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ORIGINAL ARTICLE

Methodological guidelines for the estimation of attributable mortality using a prevalence-based method: the STREAMS-P tool

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Abstract

Background: There is evidence of strong links between exposure to different risk factors and life-threatening diseases. Assessing the burden of a risk factor on the population's mortality due to a given disease provides a clear picture of these links. The estimation of attributable mortality to a risk factor is the most widely used procedure for doing this. Although different methods are available to estimate attributable mortality, the prevalence-based methodology is the most frequent. The main objective of this study is to develop guidelines and checklists to STrengthen the design and REporting of Attributable Mortality Studies using a Prevalence-based method (STREAMS-P) and also to assess the quality of an already published study which uses this methodology.

Methods: The design of the guideline and checklists has been done in two phases. A development phase, where we set recommendations based on the review of the literature, and a validation phase, where we validated our recommendations against other published studies that have estimated attributable mortality using a prevalence-based method.

Results: We have developed and tested a guideline that includes the information required to perform a prevalence-based attributable mortality study to a given risk factor; a checklist of aspects that should be present when a report or a paper on attributable mortality is written or interpreted and a checklist of quality control criteria for reports or papers estimating attributable mortality.

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Conclusion: To our knowledge, the STREAMS-P is the first set of criteria specifically created to assess the quality of such studies and it could be valuable for authors and readers interested in performing attributable mortality studies or interpreting their reliability.

Keywords: Checklist; Study guide; Risk factor; Mortality; Attributable mortality

1. Introduction

The attribution of mortality to a specific risk factor is a powerful epidemiological tool. Estimations obtained can help health authorities, health professionals, and the general population to understand the relevance, in terms of health impacts, of a given risk factor and establish measures to reduce its population burden. This attribution has been used extensively and if periodically applied it can also be helpful to determine trends on the impact of different risk factors of a certain disease. A good example is the Global Burden of Disease [1]. On other occasions, this attribution has been used to evaluate legislation [2,3].

Nevertheless, there are various methodologies available to perform such estimations and each requires the acceptance of different assumptions and/or the availability of specific data [4]. To date, no preferred method has been established, and the selection of a particular procedure is mainly dependent on data availability and, very likely, individual author preferences.

In general, methodologies used to estimate attributable mortality to a particular risk factor are dependent or independent of prevalence. Although the prevalence-independent methodology has been used in the specific case of mortality attributed to tobacco consumption [5], the prevalence-based method is most widely used for risk factors in general [6]. Despite specific differences in the procedure related to the risk factor under study, similar information requirements need to be fulfilled when a prevalence-based methodology is applied, mainly: (a) the prevalence of the risk factor in the studied population, (b) the magnitude of the association between the risk factor and the disease of interest (risk) and, (c) the observed mortality (counting of deaths) by causes of death causally associated to the risk factor under study. The combination of prevalence and risk is derived in the population attributable fraction, which after being applied to the observed mortality creates the attributable mortality to the exposure of interest. The reliability of these inputs (prevalence, risk, and observed mortality) is key to obtaining a robust output (attributable mortality estimation), and this reliability should be assessed when reading or performing an attributable mortality study.

However, to our knowledge, there are no methodological criteria, guidelines, or recommendations which assess the quality of attributable mortality studies using a prevalence-based method or serve as support when performing a study.

The main objective of this study is to develop guidelines and checklists to STrengthen the design and REporting of Attributable Mortality Studies using a Prevalence-based method (STREAMS-P tool) by: (1) assessing the quality of published papers on attributable mortality and (2) deciding to perform the attributable mortality study through the analysis of available data. It is not our aim to compare the advantages or disadvantages of the methods available, nor give preference to one over the other.

2. Methods

The design of the guideline and checklists was done in two phases.

2.1. Development phase

To establish the theoretical framework and set recommendations, we performed a scoping review in PubMed (Medline) till January 2021 focusing on the methodological literature on prevalence-based attributable mortality. To retrieve information, we used a predefined search strategy employing a combination of MeSH terms (mortality, methods) complemented with free text terms (attribut*, death*, ‘‘health consequences’’, methodol*). After an independent in-depth reading, four members of the working group discussed and proposed a preliminary list of items to establish (a) a guideline that includes the criteria required before the decision of performing an attributable mortality study, (b) a checklist to be included in reports of mortality attribution, and (c) quality control criteria for reports attributing mortality to a risk factor.

2.2. Validation phase

To validate the checklist against published studies between 2015 and 2019, we performed a bibliographic search in PubMed (Medline) to identify original research papers estimating attributable mortality. The search strategy included free text terms (attribut*, mortality, death*). Letters, simulation models, and papers published in languages other than English were excluded. Four members of the working group, two of whom were not involved in the initial elaboration of the checklist, independently reviewed the papers and thoroughly collected information to fulfill the criteria. The objective was to test the checklist applica-

What is new?

Key findings

- There are no methodological guidelines or recommendations to assess the quality of published attributable mortality studies using a prevalence-based method or to serve as support when deciding to perform such studies based on available data.

What this adds to what was known?

- We have created a set of criteria (the STREAMS-P tool) to assess the reliability of attributable mortality studies.

What is the implication and what should change now?

- The application of these checklists permits an in-depth analysis of papers estimating attributable mortality.

bility, evaluate its capacity to discriminate, and develop the final wording.

3. Results

3.1. Development phase

In the first search, 15 methodological papers were identified and analyzed [7−21]. This permitted the definition and description of key items required before performing or interpreting an attributable mortality analysis with caution (Tables 1 and 2).

We identified elements that should be present for an adequate interpretation of the results when a report or a paper on attributable mortality is written. These elements are not exclusively related to the quality of the inputs, and the scope is broader affecting the exposition of the results and their critical understanding (Table 3). Finally, the quality control checklist addressed the criteria oriented to facilitate the critical evaluation of an attributable mortality study (Table 4).

3.2. Validation phase

In the second search, 24 papers were identified and analyzed. These papers mainly focused on the tobacco or alcohol impact on mortality; the remaining comprised risk factors such as temperature, environmental tobacco smoke, obesity, pollution, or diseases such as diabetes.

We observed that no study met all established criteria and that compliance is independent of the risk factor. In the results, the reader is usually only offered attributed mortality figures. Observed mortality, attributable fractions, prevalence, or risk figures are infrequent, although their absence is not systematic.

An in-depth analysis is shown in the supplementary material.

In the data extraction for the application of the checklist, there were no doubts regarding the definition of the items.

4. Discussion

We have developed and tested a guideline and the corresponding checklist to assess the methodological requirements and the quality of reports estimating attributable mortality using prevalence-based methods. Our goal is to provide orientation for the development, publication, reading, and in-depth analysis of studies on attributable mortality. To our knowledge, this is the first set of criteria specifically created with these objectives and it could be valuable for authors and readers interested in performing attributable mortality studies or interpreting their reliability.

The STREAMS-P tool follows the layout of previous lists, such as STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) [22], so that readers familiar with them could use these checklists for attributable mortality reports easily. Of note, the STROBE checklist is intended to improve the communication of observational studies at the time of publishing and this is one of our objectives for attributable mortality studies. Nevertheless, we intend to go further with STREAMS-P and to this end we have proposed Tables 1, 2, and 4. These tables serve to assess the quality of a specific attributable mortality study and permit a rapid decision on whether a study should be performed or results should be considered with caution.

Before performing or after reading an attributable mortality analysis, it is necessary to critically reflect on the three cornerstones of the estimation: observed mortality, prevalence, and risk. In addition, it is essential to keep in mind the impact of time, in its different dimensions such as age, latency of causes of death, or duration of exposure, on the relationships between exposure and health outcomes.

4.1. Observed mortality

A clear definition of causes of mortality under study using the International Classification of Disease (ICD) rubrics is compulsory, failure to do so makes it difficult to contextualize the results [23]. The same occurs with the year of estimated mortality. Although not always the case, this must be clearly stated [24].

In some countries, the quality of observed mortality is of concern because it derives from a death registry which does not have national coverage [25], very likely resulting in under registration. Another concern is the percentage of garbage codes in death registries. This proportion can be estimated as the proportion of deaths set in a category

Table 1. Criteria required prior to the decision of performing an attributable mortality study with a prevalence-based method

Item	Information requirements	Available yes/no
Observed mortality	Mortality data with full coverage for the area under study (region, country, municipality, etc). If not, estimate the percentage of under-registration.	
Prevalence of the studied risk factor	Data source guarantees that the prevalence of the risk factor under study is representative by the characteristics used in the analysis, mainly age or gender. Prevalence is available in accordance with the categories required to describe exposure. The geographical region from which prevalence is estimated coincides with the region of interest for the calculations. The lag-time between the prevalence study and the observed mortality study is reasonable. Minimum precision of estimates is guaranteed.	
Risk	Relative risks (or hazard ratios or odds ratios) derive from relevant or well-designed studies carried out in the same population. If not, relative risks (or hazard ratios or odds ratios) derive from relevant or well-designed studies developed in other populations, where issues regarding extrapolation of results must be taken into account.	

labeled, for example, in the 10th revision of the ICD, as ''symptoms, signs, and abnormal clinical and laboratory findings not elsewhere classified''. This is an indirect indicator of the quality of the mortality data and in populations where this proportion is 10% or more it may be assumed that certification of causes of death is suboptimal [25]. Some authors corrected the under-registration by increasing the observed mortality by a ''not well-defined'' percentage, therefore increasing the uncertainty of the results [26].

Establishing and discussing the age from which attributed mortality is estimated is crucial. Setting a low age limit could lead to errors if induction times are not considered, the risk factor lacks time to cause the disease, or long patterns of exposure have not been established [11]. Although in tobacco this age limit is usually set arbitrarily at 35 years, it is important to note that individuals who begin smoking in early adolescence could have smoked for more than 15 years before turning 30 [16]. When attribution is related to alcohol consumption, age under study is usually set at 15 years and more; however, when monitoring is the goal, there is no consensus for setting an upper age limit or setting it specifically at 64 years [27]. It is crucial to differentiate estimates by age because the influence of mortality in advanced age groups outweighs the impact of risk factors in the attribution of mortality.

Last but not the least, when attributing mortality to a risk factor assessing the entire spectrum of disease for which there is evidence of causal association, a causal-linked approach must be the norm [9]. In the case of tobacco, alcohol, or obesity attributable mortality, the all-cause approach is not ruled out [7,28] and is sometimes even recommended [15]. However, including pathologies not causally linked to a risk factor, an all-causes approach overestimates the figures of smoking attributed mortality [8,29,30] or produces slight differences for alcohol related mortality [31]. The all-causes approach offers lower potential to control for confounding than the causal-linked approach, so an intermediate position has been suggested: a ''causal + suggested approach'' incorporating the causes of mortality for which evidence is suggestive but not sufficient to infer a causal relationship [19,32].

In any case, it must be borne in mind that when estimating attributable mortality, only underlying causes of death are considered, and when the causal-linked approach is applied, not assessing all contributory causes of death underestimates the burden of attributable mortality [18,32–34]. However, it is necessary to highlight that contributory causes of death data are scarcely available.

4.2. Prevalence

Prevalence data are another key factor in estimating attributable mortality. The quality of the data must be assured. For this, in-depth knowledge of the source of prevalence and the definition of the different exposure categories must be clearly stated and referenced. Related to the source of prevalence, the participation rate, representativeness, sampling, or survey technique (face-to-face, telephone, mail, online…) should be assessed to contextualize the figures. Moreover, having a standard that defines the categories of exposure would be valuable because exposure categorization varies among studies,

Table 2. Warning signs of the need for careful estimation or interpretation of an attributable mortality study with a prevalence-based method

Observed mortality	No data on observed mortality. Observed mortality is highly unreliable (i.e., only a fraction of cases registered, mortality derives from hospitals or registries not covering the total area of study, etc). The proportion of deaths in a category labeled in International Classification of Diseases (ICD) codes as ''symptoms, signs, and abnormal clinical and laboratory findings not elsewhere classified'', also known as garbage codes, is set over 10%.
Prevalence	No data on prevalence of the risk factor in the study area. Prevalence and observed mortality vary in the year to which they refer, when prevalence has changed over time and no justification is set. Prevalence extremely unreliable (i.e., convenience sampling, low participation rates, or low sampling fraction).
Risk	The available risks derive from studies performed in populations with different background than the population of interest (i.e., race, gender-specific, socioeconomic status) without adjustment for confounders. The available risks derive from studies with a low sample size and therefore the available estimations lack statistical precision (as shown by large confidence intervals).

making it difficult to compare estimations. Another aspect to keep in mind is that when a nonaccepted behavior is ascertained, social desirability bias can lead to an underestimation of the prevalence figures [35]. In the specific case of alcohol consumption, to mitigate the underestimation, various authors have suggested using a corrective factor based on alcohol sales data [7,36,37]. The underestimation may also be associated with how the exposure variable is measured. In the case of obesity, if the measurements of weight and height are self-declared, the obesity prevalence is underestimated [38]. The same can happen with exposure to second-hand tobacco smoke derived from self-declaration, which is usually an underestimation compared to objective measurements [39,40]. A similar bias is possible for diabetes diagnosis, as the proportion of undiagnosed people is high [34].

Prevalence should describe the main categories related to exposure, the pattern (intensity and duration), and the characteristics to which it can be related, such as gender or age. The latter factor is generally considered. In the seminal paper by Tanuseputro et al., the importance of a clear definition of age-dependent prevalence was established along with, in the specific case of tobacco-attributable mortality, its categorization in 5-year age groups [8].

However, neither cumulative exposure nor duration nor time-varying intensity of exposure is reflected in the summary prevalence figures. In the case of alcohol, sometimes intensity is considered by including the frequency of binge drinking [41] but the influence of duration or the time-varying intensity of exposure is not. In the definition of smoking exposure categories, it is normal that former smokers and never smokers are differentiated but, for example, alcohol life-time consumption is not ascertained and prevalence estimations target the preceding 12 months, not providing a necessary full picture of the respondent's life-time exposure to alcohol [18].

As previously mentioned, exposure to a risk factor needs time to cause the disease and then mortality. This period of time, the latency period, varies for exposures and diseases. Moreover, variations related to individual characteristics, medical care, or, among other factors, the pattern of exposure (mainly intensity, duration, and the relationship between them) can make the establishment of the latency period difficult. Latency is undoubtedly one of the most important temporal factors in epidemiology and accounting for it is essential for the valid estimation of attributable mortality. This aspect is of utmost importance for long latency periods between exposure and disease, acquiring even greater relevance if prevalence is rapidly changing in the population [8]. Therefore, the best approach for estimating attributable mortality to a risk factor should take into account, in the exposure definition, the disease-specific latency time. Nevertheless, it is difficult to summarize latency histories adequately and there are no scientific criteria to define a disease-specific latency time.

When estimating attributed mortality some authors use prevalence data before observed mortality in an effort to respect the latency period but, rather than arbitrarily establishing [42,43] or computing latencies [44], prevalence and observed mortality are generally concurrent in time, undermining one of the Bradford Hill criteria of causality; exposure must precede result. By doing this it is assumed that actual prevalence is a proxy for the cumulative effect of exposure, but the impact of this aspect is clear: if prevalence diminishes in the population, attributable mortality is underestimated and vice versa. This effect can have an even greater impact on the case of huge decreases in

Table 3. Checklist of items to include in reports of attributable mortality to a risk factor with a prevalence-based method

Section	Item should be present	Page
Title and abstract	Risk(s) factor(s) under study Country or area under study Age range under study Information about the methodology	
Introduction/Objectives	Risk(s) factor(s) under study Key aspects of the population, location, and year of study	
Methodology	Main characteristics of applied method	
Observed mortality	Cause(s) and the International Classification of Diseases (ICD) Code Causal, causal/suggested, all-causes approach Underlying/contributory causes of death Age range studied Year/s of mortality data Data sources (whether registry-based or not) Proportion of deaths in the category known as ''garbage codes''	
Prevalence	Data source (representativeness, response rate, and year of study) Definition of the categories of exposure Self-reported vs. objective measures Describes choice of groupings by category of exposure Age-dependent categories of exposure Considers intensity of exposure Considers duration of exposure Uses a correction factor (if necessary)	
Risks	Data source, including sample size, place, and date of study Age-group specific risks (if necessary) The impact of the adjustment for potential confounders	
Results	Observed mortality figures Attributed mortality figures taking into consideration selected groupings Population attributable fractions in selected groupings Prevalence and their precision (e.g., confidence intervals [CI] 95%) as handled in the analyses Risk values and their precision (e.g., CI 95%) as handled in the analyses Attributed mortality precision (e.g., CI 95%) Sensitivity analysis	
Discussion	Statement on prevalence employed and its validity Prevalence correction (if applied) Statement on the risks employed and its validity Statement on the observed mortality employed and its validity Statement on the strength of evidence regarding the exposure-risk association	

prevalence in short periods. A sensitivity analysis shows very slight changes in attributable mortality for alcohol with a 20-year lag [7] and for tobacco marginal differences appear in males but not in females [45].

Prevalence data should cover the region under study and using prevalence of a specific region for a whole country [23] or a whole country for a specific region must be avoided.

4.3. Risk

Knowledge of the excess risk of dying related to the exposure of interest is mandatory. It is unusual to have risk data derived from studies developed in the population of interest. Therefore, the possibility of extrapolating risks from other regions or using estimations derived from well-conducted and valid meta-analyses is often necessary. In-depth knowledge of the factors under study and the source of risks should inform the final decision.

Related to factors under study, it should be taken into consideration that if a risk is age-dependent, age-group specific risks must be considered. Although nonage-specific risks are applied, attributable deaths are prone to some degree of underestimation or overestimation. Also, when generating attributable fractions, these age-group-specific risks should be matched with the same age-group-specific prevalence [8,13]. When combining risk and prevalence, awareness of how the exposure was defined when the risks were calculated should be kept

Table 4. Quality control criteria for reports attributing mortality to a risk factor applying a prevalence-based method

Section	Item	Page
Observed mortality	Causes included are causally related with the risk factor under study All-cause mortality (when recommended) Mortality ages under study respect the exposure induction time Mortality data are registry-based Proportion of deaths in the category known as ''garbage codes'' is less than 10% in the studied year/s	
Prevalence	Prevalence is representative of the population under study Prevalence reflects the different categories of exposure Prevalence respects age-dependent categories of exposure Prevalence derives from objective measures Prevalence respects disease-specific latency time Prevalence estimations are precise (e.g., narrow 95% confidence intervals)	
Risk	Risk data derived from studies developed in the study region Risk derived from other regions with a similar epidemiological situation in the risk factor under study Risk derived from strongly established meta-analyses Apply age-group specific risks (if necessary) Age-groups in risk and prevalence are matched Model synergy of effect modification (if present)	
Results	Report attributed mortality figures in selected groupings Report population attributable fractions in selected groupings Report observed mortality figures in selected groupings Report prevalence figures in selected groupings Attributable and preventable deaths are differentiated (if necessary) Report additional items (potential years of life lost…) Report third-party effects (if necessary) Perform a sensitivity analysis	
Discussion	Include a statement on prevalence employed Include a statement on the risks employed Include a statement on the observed mortality employed Report the history of the risk factor on the population under study Report a statement on the strength of evidence regarding the exposure-risk association	

in mind. Both definitions should match or be as similar as possible [8].

When risks are drawn from prospective cohort studies with exposure and end points ascertained more than once, the longer length of follow-up for risk estimation should be used. This maximizes the number of end points and helps to minimize misclassification of exposure [8].

When in a cohort study the exposure is dynamic or graded, and consequentially, subjects may transition from one category to another, assessing changes between categories in detail during the follow-up period is necessary [46]. When these transitions are not ascertained, the risks could be underestimated or overestimated.

When the patterns of exposure to a risk factor are dramatically different between countries, country-specific risks are preferred. Nonetheless, some risks are fairly similar among different countries [47]. Although the application of noncountry-specific risks raises doubts regardless the risk factor under study, this is most dramatic when estimating mortality to tobacco consumption. In this case, risks are mainly derived from the American Cancer Society's Cancer Prevention Study II (CPS-II). Every study applying relative risks derived from CPS-II state as a limitation of the nonrepresentativeness of the subjects in the cohort (volunteers), the relevance of using risks without adjustments for potential confounders, and the overestimation derived from applying CPS-II risks outside the United States. Applying risks not derived from a representative sample is not a limitation itself [48], but adjusting for confounders is crucial because confounding should never be ignored. When adjusting CPS-II risk, aside from age and gender, the variation in risks is minimal [17,21] and in attributable mortality figures is negligible [17]. Applying these risks to populations with different evolution in the tobacco epidemic is usual and, exceptionally, risks have been corrected for the differences in the stage of the epidemic [49]. However, ignoring this nuance is the norm, either because ''better risks'' in terms of internal validity are not available or are derived from similar sources [20] or population [30]. However, slight changes in risk values do not always affect attributable mortality figures in the same way. Estimates of deaths related to obesity are sensitive to the precision of risk, especially in the elderly [13,50], and to the correction for bias such as regression-dilution or reverse causation [51].

Also, it is important that a risk should be estimated by modeling, if present, effect modification (synergistic interaction) between exposures. For example, alcohol-attributed mortality is estimated without considering the strong synergy with smoking for some cancers and vice versa. On the contrary, the most frequently applied risks to estimate mortality attributed to radon in Europe are smoking-adjusted [52] and in addition, because most radon-induced lung cancer arises from the synergetic effect of radon and smoking, the attributed mortality is generally estimated as per the categories of tobacco consumption.

When the risk factor under study confers a degree of protection against some conditions, to decrease uncertainty around the estimations, attributable and preventable deaths must be differentiated and not simply balance the two effects [10,41]. ''Third-party'' effects for some risk factors, such as alcohol or tobacco, represent an important contribution to mortality and must be, at least, cataloged if not quantified [10].

When discussing the results, a critical approach is necessary and pointing out limitations surrounding estimations is valuable. A sensitivity analysis is highly recommended [12].

The STREAMS-P tool has a series of limitations and strengths. Among the limitations is the difficulty of integrating the variety of circumstances that could occur when attributing mortality to risk factors. Nevertheless, we think that our work appropriately reflects the major concerns of observed mortality, prevalence, and risk and tries to unmask some of the most important assumptions underlying the estimation process. This tool does not cover prevalence-independent methodologies, which will surely be covered in future work. Notwithstanding these limitations, the main strength of these checklists is that they facilitate an easy assessment of attributable mortality studies using a prevalence-based methodology. Also, they are similar to other available tools already adopted by scientific journals, such as the STROBE statement and checklist [22], so most readers should be familiar with their application. Moreover, these checklists establish a procedure for the communication of results and can be of help for a quick assessment on the quality of attributable mortality studies.

The availability of attributable mortality data is an essential epidemiological tool for policymakers, epidemiologists, clinicians, and the general population. The headline that a given risk factor has a specific impact on mortality is a clear and powerful message for the public. Therefore, because we require this type of information, we also need to go beyond and be reliable. A poor application of the methodology could lead to diminishing trust in the tool itself and within the scientific community but also for the public. Estimates of attributed mortality are sometimes controversial [53]; however, in the field of epidemiology, the controversy generates a scholarly debate which encourages advancement in knowledge. Nevertheless, caution is needed so that this debate does not lead to public misunderstanding or, even more serious, provide support for corporate interest in debunking the evidence of strong links between exposure to different risk factors and life-threatening diseases. Differences observed between studies attributing mortality to a risk factor can be due to real or methodological aspects. Pointing out and, when necessary, mitigating the latter is our goal.

We expect the application of the STREAMS-P tool will improve the quality of attributable mortality studies, homogenize the results published, and facilitate editors', reviewers', and readers' work.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2022.03.016.

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