A practical approach to evidence-based dentistry: IV

How to use an article about harm

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ABSTRACT

Background and Overview. Questions regarding harm are common in dental practice. Observational, nonrandomized studies (that is, cohort studies and case-control studies) are the designs used by investigators to answer most of these questions. A critical appraisal of these studies should include an assessment of the risk of bias, the results, and the applicability of the study. The authors provide the concepts and guidelines that dentists can apply to most effectively use articles regarding harm to guide their clinical practice.

Practical Implications. Dentists who wish to inform their clinical decisions regarding questions of harm can use these guidelines to decide what type of studies to search, define the specific question of interest to search efficiently for these studies, and critically appraise an article about harm.

Key Words. Evidence based-dentistry; harm; observational studies; critical appraisal.

JADA 2015:146(2):94-101

http://dx.doi.org/10.1016/j.adaj.2014.12.002

FOURTH IN A SERIES

In the 3 previous articles of this series, we introduced the process of evidence-based dentistry (EBD),[1] how to search for evidence to inform clinical practice,[2] and how to use an article about therapy.[3] In this article, we will explain how to use an article to inform clinical decisions regarding questions of harm. We will introduce and describe the basic concepts needed to understand observational studies, and we will explain how to use these concepts to critically appraise such studies. In subsequent articles in this series, we will describe how to use other types of study designs.

Supplemental material is available online.

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BOX 1

Clinical scenario.

You met with a new patient who was referred to you by his family doctor. The patient explained to you that he had been having many physical problems, such as muscular pain in his shoulders, back, arms, and legs, and that his physician told him that one of the causes might be his oral health status. While examining the patient, you noticed that he has lost many teeth. The patient asks you if this tooth loss might be related to his general health problems. You are not sure, so you decide to search for evidence from a clinical study to answer this question.

CLINICAL QUESTIONS OF HARM

Questions regarding potentially harmful exposures, either to dental treatments or external agents, are common in dental practice. Some examples of these questions are the following: Do people who live in areas where the water is fluoridated have a higher risk of having enamel defects? Does smoking increase the risk of having oral cancer? Does the dentist's use of rubber dams when placing a dental restoration increase the patient's risk of allergic reactions if the patient has a latex allergy?

The classic Population-Intervention-Comparison-Outcome (PICO) framework requires only minor modifications to address questions related to harm. The population is the patients of interest. In cases that address questions related to harm, the population is those patients who may face the potentially harmful agent. The intervention becomes the exposure, which corresponds to the harmful agent. The comparison is the reference, which is the absence of the exposure to the harmful agent. The outcome is the potential negative consequence of the exposure. Table 1 shows examples of questions related to harm and the corresponding PICO components.

WHAT STUDY DESIGN BEST ADDRESSES QUESTIONS OF HARM?

Owing to the hierarchy of evidence used to answer questions about harm, even though investigators might identify randomized controlled trials as being the best type of study design to answer these types of questions, they generally cannot use this type of study design because of ethical reasons. Therefore, at the level of a primary study, an observational study is usually the most appropriate study design to answer questions regarding harm. This is not always true, however. Note, for example, that investigators could address the question listed in Table 1 about rubber dams by using a randomized controlled trial design.

An observational study is one in which the investigator does not assign an exposure or intervention; rather, these exposures or interventions occur naturally in the study setting. Although investigators have conducted descriptive observational studies in which they recruit only one group of patients and do not compare them with any other group of patients, in this article we describe the type of observational studies in which investigators use a comparison group (which can happen because either 2 groups of patients are recruited and followed, or 1 large group of patients is divided into 2 or more, on the basis of the presence of an exposure).

Observational studies can be classified according to the direction in which the exposure or outcomes are measured.[4] The intuitive design is one in which investigators enroll participants who either are exposed or are not exposed (for example, patients living in a community that has fluoride in the water or patients living in a community that does not have fluoridated water) and follow them over a period, recording whether the outcome of interest (that is, fluorosis) does or does not occur. We call these cohort studies (Figure, Table 2[5-7]).[8]

A less intuitive design is one that involves investigators recruiting samples of study participants in whom the outcome has occurred (for example, they have had fluorosis [we call these participants "cases"]) and comparing them with similar study participants who have not had the outcome of interest (that is, no fluorosis [we call these participants "controls"]). Investigators then determine—by asking questions to participants or by looking at medical records or other information sources—whether participants in either group experienced the exposure of interest (that is, water fluoridation). We call these case-control studies (Figure, Table 2[5-7]).[9]

Investigators can use another type of design only when they can assess the exposure and the outcome at the same time. Here, the investigator looks simultaneously at the exposure (for example, the current exposure to fluoridated water) and the outcome (for example, fluorosis). We call such designs cross-sectional studies.[4]

In general, cohort studies are less susceptible to bias than are case-control studies, and case-control studies are less susceptible to bias than cross-sectional studies. Thus, if available, we would choose cohort studies as our source of evidence.

Why then would investigators bother conducting case-control studies? The reason is that if an outcome is rare or if the outcome occurs over a long period, conducting a cohort study may be challenging or not feasible at all and choosing the case-control design might be a better option.

Consider the question of whether smoking increases the risk of oral cancer. Because oral cancer is (fortunately) rare and because it develops over a long period,

ABBREVIATION KEY. **DMFT:** Decayed, missing, filled teeth. **EBD:** Evidence-based dentistry. **PICO:** Population, Intervention, Comparison, Outcome. **SSB:** Sugar-sweetened beverages.

TABLE 1

Examples of questions related to harm and the corresponding PICO* framework.

CLINICAL QUESTION	POPULATION	EXPOSURE	COMPARISON	OUTCOME
Do people who live in areas where the water is fluoridated have a higher risk of having enamel defects?	Children and adults	Fluoride in water	No fluoride in water	Dental fluorosis
Does the dentist's use of rubber dams when placing a dental restoration increase the patient's risk of having an allergic reaction if the patient has a latex allergy?	Patients with allergy to latex	Rubber dams	No rubber dams	Allergic reactions

* PICO: Population, intervention, comparison, outcomes.

addressing the smoking issue would involve enrolling thousands of patients and following them for many years. Indeed, the initial studies demonstrating the association between smoking and cancer used a case-control design. Only later did investigators undertake the large cohort studies that definitively reported the association.

Sometimes, it might be completely infeasible to conduct cohort studies. Consider the question of whether pacifier use as an infant is associated with having temporomandibular disorders in adulthood. Following people from infancy to adulthood is likely to be impossible, and thus the only way to address the issue is by using a case-control design. Thus, these study designs may provide the best available evidence.

BOX 2

The study you found.

During your search, you did not identify any summary or systematic review; however, you did find an observational study with results that seem to answer your question.[10] The study investigators addressed whether there was an association between functional tooth number and physical complaints (using a cross-sectional design) and whether the functional tooth number was associated with mortality (using a prospective cohort design). The researchers recruited 5,584 people, measured the study participants' number of functional teeth and physical complaints at baseline (the cross-sectional design), and followed their cases for 15 years (the cohort design). The authors reported that "physical complaints were significantly associated with functional tooth number." You wonder about the trustworthiness of the results and the applicability of the results to your patient, and you proceed to find a more detailed appraisal.

CRITICALLY APPRAISING OBSERVATIONAL STUDIES TO INFORM CLINICAL DECISIONS

The process of using an article from the dental literature consists of three steps: assessing the risk of bias (that is, determining whether the results are systematically different from the truth), assessing the results (that is, determining the magnitude and precision of the estimates of the association between exposure and outcome), and assessing the applicability of the results (that is, determining the degree to which the results of the study can be applied to the patients who generated the clinical question).[11] We describe each of these steps in the sections that follow.

1. How serious is the risk of bias? The extent to which a study's results are likely to be correct for the sample of patients enrolled depends on how well the study was designed and conducted.[12,13]

1a. Are exposed and unexposed study participants sufficiently similar? Bias—systematic difference from the truth—will occur if exposed and unexposed study participants differ with respect to an important determinant of outcome (which we call a prognostic factor).[14] For example, if we ask whether patients with dental crowding (exposed group) are more likely to have caries than patients without dental crowding (unexposed group), misleading results caused by bias could occur if patients with dental crowding brush their teeth less frequently (the extraneous prognostic factor).

Or consider the question of whether drinking milk at night (the exposure) causes dental caries (the outcome) in children. Parents who are less aware of appropriate oral health care practices for babies may be more likely to give their babies milk at night, and they might be less likely to brush their children's teeth (the extraneous prognostic factor). As a result, the imbalance in the extraneous prognostic factor (toothbrushing) may create a spurious association between milk at night and caries. We sometimes refer to prognostic imbalance (that is, the extraneous prognostic factor being distributed differently in exposed and unexposed) as selection bias or a confounding factor.

In both cohort and case-control studies, prognostic imbalance is likely to occur. What can investigators do when faced with these situations? Fortunately, there are statistical strategies to deal with the problem that involve comparing like with like. For instance, in the example previously described, investigators could focus first on children whose parents brushed their teeth and, among these children, compare those who did and who did not receive milk at night. Then, the investigators could focus on the children whose parents did not brush their teeth and, among those children, compare those who did and who did not receive milk at night. Finally, the investigators could combine the results across these two comparisons. In this way, they could avoid

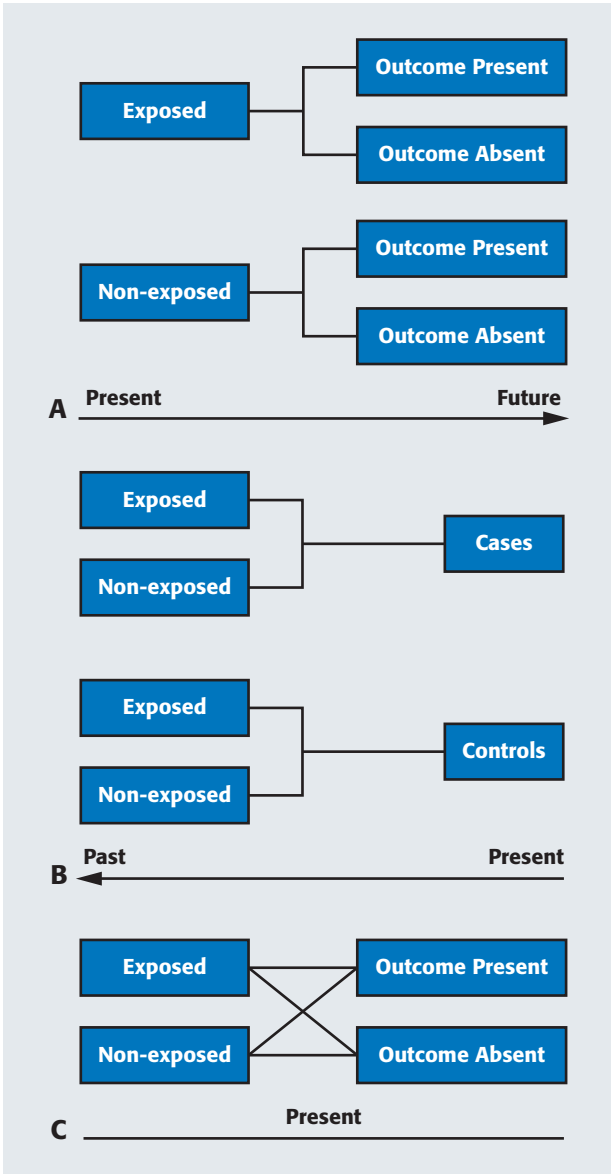

Figure. The designs of analytical observational studies. **A**. Cohort study: investigators recruit participants on the basis of the patients' exposure, and they followed up with patients over time to determine the presence of outcomes in the future. **B**. Case-control studies: investigators recruit participants on the basis of the presence or absence of an outcome, and investigators assess participants' histories to determine the presence of exposures in the past. **C**. Cross-sectional studies: investigators measure the presence of the exposure and the outcome at the same time point.

TABLE 2

Examples of analytical observational studies.

DESIGN	EXAMPLE
Cohort Study	Levin and colleagues[5] aimed to evaluate the effect of periodontal status (exposure) on implant failure (outcome). They recruited a group of patients who were undergoing implant placement surgery (population) and assessed their periodontal status (prognostic factor). Then, they followed up with these patients for an average of 12 years to determine how many of them had suffered implant failure, and the investigators compared the proportions among periodontal status categories.
Case-control Study	The objective of the study conducted by Claus and colleagues[6] was to assess whether there was an association between having had dental radiographs (exposure) and having intracranial meningioma (outcome). To assess this association, the investigators recruited patients with diagnosed intracranial meningioma (cases) and healthy patients (controls). Then, they interviewed the patients to determine their level of exposure to dental radiographs in the past and compared these levels between groups.
Cross-sectional Study	Okada and colleagues[7] aimed to assess the relationship between periodontal disease (exposure) and issues with food acceptability (outcome) in older adults (population). The investigators recruited older adults and measured, at the same time, their periodontal status and their difficulty chewing different foods. Then, they compared these difficulty levels among patients in groups with differing periodontal status.

inadvertently causing the bias that could otherwise result from prognostic imbalance. We call this analytical strategy an adjusted or stratified analysis.[15]

1b. Is information collected in the same way in exposed and unexposed study participants? Biased results will arise when investigators gather data in different ways regarding the presence of an exposure, a prognostic factor, or an outcome in the exposed and unexposed study participants, or the cases and the controls.[16] For example, in a case-control study, researchers may search more thoroughly for the presence of a past exposure if they know that the patient belongs to the group of cases rather than the group of controls. Even if the method of information collection is similar, bias will intrude if patients who are cases are more likely to remember a past exposure than patients who are controls.

Asking the following 3 questions can help clinicians assess the extent of the risk of bias in an article about harm: Were patients similar for prognostic factors known to be associated with the outcome, or did investigators conduct an adjusted analysis that considered all such factors? Were the circumstances and methods for detecting the exposure, prognostic factors, or outcome similar in both groups? In a cohort study, was the follow-up sufficiently complete? Table 3[6,17-20] lists these questions, provides some strategies to reduce bias to consider when answering them, and offers examples from the dental literature.

TABLE 3

Critically appraising the risk of bias of an article about harm.

QUESTION	STRATEGIES TO ADDRESS THE BIAS	EXAMPLES
Were patients similar for prognostic factors known to be associated with the outcome? (Selection Bias and Confounding)	Define explicit and appropriate selection criteria for entry to study, considering these prognostic factors Conduct matching according to prognostic factors Measure the prognostic factors and potential confounders to account for them in the analysis	"These randomly selected 41,346 comparison subjects were matched with the study subjects on sex, age group … , urbanization level … ."[17] "Controls were selected by random-digit-dialing by an outside consulting firm (Krieder Research) and were matched to cases by five-year age interval, sex, and state of residence …. To assess the odds of meningioma associated with risk factors, conditional logistic regression was used to provide … estimates of the odds ratios (OR) (adjusted for age, sex, race …, education …, and history of head CT)."[6]
Were the circumstances and methods for detecting the exposure or outcome similar in both groups? (Information Bias)	Use outcomes that are objective or have explicit definitions Verify self-reported information using external data Standardize interviews Mask outcome assessors to exposure status, or exposure assessors to outcome status	"All radiographs were taken with the same model x-ray machine with a long-cone, paralleling technique and standard settings of 70 kVp and 15 mA … . Preoperative, obturation, and follow-up radiographs were taken with a collimator to ensure standardized evaluation of the periradicular region … all radiographs were viewed by 2 endodontists under standardized conditions."[18] "Clinical oral examinations were conducted identically at baseline and follow-up and independent (blinded) of participants' completion of questionnaires… . A tooth was recorded as decayed if there was evidence of a carious lesion clearly extending into dentine on any coronal or root surface. The carious lesion had to be cavitated, to have penetrated the fissure and undermined the enamel, or the dentine walls to be clearly softened."[19]
In a cohort-study, was the follow-up sufficiently complete? (Selection Bias)	Ensure complete follow-up in exposed and nonexposed group Record reasons for losses to follow-up and do sensitivity analyses	"For each model, missing variables and missing or incomplete breastfeeding histories were multiply imputed … . Losses to follow-up were relatively high but not unusual among cohort studies in low-resource settings, where participants frequently change address and contact information."[20]

BOX 3

Your assessment of the risk of bias of the observational study you identified.

With respect to balance of prognostic factors, you find that there is not much information in the article. You can think of the main factors that may cause prognostic imbalance, which according to your experience and knowledge are the age of the patient, the presence of comorbidities, and the use of removable prosthesis. When you look more closely, you realize that the authors considered these factors when assessing the relationship between functional tooth number and physical complaints and mortality. With respect to exposure and outcome measurement, it seems like the same methods were used in all patients. With respect to the follow-up, the numbers reported in the article do not add up and make you doubt whether the authors were careful enough. Although your judgment leads you to believe that the prognostic balance may be in question and that the issues with follow-up are likely to bias the results, you decide to keep reading this study with caution (see the eTable,[10] available online at the end of this article).

2. What are the results? After assessing the magnitude of the risk of bias, clinicians must consider the results—in particular, the magnitude and the precision of the estimates of association between exposure and outcome—and the implications for their patient care.[21] Table 4[6,19] provides examples of the critical appraisal of the results of an article about harm.

2a. How strong is the association between exposure and outcome? As in randomized controlled trials, the authors of an observational study can present their results as mean differences when the outcome of interest is continuous (for example, probing depth) and as absolute and relative measures of effect when the outcome is dichotomous (for example, the absence or presence of some feature, such as having or not having a periapical abscess). When mean differences (that is, the differences in the mean of the outcome between the exposed and

TABLE 4

Critically appraising the results of an article about harm.

EXAMPLE	HOW STRONG IS THE ASSOCIATION BETWEEN EXPOSURE AND OUTCOME?	HOW PRECISE IS THE ESTIMATE OF THE RISK?
"[A]dults drinking 1-2 … SSB* daily had … a rate 1.31 (95% CI† 1.02-1.67) … times greater for the 4-year net DMFT‡ increments than those drinking no SSB at baseline."[19]	The relative risk is 1.31, which means that adults who drink SSB are 1.31 times more likely to have DMFT than adults who do not drink SSB. It seems like there is moderate increase in the risk of increasing the DMFT number over a 4-year period. Therefore, the magnitude of the effect is moderate.	The 95% CI of the relative risk is 1.02 to 1.67. The lower limit reflects almost no increase in the risk of increasing the number of DMFT, whereas the upper limit suggests a moderate to high risk, and we cannot be completely confident about the harmful effect of SSB. Thus, the estimate of the harm is not precise.
"Significant increases in the risk of meningioma was associated with a young age at receipt of screening as well as more frequent screening, and individuals who were aged < 10 years at the time of screening had an almost 5-fold increase in risk (OR,§ 4.9; 95% CI, 1.8-13.2)."[6]	The OR measuring the association between screening with dental radiographs at a young age (exposure) and meningioma (outcome) is 4.9. That is, when patients receive radiographs at a young age, they are 4.9 times more likely to develop meningioma than when they do not. This represents a large increase in the magnitude of effect.¶	The CI of the OR is 1.8 to 13.2. This seems to be a wide range, both 1.8 and 13.2 in which an OR of 1.8 represents a small magnitude of effect (especially considering the low prevalence of meningioma). Thus, we can be confident that there is an association between the exposure and outcome. This estimate of the harm is not precise.¶

* SSB: Sugar-sweetened beverages.
† CI: Confidence interval.
‡ DMFT: Decayed, missing, filled teeth.
§ OR: Odds ratio.
¶ The aim of this example is to illustrate how to appraise the results by appraising their magnitude and precision. Authors should assess the risk of bias of the study first to determine whether these numbers are likely to be correct or the result of bias.

nonexposed groups) and risk differences (that is, the difference in the proportion of patients with the outcome present between the groups) are used, larger numbers represent big magnitudes of effect. The clinical significance of this magnitude depends on the specific context and outcome.[22]

The relative risk, which expresses how many times more likely is one group to have the outcome with respect to another group, is the preferred relative measure for cohort studies. For example, when comparing populations exposed to fluoride in water or not exposed to fluoride in water to determine if this exposure increases the risk of dental fluorosis, finding a relative risk of 1.5 means that people exposed to fluoride in water are 1.5 times more likely to develop dental fluorosis than people who are not exposed to fluoride in water.

Two other relative measures of effect that are particularly relevant to observational studies are the odds ratio (OR) and the hazard ratio (HR). The OR is the ratio of odds of the event or outcome comparing the exposed and control group.[23] This measure of effect can be interpreted similarly to a relative risk (for example, as how many times more likely to have the outcome is the exposed group with respect to the control group) when the frequency of the outcome is low (approximately 10% or less), whereas it should be interpreted as a shift in odds when it is not (for example, as how many times the exposed group has the odds of the control group of having the outcome).[24] Although the OR can be used as the measure of association in all study designs, it is the only measure of effect that can be used in case-control studies.

The HR is a measure of effect that investigators use when they are interested not only in whether an event occurs but also when it occurs. For example, patients with bruxism (exposed group) and healthy patients (control group) can be followed because an implant is placed to determine the time to failure of such implant (outcome). The HR is the risk of the outcome in one group compared with the risk of the outcome in the other group at any specific time during the follow-up period, weighted by the number of patients available for the survival experience.[23] In other words, by using a weighted average of the relative risk, the HR accounts for the fact that some patients (for example, those who already experienced the outcome) were part of the study up to a specific time. Considering this, the interpretation of the HR is similar to that of the relative risk as well.

When authors of a study present their results using relative measures of effect, values closer to 1 (the value at which point the risk or the odds of the event is the same in the exposed group and control group) represent small effects, whereas values further from 1 represent large effects. Once again, how large this magnitude is depends on the outcome of interest.[22]

2b. How precise was the estimate of the risk? The uncertainty in the measure of association, owing to the fact that only a sample of all the population of interest is being observed, usually is described with confidence intervals (CI). A CI is a plausible range of values within which the true value actually will lie given the data observed in a study.[25] The narrower the CI, the more certain the researchers are of the estimate of effect. Similarly to what was described for interpreting the magnitude of the treatment effect, the interpretation of the width of the CI depends on the clinical context.[25]

BOX 4

Your assessment of the results of the observational study you identified.

You find that men who have fewer teeth have 1.26 times the odds of having physical complaints (such as pain of upper extremity, tinnitus, and dizziness) than men who have more teeth, and that women who have fewer teeth have 1.18 times the odds of having physical complaints than women who have more teeth. The confidence intervals range from 1.11 to 1.43 for men and 1.06 to 1.32 for women. Your judgment indicates that these numbers represent associations of small magnitude, and that the estimate for men is more precise than that for women (see the eTable,[10] available online at the end of this article, for details and explanation). Regarding the outcome mortality, you see that there are no numerical results provided, so you cannot do a critical appraisal of the results.

3. How can I apply the results to patient care? Ultimately, it is necessary to assess to what extent the results of a study are applicable to a particular context. When evaluating the applicability of articles about harm, you should consider the following factors:

3a. Were the study patients similar to the patients in my practice? To confidently apply the results to your patients, you should ensure that the patients in your practice are similar to those recruited for the study. Clinicians should look to a description of the patients participating in an observational study to determine how similar the study participants are to their own patients. If the characteristics of the included patients are similar to the patients in their practice, clinicians can confidently apply the results. If there is any characteristic that differs, such as age, medical history, or the biology of the exposure on the outcome, clinicians should assess if this difference is reason enough to think that the effect of the intervention would be different in their practice and decide to what extent the results are applicable.[21]

For example, the association between using a hard toothbrush (exposure) and having dental cervical lesions (outcome) may not be the same in a population of patients with a high prevalence of bruxism compared with a population of patients with a low prevalence of this condition. Therefore, the clinician must be careful when applying results from a study that recruited the former patients to the latter.

3b. Was the follow-up sufficiently long? A study must follow up with patients for a period long enough that the exposure could have had an effect on the outcome.[21] For instance, when determining whether chronic rhinosinusitis increases the risk of chronic periodontitis, Keller and colleagues[17] followed up with patients for 5 years after they had been diagnosed with chronic rhinosinusitis. Clinicians applying the results from this observational study to inform their clinical decisions should assess whether 5 years is a period long enough to be a contributing factor in the development of chronic periodontitis.

3c. Is the exposure similar to what might occur in my patient? Just like patients' characteristics, the exposure may not be exactly the same in all patients. For example, in the study to determine whether periodontal disease was a risk factor for implant failure,[5] approximately two-thirds of the exposed patients had severe chronic periodontitis. Therefore, clinicians must note if the results presented were for patients with chronic periodontitis, no matter what the severity, when they consider applying the results to patients with moderate chronic periodontitis. When the exposure is an external agent, such as fluoride in water, it is important to consider the dose and duration of the exposure.

3d. Are there any benefits that offset the risks associated with the exposure? Even though risk factors generally are associated with undesirable consequences, they may also be associated with some benefits. For instance, even though having fluoride in water may increase the risk of patients experiencing dental fluorosis, it may decrease the risk of patients experiencing dental caries. It is necessary, therefore, to determine whether it is worthwhile to eliminate potentially harmful exposure. When one of the outcomes is unacceptable and there are no additional benefits from the exposure, this decision is straightforward; however, in many cases, the clinician may need to decide on the balance between the outcome and the potential benefits of the exposure.

BOX 5

Your assessment of the applicability of the observational study you identified.

When assessing the applicability of the results, you noted that the patients enrolled in this study belonged to a rural population, which makes them likely to have important differences in aspects such as oral health care and occupation, causing differences between that study population and your clinic population in both exposure and outcome. For the study population, tooth extraction may be one of the few available treatment options, and rehabilitation after the tooth extraction may take different paths when compared with the options available to patients living in an urban area (see the eTable,[10] available online at the end of this article, for details). Because your practice is in a big city, you decide that this evidence is not entirely applicable to your patient.

CONCLUSION

Observational studies are the best type of study to inform clinical decisions about harm. Critical appraisal skills allow clinicians to optimally use the results of studies to inform their clinical practice. The critical appraisal of observational studies focuses on aspects of risk of bias, the results, and applicability. ■

BOX 6

What you say to your patient.

Despite the fact that the abstract of the study suggests that the number of teeth is associated with physical complaints, the risk of bias, the moderate magnitude association reported, and the limitations in applicability make you conclude that this evidence is not enough to claim that such an association actually exists and is important enough to worry about. You discuss this with your patient and suggest that he undergo oral rehabilitation because of the other benefits it would have, but you make it clear that this may not be one of the causes of his physical complaints. Even though your patient did not ask, you let him know that there is also not enough evidence to claim that there may be an association between functional tooth number and mortality.

SUPPLEMENTAL DATA

Supplemental data related to this article can be found at http://dx.doi.org/10.1016/j.adaj.2014.12.002.

Disclosure. None of the authors reported any disclosures.

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eTABLE

Example of a critical appraisal of an article regarding harm.*

1. How serious is the risk of bias?	
Were patients similar for prognostic factors that are known to be associated with the outcome (or did statistical adjustment level the playing field)?	Probably yes. Although the tables and text were not completely clear regarding the balance of prognostic factors, the researchers adjusted for the main confounding factors (age, systemic diseases, denture use) when assessing the relationship between functional tooth number and mortality physical complaints. However, there were other prognostic factors, such as socioeconomic level and physical disabilities, for which the researchers did not account.
Were the circumstances and methods for detecting the outcome similar?	Probably yes. It can be inferred from the article that the study authors measured the outcomes (physical complaints and mortality) using the same methods, irrespective of the exposures that a given patient had; however, the authors did not describe this.
Was the follow-up sufficiently complete?	For the outcome mortality, the authors reported having more patients at follow-up (5,684) than at baseline (5,584), which decreased trust in the reporting of the numbers of patients lost to follow-up. There was no information provided regarding the number of patients lost-to follow- up, if any, or the reasons for it.
2. What are the results?	
How strong was the association between exposure and outcome?	The associations between the prognostic factor "number of functional teeth" and the outcome "physical complaints" were reported separately for men (odds ratio [OR] = 1.26) and women (OR = 1.18). These values meant that men who had fewer teeth had 1.26 times the odds of having physical complaints compared with those who had more teeth, and that women who had fewer teeth had 1.18 times the odds of having physical complaints than those who had more teeth. Even though these numbers represented associations of small to moderate magnitude, it is not clear from the article whether they were calculated considering 1 tooth of difference or more than 1 tooth. Therefore, it is safer to conclude that the association magnitude of the association is small. Regarding the outcome mortality, the authors only reported that "Physical complaints were not a significant factor of survival rate of either men or women." However, no numerical data were provided, which made it impossible to appraise these results.
How precise was the estimate of the risk?	The 95% CIs† reported by sex were somewhat precise and did not include extreme values. For men, the CI of physical complaints was 1.11 to 1.43, and for women it was 1.06 to 1.32. In both groups, the upper limit of the CI may have reflected an effect that was important in clinical practice; however, in women the lower extreme of the CI represented an association of small magnitude, which made it less precise (in other words, the CI of men represented a moderate association in both extremes, whereas the CI for women represented a small to moderate association. Therefore, the CI for the association in men was more precise).
3. How can I apply the results to my patient care?	
Were the study patients similar to the patients in my practice?	Probably not. The population in the study seemed to be rural, given that their main economic activity was agriculture. This situation could lead to important differences regarding access to health care services and education if the results were applied to urban populations. On the other hand, a rural population may have had such a different lifestyle compared with urban populations (for example, sedentary or active), modifying completely the health indicators and morbidity and mortality risks.
Was follow-up sufficiently long?	Probably yes. For the outcome of mortality, 15 years seemed to be an appropriately long follow-up so that an association between the number of functional teeth could have had any influence on mortality, at least in older patients. However, depending on the main mechanism of this association considered to be plausible by the clinician, this judgment regarding the length of follow-up could change.
Is the exposure similar to what might occur in my patient?	Probably yes. Tooth loss is a reality in both rural and urban populations. However, it is very likely that rural populations are at higher risk of tooth extraction, with lack of access to restorative or conservative therapies, compared with more urbanized populations. This would cause a limitation in applicability if the population of interest were urban.
Are there any benefits that are known to be associated with exposure?	In this particular type of population (rural), tooth extraction may be the only way to manage extended caries, severe periodontitis, and other conditions. On the other hand, and on the basis of the study results, tooth loss (reduction in the number of functional teeth) would increase the risk of physical complaints, but would not increase the risk of mortality. Therefore, the benefits of the exposure would outweigh the potential harms in patients for whom dental extractions were the only available treatment.

* Source: Fukai and colleagues.[10]
† CI: Confidence interval.