ARCHAEOLOGY

Exploring climate-driven heritage loss and occupational health at the early modern whaling burial site of Likneset, Svalbard

Lukdu and Bradhet examined Arctic whalers' graves preserved in permafrost on Svalbard. As the ground thaws with climate change, these remains are rapidly deteriorating, while also revealing the harsh conditions and health struggles of early modern whalers.

REPRODUCIBILITY

What helps and hinders reproducible research?

Korpak and colleagues explore researchers' perspectives on the barriers and facilitators that shape reproducible research across different fields and career stages, using qualitative methodologies. Results highlight reproducibility as a collective responsibility, requiring coordinated action across different stakeholders.

ADDICTION

Is early childhood exposure a key predictor of adulthood problematic gaming?

Compton and colleagues investigate the relationship between frequent gaming in different childhood stages and the development and severity of symptoms of gaming addiction in adulthood. They identify high frequency gaming during preschool years as the strongest predictor, suggesting early exposure is a key risk factor.

CH4 EMISSION

The impact of water management and nitrification inhibitors on methane emissions from paddy soil

Cui and colleagues investigated three water management practices on rice paddy soil to decide which is the most effective method to control agricultural methane emissions. They prove that alternate wetting and drying irrigation combined with nitrification inhibitor DMPP can reduce cumulative methane emission by more than 90%.

EVERYONE

Twenty years of PLOS One

Over the past 20 years, PLOS One has grown from an open-access experiment into a leading multidisciplinary journal, reshaping how research is shared. This blog reflects on PLOS One's journey: scaling rapidly, strengthening standards, meeting new challenges, all while staying committed to high quality, accessible science.

EVERYONE

Behind the Papers: Fascination of Plants Day Research Highlights

Exploring the stories behind some of the excellent plant science published in PLOS One, we spoke with several authors about the questions driving their research and what continues to fascinate them about plants.

EVERYONE

Editorial Spotlight: Roberto Ariel Abeldaño Zuñiga

In an interview, Dr Roberto Zuñiga shares his insights into the importance of ethics considerations in research and publishing, and the need for well-conducted research to inform policy decisions.

PUBLISH WITH PLOS

SUBMISSION INSTRUCTIONS

SUBMIT YOUR MANUSCRIPT

EveryONE

SEE ALL BLOGS

CONNECT WITH US

PLOS Blogs

HIV HEALTHCARE WORKERS

Well-being and Self-Care Needs Among Health Workers Providing HIV Care to Children and Adolescents in Africa

Citron highlights challenges healthcare workers face when caring for young people with HIV, informing support strategies.

PLANT BIOMECHANICS

Size-curvature constraint in the closing motion of Venus flytrap leaves

Hosts and colleagues determined the Venus flytrap's size-curvature constraint using kinematics, micro-CT 3D reconstruction, and geometric modeling, supporting biomimetic soft surface design.

ECOLOGY

Ecological strategies and extinction risk in butterflies and macro-moths of Great Britain and Ireland

Roitz and colleagues studied butterflies and moths, finding multi-generation species most at risk, aiding conservation efforts.

PSYCHOLOGY

Purpose in life and coping strategies: Main associations and moderation by concurrent distress

Salin and colleagues linked life purpose to stress-regulating coping strategies, supporting better psychosocial and health outcomes.

Collections

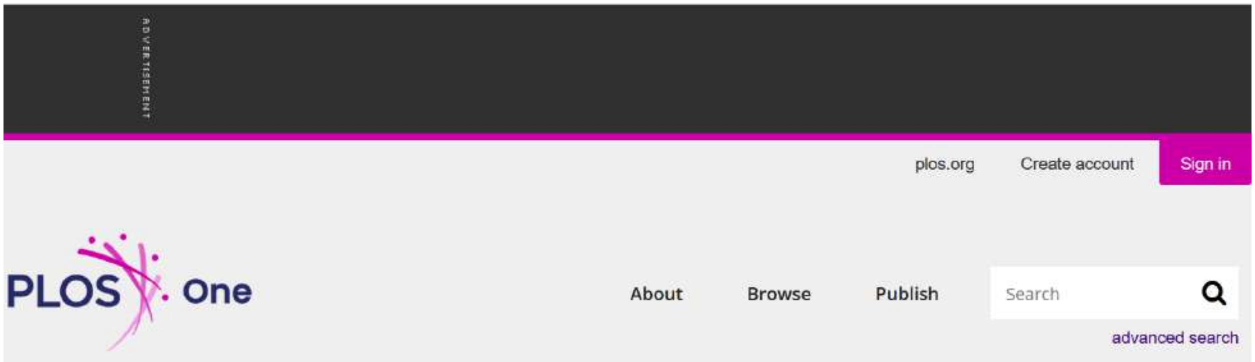
Collections

Browse the latest collections of papers from across PLOS.

Meet our staff at conferences

European Association for Cancer Research Congress

Associate Editor Jenny Tucker will be representing PLOS One at this conference in Budapest, Hungary, June 8th – 11th 2026



Editorial Board

The *PLOS ONE* Editorial Board is powered by thousands of academic experts from all over the world. Our board comprises working scientists who are established principal investigators/group leaders with extensive publication records.

Academic Editors oversee the peer review process for the journal, including evaluating submissions, selecting reviewers and assessing their comments, and making editorial decisions. Together with fellow Editorial Board Members and internal staff, Academic Editors uphold journal policies and ethics standards and work to promote the *PLOS ONE* mission to provide free public access to scientific research.

Editorial board members affiliated with the Centers for Disease Control and Prevention, the World Health Organization or any other government agency are serving in a personal capacity. The views expressed are their own and do not necessarily represent the views of the Centers for Disease Control and Prevention or the United States Government.

Interested in serving on the Editorial Board?

PLOS welcomes volunteers to the Editorial Board who support our mission, values, and commitment to providing a high-quality experience for our authors. Explore the Academic Editor role and apply online.

Academic Editors

To find a member, browse the list, or search by name, country/region, Section or Classification.

The list of Editorial Board members syncs daily with Editorial Manager. If you are a Board member and would like to update any of the information below or do not see your information listed, please contact edboardsupport@plos.org.

Displaying 1-50 of 8877 Editors.

...

- **Natraj N. A.**
  orcid.org/0000-0002-8726-5284
  Symbiosis International (Deemed University)
  India
  Sections: Computer and information sciences - Cryptography and computer security, Engineering and technology - Communication technologies, Engineering and technology - Systems science and computational engineering
  Classifications: Prototypes, Multiplexing, Science and technology workforce, Internet, Natural language processing, Medicine and health sciences, Engineering and technology, Computer architecture, Target detection, Computing systems, Broadband, Microprocessors, Telecommunications, Electronics engineering, Computer engineering, Information technology, Computer applications, Technology regulations, Carrier frequencies, Artificial neural networks, Computer inferencing, Optical computing, Internet of Things, Fuzzy logic, Electronics, Technology development, Machine learning, Health information technology, Quantum computing, Artificial intelligence, Web-based applications, Network bandwidth, Health care, Computerized simulations, Science policy, Cryptography, Databases, Computer networks, Computer hardware, Computer vision, Control sequences, Computer security, Information storage and retrieval, Cloud computing, Encryption, Mathematical computing, Computing methods, Computer and information sciences, Expert systems

- **Ahmad Khalid Aalemi**
  orcid.org/0000-0003-0111-634X
  The University of Manchester Faculty of Biology Medicine and Health
  United Kingdom of Great Britain and Northern Ireland
  Sections: Dermatology
  Classifications: Warts, Medicine and health sciences, Dermatology, Oral medicine, Blisters, Oral health, Pigmentary disorders, Dentistry, Oral diseases, Skin neoplasms

- **Katriina Aalto-Setala**
  University of Tampere
  Finland
  Sections: Developmental biology - Cell differentiation; Cell fate determination; Stem cells; Embryology; Fertilization
  Classifications: Stem cells, Genetics of disease, Cardiovascular anatomy, Human genetics, Cell differentiation, Electrophysiology, Cellular types, Animal models, Arrhythmia, Genetic testing, Cardiology, Embryonic stem cells, Clinical genetics, Induced

pluripotent stem cells, Mouse models, Genetic association studies, Molecular genetics, Personalized medicine, Medicine and health sciences, Genetics, Model organisms, Developmental biology, Biology and life sciences

- **Nik Hisamuddin Nik Ab. Rahman**
  Universiti Sains Malaysia
  Malaysia
  Sections: Health care - Health services research, Public health and epidemiology - Health policies, systems and management, Toxicology
  Classifications: Critical care and emergency medicine, Medicine and health sciences

- **Andrew Max Abaasa**
  orcid.org/0000-0002-6770-5588
  London School of Hygiene & Tropical Medicine Faculty of Epidemiology and Population Health
  Uganda
  Sections: Infectious diseases - Epidemiology and prevention, Public health and epidemiology - Biostatistics and methods
  Classifications: Medicine and health sciences, Clinical trials, Research design, Health care, Research and analysis methods, Epidemiology

- **Nidaa Ababneh**
  orcid.org/0000-0002-2155-3013
  University of Jordan
  Jordan
  Sections: Genetics - Mutation; Genetics of disease; Heredity, Neuroscience - Neurodegenerative diseases and dementia, Stem cells and regenerative medicine
  Classifications: Medicine and health sciences, Neurology

- **Yacine Abadou**
  orcid.org/0000-0002-0248-0728
  Universite Ziane Achour de Djelfa
  Algeria
  Sections: Engineering and technology - Materials and manufacturing engineering, Engineering and technology - Systems science and computational engineering, Materials science - Structural materials
  Classifications: Engineering and technology, Materials design, Physical sciences, Civil engineering, Built structures, Structural engineering, Materials science

- **Amanuel Abajobir**
  orcid.org/0000-0002-6878-0627
  African Population and Health Research Center
  Ethiopia
  Sections: Health care - Health services research, Public health and epidemiology - Health policies, systems and management, Women's and maternal health
  Classifications: Medicine and health sciences, Scientific publishing, Women's health, Research and analysis methods, Research design

- **Yared Reta Abayneh**
  orcid.org/0000-0002-8509-2287
  Hawassa University College of Medicine and Health Sciences
  Ethiopia
  Sections: Mental health and psychiatry - General
  Classifications: Medicine and health sciences, Mental health and psychiatry

- **Gianmarco Abbadessa**
  orcid.org/0000-0001-8912-3055
  Universita degli Studi della Campania Luigi Vanvitelli
  Italy
  Sections: Digital health, Neuroscience - Cellular and molecular, Neuroscience - Neurobiology of disease; Neuropathology
  Classifications: Medical services, Neurology, Autoimmune diseases, Health care, Telemedicine, Demyelinating disorders, Clinical immunology, Immunology, Medicine and health sciences, Neuroimmunology, Multiple sclerosis

- **Cristiana Abbafati**
  orcid.org/0000-0003-2811-6251
  Sapienza University of Rome
  Italy
  Sections: Economics - Health economics, Health care - General, Public health and epidemiology - Health policies, systems and management
  Classifications: Socioeconomic aspects of health, Outpatient clinics, Health care utilization, Health services administration and management, Morbidity, Community based intervention, Quality of life, Medicine and health sciences, Health statistics, Health care providers, Health care, Hospitals, Health care policy, Public and occupational health, Health economics, Health care facilities, Economics, Health care quality, Social sciences, Health services research

- **Sohail Abbas**
  orcid.org/0000-0003-1194-064X
  Henan University, Kaifeng
  China
  Sections: Agriculture - Plants, Earth sciences - Physical geography, Ecology - Ecosystems
  Classifications: Sociology, Hydrology, Climatology, Education, Environmental geography, Physical geography, Climate change, Watersheds, Atmosphere, Monsoons, Social sciences, Natural disasters, Ecology and environmental sciences, Atmospheric science, Ecology, Geography, Climate modeling, Meteorology, El Niño-Southern Oscillation, Earth systems, Earth sciences, Drought

- **Alhamzah F. Abbas**
  orcid.org/0000-0002-7508-9340
  Universiti Teknologi Malaysia
  Malaysia
  Sections: Economics - General, Management science
  Classifications: Quality of life, Health care, Medicine and health sciences, Quality of care, Health care quality

- **Mazhar Abbas**
  Universiti Utara Malaysia
  Malaysia
  Sections: Management science
  Classifications: Research and analysis methods, Social sciences, Research design, Economics

- **Asad Abbas**
  orcid.org/0000-0003-1395-4009
  Tecnologico de Monterrey
  Mexico
  Sections: Education research, Management science
  Classifications: Political science, Social sciences, Sociology, Public administration, Education

- **Faisal Abbas**
  MY University Islamad
  Pakistan
  Sections: Biotechnology - General, Immunology - General, Immunology - Immunity
  Classifications: Ecology and environmental sciences, Environmental economics, Social sciences, Economics

- **Muhammad Sibt-e-Abbas**
  orcid.org/0000-0002-0786-6742
  Muhammad Nawaz Shareef University of Agriculture
  Pakistan
  Sections: Agriculture - General, Food science and technology, Nutrition
  Classifications: Fats, Sensory perception, Garlic, Nutrition, Plant science, Protein isolation, Peanut, Wheat, Food, Protein extraction, Absorption, Biology and life sciences, Emulsions, Agriculture, Oils, Flour

- **Faisal Abbas**
  orcid.org/0000-0002-9312-5659
  National University of Sciences and Technology
  Pakistan
  Sections: Economics - Health economics, Public health and epidemiology - Global health, Public health and epidemiology - Health policies, systems and management
  Classifications: Development economics, Welfare economics, Human capital, Social sciences, Economics, Economic development, Economic models, Nutrition, Health economics, Agricultural economics, Experimental economics, Economic analysis, Macroeconomics, Economic crises

- **Sameen Abbas**
  orcid.org/0000-0002-7260-3973
  Quaid-i-Azam University
  Pakistan
  Sections: Gastroenterology and hepatology, Public health and epidemiology - Health behavior, health promotion and society, Research assessment
  Classifications: Medicine and health sciences, Gastrointestinal motility disorders, Gastroenterology and hepatology, Public and occupational health, Global health, Health promotion

- **Mahdi Abbasi**
  orcid.org/0000-0002-5373-5778
  Bu Ali Sina University
  Iran, Islamic Republic of
  Sections: Computer and information sciences - Artificial intelligence, machine learning and data science, Computer and information sciences - Computer Hardware, Computer and information sciences - General
  Classifications: Genetic programming, Network analysis, Internet of Things, Network control, Recurrent neural networks, Artificial neural networks, Computer and

information sciences, Network theory, Computer networks, Computers, Machine learning, Digital computing, Digital imaging, Feedforward neural networks, Signaling networks, Internet, Real time computing, Computing methods, Computer architecture, Random number generators, Computing systems, Computer applications, Microprocessors, Computer hardware, Computer vision, Neural networks, Expert systems, Artificial intelligence

- **Roohollah Abbasi Shureshjani**
  orcid.org/0000-0002-4141-933X
  Hazrat E Masoumeh Univ
  Iran, Islamic Republic of
  Sections: Economics - General, Management science, Mathematics - Multidisciplinary
  Classifications: Research and analysis methods, Mathematical and statistical techniques, Optimization, Decision theory, Computer and information sciences, Mathematical functions, Decision analysis, Linear programming, Computing methods, Physical sciences, Mathematics, Data management, Fuzzy logic, Applied mathematics
- **A. M. Abd El-Aty**
  orcid.org/0000-0001-6596-7907
  Cairo University
  Egypt
  Sections: Food science and technology, Pharmacology, Veterinary science
  Classifications: Pharmacologic analysis, Research and analysis methods, Solid-phase extraction, Extraction techniques, Phytopharmacology, Water analysis, Pharmacokinetic analysis, Medicine and health sciences, Drug interactions, Drugs, Chemistry, Phytochemistry, Pharmacokinetics, Phytochemicals, Chemical analysis, Environmental chemistry, Pharmacodynamics, Liquid-liquid extraction, Analytical chemistry, Chromatographic techniques, Liquid chromatography, Pharmacogenetics, Pharmacology, Liquid chromatography-tandem mass spectrometry, Antimicrobials, Supercritical fluid extraction, Drug-food interactions, Physical sciences
- **Diaa Abd El-Moneim**
  orcid.org/0000-0003-3285-0563
  Arish university, Faculty of agricultural and environmental sciences
  Egypt
  Sections: Agriculture - Plants, Genetics - Gene expression; Epigenetics; Alternative splicing; RNA splicing; Molecular genetics, Genetics - Population genetics; Evolutionary genetics

Classifications: Molecular biology, Genetics, Agriculture, Plant science, Biology and life sciences

- **Mahfouz Mohamed Mostafa Abd-Elgawad**
orcid.org/0000-0002-4731-5988
National Research Centre
Egypt
Sections: Agriculture - Plants, Pathology
Classifications: Pesticides, Agriculture, Integrated control, Pest control, Biology and life sciences

- **Yasmina Abd-Elhakim**
orcid.org/0000-0002-3646-6385
Zagazig University
Egypt
Sections: Pharmacology, Pollution research and control, Toxicology
Classifications: Immunology, Toxicology, Animal studies, Research and analysis methods, Aquatic environments, Pharmacology, Chromatographic techniques, Pharmaceutics, Medicine and health sciences, Ecology and environmental sciences, Agriculture, Veterinary science, Biology and life sciences

- **Mohamed Ezzat Abd El-Hack**
orcid.org/0000-0002-2831-8534
Zagazig University Faculty of Agriculture
Egypt
Sections: Nutrition, Veterinary science
Classifications: Agriculture, Nutrition, Zoology, Biology and life sciences

- **Hassan Abdalla**
orcid.org/0000-0001-7955-955X
University of Udine
Italy
Sections: Engineering and technology - Systems science and computational engineering, Materials science - Structural materials
Classifications: Materials science, Stiffness, Simulation and modeling, Elasticity, Composite materials, Physical sciences, Material properties, Mathematical modeling, Research and analysis methods, Mechanical properties, Materials

- **Mena Abdalla**
King's College Hospital NHS Foundation Trust

United Kingdom of Great Britain and Northern Ireland
Sections: Health care - Health services research, Obstetrics and gynecology, Women's and maternal health
Classifications: Stillbirths, Menstrual abnormalities, Female subfertility, Gynecologic cancers, Pregnancy, Pregnancy complications, Gynecologic infections, Birth, Antenatal care, Maternal health, Management of high-risk pregnancies, Obstetrics and gynecology, Contraception, Hypertensive disorders in pregnancy, Women's health, Maternal mortality, Termination of pregnancy, Chorioamnionitis, Gynecologic diseases, Medicine and health sciences, Assisted reproductive technology

- **Mervat A. Abdel-Latif**
orcid.org/0000-0002-7996-0121
Damanhour University Faculty of Veterinary Medicine
Egypt
Sections: Agriculture - Animals, Nutrition
Classifications: Nutritional deficiencies, Carbohydrate metabolism, Amino acid metabolism, Nutrients, Nutritional diseases, Animal management, Biology and life sciences, Agriculture, Micronutrient deficiencies, Antioxidants, Animal performance, Vitamin D deficiency, Metabolism, Iron deficiency, Animal production, Biochemistry, Nutrition

- **Muhammad Abdel-Gawad**
orcid.org/0000-0002-0204-4715
Al-Azhar University
Egypt
Sections: Gastroenterology and hepatology, Infectious diseases - Hepatitis
Classifications: Pancreatitis, Zollinger-Ellison syndrome, Splenomegaly, Colitis, Diarrhea, Primary biliary cirrhosis, Megacolon, Fatty liver, Liver function tests, Barrett's esophagus, Cholelithiasis, Hepatomegaly, Inflammatory bowel disease, Medicine and health sciences, Peptic ulcer disease, Alcoholic liver disease, Liver diseases, Gastrointestinal infections, Acute liver failure, Autoimmune hepatitis, Primary sclerosing cholangitis, Celiac disease, Wilson's disease, Enteropathies, Gastroesophageal reflux disease, Hemochromatosis, Liver disease and pregnancy, Hepatocellular carcinoma, Nonalcoholic steatohepatitis, Liver fibrosis, Hepatosplenomegaly, Ascites, Portal hypertension, Infectious hepatitis, Cholecystitis and biliary colic, Constipation, Gastroenterology and hepatology, Gastrointestinal cancers, Chronic liver disease, Dysentery, Cirrhosis, Crohn's disease, Biliary disorders

- **Ahmed E. Abdel Moneim**
  orcid.org/0000-0002-2654-2591
  Capital University
  Egypt
  Sections: Molecular biology, Neuroscience - General, Toxicology
  Classifications: Histology, Biochemistry, Neuroscience, Toxicology, Immunology, Biology and life sciences

- **Shady H.E. Abdel Aleem**
  orcid.org/0000-0003-2546-6352
  Institute of Aviation Engineering and Technology
  Egypt
  Sections: Engineering and technology - General, Engineering and technology - Systems science and computational engineering, Science education
  Classifications: Energy and power, Engineering and technology, Power engineering, Electrical circuits, Electrical engineering, Electrical faults

- **Muhammad Tarek Abdel Ghafar**
  orcid.org/0000-0002-0621-4291
  Tanta University Faculty of Medicine
  Egypt
  Sections: Cancer - Biomarkers, molecular diagnostics and screening, Cancer - Immunotherapy and tumor immunology, Genetics - Gene expression; Epigenetics; Alternative splicing; RNA splicing; Molecular genetics
  Classifications: Clinical medicine, Genetic causes of cancer, Medicine and health sciences, Endocrinology, Hematology, Molecular epidemiology, Clinical genetics, Epidemiology, Diagnostic medicine, Clinical immunology, Genetics of the immune system, Oncology, Cancer epidemiology, Pathology and laboratory medicine, Genetic epidemiology, Biomarker epidemiology, Autoimmunity, Cancer risk factors, Immunology

- **Ahmed S. Abdel-Moneim**
  orcid.org/0000-0002-3148-6782
  Sultan Qaboos University
  Oman
  Sections: Infectious diseases - Viral diseases, Microbiology - Virology, Virology
  Classifications: Zoonoses, Microbial pathogens, SARS coronavirus, Infectious diseases, Medicine and health sciences, Viral evolution, Influenza viruses, Emerging viral diseases, Viral diseases, Microbiology, Medical microbiology, Avian influenza, Influenza, SARS, Orthomyxoviruses, Viral genetics, Viral disease diagnosis, Viral pathogens, Virology,

Pathogens, Respiratory infections, Pathology and laboratory medicine, Coronaviruses, Pulmonology, Biology and life sciences

- **Abdelaziz Abdelaal**
orcid.org/0000-0003-3787-5970
Harvard Medical School
Egypt
Sections: Ear, nose and throat (ENT), Ophthalmology, Public health and epidemiology - Biostatistics and methods
Classifications: Research assessment, Urology, Endocrinology, Mental health and psychiatry, Medicine and health sciences, Ophthalmology, Cardiovascular medicine, Hematology, Imaging techniques, Pediatrics, Critical care and emergency medicine, Scientific publishing, Infectious diseases, Vascular medicine, Health care, Research and analysis methods, Cardiology, Pathology and laboratory medicine, Research design, Otorhinolaryngology, Nephrology, Pain management, Complementary and alternative medicine, Clinical medicine, Neurology, Epidemiology, Anesthesiology

- **Tarek Samy Abdelaziz**
orcid.org/0000-0002-1238-1045
Cairo University Kasralainy Faculty of Medicine
Egypt
Sections: Nephrology, Research assessment
Classifications: Nephrology, Medicine and health sciences

- **Hala Abdelmoneim Abdallah Abdelgaffar**
orcid.org/0000-0002-5746-6624
KIMEP University
Kazakhstan
Sections: Management science
Classifications: Refugees, Sexual harassment, Egypt, Employment, Education, Universities, Qualitative studies, Sustainability science, Careers

- **Amr Mohamed Abdelghany**
orcid.org/0000-0001-8953-0056
National Research Centre (NRC)
Egypt
Sections: Biophysics, Materials science - General, Physics and astronomy - Applied physics
Classifications: Spectrum analysis techniques, Physics, Materials characterization, States

of matter, Research and analysis methods, Materials physics, Computational techniques, Biophysics, Physical sciences, Materials science, Chemical characterization

- **Islam Abdeljawad**
orcid.org/0000-0003-2625-698X
An-Najah National University
Palestine, State of
Sections: Economics - Econometrics, Economics - Financial, Economics - General
Classifications: Futures markets, Insurance markets, Cost-benefit analysis, Cost-minimization analysis, Economics, Finance, Money markets, Cost-effectiveness analysis, Economic analysis, Financial management, Financial markets, Derivatives markets, Social sciences, Capital markets

- **Mohamed Abdelkarim**
orcid.org/0000-0002-0984-6083
Faculty of Medicine of Tunis
Tunisia
Sections: Cancer - Basic cancer research, Cancer - Biomarkers, molecular diagnostics and screening, Cell biology - General
Classifications: Metastasis, Oncology, Medicine and health sciences, Basic cancer research

- **Elsayed Abdelkreem**
orcid.org/0000-0002-8976-2989
Sohag University Faculty of Medicine
Egypt
Sections: Clinical trials, Genetics - Mutation; Genetics of disease; Heredity, Pediatrics
Classifications: Pediatric critical care, Tay-Sachs disease, Neonatal care, Autosomal recessive diseases, Congenital adrenal hyperplasia, Phenylketonuria, Sickle cell disease, Inborn errors of metabolism, Medicine and health sciences, Gaucher's disease, Developmental and pediatric neurology, Galactosemia, Child abuse, Pediatrics, Congenital disorders, Wilson's disease, Neonatology, Cystic fibrosis, Niemann-Pick disease, Clinical genetics, Glycogen storage diseases, Mucopolysaccharidoses, Chromosomal disorders, Genetic diseases, Metabolic disorders

- **Gaber Abdellrazeq**
orcid.org/0000-0002-8677-911X
Washington State University College of Veterinary Medicine
United States of America

Sections: Immunology - Immunity, Veterinary science
Classifications: Microbiology, Veterinary science, Biology and life sciences, Immunology

- **Elabbass Abdelmahmuod**
  orcid.org/0000-0001-9330-5740
  Hamad Medical Corporation
  Qatar
  Sections: Endocrinology - Cancer, Endocrinology - Diabetes and obesity, Endocrinology - General
  Classifications: Tuberculosis, Celiac disease, Thrombosis, Kidneys, Respiratory infections, Abscesses, Diabetes mellitus, COVID 19, Lymphoma, Anticoagulant therapy, Antibodies, Biopsy

- **Antoine Fakhry AbdelMassih**
  orcid.org/0000-0001-8876-3229
  Cairo University Kasralainy Faculty of Medicine
  Egypt
  Sections: Cardiovascular science and medicine - Interventional cardiology and cardiovascular surgery, Pediatrics
  Classifications: Pediatrics, Epidemiology, Medicine and health sciences, Cardiology

- **Sameh Abdelnour**
  orcid.org/0000-0002-6873-0718
  Zagazig University Faculty of Agriculture
  Egypt
  Sections: Agriculture - Animals, Reproductive biology
  Classifications: Developmental biology, Biology and life sciences, Cryobiology, Veterinary science

- **Mohammed Abdelsamea**
  orcid.org/0000-0002-2728-1127
  University of Exeter
  United Kingdom of Great Britain and Northern Ireland
  Sections: Computer and information sciences - Artificial intelligence, machine learning and data science, Computer and information sciences - Human-Computer interactions
  Classifications: Machine learning, Translational medicine, Medicine and health sciences, Neural networks, Expert systems, Diagnostic medicine, Cancer screening, Computer vision, Computer aided diagnosis, Computer-aided design, Artificial intelligence, Biology and life sciences, Computer applications, Cancer detection and diagnosis, Target

detection, Computer and information sciences, Computational neuroscience, Digital imaging, Computational biology, Artificial neural networks

- **Nourtan F. Abdeltawab**
orcid.org/0000-0002-1290-2197
Cairo University Faculty of Pharmacy
Egypt
Sections: Complementary and alternative medicine, Immunology - General, Microbiology - Host-pathogen interactions
Classifications: Taxonomy, Mammalian genetics, Immunology, Systems biology, Clinical immunology, Reverse genetics, Medicine and health sciences, Molecular biology techniques, Infectious disease immunology, Research and analysis methods, Complementary and alternative medicine, Animal genetics, Bacteriology, Phylogenetics, Database and informatics methods, Inflammatory diseases, Microbiology, Evolutionary systematics, Genetics of the immune system, Genetics, Clinical medicine, Bioinformatics, Molecular biology, Genetics of disease, Molecular genetics, Bacterial genetics, Microbial genetics, Infectious diseases, Biology and life sciences, Biochemistry

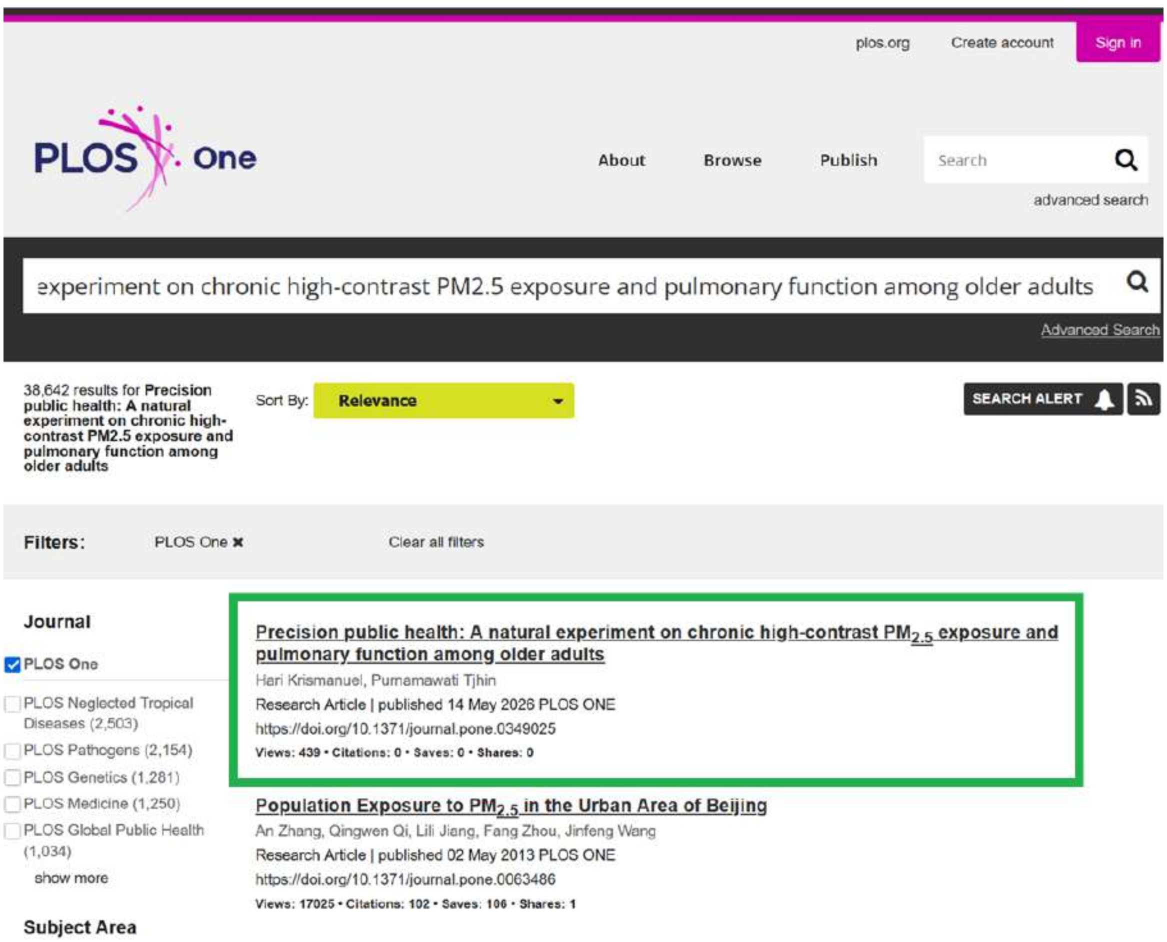
- **Zhaleh Abdi**
Tehran University of Medical Sciences
Iran, Islamic Republic of
Sections: Health care - Health policy, Health care - Health services research, Public health and epidemiology - Health policies, systems and management
Classifications: Health care, Nutrition, Medicine and health sciences, Health care providers

- **Ibrahim Abdollahpour**
orcid.org/0000-0002-8607-4507
Isfahan University of Medical Sciences
Iran, Islamic Republic of
Sections: Health care - General, Neuroscience - General, Public health and epidemiology - General
Classifications: Research and analysis methods, Public and occupational health, Nutrition, Open methodology, Biology and life sciences, Research design, Neuroscience, Medicine and health sciences, Epidemiology, Pediatrics, Neurology, Clinical trials

- **Ahmed Abdou**
orcid.org/0000-0002-4830-4594
Universiti Malaya
Malaysia

Sections: Dentistry and oral health, Health care - General
Classifications: Medicine and health sciences, Oral medicine, Dentistry

- **George Kuryan**
  orcid.org/0000-0002-9322-2918
  Christian Medical College
  India
  Sections: Cardiovascular science and medicine - General, Public health and epidemiology - Biostatistics and methods, Women's and maternal health
  Classifications: Spirometry, Labor and delivery, India, HIV, Malnutrition, Chronic obstructive pulmonary disease, Tamil people, HIV epidemiology, Medical risk factors, Diabetes mellitus, Cardiovascular disease risk, Alcohol consumption



Medicine and health sciences (36,355)
Biology and life sciences (35,021)
Research and analysis methods (16,811)
Medical conditions (14,838)
Social sciences (14,444)
show more

Article Type

Research Article (37,722)
Study Protocol (810)
Registered Report Protocol (47)
Lab Protocol (21)
Collection Review (15)
show more

Author

Wei Wang (57)
Wei Zhang (53)
Thorkild I A Sørensen (40)
Ying Zhang (37)
Li Li (31)
show more

Where my keywords appear

Body (25,251)
Results and Discussion (4,287)
References (3,721)

Respiratory health and chronic disease risks in residents of agricultural areas in Chiang Mai, Northern Thailand

Anurak Wongta, Supansa Pata, Kriangkrai Chawansuntati, Supachai Yodkeeree, Surat Hongsibsong, Wootichai Khamduang

Research Article | published 04 Apr 2025 PLOS ONE

https://doi.org/10.1371/journal.pone.0321471

Views: 1241 • Citations: 4 • Saves: 0 • Shares: 0

Impact of acute temperature and air pollution exposures on adult lung function: A panel study of asthmatics

Richard Evoy, Laurel Kincl, Diana Rohlman, Lisa M. Bramer, Holly M. Dixon, Perry Hystad, Harold Bae, Michael Barton, Aaron Phillips, Rachel L. Miller, Katrina M. Waters, Julie B. Herbstman, Kim A. Anderson

Research Article | published 28 Jun 2022 PLOS ONE

https://doi.org/10.1371/journal.pone.0270412

Views: 2134 • Citations: 9 • Saves: 16 • Shares: 2

Consequences of exposure to pollutants on respiratory health: From genetic correlations to causal relationships

Salvatore D'Antona, Isabella Castiglioni, Danilo Porro, Claudia Cava

Research Article | published 17 Nov 2022 PLOS ONE

https://doi.org/10.1371/journal.pone.0277235

Views: 1768 • Citations: 4 • Saves: 13 • Shares: 1

Study on the impact of smart city construction on the health of the elderly population——A quasi-natural experiment in China

Juqiu Deng, Dong Yao, Yue Deng, Zhenyu Liu, Jiayu Yang, Dezhao Gong

Research Article | published 21 Jun 2024 PLOS ONE

https://doi.org/10.1371/journal.pone.0305897

Views: 2566 • Citations: 5 • Saves: 0 • Shares: 0

Associations between ambient particulate matter exposure and the prevalence of arthritis: Findings from the China Health and Retirement Longitudinal Study

Yuntian Ye, Kuizhi Ma, Aifeng Liu

Research Article | published 08 Jul 2025 PLOS ONE

https://doi.org/10.1371/journal.pone.0327695

Views: 1508 • Citations: 2 • Saves: 6 • Shares: 6

Introduction (644)

Materials and Methods (607)

show more

Publication Date

to

Apply

Acute and Chronic Effects of Particles on Hospital Admissions in New-England

Itai Kloog, Brent A. Coull, Antonella Zanobetti, Petros Koutrakis, Joel D. Schwartz

Research Article | published 17 Apr 2012 PLOS ONE

https://doi.org/10.1371/journal.pone.0034664

Views: 12144 • Citations: 160 • Saves: 177 • Shares: 1

Estimation of health-related and economic impacts of $PM_{2.5}$ in Arak, Iran, using BenMAP-CE

Maryam Salehi, Amir Almasi Hashiani, Behrooz Karimi, Seyed Hamed Mirhoseini

Research Article | published 21 Dec 2023 PLOS ONE

https://doi.org/10.1371/journal.pone.0295676

Views: 1886 • Citations: 11 • Saves: 0 • Shares: 0

Analysis of PM-bound polycyclic aromatic hydrocarbons exposure among motorcycle taxi drivers in six central provinces in Thailand in winter

Kamonwan Samana, Kimihito Ito, Orasa Suthienkul, Arroon Ketsakorn

Research Article | published 01 Dec 2025 PLOS ONE

https://doi.org/10.1371/journal.pone.0336587

Views: 882 • Citations: 0 • Saves: 6 • Shares: 0

Association between long-term exposure to artificial light at night and air pollution, and cardiovascular diseases in middle-aged and older adults

Zhenzhou Liu, Xiayan Zang, Huan Li, Yingying Fan, Yujing Sun, Chi Yan, Nan Feng, Derong Guo, Jiantao Si, Pengkun Yang, Ye Zhu, Zhigang Chen, Yemin Wang

Research Article | published 05 Mar 2026 PLOS ONE

https://doi.org/10.1371/journal.pone.0338457

Views: 725 • Citations: 0 • Saves: 1 • Shares: 1

The effect of air pollution on catastrophic health expenditure among middle-aged and older adults in China

Huan He, Xuanhan Li, Lanxi Peng

Research Article | published 21 Apr 2026 PLOS ONE

https://doi.org/10.1371/journal.pone.0347317

Views: 610 • Citations: 0 • Saves: 0 • Shares: 0

Scopus Preview

Author Search Sources

Sources

Title Enter title Find sources

Title: PLOS ONE ×

CiteScore 2025 has been released. View CiteScore methodology >

Filter refine list

Apply Clear filters

Display options

Display only Open Access journals

Counts for 4-year timeframe

No minimum selected

Minimum citations

Minimum documents

Citescore highest quartile

Show only titles in top 10 percent

1st quartile

2nd quartile

3rd quartile

4th quartile

1 result

Download Scopus Source List · Learn more about Scopus Source List

All · Export to Excel · Save to source list · View metrics for year: 2025

	Source title	CiteScore	Highest percentile	Citations 2022-25	Documents 2022-25	% Cited
1	PLOS ONE Open Access	4.8	83% 38/223	309,034	64,611	72

^ Top of page

PLOS ONE

United States | Universities and research institutions | Media Ranking

Country

United States

SCIMAGO INSTITUTIONS RANKINGS

SCImago Media Rankings

Subject Area and Category

Multidisciplinary

Multidisciplinary

Publisher

Public Library of Science

SJR 2025

0.726 Q1

H-Index

500

Publication type

Journals

ISSN

19326203

Coverage

2006-2026

RESEARCH ARTICLE

Precision public health: A natural experiment on chronic high-contrast $PM_{2.5}$ exposure and pulmonary function among older adults

Hari Krismanuel*, **Purnamawati Tjhin**

Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia

* hari_krismanuel@trisakti.ac.id

Abstract

Background: While **fine particulate matter** (**$PM_{2.5}$**) is a respiratory hazard, most studies lack the temporal depth to distinguish chronic from acute effects, particularly among vulnerable older adults. This **natural experiment study employs with a 10-year stable residency filter.** To our knowledge, it is among the first in Southeast Asia to evaluate the decadal impact of $PM_{2.5}$ exposure on highly selected healthy older adults. Utilizing a Precision Public Health (PPH) framework, we provide **regional evidence in Southeast Asia** to integrate a **quasi-longitudinal approach** for isolating chronic respiratory effects using **standardized lung function** (**GLI 2012 – z-scores, adjusted for Southeast Asian populations**). **Methods:** We conducted a natural experiment involving 101 non-smoking older adults (65–80 years; normal BMI) in Indonesia. This design compared populations with **≥10-year residency** in **contrasting environments**: high-exposure urban (Kedoya) and low-exposure rural (Pangalengan). The decadal filter ensured **temporal precedence**. Spirometry included internal **BTPS (Body Temperature, Ambient Pressure, Saturated with water vapor)** compensation. **Multivariable linear regression** evaluated the association between exposure and Z-scores, adjusting for demographic and lifestyle covariates. **Results: High-exposure participants had significantly lower FEV_1_z and FVC_z than the low-exposure group, with no significant difference in FEV_1/FVC_z. Multivariable regression confirmed exposure group was the only independent predictor for FEV_1_z ($\beta = -1.42$, $p < 0.001$) and FVC_z ($\beta = -1.14$, $p < 0.001$), after adjusting for covariates. These findings indicate a subclinical reduction in lung volumes consistent with a non-obstructive, restrictive spirometric pattern.** Diagnostic testing indicated no violation of model assumptions was detected. **Conclusions:** High decadal $PM_{2.5}$ exposure is associated with significant standardized lung volume reductions. The 10-year residency stability criterion **enhances causal inference**. These findings advocate PPH approach, highlight the importance of z-score–based spirometric screening for early detection of **subclinical pollution-related lung function decline.** Integrating environmental risk assessment

Citation: Krismanuel H, Tjhin P (2026) Precision public health: A natural experiment on chronic high-contrast $PM_{2.5}$ exposure and pulmonary function among older adults. PLoS One 21(5): e0349025. https://doi.org/10.1371/journal.pone.0349025

Editor: George Kuryan, Christian Medical College, INDIA

Received: January 30, 2026

Accepted: April 23, 2026

Published: May 14, 2026

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0349025

Data availability statement: All relevant data are within the manuscript and its Supporting information files.

Funding: The author(s) received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

into geriatric care and air quality management offers a cost-effective pathway to mitigate long-term healthcare burdens in megacities.

Introduction

Ambient air pollution, particularly fine particulate matter ($PM_{2.5}$), remains one of the leading environmental risk factors for morbidity and mortality worldwide [1–5]. $PM_{2.5}$ can penetrate deep into the distal airways, triggering inflammation, oxidative stress, and structural changes that contribute to impaired pulmonary function [1,3,6–9]. Older adults are especially vulnerable due to age-related physiological decline, higher prevalence of comorbidities, and reduced capacity to respond to environmental stressors [7,10,11]. **This heightened susceptibility underscores the need for a PPH approach, which moves beyond population-wide averages to focus on tailored promotive and preventive strategies for highly vulnerable subgroups** [12–14]. In this context, identifying individuals in the **'subclinical window'**—a **critical period** where physiological decline begins due to environmental stressors but has not yet manifested as overt disease—is essential for transitioning from reactive healthcare to proactive primary prevention.

Despite extensive evidence linking $PM_{2.5}$ exposure with adverse respiratory outcomes, the majority of epidemiological research has focused on children or middle-aged adults [4,8]. Studies involving older adults—who bear a disproportionate burden of air-pollution-related disease—remain relatively scarce, particularly in low- and middle-income countries (LMICs) (2,6,10). Moreover, data from cities with extremely high ambient $PM_{2.5}$ levels are limited, restricting our understanding of how chronic exposure affects lung function in the most heavily polluted urban environments [3,6–9]. This lack of data is critical, **as it hinders the development of targeted preventive interventions tailored to the older adults, whose physiological response to extreme pollution may differ significantly from documented patterns in younger cohorts** [10].

Jakarta has repeatedly ranked among the most polluted major cities globally, with annual $PM_{2.5}$ concentrations far exceeding WHO guidelines [2,15]. However, substantial variation in $PM_{2.5}$ levels exists across districts, driven primarily by high-volume traffic emissions and localized urban construction projects [15,16]. This provides a unique opportunity to employ a **natural experiment framework** [17–20]. **Utilizing such high-contrast environmental gradients allows for a more granular understanding of how localized exposure impacts specific demographics. Such evidence is foundational for designing targeted health promotion programs and provides stronger evidence than conventional cross-sectional designs, thereby supporting evidence-informed policy-making.** Unlike standard cross-sectional studies that often lack the temporal depth to establish causal links, this study utilizes the extreme pollution contrast between two distinct regions as a **quasi-gold standard** for environmental observation [17–20]. By enforcing a strict **10-year minimum residency requirement**, we introduce a **quasi-longitudinal perspective** [21,22] that minimizes common pitfalls such as exposure misclassification and reverse causality, effectively **bridging the ethical and methodological gap** between observational surveys and randomized trials.

To our knowledge, **few studies have evaluated the chronic impact of extreme ambient $PM_{2.5}$ on highly selected healthy older adults using a 10-year stable residency filter within a natural experiment framework.** Furthermore, it applies a quasi-longitudinal approach, providing unique evidence from one of the world's most polluted megacities to **inform evidence-based preventive measures**. To address this evidence gap, we conducted a **natural experiment framework** to compare lung function, expressed as Global Lung Initiative (GLI) z-scores [23,24], between older adult residents of two areas with distinctly different annual $PM_{2.5}$ levels. Our methodology leverages this **environmental contrast** to ensure that the measured lung function **reflects long-term, cumulative impacts** rather than short-term environmental variation. Furthermore, the use of standardized spirometric z-scores (GLI-2012) specifically adjusted for Southeast Asian ethnicity allows for a detailed assessment of the aging lung in this region. **This methodological precision is essential for ensuring that clinical assessments are ethnically and age-appropriately accurate, thereby avoiding the misdiagnosis common in generalized respiratory models and improving the efficacy of primary prevention. By integrating high-resolution environmental data with precise clinical metrics, this study exemplifies the PPH mandate to transform big-data environmental monitoring into actionable, individualized clinical protection.**

The primary research questions were: (1) whether long-term exposure drives lower FEV_1 and FVC z-scores among older adults; and (2) whether exposure leads to significant differences in FEV_1/FVC z-scores. Drawing from toxicological evidence that chronic $PM_{2.5}$ exposure induces deep alveolar inflammation and systemic oxidative stress, which typically manifests as parenchymal stiffening rather than primary airway obstruction in asymptomatic cohorts, we hypothesized that older adult individuals living in the higher-exposure area would exhibit lower lung volumes (FEV_1_z and FVC_z) without overt airflow obstruction, reflecting a subclinical restrictive-like decline, with less pronounced differences in the FEV_1/FVC ratio. These findings are expected to provide the granular evidence necessary for **developing robust promotive and preventive public health strategies for aging urban populations.**

Methods

Study design

We employed **a natural experiment using a quasi-longitudinal approach** to compare lung function among older adults residing in two areas with markedly different long-term ambient exposure levels. **This design—often regarded as a quasi-gold standard for evaluating environmental exposures—was specifically chosen to bridge the ethical gap where a Randomized Controlled Trial (RCT) is impossible** [25–27]. The substantial between-area variation in levels serves as **an exogenous proxy for random assignment,** allowing for **a population-level comparison that minimizes selection bias. By utilizing these extreme environmental gradients, we created a 'quasi-experimental' condition that enhanced causal inference within the constraints of an observational design while maintaining real-world translational relevance. This design facilitates a granular assessment of environmental impact by moving beyond population-wide averages to evaluate how specific, localized environmental stressors impact a highly vulnerable sub-population.**

To strengthen the quasi-longitudinal perspective of this design, we enforced **a strict 10-year minimum residency requirement** for all participants**. This residency threshold ensures that the measured lung function reflects the cumulative, long-term impact of chronic exposure rather than acute environmental shifts.** By establishing **the necessary temporal precedence,** this **approach also significantly reduces the risk of reverse causality** often found in standard cross-sectional studies.

To our knowledge, this is the first study to utilize such a decadal exposure filter within a natural experiment to assess strictly selected older adults cohort in a high-pollution megacity.

The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplementary Materials), [28,29] to ensure transparent reporting. The completed STROBE checklist is available in the Figshare repository at https://doi.org/10.6084/m9.figshare.31659970. By comparing two geographically distinct populations that are socio-demographically similar but environmentally contrasted, we effectively utilized this **"natural contrast"** to assess the chronic impact of particulate matter on the aging lung while **minimizing confounding** through **strict eligibility criteria** and **frequency matching.**

Study setting and site selection

The study utilized a two-tiered exposure assessment strategy—a two-stage hybrid approach—to characterize exposure and select research sites by combining macro-level secondary data with micro-level direct environmental sampling. This methodology was employed to ensure a high-contrast exposure gradient while validating area-specific concentrations through ground-truthing [30]. In the first stage (Macro-level Mapping), preliminary mapping was conducted using secondary data from government air quality monitoring stations across the Jakarta and Bandung metropolitan areas to identify regions with the highest and lowest historical levels.

This was followed by a second stage of primary validation (Micro-level Direct Measurement) to capture real-time, area-specific concentrations and minimize the risk of ecological fallacy. Three specific districts within the candidate regions of Jakarta and Bandung were selected for direct on-site monitoring to validate actual ambient conditions within residential neighborhoods. This granular validation is a cornerstone of targeted environmental health surveillance, ensuring that the exposure contrast is not merely assumed from distant monitoring stations but verified at the residential level, thereby reducing exposure misclassification. Based on the synthesis of these multi-level data points, Kedoya (Jakarta) was confirmed as the high-exposure location and Pangalengan (Bandung Regency) as the lower-exposure location. Participants were subsequently assigned to exposure categories using an area-level proxy that reflected the validated chronic ambient conditions of their primary residence.

Sample size determination

An a priori minimum sample size of 34 participants per group was estimated using a **two-sample comparison of means**, assuming a significance level of $\alpha = 0.01$ and 95% power [27–29,31]. This calculation employed the standard formula for comparing two independent means:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 . 2\sigma^2}{(\mu_1 - \mu_2)^2}$$

Where:

- n: Minimum sample size required per group.
- $Z_{\alpha/2}$: The Z-score corresponding to the two-tailed significance level ($\alpha = 0.01$, $Z_{\alpha/2} \approx 2.58$).
- Z_{β}: The Z-score corresponding to the desired power ($1 - \beta = 0.95$, $Z_{\beta} \approx 1.64$).
- $\mu 1 - \mu 2$: The expected minimum mean difference between the high- and low-exposure groups.
- σ: The population standard deviation of the outcome variable (FEV_1_z).

The power calculation was based on an expected mean difference in FEV_1_z-scores ($\mu 1 - \mu 2$) of 0.8 units (assuming a standard deviation (σ) of 1.0), derived from previous similar epidemiological studies on air pollution effects in older adults. To account for potential exclusions, invalid spirometry, and data loss, the recruitment target was increased to at least 60 participants per group [27,31].

Participants recruitment and eligibility

Data collection was conducted on **May 31, 2025** and **June 14, 2025** across two districts representing high (Kedoya) and low (Pangalengan) exposure gradients. To enhance internal validity and minimize variability in major confounding factors, participants were selected through a multi-layered screening process designed to ensure that observed differences in lung function were primarily attributable to ambient exposure rather than individual health histories or lifestyle choices. This 'ultrapure' cohort selection serves a translational purpose; by isolating the impact of exposure from other major confounders, the findings provide clear, actionable evidence for clinical guidelines and public health protection for the older adults.

Eligibility was determined based on strict inclusion and exclusion criteria. Participants were **included** if they were aged between 65 and 80 years and had maintained permanent residence at their current address for at least ten continuous years. This decadal residency criterion is crucial to ensure that the measured lung function reflects the long-term, cumulative impact of chronic exposure rather than acute environmental changes, effectively establishing a retrospective temporal order between exposure and outcome. Additionally, candidates were required to demonstrate the willingness and physical ability to undergo standardized spirometry and structured interviews, and must fall within the normal Body Mass Index (BMI) range (18.5–22.9 kg/m^2) as defined by the WHO classification for Asian populations [32,33]. This BMI restriction was applied to exclude the potential restrictive effects of obesity on lung expansion [34,35].

To further minimize confounding bias, several **exclusion criteria** were rigorously applied. Individuals were excluded if they were current or former active smokers or had significant daily exposure to passive smoking. Potential participants with a known history of chronic respiratory diseases—including COPD, pulmonary fibrosis, uncontrolled asthma, or history of pulmonary tuberculosis—were also excluded, as were those with recent acute respiratory tract infections within the preceding four weeks. Furthermore, the study excluded individuals with severe cardiovascular or systemic conditions, lung cancer, or neuromuscular and cognitive impairments that could interfere with spirometry validity or the ability to follow instructions. Finally, to isolate ambient as the primary factor, individuals with significant occupational exposure to industrial dust, biomass smoke, or chemical irritants, as well as those with communication barriers such as illiteracy, were not included in the final cohort.

Sampling and final sample

The recruitment and selection process followed a systematic two-stage sampling approach to ensure a high-quality, comparable study population (See Fig 1 – STROBE Flowchart). In the first stage (area level), purposive selection was used to identify regions and specific sites (Kedoya and Pangalengan) with extreme contrast through macro-monitoring and ground-truthing. In the second stage (individual level), a sampling frame of 245 potential candidates was established through registries at community health posts (Posbindu). These candidates underwent preliminary pre-screening to verify basic eligibility based on age (65–80 years), never-smoking status, and a 10-year stable residency requirement.

From this registry, a stratified random sampling procedure was employed to invite 60 candidates from each site (total $n = 120$) for formal clinical assessment to minimize selection bias. A total of 123 individuals attended the clinical phase (68 from Kedoya and 55 from Pangalengan). These candidates underwent a rigorous one-day comprehensive clinical screening, comprising structured interviews, physical examinations, and Electrocardiography (ECG) to rule out cardiovascular abnormalities. To enhance comparability and neutralize potential confounders—such as age, gender, education level, and occupation—a frequency matching procedure was applied. After strictly adhering to the ATS/ERS 2019 quality standards for spirometry [36], the final analytical sample consisted of 101 participants (54 from the higher-exposure area and 47 from the lower-exposure area).

Research variables and operational definitions

This study involved several key variables classified into independent, dependent, and covariate variables. The independent variable was the level of chronic fine particulate matter ($PM_{2.5}$) exposure, represented by the participants' residential

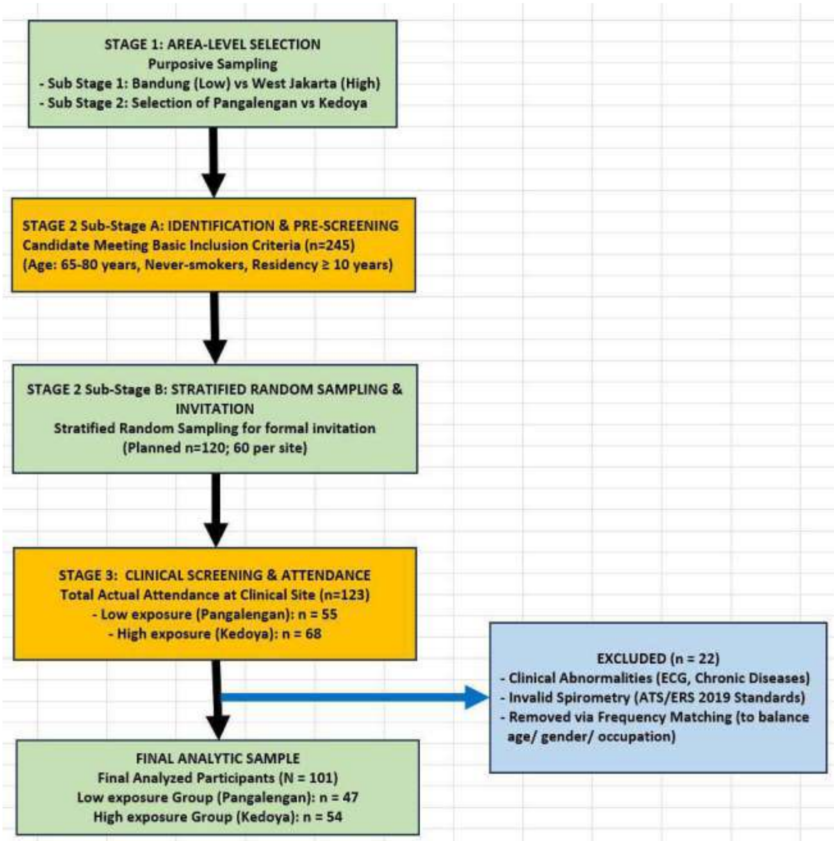


Fig 1. STROBE Flowchart of the two-stage sampling and participant selection process. The diagram illustrates the recruitment stages: Stage 1 (Area-level) involved purposive site selection (Sub-Stages 1–2), and Stage 2 (individual-level) involved participant identification, pre-screening, stratified random sampling for formal invitation. The final analytical sample was established after clinical validation, strict adherence to ATS/ERS 2019 standards, and frequency matching to ensure healthy, comparable groups.

https://doi.org/10.1371/journal.pone.0349025.g001

location, with the Kedoya area categorized as high exposure and Pangalengan as low exposure. A primary focus of this study was the assessment of lung function as a continuous physiological measure rather than a binary clinical diagnosis. This approach increases statistical power and allows for the detection of subclinical declines in respiratory health, facilitating proactive primary prevention by identifying 'at-risk' individuals before overt clinical disease manifests.

The primary outcomes were lung function indices expressed as FEV1 and FVC z-scores, calculated using the Global Lung Initiative (GLI) 2012 Southeast Asian reference equations to account for age, sex, and height. Analyzing these as continuous variables enables the detection of subtle, dose-dependent shifts in lung function associated with chronic exposure. Secondary outcomes included the FEV_1/FVC z-score and the prevalence of lung function impairment.

Participants were classified based on the Lower Limit of Normal (LLN), defined as a z-score threshold of −1.645. Clinical airflow obstruction was identified by an FEV1/FVC z-score below this threshold. Conversely, participants with an FEV_1/FVC z-score ≥ −1.645 accompanied by reduced FEV_1 and/or FVC z-scores below −1.645 were classified as having a non-obstructive spirometric impairment, characterized by reduced lung volumes with a preserved ratio. This z-score–based approach provides a more precise classification for our older adult cohort than fixed percentage thresholds by effectively accounting for age-related physiological changes and enhancing the detection of early, subclinical lung function impairment [36].

Covariate variables were collected for descriptive analysis, frequency matching, and statistical adjustment. These included age (years), gender (male or female), and height (cm). Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). In accordance with the inclusion criteria, all participants were within the WHO-defined normal range for Asian populations. BMI served both for frequency matching and as a covariate in multivariable models, with an independent sample t-test confirming no statistically significant difference in mean BMI between the two exposure groups to ensure baseline comparability of nutritional status. Socioeconomic status (SES) was captured through education level—categorized into low (no schooling/primary), middle (junior/senior high), and higher education (diploma/degree)—and occupation, which was grouped ordinally into three levels: (1) unemployed, laborer, farmer, or small trader; (2) employee; and (3) professional.

Research instruments

Data collection was facilitated through a suite of validated instruments designed to capture demographic, socioeconomic, and physiological variables. A pre-tested structured questionnaire was utilized to gather respondent identity, socioeconomic status (including education and occupation), and a detailed 10-year residency history. To ensure the 'ultrapure' nature of the cohort, the questionnaire also screened for histories of chronic or acute lung diseases and environmental confounding factors, such as passive smoking and biomass exposure. All measurements were recorded on a standardized observation sheet, which included height measurements taken with a calibrated stadiometer to the nearest centimeter. Ethical adherence was documented through signed informed consent forms, which were obtained after participants received comprehensive information regarding the study's objectives and procedures.

Pulmonary function was assessed using a portable digital spirometer to measure Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), and the FEV_1/FVC ratio. The device maintained a volume accuracy of 3% and a flow range of 0–16 L/s, with calibration performed before each session to ensure data integrity. All measurements were conducted by trained personnel in strict accordance with the American Thoracic Society/European Respiratory Society (ATS/ERS) standards. Participants received standardized instructions and demonstrations prior to the examination, with maneuvers repeated until at least two consistent, high-quality results were obtained. To further validate site conditions and technical reporting, visual documentation was utilized for location-specific field notes and activity verification, while strictly maintaining participant anonymity.

Data collection methods

Data collection was conducted directly at the two research locations by a trained survey team comprising enumerators, medical personnel, and field coordinators. The fieldwork utilized standardized procedures and instruments, beginning with a community-based recruitment process. After passing initial pre-screening and prior to any clinical procedures, participants received a comprehensive explanation of the study and provided written informed consent. Face-to-face interviews were then conducted using a piloted structured questionnaire to collect demographic data, socioeconomic factors, residency history, and detailed medical histories related to the exclusion criteria. To minimize information and observer bias, all interviews were conducted by trained enumerators who were blinded to the participants' exposure status.

Participants subsequently underwent standardized physical and supporting examinations. Anthropometric measurements, including body weight and height (measured using a portable stadiometer), were taken to confirm that all participants met the normal BMI inclusion criteria (18.5–22.9 kg/m^2). This was followed by a cardiorespiratory assessment—encompassing blood pressure, heart rate, respiratory rate, oxygen saturation, and lung/heart auscultation—and an Electrocardiogram (ECG) to exclude severe cardiovascular conditions. All clinical examinations were performed by medical personnel who were blinded to the geographic exposure classification of the participants.

Pulmonary function was measured using a portable digital spirometer in strict accordance with the American Thoracic Society (ATS) and European Respiratory Society (ERS) standards [35]. Participants performed maneuvers in a seated position, and measurements were repeated until at least dua consistent best results were obtained, with a difference in and between maneuvers not exceeding 150 mL. To ensure data validity across the geographically distinct study sites of Kedoya and Pangalengan, the following protocols were implemented. First, to account for significant differences in temperature and atmospheric pressure between the coastal Jakarta area and the highland Bandung region, the spirometer was equipped with an internal BTPS (Body Temperature, Ambient Pressure, Saturated with water vapor) sensor. This sensor automatically calibrated and adjusted measured lung volumes based on ambient conditions at each site, ensuring that the results reflected true physiological capacity. This environmental compensation ensured the precision of the biological signal across disparate geographic altitudes. Second, raw lung function values were converted into z-scores using the Global Lung Initiative (GLI) 2012 Southeast Asian-adjusted reference equations to account for ethnic-specific lung morphology. This approach minimized bias related to age, height, and ethnicity, while all spirometry technicians remained blinded to participants' exposure status to ensure objective outcome measurement.

Air pollution exposure data

Air pollution exposure data ($PM_{2.5}$ levels) were obtained from long-term environmental monitoring data at the participants' residential areas, which served as the basis for categorizing participants into the high and low exposure groups.

Data recording and quality control

All data were recorded on standardized worksheets. Data quality control involved review by a field supervisor, reconfirmation of incomplete or questionable data, and double data entry to minimize input errors and ensure accuracy.

Outcome measures

The primary outcomes of this study were standardized lung function indices, which facilitate an accurate comparison between individuals across different ages, heights, and genders. We focused on three key parameters to assess pulmonary health: Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), and the FEV_1/FVC ratio, the latter of which is used to identify obstructive ventilatory defects. To minimize the bias inherent in using absolute values or percentage of predicted values—which can vary significantly in older adultss—all raw measurements were **converted into z-scores** using the Global Lung Function Initiative (GLI-2012) reference equations.

A z-score indicates how many standard deviations an individual's measurement deviates from the mean predicted value of a healthy population. This standardization ensures that differences in lung function between the high and low exposure groups are not confounded by individual anthropometric characteristics, including age, height, gender, and ethnicity. For the clinical categorization of impairment, participants were classified as having a ventilatory defect if their FEV_1_z, FVC_z, or FEV_1/FVC_z-score fell below the Lower Limit of Normal (LLN). Following international diagnostic standards, the LLN was defined as a **z-score of less than −1.645**, which corresponds to the 5th percentile of the healthy reference population.

Data quality and handling of missing data

To ensure high data integrity, a complete case analysis was adopted. Given the direct supervision during data collection, missingness was minimal. Any participants with invalid spirometry or incomplete responses were replaced in real-time by new recruits from the same strata to maintain the required statistical power.

Statistical analysis

Participant characteristics were summarized using descriptive statistics. Initially, the effectiveness of the frequency matching procedure was verified by comparing baseline characteristics between the high and lower-exposure groups using

Independent Samples t-tests (or Mann-Whitney U tests) for continuous variables and Chi-square tests for categorical variables.

Data normality was assessed using the **Shapiro-Wilk test**, as it is more sensitive and robust for the current sample size per group ($n < 100$), supplemented by visual inspection of Q-Q plots. Homogeneity of variances was evaluated using **Levene's test**. Group differences between exposure areas were assessed using **Independent Samples t-tests** for variables meeting parametric assumptions or nonparametric alternatives (**Mann-Whitney U**) for variables that violated normality or homogeneity assumptions.

Multivariable linear regression models were fitted to estimate the association between $PM_{2.5}$ exposure category and each lung function z-score (FEV_1_z, FVC_z, and FEV_1/FVC_z-score). Models were adjusted for age, sex, body mass index, socioeconomic indicators. Although lung function outcomes were expressed as GLI-2012 z-scores, **age, sex, and height were additionally included as covariates** to account for **potential residual confounding** and to **ensure conservative model specification.** Results are reported as adjusted mean differences (Unstandardized B coefficients) with 95% confidence intervals. Model assumptions were strictly verified using the **Kolmogorov–Smirnov test to confirm the normality of unstandardized residuals (with a significance threshold of $p > 0.01$), and supplemented by visual inspection of residual Q-Q plots. Multicollinearity** was assessed using the **Variance Inflation Factor (VIF < 5.0). Model stability** and influential outliers were screened using **Cook's distance (threshold < 0.5)**, and **Mahalanobis distance with the latter evaluated against the $\chi 2$ critical value for the corresponding degrees of freedom ($p < 0.001$).** All model assumptions, including normality of residuals and homoscedasticity, were strictly verified to ensure the validity of parametric estimates.

Statistical analyses were conducted using SPSS version 26. All hypothesis tests were evaluated using a two-tailed significance level of **$\alpha = 0.01$** and **power = 95%, providing the high-precision evidence necessary for translational health applications. While the minimum required sample size to detect large effects was 68 (n = 34 per group), our final cohort of n = 101 provided superior statistical power (> 95%), ensuring high-precision evidence for evaluating decadal exposure impacts.**

Ethical considerations

The study was conducted in accordance with the **Declaration of Helsinki** and **approved by the Ethical Review Committee of the Faculty of Medicine, Universitas Trisakti** under ethical permission number 007/KER/FK/04/2025. Prior to participation, all individuals provided **written informed consent**. To ensure genuine autonomy among the older adults participants, the consent process included a comprehensive verbal explanation of the study's objectives and the non-invasive nature of the procedures.

Researchers ensured that all technical terms were explained in **lay language**, and for those with age-related visual difficulties, the form was read aloud to guarantee full comprehension before signing. Participation was strictly voluntary, with the right to withdraw at any time without consequence. Each consent form was signed by the participant and **witnessed by an impartial third party** present during the process. Individuals who were illiterate or could not speak Indonesian were excluded to ensure the integrity of the informed consent process. As the study focused exclusively on the older adults, no minors were involved.

To safeguard privacy, all data were **double-anonymized** using unique alphanumeric codes; no identifying information was stored in the final analytic dataset. All clinical examinations were conducted in private settings to maintain the dignity and comfort of the participants.

Results

A. Participant flow and selection

The flow of participants throughout the study, detailing the recruitment process, application of inclusion/exclusion criteria, and the final analytic sample size, is illustrated in Fig 1. A total of 123 older adults residents were initially screened. After applying eligibility criteria (e.g., age 65–80 years, minimum 10-years residency, no history of smoking) and excluding 22 participants, the final analytic sample consisted of 101 older adults. **The exclusions were due to clinical abnormalities identified during screening (n = 14), invalid spirometry maneuvers that did not meet the ATS/ERS 2019 quality standards (n = 3), and the frequency matching procedure to ensure group comparability (n = 5). The complete selection flow is illustrated in Fig 1.** Specifically, **47 participants** from the lowest-exposure Pangalengan group and **54 participants** from the highest-exposure Kedoya group were included in the final analysis. The Pangalengan group consisted of **37 older adults women and 10 older adults men**, while the Kedoya group comprised **47 older adults women and 7 older adults men.**

B. Study setting and exposure assessment

To establish the environmental contrast required for this study, $PM_{2.5}$ concentration measurements were conducted through a two-stage hybrid exposure assessment to establish the environmental contrast between the two study areas. In the first stage, we reviewed longitudinal ambient $PM_{2.5}$ data from government-operated monitoring stations, which provided daily records to confirm the long-term historical pollution profiles of the two regions. These records consistently indicated substantially higher ambient $PM_{2.5}$ levels in Jakarta compared to the Bandung area (characterized by generally low $PM_{2.5}$ levels).

In the second stage, to validate neighborhood-level conditions during the study period, primary measurements were conducted at six preliminary locations (three in Jakarta and three in Bandung). These validation measurements were performed using calibrated sensors over 24-hour sampling periods by an independent certified air quality monitoring company. Based on these data, Kedoya in Jakarta area was selected as the highest-exposure area and Pangalengan in Bandung area as the lowest-exposure area. To ensure the robustness of the area-level exposure proxy, all participants were recruited from a single administrative sub-district (*kelurahan*) immediately surrounding these validated sites. The measurement results for AQI (Air Quality Index), $PM_{2.5}$, and PM_{10} from all six preliminary locations are presented in Table 1.

C. Participant characteristics

Baseline demographic and clinical characteristics are detailed in Table 2. The two exposure groups were generally comparable across most variables, confirming the **effectiveness of the frequency matching procedure** outlined in the Methods section. Mean age in the low-exposure group (Group 1) was 71.32 years vs 71.52 years in the high exposure group (Group 2). The difference in mean age (Mean Differences=−0.199 years) was not statistically significant ($t=-0.317$, $p = 0.747$). Homogeneity of variance for age was also confirmed by Levene's test ($F = 5.075$, $p = 0.026$, consistent with $\alpha = 0.01$ as the criterion).

Similarly, the distribution of gender was comparable, with the majority being female in both groups (Pangalengan: 78.72% female vs. Kedoya: 87.04% female, $\chi 2$ test $p = 0.265$). The lack of significance difference in mean age and gender

Table 1. AQI (Air Quality Index), $PM_{2.5}$ and PM_{10} Concentrations in Preliminary Measurement Areas.

Area	Location	AQI	PM2.5 (μg/m³)	PM10 (μg/m³)
Bandung	Pangalengan	43	10	17
	Leuwi Panjang	179	36	87
	Padalarang	191	40	94
Jakarta	Kedoya	219	57	156
	Cilandak Barat	216	54	151
	Mangga Dua	209	45	127

https://doi.org/10.1371/journal.pone.0349025.t001

Table 2. Demographic and Anthropometric Characteristics of Study Participants by Data Collection Location.

Characteristics	Pangalengan	Kedoya	Total
Gender:			
- Male	10 (21.28%)	7 (12.96%)	17 (16.83%)
- Female	37 (78.72%)	47 (87.04%)	84 (83.17%)
Number of Participants	47 (100%)	54 (100%)	101 (100%)
Education:			
- Low: Not attending school, Elementary school	37 (72.34%)	38 (70.37%)	75 (74.26%)
- Middle: Junior and Senior High School	9 (19.14%)	14 (25.93%)	23 (22.77%)
- High: diploma, bachelor	1 (2.13%)	2 (3.70%)	3 (2.97%)
Occupation:			
- unemployed, laborers, farmers, small traders	47 (100%)	54 (100%)	101 (100%)
- employee	0 (0%)	0 (0%)	0 (0%)
- professional	0 (0%)	0 (0%)	0 (0%)
Age	Mean = 71.32, SD = 2.59	Mean = 71.52, SD = 3.57	
Height	Mean = 147.53, SD = 7.21	Mean = 151.30, SD = 6.04	
Normal Body Mass Index (18.5–22.9 kg/m2)	Mean = 20,74, SD = 0.80	Mean = 20,80, SD = 0.70	
Ethnicity	Southeast Asia	Southeast Asia	

https://doi.org/10.1371/journal.pone.0349025.t002

distribution demonstrated that the groups were well-balanced for these important covariates. No data were missing for lung function variables or covariates.

The anthropometric profile, specifically Body Mass Index (BMI), also showed no significant difference between the two groups. The mean BMI in the low-exposure group was **20.74 kg/m²** compared to **20.80 kg/m²** in the high-exposure group (**Mean Difference = −0.066 kg/m²**). This difference was not statistically significant (**t = −0.441, p = 0.661**). Homogeneity of variance for BMI was confirmed by Levene's test (**F = 1.197, p = 0.277**), further demonstrating that the groups were well-balanced regarding nutritional status.

Clinical and physiological baseline assessments showed no significant differences between the low-exposure and high-exposure groups. The median respiratory rate was 19.0 breaths/min for both groups ($p = 0.032$), while oxygen saturation remained stable with a median of 96.0% ($p = 0.947$). Other vital signs, including blood pressure, heart rate, and body temperature, were also within normal clinical ranges and did not differ significantly between groups. Detailed individual-level data for all clinical parameters are provided in S1 Table.

To compare the characteristics of the study subjects between the Pangalengan group (Group 1) and the Kedoya group (Group 2), a series of statistical tests were conducted, including normality of distribution tests, homogeneity of variances tests, and mean or median comparison tests. A comprehensive summary of these test results is presented in Table 3.

D. Lung function differences between exposure groups

Participants residing in the higher exposure area exhibited lower mean FEV_1_z-scores and FVC_z-scores compared with those living in the lower-exposure area. In contrast, the FEV_1/FVC z-score remained comparable between the two groups.

1. Comparison **of** Z-Scores (Adjusted Parameters).

For the z-scores (FEV_1_z and FVC_z), which adjust for age, gender, and height, the analysis revealed the following:
FEV_1_z (Non-parametric Test): Due to the violation of the normality assumption in group 1 ($p = 0.001$) and unequal variances (Levene's $p < 0.001$), the Mann-Whitney U test was performed. The test revealed a **highly statistically significant difference** ($p < 0.001$). The lower-exposure group showed a higher distribution (Mean Rank = 64.63; Mean = −0.45) compared to the higher-exposure group (Mean Rank = 39.14; Mean = −1.89), with a Mean Rank difference of +25.49. Notably,

Table 3. Summary of Statistical Test Results for Inter-Group Characteristic Comparisons.

Variable Compared	Normality Test Group 1/Group 2)	Variance Homogeneity (Levene's Sig.)	Comparison Test Used	Test p-value	Conclussion
Test of Difference in Proportions of Groups 1&2	N/A (Categorical)	N/A	Chi-Square Goodness of Fit Test	0.486	No significance different
Test of Difference in Gender Proportion* Group 1&2	N/A (Categorical)	N/A	Chi-Square of Independence Test	0.265	No significance different
Test of Difference in Education Proportion* Group 1&2	N/A (Categorical)	N/A	Chi-Square (Monte-Carlo exact)	0.663	No significance different
Age:					
Group 1	0.146 (Normal Distribution)	0.026 (Homogeneous)	Welch/Brown-Forsythe	0.747	No significance different
Group 2	0.102 (Normal Distribution)				
Height:					
Group 1	0.175 (Normal Distribution)	0.337 (Homogeneous)	Welch/Brown-Forsythe	0.006 (Welch/Brown-Forsythe)	Significance different
Group 2	0.162 (Normal Distribution)				
Body Mass Index:					
Group 1	0.536 (Normal Distribution)	0.277 (Homogenous)	Independent Sample t-test	0.661	No significance different
Group 2	0.111 (Normal Distribution)				

Note: Group 1: Pangalengan; Group 2: Kedoya; N/A: Not Applicable.

https://doi.org/10.1371/journal.pone.0349025.t003

while the lower-exposure group remained within the normal range, the mean of the higher-exposure group fell below the clinical threshold of **−1.645**, indicating a systematic shift toward impaired lung function.

FVC_z (Parametric Test): As the $\alpha = 0.01$ significance level, FVC_z satisfied the assumption for parametric analysis. Both groups followed a normal distribution (Shapiro-Wilk $p = 0.054$ and $p = 0.989$) and demonstrated homogeneity of variances (Levene's $p = 0.051$). Consequently, an **Independent Samples t-test** was performed. The test indicated a **highly statistically significant difference** between the two exposure groups ($p < 0.001$).

- The **Mean Difference (μ1−μ2)** was calculated as +1.2111 **z-score units** (Mean 1 = −1.2409; Mean 2 = −2.4520), corresponding to a **large effect size** (**Cohen's d=1.21**). This indicated that the average **FVC_z score** in the lower-exposure group was **1.21 Standard Deviations (SDs) higher** than the higher-exposure group.

FEV_1/FVC_z Ratio: Consistent with the primary findings, the Mann-Whitney U test for the FEV_1/FVC_z ratio showed **no statistically significant difference** between the two groups ($p = 0.464$), with a similar distribution of ranks observed in the lower-exposure group (**Mean Rank = 53.29**) compared to the higher-exposure group (**Mean Rank = 49.01**). Both groups maintained average values (+1.96 and +1.57, respectively) well above the clinical threshold for obstruction (Lower Limit of Normal = −1.645). This result is consistent with the study's recruitment process, which excluded individuals with known respiratory diseases or overt symptoms of breathlessness, thereby ensuring a study population of 'apparently healthy' older adults. Consequently, the proportional relationship between and remained preserved, confirming an absence of airway obstruction even in the higher-exposure group. **Notably, both the lower-exposure group (+1.96) and the higher-exposure group (+1.57) maintained mean values well above the clinical threshold for obstruction (LLN=−1.64). This result aligns with the study's recruitment process, which excluded individuals with known respiratory diseases or overt symptoms of breathlessness to ensure a population of 'apparently healthy' older**

adults. Consequently, while absolute volumes (FEV1_z and FVCz) were significantly reduced, the proportional relationship between them remained preserved, confirming an absence of airway obstruction even in the higher-exposure group.

2. Consistency in Actual Parameters

This pattern was consistently mirrored in the analysis of actual lung function parameters (FEV_1_actual and FVC_actual):

- The mean FEV_1_actual was significantly lower in the high-exposure group (Independent -test, $p < 0.001$).
- The median FVC_actual also showed a statistically significant difference (Mann-Whitney U test, $p = 0.002$).
- Correspondingly, no significant difference was detected in the median FEV_1/FVC_actual ($p = 0.687$).

These findings strongly suggest that differences in $PM_{2.5}$ exposure were primarily associated with reductions in absolute **lung volumes** (FEV_1_z and FVC_z), rather than an alteration in the underlying **airway resistance pattern** (as indicated by the non-significant FEV_1/FVC_z ratio). Overall, chronic exposure to higher levels was associated with a pattern consistent with reduced lung volumes without airflow obstruction, as indicated by significantly lower and scores but preserved ratios.

The complete comparison results for both actual and z-scores lung function parameters are detailed in Table 4.

E. Correlation analysis between covariates and lung function

To explore potential confounders and inform the subsequent multivariable model, bivariate correlations were examined between selected participant characteristics (covariates) and lung function z-scores. The complete correlation matrix, including the results of both Pearson (r) and Spearman (ρ) tests, is summarized in Table 5.

The key finding confirmed the inverse association observed in the descriptive analysis: Ambient $PM_{2.5}$ exposure demonstrated a significant and moderate negative correlation with both FEV_1_z (Pearson $r = -0.469$, $p < 0.001$) and FVC_z (Pearson $r = -0.462$, $p < 0.001$). This suggests that higher levels are associated with lower lung volumes relative to reference

Table 4. Summary of Statistical Tests for FEV_1, FVC, and FEV_1/FVC Variables.

Variable	Group	Normality Test (Shapiro-Wilk Sig.)	Homogeneity of Variance (Levene's Sig.)	Tests Performed	Sig. Test Results	Conclusion (Differences Between Groups)
FEV_1_actual	1	0.019 (Normal)	0.672 (Homogeneous)	Independent Samples t-test	<0.001	Significant Difference
	2	0.058 (Normal)				
FVC_actual	1	0.008 (Non Normal)	0.634 (Homogeneous)	Mann-Whitney U	0.002	Significant Difference
	2	0.520 (Normal)				
FEV_1FVC_actual	1	<0.001 (Non Normal)	0.058 (Homogeneous)	Mann-Whitney U	0.687	No Significant Difference
	2	<0.001 (Non Normal)				
FEV_1_z	1	0.001 (Non Normal)	0.000 (Not Homogeneous)	Mann-Whitney U	<0.001	Significant Difference
	2	0.369 (Normal)				
FVC_z	1	0.054 (Normal)	0.051 (Homogeneous)	Independent Samples t-test	<0.001	Significant Difference
	2	0.989 (Normal)				
FEV_1FVC_z	1	<0.001 (Non Normal)	0.017 (Homogeneous)	Mann-Whitney U	0.464	No Significant Difference
	2	<0.001 (Non Normal)				

Abbreviations: FEV_1 – Forced Expiratory Volume in 1 second; FVC – Forced Vital Capacity; FEV_1/FVC – Ratio of FEV_1 to FVC; FEV_1_actual – Measured absolute value of FEV_1 (in liters); FVC_actual – Measured absolute value of FVC (in liters);FEV_1/FVC_actual – Measured absolute ratio of FEV_1 to FVC; FEV_1_z – Standardized Z-score of FEV_1 (adjusted for age, gender, and height); FVC_z – Standardized Z-score of FVC (adjusted for age, sex, and height); FEV_1/FVC_z – Standardized Z-score of the FEV_1/FVC ratio; Sig. – Significance (p-value); Levene's Sig. – p-value from Levene's test for homogeneity of variances.

https://doi.org/10.1371/journal.pone.0349025.t004

Table 5. Pearson Correlation and Spearman's rho Matrix between $PM_{2.5}$ Exposure, Covariates and Lung Function Variables in the Older adults.

Variables	Pearson r Correlation Coeff. (p)	Spearman's ρ Correlation Coeff. (p)	Conclusion
PM2.5 vs FEV_1_z	−0.469 (p < 0.001)	−0.436 (p < 0.001)	Significant and moderate negative correlation
PM2.5 vs FVC_z	−0.442 (p < 0.001)	−0.415 (p < 0.001)	Significant and moderate negative correlation
PM2.5 vs FEV_1/FVC_z	−0.136 (p = 0.176)	−0.073 (p = 0.467)	Not statistically significant
Gender vs FEV1_z	0.078 (p = 0.439)	0.058 (p = 0.564)	Not statistically significant
Gender vs FVC_z	0.099 (p = 0.324)	0.118 (p-0.240)	Not statistically significant
Gender vs FEV_1/FVC_z	0.039 (p = 0.699)	0.031 (p = 0.759)	Not statistically significant
Age vs FEV_1_z	−0,111 (p = 0.269)	−0,136 (p = 0.175)	Not statistically significant
Age vs FVC_z	−0,118 (p = 0.239)	−0.122 (p = 0.223)	Not statistically significant
Age vs FEV_1/FVC_z	−0.085 (p = 0.397)	−0,138 (p = 0.168)	Not statistically significant
Height vs FEV_1_z	−0,238 (p = 0.016)	−0,124 (p = 0.218)	Not statistically significant
Height vs FVC_z	−0.273 (p = 0.006)	−0.184 (p = 0.066)	Significant and weak negative correlation
Height vs FEV_1/FVC_z	0.016 (p = 0,876)	0.065 (p = 0.517)	Not statistically significant
Education vs FEV_1_z	0.086 (p = 0.393)	0.162 (p = 0.106)	Not statistically significant
Education vs FVC_z	0.046 (p = 0.649)	0.095 (p = 0.345)	Not statistically significant
Education vs FEV_1/FVC_z	0.184 (p = 0.066)	0.146 (p = 0.146)	Not statistically significant
BMI vs FEV_1_z	0.214 (p = 0.031)	0.146 (p = 0.145)	Not statistically significant
BMI vs FVC_z	0.099 (p = 0.327)	0.078 (p = 0.440)	Not statistically significant
BMI vs FEV_1/FVC_z	0.210 (p = 0.035)	0.150 (p = 0.135)	Not statistically significant

Note: Significance evaluated at $p < 0.01$ (two-tailed); $p \geq 0.01$ was interpreted as not statistically significant (NS). Conclusions were based on the appropriate correlation test according to data distribution: Spearman's rho was applied when at least one variable was non-normally distributed, and Pearson's correlation was applied when both variables were normally distributed. Magnitude guidelines (absolute coefficient): **weak** = 0.10–0.29; **moderate** = 0.30–0.49; **strong** ≥ 0.50. The sign indicates direction (negative/positive). See Table 4 for variable abbreviations.

https://doi.org/10.1371/journal.pone.0349025.t005

values. Consistent with the group comparison results, $PM_{2.5}$ exposure was not statistically significantly associated with the FEV_1/FVC_z ratio (Pearson r=−0.136, p = 0.176).

Regarding the covariates, Age, Gender, Education, and Body Mass Index (BMI) showed no statistically significant correlations with any of the lung function outcomes when evaluated at the prespecified significance level of p < 0.01. However, Height showed a significant, weak negative correlation with FVC_z (Pearson r=−0.273, p = 0.006), suggesting a potential weak confounding effect that should be controlled for in the regression analysis.

F. Multivariable linier regression

Multivariable linear regression was employed to determine the independent association between exposure (group status) and lung function Z-scores. The models were **adjusted for potential confounders**, including age, gender, education, height, and BMI. The results of the three adjusted models are summarized in Table 6.

Model for FEV_1_z

The overall model for FEV_1_z was **statistically significant** (F(6,94)=7.189, p < 0.001), explaining approximately **31.5%** of the variance in FEV_1_z ($R^2 = 0.315$). In this adjusted model, **residence in the high-exposure area emerged as the only significant driver** of lower FEV_1_z (Unstandardized Coefficient B=−1.434, p < 0.001). This indicates that, after controlling for all listed covariates, participants in the high $PM_{2.5}$ area had an FEV_1_z score that was 1.434 units lower than those in the low $PM_{2.5}$ area. While BMI showed a positive association (B = 0.443, p = 0.015), it did not meet the stringent

Table 6. Summary of Multivariable Linear Regression Analysis.

Variables	R^2 (Adj. R^2)	F (df)	p-value Model	Prediktor Signifikan ($p<0.01$)	VIF Maks	Tolerance Min	Std. Residual Range	Cook's D Max	Mahalanobis D Max	Remarks
FEV_1_z	0.315 (0.271)	F(6, 94) = 7.189	< 0.001	Group ($PM_{2.5}$), $p<0.001$	1.562	0.64	−2.058 to +2.676	0.149	20.338	Model significant; assumptions met; no outliers or multicollinearity detected.
FVC_z	0.259 (0.212)	F(6, 94) = 5.475	< 0.001	Group ($PM_{2.5}$), $p<0.001$	1.562	0.64	−1.869 to 2.282	0.123	20.338	Model significant; assumptions met; no outliers or multicollinearity detected.
FEV_1FVC_z	0.110 (0.054)	F(6, 94) = 1.943	0.082	None	1.562	0.64	−2.636 to +1.518	0.104	20.338	Model not significant; all predictors $p\geq 0.01$; no assumption violations detected.

Note: All variable abbreviations (e.g., FEV_1_actual, FEV_1_z, FVC_z) are defined in Table 4. Statistical terms (e.g., R^2, Adj. R^2, VIF, Cook's D, Mahalanobis D) follow standard statistical nomenclature.

https://doi.org/10.1371/journal.pone.0349025.t006

significance threshold of 0.01. The model's validity was confirmed by a maximum Cook's distance of 0.149 and VIF values below 1.6, indicating no influential outliers or multicollinearity issues.

Model for FVC_z

Similarly, the model for FVC_z was also **statistically significant** (F(6,94)=5.475, $p<0.001$), accounting for **25.9%** of the variance ($R^2=0.259$). The $PM_{2.5}$ exposure group was the **sole significant predictor** (Unstandardized Coefficient B = −1.145, $p<0.001$), demonstrating that the impact of higher exposure on reduced lung volume remains robust after adjustment.

Model for FEV_1/FVC_z

In contrast, the model for FEV_1/FVC_z was **not statistically significant** (F(6,94)=1.943, $p=0.082$), accounting for only 11.0% of the variance ($R^2=0.110$). Consistent with the unadjusted results, **no predictor variable**, including $PM_{2.5}$ exposure (B=−0.560, $p=0.071$), showed a statistically significant association with the FEV_1/FVC_z ratio after adjustment.

Overall, these findings indicate that long-term exposure to elevated $PM_{2.5}$ levels is significantly associated with reduced lung volumes (FEV_1_z and FVC_z) but not with evidence of obstructive impairment (indicated by the FEV_1/FVC_z ratio) in this older adults population.

Assessment of model assumptions

Prior to final interpretation, key assumptions of the multivariable linear regression models were assessed. Multicollinearity was confirmed to be minimal, with Variance Inflation Factor (VIF) values remaining well below the threshold of 5 for all models. Furthermore, residual normality was formally tested for each model, with results summarized in Table 7.

Based on the strict $\alpha=0.01$ criterion, the residuals for the FEV_1_z model met the criteria for normality (K–S $p=0.176$; S–W $p=0.018$). Similarly, the FVC_z model residuals demonstrated strong normality (K–S $p=0.200$;S–W $p=0.114$), validating the use of parametric tests in these models. While the residuals for the FEV_1/FVC_z ratio model showed a deviation from formal normality (S–W $p=0.001$), they were considered approximately normal given the large sample size ($n=101$). As shown in Table 6, the multivariable linear regression models demonstrated high stability. **The sensitivity analysis**, integrated through the assessment of **Cook's Distance (max < 0.15) and Mahalanobis Distance (max = 20.338), confirmed that no influential outliers biased the model estimates**, further **validating the robustness**

Table 7. **Residual Normality Tests for Multivariable Linear Regression Models.**

Dependent Variable	n	Kolmogorov–Smirnov (Stat; p)	Shapiro–Wilk (Stat; p)	Normality Verdict*	Brief Interpretive Note
FEV_1_zRES_8	101	(K–S Stat); 0.176	(S–W Stat); 0.018	Accepted	Residuals follow a normal distribution at α = 0,01.
FVC_zRES_9	101	(K–S Stat); 0.200	(S–W Stat); 0.114	Accepted	High degree of normality; no transformation required.
FEV_1/FVC_z RES_10	101	(K–S Stat); 0.020	(S–W Stat); 0.001	Approximately normal	n is large; Q-Q plot shows minimal deviation from diagonal.

Note: *Rows show* ***unstandardized residuals*** *from the corresponding multivariable regression models (SPSS saved variables:* ***FEV_1_zRES_5*** *= residuals from the FEV_1_z model;* ***FVC_zRES_6*** *= residuals from the FVC_z model;* ***FEV_1/FVC_zRES_7*** *= residuals from the FEV_1/FVC_z model).*

Abbreviations: K–S = Kolmogorov–Smirnov test; S–W = Shapiro–Wilk test.

Normality decision rules (α = 0.01): **Accepted** = both tests p ≥ 0.01 and Q–Q plot shows no material deviation; **Partially rejected** = tests disagree (one p ≥ 0.01, one p < 0.01) and only mild tail departure on visual inspection—treated as approximately normal for regression at n = 101; **Rejected** = p < 0.01 on both tests and/or clear departure from normality on Q–Q/detrended plots (interpret model cautiously).

https://doi.org/10.1371/journal.pone.0349025.t007

of the findings despite the focused sample size. These findings validate the robustness of the parametric tests used in this study.

Overall, these results demonstrate that **chronic decadal $PM_{2.5}$ exposure is strongly and independently associated with reduced lung volumes** (FEV_1_z and FVC_z), while no such impact was observed for obstructive patterns. This enhances the conclusion that the observed lung function deficits are linked to the long-term environmental contrast inherent in this natural experiment.

Discussion

Principal findings and comparison with previous studies

In this natural experiment employing a quasi-longitudinal approach and focusing on older adults residing in two urban areas with substantially different ambient PM2.5 concentrations, we found that long-term exposure to higher PM2.5 levels was significantly associated with reduced lung function, specifically reflected by lower FEV_1_z and FVC_z scores. This association remained consistent and robust after rigorous adjustment for demographic, socioeconomic, and anthropometric covariates, including Body Mass Index (BMI). The persistence of these findings after controlling for BMI—a known physiological determinant of lung capacity—suggests that the observed decline is independently driven by particulate exposure rather than variations in body composition.

A key methodological strength of this study is the requirement that participants had resided at their current address for at least ten continuous years. This decadal residency threshold provides a quasi-longitudinal perspective that represents a substantial advance over most air pollution epidemiological studies, which often rely on current residence or short-term exposure windows of one to three years. By enforcing this criterion, we minimized exposure misclassification and migration-related bias, thereby strengthening causal inference. Ensuring that prolonged exposure clearly preceded lung function assessment establishes temporal precedence and reduces the risk of reverse causality inherent in standard cross-sectional designs.

Notably, no statistically significant difference was observed in FEV_1/FVC_z scores between exposure groups. This pattern—characterized by concurrent reductions in FEV_1_z and FVC_z with a preserved ratio—indicates a **non-obstructive, restrictive-pattern spirometry** rather than airflow obstruction. The GOLD 2023 report emphasizes that clinically meaningful lung function impairment may exist in the absence of overt airflow obstruction, particularly among individuals exposed to chronic environmental risk factors such as air pollution [37]. Within this framework, our findings suggest that the dominant physiological impact of long-term PM2.5 exposure in this older adults manifests primarily as reduced lung volumes, consistent with impaired lung expansion or accelerated pulmonary aging. **The observed effect sizes for (FEV_1_z) and (FVC_z) indicate a substantial clinical impact, corresponding to large Cohen's values of 1.21 and 1.02, respectively. In the context of GLI-2012 z-scores, a reduction of more than 1 Standard Deviation (SD) signifies that a significant portion of the exposed population has shifted downward by approximately 35–40 percentile points (e.g., from the median/50th percentile to below the 15th percentile). This framing highlights that the effect is not merely statistically significant but clinically profound at the population level.**

The absence of airflow obstruction is consistent with our study design, which applied stringent exclusion criteria to include only "apparently healthy" older adults, effectively excluding individuals with known chronic respiratory disease, asthma, or significant smoking histories. By isolating the effects of environmental exposure in a clinically asymptomatic cohort, our results demonstrate that substantial physiological impairment can occur before the onset of respiratory symptoms. Accordingly, the lower FEV_1_z and FVC_z scores observed in the high-exposure group represent a **subclinical decline in lung capacity** that would likely remain undetected using symptom-based screening or conventional diagnostic thresholds alone. From a clinical standpoint, this 'silent' reduction in lung reserve is critical; while these individuals are currently asymptomatic, their diminished physiological buffer makes them disproportionately vulnerable to acute respiratory failure during minor infections or peak pollution events—a major contributing factor to avoidable emergency hospitalizations.

While clinical practice often relies on fixed spirometric cut-offs for diagnostic convenience, the GOLD 2023 report recognizes the limitations of such approaches in older populations and acknowledges the value of lower-limit-of-normal–based methods for identifying early impairment [37]. **Our study adopts an even more sensitive approach in this regard; as demonstrated by Torén et al. (2020), individuals with ratios between 0.70 and 0.80 already exhibit a significantly higher prevalence of respiratory symptoms, such as dyspnoea (shortness of breath), compared to those with ratios above 0.80. This suggests that the optimal threshold for respiratory health is likely higher, around 0.80–0.85—than the conventional 0.70 cut-off** [38]. In line with this guidance, our use of GLI-2012 z-scores allowed for age-, sex-, height-, and ethnicity-adjusted assessment of lung function, minimizing age-related misclassification and improving sensitivity to early, non-obstructive decline. This approach underscores the importance of volume-based spirometric measures when evaluating the long-term respiratory effects of environmental exposures, particularly in aging populations.

Our findings align with a large body of literature demonstrating the detrimental effects of particulate air pollution on lung function. **However, while massive cohort studies in Europe and North America often struggle with exposure homogeneity or residential mobility** [39–41], **our natural experiment design isolates the impact of extreme environmental contrast with unprecedented precision** [14–17,40]. Previous research has often found stronger associations for FEV_1_z and FVC_z compared with the FEV_1/FVC_z ratio, supporting the idea that chronic exposure may contribute more to restrictive-like patterns or reduced lung expansion capacity than to airway obstruction [42]. Our findings contribute additional evidence from Jakarta, one of the most polluted megacities in the world, where older adults may experience particularly high cumulative exposure over the life course.

Strengths and limitations

This study has several methodological strengths. It focuses on an understudied yet vulnerable population—older adults living in an exceptionally polluted urban environment. Its methodological novelty lies in the application of a strict decade-long residency requirement within a rigorously screened cohort, enabling a cleaner isolation of pollution-related lung function decline than has been achieved in prior global assessments. Unlike conventional environmental studies that treat exposure as a short-term snapshot [43,44], our approach recognizes the aging lung as a product of cumulative environmental insults. By employing a natural experiment design [17–20], this study exploited substantial environmental contrast between two geographically distinct areas, an approach widely regarded as a quasi-gold standard for observational research. This design was intentionally chosen to address the ethical infeasibility of randomized controlled trials in environmental exposure research, while providing a quasi-experimental framework that strengthens the interpretability of exposure–outcome associations [25–27]. The robustness of the findings is further supported by a post-hoc power analysis indicating that with n = 101 and the observed large effect sizes, the study achieved a statistical power of >0.95 at $\alpha = 0.01$.

Standardized lung function assessments were conducted in accordance with ATS/ERS guidelines [36], ensuring methodological consistency across measurement conditions. Lung function was evaluated using GLI-2012 z-scores derived from Southeast Asian reference equations, allowing for age-, sex-, height-, and ethnicity-adjusted comparisons and minimizing bias related to ethnic physiological variation. Adherence to GLI-2012 standards and data transparency responds to long-standing calls for methodological consistency and open data practices in respiratory cohort research [41]. Rigorous restriction, frequency matching, and multivariable regression adjustment were employed to control confounding, and residual-based diagnostic tests, **supplemented by Q-Q plots and sensitivity analyses (Cook's Distance < 0.15)**, confirmed the normality, stability and validity of our parametric estimates.

Several limitations should be acknowledged. **Exposure classification was assigned at the area level (Kedoya vs. Pangalengan) and therefore represents an ecological proxy for long-term $PM_{2.5}$ exposure. This approach did not incorporate individual-level personal exposure monitoring, cumulative dose modeling, indoor air quality assessment, or time–activity pattern analysis. Consequently, within-area variability in pollution exposure was not captured, and some degree of residual exposure misclassification cannot be completely excluded. Because exposure was assigned ecologically at the area level, individual heterogeneity in long-term exposure may not be fully represented, and historical exposure trajectories at the individual level were not modeled. These constraints are inherent to ecological exposure assignment and should be considered when interpreting the estimated magnitude of the pollution effect. However, this limitation does not undermine the natural experiment framework, which relies primarily on environmental contrast between populations rather than precise individual-level exposure quantification.**

While the use of two study areas with contrasting exposure profiles enhanced internal validity by maximizing exposure contrast and minimizing contextual heterogeneity, it necessarily constrained exposure variability [45–48]. However, unlike large longitudinal cohorts that may suffer from exposure homogeneity and bias due to unmeasured residential mobility [39–41], our natural experiment design provided a necessary baseline comparison to disentangle pollution-induced deficits from biological aging [14–17,40]. This trade-off between internal validity and exposure variability reflects a deliberate methodological choice to prioritize causal inference. As articulated in the causal uncertainty principle, population restriction can strengthen causal identification at the expense of evidential breadth [49]. **Furthermore, the external validity of these findings is constrained by our strict inclusion criteria. By focusing on a 'highly selected' cohort of non-smoking, non-obese older adults without significant comorbidities, we prioritized internal validity to isolate the independent effect of decadal exposure. Consequently, these results may not be generalizable to populations with different clinical profiles, such as active or former smokers, individuals with obesity, or those with multi-morbidities, in whom the physiological response to chronic air pollution may be further exacerbated or modified by existing systemic inflammation.**

Translational implications for precision public health

Our findings have direct implications for public health policy in rapidly urbanizing Southeast Asian megacities. The evidence of significant lung volume reduction—even in 'apparently healthy' older adults—suggests that current public health advisories based on general population averages may be insufficient for vulnerable age groups. Consequently, this study underscores the urgent need for robust promotive and preventive public health strategies tailored to the unique risks of the urban older adults.

From a **translational perspective**, this study advocates for **Precision Public Health** that moves beyond broad monitoring toward targeted **respiratory screening and primary prevention** [50,51]. **From a promotive standpoint, health**

authorities should utilize these findings to enhance community-based education, raising awareness among older adults residents and their caregivers regarding the long-term respiratory hazards of decadal exposure. Specifically, **integrating spirometry z-score assessments into routine older adults community health posts (*Posbindu*) in high-exposure districts, such as Kedoya, could allow for the early detection of subclinical decline** [51]. Furthermore, these results provide actionable evidence for urban planners to prioritize localized **"clean air zones"** and **specialized indoor filtration subsidies for long-term older adults residents** in areas validated as **high-contrast pollution zones, effectively bridging the gap between environmental data and clinical protection** [52]. **Finally, from a clinical advocacy standpoint,** these findings **empower healthcare practitioners to utilize decadal residential history as a critical, independent risk factor for respiratory decline, ensuring that long-term pollution exposure is prioritized in clinical screenings regardless of a patient's smoking status** [53,54].

Critically, this transition toward a data-driven preventive model serves as a vital safeguard for national healthcare sustainability. By prioritizing early detection within the subclinical window, these targeted surveillance strategies directly mitigate the looming economic burden of chronic respiratory care [54]. Shifting the focus from generalized individual precautions, such as mask-wearing, to systematic screenings and structural interventions ensures a more cost-effective allocation of resources [50,52]. Ultimately, such data-driven prevention at the community level (e.g., Posbindu) acts as a high-value investment, potentially reducing long-term national health insurance (BPJS) expenditures for acute exacerbations and chronic respiratory morbidity among the burgeoning urban elderly population.

Conclusions

By utilizing a natural experiment design with a strict 10-year residency requirement, this study demonstrates that long-term exposure to elevated ambient levels is associated with **markedly reduced lung volumes (FEV_1 and FVC z-scores)** among older adults. **By exploiting extreme environmental contrasts as an ethical alternative to randomized trials, this framework—supported by ethnicity-adjusted z-scores—strengthens the interpretation that the observed deficits are attributable to pollution rather than geographic or biological variations. The stability of exposure over a decade, combined with robust model diagnostics confirming the normality of residuals, and model stability (Cook's distance < 0.15), strengthens the evidence for a chronic, cumulative impact compared with standard cross-sectional assessments.**

Crucially, these reductions were observed in a **rigorously screened** population of apparently healthy individuals, indicating that chronic particulate exposure primarily contributes to a subclinical, restrictive-pattern lung function deficit characterized by reduced lung volumes rather than airflow obstruction. In line with the GOLD 2023 report, which emphasizes that clinically meaningful lung function impairment may occur before the development of overt obstructive disease—particularly in the context of chronic environmental exposures—our findings highlight the presence of early physiological vulnerability that remains undetected by traditional symptom-based or fixed-ratio diagnostic thresholds.

From a socio-economic perspective, these findings suggest that long-term urban residency may function as a structural determinant of health, where geography influences patterns of respiratory aging. This underscores the necessity of a targeted public health approach that moves beyond individual-focused advice, such as intermittent mask-wearing, toward systemic interventions. Utilizing standardized z-score–based spirometry to identify pollution-related lung function decline at a subclinical stage enables **earlier risk stratification** and **preventive intervention** among vulnerable aging populations. Furthermore, **institutionalizing this framework within national health systems (such as Indonesia's BPJS)** may offer a strategic pathway to **mitigate the future economic burden of emergency hospitalizations** and **chronic respiratory morbidity.**

Ultimately, this research provides the evidentiary foundation for a dual-track strategy in public health: robust health promotion to increase community awareness of long-term hazards, and precise primary prevention

through routine respiratory screening in high-pollution corridors. These findings provide **actionable translational evidence** for shifting public health strategies from broad, population-wide advisories toward **targeted, data-driven interventions**.

Beyond general air-quality regulations, this study advocates for the integration of decadal environmental risk assessments into routine geriatric clinical care. **The translational value of this research** lies in **its capacity to bridge the gap between environmental monitoring** and **clinical protection**, **supporting a framework that prioritizes high-resolution screening for long-term residents in validated pollution hotspots.** While our **quasi-longitudinal approach** provides **robust evidence of the chronic impact of decadal exposure, future prospective longitudinal studies could further illuminate the real-time rate of lung function decline and the potential reversibility of these subclinical deficits in populations transitioning between different pollution trajectories.**

Recommendations

Based on the evidence of subclinical lung function deficits associated with long-term $PM_{2.5}$ exposure among biologically and environmentally vulnerable older adults, this study supports **risk-stratified prevention and surveillance** that moves beyond population-wide recommendations toward risk-stratified prevention and surveillance.

At the policy and macro-economic level, our findings underscore the need for **precision regulation** in high-burden urban corridors. Rather than uniform air quality interventions, municipalities should prioritize **high-resolution $PM_{2.5}$ monitoring** in densely populated areas with long-standing exposure, particularly where older adults reside. These data can inform the designation of **respiratory protection priority zones, in which environmental mitigation efforts**—such as **stricter localized emission controls**, **traffic regulation, and urban greening**—are preferentially implemented to protect populations with the highest cumulative exposure and biological vulnerability. **Crucially, we recommend that health policymakers integrate these findings into national health insurance frameworks (e.g., BPJS) by reallocating resources toward preventive respiratory screenings within these designated zones. Investing in early detection at the community level acts as a fiscal safeguard, potentially reducing the long-term economic burden of emergency hospitalizations and chronic oxygen dependency.**

At the **clinical and public health service perspective**, the observed reductions in FEV_1_z and FVC_z among asymptomatic older adults highlight the **importance of early, risk-based detection strategies. Routine spirometric screening using standardized GLI-2012 z-scores** should be **integrated** into **primary care and community health services** for older adults living in high-pollution areas, particularly those with long-term residential stability. This targeted surveillance approach enables the identification of subclinical lung function decline before overt disease develops, allowing **preventive interventions** to be initiated at a reversible stage. For individuals identified as highly vulnerable—based on cumulative exposure and genetic susceptibility—**enhanced follow-up** and **individualized respiratory health monitoring** may be warranted.

At **the individual and household level**, **precision prevention** should focus on **environmental modification** rather than reliance on behavioral restriction alone. Interventions such as **improving indoor air quality through ventilation optimization**, **the use of air filtration systems**, and **tailored activity planning** during periods of elevated pollution represent more sustainable strategies for protecting the aging lung. While **personal protective measures**, including the use of well-fitted respirators (e.g., N95 or KN95 masks), may serve as **supplementary short-term mitigation** during peak pollution events, they **should be viewed as part of a broader**, **integrated prevention strategy rather than a standalone solution.**

Finally, this study provides a **foundation for future research** aimed at strengthening mechanistic and causal understanding. **Longitudinal follow-up** with repeated spirometric assessments would allow estimation of individual rates of lung function decline, while the incorporation of inflammatory and oxidative stress **biomarkers** could further elucidate biological pathways underlying pollution-related lung impairment. Additionally, **intervention studies** evaluating indoor air quality improvements or community-level emission reductions would be valuable to determine whether targeted environmental modifications can **halt or potentially reverse subclinical lung function loss** in high-risk older adults.

Supporting information

S1 File. Supplementary materials. This file contains the completed STROBE checklist, S1 Table, S2 Table, and S1 Fig. (PDF)

Author contributions

Conceptualization: Hari Krismanuel.

Data curation: Purnamawati Tjhin.

Formal analysis: Hari Krismanuel.

Investigation: Hari Krismanuel.

Methodology: Hari Krismanuel.

Visualization: Purnamawati Tjhin.

Writing – original draft: Hari Krismanuel.

Writing – review & editing: Hari Krismanuel.

References

1. United States Environmental Protection Agency. Particulate Matter (PM) Basics. 2023. [cited 2025 July 19]. https://www.epa.gov/pm-pollution/particulate-matter-pm-basics
2. Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. Lancet. 2017;389(10082):1907–18. https://doi.org/10.1016/S0140-6736(17)30505-6 PMID: 28408086
3. Li T, et al. Fine particulate matter ($PM_{2.5}$): the culprit for chronic lung diseases in China. Chronic Dis Transl Med. 2018;4(3):176–86. https://doi.org/10.1016/j.cdtm.2018.07.002
4. Kim D, Chen Z, Zhou L-F, Huang S-X. Air pollutants and early origins of respiratory diseases. Chronic Dis Transl Med. 2018;4(2):75–94. https://doi.org/10.1016/j.cdtm.2018.03.003 PMID: 29988883
5. Jia L, Zhou X, Wang Q. Effects of agricultural machinery operations on PM2.5, PM10 and TSP in Farmland under different Tillage patterns. Agriculture. 2023;13(5):930. https://doi.org/10.3390/agriculture13050930
6. Lim EY, Kim G-D. Particulate matter-induced emerging health effects associated with oxidative stress and inflammation. Antioxidants (Basel). 2024;13(10):1256. https://doi.org/10.3390/antiox13101256 PMID: 39456509
7. Thangavel P, Park D, Lee Y-C. Recent insights into Particulate Matter (PM2.5)-mediated toxicity in humans: an overview. Int J Environ Res Public Health. 2022;19(12):7511. https://doi.org/10.3390/ijerph19127511 PMID: 35742761
8. Xing Y-F, Xu Y-H, Shi M-H, Lian Y-X. The impact of PM2.5 on the human respiratory system. J Thorac Dis. 2016;8(1):E69-74. https://doi.org/10.3978/j.issn.2072-1439.2016.01.19 PMID: 26904255
9. Yang L, Li C, Tang X. The impact of PM2.5 on the host defense of respiratory system. Front Cell Dev Biol. 2020;8:91. https://doi.org/10.3389/fcell.2020.00091 PMID: 32195248
10. Amnuaylojaroen T, Parasin N. Pathogenesis of $PM_{2.5}$-related disorders in different age groups: children, adults, and the elderly. Epigenomes. 2024;8(2):13. https://doi.org/10.3390/epigenomes8020013 PMID: 38651366
11. Croft DP, Zhang W, Lin S, Thurston SW, Hopke PK, Masiol M, et al. The association between respiratory infection and air pollution in the setting of air quality policy and economic change. Ann Am Thorac Soc. 2019;16(3):321–30. https://doi.org/10.1513/AnnalsATS.201810-691OC PMID: 30398895
12. BreathSafeAir. Air pollution in Indonesia: understanding the crisis and how to protect yourself. [cited in 2025 July 19]. https://breathesafeair.com/air-pollution-in-indonesia/
13. Rosman PS, Samah MAA, Yunus K, Hussain MRM. Particulate Matter (PM 2.5) at construction site: a review. Int J Recent Technol Eng. 2019;8(1C2):255–9.

14. Craig P, Campbell M, Deidda M, Dundas R, Green J, Katikireddi SV, et al. Using natural experiments to evaluate population health interventions: a framework for producers and users of evidence. Public Health Res (Southampt). 2025;13(3):1–59. https://doi.org/10.3310/JTYW6582 PMID: 40163348

15. Albers PN, Rinaldi C, Brown H, Mason KE, d'Apice K, McGill E, et al. Natural experiments for the evaluation of place-based public health interventions: a methodology scoping review. Front Public Health. 2023;11:1192055. https://doi.org/10.3389/fpubh.2023.1192055 PMID: 37427271

16. Ogilvie D, Adams J, Bauman A, Gregg EW, Panter J, Siegel KR, et al. Using natural experimental studies to guide public health action: turning the evidence-based medicine paradigm on its head. J Epidemiol Community Health. 2020;74(2):203–8. https://doi.org/10.1136/jech-2019-213085 PMID: 31744848

17. Crane M, Bohn-Goldbaum E, Grunseit A, Bauman A. Using natural experiments to improve public health evidence: a review of context and utility for obesity prevention. Health Res Policy Syst. 2020;18(1):48. https://doi.org/10.1186/s12961-020-00564-2 PMID: 32423438

18. Xanthopoulou P, Sahinidis A, Vassiliou EE, Kavoura A. When intentions stall: exploring the quasi-longitudinal divide between entrepreneurial intention and action. Adm Sci. 2026;16(1):14. https://doi.org/10.3390/admsci16010014

19. Kim TY, Kim YK. A quasi-longitudinal study on English learning motivation and attitudes: the case of South Korean students. The Journal of Asia TEFL. 2016;13(2):138–55. https://doi.org/10.18823/asiatefl.2016.13.2.5.138

20. Ong-Salvador R, Laveneziana P, de Jongh F. ERS/ATS global lung function initiative normal values and classifying severity based on z-scores instead of per cent predicted. Breathe (Sheff). 2024;20(3):230227. https://doi.org/10.1183/20734735.0227-2023 PMID: 39660084

21. Kanj AN, Scanlon PD, Yadav H, Smith WT, Herzog TL, et al. Application of global lung function initiative global spirometry reference equations across a large, multicenter pulmonary function lab population. Am J Respir Crit Care Med. 2023;209(1). https://doi.org/10.1164/rccm.202303-0613OC

22. Council for International Organizations of Medical Sciences (CIOMS). International ethical guidelines for health-related research involving humans. 4th ed. Geneva: CIOMS; 2016.

23. Hosseini A, Jackson AC, Bahramnezhad F. Ethical considerations in interventional studies: a systematic review ethics and interventional study. Ethics Interv Stud. 2023;23.

24. Kaye DK. Navigating ethical challenges of conducting randomized clinical trials on COVID-19. Philos Ethics Humanit Med. 2022;17(1):2. https://doi.org/10.1186/s13010-022-00115-3 PMID: 35086524

25. STROBE Statement. STROBE Checklists. 2025. [cited 2025 July 24]. https://www.strobe-statement.org/checklists/

26. Cuschieri S. The STROBE guidelines. Saudi J Anaesth. 2019;13(Suppl 1):S31–4. https://doi.org/10.4103/sja.SJA_543_18 PMID: 30930717

27. Serdar CC, Cihan M, Yücel D, Serdar MA. Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. Biochem Med (Zagreb). 2021;31(1):010502. https://doi.org/10.11613/BM.2021.010502 PMID: 33380887

28. Marsh J. Sample size calculations. Research Skills Seminar Series 2019 CAHS Research Education Program. 2019. [cited 2025 July 19]. https://pch.health.wa.gov.au/-/media/Files/Hospitals/PCH/General-documents/Research/Research-Education/Handouts/SampleSizeCalcHandouts.ashx

29. Beard J. Sample size calculations for cross-sectional studies. Sudan J Med Sci. 2024.

30. Whelan MJ, Pemberton E, Hughes CB, Swansborough C, Goslan EH, Gouin T, et al. A tiered assessment of human health risks associated with exposure to persistent, mobile and toxic chemicals via drinking water. Sci Total Environ. 2025;958:177868. https://doi.org/10.1016/j.scitotenv.2024.177868 PMID: 39642616

31. Buckley J. Conducting power analyses to determine sample sizes in quantitative research: a primer for technology education researchers using common statistical tests. J Technol Educ. 2024;35(2):81–109. https://doi.org/10.21061/jte.v35i2.a.5

32. Sruthi KG, Aditya C, Panda P, Ranjan Mohanty J, Behera MR. Prevalence of normal weight obesity among adults in Southeast Asia: insights from a systematic review and meta-analysis. Metabol Open. 2025;28:100416. https://doi.org/10.1016/j.metop.2025.100416 PMID: 41321405

33. Okawa Y, Mitsuhashi T, Tsuda T. The asia-pacific body mass index classification and new-onset chronic kidney disease in non-diabetic japanese adults: a community-based longitudinal study from 1998 to 2023. Biomedicines. 2025;13(2):373. https://doi.org/10.3390/biomedicines13020373 PMID: 40002785

34. Silva-Reis A, Brill B, Brandao-Rangel MAR, Moraes-Ferreira R, Melamed D, Aquino-Santos HC, et al. Association between visceral fat and lung function impairment in overweight and grade I obese women: a cross-sectional study. Adv Respir Med. 2024;92(6):548–58. https://doi.org/10.3390/arm92060048 PMID: 39727499

35. Dixon AE, Peters U. The effect of obesity on lung function. Expert Rev Respir Med. 2018;12(9):755–67. https://doi.org/10.1080/17476348.2018.1506331 PMID: 30056777

36. Graham BL, Steenbruggen I, Miller MR, Barjactarevic IZ, Cooper BG, et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society Technical Statement. Am J Respir Crit Care Med. 2019;200(8):e71–88. https://doi.org/10.1164/rccm.201908-1590ST

37. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. Respirology. 2023;28(4):325–38. https://doi.org/10.1111/resp.14486

38. Torén K, Schiöler L, Lindberg A, Andersson A, Behndig AF, Bergström G, et al. The ratio FEV1 /FVC and its association to respiratory symptoms-A Swedish general population study. Clin Physiol Funct Imaging. 2021;41(2):181–91. https://doi.org/10.1111/cpf.12684 PMID: 33284499

39. Hoek G, Vienneau D, de Hoogh K. Does residential address-based exposure assessment for outdoor air pollution lead to bias in epidemiological studies?. Environ Health. 2024;23(1):75. https://doi.org/10.1186/s12940-024-01111-0 PMID: 39289774

40. Wang X, Kattan MW. Cohort studies: design, analysis, and reporting. Chest. 2020;158(1S):S72–8. https://doi.org/10.1016/j.chest.2020.03.014

41. Lenney W, Gilchrist FJ, Kouzouna A, Pandyan AD, Ball V. The problems and limitations of cohort studies. Breathe. 2014;10(4):306–11. https://doi.org/10.1183/20734735.002313

42. de Jong K, Vonk JM, Zijlema WL, Stolk RP, van der Plaat DA, Hoek G, et al. Air pollution exposure is associated with restrictive ventilatory patterns. Eur Respir J. 2016;48(4):1221–4. https://doi.org/10.1183/13993003.00556-2016 PMID: 27492831

43. Moffat I, Chepelev N, Labib S, Bourdon-Lacombe J, Kuo B, Buick JK, et al. Comparison of toxicogenomics and traditional approaches to inform mode of action and points of departure in human health risk assessment of benzo[a]pyrene in drinking water. Crit Rev Toxicol. 2015;45(1):1–43. https://doi.org/10.3109/10408444.2014.973934 PMID: 25605026

44. Tuo J-Y, Shen Q-M, Li Z-Y, Tan J-Y, Fang J, Gao L-F, et al. Residential mobility and liver cancer risk: findings from a prospective cohort study in Chinese women. BMC Public Health. 2024;24(1):1196. https://doi.org/10.1186/s12889-024-18574-y PMID: 38685025

45. Bulbulia JA. Methods in causal inference. Part 1: causal diagrams and confounding. Evol Hum Sci. 2024;6:e40. https://doi.org/10.1017/ehs.2024.35 PMID: 39600624

46. Weaver J, Voss EA, Cafri G, Beyrau K, Nashleanas M, Suruki R. The necessity of validity diagnostics when drawing causal inferences from observational data: lessons from a multi-database evaluation of the risk of non-infectious uveitis among patients exposed to Remicade®. BMC Med Res Methodol. 2024;24(1):322. https://doi.org/10.1186/s12874-024-02428-7 PMID: 39731030

47. Miller LC, Shaikh SJ, Jeong DC, Wang L, Gillig TK, Godoy CG, et al. Causal inference in generalizable environments: systematic representative design. Psychol Inq. 2019;30(4):173–202. https://doi.org/10.1080/1047840x.2019.1693866 PMID: 33093760

48. Hernán MA, Robins JM. Causal inference: what if. Boca Raton (FL): Chapman & Hall/CRC; 2020.

49. Reidpath DD. The causal uncertainty principle. 2025. https://doi.org/arXiv:2511.22649

50. Khoury MJ, Iademarco MF, Riley WT. Precision public health for the era of precision medicine. Am J Prev Med. 2016;50(3):398–401. https://doi.org/10.1016/j.amepre.2015.08.031 PMID: 26547538

51. Roberts MC, Holt KE, Del Fiol G, Baccarelli AA, Allen CG. Precision public health in the era of genomics and big data. Nat Med. 2024;30(7):1865–73. https://doi.org/10.1038/s41591-024-03098-0 PMID: 38992127

52. Gallego E, Hinz EM, Massey B, Tilson EC, Tenenbaum JD. Precision prevention: using data to target the right intervention at the right intensity in the right community at the right time. Yearb Med Inform. 2024;33(1):6–17. https://doi.org/10.1055/s-0044-1800713 PMID: 40199283

53. Bilkey GA, Burns BL, Coles EP. Optimizing precision medicine for public health. Front Public Health. 2019;7:42.

54. August GJ, Gewirtz A. Moving toward a precision-based, personalized framework for prevention science. Prev Sci. 2019;20(1):1–9. https://doi.org/10.1007/s11121-018-0955-9

Precision Public Health Approach to Chronic PM2.5 Exposure

by Hari Krismanuel

Precision Public Health Approach to Chronic $PM_{2.5}$ Exposure: A Natural Experiment on Pulmonary Function Among Older Adults Across High-Contrast Gradients

Hari Krismanuel[1*], Purnamawati Tjhin[2]

[1]Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia.

[2]Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia.

*Corresponding author: Hari Krismanuel

Email: hari_krismanuel@trisakti.ac.id

https://orcid.org/0009-0002-2615-2363

ABSTRACT

Background: While $PM_{2.5}$ is a known respiratory hazard, most studies lack the temporal depth to distinguish chronic impacts from acute effects, particularly among vulnerable older adults. Addressing the inherent limitations of standard cross-sectional surveys, this study employs a **pioneering natural experiment design** with a 10-year stable residency filter. **To our knowledge, this represents the first study globally to evaluate the chronic impact of extreme ambient on an 'ultrapure' healthy older adults population using such a decadal filter, providing the first regional evidence in Southeast Asia that integrates a quasi-longitudinal framework to isolate respiratory effects. Utilizing a Precision Public Health (PPH) framework, this study aimed to determine the translational impact** of chronic $PM_{2.5}$ exposure on **standardized lung function** (**GLI 2012 - z-scores, adjusted for South East Asian populations**) among **'apparently healthy'** older adults Indonesians, thereby providing a unique regional evidence for targeted promotive and preventive public health strategies. **Methods:** We conducted **a natural experiment with quasi-longitudinal approach. Applying a two-tiered assessment strategy, this study involved 101 non-smoking older adults adults (age 65–80 years; normal BMI). This design compared two populations with a minimum 10-year residency in areas of contrasting $PM_{2.5}$ levels: a high-exposure urban area (Kedoya) and a low-exposure rural area (Pangalengan). The decade-long residency requirement ensured that exposure preceded the outcome, thereby minimizing reverse causality. To ensure comparability across different altitudes and temperatures, spirometry was performed using internal BTPS (Body Temperature, Ambient Pressure, Saturated with water vapor) compensation. Multivariable linear regression** was used to evaluate the association between residential $PM_{2.5}$ exposure and lung function, **adjusting for key demographic and lifestyle covariates. Results:** Older adult participants in the high-exposure area had significantly lower FEV1_z and FVC_z values compared to those in the low-exposure area. No significant difference was observed for the FEV1/ FVC_z ratio. Multivariate regression confirmed that exposure group (urban vs. rural) was the only independent predictor of FEV1_z ($\beta=-1.42$, $p<0.001$) and FVC_z ($\beta=-1.14$, $p<0.001$), after adjusting for covariates. No violation of model assumptions was detected for these outcomes. **Conclusions: By utilizing a natural experiment design with a decade of stable exposure, this study demonstrates** that high $PM_{2.5}$ exposure is associated with significant reductions in standardized lung volumes (FEV1_z, and FVC_z) among older adults, even after adjusting for demographic factors. The finding that the FEV1/FVC_z ratio remains unaffected suggests that chronic particulate exposure primarily contributes to **restrictive-type impairment**. **The 10-year exposure stability strengthens the causal inference by ensuring temporal precedence.** This study provides **actionable translational evidence** for **robust promotive and preventive measures**, emphasizing the urgent need for stringent air quality management—including **expanding green spaces** and **integrating environmental risk assessments into geriatric care. Ultimately, these findings support a shift toward early detection through targeted respiratory screening and individualized risk assessments to protect vulnerable older adults in highly polluted megacities.**

Keywords: GLI-2012 z-scores, **natural experiment design**, older adults, $PM_{2.5}$ exposure, **Precision Public Health**, **promotive and preventive strategies**, **quasi-longitudinal approach**.

INTRODUCTION

Ambient air pollution, particularly fine particulate matter ($PM_{2.5}$), remains one of the leading environmental risk factors for morbidity and mortality worldwide [1,2,3,4,5]. $PM_{2.5}$ can penetrate deep into the distal airways, triggering inflammation, oxidative stress, and structural changes that contribute to impaired pulmonary function [1,3,6,7,8,9]. Older adults are especially vulnerable due to age-related physiological decline, higher prevalence of comorbidities, and reduced capacity to respond to environmental stressors [7,10,11]. **This heightened susceptibility underscores the need for a Precision Public Health approach, which moves beyond population-wide averages to focus on tailored promotive and preventive strategies for highly vulnerable subgroups** [12,13,14].

Despite extensive evidence linking $PM_{2.5}$ exposure with adverse respiratory outcomes, the majority of epidemiological research has focused on children or middle-aged adults [4,8]. Studies involving older adult populations—who bear a disproportionate burden of air-pollution-related disease—remain relatively scarce, particularly in low- and middle-income countries (LMICs) (2,6,10). Moreover, data from cities with extremely high ambient $PM_{2.5}$ levels are limited, restricting our understanding of how chronic exposure affects lung function in the most heavily polluted urban environments [3,6,7,8,9]. This lack of data is critical, **as it hinders the development of precision-based preventive interventions tailored to the older adults, whose physiological response to extreme pollution may differ significantly from documented patterns in younger cohorts** [10].

Jakarta has repeatedly ranked among the most polluted major cities globally, with annual $PM_{2.5}$ concentrations far exceeding WHO guidelines [2,15]. However, substantial variation in $PM_{2.5}$ levels exists across districts, driven primarily by high-volume traffic emissions and localized urban construction projects [15, 16]. This provides a unique opportunity to employ a **natural experiment framework** [17,18,19,20]. **In the context of Precision Public Health, utilizing such high-contrast environmental gradients allows for a more granular understanding of how localized exposure impacts specific demographics. Such evidence is foundational for designing targeted health promotion programs and providing the causal rigor needed for effective policy-making.** Unlike standard cross-sectional studies that often lack the temporal depth to establish causal links, this study utilizes the extreme pollution contrast between two distinct regions as a **quasi-gold standard** for environmental observation [17,18,19,20]. By enforcing a strict **10-year minimum residency requirement**, we introduce a **quasi-longitudinal perspective** [21,22] that minimizes common pitfalls such as exposure misclassification and reverse causality, effectively **bridging the ethical and methodological gap** between observational surveys and randomized trials.

To our knowledge, **this is the first study globally to apply a Precision Public Health lens by evaluating the chronic impact of extreme ambient $PM_{2.5}$ on an 'ultrapure' healthy older adult population using a 10-year stable residency filter within a natural experiment framework.** Furthermore, it represents **a pioneering application** of this quasi-longitudinal approach globally, providing unique evidence from one of the world's most polluted megacities to **inform evidence-based preventive measures**.

To address this evidence gap, we conducted a **natural experiment framework** to compare lung function, expressed as Global Lung Initiative (GLI) z-scores [23,24], between older adult residents of two areas with distinctly different annual $PM_{2.5}$ levels. Our methodology leverages this this **'as-if random' assignment** to ensure that the measured lung function **reflects long-term, cumulative impacts** rather than acute environmental shifts, thereby establishing the necessary **temporal precedence for causal inference**. Furthermore, the use of standardized spirometric z-scores (GLI-2012) specifically adjusted for South East Asian ethnicity allows for a pioneering assessment of the aging lung in this region. **This methodological precision is essential for Precision Public Health, ensuring that clinical assessments are ethnically and age-appropriately accurate, thereby avoiding the misdiagnosis common in generalized respiratory models and improving the efficacy of primary prevention.**

The primary research questions were: (1) whether long-term exposure drives lower and z-scores among older adults; and (2) whether exposure leads to significant differences in z-scores. We hypothesized that older adult individuals living in the higher-exposure area would exhibit lower lung volumes (FEV_1_z and FVC_z), reflecting a subclinical restrictive-like decline, with less pronounced differences in the FEV_1/ FVC ratio. **These findings are expected to provide the granular evidence necessary for developing robust promotive and preventive public health strategies for aging urban populations.**

METHODS

Study Design

We employed **a natural experiment using a quasi-longitudinal approach** to compare lung function among older adults residing in two areas with markedly different long-term ambient exposure levels. **This design—often regarded as a quasi-gold standard for evaluating environmental exposures—was specifically chosen to bridge the ethical gap where a Randomized Controlled Trial (RCT) is impossible** [25,26,27]. The substantial between-area variation in levels serves as **an exogenous proxy for random assignment,** allowing for **a population-level comparison that minimizes selection bias. By utilizing these extreme environmental gradients, we simulated a 'quasi-experimental' condition that approaches the causal rigor of an RCT while maintaining real-world translational relevance. This design aligns with the Precision Public Health framework by moving beyond population-wide averages to evaluate how specific, localized environmental stressors impact a highly vulnerable sub-population.**

To strengthen the quasi-longitudinal perspective of this design, we enforced **a strict 10-year minimum residency requirement** for all participants. **This residency threshold ensures that the measured lung function reflects the cumulative, long-term impact of chronic exposure rather than acute environmental shifts.** By establishing **the necessary temporal precedence,** this design addresses **a key requirement for causal inference and significantly reduces the risk of reverse causality** often found in standard cross-sectional studies.

To our knowledge, this is the first study globally to utilize such a decadal exposure filter within a natural experiment to assess an 'ultrapure' older adults cohort in a high-pollution megacity.

The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [28,29] to ensure transparent reporting. By comparing two geographically distinct populations that are socio-demographically similar but environmentally contrasted, we effectively utilized this **"natural contrast"** to assess the chronic impact of particulate matter on the aging lung while **minimizing confounding** through **strict eligibility criteria** and **frequency matching.**

Study Setting and Site Selection

The study utilized a two-tiered exposure assessment strategy—a two-stage hybrid approach—to characterize exposure and select research sites by combining macro-level secondary data with micro-level direct environmental sampling. This methodology was employed to ensure a high-contrast exposure gradient while validating area-specific concentrations through ground-truthing [30]. In the first stage (Macro-level Mapping), preliminary mapping was conducted using secondary data from government air quality monitoring stations across the Jakarta and Bandung metropolitan areas to identify regions with the highest and lowest historical levels.

This was followed by a second stage of primary validation (Micro-level Direct Measurement) to capture real-time, area-specific concentrations and minimize the risk of ecological fallacy. Three specific districts within the candidate regions of Jakarta and Bandung were selected for direct on-site monitoring to validate actual ambient conditions within residential neighborhoods. This granular validation is a cornerstone of the Precision Public Health framework, ensuring that the exposure contrast is not merely assumed from distant monitoring stations but verified at the residential level, thereby reducing exposure misclassification. Based on the synthesis of these multi-level data points, Kedoya (Jakarta) was confirmed as the high-exposure location and Pangalengan (Bandung Regency) as the lower-exposure location. Participants were subsequently assigned to exposure categories using an area-level proxy that reflected the validated chronic ambient conditions of their primary residence.

Sample Size Determination

A minimum sample size of 34 participants per group was estimated using a **two-sample comparison of means**, assuming a significance level of α=0.01 and 95% power [31,32,33,34]. This calculation employed the standard formula for comparing two independent means:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \cdot 2\sigma^2}{(\mu_1 - \mu_2)^2}$$

Where:

- n: Minimum sample size required per group.
- $Z_{\alpha/2}$: The Z-score corresponding to the two-tailed significance level ($\alpha=0.01$, $Z_{\alpha/2}\approx2.58$).
- Z_{β}: The Z-score corresponding to the desired power ($1-\beta=0.95$, $Z_{\beta}\approx1.64$).
- $\mu1-\mu2$: The expected minimum mean difference between the high- and low-exposure groups.
- σ: The population standard deviation of the outcome variable (FEV1_z).

The power calculation was based on an expected mean difference in FEV1_z-scores ($\mu1-\mu2$) of 0.8 units (assuming a standard deviation (σ) of 1.0), derived from previous similar epidemiological studies on air pollution effects in older adult populations. To account for potential exclusions, invalid spirometry, and data loss, the recruitment target was increased to at least 60 participants per group [31,34].

Participants Recruitment and Eligibility

Data collection was conducted between May and June 2025 across two districts representing high (Kedoya) and low (Pangalengan) exposure gradients. To enhance internal validity and minimize variability in major confounding factors, participants were selected through a multi-layered screening process designed to ensure that observed differences in lung function were primarily attributable to ambient exposure rather than individual health histories or lifestyle choices. This 'ultrapure' cohort selection serves a translational purpose; by isolating the impact of exposure from other major confounders, the findings provide clear, actionable evidence for clinical guidelines and public health protection for the older adult population.

Eligibility was determined based on strict inclusion and exclusion criteria. Participants were **included** if they were aged between 65 and 80 years and had maintained permanent residence at their current address for at least ten continuous years. This decadal residency criterion is crucial to ensure that the measured lung function reflects the long-term, cumulative impact of chronic exposure rather than acute environmental changes, effectively establishing a retrospective temporal order between exposure and outcome. Additionally, candidates were required to demonstrate the willingness and physical ability to undergo standardized spirometry and structured interviews, and must fall within the normal Body Mass Index (BMI) range (18.5–22.9 kg/m^2) as defined by the WHO classification for Asian populations [35,36]. This BMI restriction was applied to exclude the potential restrictive effects of obesity on lung expansion [37,38].

To further minimize confounding bias, several **exclusion criteria** were rigorously applied. Individuals were excluded if they were current or former active smokers or had significant daily exposure to passive smoking. Potential participants with a known history of chronic respiratory diseases—including COPD, pulmonary fibrosis, uncontrolled asthma, or history of pulmonary tuberculosis—were also excluded, as were those with recent acute respiratory tract infections within the preceding four weeks. Furthermore, the study excluded individuals with severe cardiovascular or systemic conditions, lung cancer, or neuromuscular and cognitive impairments that could interfere with spirometry validity or the ability to follow instructions. Finally, to isolate ambient as the primary factor, individuals with significant occupational exposure to industrial dust, biomass smoke, or chemical irritants, as well as those with communication barriers such as illiteracy, were not included in the final cohort.

Sampling and Final Sample

The recruitment and selection process followed a systematic multi-stage purposive sampling approach to ensure a high-quality, comparable study population (See Figure 1 – STROBE Flowchart). In the first and second stages, purposive selection was used to identify regions and specific sites (Kedoya and Pangalengan) with extreme contrast. In the third stage, a sampling frame of 245 potential candidates was established through registries at community health posts (Posbindu). These candidates underwent preliminary pre-screening to verify basic eligibility based on age (65–80 years), never-smoking status, and a 10-year stable residency requirement.

From this registry, a simple random sampling procedure was employed to invite 60 candidates from each site (total n=120) for formal clinical assessment to minimize selection bias. A total of 123 individuals attended the clinical phase (68 from Kedoya and 55 from Pangalengan). These candidates underwent a rigorous one-day comprehensive clinical screening, comprising structured interviews, physical examinations, and Electrocardiography (ECG) to rule out cardiovascular abnormalities. To enhance comparability and neutralize potential confounders—such as age, gender, education level, and occupation—a frequency matching procedure was applied. After strictly adhering to the ATS/ERS 2019 quality standards for spirometry [39], the final analytical sample consisted of 101 participants (54 from the higher-exposure area and 47 from the lower-exposure area).

Research Variables and Operational Definitions

This study involved several key variables classified into independent, dependent, and covariate variables. The independent variable was the level of chronic fine particulate matter () exposure, represented by the participants' residential location, with the Kedoya area categorized as high exposure and Pangalengan as low exposure. A primary focus of this study

was the assessment of lung function as a continuous physiological measure rather than a binary clinical diagnosis. This approach increases statistical power and allows for the detection of subclinical declines in respiratory health, representing a key feature of the Precision Public Health framework by identifying 'at-risk' individuals before overt clinical disease manifests.

The primary outcomes were lung function indices expressed as and z-scores, calculated using the Global Lung Initiative (GLI) 2012 Southeast Asian reference equations to account for age, sex, and height. Analyzing these as continuous variables enables the detection of subtle, dose-dependent shifts in lung function associated with chronic exposure. Secondary outcomes included the z-score and the prevalence of lung function impairment. Clinical obstruction was defined using an age-appropriate threshold for older adults, specifically an z-score below −1.64 (the Lower Limit of Normal), while participants with a z-score ≥−1.64 were classified as having a normal ventilatory pattern.

Covariate variables were collected for descriptive analysis, frequency matching, and statistical adjustment. These included age (years), gender (male or female), and height (cm). Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters (). In accordance with the inclusion criteria, all participants were within the WHO-defined normal range for Asian populations. BMI served both for frequency matching and as a covariate in multivariable models, with an independent sample t-test confirming no statistically significant difference in mean BMI between the two exposure groups to ensure baseline comparability of nutritional status. Socioeconomic status (SES) was captured through education level—categorized into low (no schooling/primary), middle (junior/senior high), and higher education (diploma/degree)—and occupation, which was grouped ordinally into three levels: (1) unemployed, laborer, farmer, or small trader; (2) employee; and (3) professional.

Research Instruments

Data collection was facilitated through a suite of validated instruments designed to capture demographic, socioeconomic, and physiological variables. A pre-tested structured questionnaire was utilized to gather respondent identity, socioeconomic status (including education and occupation), and a detailed 10-year residency history. To ensure the 'ultrapure' nature of the cohort, the questionnaire also screened for histories of chronic or acute lung diseases and environmental confounding factors, such as passive smoking and biomass exposure. All measurements were recorded on a standardized observation sheet, which included height measurements taken with a calibrated stadiometer to the nearest centimeter. Ethical adherence was documented through signed informed consent forms, which were obtained after participants received comprehensive information regarding the study's objectives and procedures.

Pulmonary function was assessed using a portable digital spirometer to measure Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), and the FEV_1/ FVC ratio. The device maintained a volume accuracy of 3% and a flow range of 0–16 L/s, with calibration performed before each session to ensure data integrity. All measurements were conducted by trained personnel in strict accordance with the American Thoracic Society/European Respiratory Society (ATS/ERS) standards. Participants received standardized instructions and demonstrations prior to the examination, with maneuvers repeated until at least two consistent, high-quality results were obtained. To further validate site conditions and technical reporting, visual documentation was utilized for location-specific field notes and activity verification, while strictly maintaining participant anonymity.

Data Collection Methods

Data collection was conducted directly at the two research locations by a trained survey team comprising enumerators, medical personnel, and field coordinators. The fieldwork utilized standardized procedures and instruments, beginning with a community-based recruitment process. After passing initial pre-screening and prior to any clinical procedures, participants received a comprehensive explanation of the study and provided written informed consent. Face-to-face interviews were then conducted using a piloted structured questionnaire to collect demographic data, socioeconomic factors, residency history, and detailed medical histories related to the exclusion criteria. To minimize information and observer bias, all interviews were conducted by trained enumerators who were blinded to the participants' exposure status.

Participants subsequently underwent standardized physical and supporting examinations. Anthropometric measurements, including body weight and height (measured using a portable stadiometer), were taken to confirm that all participants met the normal BMI inclusion criteria (18.5–22.9 kg/m^2). This was followed by a cardiorespiratory assessment—encompassing blood pressure, heart rate, respiratory rate, oxygen saturation, and lung/heart auscultation—and an Electrocardiogram (ECG) to exclude severe cardiovascular conditions. All clinical examinations were performed by medical personnel who were blinded to the geographic exposure classification of the participants.

Pulmonary function was measured using a portable digital spirometer in strict accordance with the American Thoracic Society (ATS) and European Respiratory Society (ERS) standards [38]. Participants performed maneuvers in a seated position, and measurements were repeated until at least dua consistent best results were obtained, with a difference in and between maneuvers not exceeding 150 mL. To ensure data validity across the geographically distinct study sites of Kedoya and Pangalengan, the following protocols were implemented. First, to account for significant differences in temperature and atmospheric pressure between the coastal Jakarta area and the highland Bandung region, the spirometer was equipped with an internal BTPS (Body Temperature, Ambient Pressure, Saturated with water vapor) sensor. This sensor automatically calibrated and adjusted measured lung volumes based on ambient conditions at each site, ensuring that the results reflected true physiological capacity. This environmental compensation ensured the precision of the biological signal across disparate geographic altitudes. Second, raw lung function values were converted into z-scores using the Global Lung Initiative (GLI) 2012 South East Asian-

adjusted reference equations to account for ethnic-specific lung morphology. This approach minimized bias related to age, height, and ethnicity, while all spirometry technicians remained blinded to participants' exposure status to ensure objective outcome measurement.

Air Pollution Exposure Data

Air pollution exposure data ($PM_{2.5}$ levels) were obtained from long-term environmental monitoring data at the participants' residential areas, which served as the basis for categorizing participants into the high and low exposure groups.

Data Recording and Quality Control

All data were recorded on standardized worksheets. Data quality control involved review by a field supervisor, reconfirmation of incomplete or questionable data, and double data entry to minimize input errors and ensure accuracy.

Outcome Measures

The primary outcomes of this study were standardized lung function indices, which facilitate an accurate comparison between individuals across different ages, heights, and genders. We focused on three key parameters to assess pulmonary health: Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), and the FEV_1/ FVC ratio, the latter of which is used to identify obstructive ventilatory defects. To minimize the bias inherent in using absolute values or percentage of predicted values—which can vary significantly in older adult populations—all raw measurements were **converted into z-scores** using the Global Lung Function Initiative (GLI-2012) reference equations.

A z-score indicates how many standard deviations an individual's measurement deviates from the mean predicted value of a healthy population. This standardization ensures that differences in lung function between the high and low exposure groups are not confounded by individual anthropometric characteristics, including age, height, gender, and ethnicity. For the clinical categorization of impairment, participants were classified as having a ventilatory defect if their FEV_1_z, FVC_z, or FEV_1/ FVC_z-score fell below the Lower Limit of Normal (LLN). Following international diagnostic standards, the LLN was defined as a **z-score of less than -1.645**, which corresponds to the 5th percentile of the healthy reference population.

Data Quality and Handling of Missing Data

To ensure high data integrity, a complete case analysis was adopted. Given the direct supervision during data collection, missingness was minimal. Any participants with invalid spirometry or incomplete responses were replaced in real-time by new recruits from the same strata to maintain the required statistical power.

Statistical Analysis

Participant characteristics were summarized using descriptive statistics. Initially, the effectiveness of the frequency matching procedure was verified by comparing baseline characteristics between the high and lower-exposure groups using Independent Samples t-tests (or Mann-Whitney U tests) for continuous variables and Chi-square tests for categorical variables.

Data normality was assessed using the **Shapiro-Wilk test**, as it is more sensitive and robust for the current sample size per group ($n<100$), supplemented by visual inspection of Q-Q plots. Homogeneity of variances was evaluated using **Levene's test**. Group differences between exposure areas were assessed using **Independent Samples t-tests** for variables meeting parametric assumptions or nonparametric alternatives (**Mann-Whitney U**) for variables that violated normality or homogeneity assumptions.

Multivariable linear regression models were fitted to estimate the association between $PM_{2.5}$ exposure category and each lung function z-score (FEV_1_z, FVC_z, and FEV_1/FVC_z-score). Models were adjusted for age, sex, body mass index, socioeconomic indicators. Results are reported as adjusted mean differences (Unstandardized B coefficients) with 95% confidence intervals. Model assumptions were strictly verified using **the Kolmogorov–Smirnov test was used to confirm the normality of unstandardized residuals (with a significance threshold of p>0.01), multicollinearity** was assessed using the **Variance Inflation Factor (VIF < 5.0)**, and influential outliers were screened using **Cook's distance (threshold < 1.0)**, and **Mahalanobis distance with the latter evaluated against the $\chi 2$ critical value for the corresponding degrees of freedom ($p<0.001$).** Statistical analyses were conducted using SPSS version 26. All hypothesis tests were evaluated using a two-tailed significance level of **α=0.01** and **power=95%, providing the high-precision evidence necessary for translational health applications.**

Ethical considerations

The study was conducted in accordance with the **Declaration of Helsinki** and **approved by the Ethical Review Committee of the Faculty of Medicine, Universitas Trisakti** under ethical permission number 007/KER/FK/04/2025. Prior to participation, all individuals provided **written informed consent**. To ensure genuine autonomy among the older adults participants, the consent process included a comprehensive verbal explanation of the study's objectives and the non-invasive nature of the procedures.
Researchers ensured that all technical terms were explained in **lay language**, and for those with age-related visual difficulties, the form was read aloud to guarantee full comprehension before signing. Participation was strictly voluntary, with the right to withdraw at any time without consequence. Each consent form was signed by the participant and **witnessed by an impartial third party** present during the process. Individuals who were illiterate or could not speak Indonesian were excluded to ensure the integrity of the informed consent process. As the study focused exclusively on the older adults, no minors were involved.
To safeguard privacy, all data were **double-anonymized** using unique alphanumeric codes; no identifying information was stored in the final analytic dataset. All clinical examinations were conducted in private settings to maintain the dignity and comfort of the participants.

RESULTS

A. Participant Flow and Selection. The flow of participants throughout the study, detailing the recruitment process, application of inclusion/exclusion criteria, and the final analytic sample size, is illustrated in Figure 1. A total of 123 older adults residents were initially screened. After applying eligibility criteria (e.g., age 65–80 years, minimum 10-years residency, no history of smoking) and excluding 22 participants, the final analytic sample consisted of 101 older adults adults. Specifically, **47 participants** from the low-exposure Pangalengan group and **54 participants** from the high-exposure Kedoya group were included in the final analysis. The Pangalengan group consisted of **37 older adults women and 10 older adults men**, while the Kedoya group comprised **47 older adults women and 7 older adults men.**

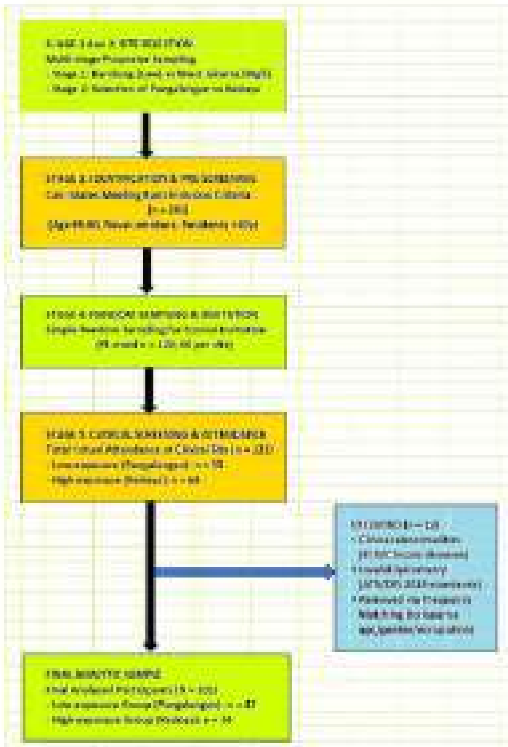


Figure 1. STROBE Flowchart of the multi-stage participant selection process. The diagram illustrates the recruitment stages, including site selection (Stages 1–2), identification and pre-screening (Stage 3), random sampling for invitation (Stage 4), and clinical validation. The final analytical sample was established after frequency matching and rigorous filtration to ensure a healthy, comparable groups.

B. Study Setting and Exposure Assessment

$PM_{2.5}$ concentration measurements were conducted at six preliminary locations: three in the Bandung area (characterized by generally low $PM_{2.5}$ levels) and three in Jakarta (characterized by generally high $PM_{2.5}$ levels). This initial screening was performed to identify the most suitable study locations for participant recruitment. Based on the collected data, one location in the Bandung area exhibiting the lowest $PM_{2.5}$ concentration and one location in Jakarta with the highest $PM_{2.5}$ concentration were subsequently selected for the

study. The measurement results for AQI (Air Quality Index), , and from all six preliminary locations are presented in Table 1.

Table 1. AQI (Air Quality Index), PM2.5 and PM10 Concentrations in Preliminary Measurement Areas.

Area	Location	AQI	PM2.5 (µg/m3)	PM10 (µg/m3)
Bandung	Pangalengan	43	10	17
	Leuwi Panjang	179	36	87
	Padalarang	191	40	94
Jakarta	Kedoya	219	57	156
	Cilandak barat	216	54	151
	Mangga Dua	209	45	127

C. Participant Characteristics

Baseline demographic and clinical characteristics are detailed in **Table 2.** The two exposure groups were generally comparable across most variables, confirming the **effectiveness of the frequency matching procedure** outlined in the Methods section. Mean age in the low-exposure group (Group 1) was 71.32 years vs 71.52 years in the high exposure group (Group 2). The difference in mean age (Mean Differences=−0.199 years) was not statistically significant ($t=-0.317$, $p=0.747$). Homogeneity of variance for age was also confirmed by Levene's test ($F=5.075$, $p=0.026$, consistent with $\alpha=0.01$ as the criterion).

Similarly, the distribution of gender was comparable, with the majority being female in both groups (Pangalengan: 78.72% female vs. Kedoya: 87.04% female, $\chi 2$ test $p = 0.265$). The lack of significance difference in mean age and gender distribution demonstrated that the groups were well-balanced for these important covariates. No data were missing for lung function variables or covariates.

The anthropometric profile, specifically Body Mass Index (BMI), also showed no significant difference between the two groups. The mean BMI in the low-exposure group was **20.74 kg/m^2** compared to **20.80 kg/m^2** in the high-exposure group (**Mean Difference = -0.066 kg/m^2**). This difference was not statistically significant (**$t = -0.441$, $p = 0.661$**). Homogeneity of variance for BMI was confirmed by Levene's test (**$F = 1.197$, $p = 0.277$**), further demonstrating that the groups were well-balanced regarding nutritional status.

Table 2. Demographic and Anthropometric Characteristics of Study Participants by Data Collection Location.

Characteristics	Pangalengan	Kedoya	Total
Gender:			
- Male	**10 (21.28%)**	**7 (12.96%)**	**17 (16.83%)**
- Female	**37 (78.72%)**	**47 (87.04%)**	**84 (83.17%)**
Number of Participants	**47 (100%)**	**54 (100%)**	**101 (100%)**
Education:			
- Low: Not attending school, Elementary school	**37 (72.34%)**	**38 (70.37%)**	**75 (74.26%)**
- Middle: Junior and Senior High School	**9 (19.14%)**	**14 (25.93%)**	**23 (22.77%)**
- High: diploma, bachelor	**1 (2.13%)**	**2 (3.70%)**	**3 (2.97%)**
Occupation:			
- unemployed, laborers, farmers, small traders	**47 (100%)**	**54 (100%)**	**101 (100%)**
- employee	**0 (0%)**	**0 (0%)**	**0 (0%)**
- professional	**0 (0%)**	**0 (0%)**	**0 (0%)**
Age	**Mean=71.32, SD=2.59**	**Mean=71.52, SD=3.57**	
Height	**Mean=147.53, SD=7.21**	**Mean=151.30, SD=6.04**	
Normal Body Mass Index (18.5-22.9 kg/m2)	**Mean=20,74, SD=0.80**	**Mean=20.80, SD=0.70**	
Ethnicity	**Southeast Asia**	**Southeast Asia**	

To compare the characteristics of the study subjects between the Pangalengan group (Group 1) and the Kedoya group (Group 2), a series of statistical tests were conducted, including normality of distribution tests, homogeneity of variances tests, and mean or median comparison tests. A comprehensive summary of these test results is presented in **Table 3.**

Table 3. Summary of Statistical Test Results for Inter-Group Characteristic Comparisons.

Variable Compared	Normality Test Group 1 / Group 2)	Variance Homogeneity (Levene's Sig.)	Comparison Test Used	Test p-value	Conclusion
Test of Difference in Proportions of Groups 1&2	N/A (Categorical)	N/A	Chi-Square Goodness of Fit Test	0.486	No significance different
Test of Difference in Gender Proportion* Group 1&2	N/A (Categorical)	N/A	Chi-Square of Independence Test	0.265	No significance different
Test of Difference in Education Proportion* Group 1&2	N/A (Categorical)	N/A	Chi-Square (Monte-Carlo exact)	0.663	No significance different
Age: Group 1 Group 2	0.146 (Normal Distribution) 0.102 (Normal Distribution)	0.026 (Homogeneous)	Welch / Brown-Forsythe	0.747	No significance different
Height: Group 1 Group 2	0.175 (Normal Distribution) 0.162 (Normal Distribution)	0.257 (Homogeneous)	Welch / Brown-Forsythe	0.006 (Welch/Brown-Forsythe)	Significance different
Body Mass Index: Group 1 Group 2	0.526 (Normal Distribution) 0.111 (Normal Distribution)	0.277 (Homogenous)	Independent Sample t-test	0.661	No significance different

Note: Group 1: Pangalengan; Group 2: Kedoya; N/A: Not Applicable.

D. Lung Function Differences Between Exposure Groups

Participants residing in the higher exposure area exhibited lower mean FEV1_z-scores and FVC_z-scores compared with those living in the lower-exposure area. In contrast, the FEV1/FVC z-score remained comparable between the two groups.

1. Comparison of Z-Scores (Adjusted Parameters)

For the z-scores (FEV1_z and FVC_z), which adjust for age, gender, and height, the analysis revealed the following:

FEV1_z (Non-parametric Test): Due to the violation of the normality assumption in group 1 ($p=0.001$) and unequal variances (Levene's $p<0.001$), the Mann-Whitney U test was performed. The test revealed **a highly statistically significant difference** ($p<0.001$). The lower-exposure group showed a higher distribution (Mean Rank = 64.63) compared to the higher-exposure group (Mean Rank = 39.14), with a Mean Rank difference of +25.49.

FVC_z (Parametric Test): As the $\alpha=0.01$ significance level, FVC_z satisfied the assumption for parametric analysis. Both groups followed a normal distribution (Shapiro-Wilk $p=0.054$ and $p=0.989$) and demonstrated homogeneity of variances (Levene's $p=0.051$). Consequently, an **Independent Samples t-test** was performed. The test indicated a **highly statistically significant difference** between the two exposure groups ($p<0.001$).

- **The Mean Difference ($\mu_1-\mu_2$)** was calculated as +1.2111 **z-score units** (Mean 1 = −1.2409; Mean 2 = −2.4520), corresponding to a **large effect size (Cohen's d=1.21**). This indicated that the average **FVC_z score** in the lower-exposure group was **1.21 Standard Deviations (SDs) higher** than the higher-exposure group.

FEV1/ FVC_z Ratio: Consistent with the primary findings, the Mann-Whitney U test for the FEV1/ FVC_z ratio showed **no statistically significant difference** between the two groups ($p=0.464$). Both groups maintained average values (+1.96 and +1.57, respectively) well above the clinical threshold for obstruction (Lower Limit of Normal = −1.64). This result is consistent with the study's recruitment process, which excluded individuals with known respiratory diseases or overt symptoms of breathlessness, thereby ensuring a study population of 'apparently healthy' older adults. Consequently, the proportional relationship between and remained preserved, confirming an absence of airway obstruction even in the higher-exposure group. **Notably, both the lower-exposure group (+1.96) and the higher-exposure group (+1.57) maintained mean values well above the clinical threshold for obstruction (LLN=−1.64). This result aligns with the study's recruitment process, which excluded individuals with known respiratory diseases or overt symptoms of breathlessness to ensure a population of 'apparently healthy' older adults. Consequently, while absolute volumes (FEV1_z and FVCz) were significantly reduced, the proportional relationship between them remained preserved, confirming an absence of airway obstruction even in the higher-exposure group.**

2. Consistency in Actual Parameters

This pattern was consistently mirrored in the analysis of actual lung function parameters (FEV1_actual and FVC_actual):

- The mean FEV1_actual was significantly lower in the high-exposure group (Independent -test, $p<0.001$).
- The median FVC_actual also showed a statistically significant difference (Mann-Whitney U test, $p=0.002$).
- Correspondingly, no significant difference was detected in the median FEV1/ FVC_actual ($p=0.687$).

These findings strongly suggest that differences in $PM_{2.5}$ exposure were primarily associated with reductions in absolute **lung volumes** (FEV1_z and FVC_z), rather than an alteration in the underlying **airway resistance pattern** (as indicated by the non-significant FEV1/ FVC_z ratio).

The complete comparison results for both actual and z-scores lung function parameters are detailed in **Table 4.**

Table 4. Summary of Statistical Tests for FEV_1, FVC, and FEV_1/FVC Variables.

Variable	Group	Normality Test (Shapiro-Wilk Sig.)	Homogeneity of Variance (Levene's Sig.)	Tests Performed	Sig. Test Results	Conclusion (Differences Between Groups)
FEV1_actual	1	0.019 (Normal)	0.672 (Homogeneous)	Independent Samples t-test	<0.001	Significant Difference
	2	0.058 (Normal)				
FVC_actual	1	0.008 (Non Normal)	0.634 (Homogeneous)	Mann-Whitney U	0.002	Significant Difference
	2	0.520 (Normal)				
FEV1FVC_actual	1	0.000 (Non Normal)	0.058 (Homogeneous)	Mann-Whitney U	0.687	No Significant Difference
	2	0.000 (Non Normal)				
FEV1_z	1	0.001 (Non Normal)	0.000 (Not Homogeneous)	Mann-Whitney U	<0.001	Significant Difference
	2	0.369 (Normal)				
FVC_z	1	0.054 (Normal)	0.051 (Homogeneous)	Independent Samples t-test	<0.001	Significant Difference
	2	0.989 (Normal)				
FEV1FVC_z	1	0.000 (Non Normal)	0.017 (Not Homogeneous)	Mann-Whitney U	0.464	No Significant Difference
	2	0.000 (Non Normal)				

Abbreviations: FEV_1 – Forced Expiratory Volume in 1 second; FVC – Forced Vital Capacity; FEV_1/FVC – Ratio of FEV_1 to FVC; FEV_1_actual – Measured absolute value of FEV_1 (in liters); FVC_actual – Measured absolute value of FVC (in liters);FEV_1/FVC_actual – Measured absolute ratio of FEV_1 to FVC; FEV_1_z – Standardized Z-score of FEV_1 (adjusted for age, gender, and height); FVC_z – Standardized Z-score of FVC (adjusted for age, sex, and height); FEV_1/FVC_z – Standardized Z-score of the FEV_1/FVC ratio; Sig. – Significance (p-value); Levene's Sig. – p-value from Levene's test for homogeneity of variances.

E. Correlation Analysis between Covariates and Lung Function

To explore potential confounders and inform the subsequent multivariable model, bivariate correlations were examined between selected participant characteristics (covariates) and

lung function z-scores. The complete correlation matrix, including the results of both Pearson (r) and Spearman (ρ) tests, is summarized in Table 5.

The key finding confirmed the inverse association observed in the descriptive analysis: Ambient $PM_{2.5}$ exposure demonstrated a significant and moderate negative correlation with both FEV1_z (Pearson r=−0.469, p<0.001) and FVC_z (Pearson r=-0.462, p<0.001). This suggests that higher levels are associated with lower lung volumes relative to reference values. Consistent with the group comparison results, $PM_{2.5}$ exposure was not statistically significantly associated with the FEV_1/FVC_z ratio (Pearson r=−0.136, p=0.176).

Regarding the covariates, Age, Gender, Education, and Body Mass Index (BMI) showed no statistically significant correlations with any of the lung function outcomes when evaluated at the prespecified significance level of p<0.01. However, Height showed a significant, weak negative correlation with FVC_z (Pearson r=−0.273, p=0.006), suggesting a potential weak confounding effect that should be controlled for in the regression analysis.

Table 5. Pearson Correlation and Spearman's rho Matrix between $PM_{2.5}$ Exposure, Covariates and Lung Function Variables in the Older adults.

Variables	Pearson r Correlation Coeff. [illegible]	Spearman's ρ Correlation Coeff. [illegible]	Conclusion
PM2.5 vs FEV1_z	-0.469 (p<0.001)	[illegible]	Significant and moderate negative correlation
PM2.5 vs FVC_z	-0.462 (p<0.001)	[illegible]	Significant and moderate negative correlation
PM2.5 vs FEV1/FVC_z	-0.136 (p=0.176)	[illegible]	Not statistically significant
Gender vs FEV1_z	[illegible]	[illegible]	Not statistically significant
Gender vs FVC_z	[illegible]	[illegible]	Not statistically significant
Gender vs FEV1/FVC_z	[illegible]	[illegible]	Not statistically significant
Age vs FEV1_z	[illegible]	[illegible]	Not statistically significant
Age vs FVC_z	[illegible]	[illegible]	Not statistically significant
Age vs FEV1/FVC_z	[illegible]	[illegible]	Not statistically significant
Height vs FEV1_z	[illegible]	[illegible]	Not statistically significant
Height vs FVC_z	-0.273 (p=0.006)	[illegible]	Significant and weak negative correlation
Height vs FEV1/FVC_z	[illegible]	[illegible]	Not statistically significant
Education vs FEV1_z	[illegible]	[illegible]	Not statistically significant
Education vs FVC_z	[illegible]	[illegible]	Not statistically significant
Education vs FEV1/FVC_z	[illegible]	[illegible]	Not statistically significant
BMI vs FEV1_z	[illegible]	[illegible]	Not statistically significant
BMI vs FVC_z	[illegible]	[illegible]	Not statistically significant
BMI vs FEV1/FVC_z	[illegible]	[illegible]	Not statistically significant

Note: Significance evaluated at $p < 0.01$ (two-tailed); $p \geq 0.01$ was interpreted as not statistically significant (NS). Conclusions were based on the appropriate correlation test according to data distribution: Spearman's rho was applied when at least one variable was non-normally distributed, and Pearson's correlation was applied when both variables were normally distributed. Magnitude guidelines (absolute coefficient): **weak** = 0.10–0.29; **moderate** = 0.30–0.49; **strong** ≥ 0.50. The sign indicates direction (negative/positive). See Table 4 for variable abbreviations.

F. Multivariable Linier Regression

Multivariable linear regression was employed to determine the independent association between exposure (group status) and lung function Z-scores. The models were **adjusted for potential confounders**, including age, gender, education, height, and BMI. The results of the three adjusted models are summarized **in Table 6**.

Model for FEV_1_z

The overall model for was **statistically significant** ($F(6.94)=7.189$, $p<0.001$), explaining approximately **31.5%** of the variance in FEV_1_z ($R^2=0.315$). In this adjusted model, **residence in the high-exposure area emerged as the only significant driver** of lower FEV_1_z (Unstandardized Coefficient B=−1.434, $p<0.001$). This indicates that, after controlling for all listed covariates, participants in the high $PM_{2.5}$ area had an FEV_1_z score that was 1.434 units lower than those in the low $PM_{2.5}$ area. While BMI showed a positive association (B=0.443, p=0.015), it did not meet the stringent significance threshold of 0.01. The model's validity was confirmed by a maximum Cook's distance of 0.149 and VIF values below 1.6, indicating no influential outliers or multicollinearity issues.

Model for FVC_z

Similarly, the model for FVC_z was also **statistically significant** ($F(6,94)=5.475$, $p<0.001$), accounting for **25.9%** of the variance ($R^2=0.259$). The $PM_{2.5}$ exposure group was the **sole significant predictor** (Unstandardized Coefficient B = −1.145, $p<0.001$), demonstrating that the impact of higher exposure on reduced lung volume remains robust after adjustment.

Model for FEV_1/ FVC_z

In contrast, the model for FEV_1/ FVC_z was **not statistically significant** ($F(6,94)=1.943$, $p=0.082$), accounting for only 11.0% of the variance ($R^2=0.110$). Consistent with the unadjusted results, **no predictor variable**, including $PM_{2.5}$ exposure (B=−0.560, p=0.071), showed a statistically significant association with the FEV_1/FVC_z ratio after adjustment.

Overall, these findings indicate that long-term exposure to elevated $PM_{2.5}$ levels is significantly associated with reduced lung volumes (FEV_1_z and FVC_z) but not with evidence of obstructive impairment (indicated by the FEV_1/FVC_z ratio) in this older adults population.

Table 6. Summary of Multivariable Linear Regression Analysis

Variables	R^2 (Adj. R^2)	F (df)	p-value Model	Prediktor Signifikan (p < 0.01)	VIF Maks	Tolerance Min	Std. Residual Range	Cook's D Max	Mahalanobis D Max	Remarks
FEV₁_z	0.315 (0.271)	F(6, 94) = 7.189	< 0.001	Group ($PM_{2.5}$), p < 0.001	1.562	0.64	-2.058 to +2.676	0.149	20.338	Model significant; assumptions met; no outliers or multicollinearity detected.
FVC_z	0.259 (0.212)	F(6, 94) = 5.475	< 0.001	Group ($PM_{2.5}$), p < 0.001	1.562	0.64	-1.869 to 2.282	0.123	20.338	Model significant; assumptions met; no outliers or multicollinearity detected.
FEV₁FVC_z	0.110 (0.054)	F(6, 94) = 1.943	0.082	None	1.562	0.64	-2.636 to +1.518	0.104	20.338	Model not significant; all predictors p ≥ 0.01; no assumption violations detected.

Note: All variable abbreviations (e.g., FEV_1_actual, FEV_1_z, FVC_z) are defined in Table 4. Statistical terms (e.g., R^2, Adj. R^2, VIF, Cook's D, Mahalanobis D) follow standard statistical nomenclature.

Assessment of Model Assumptions.

Prior to final interpretation, key assumptions of the multiple linear regression models were assessed. Multicollinearity was confirmed to be minimal, with Variance Inflation Factor (VIF) values remaining well below the threshold of 5 for all models. Furthermore, residual normality was formally tested for each model, with results summarized in **Table 7**.

Based on the strict α=0.01 criterion, the residuals for the FEV1_z model met the criteria for normality (K–S p=0.176; S–W p=0.018), a conclusion supported by visual inspection of the Q–Q plot (see Supplementary Figure 1). Similarly, the FVC_z model residuals demonstrated strong normality (K–S p=0.200;S–W p=0.114), validating the use of parametric tests in these models. While the residuals for the FEV1/FVC_z ratio model showed a deviation from formal normality (S–W p=0.001), they were considered approximately normal given the large sample size (n=101) and visual alignment in Q–Q plots. These findings validate the robustness of the parametric tests used in this study.

Overall, these results demonstrate that **chronic decadal exposure to higher levels** is a **primary driver of reduced lung volumes** (FEV_1_z and FVC_z), while no such impact was observed for obstructive impairment. This reinforces the conclusion that the observed lung function deficits are driven by the long-term environmental contrast inherent in this natural experiment.

Table 7. Residual Normality Tests for Multiple Linear Regression Models

Dependent Variable	n	Kolmogorov–Smirnov (Stat; p)	Shapiro–Wilk (Stat; p)	Normality Verdict*	Brief Interpretive Note
FEV$_1$_zRES_8	101	(K–S Stat); 0.176	(S–W Stat); 0.018	Accepted	Residuals follow a normal distribution at α=0,01.
FVC_zRES_9	101	(K–S Stat); 0.200	(S–W Stat); 0.114	Accepted	High degree of normality; no transformation required.
FEV$_1$/FVC_z RES_10	101	(K–S Stat); 0.020	(S–W Stat); 0.001	Approximately normal	n is large; Q-Q plot shows minimal deviation from diagonal.

Note: *Rows show* ***unstandardized residuals*** *from the corresponding multivariable regression models (SPSS saved variables:* ***FEV$_1$_zRES_5*** *= residuals from the FEV$_1$_z model;* ***FVC_zRES_6*** *= residuals from the FVC_z model;* ***FEV$_1$/FVC_zRES_7*** *= residuals from the FEV$_1$/FVC_z model).*

Abbreviations: K–S = Kolmogorov–Smirnov test; S–W = Shapiro–Wilk test.

Normality decision rules (α = 0.01): **Accepted** = both tests $p \geq 0.01$ and Q–Q plot shows no material deviation; **Partially rejected** = tests disagree (one $p \geq 0.01$, one $p < 0.01$) and only mild tail departure on visual inspection—treated as approximately normal for regression at n = 101; **Rejected** = $p < 0.01$ on both tests and/or clear departure from normality on Q–Q / detrended plots (interpret model cautiously).

DISCUSSION

Principal Findings and Comparison With Previous Studies

In this **natural experiment employing a quasi-longitudinal approach,** focusing on older adults adults residing in two urban areas with substantially different ambient $PM_{2.5}$ concentrations, we found that long-term exposure to higher $PM_{2.5}$ levels was significantly associated with reduced lung function, specifically reflected by lower FEV1_z and FVC_z scores. **This association remained consistent and robust after rigorous adjustment for demographic, socioeconomic, and anthropometric covariates, including Body Mass Index (BMI). The persistence of these findings after controlling for BMI—a known physiological determinant of lung capacity—suggests that the observed decline is independently driven by particulate exposure rather than variations in body composition.**

A key strength of this study is the requirement for participants to have resided at their current address for **at least ten continuous years, which provides a quasi-longitudinal perspective. This decadal residency threshold represents a significant methodological advancement over most large-scale global air pollution studies, which typically rely on current addresses or short-term exposure windows (1–3 years). By implementing this strict filter, we effectively eliminated the "exposure noise" and migration bias that often weaken the causal claims of standard epidemiological research.** By ensuring that the exposure period significantly precedes the lung function measurement, **this residency threshold establishes a clear temporal relationship and addresses the issue of temporal precedence—a key requirement for causal**

inference—thereby reducing the risk of reverse causality often found in standard cross-sectional studies. Notably, **no statistically significant difference was observed in FEV_1/ FVC_z scores**, suggesting that the primary impact of chronic $PM_{2.5}$ exposure in this older adults population reflects a reduction in lung volumes rather than obstructive impairment.

This lack of obstructive impairment is consistent with our study design, which applied stringent exclusion criteria to select only "apparently healthy" older adults participants, effectively screening out individuals with symptomatic chronic obstructive pulmonary disease (COPD), asthma, or significant smoking histories. Consequently, while the participants appeared clinically normal, the lower FEV1_z and FVCz scores in the high-exposure group reveal a **subclinical decline** in lung capacity that would otherwise remain undetected by traditional diagnostic thresholds. **This identification of subclinical risk is a cornerstone of early detection, providing a critical window for intervention before irreversible damage occurs. This exemplifies the Precision Public Health approach, which seeks to move beyond reactive medicine by using granular data to identify physiological vulnerability in specific high-risk groups before clinical symptoms arise.**

Our findings align with a large body of literature demonstrating the detrimental effects of particulate air pollution on lung function. **However, while massive cohort studies in Europe and North America often struggle with exposure homogeneity or residential mobility** [40], **our natural experiment design isolates the impact of extreme environmental contrast with unprecedented precision.** Research has often found stronger associations for FEV1_z and FVC_z compared with the FEV1/FVC_z ratio, supporting the idea that chronic exposure may contribute more to restrictive-like patterns or reduced lung expansion capacity than to airway obstruction. Our findings contribute additional evidence from Jakarta, one of the most polluted megacities in the world, where older adults may experience particularly high cumulative exposure.

Strengths and Limitations

This study has several methodological strengths. It focuses on an understudied but vulnerable population—older adults individuals—living in an exceptionally polluted urban environment. **The methodological novelty of this study is anchored in its decade-long exposure filter applied to a strictly screened older adults population, allowing for a cleaner isolation of pollution-induced deficits than has been achieved in prior global assessments. Unlike conventional toxicogenomic or environmental studies that treat exposure as a snapshot in time** [41,42], **our approach recognizes that the "aging lung" is a product of cumulative environmental insults. By employing a natural** experiment **design** [17,18,19,20], **this study exploited the significant environmental contrast between two geographically distinct areas, which is considered a quasi-gold standard for observational research.** This design was **intentionally chosen to bridge the ethical gap where a Randomized Controlled Trial (RCT) is impossible** [25,26,27]; **by utilizing existing extreme environmental gradients, we simulated a 'quasi-experimental' condition** that **approaches the causal rigor of an RCT** while **maintaining real-world**

translational relevance. The translational value of this research lies in its ability to bridge the gap between environmental monitoring and clinical respiratory outcomes. Furthermore, the use of GLI-2012 z-scores provides a standardized and ethnically sensitive threshold that serves as a robust tool for preventive screening, ensuring that lung function decline is identified accurately even in asymptomatic populations. By isolating $PM_{2.5}$ as an independent driver of lung decline in an 'ultrapure' cohort, we provide actionable evidence that can be directly translated into clinical screening guidelines for older adults residents in high-pollution corridors.

Standardized lung function assessments were performed according to **ATS/ERS guidelines** [39]. **To ensure data validity across the contrasting altitudes and temperatures of coastal Jakarta and highland Bandung, all measurements utilized internal BTPS (Body Temperature, Ambient Pressure, Saturated with water vapor) compensation.** Furthermore, the use of GLI-2012 z-scores **calculated using South East Asian-specific equations** allowed for age-, sex-, height-, and ethnicity-adjusted comparisons, eliminating potential bias from ethnic physiological variations.

The stringent exclusion of participants with pre-existing respiratory diseases ensures that the observed differences in lung function z-scores reflect the chronic impact of ambient PM2.5 exposure on the 'healthy' aging lung, rather than the confounding effects of clinical pathologies. Although confounding was rigorously addressed through restriction, frequency matching, and multivariable regression adjustment, residual confounding due to unmeasured or imperfectly measured factors cannot be entirely excluded, as is inherent to observational research. This clinical rigor was complemented by high statistical validity; residual-based diagnostic tests confirmed that the unstandardized residuals for the primary lung volume models using FEV_1 and FVC Z-scores outcomes demonstrated clear normal distributions in Shapiro-Wilk tests, ensuring the appropriateness and reliability of the parametric regression estimates.

A further limitation relates to the use of two study areas with contrasting exposure profiles. While this design enhances internal validity by maximizing exposure contrast and minimizing heterogeneity in contextual factors, it necessarily limits the variability of exposure levels [43,44,45,46]. **However, unlike standard longitudinal cohorts that may suffer from exposure homogeneity, our natural experiment design provided the necessary baseline comparison to isolate pollution-induced deficits from natural biological aging.** This trade-off between internal validity and exposure variability reflects a deliberate methodological choice to prioritize causal inference over broad exposure representation.

The integration of this natural experiment framework with a strict 10-year residency requirement significantly strengthened the internal validity of the study by reducing exposure misclassification and establishing a clear temporal link between long-term pollution and subclinical lung function decline.

Translational Implications for Precision Public Health

Our findings have direct implications for public health policy in rapidly urbanizing Southeast Asian megacities. The evidence of significant lung volume reduction—even in 'apparently healthy' older adults—suggests that current public health advisories based on general population averages may be insufficient for vulnerable age groups. Consequently, this study underscores the urgent need for robust promotive and preventive public health strategies tailored to the unique risks of the urban older adults. **Consequently, this study underscores the urgent need for robust promotive and preventive public health strategies tailored to the unique risks of the urban older adults.**

From a **translational perspective**, this study advocates for a **Precision Public Health framework that moves beyond broad monitoring toward targeted respiratory screening and primary prevention. From a promotive standpoint, health authorities should utilize these findings to enhance community-based education, raising awareness among older adults residents and their caregivers regarding the long-term respiratory hazards of decadal exposure. Specifically, integrating spirometry z-score assessments into routine older adults community health posts (*Posbindu*) in high-exposure districts, such as Kedoya, could allow for the early detection of subclinical decline. Furthermore, these results provide actionable evidence for urban planners to prioritize localized "clean air zones" and specialized indoor filtration subsidies for long-term older adults residents in areas validated as high-contrast pollution zones, effectively bridging the gap between environmental data and clinical protection. Finally, from a clinical advocacy standpoint, these findings empower healthcare practitioners to utilize decadal residential history as a critical, independent risk factor for respiratory decline, ensuring that long-term pollution exposure is prioritized in clinical screenings regardless of a patient's smoking status.**

CONCLUSIONS

By utilizing a natural experiment design with a strict 10-year residency requirement, this study demonstrates that long-term exposure to elevated ambient levels is associated with markedly reduced lung volumes (FEV_1 and FVC z-scores) among older adults adults. **By exploiting extreme environmental contrasts as an ethical alternative to randomized trials, this framework—supported by BTPS-compensated measurements and ethnicity-adjusted z-scores—ensures that the observed deficits are attributable to pollution rather than geographic or biological variations. The stability of exposure over a decade, combined with robust model diagnostics confirming the normality of residuals, strengthens the evidence for a chronic, cumulative impact, providing a superior causal inference compared to standard cross-sectional assessments.**

Crucially, these reductions were observed in an **'ultrapure' population of apparently healthy individuals**, indicating that chronic particulate exposure primarily contributes to **subclinical, restrictive-pattern impairment**—characterized by volume loss—rather than airflow obstruction.

This finding underscores the necessity of a Precision Public Health approach, utilizing standardized z-scores to detect environmental lung damage that remains hidden under traditional clinical thresholds, thereby allowing for earlier identification of at-risk individuals within vulnerable aging populations.

Ultimately, this research provides the evidentiary foundation for a dual-track strategy in public health: robust health promotion to increase community awareness of long-term hazards, and precise primary prevention through routine respiratory screening in high-pollution corridors. These findings provide **actionable translational evidence** for shifting public health strategies from broad, population-wide advisories toward **targeted, data-driven interventions**. Beyond general air-quality regulations, this study advocates for the integration of decadal environmental risk assessments into routine geriatric clinical care. **The translational value of this research** lies in its capacity to bridge the gap between environmental monitoring and clinical protection, **supporting a Precision Public Health framework that prioritizes high-resolution screening for long-term residents in validated pollution hotspots.** While our **quasi-longitudinal approach** provides **robust evidence of the chronic impact of decadal exposure, future prospective longitudinal studies could further illuminate the real-time rate of lung function decline and the potential reversibility of these subclinical deficits in populations transitioning between different pollution trajectories.**

Recommendations

Based on the evidence of subclinical lung function deficits in long-term residents, this study proposes a multi-sectoral framework for protecting vulnerable aging populations:

1. **For Government and Urban Policy (Precision Regulation)**
   - **Localised Monitoring:** Strengthen high-resolution ambient air quality monitoring ($PM_{2.5}$) in densely populated corridors and establish "Respiratory Protection Zones" where long-term residents are prioritized for health surveillance.
   - **Emission Control:** Tighten localized emissions standards for transport and industry in high-burden areas, and integrate real-time pollution alerts into municipal disaster-readiness systems specifically tailored for geriatric protection.
2. **For Clinical and Public Health Services (Early Detection)**
   - **Screening Integration:** Incorporate routine spirometry with standardized z-scores into primary care for asymptomatic older adults in high-pollution areas.
   - **Targeted Interventions:** Promote the use of well-fitted masks (e.g., N95/KN95) and limit outdoor exposure during peak pollution hours as a precision health advisory for "ultrapure" but vulnerable populations.
3. **Future Research Directions (Mechanistic Clarity)**

- **Longitudinal & Biomarker Studies:** To build upon this natural experiment, future research should employ repeated spirometry to track the real-time rate of decline. Incorporating inflammatory biomarkers and personal exposure monitoring will further clarify the causal pathways of chronic particulate impact.
- **Intervention Trials:** Research should evaluate modifiable strategies, such as indoor air filtration and community-led emission reduction, to determine their efficacy in reversing or halting subclinical lung function loss.

- **Author Contributions**
- Conceptualization: Hari Krismanuel.
- Data curation: Purnamawati Tjhin.
- Formal analysis: Hari Krismanuel.
- Investigation: Hari Krismanuel.
- Methodology: Hari Krismanuel.
- Visualization: Purnamawati Tjhin.
- Writing – original draft: Hari Krismanuel.
- Writing – review & editing: Hari Krismanuel

Conflicts of interest.

- The authors declare no conflict of interest.

Declaration of funding.

- There is no financial funding of this research.

Acknowledgements

- We would like to thank the village heads of Pangalengan and Kedoya sub-districts, village officials, research participants, and personnel for their participation in this study.

REFERENCES

1. United States Environmental Protection Agency. Particulate Matter (PM) Basics [Internet]. 2023 Jul 11 [cited 2025 Jul 19]. Available from: https://www.epa.gov/pm-pollution/particulate-matter-pm-basics
2. Cohen AJ, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet.* 2017 May 13; 389(10082): 1907–1918. doi: 10.1016/S0140-6736(17)30505-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC5439030/pdf/main.pdf.
3. Li T, et al. Fine particulate matter ($PM_{2.5}$): The culprit for chronic lung diseases in China. *Chronic Dis Transl Med.* 2018 Sep; 4(3): 176–186. doi: 10.1016/j.cdtm.2018.07.002. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6160608/pdf/main. pdf.
4. Kim D, Chen Z, Zhou LF, Huang SX. Air pollutants and early origins of respiratory diseases. *Chronic Dis Transl Med.* Jun 2018; 4(2): 75-94. https://doi.org/10.1016%2Fj.cdtm.2018.03.003 Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC6033955/

5. Jia L, Zhou X, Wang Q. Effects of Agricultural Machinery Operations on $PM_{2.5}$, PM_{10} and TSP in Farmland under Different Tillage Patterns. *Agriculture*. 2023; *13*(5): 930, https://doi.org/10.3390/agriculture13050930. Available from: https://www.mdpi.com/ 2077-0472/13/5/930
6. Lim EY, Kim GD. Particulate Matter-Induced Emerging Health Effects Associated with Oxidative Stress and Inflammation. *Antioxidants* 2024, *13*(10), 1256; https://doi.org/10.3390/antiox13101256
7. Thangavel P, Park D, Lee YC. Recent Insights into Particulate Matter ($PM_{2.5}$)-Mediated Toxicity in Humans : An Overview. *Int J Environ Res Public Health*. 2022 Jun; 19(12): 7511. https://doi.org/10.3390%2Fijerph19127511
8. Xing YF, Xu YH, Shi MH, Lian YX. The impact of $PM_{2.5}$ on the human respiratory system. *J Thorac Dis*. 2016 Jan;8(1):E69-E74. doi: https://doi.org/10.3978/j.issn.2072-1439.2016.01.19. Available from: https://pubmed. ncbi.nlm.nih.gov/26904255/.
9. Yang L, Li C, Tang X. The Impact of PM 2.5 on the Host Defense Of Respiratory System. *Front Cell Dev Biol*. 2020 March;8:91. https://doi.org/10.3389/fcell.2020. 00091. Available from: https://www.frontiersin.org/journals/cell-and-developmental-biology/
10. Amnuaylojaroen T, Parasin N. Pathogenesis of $PM_{2.5}$-Related Disorders in Different Age Groups: Children, Adults, and the Older adults. *Epigenomes*. 2024 Jun; 8(2): 13. doi: 10.3390/epigenomes8020013. Available from: https://www.ncbi.nlm.nih.gov/pmc/ articles/PMC11036283/pdf/epigenomes-08-00013.pdf.
11. Croft DP, et al. The Association between Respiratory Infection and Air Pollution in the Setting of Air Quality Policy and Economic Change. *Multicenter Study Ann Am Thorc Soc*. 2019 March; 16(3): 321-330. https://doi.org/10.1513/AnnalsATS.201810-691OC. Available from: https://pubmed.ncbi.nlm. nih.gov/30398895/.
12. BreathSafeAir. Air Pollution in Indonesia: Understanding the Crisis and How to Protect Yourself *[Internet]*. 2024 *[cited 2025 Jul 19]*. Available from: https://breathesafeair.com/ air-pollution-in-indonesia/
13. Rosman PS, Samah MAA, Yunus K, Hussain MRM. Particulate Matter (PM 2.5) At Construction Site: A Review. *Int J Recent Technol Eng*. 2019 May;8(1C2):255-259. Available from: https://www.ijrte.org/wp-content/uploads/papers/v8i1C2/A10430581C 219.pdf
14. Craig P, Campbell M, Deidda M, Dundas R, Green J, Katikireddi SV, et al. Using natural experiments to evaluate population health interventions: a framework for producers and users of evidence. *Public Health Res* 2025;13(3). https://doi.org/10.3310/JTYW6582
15. Albers PN, Rinaldi C, Brown H, Mason KE, d'Apice K, et al. Natural experiments for the evaluation of place-based public health interventions: a methodology scoping review. *Front. Public Health*. 2023; 11:1192055. doi: 10.3389/fpubh.2023.1192055
16. Ogilvie D, Adams J, Bauman A, Gregg EW, Panter J, et al. Using natural experimental studies to guide public health action: turning the evidence-based medicine paradigm on its head. *J Epidemiol Community Health*. 2019 Nov 19;74(2):203–208. doi: 10.1136/jech-2019-213085
17. Crane M, Bohn-Goldbaum E, Grunseit A, Bauman A. Using natural experiments to improve public health evidence: a review of context and utility for obesity prevention. *Health Res Policy Syst*. 2020 May 18;18:48. doi: 10.1186/s12961-020-00564-2
18. Xanthopoulou P, Sahinidis A, Vassiliou EE, Kavoura A. When Intentions Stall: Exploring the Quasi-Longitudinal Divide Between Entrepreneurial Intention and Action. *Adm. Sci.* 2026, *16*(1), 14; https://doi.org/10.3390/admsci16010014

19. Kim TY, Kim YK. A Quasi-Longitudinal Study on English Learning Motivation and Attitudes: The Case of South Korean Students. The Journal of Asia Tefl 2016; 13(2): 138-155. http://dx.doi.org/10.18823/asiatefl.2016.13.2.5.138
20. Ong-Salvador R, Laveneziana P, de Jongh F. ERS/ATS Global Lung Function Initiative normal values and classifying severity based on z-scores instead of per cent predicted. Breathe (Sheff). 2024 Dec 10;20(3):230227. doi: 10.1183/20734735.0227-2023
21. Kanj AN, Scanlon PD, Yadav H, Smith WT, Herzog TL, et al. Application of Global Lung Function Initiative Global Spirometry Reference Equations across a Large, Multicenter Pulmonary Function Lab Population. Am J Respir Crit Care Med. 2023; 209(1). https://doi.org/10.1164/rccm.202303-0613OC
22. Council for International Organizations of Medical Sciences (CIOMS). International Ethical Guidelines for Health-related Research Involving Humans. 4th ed. Geneva: CIOMS; 2016.
23. Hosseini A, Jackson AC, Bahramnezhad F. Ethical Considerations in Interventional Studies: A Systematic Review Ethics and Interventional Study.
24. Kaye DK. Navigating ethical challenges of conducting randomized clinical trials on COVID-19. *Philos Ethics Humanit Med.* 2022;17(2):1-11. https://doi.org/10.1186/s13010-022-00115-3
25. STROBE Statement. STROBE Checklists [Internet]. [Place unknown]. STROBE Initiative; 2025 [cited 24 Jul 2025]. Available from: https://www.strobe-statement.org/checklists/.
26. Cushieri S. The STROBE guidelines. Saudi J Anaesth. 2019;13(Suppl 1):S31–S34. https://doi.org/10.4103/sja.SJA_543_18
27. Serdar CC, Cihan M, Yücel D, Serdar MA. Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. Biochem Med. 2020 Dec 15; 31(1):010502. doi: 10.11613/BM.2021.010502. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7745163/pdf/bm-31-1-010502.pdf
28. Marsh J. Sample Size Calculations. *Research Skills Seminar Series 2019 CAHS Research Education Program [Internet]. 2019 [cited 2025 Jul 19].* Available from: https://pch.health.wa.gov.au/-/media/Files/Hospitals/PCH/General-documents/Research/Research-Education/Hand outs/Sample SizeCalcHand outs.ashx.
29. Beard J. (2024). Sample size calculations for cross-sectional studies. *Sudan J Med Sci [Internet]. 2024 [cited 2025 Jul 19].* Available from: https://www.ajol.info/ssmj/ article/view
30. Whelan MJ, Pemberton E, Hughes CB, Swansborough C, Goslan EH, Gouin T, et al. A tiered assessment of human health risks associated with exposure to persistent, mobile and toxic chemicals via drinking water. Sci Total Environ. 2025;958:177868.
31. Serdar CC, Cihan M, Yücel D, Serdar MA. Sample size, power and effect size revisited: simplified and practical approaches in pre-clinical, clinical and laboratory studies. Biochem Med. 2020 Dec 15; 31(1):010502. doi: 10.11613/BM.2021.010502. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7745163/pdf/bm-31-1-010502.pdf
32. Marsh J. Sample Size Calculations. *Research Skills Seminar Series 2019 CAHS Research Education Program [Internet]. 2019 [cited 2025 Jul 19].* Available from: https://pch.health.wa.gov.au/-/media/Files/Hospitals/PCH/General-documents/Research/Research-Education/Hand outs/Sample SizeCalcHand outs.ashx.
33. Beard J. (2024). Sample size calculations for cross-sectional studies. *Sudan J Med Sci [Internet]. 2024 [cited 2025 Jul 19].* Available from: https://www.ajol.info/ssmj/ article/view

34. Buckley J. Conducting Power Analyses to Determine Sample Sizes in Quantitative Research: A Primer for Technology Education Researchers Using Common Statistical Tests. *J Technol Educ.* 2024;35(2): 81-109. DOI: 10.21061/jte.v35i2.a.5. Available from: https://jte-journal.org/articles/10.21061/ jte.v35i2. a.5
35. Sruthi KG, Aditya, Panda P, Mohanty JR, Behera MR. Prevalence of normal weight obesity among adults in Southeast Asia: Insights from a systematic review and meta-analysis. Metab Open. 2025 Dec;28:100416. https://doi.org/10.1016/j.metop.2025.100416
36. Okawa Y, Mitsuhashi T, Tsuda T. The Asia-Pacific Body Mass Index Classification and New-Onset Chronic Kidney Disease in Non-Diabetic Japanese Adults: A Community-Based Longitudinal Study from 1998 to 2023. *Biomedicines* 2025, *13*(2), 373; https://doi.org/10.3390/biomedicines13020373
37. Silva-Reis A, Brill B, Rangel MARB, Ferreira RM, Melamed D, et al. Association Between Visceral Fat and Lung Function Impairment in Overweight and Grade I Obese Women: A Cross-Sectional Study. *Adv. Respir. Med.* 2024; *92*(6): 548-558; https://doi.org/10.3390/ arm92060048
38. Peters U, Dixon AE. The effect of obesity on lung function. *Expert Rev Respir Med.* 2018 Aug 14;12(9):755–767. doi: 10.1080/17476348.2018.1506331
39. Graham BL, Steenbruggen I, Miller MR, Barjactarevic IZ, Cooper BG, et al. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med.* 2019;200(8):e71-e88. https://doi.org/10.1164/rccm.201908-1590ST
40. Hoek G, Vienneau D, de Hoogh K. Does residential address-based exposure assessment for outdoor air pollution lead to bias in epidemiological studies?. *Environ Health.* 2024: 23:75. https://doi.org/10.1186/s12940-024-01111-0
41. Moffat I, Chepelev N, Labib S, Bourdon-Lacombe J, Kuo B, Buick JK, et al. Comparison of toxicogenomics and traditional approaches to inform mode of action and points of departure in human health risk assessment of benzo[a]pyrene in drinking water. *Crit Rev Toxicol.* 2015;45(1):1-43. doi: 10.3109/10408444.2014.973934.
42. Tuo JY, Shen QM, Li ZY, Tan JY, Fang J, et al. Residential mobility and liver cancer risk: findings from a prospective cohort study in Chinese women. *BMC Public Health.* 2024; 24:1196. https://doi.org/10.1186/s12889-024-18574-y
43. Bulbulia JA. Methods in causal inference. Part 1: causal diagrams and confounding. *Evol Hum Sci.* 2024;6:640. doi:10.1017/ehs.2024.35.
44. Weaver J, Voss EA, Cafri G, Beyrau K, Nashleanas M, Suruki R. The necessity of validity diagnostics when drawing causal inferences from observational data: lessons from a multi-database evaluation of the risk of non-infectious uveitis among patients exposed to Remicade®. *BMC Med Res Methodol.* 2024;24:322. doi:10.1186/s12874-024-02428-7.
45. Miller LC, Shaikh SJ, Jeong DC, Wang L, Gillig TK, Godoy CG, et al. Causal inference in generalizable environments: systematic representative design. *Psychol Inq.* 2019;30(4):173–202. doi:10.1080/1047840x.2019.1693866.
46. Hernán MA, Robins JM. *Causal inference: What if.* Boca Raton (FL): Chapman & Hall/CRC; 2020.

Precision Public Health Approach to Chronic PM2.5 Exposure

ORIGINALITY REPORT

10%	9%	7%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1 pmc.ncbi.nlm.nih.gov
Internet Source

2 www.mdpi.com
Internet Source

3 www.science.gov
Internet Source

4 academic.oup.com
Internet Source

5 public-pages-files-2025.frontiersin.org
Internet Source

6 Yi-Giien Tsai, Jiu-Yao Wang, Kuender D. Yang, Hsiao-Yu Yang et al. " Long-term PM exposure impairs lung growth and increases airway inflammation in Taiwanese school children ", ERJ Open Research, 2025
Publication

7 research.tees.ac.uk
Internet Source

8 www.aimspress.com
Internet Source

9 Leonard B. Bacharier, Theresa W. Guilbert, Constance H. Katelaris, Antoine Deschildre e al. "Dupilumab Improves Lung Function Parameters in Pediatric Type 2 Asthma: VOYAG Study", The Journal of Allergy and Clinical Immunology: In Practice, 2023
Publication

10 journal.copdfoundation.org
Internet Source

11 www.ncbi.nlm.nih.gov
Internet Source

12 bmcgeriatr.biomedcentral.com
Internet Source

13 Submitted to University of Cincinnati
Student Paper

14 vdoc.pub
Internet Source

15 www.scivisionpub.com
Internet Source

16 Guoyong Ding, Jingjing Xia, Jayant M. Pinto, Zahia Esber et al. "Poor olfaction is associat with lower pulmonary function in older adults", CHEST, 2025
Publication

17 K.G. Sruthi, C. Aditya, Paramjot Panda, Jyoti Ranjan Mohanty, Manas Ranjan Behera. "Prevalence of Normal Weight Obesity Among Adults in Southeast Asia: Insights from a Systematic Review and Meta-Analysis", Metabolism Open, 2025
Publication

18 journals.sagepub.com
Internet Source

19 Chi-Hsin S. Chen, Tien-Chueh Kuo, Han-Chun Kuo, Yufeng J. Tseng, Ching-Hua Kuo, Tzu-Hsuen Yuan, Chang-Chuan Chan. "Metabolomics of Children and Adolescents Exposed Industrial Carcinogenic Pollutants", Environmental Science & Technology, 2019
Publication

20 Sjostrom, M., M. Lewne, M. Alderling, P. Willix, P. Berg, P. Gustavsson, and M. Svartengr "A Job-Exposure Matrix for Occupational Noise: Development and Validation", Annals o Occupational Hygiene, 2013.
Publication

21 Yueh-Ying Han, Kristina Gaietto, Molin Yue, Franziska J. Rosser, Wei Chen, Juan C. Celed "Prevalence and Potential Risk Factors for T2-Low Asthma Among School-Aged Childrer the National Health and Nutrition Examination Survey, 2007–2012", The Journal of Aller and Clinical Immunology: In Practice, 2025
Publication

22 bmcpublichealth.biomedcentral.com
Internet Source

23 pubmed.ncbi.nlm.nih.gov
Internet Source

24 usir.salford.ac.uk
Internet Source

25 Submitted to National School of Healthcare Science
Student Paper

26 Submitted to The University of Texas at Arlington
Student Paper

27 www.frontiersin.org
Internet Source

28	www.seejph.com Internet Source	
29	"Ambient Air Pollution and Health Impact in China", Springer Science and Business Mec LLC, 2017 Publication	
30	Yang, Hong-Qi, Qi Zhang, San-Shan Tu, You Wang, Yi-Min Li, and Yi Huang. "Effects of inhomogeneous elastic stress on corrosion behaviour of Q235 steel in 3.5% NaCl soluti using a novel multi-channel electrode technique", Corrosion Science, 2016. Publication	
31	jped.elsevier.es Internet Source	
32	pure.eur.nl Internet Source	
33	Submitted to University of Technology, Sydney Student Paper	
34	clinmedjournals.org Internet Source	
35	doczz.net Internet Source	
36	link.springer.com Internet Source	
37	www.researchgate.net Internet Source	
38	Yulong Chen. "Early exposure to air pollution and cognitive development later in life: Evidence from China", China Economic Review, 2024 Publication	
39	bjsm.bmj.com Internet Source	
40	bmchealthservres.biomedcentral.com Internet Source	
41	f1000research-files.f1000.com Internet Source	
42	oup.silverchair-cdn.com Internet Source	

43	www.jornaldepneumologia.com.br Internet Source
44	www.naturalgrocers.com Internet Source

Exclude quotes	On	Exclude matches	< 10 words
Exclude bibliography	On		

Precision Public Health Approach to Chronic PM2.5 Exposure

GRADEMARK REPORT

FINAL GRADE	GENERAL COMMENTS
/100	

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8

PAGE 9

PAGE 10

PAGE 11

PAGE 12

PAGE 13

PAGE 14

PAGE 15

PAGE 16

PAGE 17

PAGE 18

PAGE 19

PAGE 20

PAGE 21

PAGE 22

PAGE 23

PAGE 24

PAGE 25

PAGE 26

PAGE 27

PAGE 28

DOKUMEN BUKTI REVIEW ARTIKEL

Peer Review History

Original Submission January 30, 2026

16 Feb 2026

Decision Letter - George Kuryan, Editor

-->PONE-D-26-04311-->-->Precision public health: a natural experiment on chronic high-contrast PM2.5 exposure and pulmonary function among older adults-->-->PLOS One

Dear Dr. Krismanuel,

Thank you for submitting your manuscript to PLOS ONE. After careful consideration, we feel that it has merit but does not fully meet PLOS ONE's publication criteria as it currently stands. Therefore, we invite you to submit a revised version of the manuscript that addresses the points raised during the review process.

Please submit your revised manuscript by Apr 02 2026 11:59PM. If you will need more time than this to complete your revisions, please reply to this message or contact the journal office at plosone@plos.org. When you're ready to submit your revision, log on to https://www.editorialmanager.com/pone/ and select the 'Submissions Needing Revision' folder to locate your manuscript file.

Please include the following items when submitting your revised manuscript:-->

- A letter that responds to each point raised by the academic editor and reviewer(s). You should upload this letter as a separate file labeled 'Response to Reviewers'.
- A marked-up copy of your manuscript that highlights changes made to the original version. You should upload this as a separate file labeled 'Revised Manuscript with Track Changes'.
- An unmarked version of your revised paper without tracked changes. You should upload this as a separate file labeled 'Manuscript'.

If you would like to make changes to your financial disclosure, please include your updated statement in your cover letter. Guidelines for resubmitting your figure files are available below the reviewer comments at the end of this letter.

If applicable, we recommend that you deposit your laboratory protocols in protocols.io to enhance the reproducibility of your results. Protocols.io assigns your protocol its own identifier

(DOI) so that it can be cited independently in the future. For instructions see: https://journals.plos.org/plosone/s/submission-guidelines#loc-laboratory-protocols. Additionally, PLOS ONE offers an option for publishing peer-reviewed Lab Protocol articles, which describe protocols hosted on protocols.io. Read more information on sharing protocols at https://plos.org/protocols?utm_medium=editorial-email&utm_source=authorletters&utm_campaign=protocols.

We look forward to receiving your revised manuscript.

Kind regards,

George Kuryan

Academic Editor

PLOS One

Journal Requirements:

When submitting your revision, we need you to address these additional requirements.

1. Please ensure that your manuscript meets PLOS ONE's style requirements, including those for file naming. The PLOS ONE style templates can be found at

https://journals.plos.org/plosone/s/file?id=wjVg/PLOSOne_formatting_sample_main_body.pdf and

https://journals.plos.org/plosone/s/file?id=ba62/PLOSOne_formatting_sample_title_authors_affiliations.pdf

2. We note that your Data Availability Statement is currently as follows:

“All relevant data are within the manuscript and its Supporting Information files.”

Please confirm at this time whether or not your submission contains all raw data required to replicate the results of your study. Authors must share the “minimal data set” for their submission. PLOS defines the minimal data set to consist of the data required to replicate all study findings reported in the article, as well as related metadata and methods (https://journals.plos.org/plosone/s/data-availability#loc-minimal-data-set-definition).

For example, authors should submit the following data:

- The values behind the means, standard deviations and other measures reported;

- The values used to build graphs;

- The points extracted from images for analysis.

Authors do not need to submit their entire data set if only a portion of the data was used in the reported study.

If your submission does not contain these data, please either upload them as Supporting Information files or deposit them to a stable, public repository and provide us with the relevant URLs, DOIs, or accession numbers. For a list of recommended repositories, please see https://journals.plos.org/plosone/s/recommended-repositories.

If there are ethical or legal restrictions on sharing a de-identified data set, please explain them in detail (e.g., data contain potentially sensitive information, data are owned by a third-party organization, etc.) and who has imposed them (e.g., an ethics committee). Please also provide contact information for a data access committee, ethics committee, or other institutional body to which data requests may be sent. If data are owned by a third party, please indicate how others may request data access.

3. If the reviewer comments include a recommendation to cite specific previously published works, please review and evaluate these publications to determine whether they are relevant and should be cited. There is no requirement to cite these works unless the editor has indicated otherwise.

[Note: HTML markup is below. Please do not edit.]

Reviewers' comments:

Reviewer's Responses to Questions

-->**Comments to the Author**

1. Is the manuscript technically sound, and do the data support the conclusions?

The manuscript must describe a technically sound piece of scientific research with data that supports the conclusions. Experiments must have been conducted rigorously, with appropriate controls, replication, and sample sizes. The conclusions must be drawn appropriately based on the data presented. -->

Reviewer #1: Partly

Reviewer #2: Yes

****

-->2. Has the statistical analysis been performed appropriately and rigorously? -->

Reviewer #1: No

Reviewer #2: Yes

****

-->3. Have the authors made all data underlying the findings in their manuscript fully available?

The PLOS Data policy requires authors to make all data underlying the findings described in their manuscript fully available without restriction, with rare exception (please refer to the Data Availability Statement in the manuscript PDF file). The data should be provided as part of the manuscript or its supporting information, or deposited to a public repository. For example, in addition to summary statistics, the data points behind means, medians and variance measures should be available. If there are restrictions on publicly sharing data—e.g. participant privacy or use of data from a third party—those must be specified.-->

Reviewer #1: Yes

Reviewer #2: Yes

****

-->4. Is the manuscript presented in an intelligible fashion and written in standard English?

PLOS ONE does not copyedit accepted manuscripts, so the language in submitted articles must be clear, correct, and unambiguous. Any typographical or grammatical errors should be corrected at revision, so please note any specific errors here.-->

Reviewer #1: Yes

Reviewer #2: Yes

****

-->5. Review Comments to the Author

Please use the space provided to explain your answers to the questions above. You may also include additional comments for the author, including concerns about dual publication, research ethics, or publication ethics. (Please upload your review as an attachment if it exceeds 20,000 characters)-->

Reviewer #1: This manuscript presents a natural experiment evaluating decadal $PM_{2.5}$ exposure and lung function in an “ultrapure” cohort of non-smoking older adults in Indonesia. The 10-year residency filter and use of GLI-2012 Southeast Asian z-scores represent notable methodological strengths. The findings demonstrate robust associations between chronic exposure and reduced FEV_1_z and FVC_z without obstructive impairment.

The study is innovative, clinically relevant, and translationally ambitious. However, several conceptual and methodological claims are overstated, and causal language exceeds the evidentiary strength of the design.

MAJOR STRENGTHS

1. Methodological Innovation

10-year stable residency filter is a genuine strength.

BTPS compensation explicitly described (rarely reported in field studies).

GLI-2012 SEA z-scores appropriately used.

Strict exclusion criteria minimize confounding.

2. Clean Physiological Signal

The restrictive-type pattern (↓FEV_1_z + ↓FVC_z with preserved ratio) is biologically coherent for chronic particulate exposure.

3. Internal Validity

Frequency matching verified.

Strong regression diagnostics.

Conservative $\alpha = 0.01$ threshold.

Assumptions carefully tested.

4. Translational Framing

The Precision Public Health (PPH) positioning is forward-thinking and policy-oriented.

MAJOR CONCERNS

1. Overstatement of “Global First”

You repeatedly state:

“first globally”

“pioneering application globally”

“unprecedented precision”

This is not entirely accurate.

Natural experiments + long residency filters have been used before (though not identically).

Recommendation:

Reframe as:

“To our knowledge, among the first in Southeast Asia…”

Avoid global-first claims unless you provide a systematic citation gap analysis.

2. Causal Language Exceeds Design

You use phrases like:

“primary driver”

“causal rigor”

“as-if random assignment”

“approaches RCT-level inference”

This is problematic.

This is still:

Cross-sectional measurement of outcome

Area-level exposure proxy

No individual-level long-term $PM_{2.5}$ quantification

The 10-year filter strengthens temporal plausibility — but does not create causal equivalence to RCT.

Suggested Reframe:

Replace:

“primary driver”

With:

“strong independent association consistent with a chronic exposure effect”

Replace:

“approaches causal rigor of RCT”

With:

“strengthens causal inference within observational constraints”

3. Area-Level Exposure Proxy Limitation Underplayed

Exposure classification is binary (Kedoya vs Pangalengan).

Issues:

No personal exposure monitoring

No cumulative dose modeling

No indoor exposure adjustment

No time-activity pattern analysis

This is fine for a natural experiment — but you must emphasize it more clearly in limitations.

Currently limitations are discussed, but defensively rather than transparently.

Add explicitly:

Ecological exposure assignment risk

Within-area variability not captured

No historical exposure trajectory modeling

4. Restrictive Pattern Interpretation Needs Caution

You interpret reduced volumes with preserved ratio as:

“restrictive-type impairment”

Important nuance:

Spirometry alone cannot diagnose true restriction.

You need TLC for confirmation.

You should say:

“restrictive-pattern spirometry”

Not imply parenchymal stiffening definitively

5. Residual Normality Justification Is Slightly Weak

For FEV_1/FVC_z model:

S–W $p = 0.001$

You justify approximate normality due to n=101.

Better to add:

Q-Q plot visual confirmation

Possibly robust regression sensitivity analysis (even briefly stated)

That strengthens credibility.

STATISTICAL COMMENTS

Effect Sizes

Cohen's d = 1.21 for FVC_z is large.

That is substantial and clinically meaningful.

You should:

Explicitly interpret clinical magnitude (e.g., ">1 SD reduction corresponds to X percentile shift").

R^2 Values

31.5% for FEV_1_z

25.9% for FVC_z

These are strong for environmental health.

You should highlight:

Exposure explained a substantial proportion of variance relative to demographic variables.

CONCEPTUAL COMMENTS

Precision Public Health Framing

The PPH narrative is strong — but slightly repetitive.

You mention PPH ~25+ times.

Suggestion:

Reduce repetition

Focus PPH section into a sharper translational paragraph

Make it tighter and more strategic

Right now it feels slightly promotional.

STRUCTURAL SUGGESTIONS

Abstract

Excellent clarity.

However:

Reduce “global first”

Tone down causal phrasing

Discussion

Strong.

But trim redundancy in:

Causal inference justification

RCT comparisons

Repeated BTPS emphasis

Conclusion

Very strong but could be 15% shorter.

EXTERNAL VALIDITY

Sample is:

Non-smokers

Normal BMI

No comorbidities

Stable 10-year residents

This maximizes internal validity but limits generalizability.

You should explicitly state:

Findings may not apply to obese, smokers, or multi-morbid elderly populations.

Reviewer #2: 1. The manuscript frequently employs strong novelty-related descriptors (e.g., “global first,” “pioneering,” “ultrapure”), which may be perceived as overstated unless supported by comprehensive evidence. The authors are encouraged to soften such language and adopt a more cautious tone (e.g., “To our knowledge, few studies have applied a decadal residency filter…”).

2. The sample size (n = 101) is relatively modest. The authors should consider including an a priori power calculation or provide a clear justification demonstrating that the study is adequately powered to detect clinically meaningful differences in lung function outcomes.

3. Further clarification is required regarding how PM2.5 exposure was quantified. Specifically, the authors should state whether exposure estimates were derived from satellite-based data, fixed-site monitoring stations, modeled annual averages, or a combination of these approaches, and briefly describe the spatial and temporal resolution.

4. The phrase “non-obstructive, restrictive-type lung function impairment” may be imprecise. The authors are advised to replace this with “pattern consistent with reduced lung volumes without airflow obstruction,” which more accurately reflects the spirometric findings.

5. The statement that the 10-year stability “strengthens causal inference” should be modified to a more conservative phrasing such as “enhances causal inference,” in keeping with the observational nature of the study.

****

-->6. PLOS authors have the option to publish the peer review history of their article (what does this mean?). If published, this will include your full peer review and any attached files.

If you choose “no”, your identity will remain anonymous but your review may still be made public.

Do you want your identity to be public for this peer review? For information about this choice, including consent withdrawal, please see our Privacy Policy.-->

Reviewer #1: No

Reviewer #2: **Yes:** Manu Chopra

****

[NOTE: If reviewer comments were submitted as an attachment file, they will be attached to this email and accessible via the submission site. Please log into your account, locate the manuscript record, and check for the action link "View Attachments". If this link does not appear, there are no attachment files.]

To ensure your figures meet our technical requirements, please review our figure guidelines: https://journals.plos.org/plosone/s/figures

You may also use PLOS's free figure tool, NAAS, to help you prepare publication quality figures: https://journals.plos.org/plosone/s/figures#loc-tools-for-figure-preparation.

NAAS will assess whether your figures meet our technical requirements by comparing each figure against our figure specifications.

https://doi.org/10.1371/journal.pone.0349025.r001

Revision 1

13 Mar 2026

Author Response

23 Apr 2026

Response to Academic Editor

Manuscript ID: PONE-D-26-04311

Title: Precision public health: a natural experiment on chronic high-contrast PM2.5 exposure and pulmonary function among older adults

Dear Dr. George Kuryan,

Academic Editor, PLOS ONE,

Thank you for the opportunity to revise our manuscript. We sincerely appreciate the constructive guidance provided by you and the reviewers. Below, we address the specific journal requirements:

1. Style Requirements and File Naming

Response: We have carefully reviewed the PLOS ONE formatting guidelines and templates. The revised manuscript has been reformatted to comply fully with the journal's style requirements, including title page structure, author affiliations, section organization, heading hierarchy, and main body formatting. All tables and figures have been prepared according to PLOS ONE specifications, and all submission files have been named in accordance with the journal's file naming conventions.

2. Data Availability Statement

Response: We confirm that the submission includes the full de-identified participant-level dataset constituting the minimal data set required to replicate all findings reported in the manuscript. The Supporting Information files contain all variables used in the statistical analyses, including exposure group, sociodemographic characteristics, anthropometric measurements, and absolute spirometric parameters. These data provide the values underlying all reported means, standard deviations, regression analyses, and figures.

There are no ethical or legal restrictions on sharing the de-identified dataset.

3. Recommendations to Cite Specific Works

Response: The reviewers did not request citation of specific additional publications. We have nevertheless carefully reviewed the reference list to ensure that all references are appropriate, relevant, and up to date.

We have also addressed all comments from Reviewer #1 and Reviewer #2 in the accompanying 'Response to Reviewers' document.

Thank you for your continued consideration of our work.

Sincerely,

Dr. Hari Krismanuel

Response to Reviewers (Rebuttal)

Response to Reviewers' General Assessments

1. Technical Soundness and Support for Conclusions

• Reviewer #1: Partly

• Reviewer #2: Yes

Response: We thank Reviewer #2 for their positive evaluation of the study's technical soundness. We also appreciate Reviewer #1's assessment and have carefully reviewed the manuscript to ensure that all conclusions are fully supported by the data presented.

In response, we have:

• Moderated causal language to ensure conclusions remain consistent with the observational design

• Clarified that associations are interpreted within the constraints of area-level exposure assignment

• Refined the spirometric interpretation to avoid overdiagnosis (i.e., “pattern consistent with reduced lung volumes”)

• Strengthened statistical justification and model diagnostics reporting

These revisions ensure that the conclusions are proportionate to the data presented, methodologically justified, and fully supported by the analytical framework.

2. Has the statistical analysis been performed appropriately and rigorously?

• Reviewer #1: No

• Reviewer #2: Yes

Response: We acknowledge Reviewer #1’s concerns regarding the statistical presentation and have implemented the following improvements to ensure methodological rigor:

• Normality & Robustness: We added a Q-Q plot and conducted a sensitivity analysis (Cook’s Distance < 0.15), confirming that no influential outliers affected the regression estimates despite slight deviations in formal normality tests.

• Clinical Interpretation of Effect Sizes: We have expanded the discussion on effect sizes, specifically interpreting the large Cohen’s d (1.21 for FEV1_z, and 1.02 for FVC_z). We now explicitly state that a reduction of more than 1 SD corresponds to a significant percentile shift in lung function (e.g., from the 50th to the 15th percentile), highlighting its clinical magnitude.

• Variance Explanation (R2): We have highlighted the strong R2 values (31.5% for FEV1_z and 25.9% for FVC_z) to emphasize that PM2.5 exposure explains a substantial proportion of the variance in pulmonary function relative to other demographic variables.

• Power Calculation: To further clarify the adequacy of our sample size, we provided an achieved power estimation based on the observed effect sizes. With n=101 and the observed large effect sizes, the study achieved a statistical power of >0.95 at α=0.01, confirming the study was more than adequately powered to detect the reported differences.

3. Data Availability

• Reviewer #1: Yes

• Reviewer #2: Yes

Response: We are pleased that both reviewers found our data availability to be transparent and compliant with the journal's requirements. We confirm that all relevant data underlying the findings of this study are available within the manuscript and its Supporting Information files. Specifically, we have ensured the following:

• The minimal data set required to replicate all study findings, including individual data points behind the means, standard deviations, and measures reported, is included.

• The data used to build all graphs and tables presented in the manuscript are fully available as Supporting Information.

• There are no ethical or legal restrictions on sharing the de-identified data set.

4. Manuscript Presentation and English Language

• Reviewer #1: Yes

• Reviewer #2: Yes

Response: We thank both reviewers for their positive assessment of the clarity and quality of our English writing. To ensure that the manuscript remains clear, correct, and unambiguous as per PLOS ONE’s standards:

• We have conducted a final thorough proofreading of the entire manuscript to eliminate any remaining minor typographical or grammatical errors.

• We have ensured that all technical and physiological terms are used consistently and correctly throughout the revised text.

5. Response to Reviewer #1 Comments

We sincerely thank Reviewer #1 for the thorough, constructive critique and highly insightful evaluation of our manuscript. We appreciate the recognition of our methodological strengths, including the 10-year residency filter, the use of GLI-2012 z-scores, and the study’s translational relevance. Below, we provide a detailed, point-by-point response to all comments and describe the revisions made in the revised manuscript. All major concerns have been carefully addressed as outlined below.

1. Overstatement of “Global First”

• Reviewer Comment: Claims of "first globally" and "pioneering application globally" are overstated.

• Response: We appreciate this important observation and agree that our original wording may have overstated the novelty of the study. While the integration of a decade-long residency filter, high-contrast exposure setting, and GLI-2012 SEA z-scores is relatively uncommon, we acknowledge that similar methodological elements have been used in other contexts.

• Revision: We have removed all “global first” and “pioneering” claims throughout the manuscript. The text has been reframed to: "To our knowledge, this study is among the first in the Southeast Asian context to utilize a decade-long stable residency filter..." (See page 1, lines 30-35).

2. Causal Language and RCT Comparisons

• Reviewer Comment: Causal language exceeds the evidentiary strength; design is not equivalent to RCT.

• Response: We agree that as an observational study, we must be more conservative. We have toned down the causal language. We now explicitly state that while the 10-year residency filter strengthens temporal plausibility and internal validity, the study strengthens causal inference within observational constraints but does not establish definitive causality.

• Revision:

o Changed "primary driver" to "strong independent association consistent with a chronic exposure effect."

o Changed "approaches causal rigor of RCT" to "strengthens causal inference within the inherent constraints of an observational design."

3. Area-Level Exposure Proxy Limitations

• Reviewer Comment: Limitation of binary exposure (Kedoya vs. Pangalengan) and lack of personal monitoring are underplayed.

• Response: We agree and thank the reviewer for highlighting this important issue. While the high-contrast natural experiment design provides strong exposure differentiation, we acknowledge limitations inherent to ecological exposure assignment. We have revised the Limitations section to be more transparent and less defensive.

• Revision: The manuscript now explicitly acknowledges the following limitations: (1) Potential risk of ecological exposure assignment; (2) Uncaptured within-area variability; (3) Absence of personal/indoor exposure monitoring; (4) Lack of cumulative dose quantification; (5) Absence of time–activity pattern analysis; and (6) Absence of historical exposure trajectory modeling.

These clarifications have been added to the Limitations section (Please see Revised Manuscript, page 23, lines 736–748).

4. Restrictive Pattern Interpretation

• Reviewer Comment: Spirometry alone cannot diagnose "restriction"; it shows a "restrictive pattern."

• Response: We appreciate this physiological nuance. We have corrected the terminology to avoid any definitive implication of parenchymal stiffening, acknowledging that spirometry measures airflow and volumes rather than tissue compliance.

• Revision: We have replaced "restrictive-type impairment" with "restrictive-pattern spirometry" or "pattern consistent with reduced lung volumes" throughout the manuscript, including the Abstract, Results, and Discussion sections. (Please see Revised Manuscript, page 1, lines 45-47)

5. Statistical Justification (Normality and Effect Sizes)

• Reviewer Comment: S-W for needs better justification. Also, clinical magnitude of Cohen's should be interpreted.

• Response: We appreciate this important statistical observation. We have significantly strengthened the reporting of model diagnostics and clarified the robustness of our parametric estimates. Although the Shapiro–Wilk test indicated deviation from strict normality in the FEV_1/FVC_z model ($p = 0.001$), visual inspection of residual Q–Q plots demonstrated approximate normal distribution without substantial skewness or kurtosis. Moreover, given the moderate sample size ($n = 101$), linear regression estimates are generally robust to minor deviations from normality. We further clarify that the normality assumption in linear regression pertains to the distribution of model residuals rather than the raw outcome variables. Therefore, residual diagnostics such as Q–Q plots and influence statistics provide the appropriate basis for evaluating model validity. We have also expanded the interpretation of effect size magnitude to clarify clinical relevance. In addition, we clarified in the Results section that exposure status accounted for a substantial proportion of explained variance relative to demographic covariates, highlighting its comparative contribution within the multivariable models.

• Revision:

o Visual Confirmation: We added a Q-Q plot as Supplementary Material to visually confirm the residual distribution, providing robust evidence for the "approximately normal" assumption despite formal test deviations.

o Clinical Magnitude: We added a paragraph interpreting the clinical magnitude of Cohen's d (1.21 for FEV1_z and 1.02 for FVC_z). We noted that a reduction of >1 SD represents a significant shift in population lung function percentiles, moving an average individual from approximately the 50th percentile to near the 15th percentile. This demonstrates that the observed differences are not only statistically significant but clinically meaningful at the population level.

o Model Stability (Sensitivity Analysis): We clarified and expanded the reporting of regression sensitivity diagnostics presented in Table 6. Specifically, we explicitly interpreted Cook's Distance (max < 0.15) and Mahalanobis Distance value to demonstrate that the model estimates are stable and not biased by influential outliers. Mahalanobis distance values were examined to detect potential multivariate outliers, and no observations exceeded conventional influence thresholds, indicating that the regression estimates were not driven by extreme cases. This strengthened the justification of model robustness within the manuscript text. (Please see Revised Manuscript, pages 18-22, lines 579-640 and lines 669-675).

6. Precision Public Health (PPH) Narrative

• Reviewer Comment: PPH narrative is repetitive.

• Response: We appreciate this observation and agree that the Precision Public Health (PPH) framing required refinement to avoid repetition and promotional tone. We have streamlined the narrative to ensure that PPH is presented as a contextual framework rather than a central rhetorical theme.

• Revision: We reduced the mentions of PPH by approximately 50%, and consolidated the conceptual framing into a single, sharp paragraph in the Discussion section. Redundant references across the manuscript were streamlined to improve clarity, balance, and scholarly tone.

7. External Validity (Generalizability)

• Reviewer Comment: Findings may not apply to smokers, obese, or multi-morbid populations.

• Response: We agree. The "ultrapure" nature of our cohort is a strength for internal validity but a trade-off for generalizability.

• Revision: We have added a statement in the Limitations section explicitly clarifying that these findings should not be generalized to smokers, obese individuals, or elderly populations with significant comorbidities, in whom physiological responses to chronic $PM_{2.5}$ exposure may differ. (See page 24, lines 756-763).

8. Structural Revisions (Abstract, Discussion, Conclusion)

• Reviewer Comment: Abstract and Discussion require tone moderation and reduced redundancy.

• Response: We agree and have carefully revised the relevant sections to moderate tone, reduce redundancy, and improve clarity and conciseness.

• Revision:

– Abstract: Global-first language and strong causal phrasing have been moderated.

– Discussion: Redundant RCT comparisons have been reduced, repeated emphasis on BTPS has been streamlined, and overlapping explanations regarding causal inference have been consolidated to improve clarity and avoid redundancy.

– Conclusion: Reduced by approximately 15% for clarity and focus.

Response to Reviewer #2 (Dr. Manu Chopra)

We thank Dr. Manu Chopra for the positive and constructive evaluation of our work. We have carefully addressed each of the points raised to ensure a more cautious and academically rigorous presentation.

1. Softening Novelty Descriptors

• Reviewer Comment: Suggestions to soften terms like “global first,” “pioneering,” and “ultrapure.”

• Response: We have followed this suggestion and revised the manuscript to adopt a more cautious tone.

• Revision: We removed the terms “global first” and “pioneering.” The phrase has been revised to: "To our knowledge, few studies in Southeast Asia have applied such a strict decadal residency filter..." (See page 1, lines 30-32).

2. Sample Size Justification and Power Calculation

• Reviewer Comment: Request for a priori power calculation or justification for n=101.

• Response: We have strengthened the methodological justification for our sample size by providing both an effect size–based justification and achieved power estimation. Rather than relying solely on conventional post-hoc power testing, we provided an achieved power estimation based on the observed effect sizes to demonstrate that the study was adequately powered to detect clinically meaningful differences. This approach aligns with contemporary methodological recommendations emphasizing effect size magnitude and precision over retrospective hypothesis testing.

• Revision:

- o Statistical Power: We have updated the Statistical Analysis section to clarify that an a priori detectable effect size calculation informed the study design assumptions, and we subsequently reported an achieved statistical power estimation based on the observed large effect sizes (Cohen's d ranging from 1.02 to 1.21). Given these magnitudes, our final cohort of n = 101 achieved statistical power >0.95 at $\alpha = 0.01$. While the minimum required sample size to detect such large effects was approximately 68 (n = 34 per group), our actual sample size provides an adequate margin to ensure statistical stability.
- **Model Stability (Sensitivity Analysis):** To further address potential concerns regarding the focused sample size, we have **highlighted the stability diagnostics already provided in Table 6**. Sensitivity analysis using **Cook's Distance (max < 0.15)** and **Mahalanobis Distance (max = 20.338)** confirmed that the regression estimates are robust and not driven by influential outliers. This demonstrates that despite the focused cohort of 101 participants, our findings remain statistically stable and reliable.

Detailed Justification in Revised Manuscript:

- **Statistical Power:** See *Statistical Analysis* section on **page 11, lines 376-395**.
- **Stability Diagnostics:** See *Assessment of Model Assumptions* section on **pages 19-21, lines 611-640**.
- **Clinical Meaningfulness:** See *Discussion* section on **pages 21-22, lines 669-675**.

3. **PM2.5 Exposure Quantification**

- **Reviewer Comment: Clarification on how PM2.5 was quantified (satellite, stations, etc.) and the spatial/temporal resolution.**
- **Response: We have updated the manuscript to provide a more granular description of our two-stage hybrid exposure assessment. We clarified that historical $PM_{2.5}$ information was obtained from government-operated air quality monitoring stations to establish the long-term difference in ambient pollution levels between the two study areas. These publicly available monitoring records report $PM_{2.5}$ concentrations on a daily basis and were used to confirm that Kedoya consistently exhibits substantially higher pollution levels than Pangalengan.**

- **To validate exposure conditions at the residential level during the study period, additional direct field measurements were conducted at three locations within each district using calibrated sensors during 24-hour sampling. We also clarified that participants were recruited from a single administrative sub-district (kelurahan) surrounding the validated measurement sites to minimize within-area exposure variability and strengthen the area-level exposure assignment.**
- **Revision: We have clarified the quantification process as follows:**
  1. **Stage 1 (Historical monitoring data): Publicly available $PM_{2.5}$ monitoring records from government-operated air quality monitoring stations were reviewed to characterize the ambient pollution profile of the two study areas. These monitoring systems report $PM_{2.5}$ concentrations on a daily basis and indicate substantially higher pollution levels in Kedoya compared with Pangalengan in publicly reported monitoring records.**
  2. **Stage 2 (Residential-level validation):** To validate exposure conditions at the neighborhood level during the study period, primary measurements were conducted across three locations in each district using calibrated sensors with 24-hour sampling performed by an independent certified air quality monitoring company.
  3. **Participant assignment:** Participants were exclusively recruited from a single administrative sub-district (kelurahan) surrounding the validated monitoring sites to minimize within-area exposure variability and ensure that the exposure classification reflected neighborhood-level ambient conditions.

  This strategy provided a robust area-level proxy for chronic exposure while reducing the risk of ecological fallacy by ensuring that the exposure contrast was verified at the residential level. (Please see Revised Manuscript, page 13, lines 435-455).

4. **Spirometric Terminology**
   - **Reviewer Comment: Suggestion to replace "restrictive-type lung function impairment" with more precise terminology.**
   - **Response: We agree and have updated the terminology throughout the manuscript.**
   - **Revision: We now use the phrase *"pattern consistent with reduced lung volumes without airflow obstruction"* to more accurately reflect the spirometric findings. (See page 17, lines 544-546).**
5. **Causal Inference Phrasing**
   - **Reviewer Comment: Suggestion to change "strengthens causal inference" to "enhances causal inference."**

- **Response: We have adopted this more conservative phrasing to stay consistent with the observational nature of the study.**
- **Revision: All instances of "strengthened causal inference" have been changed to *"enhanced causal inference."***

We hope these revisions address all concerns and demonstrate the robustness of our study. We look forward to your further assessment. We also acknowledge the reviewer's decision to make their identity public and appreciate the transparency of the peer review process.

Best regards,

Dr. Hari Krismanuel
Universitas Trisakti
Hari_krismanuel@trisakti.ac.id

Decision Letter - George Kuryan, Editor

Precision public health: a natural experiment on chronic high-contrast PM2.5 exposure and pulmonary function among older adults

PONE-D-26-04311R1

Dear Dr.Hari-Krismanuel

We're pleased to inform you that your manuscript **has been judged scientifically suitable for publication and will be formally accepted for publication once it meets all outstanding technical requirements.**

Within one week, you'll receive an e-mail detailing the required amendments. When these have been addressed, you'll receive a formal acceptance letter and your manuscript will be scheduled for publication.

An invoice will be generated when your article is formally accepted. Please note, if your institution has a publishing partnership with PLOS and your article meets the relevant criteria, all or part of your publication costs will be covered. Please make sure your user information is up-to-date by logging into Editorial Manager at Editorial Manager® and clicking the 'Update My Information' link at the top of the page. For questions related to billing, please contact billing support.

If your institution or institutions have a press office, please notify them about your upcoming paper to help maximize its impact. If they'll be preparing press materials, please inform our press team as soon as possible -- no later than 48 hours after receiving the formal acceptance.

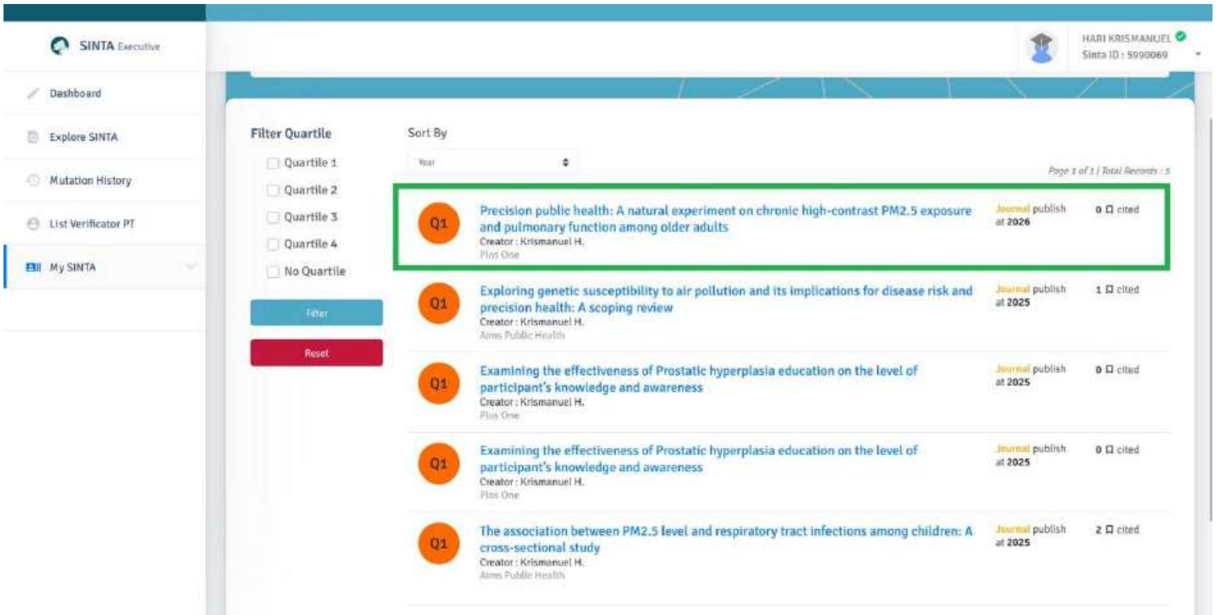
Your manuscript will remain under strict press embargo until 2 pm Eastern Time on the date of publication. For more information, please contact onepress@plos.org.

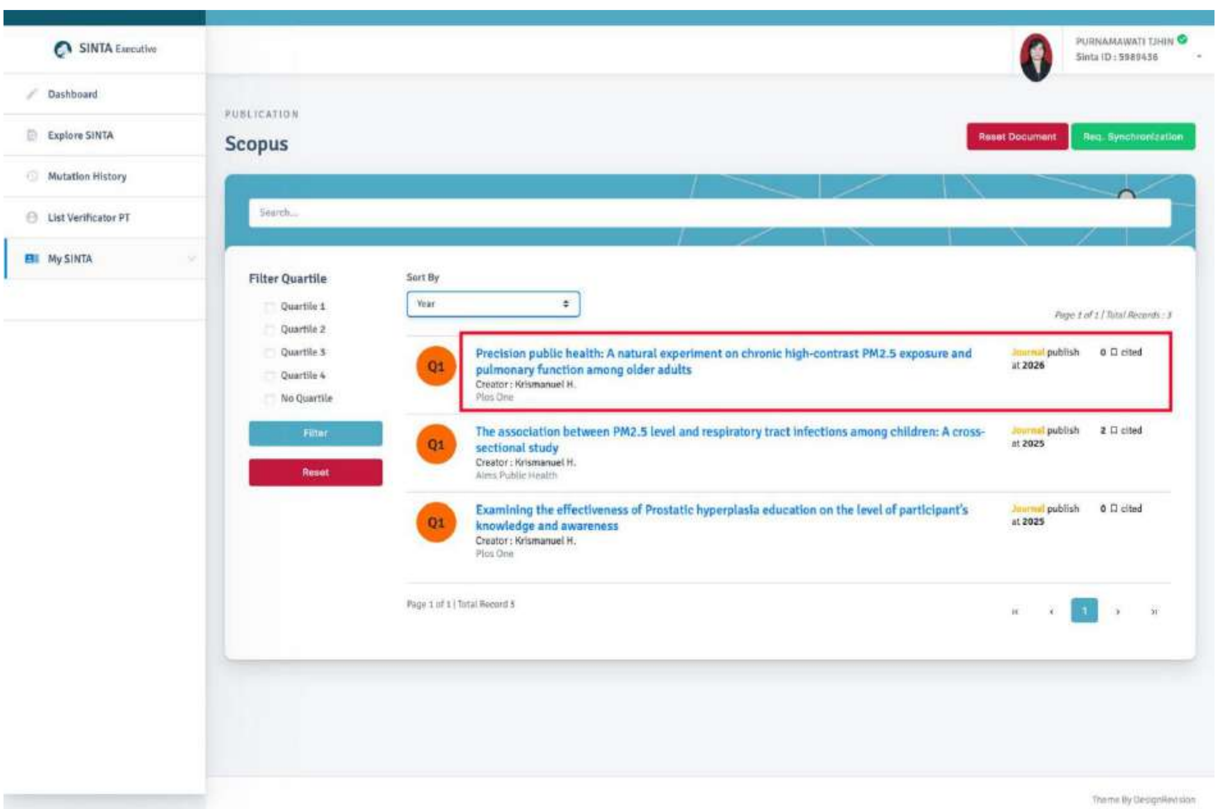
Kind regards,

Kuryan George

Academic Editor

PLOS One


SINTA Executive
HARI KRISMANUEL
Sinta ID : 5990069
Dashboard
Explore SINTA
Mutation History
List Verificator PT
My SINTA
Filter Quartile
Quartile 1
Quartile 2
Quartile 3
Quartile 4
No Quartile
Filter
Reset
Sort By
Year
Page 1 of 1 | Total Records : 5
Q1
Precision public health: A natural experiment on chronic high-contrast PM2.5 exposure and pulmonary function among older adults
Creator : Krismanuel H.
Plos One
Journal publish at 2026
0 cited
Q1
Exploring genetic susceptibility to air pollution and its implications for disease risk and precision health: A scoping review
Creator : Krismanuel H.
Aims Public Health
Journal publish at 2025
1 cited
Q1
Examining the effectiveness of Prostatic hyperplasia education on the level of participant's knowledge and awareness
Creator : Krismanuel H.
Plos One
Journal publish at 2025
0 cited
Q1
Examining the effectiveness of Prostatic hyperplasia education on the level of participant's knowledge and awareness
Creator : Krismanuel H.
Plos One
Journal publish at 2025
0 cited
Q1
The association between PM2.5 level and respiratory tract infections among children: A cross-sectional study
Creator : Krismanuel H.
Aims Public Health
Journal publish at 2025
2 cited


SINTA Executive
PURNAMAWATI TJHIN
Sinta ID : 5989436
Dashboard
Explore SINTA
Mutation History
List Verificator PT
My SINTA
PUBLICATION
Scopus
Reset Document
Req. Synchronization
Search...
Filter Quartile
Quartile 1
Quartile 2
Quartile 3
Quartile 4
No Quartile
Filter
Reset
Sort By
Year
Page 1 of 1 | Total Records : 3
Q1
Precision public health: A natural experiment on chronic high-contrast PM2.5 exposure and pulmonary function among older adults
Creator : Krismanuel H.
Plos One
Journal publish at 2026
0 cited
Q1
The association between PM2.5 level and respiratory tract infections among children: A cross-sectional study
Creator : Krismanuel H.
Aims Public Health
Journal publish at 2025
2 cited
Q1
Examining the effectiveness of Prostatic hyperplasia education on the level of participant's knowledge and awareness
Creator : Krismanuel H.
Plos One
Journal publish at 2025
0 cited
Page 1 of 1 | Total Record 3
1
Theme By DesignRevision