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WHAT A PHARMACIST/PRACTITIONER SHOULD KNOW ABOUT EVALUATING SYSTEMATIC REVIEWS AND META-ANALYSES

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Abstract : Trials/Studies of published systematic reviews/meta-analysis have shown little consistency and often poor quality in proper reporting, introducing potential errors and biases to the overall study results. As the pharmacy profession continues its quest for provider status to provide patient care services, it is pivotal for pharmacists to efficiently evaluate and interpret the quality of systematic reviews before applying the results to patient care. This review aims to educate pharmacists, practitioners, and students on how to evaluate systematic reviews in the context of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement. An example is also provided to illustrate how to apply PRISMA in evaluating a published meta-analysis. As pharmacists become increasingly involved in medication optimization services within the patient care process, the ability to properly evaluate systematic reviews and the application of evidence-based medicine will be essential components in providing optimal patient care.

Keywords: systematic review, meta-analysis, evidence-based medicine, pharmacist, PRISMA

INTRODUCTION

As the pharmacy profession looks to gain provider status and move into greater clinical roles, pharmacists are increasingly called upon to practice evidence-based medicine. In fact, practicing evidence-based medicine has been deemed an essential skill in pharmacy education by its inclusion in the 2013 Center for the Advancement of Pharmacy Education (CAPE) outcomes (Medina *et al*., 2013) and the Accreditation Council for Pharmacy Education (ACPE) accreditation standards (ACPE, 2015). In the practice of evidence-based medicine, systematic reviews are considered the top level of evidence (OCEBM, 2011) and large numbers are published each year (Moher *et al*., 2007). However, studies of published systematic reviews have shown little consistency, and are often insufficient quality, in proper reporting (Moher *et al*., 2007; Wen *et al*., 2008). In addition, protocols for reviews are often changed before the

review is published, creating concern for the introduction of potential bias (Silagy *et al*., 2002). Thus, it is important for pharmacists to be able to judge the quality of systematic reviews before applying the results to patient care.

Review articles fall under two main categories--narrative and systematic. Narrative reviews or overviews provide a summary of research without describing systematic methods of identifying relevant primary literature and authors oftentimes introduce expert opinions and find studies to support their conclusions, which may lead to publication and selection biases. On the other hand, systematic reviews attempt to gather all relevant evidence that fits pre-specified eligibility criteria in order to answer a specific research question (Bryant *et al*., 2014). Unlike narrative reviews, systematic reviews use explicit, reproducible, systematic methods to perform a thorough literature search, identify, select, evaluate, qualitatively and/or quantitatively synthesize and summarize the findings to answer a specific clinical question that helps practitioners in practice. Often systematic reviews include meta-analysis, which uses statistical techniques to combine and quantitatively summarize the results of similar but separate studies. Not all systematic reviews contain meta-analysis, and the use of meta-analysis is not restricted to systematic reviews (Shamseer *et al*., 2015). When multiple systematic reviews on the same clinical question are conducted, conclusions can be similar and this reinforces our confidence in the findings. Conclusions can also be different and this forces the reader to critically evaluate the methods of each review to justify the reason for discordances.

In order to help create consistency in reporting, the Quality of Reporting of Meta-Analyses (QUORUM) guidelines were created in 1999, followed by an update, the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA), in 2009. The PRISMA statement provides a list of 27 items that should be reported in every systematic review, whether or not meta-analysis is conducted. Items on the checklist need not be in any particular order (Liberati *et al*., 2009), as formatting will usually be dictated by the publishing journal, and journals may have their own standards for what they expect in a review article. The 2015 Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines for review protocols and the 2011 Cochrane Handbook for Systematic Reviews of Interventions also provide valuable and more up-to-date guidance in evaluating proper methodology in systematic reviews (Shamseer *et al*., 2015; Higgins *et al*., 2011). Generally, systematic reviews have sections in the following order: title and authors, abstract, methods, results, discussion and conclusion, acknowledgments and funding, references, and appendices if applicable. The purpose of this review is to familiarize pharmacists with the components of systematic reviews and the importance of each component.

EVALUATION OF TITLE, ABSTRACT AND INTRODUCTION

The title should identify an article as a systematic review, meta-analysis or both. Ideally, the title will also clearly identify the topic in the PICOS format (P=patient; I=intervention; C=comparator; O=outcome; S=study design). This allows readers to clearly understand the type of article and the basic scope of the review (Shamseer *et al*., 2015; Liberati *et al*., 2009). The abstract serves to summarize the review and allows readers to understand the key information about the article without having to read the full text. An abstract may contain the following sections, depending on applicability and length limitations for review publication: background; objectives; data sources; study eligibility criteria, including participants and interventions of

note; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; funding source; and registration number (Liberati *et al*., 2009).

Next, the introduction should succinctly explain the rationale for the review and provide an explicit statement of the questions being asked and answered by the authors. The rationale should include a statement of whether the report is a new review or an update of an existing one (Liberati *et al*., 2009). A good rationale will explain why the review was conducted and will set the context of the article by summarizing how the review builds upon and adds to current knowledge (Shamseer *et al*., 2015). The questions being asked in the study, also referred to as objectives, should be clearly stated (Liberati *et al*., 2009). At a minimum, they should include the population, intervention, comparator, and outcome. Other aspects such as setting, study design and time frame may also be included in the objective, but may appear elsewhere in the article (Shamseer *et al*., 2015). Depending on the scope of the article, the questions may be broad or specific, and multiple questions may be necessary to fully describe the objectives of the study (Liberati *et al*., 2009).

EVALUATION OF METHODS

The methods section is arguably the most important section for determining the quality of a review article, since it describes exactly how the authors conducted the systematic review. Improperly reported methods can introduce concerns about bias and can make the results impossible to reproduce for independent verification. In this section, authors should indicate if a review protocol exists and where to find it; define eligibility criteria of the studies; list information sources; give a full search strategy; describe the study selection and data extraction processes; list the principle summary measures; describe how data was handled and how results were combined; provide a description of how bias was assessed within and across studies analyzed; and describe any additional analyses performed, including sensitivity analyses (Liberati *et al*., 2009). Not all published systematic reviews have an associated protocol. However, there is an increasing push for authors of reviews to publish protocols before proceeding, and some publishers, prominently the Cochrane Collaboration, require their reviews to have published protocols. Often, there are changes between protocols and the final review article, and the published protocols allow readers to assess the impact of these changes and gauge the extent of selective reporting of results. Thus, including protocols in the systematic review can provide valuable information (Shamseer *et al*., 2015; Green *et al*., 2011).

Eligibility criteria for studies included in both qualitative or quantitative analyses should be specific and define study patients, interventions, controls, outcomes, study design, and length of follow up. This allows readers to evaluate the external validity of the review to their practice. Year of publication, language, and publication status used in searching for studies should also be listed (Liberati *et al*., 2009). Inclusion of certain studies, for example, studies not published in English, may affect the quality of studies included in the review and possibly influence the results (Jüni *et al*., 2002). All sources searched for potentially eligible studies should be reported, including any database platform used and a time frame when the search was performed (Liberati *et al*., 2009). Databases used for information may include Medline; CENTRAL; EMBASE; regional databases, such as WPRIM for the western Pacific and PASCAL for Europe; and subject specific databases, such as AMED, CINAHL, and PsycInfo. As databases do not always overlap, multiple databases should be searched (LeFebvre *et al*., 2011). Review authors may also use supplementary approaches such as checking reference lists, searching clinical trial

registries, or hand-searching journals. Any efforts to obtain unpublished literature or obtain additional results from study authors should also be described in the methods section. In the review, a full electronic search strategy should be presented for each part of the objective for at least one database. The text of the article may contain only limited information such as search terms to comply with journal space requirements, with the full strategy presented as a supplement or appendix to the review. The full text should include any limits used and should be thorough enough allow interested readers to duplicate the search. Stating whether search strategies were peer reviewed is also encouraged (Liberati *et al*., 2009).

Next, review authors need to describe how they selected the studies included in the review from the search results. This description should detail which investigators were involved in screening studies for eligibility, the level of agreement, and how disagreements were resolved (Liberati *et al*., 2009). Agreement between investigators is usually assessed using the Kappa statistic, with the values between 0.6 and 0.75 representing good agreement and values greater than 0.75 representing excellent agreement (Higgins *et al*., 2011). Using two or more investigators to screen for relevant articles may help enhance objectivity and has been shown to reduce the possibility of rejecting relevant reports (Edwards *et al*., 2002). The description should also be accompanied by a flow diagram, which illustrates the number of results the search obtained, the number and reasons why studies were excluded at each screening step, and how many studies were included in the final analysis. The systematic search used in the review may find multiple reports of the same study, so investigators should explain how they identified such duplicates (Liberati *et al*., 2009). A thorough process would include both computer based algorithms and hand searching (Qi *et al*., 2013).

The review authors should list what data was extracted from each selected article and how the extraction was performed. Possible data items include characteristics of study participants, interventions, sample size, outcomes, results, and other variables of interest needed to evaluate the quality and results of the studies. As with study selection, enumerated data extraction procedures should include which investigators were involved in the process and how disagreements were resolved. In addition, review authors should report if any particular algorithm, form, or computer program was used to assist in data extraction and how it was piloted. Some published studies may not contain all the desired data points, so authors should explain if and how they tried to obtain missing data from study authors and how they handled any missing data in the final analysis (Liberati *et al*., 2009).

In any study, whether original research or review, there is a risk of bias. As such, authors of systematic reviews should discuss how they assessed the risk of bias within the selected studies and across the studies. If no assessment of bias was undertaken, a rationale should be provided (Liberati *et al*., 2009). An appropriate assessment of bias within studies would include analysis of such items as appropriate generation of random allocation sequence, concealment of allocation sequence, blinding, and proportion of patients lost to follow up. Other items reviewers may include in the assessment are early stopping of trials for benefit, industry sponsorship, single trial centers, and improper analyses or fabrication of primary study data (Shamseer *et al*., 2015). Use of summary scales that report quality as a single number can be misleading, and is thus discouraged. Though, some quality weighting scales include Jadad score, Detsky criteria, PEDro score are still commonly used.

Similar to study selection and data extraction, reviewers should report the exact process used in bias assessment including the involved investigators and if any blinding was performed (Liberati *et al*., 2009). The effect of blinding on the assessment of bias remains unclear, but

readers should have this information available to help form their opinions (Higgins *et al*., 2011). Review authors may choose to alter the data analysis based on the quality of selected studies, by methods such as excluding poor quality studies or weighting data based on a quality score. Because of this variety, authors should report what method they utilized in their review, thus allowing readers to better interpret the results (Liberati *et al*., 2009). Bias across studies commonly manifests as publication bias (e.g., the lower likelihood of being published for studies with negative results or small study effect, or those originating in non-English speaking countries) and outcome reporting bias. Published studies are more likely to have positive or significant results (Dwan *et al*., 2013). Such bias can be expected to yield generally more positive results in systematic reviews and meta-analyses. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests e.g., trim and fill method, fail-safe N method) and/or more conclusive statistical regression tests. Common statistical tests include those by Begg, Egger, Tang, Macaskill, Deeks, Harbord, Peters, Schwarzer, and Rücker have been proposed to appraise the likelihood of such small study bias (Dwan *et al.*, 2013).

The methods section should also include a description of how individual study data was synthesized, including how heterogeneity was measured, any statistical methods used to combine data, and the summary measures to be reported to asses for heterogeneity, a combination of visual inspection (e.g., forest plot, L'Abbe diagram) and statistical tests for heterogeneity (Liberati *et al.*, 2009). Statistical heterogeneity tests serve to measure differences in study populations and designs and determine which methods are appropriate for combining study data. The most common tests for heterogeneity are the chi-square (χ^2), also known as Cochran's Q, and I^2 tests. Synthesis of results using meta-analysis can be performed using fixed effects or random effects models (Deeks *et al*., 2011). Random effects models take into account of variation between studies, can control the effects of heterogeneity statistically, should be used for heterogeneous data, and generally offer broader estimates of treatment effects. Fixed effects models assume no difference between study populations and often provide inappropriately narrow estimates of effect (Schmidt *et al*., 2009). Thus, fixed effects models should only be used if heterogeneity measures are low or when the data are homogeneous. Generally, if heterogeneity is minimal, both models provide similar estimates of effect. Reviews including studies with significant variation in study design should not be combined statistically with meta-analysis, instead reporting and combining the studies qualitatively. Nevertheless, some authors still statistically pool the results, if heterogeneity exists by using a random effect model. Different outcome measures are used in meta-analysis depending on the type of data to be combined. Binary outcomes are usually reported as an overall risk ratio, odds ratio, or risk difference; continuous outcomes are often reported as the difference in means of the outcome variable, weighted mean difference, and/or standardized mean difference; and time-to-event outcomes are commonly reported as hazard ratios (Liberati *et al*., 2009). Studies included in the review may not use different outcome scales, so review authors may need to adjust scales so they are aligned for statistical analysis and should describe these adjustments in the review (Shamseer *et al*., 2015).

Lastly, the methods section should include a discussion of all additional analyses the reviewers conducted, and indicating which were pre-specified. Additional analyses should prove the robustness of the findings to any assumptions made during the study process, and may include sensitivity analysis, subgroup analysis, and meta-regression. Examples of sensitivity analyses include combining the data of only studies of a certain quality, adding in the data of

studies which do not definitively fit the inclusion criteria, or eliminating any unpublished data. Subgroup analyses address the effects of specific characteristics of trials and trial participants, for instance, age, gender, or control intervention. Meta-regression, while rarely used, allows for the examination of how different variables contribute to any heterogeneity in study findings (Liberati *et al*., 2009).

EVALUATION OF RESULTS

The results section of a systematic review will present the findings of the reviewers. This section should include a summary of the study selection process, the characteristics of included studies, data on the risk of bias within and across studies, the results of each study, results of any data synthesis performed, and results for any additional analyses performed. The study selection results should include the number of studies found from the search, the number and reason why studies were excluded at each stage of selection, and how many were included in the final analysis. Often these numbers are included in the flow chart presented in the methods section. A summary of study characteristics will present the citations of each included study along with any characteristics listed in the methods section for which data was extracted. Such a summary allows the readers to judge for themselves the validity of including each study in the analysis and to conduct their own subgroup analyses. It should be noted if any information from the studies is missing or assumed. In addition to individual study characteristics, review authors should summarize overall characteristics for their readers (Liberati *et al*., 2009).

In presenting their assessment of the risk of bias within studies, review authors should report the study characteristics (subjects, methods, data analytic techniques, results, quality using quality weighting scales e.g., Jadad score, Detsky criteria, PEDro score) for each study individually. Such a summary of a listing of the studies used for meta-analysis allows readers to judge whether the studies selected are sufficiently similar in key characteristics or have quality issues to merit a quantitative synthesis or pooling. It is important to note that if there is methodological limitation to the quality of all the studies in the meta-analysis. The meta-analysis itself will have serious limitations. Meta-analysis cannot correct the flaws of the existing research studies and may tend to intensify these flaws.

The format for reporting the reviewers' analysis of study results will depend on whether the study includes meta-analysis. However, both studies with meta-analysis and those with qualitative synthesis should report both the findings of individual studies and the overall result, thus allowing readers to identify any studies with outlying results and assess how each study contributed to the final conclusion. Results should be presented for each outcome outlined in the methods section. Often in qualitative reviews, the results will be summarized in narrative form or in a table with the citations of each included study, and conclusions made primarily by the authors' opinions. Meta-analysis data is often presented in a forest plot. In this type of plot, each study citation will be listed along with the sample size for each group in the study and the result for the outcome of interest (including a confidence interval). This data is also depicted graphically, with the primary axis representing no effect and the area to each side representing results favoring one intervention or the other, onto which the study result and confidence interval are plotted. The summary result will often be represented on this plot as the last line. The forest plot serves not only to summarize data but can act as a way for readers to assess heterogeneity. If the results of each study appear to be around the same effect, they are likely homogeneous (Liberati *et al*., 2009). But if, for instance, only one-half significantly favors one intervention,

then the data is likely heterogeneous. To statistically prove homogeneity, the authors should include the result of the statistical test they used. If the Cochrane Q test is used, a p-value of <0.05 indicates significant heterogeneity. Values of the I^2 statistic will fall into four categories: 0%-40% may not be important; 30%-60% may indicate moderate heterogeneity; 50%-90% may represent significant heterogeneity; and 75%-100% represents considerable heterogeneity (Deeks *et al*., 2011).

To allow readers to assess the risk of publication bias across studies, the funnel plot and results of any statistical tests used should be reported (Liberati *et al*., 2009). In the funnel plot, results of each study are plotted against a measure of study size, such as sample size, standard error, or inverse variance. If publication bias is negligible, the plot should be symmetric and any statistical tests for asymmetry should yield insignificant results. However, publication bias is not the only contributing factor to asymmetry, and even studies with publication bias may have symmetrical funnel plots. Also, if a review involves only a few studies, the funnel plot may not present very much data (Sterne *et al*., 2011). Additional tests (e.g., trim and fill analysis, fail-safe N, Egger regression) should also be taken into consideration. Egger's, Peter's, Begg's test provide a p-value and a p-value < 0.05 indicates a higher likelihood of publication bias exists (Sterne *et al*., 2011). Thus, readers should interpret the results with caution and refer to the methods section to ensure the review authors took steps to try and minimize publication bias, such as trying to obtain data from unpublished studies.

After the primary results are presented, results of any additional analyses, such as checking for sensitivity analyses, should be reported, including statistical significance. This reporting may be presented in text or as additional forest plots, if applicable. All pre-specified analyses should be presented, whether or not they yielded significant results, in order to avoid reporting bias (Liberati *et al*., 2009). If the results of the analyses are similar to the primary findings, the results of the review are likely robust; the opposite is true if the sensitivity analyses provide dissimilar results. Subgroup analyses may suggest certain populations react differently to a given intervention compared to the population as a whole, and may be a starting point for future investigations (Schmidt *et al*., 2009). As mentioned earlier, meta-regression may elucidate which variables are the sources of heterogeneity, but caution should be used to ensure results are not over-interpreted (Liberati *et al*., 2009).

EVALUATION OF DISCUSSION AND FUNDING

The discussion section of a systematic review acts as the author's evaluation of their work, and should summarize their main findings, list any limitations, and offer their conclusion. Based on the evidence and methods presented, readers may disagree with the authors' opinions. In the summary of evidence, the authors should again present any significant findings and elaborate on the utility of the results to different potential audiences, including clinicians and public health officials. A discussion of limitations should address potential concerns related to internal and external validity. Common limitations include a limited number of studies, poor quality of studies, significant evidence of publication bias, and limits imposed by search criteria. In the conclusion, the authors should put their results into the context of other available research on the topic and offer specific suggestions for future research. The authors should also list the source of funding and what role that source had in the research itself and the decision to publish, since this can reflect a potential for bias in the review (Liberati *et al*., 2009). Non-profit funding sources or Cochrane reviews tend to be of better quality than industry-supported reviews and

tend to be less likely to unreservedly recommend the study intervention, even though the data may be similar (Jørgensen *et al*., 2006).

EXAMPLE HOW TO APPLY GUIDELINES

To illustrate how to apply these guidelines to a real systematic review, an example is provided below. The article was randomly selected by searching PubMed with the keyword "obesity" and limiting search criteria to meta-analyses published between 1/1/2014 and 1/27/2015. The selected article, "The obesity paradox in acute coronary syndrome: a meta-analysis" was published in November 2014 in the *European Journal of Epidemiology* (Niedziela *et al*., 2014)

1. Title (p. 801): The article is identified as a meta-analysis, per the guidelines. However, the article contains a substantial systematic review, so this title is inadequate. Also, while it can be argued that the title describes the patient population and intervention, other key details of PICOS are missing, making the title very vague. A more proper title would be "The effect of BMI on mortality in patients with acute coronary syndrome: a systematic review and meta-analysis."

2. Abstract (p. 801): The abstract of this article contains the background, objectives, and a summary of results and conclusions. Elements that are missing or vague are the data sources, study eligibility criteria, type of meta-analysis or systematic review, study appraisal, funding source, and protocol registration.

3. Introduction: The rationale for the review is explained (p. 801-2) and the objective is stated (p. 802). The objective could be clearer and adhere better to the PICOS format by mentioning the study types examined, and specifying which BMIs were being compared (for instance, underweight, overweight and obese vs. normal weight).

4. Methods

- **a.** No protocol registration number is provided, and nowhere do the authors mention if they worked from a protocol.
- **b.** The inclusion and exclusion criteria for studies are clearly presented in Table 1 (p. 803). However, neither the text nor table mentions any limits on language, time frame, or inclusion of unpublished literature. The supplement provided with the article clarifies that only English language studies were included and all time frames were searched.
- **c.** Data sources are clearly stated (p. 802), and multiple, valid databases were searched. However, the flow diagram presented includes a box labeled "other sources". These other sources are not specified.
- **d.** The search strategy description (p. 802) is inadequate. The in-text description with the keywords used is appropriate if it were accompanied by a more detailed strategy, which the authors claim is in the supplement but is not. Thus, the reader does not have enough information to duplicate the search. In addition, although it is not critical, the reviewers never mention whether the strategy was peer reviewed.
- **e.** The flow chart showing the study selection process (p. 804) is well done, including the presentation of numbers of studies at each step and reasons for exclusion. While the investigators who were involved in the screening is clear, how disagreements were resolved and a measure of inter-rater agreement is not provided (p. 802). The resolution of disagreements appears to be stated for data extraction, but not for screening. Also, the flow chart indicates that the reviewers screened for duplicates, but the authors do not

describe the process they used--whether they used a computer program, hand-screened, or both.

f. The data extraction process (p. 802) is very vague. The article seems to imply that the authors who screened also performed the data extraction, but this is not clearly stated. It is also unclear which data items were extracted, since the form the reviewers say they used and is provided in the supplement is not present. Furthermore, the reviewers do not state how missing data was handled, for instance, if study authors were contacted for the data.

g. In assessing the quality of the study (p. 802), the reviewers identify the scale that was used and a level of inter-rater agreement but fail to mention which authors were involved in the assessment, if they were blinded, and how quality scores affected data handling. In addition, their choice of a rating scale was inappropriate. Firstly, the use of composite scores is discouraged, and they should have listed what quality measures they looked at. Secondly, the scale they used is still being investigated for validity and is only used for non-randomized studies (Wells *et al*., 2014). Since the inclusion criteria include randomized controlled trials, a different scale may be more useful.

h. Bias across studies such as publication bias is assessed using established methods (p. 803).

i. The summary measures are listed (p. 803) and appropriate, as relative risk is a common summary measure for binary data such as mortality.

j. The description of how data was combined (p. 802-3) is, for the most part, adequate. The reviewers state how heterogeneity was measured, what kind of meta-analysis was used, how the data was weighted, and how variations in the studies' BMI classifications were accounted for in the definitions they used for meta-analysis. Given the high levels of heterogeneity they observed, use of a random-effects model was the most appropriate assessment, besides possibly qualitative analysis, but which specific model they used is unclear. The authors also fail to mention what software was used for the analysis, and completely omit the fact that they also performed a qualitative synthesis.

k. While the authors describe the sensitivity analysis they performed (p. 803), additional analyses may be appropriate to properly establish the robustness of the findings. Some other analyses that could be conducted include reanalyzing the data using different weighting scales and altering the definitions of BMI categories.

5. Results

a. The results of the study selection process are adequately summarized in the text (p.803-4) and detailed in the flow chart (p. 804).

b. The study characteristics are clearly presented in Table 2 (p.805). Most of the relevant data is presented, but some information critical to evaluating the studies' inclusion in the review is missing, namely, the type of study (randomized control trial, controlled clinical trial, cohort study, etc.) and age of the study population. The in-text summary of the characteristics (p. 803) can be more detailed, for example, listing the general locations and types of acute coronary syndrome. A critical oversight in both aspects of this summary is that the studies included in the qualitative analysis only were omitted, which made it unclear at this point in the review whether they were going to be analyzed at all.

c. The results of the quality assessment are not presented. In the methods section (p. 802), the reviewers mention quality was "high" for all included studies, but this description is inadequate. Ideally, the authors would have listed all the data items assessed and the

value of each item for each article, so the readers are able to evaluate quality for themselves. But at a minimum, the cumulative score should have been listed for each included study, possibly in the study characteristics table.

d. Results for the assessment of publication bias for each comparison are included along with how data was handled if bias was detected (p. 804). A figure of the actual funnel plot would be useful but is not necessary since the results were analyzed statistically and the results of that analysis are presented.

e. The results of each comparison are presented clearly in the text (p. 804) and forest plots (Figures 2-5, p. 806-9). The forest plots include the essential items--study citation, results in graphical and numerical format, weighting of each result, summary result, and heterogeneity scores. Presenting the weight of each study instead of the event rates is acceptable as long as this was the measure used in the meta-analysis model. The heterogeneity measures are generally high and some of the results in the forest plots appear scattered, but combining the data was appropriate since a random effects model was used. The review authors also nicely summarize the results across BMIs in Figure 6 (p. 809).

f. The results of the sensitivity analysis detailed in the methods section is not presented in the text or as a figure or table.

6. Discussion:

a. The authors provide a very detailed summary of the evidence they found (p. 804-10), which appears to be their qualitative systematic review, since it cites studies not included in the meta-analysis and presented a breakdown of findings regarding specific areas. While the fact remains that the qualitative review should have been more clearly identified as such and characteristics of the additional studies should have been presented, the discussion provides an in-depth summary of the evidence the authors found.

b. The authors also appropriately list the limitations they found in their study (p. 810). The listed limitations are a matter of opinion, and can arguably be added to, but this is the case for most articles, both original research and reviews. An example of an additional limitation, apart from inadequate reporting, would be the lack of results for sensitivity analysis, and thus any ability to claim that the results were robust.

c. The authors clearly state their opinion in the conclusion (p. 810), which is appropriate, whether or not the reader agrees with the opinion. However, the reviewers inappropriately fail to suggest ideas for future research

7. Funding: The reviewers fail to report their funding source or lack thereof, so readers are unable to assess the potential impact for bias in the review.

8. Comments: The selected article has some strengths, including clear use of tables and figures, and generally proper statistical methods. But despite reporting that they followed the PRISMA statement (p. 802), the review authors inadequately report many aspects of their analysis, making it unclear whether the methods themselves were inadequate or whether the authors just failed to report all of what was done. This makes it difficult to judge how the results can be applied to practice settings, which is the primary purpose of the reader when reading these types of articles.

CONCLUSION

In this article, important items to look for in evaluating systematic reviews and meta-analyses were summarized in the context of the PRISMA statement, the established guide for systematic review reporting. An example was provided to illustrate how these items can be used in evaluating a published meta-analysis. Systematic reviews can be very valuable resources in answering clinical questions, and such evaluation of reviews is important in properly assessing their utility in practice. As pharmacists become increasingly involved in medication management, such analysis and use of evidence-based medicine is an essential tool in providing optimal patient care, the ultimate goal of health professionals.

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