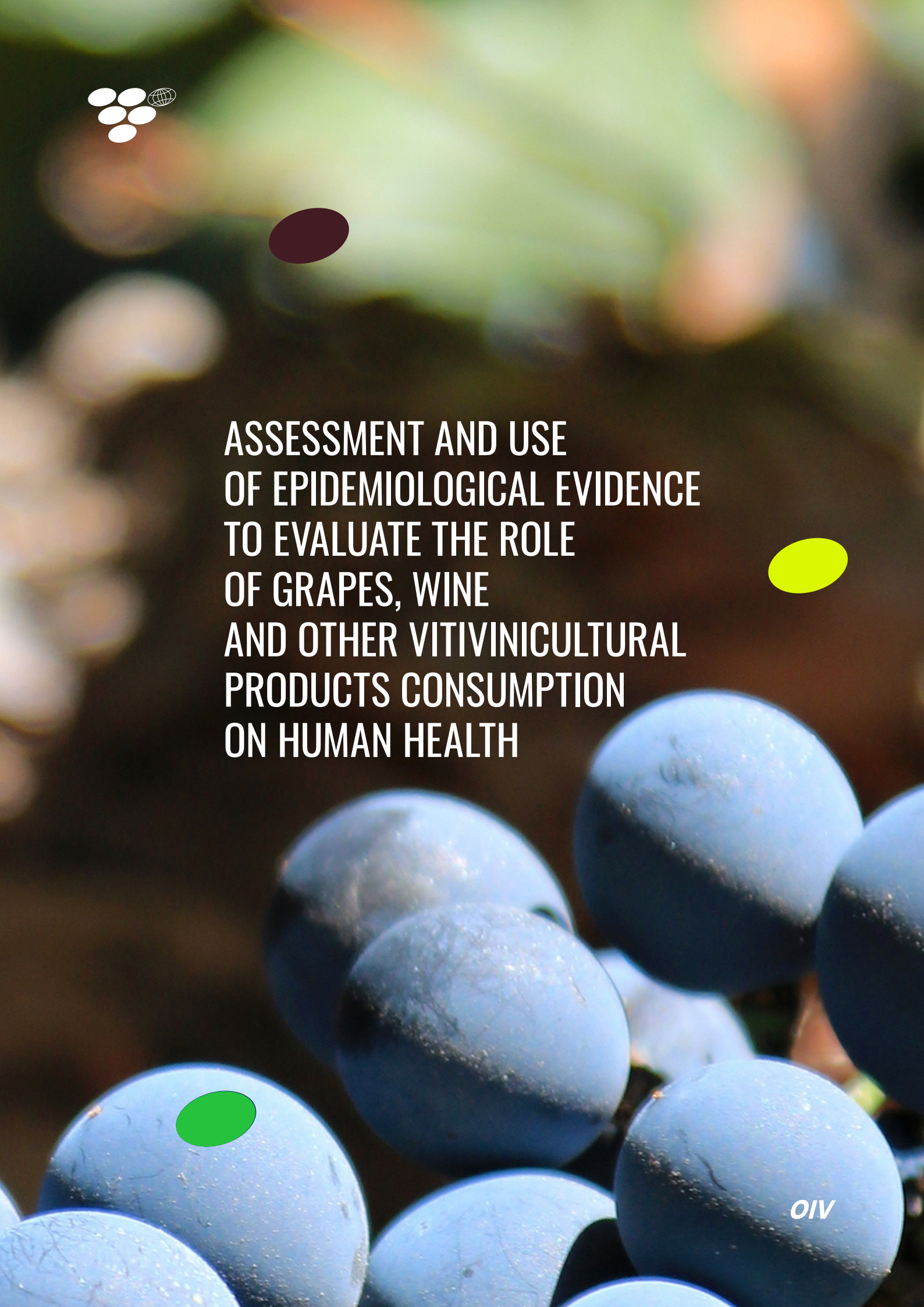
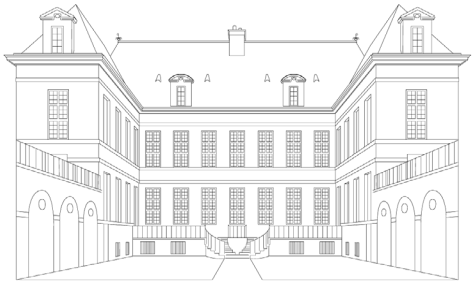


ASSESSMENT AND USE OF EPIDEMIOLOGICAL EVIDENCE TO EVALUATE THE ROLE OF GRAPES, WINE AND OTHER VITIVINICULTURAL PRODUCTS CONSUMPTION ON HUMAN HEALTH

OIV



OIV 100

International Year of Vine and Wine 1924 • 2024

DISCLAIMER

OIV collective expertise documents are not submitted to the Step Procedure for Examining Resolutions and can under no circumstances be treated as OIV resolutions. Only resolutions adopted by the Member States of the OIV have an official character. This document has been drafted by the Safety and Health Commission's "Consumption, Nutrition and Health" (CONUSA) Group.

Illustrated examples of the information provided can be seen throughout this document with a series of images, which are indicated by the icon. The current document has been drafted and developed on the initiative of the OIV and constitutes a collective expert report.

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TABLE OF CONTENTS

SUMMARY

The “Consumption, Nutrition and Health” group of experts of the OIV has made an effort to create a guide that elaborates the types of epidemiological studies that collectively assist in the comprehension of wine or grape-derived products consumption.
The purpose of this report is to develop clear and consistent guidelines that can identify the set of processes used to assess the consumption of wine and/or grapes-derived products and its consequences in terms of health issues for the general population or individuals.

The current report presents what epidemiology is, the different types of epidemiological studies used to measure health and disease as well as possible bias existing in those studies. Methods, procedures, data analysis, and results integrity were considered.

The target audiences of this report are experts, researchers, reviewers and readers of epidemiological publications and results. The proper evaluation of the research evidence through a proven scientific process permits the avoidance of the potential use of papers whose scientific value is uncertain or biased.

BACKGROUND

In June 2020, during the OIV “Consumption, Nutrition and Health” experts’ group meeting it was decided to create an electronic working group (eWG), with main task being to elaborate a set of guidelines on: 1) which type of epidemiological studies considers the analysis of the consumption of wine and grapes derivatives in relation to its effects on health and 2) on the basis of which criteria the study was selected or rejected. The main advantage of this report is that papers with scientific uncertainty will not been taken into consideration in analyses.

Careful evaluation of published study results is extremely important when considering the effects of alcohol consumption on general health status. In particular, the authors' conclusions must highlight that an adjustment has been applied that takes into account the underlying dietary pattern as a potential confounding factor. Furthermore, in the direct comparison between the different research results, the type of exposure (i.e. alcoholic beverage, consumption pattern) should also be considered (Sluik et al., 2016).

SCOPE AND PURPOSE

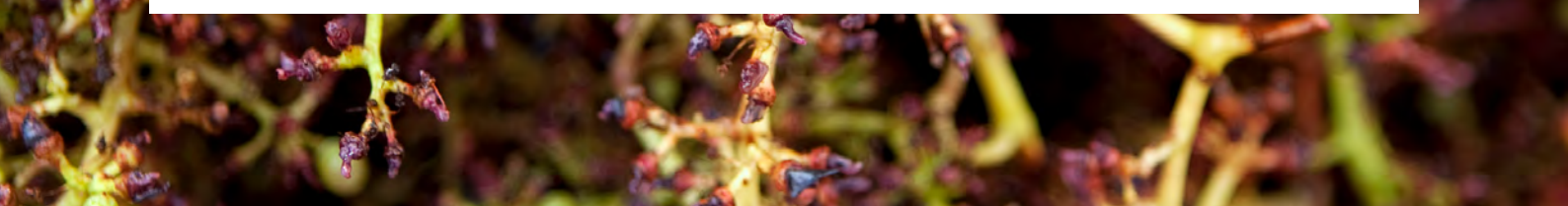
Assessing the quality of an epidemiological study equates to assessing whether the conclusions drawn from it are warranted, considering the methods, the representativeness of the study sample and the nature of the population. Bias, confounding factors, and randomness can threaten the quality of an epidemiological study at any phase. Nevertheless, their presence does not necessarily imply that a study should be disregarded. An in-depth analysis must first assess any of these threats or missing information and evaluate their potential impact on the conclusions.

The purpose of this report is to develop guidelines that will assist in the identification of processes necessary in order to assess clarity and consistency of epidemiological information, when it comes to the consumption of wine and/or grapes derived products and its consequences in terms of health issues for the general population or individuals.

It is important that the processes and methods used to evaluate the evidence and to estimate possible health effects of wine consumption, are clear, explicit, and based on valid epidemiological theory and practices. **This work will have the advantage of avoiding potential use of doubtful papers with bias when analysing the health effects of wine and grape products.**

The primary target audiences of the document are experts, investigators, communication experts, and users of epidemiological publications and results.





WHAT IS EPIDEMIOLOGY?

Through the years, the definition of epidemiology has been altered many times, with more than 100 definitions being found (1). Epidemiology is a discipline that is ever evolving along with the society changes and the appearance of new diseases and their related disciplines.

According to the USA Centers for Disease Control and Prevention (CDC) (2, 3) "epidemiology is the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems". Various methods can be used to carry out epidemiological investigations: surveillance and descriptive studies can be used to study distribution; analytical studies can be used to study determinants.

It could be of great interest to indicate that epidemiology underpins good clinical research. Epidemiological study is any research with a defined numerator, which describes, quantifies, and postulates causal mechanisms for health phenomena. Epidemiology gives insight into the natural history and causes of disease and can provide evidence to help prevent the occurrence of the disease. It promotes effective treatments which either cure or help prolong the lives of those with disease. Epidemiology, also referred to as "population medicine", is used to estimate the individual risk of a disease and the chances of avoiding it by using the average from the group experience.

1. The different types of epidemiological studies to measure health and disease

Types of Epidemiological Studies

Observation and experience
Observational studies
Experimental studies

Observational epidemiology
Descriptive studies
Ecological studies
Ecological error studies
Cross-sectional studies
Case-control studies
Cohort studies

Experimental epidemiology
Randomized controlled trials
Field trials
Community trials

2. Possible bias in epidemiological studies and related terms

Can epidemiological studies be wrong? How can we identify incorrect study outcomes?

In epidemiology, bias is defined as 'an error in the conception and design of a study – or in the collection, analysis, interpretation, reporting, publication, or review or data – leading to results or conclusions that are systematically (as opposed to randomly) different from truth' (Int. J. Epidemiology https://academic.oup.com/ije/pages/bias-in-epidemiology).

Methodological quality (risk of bias) assessment is an important step to be implemented prior to the initiation of the study. Therefore, it is important to accurately plan the type of study in order to choose the proper tool (4).

Types of bias

Random error
Chance is a random error that appears to indicate an association between the exposure and the outcome. A main assumption in epidemiology is that conclusions can be drawn about the whole population based on a sample of the population. Random error is the result of variations that occur by chance and affect the reliability of the investigation. It can be estimated and expressed quantitatively using p-values and confidence intervals. It cannot be eliminated, but it can be controlled by using larger sample sizes and efficient statistical analysis.

Sample size
Increasing the sample size tends to reduce the sampling error by making the sample statistic less variable. However, **increasing sample size does not affect survey bias**. A large sample size cannot compensate for methodological problems, such as under coverage, nonresponse bias among others that can lead to survey bias.

Sampling bias occurs when some members of a population are systematically more likely to be selected in a sample compared to others. In medical fields this is called ascertainment bias.
Sampling bias limits the generalizability of findings because it is a threat to external validity, specifically population validity. In other words, findings from biased samples can only be generalized to populations that share characteristics with the sample.

Systematic error
Systematic error (bias) is associated with weaknesses in methodological design or study execution that can affect the validity of the study results. It can be assessed qualitatively and avoided.

Selection bias
Refers to a systematic error resulting from a differential access to the study population for different exposure-disease subgroups.

Information bias
Refers to systematic error resulting from inaccuracy in measurement or classification of study variables, including disease, exposure, and other risk factors.

Confounding bias differs somewhat from the aforementioned two other forms, in way that the actual data may be fully accurate. Confounding bias is a systematic misinterpretation that results from making an unfair comparison, i.e., to take into account important differences between exposed and unexposed groups from a failure.
We will take up each of these types of bias.

Confounding factors need to be taken into account. A confounder variable is an important concept in epidemiology, because, if present, it can cause an over- or under- estimation of the observed association between exposure and health outcome. The distortion generated by a confounding factor can be profound and it can even alter the apparent direction of an effect.

Validity
Internal validity: study measured what was set out.
External validity: ability to generalise beyond the study population.

Ethical questions
Specific ethical issues arising in epidemiologic research and public health practice, that have been highlighted in ethics guidelines, include minimizing risks and providing benefits, informed consent, avoiding and disclosing conflicts of interest, obligations to communities, and the institutional review board system.
One of the most basic ethical principles of medicine and epidemiology is the moral obligation to cause no harm to participants (non-malfeasance), whether physical or psychological. Although the risk in an epidemiological investigation is usually minimal, most people who take part gain no personal benefit.

Risk: probability that an event will occur (an individual becoming diseased) or the number of new cases in a particular time frame period/number of total participants at start of time period.

Odds: the ratio between the probability that an event (disease) will occur and the probability of that event not happening (no disease) or the number of new cases on a time period/number of disease-free participants (non-cases).

Relative risk (RR): risk in the exposed group divided by the risk in the unexposed group.

Absolute risk: overall likelihood of getting a disease/condition during a given period of time i.e. (likelihood that a person who is free of a certain disease will develop this disease by a specific age).

Odds ratio (OR): odds in an exposed group divided by the odds in an unexposed group
A relative risk (RR) or odds ratio (OR) greater than one (>1), indicates an exposure to be harmful, while a value less than one (<1) indicates a protective effect. RR = 1.3 means exposed people are 30% more likely to be affected and get diseased, while OR = 1.3 means that the odds of being affected and get diseased is higher by 30% in exposed people.

Absolute risk reduction/Risk difference: risk in exposed group minus risk in unexposed group.

Baseline risk: risk in unexposed group.

The number needed to treat (NNT): is the number of patients requiring treatment (exposure) for one extra successful outcome (effect) and is calculated as 1/ (Risk in unexposed*(RR-1)).

Confidence interval (CI): Range considered to contain the population mean, derived from the sample interval mean and standard deviation. Usually, 95%

3. Study selection

Listed below are a set of processes that will help in the selection of the most accurate epidemiological studies when analysing wine and other grape derived products consumption and its effects on the health.

ASSESSING THE ANALYSIS PHASE OF AN EPIDEMIOLOGICAL STUDY
Statistical analysis versus biological interpretation

Most results of epidemiological studies are analysed using formal statistics. The type of statistical test that should be used is determined by the goal of the analysis (for example, to compare groups, to explore an association, or to predict an outcome) and the types of variables used in the analysis (for example, categorical, ordinal, or continuous variables).
The statistical results are often presented with a p value, which is a number, calculated from a statistical test, that describes how likely it is for a particular set of observations to exist if the null hypothesis is true. For example, in a two-tailed t-test, the null hypothesis is obtained when the difference between two groups is zero.

Confidence intervals are more useful to be considered, compared to p values, when assessing whether results are significant as they reflect both the degree of variability in the factor being investigated and the limited size of the study. The wider the confidence intervals, the less powerful the study is.

BEST PRACTICES FOR EPIDEMIOLOGICAL STUDIES

Research integrity and research fairness have gained considerable momentum in the past decade and have direct implications when it comes to global health epidemiology. The existing good epidemiological practice guidelines that have been developed by national epidemiological associations, are not tailored to the idiosyncrasies of global health, and seem to lack of international legitimacy.

Epidemiology, like any other discipline, is liable to malpractice. Questionable research practices must have no place in the global health research, as they steer research in the wrong direction, misguiding public policies and undermining society's trust (5).

• Guidelines can address part of the problem by facilitating structured and transparent processes.

• Key features of global health epidemiology revolve around the transnational and interdisciplinary nature of global health, its focus on equity, large-scale use and sustainability.

• Guidelines for good epidemiological practice (GEP) in global health are not available, but a number of documents have laid the foundation for their development.

Stakeholders involved in the commissioning, conduct, appraisal and publication of global health research should endorse a common set of GEP guidelines.

It can be recommended that epidemiological studies respect and use the PRISMA 2020 statement and checklist (6-12) (Annex 1) for a transparent reporting of systematic reviews and meta-analysis.

The professional standards that govern the practice of epidemiology, are based on rules about the scientific and methodological quality of the studies, their quality and confidentiality (as well as the ownership) of the data, conflicts of interest, reuse of data, and the use and communication of study results. If studies do not comply with these rules, their implementation and continuation become contrary to set professional standards, which are part of the more general rules of health ethics.

The professional and technical independence of the epidemiologists in the exercise of their scientific activity is an inviolable principle that must exist and be the basis of the relationship between the epidemiologist and the funder, public or private, of an epidemiological study, regardless of their relationship (employer-employee or another type of contract). In particular, the professional status or work contract of epidemiologists should not include any condition incompatible with their professional and technical independence, or any clause that might prevent them from doing their job in conformity with good epidemiological practices. When epidemiologists conduct their activity within a regulated profession or belong to a body regulated by a particular status, they must always ensure that the rules applying to that profession otherwise the status cannot be opposed to their independence or comply with the good epidemiological practices.

Analysis

The data collected or obtained during an epidemiological study must be analysed in conformity with the study protocol. Nonetheless, data collected in a study may legitimately be analysed to evaluate hypotheses that have not being explicitly formulated in the initial protocol, or were created for secondary purposes, different from what was originally intended. Any significant change from the statistical methodology described in the study protocol must be extensively? mentioned in any publication or presentation of the study results.

Quality control for the study

Standard procedures must be developed to guarantee the quality of the data collected, obtained, produced, or published during or as part of an epidemiological study.

Filing and archiving data

During the study period, it is imperative that an archiving system is organized and ensures to the guarantee of confidentiality of personal data; it must be easy to access and allow easy archiving of all data and documents.

Upon study completion, personal data can be stored only in anonymised form, which does not in any case allow the identification of individuals.

Scientific integrity and communication
All study results, regardless of whether the funders are public or private, are under the scientific supervision of the epidemiologist who is the principal investigator, and not under the funder, and the results must always be made public if their scientific validity is sufficient. All requests to hide the results, change or attenuate the content of a report or even to delay publication must be categorically rejected.

Impartiality of publications
Such publications must describe every aspect of the study in an honest and balanced manner, without considering other interests, especially non-scientific ones. Epidemiologists must not exaggerate results in the aim of increasing the likelihood of further funding for future research or in an effort to make their articles more attractive to journal editors. Published results generally constitute only a small fraction of the available information, and some bias may affect the choice of data to be published, which may be limited to selecting the results that agree with the epidemiologist' point of view, excluding those that contradict it. This type of partiality or bias must be avoided. The authors of epidemiological articles must comply with the rules of the well-established journals in their reporting of possible conflicts of interest. The definition and order of authors must comply with good practices for scientific publication.

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ANNEX 1
PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
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.	

Section and Topic	Item #	Checklist item	Location where item is reported
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.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

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