An Overview of Reviews on the Human Health Effects from Exposure to Near Roadway Air Pollution (NRAP): Protocol

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Abstract

Background: Globally, across the United States, and California, transportation is a substantial contributor to air pollution, which represents a significant public health concern. Many primary studies and systematic reviews have been conducted evaluating the health impacts from exposure to near roadway air pollution (NRAP), however, it is unclear what the current overall body of the evidence demonstrates and whether the evidence has been evaluated using rigorous scientific methods. Therefore, we will conduct an overview of reviews to summarize and evaluate the quality of the current evidence.

Objective: Inform a California State Policy Evidence Consortium (CalSPEC) report for the California Senate Committee on Environmental Quality and Assembly Committee on Natural Resources on the human health effects of near roadway air pollution.

Search and study eligibility: We will perform electronic searches in EMBASE, PubMed, CABI Global Health, Cochrane CENTRAL, Cochrane Reviews, Web of Science, TRIP Pro database, MEDNAR, NTIS, and Base. Reviews are eligible if they meet our PECO statement and additional eligibility criteria.

Study appraisal, data analysis and synthesis: Eligible reviews will be assessed using a modified version of the AMSTAR 2.0 tool. We will extract and present results as reported by the review authors. We will produce summary statistics, when necessary, but we will not re-analyze data.

Conclusion: Findings from this overview will support additional research and policy efforts on mitigating the health effects of NRAP.

Previous Version of the Protocol (v1.0, posted September 25, 2023) can be found here: https://osf.io/ufjqa

Summary of Changes

- Expanded on methods for examining the disproportionate impacts of NRAP in California (pp. 10)

Background

Globally, air pollution is one of the leading risk factors for death and disease burden.[1] In 2019, air pollution contributed to 6.67 million deaths; 2.31 million from household air, 4.14 million from ambient particulate matter, and 0.37 million from ambient ozone.[2,3] The World Health Organization (WHO) has attributed outdoor air pollution-related deaths to ischemic heart disease and stroke (37%), acute lower respiratory infections (23%), chronic obstructive pulmonary disease (COPD) (18%), and cancer within the respiratory tract (11%).[4] Globally, children, pregnant people, older adults, and individuals with pre-existing cardiovascular and respiratory disease are particularly susceptible to the health effects of air pollutants.[5,6] Communities with low socio-economic status, access to health care, and social support are also uniquely vulnerable to air pollution.[5,6] In the United States (US), vast racial and ethnic disparities in air pollution exposure and adverse health outcomes exist.[7,8] Thus, it is critical that we understand the human health effects of air pollution and the injustices that give rise to such disparities so we can inform equitable policies and programs that protect public health.

Motor vehicles are a substantial source of air pollution, especially in urban areas around the world and across the US.[9–11] In California, it is estimated that transportation is responsible for 80% of air pollution.[12] This is therefore an issue of public health concern as 59.5 million people in the US live within 500 meters of a high volume road,[a] while in California, 40% of the population live near high volume roads, the highest share of any state.[13] The Centers for Disease Control and Prevention (CDC) also approximates that in the US, 11.3 million people live within 150 meters of a major highway.[b14]

This proximity to high volume roads exposes individuals to traffic-related air pollution (TRAP), which is defined broadly as "ambient air pollution resulting from the use of motorized vehicles such as heavy-duty and light-duty vehicles, buses, coaches, passenger cars, and motorcycles."[15] Traffic-related air pollution encompasses combustion emissions, including carbon dioxide (CO_2), carbon monoxide (CO), black carbon (BC), elemental carbon (EC), hydrocarbons (HC), nitrogen oxides (NO_x), particulate matter (PM), and mobile source air toxics (i.e., benzene, formaldehyde, acetaldehyde, 1,3-butadiene), as well as secondary pollutants formed in the atmosphere (i.e., nitrogen dioxide (NO_2), ozone) and brake and tire debris.[16] TRAP is most prevalent near roadways; hence it is sometimes referred to as near roadway air pollution (NRAP).

The definition for NRAP based on the air pollution that can be attributed to roadways varies. For example, the US Environmental Protection Agency (EPA) specifies "Research findings indicate that roadways generally influence air quality within a few hundred meters – about 500-600 feet downwind from the vicinity of heavily traveled roadways or along corridors

[a] Defined as having greater than 25,000 average annual daily traffic (AADT)

[b] Defined as interstates, freeways, or expressways based on the Federal Highway Administration Functional Classification System

with significant trucking traffic or rail activities. This distance will vary by location and time of day or year, prevailing meteorology, topography, nearby land use, traffic patterns, as well as the individual pollutant."[16] The California Air Resources Board (CARB) indicates that individuals living as much as 1000 feet away could experience consequences from their proximity to a freeway.[17] This variability in definitions poses a challenge in evaluating the health effects attributable to NRAP.

Although there are challenges specific to the evaluation of NRAP, numerous systematic reviews have been conducted on the health effects of exposure to indirect measures of NRAP including distance to roadway as well as components of NRAP, including but not limited to NO_2 and EC.[18] Systematic reviews have evaluated a wide range of health outcomes, including cardiorespiratory diseases and mortality, asthma, fertility, diabetes risk, childhood cancers, and cognition.[18] However, the results from systematic reviews are inconsistent for several outcomes including but not limited to childhood leukemia,[19,20] birth outcomes,[21,22] and cardiovascular events.[23,24] As systematic reviews in environmental health also vary in quality,[18,25] it is difficult to ascertain if differences in results are due to true differences in the evidence base or differences in the quality of systematic reviews. As urbanization and traffic congestion increases, there is considerable need to understand what the current overall body of the evidence demonstrates on the health effects from exposure to NRAP, whether the evidence has been evaluated using rigorous scientific methods, and if disparities in exposures and health outcomes exist based on social factors e.g., race, income, education, linguistic isolation.

The motivation for this current work on NRAP comes from the California State Policy Evidence Consortium (CalSPEC) which "seeks to build an evidence pipeline that enhances policy decision-making through rapid evidence and policy reviews on complex topics of concern or interest to the State Legislature."[26] In 2023, CalSPEC was charged with identifying the health effects from near roadway indoor air pollution. Due to limited evidence on the health effects of near roadway *indoor* air pollution, reflective of the challenges of measuring the indoor air component of near roadway pollution,[27,28] and consistent evidence demonstrating that outdoor air pollution levels are indicative of indoor exposures,[27,29–31] we are conducting an overview of reviews (referred to hereafter as an "overview") on the human health effects of NRAP, adhering to the steps of the Navigation Guide systematic review methodology,[32] and Cochrane's Overviews of Reviews[33] and Rapid Review guidance.[34]

Overviews also referred to as "umbrella reviews," "reviews of reviews," and "meta-reviews," follow the steps of a full systematic review, however, instead of an evaluation of primary studies, overviews evaluate systematic reviews.[33] Systematic reviews are a type of study in which researchers "identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question."[35] Due to the need for timely evidence on the health effects of NRAP, we will conduct an overview using rapid review methods. Rapid review methodology allows for the omission of specific steps to accelerate the study timeline, producing prompt evidence to inform policymakers.[34]

Aim

The aim of this overview is to inform a California State Policy Evidence Consortium (CalSPEC) report for the California Senate Committee on Environmental Quality and Assembly Committee on Natural Resources on the human health effects of NRAP. Our specific questions are:

1. What are the human health effects of exposure to NRAP?
2. To what extent are specific groups of Californians (identified by age, gender, race/ethnicity, or health history) at increased risk for negative health effects of NRAP?

Objectives

Our specific objectives are to:

- Identify systematic reviews evaluating the human health effects of NRAP.
- Assess methodological quality of included systematic reviews.
- As appropriate, summarize the data presented in the systematic reviews.
- Provide a conclusive summary statement about the human health effects of NRAP.
- Address the extent to which specific groups of Californians (identified by age, gender, race/ethnicity, or health history) are at increased risk for negative health effects of NRAP.

Methods

Review Team

The human health effects overview of NRAP is led by Professor Tracey Woodruff (TW) and consists of four primary members: Dr. Nicholas Chartres (NC), Courtney Cooper, MPH (CC), Emily Lasher (EL), and Olivia Stoddard (OS). The team has expertise in environmental health, air pollution, systematic review, and public health. The project will be informed by the Navigation Guide systematic review methodology,[36] Cochrane Overviews of Reviews,[33] and, given the timeline for this project (approximately four months to complete the review), we will also employ rapid systematic review (rapid review) guidance.[34]

Search Strategy

We will utilize a search that has been previously conducted[18] and updated with support from an information specialist at UC Davis (BA). Our search will not be limited by publication date or language. We will perform electronic searches in EMBASE, PubMed, CABI Global Health, Cochrane CENTRAL, Cochrane Reviews, Web of Science, TRIP Pro database, MEDNAR, NTIS, and Base to capture both peer reviewed and grey literature. The search strings that will be used for each database can be found in **Appendix A**.

Data Management

A study flow diagram will track the number of references retrieved and processed in the review (**Appendix B**). We will download all references into EndNote 20[37] where they will be de-duplicated using EndNote's reference de-duplication feature. We will then export them to DistillerSR and use the Duplicate Detection feature to catch any references not caught in the first round of de-duplication. DistillerSR[38] will then be used for screening, data collection, and study evaluation. The reviews will all have a unique identification number in DistillerSR that will carry through until the end of the project.

Study Selection Criteria

This overview will only include systematic reviews, with or without meta-analyses. Eligible reviews will address the study question and characteristics as outlined in the following population, exposure, comparator, and outcome (PECO) statement along with additional eligibility criteria.

PECO Statement

Population: Systematic reviews (as defined by study authors and our specific criteria, using the modified PRISMA guidelines, available in **Appendix C**[18,39]) on human epidemiological studies, with or without meta-analyses.

Exposure: Exposure to NRAP (as defined by study authors).*

Comparator: N/A

Outcome: Any adverse health outcome in humans.**

**Authors may have used different terminology and we will be inclusive of other phrasing, like traffic related air pollution, or pollutants that were measured on or near a roadway. At evaluation, we will prioritize reviews in which authors have focused on TRAP/NRAP, and the single pollutants of NO_2 and EC that are reflective of TRAP/NRAP exposures given timeline considerations.*

***Given our timeline for this project, we will prioritize clinical, apical outcomes after full text screen with a specific focus on the following outcomes: mortality, respiratory health, cardiovascular health, cognitive decline, and fertility. Apical outcomes: observable outcomes in an organism (such as a clinical sign or pathological state) that indicate disease. Clinical outcomes: measurable change in symptoms, overall health, ability to function, quality of life, or survival outcomes.*

Additional Inclusion/Exclusion Criteria

Along with fitting our PECO statement, we will include the following:

- Full text systematic reviews.
- English language systematic reviews.

- Systematic reviews which feature quantitative measures of one or more, direct or indirect, NRAP related exposures.
- Systematic reviews that include studies with a comparison group.

We will exclude:

- Any review that is not systematic, including narrative reviews, based upon the definition provided by the study authors and our specific criteria (which will be assessed thoroughly at full text screening).
- Systematic review protocols with no available full systematic review. *
- Conference abstracts with no available full systematic review. *
- Non full text references.
- Reviews which do not contain human data.
- Systematic reviews in a language other than English (and are not available at all in English).
- Original studies (including studies which used meta-analyses on individual participant data or cohorts to obtain their effect estimate).
- Systematic reviews which do not have a health-related outcome.
- Reviews which do not include quantitative measures of direct or indirect exposure to NRAP.
- Studies which have a non-near roadway related exposure including cigarette smoke (active or passive inhalation) regardless of whether some of the chemicals in the exposure may be known near roadway related air pollutants. The reason for excluding these studies is due to the likely difference in the magnitude of exposure vs near roadway-related exposures, and the non-specificity of the exposure itself (i.e., cigarette smoke has many other exposures not typically associated with NRAP).
- After full text, but before data extraction, we will exclude any systematic reviews that do not indicate the availability of a protocol or pre-published method. This will allow us to remove any reviews that are of critically low quality to focus on higher quality reviews. Furthermore, this prioritization will allow us to meet the timeline needs for this project.

**We will contact the authors of protocols and conference abstracts that are identified at title/abstract screening to identify a full study report for inclusion at full text screening as needed.*

Study Screening

A team of three reviewers (CC, EL, and OS) will employ rapid review guidance in which one reviewer is needed to include a reference and two are needed to exclude a reference[34] during Title/Abstract screen in DistillerSR. The same team will adhere to this guidance during full text screen. Any discrepancies will be discussed between the reviewers with the final judgement coming from NC.[33] Ahead of conducting the screening for both T/A and full text screen, EL, OS,

and CC will pilot 8 of the same references to test the forms, refine eligibility criteria, and for training purposes.[40] We will report reasons for exclusion at the full text stage in a supplemental file along with the results of the review.

We will also look for the full text of the reviews in English if we determine the study is not written in English, given the language capacities of our study team. Furthermore, we will assess if there are full systematic reviews available for conference abstracts and protocols through an internet search and, if necessary, outreach to authors. We will adhere to Cochrane's guidance on obtaining information from authors via email.[41,42] To ensure this process is efficient given a short timeline, we will send one email, and one follow-up email. If no response is received after the second email, we will exclude the reference.

Data Collection

The team of reviewers (EL, OS, and CC) will collect data from literature included after the full text screen in DistillerSR. One individual will do the primary collection (EL, OS), and another will QC (CC). Any discrepancies will be discussed between the reviewers with the final judgement coming from NC.[33] Ahead of collecting data, OS, CC, and EL will pilot at least 2 of the same references to test the form and for training purposes.[41] Please see **Appendix D** for the data collection form.

Quality Assessment

We will apply a modified version of AMSTAR (A MeaSurement Tool to Assess Systematic Reviews) 2.0[43] as done in previous evaluations of environmental health systematic review methods.[41,44] The AMSTAR 2.0 tool notes that amendments are justifiable and the authors have provided the criteria as suggestions.[43] We modified the tool based on past use to reflect the evidence base available in the environmental health literature to ensure judicious, reasonable, and expeditious evaluation of studies. Modifications were guided by two experts in environmental health and systematic review (NC & TW). We amended the criteria for 'partial yes' in domains 4, 5, 6, and 7. We amended the criteria for 'yes' in domains 3, 4, 10-14, and 16. In domain 9, we amended the criteria for 'yes,' 'partial yes,' and 'no.' In **Appendix E** we present the modified tool, with reference to the original tool. We will use both the publication and the protocol of each review to identify information to assess each criterion of the AMSTAR tool. We will evaluate the systematic reviews at the outcome level.

We will follow rapid review guidance during this stage in which one person evaluates and another person verifies. We will conduct these ratings in Excel with the following individuals: EL, OS, NC.

To rate the overall confidence in the results of the included systematic reviews in this overview, we will assess each of the 16 AMSTAR 2.0 domains and will consider the following 6 domains 'critical':

- Protocol registered before the commencement of the review (item 2)

- Adequacy of the literature search (item 4)
- Justification for excluding individual studies (item 7)
- Risk of bias from individual studies being included in the review (item 9)
- Appropriateness of meta-analytical methods (item 11)
- Consideration of risk of bias when interpreting the results of the review (item 13)

Included systematic reviews will then be rated as:

High – The systematic review has no or one non-critical weakness and provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.

Moderate – The systematic review has more than one non-critical weakness and may provide an accurate summary of the results of the available studies that were included in the review.

Low – The systematic review has one critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.

Critically low – The systematic review has more than one critical flaw with or without non-critical weaknesses and should not be relied on to provide an accurate and comprehensive summary of the available studies.

If a systematic review contains multiple non-critical weaknesses, we will consider moving the overall appraisal down from moderate to low confidence.

Data Analysis

We will summarize outcome data by presenting data in the overview exactly as they are reported in the included systematic reviews, including narratively reported study results and the results of any meta-analyzed data. We will extract and report effect estimates, 95% confidence intervals, and measures of heterogeneity if meta-analyses have been conducted for each exposure/outcome in our overview related to near roadway air pollution. We will extract the results of the most appropriately adjusted model. We will describe the results narratively and present them in a summary of findings table.

We will not re-analyze outcome data from the included systematic reviews, however, when review authors have reported study results narratively, we will consider vote counting based on the direction of effect.[45] We will categorize each effect estimate as showing benefit or harm based on the observed direction of effect alone to create a standardized binary metric. A noted limitation of vote counting is that effect size and/or statistical significance are not considered in the categorization. Will then use a sign test to answer the question ‘is there any evidence of an effect?’ We will consider the use of harvest plots to display the results with characteristics of the studies including sample size and risk of bias of individual studies represented using different heights and shading.[45]

Overlap Between Systematic Reviews' Primary Studies

We will identify the overlap of the primary studies in the included systematic reviews to establish the independence of the results for each exposure/outcome in the overview.[46] We will create a citation matrix and conduct an overlap calculation across and between reviews following recommended guidance for overviews.[46–48] We will calculate the corrected covered area (CCA) and consider CCA lower than 5% as indicating slight overlap, 5% to 10% as moderate overlap, 10% to 15% as high overlap, and more than 15% as very high overlap.[46] We will present the CCA for each pair of systematic reviews using the Graphical Representation of Overlap for Overviews (GROOVE) tool to transparently report separate contributions for the total overlap in the Overview.[47] We will report data from the most recent, highest quality systematic review to manage the overlap in primary studies in the reviews that reported results for the same exposure/outcome but with different years of publication.[33]

Addressing Disproportionate Impacts of NRAP in California

We will use CalEnviroScreen 4.0 to assess which subpopulations of Californians have higher exposure to NRAP.[49] CalEnviroScreen contains a traffic impact metric, which is defined as the "sum of traffic volumes adjusted by road segment length (vehicle kilometers per hour) divided by total road length (kilometers) within 150 meters of the census tract (traffic volumes estimates for 2017)."[49] We will use this indicator to identify the census tracts of Californians living in the top 10, 20, and 50 percent of traffic impact. We will examine associations between population characteristics and NRAP exposure across exposure groups using a multivariate regression model, accounting for possible confounding variables. Covariates that are significantly associated with NRAP exposure will be retained in adjusted models. Demographic variables that will be evaluated include age, race/ethnicity, linguistic isolation, and sex. Socioeconomic variables will include poverty, unemployment, health insurance status, and educational attainment. Health status indicators that will be evaluated include asthma, cardiovascular disease, and low birth weight infants. These factors have been shown to increase the vulnerability or susceptibility of populations to the health effects of air pollution. Data will be obtained from CalEnviroScreen[49] and the American Community Survey.[50] Analyses will be conducted using STATA statistical software (v17.0).[51] UCSF's Health Atlas will also be used to generate a map of traffic impact by census tract.[52]

Conclusion

Motor vehicles are a substantial source of air pollution, especially in urban areas around the world and across the US. As urbanization and traffic congestion increases there is considerable need to understand the totality of the evidence on the health effects from NRAP, and if disparities exist based on social factors e.g., race, income, education, linguistic isolation. Current systematic reviews report inconsistent findings on the human health effects of NRAP and are of varying quality. Our overview of reviews will therefore aim to (1) evaluate and summarize what is known about the health effects of NRAP, (2) help future researchers prioritize exposures and/or health outcomes to further investigate, and (3) aid policy makers, including the California State Legislature and the US EPA in developing recommendations to protect and foster human

health, particularly for the historically marginalized communities who are disproportionately affected by hazardous environmental exposures. Furthermore, research on NRAP is highly relevant, as several motor vehicle emissions are included in the next set of chemicals the United States Environmental Protection Agency (EPA) will evaluate under the Toxic Substances Control Act (TSCA) (e.g., 1,1-Dichloroethane, 1,2-Dichloroethane) and this is an important source for criteria air pollutants regulated under the Clean Air Act.

Declarations of interest:

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

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Authors & review team contributions:

CC, EL, and NC designed and wrote the review protocol. TW reviewed the protocol. CC will provide project management expertise for the project. CC, EL, and OS will screen reviews for inclusion and collect data with NC adjudicating if consensus cannot be reached. OS, NC, and EL will conduct evaluations of the reviews. NC and TW will provide technical expertise on systematic review and air pollution. CC, NC, EL, and TW will all be involved in the writing of the report chapter to narratively summarize the results of this review. NC and TW are guarantors.

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Appendix A

Search Strings

 # Web of Science Search Strategy (v0.1)

Database: Web of Science Core Collection

Entitlements:

- WOS.IC: 1993 to 2023
- WOS.CCR: 1985 to 2023
- WOS.SCI: 1900 to 2023
- WOS.AHCI: 1975 to 2023
- WOS.BHCI: 2005 to 2023
- WOS.BSCI: 2005 to 2023
- WOS.ESCI: 2005 to 2023
- WOS.ISTP: 1990 to 2023
- WOS.SSCI: 1900 to 2023
- WOS.ISSHP: 1990 to 2023

Searches:

1: ALL=((systematic review OR systematic literature review OR systematic scoping review OR systematic narrative review OR systematic qualitative review OR systematic evidence review OR systematic quantitative review OR systematic meta-review OR systematic critical review OR systematic mixed studies review OR systematic mapping review OR systematic cochrane review OR systematic search and review OR systematic integrative review OR Meta-analysis OR systematic review OR evidence synthesis OR meta-synthesis OR (systematic AND (search OR review)))) Date Run: Wed May 17 2023 10:55:21 GMT-0700 (Pacific Daylight Time) Results: 717876

2: TS=(("Vehicle Emissions"[Mesh] OR "Vehicle Emission" OR "Vehicle Emissions" OR "Traffic-Related Pollution"[Mesh] OR "Traffic-Related Pollution" OR Traffic-Related Pollutant OR Traffic-related pollutants OR "Traffic Related Pollution" OR Traffic Related Pollutant OR Traffic related pollutants OR Traffic related air pollution OR Traffic related air pollutant OR Traffic related air pollutants OR Traffic-related air pollution OR Traffic-related air pollutant OR Traffic-related air pollutants OR Traffic Pollution OR traffic pollutant OR traffic pollutants OR Vehicle Pollution OR vehicle pollutant OR vehicle pollutants OR "Automobile Exhaust OR "Engine Exhaust" OR "Transportation Emissions) OR ((Nitrogen Oxides [mesh] OR Nitrogen Oxides OR Nitrogen Oxide OR NOx OR Carbon monoxide [mesh] OR Carbon Monoxide OR Carbon Dioxide [mesh] OR carbon dioxide OR Volatile Organic Compounds [mesh] OR Volatile Organic Compound OR Volatile Organic Compounds OR VOCs OR PM10 OR PM5 OR PM2.5 OR PM1 OR Pollut* OR sulfur dioxide [mesh] OR sulphur dioxide OR sulfur dioxide OR S02 OR ozone OR O3 OR urban pollution OR urban pollutant OR urban pollutants OR black carbon OR polycyclic aromatic hydrocarbon OR polycyclic aromatic hydrocarbons OR benzene OR formaldehyde OR Particulate Matter[mh] OR Particulate Matter OR Particulate Air Pollutants OR Particulate Air Pollutant OR Particulate Air Pollution OR Ambient Particulate Matter OR PM coarse OR MSATs OR "mobile-source air toxics" OR PAH OR OPAH or NPAH OR petroleum pollution [mesh] OR petroleum pollution) AND (motor

vehicles[mh] OR traffic OR automobiles [mesh] OR auto OR autos OR automobile OR automobiles OR car OR cars OR truck OR trucks OR diesel OR vehicle OR vehicles OR vehicular OR bus OR buses OR motorcycle OR motorbike OR motor-bike OR motorcycles OR motorbikes OR motor-bikes OR traffic OR internal combustion OR exhaust OR tailpipe* OR ("Vehicle Emissions"[Mesh] OR vehicle emission OR vehicle emissions OR taxi*)))) Date Run: Wed May 17 2023 11:04:32 GMT-0700 (Pacific Daylight Time) Results: 107805

3: #2 AND #1 Date Run: Wed May 17 2023 11:04:50 GMT-0700 (Pacific Daylight Time) Results: 793

Embase

Session Results

.....

No.	Query	Results	Date
#5.	(#1 OR #2) AND #3 AND #4	320	17 May 2023
#4.	((((((((((((systematic AND review:ti OR systematic) AND literature AND review:ti OR systematic) AND scoping AND review:ti OR systematic) AND narrative AND review:ti OR systematic) AND qualitative AND review:ti OR systematic) AND evidence AND review:ti OR systematic) AND quantitative AND review:ti OR systematic) AND 'meta review':ti OR systematic) AND critical AND review:ti OR systematic) AND mixed AND studies AND review:ti OR systematic) AND mapping AND review:ti OR systematic) AND cochrane AND review:ti OR systematic) AND search AND review:ti OR systematic) AND integrative AND review:ti OR 'meta-analysis':ab,ti OR 'systematic review':ab,ti OR 'evidence synthesis':ab,ti OR 'meta-synthesis':ab,ti OR 'systematic':ab,ti) AND ('search':ab,ti OR 'review':ab,ti)	438,015	17 May 2023
#3.	'motor vehicle'/exp OR 'car'/exp OR auto OR autos OR automobile OR automobiles OR car OR cars OR truck OR trucks OR diesel OR vehicle OR vehicles OR vehicular OR bus OR buses OR taxi* OR motorcycle OR motorbike OR 'motor bike' OR motorcycles OR motorbikes OR 'motor bikes' OR traffic OR 'internal combustion' OR exhaust OR tailpipe* OR 'exhaust gas'/exp OR 'vehicle emission' OR 'vehicle emissions'	566,183	17 May 2023
#2.	'nitrogen oxide'/exp OR 'nitrogen oxides' OR 'nitrogen oxide' OR 'nox' OR 'carbon monoxide'/exp OR 'carbon monoxide' OR 'carbon dioxide'/exp OR 'carbon dioxide' OR 'volatile organic compound'/exp OR 'volatile organic compound' OR 'volatile organic compounds' OR 'vocs' OR pm10 OR pm5 OR pm2.5 OR pm1 OR pollut*	1,070,441	17 May 2023

	OR 'sulfur dioxide'/exp OR 'sulphur dioxide' OR 'sulfur dioxide' OR s02 OR ozone OR o3 OR 'urban pollution' OR 'urban pollutant' OR 'urban pollutants' OR 'black carbon' OR 'polycyclic aromatic hydrocarbon'/exp OR 'polycyclic aromatic hydrocarbon derivative'/exp OR 'polycyclic aromatic hydrocarbons' OR benzene OR formaldehyde OR 'particulate matter'/exp OR 'particulate organic carbon'/exp OR 'particulate organic carbon' OR 'particulate organic matter'/exp OR 'particulate organic matter' OR 'particulate matter' OR 'particulate air pollutants' OR 'particulate air pollutant' OR 'particulate air pollution' OR 'ambient particulate matter' OR 'pm coarse' OR msats OR 'mobile-source air toxics' OR pah OR opah OR npah OR 'petroleum pollution'		
#1.	'exhaust gas'/exp OR 'exhaust gas' OR 'vehicle emission' OR 'vehicle emissions'/exp OR 'vehicle emissions' OR 'traffic-related pollution'/exp OR 'traffic-related pollution' OR 'traffic-related pollutant' OR 'traffic-related pollutants' OR 'traffic related pollution'/exp OR 'traffic related pollution' OR 'traffic related pollutant' OR 'traffic related pollutants' OR 'traffic related air pollution'/exp OR 'traffic related air pollution' OR 'traffic related air pollutant' OR 'traffic related air pollutants' OR 'traffic-related air pollution' OR 'traffic-related air pollutant' OR 'traffic-related air pollutants' OR 'traffic pollution'/exp OR 'traffic pollution' OR 'traffic pollutant' OR 'traffic pollutants' OR 'vehicle pollution' OR 'vehicle pollutant' OR 'vehicle pollutants' OR 'automobile exhaust'/exp OR 'automobile exhaust' OR 'engine exhaust' OR 'transportation emissions'	25,801	17 May 2023

.....

Search	Actions	Details	Query	Results	Time
#5					
Search: **(#1 OR #2) AND #3 AND #4**				337	13:42:04
#4					
Search: **(((systematic review[ti] OR systematic literature review[ti] OR systematic scoping review[ti] OR systematic narrative review[ti] OR**				455,549	13:41:27

systematic qualitative review[ti] OR systematic evidence review[ti] OR systematic quantitative review[ti] OR systematic meta-review[ti] OR systematic critical review[ti] OR systematic mixed studies review[ti] OR systematic mapping review[ti] OR systematic cochrane review[ti] OR systematic search and review[ti] OR systematic integrative review[ti]) NOT comment[pt] NOT (protocol[ti] OR protocols[ti])) NOT MEDLINE [subset]) OR (Cochrane Database Syst Rev[ta] AND review[pt]) OR systematic review[pt] OR "Meta-analysis" [tiab] OR "systematic review" [tiab] OR "evidence synthesis" [tiab] OR "meta-synthesis" [tiab] OR (systematic [tiab] AND (search[tiab] OR review[tiab]))		
#3		
Search: **("motor vehicles"[mh] OR traffic OR automobiles [mesh] OR auto OR autos OR automobile OR automobiles OR car OR cars OR truck OR trucks OR diesel OR vehicle OR vehicles OR vehicular OR bus OR buses OR motorcycle OR motorbike OR motor-bike OR motorcycles OR motorbikes OR motor-bikes OR traffic OR "internal combustion" OR exhaust OR tailpipe* OR ("Vehicle Emissions"[Mesh] OR "vehicle emission" OR "vehicle emissions" OR taxi*))**	388,992	13:41:05
#2		
Search: **("Nitrogen Oxides" [mesh] OR "Nitrogen Oxides" OR "Nitrogen Oxide" OR "NOx" OR "Carbon monoxide" [mesh] OR "Carbon Monoxide" OR "Carbon Dioxide" [mesh] OR "carbon dioxide" OR "Volatile Organic Compounds" [mesh] OR "Volatile Organic Compound" OR "Volatile Organic Compounds" OR "VOCs" OR PM10 OR PM5 OR PM2.5 OR PM1 OR Pollut* OR "sulfur dioxide" [mesh] OR "sulphur dioxide" OR "sulfur dioxide" OR S02 OR ozone OR O3 OR "urban pollution" OR "urban pollutant" OR "urban pollutants" OR "black carbon" OR "polycyclic aromatic hydrocarbon" OR "polycyclic aromatic hydrocarbons" OR benzene OR formaldehyde OR "Particulate Matter"[mh] OR "Particulate Matter" OR "Particulate Air Pollutants" OR "Particulate Air Pollutant" OR "Particulate Air Pollution" OR "Ambient Particulate Matter" OR "PM coarse" OR MSATs OR "mobile-source air toxics" OR PAH OR OPAH or NPAH OR "petroleum pollution" [mesh] OR "petroleum pollution")**	994,026	13:40:38
#1		
Search: **("Vehicle Emissions"[Mesh] OR "Vehicle Emission" OR "Vehicle Emissions" OR "Traffic-Related Pollution"[Mesh] OR "Traffic-Related Pollution" OR "Traffic-Related Pollutant" OR "Traffic-related pollutants" OR "Traffic Related Pollution" OR "Traffic Related Pollutant" OR "Traffic related pollutants" OR "Traffic related air pollution" OR "Traffic related air pollutant" OR "Traffic related air pollutants" OR "Traffic-related air pollution" OR "Traffic-related air pollutant" OR "Traffic-related air pollutants" OR "Traffic Pollution" OR**	14,199	13:40:18

"traffic pollutant" OR "traffic pollutants" OR "Vehicle Pollution" OR "vehicle pollutant" OR "vehicle pollutants" OR "Automobile Exhaust" OR "Engine Exhaust" OR "Transportation Emissions")

Cochrane Library

Date Run: 17/05/2023 17:40:13
Comment:

ID Search Hits
#1 ([mh "Vehicle Emissions"] OR "Vehicle Emission"
OR "Vehicle Emissions"
OR [mh "Traffic-Related Pollution"] OR "Traffic-Related Pollution"
OR "Traffic-Related Pollutant"
OR "Traffic-related pollutants"
OR "Traffic Related Pollution"
OR "Traffic Related Pollutant"
OR "Traffic related pollutants"
OR "Traffic related air pollution"
OR "Traffic related air pollutant"
OR "Traffic related air pollutants"
OR "Traffic-related air pollution"
OR "Traffic-related air pollutant"
OR "Traffic-related air pollutants"
OR "Traffic Pollution"
OR "traffic pollutant"
OR "traffic pollutants"
OR "Vehicle Pollution"
OR "vehicle pollutant"
OR "vehicle pollutants"
OR "Automobile Exhaust"
OR "Engine Exhaust"
OR "Transportation Emissions"
) 206
#2 ([mh "Nitrogen Oxides"] OR "Nitrogen Oxides"
OR "Nitrogen Oxide"
OR NOx
OR [mh "Carbon monoxide"] OR "Carbon Monoxide"
OR [mh "Carbon Dioxide"] OR "carbon dioxide"
OR [mh "Volatile Organic Compounds"] OR "Volatile Organic Compound"
OR "Volatile Organic Compounds"
OR VOCs
OR PM10
OR PM5
OR PM2.5
OR PM1
OR Pollut*
OR [mh "sulfur dioxide"] OR "sulphur dioxide"
OR "sulfur dioxide"

OR S02
OR ozone
OR O3
OR "urban pollution"
OR "urban pollutant"
OR "urban pollutants"
OR "black carbon"
OR "polycyclic aromatic hydrocarbon"
OR "polycyclic aromatic hydrocarbons"
OR benzene
OR formaldehyde
OR [mh "Particulate Matter"] OR "Particulate Matter"
OR "Particulate Air Pollutants"
OR "Particulate Air Pollutant"
OR "Particulate Air Pollution"
OR "Ambient Particulate Matter"
OR "PM coarse"
OR MSATs
OR "mobile-source air toxics"
OR PAH
OR OPAH
OR NPAH
OR [mh "petroleum pollution"] OR "petroleum pollution"
) 23939
#3 ([mh "motor vehicles"] OR traffic
OR [mh automobiles] OR auto
OR autos
OR automobile
OR automobiles
OR car
OR cars
OR truck
OR trucks
OR diesel
OR vehicle
OR vehicles
OR vehicular
OR bus
OR buses
OR motorcycle
OR motorbike
OR motor-bike
OR motorcycles
OR motorbikes
OR motor-bikes
OR traffic
OR "internal combustion"
OR exhaust

OR tailpipe*
OR ([mh "Vehicle Emissions"] OR "vehicle emission"
OR "vehicle emissions"
OR taxi*
)) 22103
#4 ((("systematic review":ti OR "systematic literature review":ti OR "systematic scoping review":ti OR "systematic narrative review":ti OR "systematic qualitative review":ti OR "systematic evidence review":ti OR "systematic quantitative review":ti OR "systematic meta-review":ti OR "systematic critical review":ti OR "systematic mixed studies review":ti OR "systematic mapping review":ti OR "systematic cochrane review":ti OR "systematic search"
AND review:ti OR "systematic integrative review":ti) NOT comment:pt NOT (protocol:ti OR protocols:ti)) NOT MEDLINE) OR ("Cochrane Database Syst Rev":so AND review:pt) OR "systematic review":pt OR Meta-analysis:ti,ab OR "systematic review":ti,ab OR "evidence synthesis":ti,ab OR meta-synthesis:ti,ab OR (systematic:ti,ab AND (search:ti,ab OR review:ti,ab)) 18095
#5 (#1 OR #2) AND #3 AND #4 154
#6 #5 AND #1 5

CABI Global Health

("systematic reviews" OR "meta-analysis") AND ("vehicles" OR "traffic" OR "tracks" OR "cabs" OR "trucks" OR "motor cars" OR "motoring" OR "road transport" OR "bus transport" OR "automobile*") AND ("air pollution" OR "indoor air pollution" OR "air pollutants" OR "air quality" OR "vehicle emissions")

PubMed

#1	("Vehicle Emissions"[Mesh] OR "Vehicle Emission" OR "Vehicle Emissions" OR "Traffic-Related Pollution"[Mesh] OR "Traffic-Related Pollution" OR "Traffic-Related Pollutant" OR "Traffic-related pollutants" OR "Traffic Related Pollution" OR "Traffic Related Pollutant" OR "Traffic related pollutants" OR "Traffic related air pollution" OR "Traffic related air pollutant" OR "Traffic related air pollutants" OR "Traffic-related air pollution" OR "Traffic-related air pollutant" OR "Traffic-related air pollutants" OR "Traffic Pollution" OR "traffic pollutant" OR "traffic pollutants" OR "Vehicle Pollution" OR "vehicle pollutant" OR "vehicle pollutants" OR "Automobile Exhaust" OR "Engine Exhaust" OR "Transportation Emissions")
#2	("Nitrogen Oxides" [mesh] OR "Nitrogen Oxides" OR "Nitrogen Oxide" OR "NOx" OR "Carbon monoxide" [mesh] OR "Carbon Monoxide" OR "Carbon Dioxide" [mesh] OR "carbon dioxide" OR "Volatile Organic Compounds" [mesh] OR "Volatile Organic Compound" OR "Volatile Organic Compounds" OR "VOCs" OR PM10 OR PM5 OR PM2.5 OR PM1 OR Pollut* OR "sulfur dioxide" [mesh] OR "sulphur dioxide" OR "sulfur dioxide" OR S02 OR ozone OR O3 OR "urban pollution" OR "urban pollutant" OR "urban pollutants" OR "black carbon" OR "polycyclic aromatic hydrocarbon" OR "polycyclic aromatic hydrocarbons" OR benzene OR formaldehyde OR "Particulate Matter"[mh] OR "Particulate Matter" OR "Particulate Air Pollutants" OR "Particulate Air Pollutant" OR "Particulate Air Pollution" OR "Ambient Particulate Matter" OR "PM coarse" OR MSATs OR "mobile-source air toxics" OR PAH OR OPAH or NPAH OR "petroleum pollution" [mesh] OR "petroleum pollution")
#3	("motor vehicles"[mh] OR traffic OR automobiles [mesh] OR auto OR autos OR automobile OR automobiles OR car OR cars OR truck OR trucks OR diesel OR vehicle OR vehicles OR vehicular OR bus OR buses OR motorcycle OR motorbike OR motor-bike OR motorcycles OR motorbikes OR motor-bikes OR traffic OR "internal combustion" OR exhaust OR tailpipe* OR ("Vehicle Emissions"[Mesh] OR "vehicle emission" OR "vehicle emissions" OR taxi*))
#4	(((systematic review[ti] OR systematic literature review[ti] OR systematic scoping review[ti] OR systematic narrative review[ti] OR systematic qualitative review[ti] OR systematic evidence review[ti] OR systematic quantitative review[ti] OR systematic meta-review[ti] OR systematic critical review[ti] OR systematic mixed studies review[ti] OR systematic mapping review[ti] OR systematic cochrane review[ti] OR systematic search and review[ti] OR systematic integrative review[ti]) NOT comment[pt] NOT (protocol[ti] OR protocols[ti])) NOT MEDLINE [subset]) OR (Cochrane Database Syst Rev[ta] AND review[pt]) OR systematic review[pt] OR "Meta-analysis" [tiab] OR "systematic review" [tiab] OR "evidence synthesis" [tiab] OR "meta-synthesis" [tiab] OR (systematic [tiab] AND (search[tiab] OR review[tiab]))
#5	(#1 OR #2) AND #3 AND #4

TRIP Pro database and MEDNAR

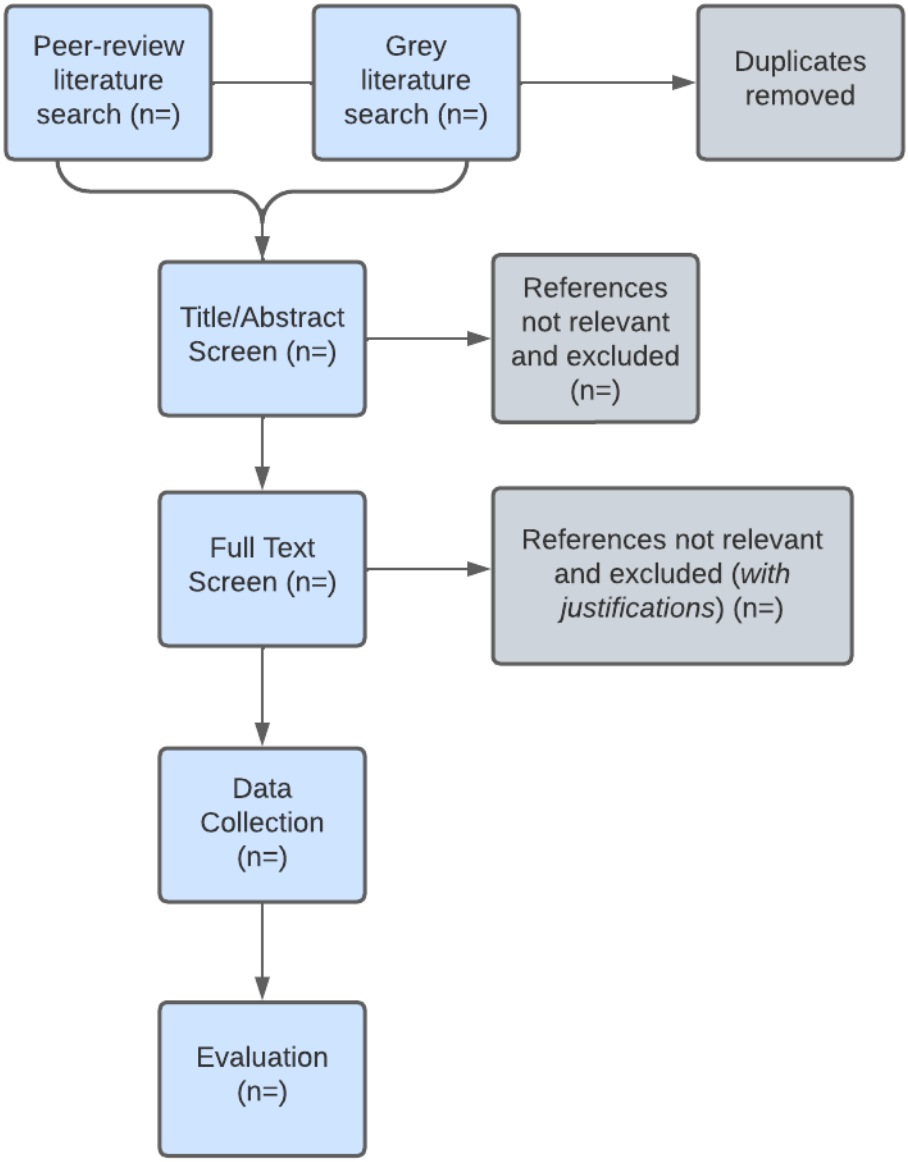
Search terms: "indoor air pollution" AND "traffic related"

NTIS and Base

Search terms: air pollution; systematic review

Appendix B

Study Flow Diagram Example



Appendix C

PRISMA Guidelines to meet the minimum criteria for systematic review, the paper must include all of the following highlighted information:*

Section and Topic	Item #	Checklist item
TITLE		
Title	1	Identify the report as a systematic review.
ABSTRACT		
Abstract	2	See the PRISMA 2020 for Abstracts checklist.
INTRODUCTION		
Rationale	3	Describe the rationale for the review in the context of existing knowledge.
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.
METHODS		
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.(
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.
RESULTS		

Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.
Study characteristics	17	Cite each included study and present its characteristics.
Risk of bias in studies	18	Present assessments of risk of bias for each included study.
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.
	20c	Present results of all investigations of possible causes of heterogeneity among study results.
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.
DISCUSSION		
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.
	23b	Discuss any limitations of the evidence included in the review.
	23c	Discuss any limitations of the review processes used.
	23d	Discuss implications of the results for practice, policy, and future research.
OTHER INFORMATION		
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.
	24c	Describe and explain any amendments to information provided at registration or in the protocol.
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.
Competing interests	26	Declare any competing interests of review authors.
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.

* Section and Topic, and Checklist items used as inclusion criteria for reviews. Reviews were required to report all components to be included in the Overview.

Appendix D

Data Collection Form

Information for Evidence Table(s):

- Citation (Author, Publication Year)
- Review Specific Acronyms
- Review Corresponding Author Country
- Review Objective
- Review Publication Search Criterion
- Review Population(s)
- Review Exposure(s)
- Review Comparison(s)
- Review Outcome(s)
- Number of Primary Studies Included in Review
- Number of Primary NRAP Studies Included in Review
- Primary NRAP Studies Included in Review (Citations)
- Primary NRAP Study Sample Sizes
- Exposures (of primary NRAP studies)
- Outcomes (of primary NRAP studies)
- Review Relative effects or narrative results
- Review Author Affiliations
- Review Funding Statement
- Review Conflict of Interest Statement
- Review Acknowledgement Statement

We will also collect information for AMSTAR Criteria 1-16 to evaluate the reviews (see Appendix E for more detail).

Appendix E

Guidance: Use both the publication and the protocol to identify relevant information for the AMSTAR evaluation.

---

1. Did the research questions and inclusion criteria for the review include the components of PI/ECO?

For Yes:
- ☐ Population
- ☐ Intervention/ Exposure
- ☐ Comparator group
- ☐ Outcome

Optional (recommended)
- ☐ Timeframe for follow-up

Yes
No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:
The authors state that they had a written protocol or guide that included ALL the following:
- ☐ review question(s)
- ☐ a search strategy
- ☐ inclusion/exclusion criteria
- ☐ a risk of bias assessment

For Yes:
As for partial yes, plus the protocol should be registered/was made publicly available before the review commenced and should also have specified:
- ☐ a meta-analysis/synthesis plan, if appropriate, *and*
- ☐ a plan for investigating causes of heterogeneity
- ☐ justification for any deviations from the protocol

Yes
Partial Yes
No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:
- ☐ *Explanation for* including only RCTs
- ☐ OR *Explanation for* including only NRSI
- ☐ OR *Explanation* for the type of epidemiological exposure studies
- ☐ OR *Explanation for* including both RCTs and NRSI

Yes
No

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):
- ☐ searched at least 2 databases (relevant to research question)
- ☐ provided key word and/or search strategy
- ☐ justified publication restrictions (e.g., language)/had no publication restrictions

For Yes, should also have (all the following):
- ☐ searched the reference lists / bibliographies of included studies
- ☐ included/consulted content experts in the field *(optional)*
- ☐ where relevant, searched for grey literature
- ☐ conducted search within 24 months of submission of the review

Yes
Partial Yes
No

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:

- ☐ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include — Yes
- ☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer. — Partial Yes

☐ No

For Partial Yes:

One reviewer selected eligible studies (no second reviewer), however this was noted as a limitation

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following:
- ☐ at least two reviewers achieved consensus on which data to extract from included studies
- ☐ OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.

☐ Yes
☐ Partial Yes
☐ No

For Partial yes:
One reviewer selected eligible studies (no second reviewer), however this was noted as a limitation

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes:
- ☐ provided a list of all potentially relevant studies that were read in full-text form but excluded from the review
  OR
  if a reason (usually in the PRISMA flow and a summary of XX studies for XX reason) for the exclusions was summarized

For Yes, must also have:
- ☐ Justified the exclusion from the review of each potentially relevant study

☐ Yes
☐ Partial Yes
☐ No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following):
- ☐ described populations
- ☐ described interventions/exposures
- ☐ described comparators
- ☐ described outcomes
- ☐ described research designs

For Yes, should also have ALL the following:
- ☐ described population in detail
- ☐ described intervention/exposures in detail (including doses where relevant)
- ☐ described comparator in detail (including doses where relevant)
- ☐ described study's setting
- ☐ timeframe for follow-up

☐ Yes
☐ Partial Yes
☐ No

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs
For **Partial Yes**, must have assessed RoB from
- ☐ unconcealed allocation, *and*
- ☐ lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality)

AND
Explicitly conducting tests of internal validity using a known qualitative domain-based tool, but the authors develop an overall qualitative rating for the study

For **Yes**, must also have assessed RoB from:
- ☐ allocation sequence that was not truly random, *and*
- ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome

AND you need to have both of the below.
- o Explicitly conducting tests of internal

☐ Yes
☐ Partial Yes
☐ No
☐ Includes only NRSI

(studies that cited the WHO/ILO approach (or ROBINS) which used the Nav Guide).

NO

- No mention of internal validity nor any tests conducted to assess RoB/validity.
- If the study uses a scoring system (quantitative) to numerically score studies

validity using a known qualitative domain-based tool (a citable protocol). They may use different ones.

- Presents results from the entire internal validity tool (e.g., responses to each question and not only the overall ROB rating for each study)

NRSI

For **Partial Yes**, must have assessed RoB:

Partial

Explicitly conducting tests of internal validity using a known qualitative domain-based tool, but the authors develop an overall qualitative rating for the study (studies that cited the WHO/ILO approach (or ROBINS) which used the Nav Guide).

NO

- No mention of internal validity nor any tests conducted to assess RoB/validity.
- If the study uses a scoring system (quantitative) to numerically score studies

For **Yes**, you need to have both of the below:

- Explicitly conducting tests of internal validity using a known qualitative domain-based tool (a citable protocol). They may use different ones.
- Presents results from the entire internal validity tool (e.g., responses to each question and not only the overall ROB rating for each study).

- ☐ Yes
- ☐ Partial Yes
- ☐ No
- ☐ Includes only RCTs

10. Did the review authors report on the sources of funding and COI for the studies included in the review?

For Yes

☐ Must have reported on the sources of funding & COI for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies

Options: Yes/No

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

For Yes:

- ☐ The authors justified combining the data in a meta-analysis
  - ☐ AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available

☐ Yes
☐ No
☐ No meta-analysis conducted

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes:

☐ If the pooled estimate was based on RCTs/exposure studies and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.

☐ Yes
☐ No
☐ No meta-analysis conducted

13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?

For Yes:

☐ If RCTs/Exposure studies with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results

☐ Yes
☐ No

14. If meta-analysis was performed, did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes:

- ☐ There was no significant heterogeneity in the results
- ☐ OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review

If meta-analysis was not performed, did the review authors discuss the reasons why, including a discussion of heterogeneity?

☐ Yes
☐ No

15. Did the review authors assess publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes:

☐ performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias

☐ Yes
☐ No
☐ No meta-analysis conducted

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	
For Yes: □ For "Yes", "1) There is an author COI statement and it is concordant with the authors affiliations and 2) there is a study funding statement" - If any of this information is missing, or it isn't concordant, then it is a "NO"	□ Yes □ No

To cite this tool: Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.