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ABSTRACT

Introduction Globally, the prevalence of obesity tripled from 1975 to 2016. There is evidence that air pollution may contribute to the obesity epidemic through an increase in oxidative stress and inflammation of adipose tissue. However, the impact of air pollution on body weight at a population level remains inconclusive. This systematic review and meta-analysis will estimate the association of ambient air pollution with obesity, distribution of ectopic adipose tissue, and the incidence and prevalence of non-alcoholic fatty liver disease among adults.

Methods and analysis The study will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for conduct and reporting. The search will include the following databases: Ovid Medline, Embase, PubMed, Web of Science and Latin America and the Caribbean Literature on Health Sciences, and will be supplemented by a grey literature search. Each article will be independently screened by two reviewers, and relevant data will be extracted independently and in duplicate. Study-specific estimates of associations and their 95% Confidence Intervals will be pooled using a DerSimonian and Laird random-effects model, implemented using the RevMan software. The I^2 statistic will be used to assess interstudy heterogeneity. The confidence in the body of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Ethics and dissemination As per institutional policy, ethical approval is not required for secondary data analysis. In addition to being published in a peer-reviewed journal and presented at conferences, the results of the meta-analysis will be shared with key stakeholders, health policymakers and healthcare professionals.

PROSPERO registration number CRD42023423955.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Using different measures of obesity, this review will provide a comprehensive and systematic overview of the association of air pollution with ectopic fat deposition, obesity and non-alcoholic fatty liver disease.
⇒ This study will follow the methodology outlined in the Cochrane Handbook for Systematic Reviews of Interventions.
⇒ In collaboration with an experienced librarian, we have developed a search algorithm tailored to five large databases, without language restrictions.
⇒ The review is limited by the anticipated heterogeneity resulting from the different methods used to measure air pollution.
⇒ The review is not able to assess the joint effects of diet and genetics on pollution-induced obesity.

INTRODUCTION

Over the past few decades, obesity has become a global health concern,[1] resulting in excess morbidity and premature deaths.[2 3] Globally, the prevalence of obesity tripled from 1975 to 2016.[4] If this trend does not slow, by 2030, the worldwide prevalence of obesity will reach 1.12 billion.[5] In addition to causing many diseases, such as hypertension, diabetes mellitus (DM),[6] kidney disease,[7] sleep apnoea and various types of cancer,[8] obesity increases the risk of other multifactorial conditions, such as metabolic syndrome[9] and cardiovascular disease (CVD).[10–14] It is estimated that obesity causes 4 million deaths annually, most of which are from CVD.[15]

Obesity refers to an increase in body fat tissue above a normal level.[16 17] General/peripheral obesity is measured by the body mass index (BMI), whereas abdominal/central obesity is more accurately captured by measures such as waist circumference (WC),[18] waist-to-hip ratio (WHR) or waist-to-height ratio (WHtR).[19] Both general obesity and central obesity increase CVD risk factors and disease incidence.[20] Recently, it has been shown that central obesity is more closely associated with metabolic dysfunction than general obesity. In individuals with central obesity, visceral obesity, a condition in which adipose tissue depots enlarge around visceral organs, results in glucose intolerance, insulin

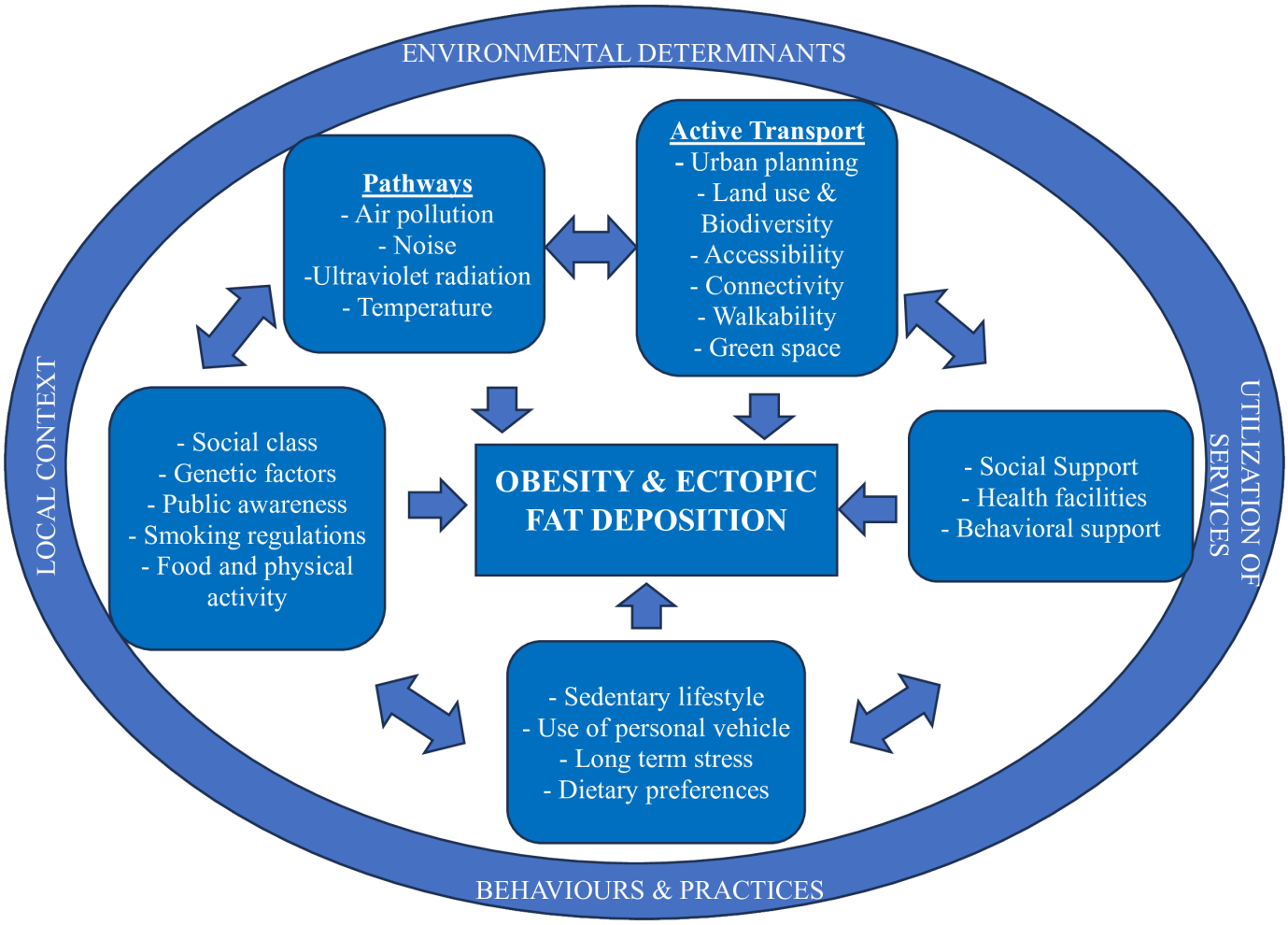

Figure 1 Diagram illustrating how spatial environmental factors and other determinants influence obesity.

resistance and metabolic dysfunction, which cannot be fully accounted for BMI.[21]

Air pollution is the combination of particulate matter (PM)[22] and gaseous pollutants composing of sulfur oxides, nitrogen oxides, ozone (O_3) and carbon monoxide emitted from different sources including exhaust of traffic vehicles, fossil fuel combustion, biomass burning, agriculture and forest fires.[23] Apart from other well-established risk factors for obesity such as unhealthy diet, sedentary lifestyle and genetic factors, air pollution is considered a potential contributor to the obesity epidemic.[24–26] Obesity increases oxidative stress and adipose tissue inflammation.[27] Furthermore, both prolonged[28] and short-term exposure to air pollutants are associated with weight gain.[24 29 30] Figure 1 illustrates how different determinants may interact to cause obesity.

Several mechanisms studied in animal models underlie the relationship between air pollution and body fat. Prolonged and repeated exposure to air pollution sets in motion a 'vicious cycle' for the human body.[31] First, air pollution causes oxidative stress in adipose tissue, resulting in mitochondrial damage and adipose tissue inflammation, leading to an upregulation of energy-saving white adipocytes and a downregulation of energy-consuming brown adipocytes.[22] Adipocyte differentiation disrupts adipose tissue energy equilibrium, leading to fat accumulation and likely obesity, and associated metabolic imbalances.[32] Second, air pollutants increase liver fat cell proliferation[33] and reduce skeletal muscle glucose utilisation.[34] Fat and liver cells communicate efficiently with pancreatic islets and skeletal muscle, and they share an architectural closeness with a wide network of vascular and immune cells (ie, Kupffer cells or macrophages), which enables continuous and dynamic interactions between immune and metabolic responses.[35] During immune or inflammatory responses, the energy balance in insulin-sensitive tissues (liver and visceral fat cells) is disturbed, increasing visceral fat and insulin resistance.[35] Insulin resistance decreases mitochondrial activity, resulting in muscle atrophy and fat accumulation in muscles. These two organs play a significant role in the development of type 2 diabetes and obesity,[32] and muscle atrophy and central obesity further contribute to insulin resistance. Third, air pollution is often a barrier to physical activity because it forces people to stay indoors,[36] which increases sedentary time, leading to diminished muscle mass and functionality. Consequently, exercise capacity

is further reduced, reducing energy expenditure and promoting obesity.[37] Fourth, O_3 inhalation triggers the hypothalamus to release both adrenocorticotropic and glucocorticoid hormones,[38] suppressing the immune system and causing increased glycogenolysis and insulin resistance.[39] As a result, chronic activation of the stress response system may also contribute to obesity following exposure to air pollution.[38] Fifth, air pollution contributes to CVD, respiratory disease and cancer.[40] This can indirectly impact weight by reducing muscle mass and energy consumption.[37 41] Furthermore, some of these conditions impair the ability to ventilate adequately during physical activity, which may lead to a sedentary lifestyle.[42 43] Therefore, the relationship between air pollution and body fat is complex and may vary according to the type and severity of exposure to each pollutant.

Obesity has recently become an epidemic in Asian countries such as China.[44] This continent is experiencing a rapidly rising incidence of obesity-related morbidities, including DM and CVD.[45 46] This systematic review will address a gap that previous systematic reviews have not addressed: China's most recent data have not been included in previous systematic reviews. China is one of the countries facing rising obesity and air pollution rates.[47] Therefore, it is necessary to incorporate the latest evidence from Asia and other regions of the world to enhance the generalisability of pooled analyses. Moreover, no systematic review has been conducted concerning the effects of air pollution on body fat based on sex.

Systematic reviews of human studies support a link between air pollution and obesity.[48 49] However, inconsistencies across the contributing studies remain, likely due to variations in demographic characteristics and use of different units and methods of measuring air pollutants. Only one previous systematic review has presented pooled estimates of the association between air pollution exposure and body fat, and this is limited because it was primarily based on cross-sectional studies and failed to measure abdominal obesity as an outcome.[47] Therefore, a systematic review and meta-analysis of prospective cohort studies, including recent studies from China, will advance this field by clarifying the temporal relationship between air pollution and general and abdominal obesity.

Another unresolved gap will be the pooling of available evidence regarding the association between air pollution and body fat distribution, such as subcutaneous and visceral fat, as well as non-alcoholic fatty liver disease (NAFLD). No systematic review has yet examined these outcomes.

The aim of this study will be to estimate the effect of different air pollutants on the incidence and prevalence of obesity, and the distribution of ectopic adipose tissue (EAT). The research question is: Globally, what are the associations between exposure to air pollutants (fine particles of 2.5 microns or less in diameter ($PM_{2.5}$), nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and O_3) and the risk of obesity, EAT deposition, and NAFLD in adults?

METHODS AND ANALYSIS

This protocol is written to meet the requirements of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols.[50] This systematic review approach will follow Cochrane Handbook for Systematic Reviews of Interventions.[51]

Criteria for considering studies for inclusion and exclusion

Types of studies

Observational studies, specifically, cross-sectional, prospective, retrospective, time series, case cross-over and case–control designs will be eligible for inclusion in this review. We will exclude controlled trials (randomised and non-randomised) as well as ecological studies. Abstracts, conference proceedings, review articles and editorial letters (systematic, scoping and mini reviews) will not be eligible.

Types of participants

Our research will include studies with participants over the age of 18 years,[52] including both males and females. To improve generalisability, we will exclude studies that included participants engaged in specific occupations known to carry high burden of pollution exposure (eg, mining, occupational factories), even if these occupational exposures are related to air pollution. In the same manner, we will exclude studies conducted on only first-hand and secondhand cigarette smokers, children, pregnant women and individuals with previous respiratory system comorbidities such as asthma and COVID-19.

Types of exposures

The exposures include major air pollutants: $PM_{2.5}$, NO_2, O_3 and SO_2.[53] Exposure to outcome estimates measured in 10 micro-gram per meter cube ($\mu g/m^3$) increment for $PM_{2.5}$, and per 10 parts per billion (ppb) increment for SO_2, NO_2 and O_3. We will include any study that assesses exposure to at least one of these pollutants. If the exposure–outcome estimate cannot be converted to the above-mentioned units, the results of that study will not be included in the meta-analysis.

Types of outcome measures

The main outcomes of our review will be BMI, WC, WHR, WHtR, body fat per cent, subcutaneous abdominal adipose tissue, visceral adipose tissue, hepatic fat fraction, cardiac fat and NAFLD. Outcomes will not be labelled as primary or secondary outcomes. To be eligible, a study report must include at least one of the outcomes under consideration.

Search methods for identification of studies

OVID Medline, Embase, PubMed, Web of Science and Latin America and the Caribbean Literature on Health Sciences (LILACS) will be searched from

inception through 30 October 2023, using the search strategy provided in online supplemental appendix 1. Neither a date restriction nor a language restriction will be imposed. Any article that meets the eligibility criteria but is not in English language will be translated. As part of our search, we will also explore the websites of the Centers for Disease Control and Prevention (https://www.cdc.gov/), the Health Effects Institute (https://www.healtheffects.org/) and the WHO (https://www.who.int/) and Google Scholar for grey literature.

Data collection and analysis

Selection of studies

One author will screen the titles and abstracts of all studies identified from the database searches, and code them as relevant, unclear or irrelevant for the review. The full text of articles deemed to be unclear or relevant will be retrieved and independently screened by two reviewers. The two reviewers will identify the article as included or excluded and note the reasons for exclusion for all excluded studies. The two reviewers will resolve any conflicts through discussion. Where multiple publications report on the same cohort, the report with the largest sample size and, if multiple reports satisfy this, the longest follow-up duration that aligns most closely with the research question will be selected.

Data extraction and management

We will develop and use data extraction forms to collect information regarding exposures and outcomes, in accordance with the Cochrane Handbook for Systematic Reviews of Interventions.[54] Following training and calibration exercises, two reviewers will independently extract data. Data will be cross-checked, and conflicts will be resolved by a consensus. Data will be extracted in a Covidence data extraction form and then exported as CSV file. Data for the meta-analysis will be entered into the Review Manager (RevMan) software for statistical pooling.[55]

As part of the data extraction process, information about the year of publication, country of data collection, design of the study, start and end date, duration of the follow-up, if applicable, population composition (mean age and sex distribution), sample size, pollutant type, average exposure level, duration of exposure, scale and methods of measuring exposure, methods of measuring outcomes, minimally and fully adjusted measures of association between exposure and outcomes, sources of funding, and the authors' conflicts of interest and contact details will be captured.

A pilot study of the data extraction form will be conducted for the first five studies before the actual data extraction process begins. For prospective or retrospective cohort studies, in order to calculate the difference in estimates from baseline to follow-ups, we will extract the baseline effect estimates and the follow-up effect estimates, if available.

All air pollutants' units and outcomes' units will be converted to comparable and combinable units across studies (online supplemental appendix 2). For the meta-analysis of exposure to outcome estimates, the estimates will be computed per 10 $\mu g/m^3$ increment for $PM_{2.5}$, and per 10 ppb increment for SO_2, NO_2 and O_3 according to the formulas mentioned below. The formula for odds ratio (OR) calculation will also be applicable to hazard ratio (HR), risk ratio (RR) and incidence risk (IR).

$$OR_{(standardised)} = OR_{(original)}^{\text{increment (10)/increment (original)}}$$

Beta coefficient [56] $(\beta)_{(standardised)} = \beta_{(original)} \times \text{increment}_{(10)} / \text{increment}_{(original)}$

Assessment of risk of bias in included studies

Included articles will be assessed for risk of bias (ROB) by two reviewers independently and in duplicate using the Joanna Briggs Institute's critical appraisal tools as appropriate for each different study design.[54] We will evaluate each study based on the following seven domains: (1) ROB due to confounding, (2) ROB arising from measurement of the exposure, (3) ROB in selection of participants into the study (or into the analysis), (4) ROB due to post-exposure interventions, (5) ROB due to missing data, (6) ROB arising from measurement of the outcome and (7) ROB in selection of the reported result. A cross-sectional study will be rated as low if 7–8 (87–100%) of the domains are low ROB; moderate if 4–6 (50–75%) domains are low ROB; and high ROB if fewer than 4 (less than 50%) domains are low ROB. A prospective cohort study will be rated as low ROB if 9–11 domains have low ROB, moderate if 5–8 domains have low risk and high if fewer than 5 domains have low ROB.

Measures of exposure effect

We will extract point estimates of measures of association along with 95% confidence intervals (CIs), standard errors (SEs) or standard deviations (SDs). We anticipate these measures to be HR, RR, IR or OR for categorical outcomes and beta coefficient for continuous variables. The exposure effect will use standardised measures of exposure and outcomes as described above.

Dealing with missing data

We will contact authors of studies to obtain any data necessary of analysis that are missing from published reports, in accordance with the guidelines provided in the Cochrane Handbook for Systematic Reviews of Interventions.[54] We will conduct a sensitivity analysis if the study authors do not respond to our requests for information. We will exclude studies that have missing data to determine whether the lack of missing data has a significant impact on the outcome. To estimate exposure effects and variance, we will employ published methods of sensitivity analyses, as well as formulas for estimating exposure effects from p values, t-values or Z-values.[57]

Assessment of heterogeneity

Where at least two studies are available, between-study heterogeneity will be assessed using Cochran's Q statistics and quantified using the I^2 statistic. We will use the criteria suggested in the Cochrane Handbook to interpret I^2 statistics for heterogeneity. Specifically, 0–40% might not be important; 30–60% may represent moderate heterogeneity; 50–90% may represent substantial heterogeneity and 75–100% may represent considerable heterogeneity.[58] If there is substantial heterogeneity among the studies, we will attempt to explain this through subgroup analysis or meta-regression.[58]

Publication bias

We will visually inspect and conduct statistical tests (ie, Egger's regression) if there are ≥10 studies, to assess the potential for publication bias as per published guidelines.[59] We will use Duvall and Tweedie's trim-and-fill method to correct for publication bias, if this is detected.

Data synthesis

Following the extraction of data from two or more studies with similar exposures and outcomes, the data will be meta-analysed using the RevMan software. Since we are considering observational studies, there is an inherent degree of heterogeneity across study settings, so we will use the DerSimonian and Laird random-effects model. For analyses with fewer than six studies, we will also compute the fixed-effect estimate, because random-effects models have low power to estimate between-study heterogeneity (tau) in the presence of few studies. If there is only a single study for a given exposure–outcome association, it will be described narratively and presented in a summary of the findings table.

Subgroup analysis

We will conduct the following subgroup analyses or meta-regression if we find at least two studies with similar exposure–outcome relationships within each subgroup, otherwise we will narratively describe the results:

1. Economic status of the included country of conduct: It is estimated that 98% of low-income and middle-income countries (LICs and MICs) failed to comply with the WHO air pollution guidelines, compared with 56% of high-income countries (HICs).[27] Perhaps this is due to the fact that less research has been conducted in LICs and MICs. Thus, we hypothesise that air pollution affects adults more significantly in LICs and MICs than in HICs. Based on the World Bank's classification, we will compare LICs', MICs' and HICs' estimates.[60]
2. By sex: There is evidence that ambient air pollution has stronger impact on obesity among women than it does on men.[27 28 48] The outcome measures for males and females will be compared.
3. By obesity cut-offs: The cut-off values (in kg/m^3) for overweight and obesity according to the WHO are ≥25 and ≥30, respectively, for white or European populations.[61] For Asian populations, the WHO set the criteria for overweight and obesity as ≥22[62] and ≥27.5, respectively.[63] For the same BMI, Asians have a higher percentage of body fat than Europeans. The same applies to WC.[62] Therefore, we hypothesised that air pollution would have a different impact on different BMI and WC cut-offs, and we will examine this hypothesis by examining obesity subgroups.
4. By ROB: Since high or unclear ROB studies may inflate estimates of their overall effects,[64] we will compare the results of studies with a high or unclear ROB with those of studies with a medium or low ROB.
5. By study duration: We hypothesise that increasing duration of air pollution exposure increases the risk of becoming obese.[65] Therefore, we will aggregate the results according to the duration of exposure: short-term (≤3 months), medium-term (>3 months but ≤1 year) and long-term (>1 year) duration.[47]
6. By ethnic groups: Some ethnic groups are more prone to obesity.[66] We will extract ethnicity data from included studies and create subgroups according to major categories; we will also consider a continuous meta-regression by 'per cent white'. We anticipate six major ethnic groups will make up most of the study samples: (1) white, (2) Southeast and East Asian, (3) South Asian, (4) Hispanic, (5) Indigenous Peoples, First Nations, Inuit and Métis, and (6) black. We will perform meta-regression treating percentage of participants from each ethnic groups as predictor variables described above.

Sensitivity analysis

All analyses will be repeated excluding studies with high ROB to determine the impact of these studies on the overall results.

Certainty of the evidence

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach will be used to assess the certainty of evidence for an association between each of the pollutants and the adiposity outcomes. Studies with similar outcomes will be evaluated based on the following criteria: ROB (limitations in study design or implementation), inconsistency, indirectness (whether or not the outcomes directly answer the research question), imprecision, unexplained heterogeneity, publication bias, etc.[67] We will rate the evidence for each exposure–outcome association as high, moderate, low or very low certainty of evidence based on these domains.

Summary of findings table

A summary of findings provides a succinct summary of the key information from systematic reviews needed by decision-makers.[68] We will prepare the GRADE summary of findings tables to report the main comparisons of this review.[68]

Transparency

The review will be conducted according to the published protocol and any deviations will be immediately reported.

Patient and public involvement

Patients and/or the public were not involved in any phase of this research.

ETHICS AND DISSEMINATION

Consistent with our institution's policy, ethics approval is not required for secondary analysis of already published data. We will publish the reviews in a peer-reviewed journal. We will also present the results of these reviews in conferences and meetings with other researchers and clinicians.

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Contributors RJdS is the guarantor of this study. RJdS conceived the work. MM drafted the manuscript. LB contributed to the search strategy development. RJdS, SMA, LB, OK, SB, JB and DD revised the manuscript critically for important intellectual content.

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REFERENCES

1 Ellulu M, Abed Y, Rahmat A, *et al*. Epidemiology of obesity in developing countries: challenges and prevention. *Glob Epidemi Obes* 2014;2:2.
2 Adair T, Lopez AD. The role of overweight and obesity in adverse cardiovascular disease mortality trends: an analysis of multiple cause of death data from Australia and the USA. *BMC Med* 2020;18:199.
3 Prentice AM. The emerging epidemic of obesity in developing countries. *Int J Epidemiol* 2006;35:93–9.
4 Dong G, Qian Z (Min), Liu M, *et al*. Ambient air pollution and the prevalence of obesity in chinese children: the seven northeastern cities study. *Obesity* 2014;22:795–800.
5 Kelly T, Yang W, Chen C-S, *et al*. Global burden of obesity in 2005 and projections to 2030. *Int J Obes* 2008;32:1431–7.
6 Bassuk SS, Manson JE. Lifestyle and risk of cardiovascular disease and type 2 diabetes in women: a review of the epidemiologic evidence. *Am J Lifestyle Med* 2008;2:191–213.
7 Vivante A, Golan E, Tzur D, *et al*. Body mass index in 1.2 million adolescents and risk for end-stage renal disease. *Arch Intern Med* 2012;172:1644–50.
8 Behan DF, Cox SH, Lin Y, *et al*. Obesity and its relation to mortality and morbidity costs. *Society of Actuaries* 2010;59.
9 Cave MC, Samala NR, Smith MR, *et al*. Environmental pollutant exposures are associated with nonalcoholic fatty liver disease severity and enrichment in the metabolic pathways associated with liver fibrosis. *Hepatology* 2021;74:82A.
10 Singh GM, Danaei G, Farzadfar F, *et al*. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One* 2013;8:e65174.
11 Juonala M, Magnussen CG, Berenson GS, *et al*. Childhood adiposity, adult adiposity, and cardiovascular risk factors. *N Engl J Med* 2011;365:1876–85.
12 Alderete TL, Habre R, Toledo-Corral CM, *et al*. Longitudinal associations between ambient air pollution with insulin sensitivity, β-cell function, and adiposity in Los Angeles Latino children. *Diabetes* 2017;66:1789–96.
13 Brook RD, Sun Z, Brook JR, *et al*. Extreme air pollution conditions adversely affect blood pressure and insulin resistance: the air pollution and cardiometabolic disease study. *Hypertension* 2016;67:77–85.
14 Li J, Zhou C, Xu H, *et al*. Ambient air pollution is sssociated with HDL (high-density lipoprotein) dysfunction in healthy adults. *Arterioscler Thromb Vasc Biol* 2019;39:513–22.
15 Afshin A, Reitsma MB, Murray CJL. Health effects of overweight and obesity in 195 countries. *N Engl J Med* 2017;377:1496–7.
16 Abildgaard J, Danielsen ER, Dorph E, *et al*. Ectopic lipid deposition is associated with insulin resistance in postmenopausal women. *J Clin Endocrinol Metab* 2018;103:3394–404.
17 Yu SY, Kim BS, Won CW, *et al*. Body mass index and mortality according to gender in a community-dwelling elderly population: the 3-year follow-up findings from the living profiles of older people surveys in Korea. *Korean J Fam Med* 2016;37:317–22.
18 Ross R, Neeland IJ, Yamashita S, *et al*. Waist circumference as a vital sign in clinical practice: a consensus statement from the IAS and ICCR Working Group on visceral obesity. *Nat Rev Endocrinol* 2020;16:177–89.
19 Jebb S. Obesity: causes and consequences. *Women's Health Medicine* 2004;1:38–41.
20 Prospective Studies Collaboration, Whitlock G, Lewington S, *et al*. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009;373:1083–96.
21 Rattarasarn C. Dysregulated lipid storage and its relationship with insulin resistance and cardiovascular risk factors in non-obese Asian patients with type 2 diabetes. *Adipocyte* 2018;7:71–80.
22 Xu Z, Xu X, Zhong M, *et al*. Ambient particulate air pollution induces oxidative stress and alterations of mitochondria and gene expression in brown and white adipose tissues. *Part Fibre Toxicol* 2011;8:20.
23 Boogaard H, Patton AP, Atkinson RW, *et al*. Long-term exposure to traffic-related air pollution and selected health outcomes: a systematic review and meta-analysis. *Environment International* 2022;164:107262.
24 Kim JS, Chen Z, Alderete TL, *et al*. Associations of AIR pollution, obesity and cardiometabolic health in young adults: the Meta-AIR study. *Environ Int* 2019;133:105180.

25 Kim JS, Alderete TL, Chen Z, *et al*. Longitudinal associations of in utero and early life near-roadway air pollution with trajectories of childhood body mass index. *Environ Health* 2018;17:64.
26 McConnell R, Shen E, Gilliland FD, *et al*. A longitudinal cohort study of body mass index and childhood exposure to secondhand tobacco smoke and air pollution: the Southern California Children's Health Study. *Environ Health Perspect* 2015;123:360–6.
27 An R, Ji M, Yan H, *et al*. Impact of ambient air pollution on obesity: a systematic review. *Int J Obes* 2018;42:1112–26.
28 Liu X, Tu R, Qiao D, *et al*. Association between long-term exposure to ambient air pollution and obesity in a Chinese rural population: the Henan Rural Cohort study. *Environmental Pollution* 2020;260:114077.
29 Kloog I, Zanobetti A, Nordio F, *et al*. Effects of airborne fine particles (PM2.5) on deep vein thrombosis admissions in the northeastern United States. *J Thromb Haemost* 2015;13:768–74.
30 Qin X-D, Qian Z, Vaughn MG, *et al*. Gender-specific differences of interaction between obesity and air pollution on stroke and cardiovascular diseases in Chinese adults from a high pollution range area: a large population based cross sectional study. *Sci Total Environ* 2015;529:243–8.
31 Chen C-H, Huang L-Y, Lee K-Y, *et al*. Effects of $PM_{2.5}$ on skeletal muscle mass and body fat mass of the elderly in Taipei, Taiwan. *Sci Rep* 2019;9:11176.
32 Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. *J Clin Invest* 2006;116:1793–801.
33 Toledo-Corral CM, Alderete TL, Habre R, *et al*. Effects of air pollution exposure on glucose metabolism in Los Angeles minority children. *Pediatr Obes* 2018;13:54–62.
34 Liu C, Xu X, Bai Y, *et al*. Air pollution-mediated susceptibility to inflammation and insulin resistance: influence of CCR2 pathways in mice. *Environ Health Perspect* 2014;122:17–26.
35 Hotamisligil GS. Inflammation and metabolic disorders. *Nature* 2006;444:860–7.
36 Roberts JD, Voss JD, Knight B. The association of ambient air pollution and physical inactivity in the United States. *PLoS One* 2014;9:e90143.
37 Choi KM. Sarcopenia and sarcopenic obesity. *Korean J Intern Med* 2016;31:1054–60.
38 Thomson EM. Neurobehavioral and metabolic impacts of inhaled pollutants: a role for the hypothalamic-pituitary-adrenal axis? *Endocrine Disruptors* 2013;1:e27489.
39 Lucassen EA, Cizza G. The hypothalamic-pituitary-adrenal axis, obesity, and chronic stress exposure: sleep and the HPA axis in obesity. *Curr Obes Rep* 2012;1:208–15.
40 Mannucci PM, Harari S, Martinelli I, *et al*. Effects on health of air pollution: a narrative review. *Intern Emerg Med* 2015;10:657–62.
41 Chen C-H, Huang L-Y, Lee K-Y, *et al*. Effects of PM2.5 on skeletal muscle mass and body fat mass of the elderly in Taipei, Taiwan. *Sci Rep* 2019;9.
42 An R, Zhang S, Ji M, *et al*. Impact of ambient air pollution on physical activity among adults: a systematic review and meta-analysis. *Perspect Public Health* 2018;138:111–21.
43 Cakmak S, Dales R, Leech J, *et al*. The influence of air pollution on cardiovascular and pulmonary function and exercise capacity: Canadian Health Measures Survey (CHMS). *Environmental Research* 2011;111:1309–12.
44 Wu Y. Overweight and obesity in China. *BMJ* 2006;333:362–3.
45 Diet, nutrition and the prevention of chronic diseases[backcover]. *World Health Organ Tech Rep Ser* 2003;916:i–viii, 1-149.
46 Aguirre F, Brown A, Cho NH, *et al*. IDF diabetes Atlas; 2013.
47 Huang S, Zhang X, Huang J, *et al*. Ambient air pollution and body weight status in adults: a systematic review and meta-analysis. *Environ Pollut* 2020;265:114999.
48 Li M, Qian Z, Vaughn M, *et al*. Sex-specific difference of the association between ambient air pollution and the prevalence of obesity in Chinese adults from a high pollution range area: 33 communities Chinese health study. *Atmospheric Environment* 2015;117:227–33.
49 Shamy M, Alghamdi M, Khoder MI, *et al*. Association between exposure to ambient air particulates and metabolic syndrome components in a Saudi Arabian population. *Int J Environ Res Public Health* 2017;15:27.
50 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4.
51 Higgins J, Thomas J, Chandler J, *et al*. Cochrane handbook for systematic reviews of interventions version 6.2. Cochrane; 2021. Available: www.training.cochrane.org/handbook
52 WHO. World Health Organization (WHO) definition of key terms. 2016. Available: http://www.who.int/hiv/pub/guidelines/arv2013/intro/keyterms/en
53 Shin HH, Owen J, Maquiling A, *et al*. Circulatory health risks from additive multi-pollutant models: short-term exposure to three common air pollutants in Canada. *Environ Sci Pollut Res Int* 2023;30:15740–55.
54 Higgins JPT, Green S, Collaboration C. Cochrane Handbook for systematic reviews of Interventions.Version 5.1. 0. 2013; 2015.
55 Review manager web (Revman web) [The Cochrane Collaboration]. 2020. Available: revman.cochrane.org
56 Yang B-Y, Qian Z, Howard SW, *et al*. Global association between ambient air pollution and blood pressure: a systematic review and meta-analysis. *Environ Pollut* 2018;235:576–88.
57 Guyatt GH, Ebrahim S, Alonso-Coello P, *et al*. GRADE guidelines 17: assessing the risk of bias associated with missing participant outcome data in a body of evidence. *J Clin Epidemiol* 2017;87:14–22.
58 Higgins JPT, Thomas J, Chandler J, *et al*. Cochrane handbook for systematic reviews of interventions version 6.2. Cochrane; 2021. Available: www.training.cochrane.org/handbook
59 Sterne JAC, Sutton AJ, Ioannidis JPA, *et al*. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:bmj.d4002.
60 Bank TW. World Bank country and lending groups. n.d. Available: https://datahelpdeskworldbankorg/knowledgebase/articles/906519-world-bank-country-and-lending-groups2023
61 WHO. Cut-off for BMI according to WHO standards. 2018. Available: https://gateway.euro.who.int/en/indicators/mn_survey_19-cut-off-for-bmi-according-to-who-standards
62 Consultation WE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157–63.
63 Li Z, Daniel S, Fujioka K, *et al*. Obesity among Asian American people in the United States: a review. *Obesity (Silver Spring)* 2023;31:316–28.
64 Savović J, Turner RM, Mawdsley D, *et al*. Association between risk-of-bias assessments and results of randomized trials in cochrane teviews: the ROBES meta-epidemiologic study. *Am J Epidemiol* 2018;187:1113–22.
65 Parasin N, Amnuaylojaroen T, Saokaew S. Effect of air pollution on obesity in children: a systematic review and meta-analysis. *Children (Basel)* 2021;8:327.
66 Saxena S, Ambler G, Cole TJ, *et al*. Ethnic group differences in overweight and obese children and young people in England: cross sectional survey. *Arch Dis Child* 2004;89:30–6.
67 GRADEpro G. Computer program. McMaster University (developed by evidence prime). GRADEpro GDT. Hamilton (ON) McMaster University (developed by Evidence Prime); 2015.
68 Guyatt G, Oxman AD, Akl EA, *et al*. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383–94.