The intensity of these negative behaviours in the offspring increased with an increase in the particulate matter concentration injection rate during prenatal and postnatal periods. These behaviours persisted throughout the postnatal monitoring period, even when there was no injection of ultrafine particles during the first 3 months of the postnatal stage, indicating a lasting impact of prenatal ultrafine particle exposure on neurodevelopment and behaviour.

In contrast, offspring from the fine particle-exposed group exhibited moderately elevated levels of autism spectrum disorder-like behaviours compared to the control group but demonstrated significantly lower ($p < 0.05$) severity and incidence rates compared to the ultrafine particle-

exposed group. While the differences were less pronounced, they were still statistically significant.

These findings highlight the importance of considering the size and composition of particulate matter when assessing its impact on neurodevelopmental outcomes. Ultrafine particles, with their smaller size and greater ability to penetrate biological barriers, may exert a more profound influence on foetal brain development and autism spectrum disorder-related development risk compared to larger particles.

The research provides compelling evidence linking prenatal exposure to ultrafine particles with an increased risk of autism spectrum disorder-like behaviours in offspring, underscoring the need for further investigation into the underlying mechanisms and potential interventions to mitigate the adverse effects of environmental exposures on neurodevelopment.

The severity of autism spectrum disorder-related development and behaviours with an increase in exposure dose through an increase in injection rates highlights the importance of reducing the exposure dose as much as possible.

Additionally, the observed superiority in the detrimental effects of ultrafine particles on brain structural and functional abnormalities was consistent with the observed behavioural phenotype, suggesting a direct link between the seriousness of the impact of prenatal ultrafine particle exposure and neurobiological changes underlying autism spectrum disorder.

The significant increase in the severity of the disruption to the offspring's brain structural and functional abnormalities and autism spectrum disorder-like behaviour during the postnatal period when they were exposed to ultrafine and fine particles than when they were not exposed suggests the need to reduce exposure to particulate matter during this period.

The research findings effectively address the overarching research questions and objectives regarding: (i) the correlation between prenatal exposure to particulate matter, particularly ultrafine particles, and the risk of prenatal autism spectrum disorder-related development; (ii) the correlation between prenatal exposure to particulate matter, particularly ultrafine particles, and the risk of young offspring's autism spectrum disorder-related behaviour; (iii) the correlation between early-life exposure to particulate matter, especially ultrafine particles, and the risk of autism spectrum-related disorder development and behaviour in young offspring; and (iv) the correlation between an increase in injection rate or exposure dose rate during prenatal and postnatal periods on autism spectrum disorder-related development during prenatal and postnatal periods, and autism spectrum disorder-like behaviour during postnatal periods.

These findings contribute to the understanding of the impact of environmental exposures on neurodevelopment and underscore the importance of implementing measures to reduce exposure to particulate matter, particularly during critical periods of development.

While the current study utilised mouse models, its findings carry implications for understanding human neurodevelopment and behavioural outcomes. Mice were chosen as models for studying neurodevelopmental disorders like autism spectrum disorder due to their genetic,

neurobiological, and behavioural similarities to humans. These similarities extend to the fundamental neurodevelopmental pathways and responses to environmental exposures.

Neurodevelopment in mice shares many parallels with humans, including the formation of neural circuits, synaptic connectivity, and neurotransmitter systems. Moreover, both mice and humans exhibit similar behavioural traits and responses, making mouse models valuable tools for studying complex behaviours associated with neurodevelopmental disorders.

In this study, the observed alterations in brain structure and function, as well as the manifestation of autism spectrum disorder-like behaviours in mouse offspring exposed to particulate matter during pregnancy, provide insights into potential effects in humans. While direct translation from mice to humans requires caution due to species differences, the underlying neurobiological processes affected by environmental exposures are often conserved across species.

Furthermore, the study's findings suggest a plausible transferability to human populations based on shared responses to environmental exposures. The demonstrated correlations between particulate matter exposure and autism spectrum disorder-related outcomes in mice highlight the importance of considering similar risks in humans, particularly during critical periods of neurodevelopment.

While acknowledging the limitations of extrapolating findings from mouse models to humans, the study provides valuable insights into potential neurodevelopmental and behavioural consequences of prenatal particulate matter exposure in humans.

Further research in human populations is warranted to confirm and expand upon these findings, but the study's results offer a foundation for understanding the impact of environmental exposures on neurodevelopment and advocating for preventive measures to mitigate autism spectrum disorder-related risks.

5.…….

After completing his PhD, Alonso's groundbreaking research on the effects of particulate matter exposure on neurodevelopment of foetuses and young offspring catapulted him into the forefront of environmental health and science. His study's findings not only shed light on the potential risks of environmental exposures but also paved the way for future research and advocacy efforts aimed at protecting vulnerable populations.

With his reputation as a leading expert in the field firmly established, Alonso was offered a prestigious postdoctoral fellowship at a renowned research institution. During his postdoc, he continued to dig deeper into the mechanisms underlying neurodevelopmental disorders, using advanced imaging techniques and cutting-edge methodologies to unravel the complexities of brain structure and function.

From the moment Alonso completed his PhD, it became evident that he possessed an extraordinary intellect, one that transcended conventional boundaries and defied easy categorisation. His mind, honed by years of navigating the intricacies of autism, operated on a

level of complexity and depth that set him apart from his peers.

As Alonso delved into his research, he found himself drawn to the complex interplay between environmental factors and human health, a subject that ignited his passion and fuelled his insatiable curiosity. His autism, far from being a hindrance, became a powerful tool in his arsenal, enabling him to perceive the world with a clarity and precision that bordered on the extraordinary.

Where others saw complexity, Alonso saw patterns. Where others stumbled, Alonso soared. His ability to dissect complex problems and distil them down to their essence was nothing short of genius, a testament to the unique wiring of his brain and the depth of his intellectual capabilities.

As Alonso's career progressed, so too did his reputation as a leading authority in environmental health and science. His research papers, filled with insights that bordered on the prophetic, garnered international acclaim and transformed the way the world thought about the relationship between the environment and human health.

But perhaps what truly set Alonso apart was his ability to harness the benefits of his autism to push the boundaries of knowledge even further. His intense focus, unwavering determination, and relentless pursuit of excellence were the hallmarks of his genius, propelling him to heights that few could reach and earning him the respect and admiration of colleagues and peers worldwide.

As Alonso's expertise and influence grew, so did his career prospects. He was soon appointed as an assistant professor at a top-tier university, where he continued to conduct groundbreaking research, mentor the next generation of scientists, and advocate for policies aimed at promoting environmental health and sustainability.

In recognition of his contributions to the field, Alonso was promoted to the rank of associate professor, where he further expanded his research portfolio with interdisciplinary collaborators in public health, epidemiology, and toxicology. Together, they worked tirelessly to translate their findings into actionable strategies for mitigating environmental risks and improving public health outcomes.

Over the years, Alonso dedicated himself to providing scientific data that supported and expanded upon the findings of his groundbreaking study during his PhD building upon the observed alterations in brain structure and function in mouse offspring exposed to particulate matter during pregnancy, Alonso conducted numerous follow-up studies aimed at elucidating the potential effects of environmental exposures on human neurodevelopment.

One of Alonso's key contributions was his innovative use of advanced imaging techniques to assess brain development in human populations exposed to environmental pollutants. By employing state-of-the-art neuroimaging methods such as MRI and fMRI (Functional Magnetic Resonance Imaging), he was able to identify subtle changes in brain structure and function that mirrored those observed in mouse models, providing compelling evidence of a link between prenatal particulate matter exposure and neurodevelopmental disorders in humans.

Alonso's research did not stop at highlighting problems; he, with the support of his team, made conscious efforts to develop effective solutions, now available in the market, that can effectively solve the highlighted problems. An example of such a solution is the development of a solution to the problem he first highlighted during his PhD research studies.

Alonso and his team embarked on a pioneering endeavour to develop the Nanotechnology Enhanced Filtration System (NEFS) in response to the growing concern over the health impacts of ultrafine particles present in indoor air. Recognising the limitations of existing filtration technologies in effectively capturing these tiny particles, they sought to harness the power of nanotechnology to address this critical challenge.

The development process of NEFS was a meticulous journey of innovation and experimentation. Drawing upon their expertise in environmental engineering, materials science, and nanotechnology, the team explored various nanomaterials and filtration techniques to design a system capable of efficiently capturing ultrafine particles in indoor air.

The cornerstone of NEFS was its use of advanced nanomaterials with tailored properties to enhance filtration efficiency. NEFS has a highly porous nanofiber matrix composed of nanomaterials, meticulously engineered at the nanoscale, offered superior filtration capabilities compared to conventional filters, enabling effective trapping of ultrafine particles with remarkable precision.

Furthermore, NEFS incorporated state-of-the-art filtration mechanisms and airflow optimisation techniques to ensure optimal performance in real-world environments. The system was designed to seamlessly integrate into existing HVAC (Heating, Ventilation, and Air Conditioning) systems, providing a cost-effective and scalable solution for indoor air quality improvement.

Alonso's further research during his career provided compelling evidence of the efficacy of NEFS in mitigating the adverse effects of particulate matter, especially ultrafine particles, on neurodevelopmental disorders and compromised behaviour such as autism spectrum disorder-related development.

Through comprehensive experimental studies and rigorous data analysis spanning many years in his career and involving several undergraduate, master's, and PhD students, postdoc fellows, researchers, and academic staff, Alonso demonstrated that the use of NEFS in air conditioning systems significantly reduced building occupants' exposure to ultrafine particles, thereby diminishing the risk of neurodevelopmental disorders and behavioural abnormalities associated with particulate matter exposure.

Moreover, Alonso's research shed light on the underlying mechanisms by which NEFS exerted its protective effects, highlighting the importance of ultrafine particle removal in mitigating the neurotoxic effects of indoor air pollution. By elucidating these mechanisms, Alonso and co-developers provided valuable insights that informed the development and implementation of NEFS in various indoor environments.

Ultimately, Alonso's pioneering work and leadership in developing and validating NEFS represented a paradigm shift in indoor air quality management, offering a transformative solution to address the growing public health concern posed by ultrafine particles. Through his unwavering dedication to scientific inquiry and innovation, Alonso forged a path towards healthier and more sustainable indoor environments, leaving a lasting impact on the field of environmental health and science.

Alonso and his team also provided evidence on the importance of adequate adoption of ventilation and its rate and source elimination or control in reducing the risk of neurodevelopmental disorders and behavioural abnormalities associated with particulate matter exposure.

His research on the impact of indoor air pollution, particularly particulate matters, on human neurodevelopment and behaviour and sustainable solutions he and his team developed, permeates his teachings. Below is an extract from one of his teachings.

[Student]: "Professor! Why is $PM_{0.1}$ potentially more dangerous to human health than $PM_{2.5}$? My question is in the context of assuming the initial toxicity of $PM_{0.1}$ and $PM_{2.5}$ and their surroundings are the same or similar."

[Professor Alonso Afonso]: "The precision of attack and size make $PM_{0.1}$ more dangerous.… $PM_{0.1}$'s higher precision of attack due to its higher surface area to volume (A/V) ratio makes its interactions and chemical reactions with its surroundings (air pollutants, human organs, cells…) more intense and have greater consequences than that of a $PM_{2.5}$, which has a lower surface area to volume (A/V) ratio.

$PM_{0.1}$, with its smaller size, occupies less space (volume), whereas $PM_{2.5}$, being larger, occupies a greater volume. The explanation for the A/V ratio is that as particle size increases, its volume with r^3 increases at a rate faster than that of its surface area with r^2. That is, the rate of increase for surface area, dA/dr, is 2r, while the rate of increase for volume, dV/dr, is $3r^2$. Thus, as a larger particle size occupies more volume, its A/V ratio decreases."

[Another student]: "Professor! Although $PM_{2.5}$ has a lower A/V ratio than $PM_{0.1}$, it still has a larger surface area than $PM_{0.1}$. Shouldn't that count for something? I would expect that the relatively higher surface area of a $PM_{2.5}$ than a $PM_{0.1}$ would lead to a $PM_{2.5}$ having more interactions and chemical reactions with air pollutants, human organs, cells, etc. Do you mean a $PM_{2.5}$ has a higher quantity but a lesser quality of interactions and chemical reactions than a $PM_{0.1}$, but the higher quality $PM_{0.1}$ has due to its higher A/V ratio makes it more precise and potent than a $PM_{2.5}$?"

[Professor Alonso Afonso]: "Precisely, gentlemen! You've answered your question! With higher precision of attack and potency, imagine the adverse health problems… if a $PM_{0.1}$ can penetrate and remain more in the human body than $PM_{2.5}$? Unfortunately, it does. A higher surface area per unit volume leads to more precise interactions and reactions and potent implications.

Due to its size, a $PM_{0.1}$ can bypass human protection systems more easily and reach every part of the human body more thoroughly. With potentially higher toxic contents, a more precise attack, and a longer residence in the body, vulnerability will be higher. The concern here is that the sources of particle matter, including ultrafine particles, are prevalent around us.

Indoor sources of toxic particulate matter include cooking, tobacco or cigarette smoking, cleaning products, heating systems, pet dander, virus-infected and bacteria-infected individuals, and infiltration of outdoor air. Outdoor sources of toxic particulate matter include vehicle emissions, industrial activities, agricultural operations, natural sources, and construction and demolition."

While Alonso answered his students' questions, his postdoctoral fellow and teaching assistant, Dr. Fathia Alabi, stood in front of the class with him, thinking to herself that $PM_{0.1}$, $PM_{2.5}$, and PM_{10} are air pollutants in outdoor and indoor air (where a higher exposure rate occurs). She later shared her thoughts with the students.

She further told the students, "Guys! The explanations given by Prof about $PM_{0.1}$ and $PM_{2.5}$ also explain why $PM_{2.5}$ has more adverse health effects than PM_{10}. Particulate matter's health problems are related to organs, irritations, and other discomforts." Alonso went on to share more details on NEFS and how it could effectively reduce exposure to ultrafine particles.

As Alonso's reputation continued to soar, he was eventually appointed as a full professor of environmental health and science, a position that allowed him to influence policy at the highest levels and make a lasting impact on a global scale. His research was widely cited and respected, and he was frequently invited to speak at international conferences and symposiums, where his insights and expertise were sought after by colleagues and policymakers alike.

However, perhaps Alonso's greatest legacy lies in the tangible impact of his work on communities around the world. Through his research, advocacy, and outreach efforts, he helped raise awareness about the link between environmental exposures and neurodevelopmental disorders, empowering individuals and policymakers to protect the health and well-being of future generations.

6.…….

As Alonso's career flourished, so too did his personal life. Amidst his groundbreaking research and global advocacy efforts, he found love in the most unexpected of places: the intersection of academia and architecture practice.

It was at a conference on the sustainable built environment that Alonso first met Isabella, a talented architect whose passion for design and sustainability mirrored his own. Their shared interests sparked a deep connection, and before long, they found themselves embarking on a journey of love and partnership.

Despite their demanding careers, Alonso and Isabella carved out time for each other, nurturing their relationship with shared adventures, intellectual debates, and moments of quiet companionship. Their bond only grew stronger with each passing year as they supported and uplifted each other through life's triumphs and challenges.

In the fullness of time, Alonso and Isabella exchanged vows in a ceremony that celebrated their love and commitment to each other. Surrounded by family, friends, and colleagues from around the world, they embarked on a new chapter of their lives together, united in their shared vision of a brighter future. Alonso was an assistant professor when he got married.

As Alonso's career continued to thrive, so did his family. He and Isabella welcomed two children into their lives, each inheriting their parents' passion for knowledge and creativity. From a young age, their children displayed an extraordinary intellect and curiosity, traits that mirrored Alonso's own genius and Isabella's artistic flair.

As their children grew and flourished, Alonso and Isabella found joy in watching them pursue their passions and achieve their dreams. From academic achievements to artistic endeavours, their children's accomplishments filled their hearts with pride and gratitude, reminding them of the boundless potential of the human spirit.

Years passed, and Alonso and Isabella were blessed with the arrival of grandchildren, who brought even more love and laughter into their lives. As they revelled in the joy of being grandparents, Alonso and Isabella cherished the opportunity to impart wisdom and share their experiences with the next generation.

Despite the demands of their careers, Alonso and Isabella made it a priority to create cherished memories with their family, whether through weekend outings to the countryside, family vacations to exotic destinations, or simple moments spent gathered around the dinner table.

As they grew older, Alonso and Isabella found solace and fulfilment in the bonds they had forged with each other and their loved ones. Theirs was a life filled with love, laughter, and endless possibilities, a testament to the power of passion, perseverance, and the unwavering belief in the potential for positive change.

Alonso's journey from orphanhood to troubled youth and from struggling with autism to harnessing its benefits to make a profound impact on people's lives through his scientific discoveries are a testament to the power of resilience, determination, and the human spirit. Despite facing seemingly insurmountable challenges, Alonso never lost sight of his dreams or his belief in the potential for positive change.

Through his groundbreaking research and unwavering commitment to improving public health, Alonso not only transformed the way we understand the impact of environmental exposures on neurodevelopment but also inspired countless individuals to advocate for a healthier, more sustainable world.

Perhaps Alonso's greatest achievement was not in the accolades and recognition he received for his work, but in the love and connection he shared with his wife, Isabella, and their family. Together, they overcame obstacles, celebrated triumphs, and created a legacy of love and compassion that would endure for generations to come.

As Alonso looked back on his remarkable journey–from the depths of despair to the pinnacle of success–he knew that every challenge he faced, every obstacle he overcame, had led him to this moment of fulfilment and happiness. As Alonso embraced his loved ones and cherished the life they had built together, he realised that the greatest discoveries were not made in the laboratory, but in the depths of the human heart.

It was the goodness of Mr. Ramirez's heart that set him on the journey of great transformation. Mr. Ramirez made him realise that his weakness as someone with autism spectrum disorder was actually his strength and secret weapon for success in his professional and personal endeavours.

It was Professor Jacob's goodness of heart that made her provide Alonso with world-class guidance and mentorship, which led him on a journey to becoming a world-class researcher and educator. It was the goodness of his loving wife's heart that made it easy for him to have a happy family and loving children and grandchildren and made life truly meaningful for him. **The End!**