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Review article

"Assessing the methodological quality of systematic reviews in radiation oncology: A systematic review"

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ABSTRACT

Objective: The objective of our study was to evaluate the methodological quality of systematic reviews and meta-analyses in Radiation Oncology.
Methods: A systematic literature search was conducted for all eligible systematic reviews and meta-analyses in Radiation Oncology from 1966 to 2015. Methodological characteristics were abstracted from all works that satisfied the inclusion criteria and quality was assessed using the critical appraisal tool, AMSTAR. Regression analyses were performed to determine factors associated with a higher score of quality.
Results: Following exclusion based on a priori criteria, 410 studies (157 systematic reviews and 253 meta-analyses) satisfied the inclusion criteria. Meta-analyses were found to be of fair to good quality while systematic reviews were found to be of less than fair quality. Factors associated with higher scores of quality in the multivariable analysis were including primary studies consisting of randomized control trials, performing a meta-analysis, and applying a recommended guideline related to establishing a systematic review protocol and/or reporting.
Conclusions: Systematic reviews and meta-analyses may introduce a high risk of bias if applied to inform decision-making based on AMSTAR. We recommend that decision-makers in Radiation Oncology scrutinize the methodological quality of systematic reviews and meta-analyses prior to assessing their utility to inform evidence-based medicine and researchers adhere to methodological standards outlined in validated guidelines when embarking on a systematic review.

1. Introduction

Systematic reviews and meta-analyses are undeniably strong study designs that are able to provide high quality evidence through critically summarizing numerous studies into a succinct and thorough document with the aim of answering a precise research question [1,2]. These studies however, rely on the methodology of the included studies and thus are prone to flaws that can threaten the validity and quality of systematic reviews. In turn, these methodological flaws can erroneously influence clinical and policy decision-making [3,4]. Consequently, a high level of evidence and quality in systematic reviews is contingent on high methodological quality, which can only be achieved through strict adherence to methods that minimize bias and error [3].

There has been a significant increase in the number of published systematic reviews in the literature over the last decade [5,6], which has created an excellent opportunity to inform evidence-based medicine. However, the increase in quantity has not necessarily been associated with quality. A significant number of systematic reviews in numerous fields of medicine have been shown to have significant variability and alarming deficiencies [3,4,7–10]. For example, studies evaluating methodological quality of systematic reviews in Pediatric Oncology, Pediatric Urology, Orthopedic Surgery, General Surgery, and

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Periodontal Regeneration were all found to be of less than fair quality [1,3,6,7,11].

There are no systematic reviews that evaluate the methodological quality of systematic reviews in the field of Radiation Oncology. Radiation Oncology has seen impressive advances, which have significantly contributed towards an increase in cure rates for cancers that were previously associated with high mortality [12,13]. Continuing advances in Radiation Oncology make it essential that systematic reviews are rigorous and conducted with the highest methodological quality for reliable evidence-based decision-making. The aim of this study is to evaluate the methodological quality of systematic reviews using the Assessment of Multiple Systematic Reviews (AMSTAR) tool in the field of Radiation Oncology in order to identify whether serious methodological flaws exist, which in turn could mislead clinical decision-making.

2. Methods

2.1. Study Selection

We identified eligible studies by a search in MEDLINE/Ovid (from 1966 to September 2015), EMBASE/Ovid (from 1980 to September 2015) and The Cochrane Database of Systematic Reviews (CDSR) (from 2005 to September 2015). The search strategy was tailored to each database and adapted to the search filter developed by Shojania et al. [14] to identify systematic reviews (Appendix A). Furthermore, we screened reference lists of included studies to ensure our search was comprehensive.

Two authors (T. Muhammad and K. Taguchi) reviewed the title and abstract of studies identified in the database searches to assess inclusion eligibility. The full text was downloaded and reviewed if the title and abstract were insufficient to determine fulfillment of inclusion criteria. In a second round of screening, two authors (H. Hasan and T. Muhammad) reviewed the full text of all studies that passed through the first round of screening for inclusion eligibility. Studies were subsequently stratified into two groups: meta-analyses and systematic reviews. Any disagreements were settled by discussion, and the principle investigator (K. Goddard) was available as an arbitrator.

2.2. Study inclusion and exclusion criteria

To meet the inclusion criteria, a study had to be described as "*a systematic review or meta-analysis that explicitly indicates the use of a strategy for locating evidence*" based on criteria proposed by Lundh et al. [6], which we modified, focused on Radiation Oncology (i.e., with the main topic being Radiation Oncology), and available in the English language with full-text available. We excluded studies without a focused research question, individual case reports, case series associated with literature reviews, conference abstracts, letters to the editor and meta-analyses supplementing randomized control trials (RCTs). In the event of multiple publications (i.e., updating a review) or publication of the same review in multiple journals, the most recent publication was included.

2.3. Characteristics of Systematic Reviews

Two authors (T. Muhammad and J. Yu) extracted data pertinent to the AMSTAR questionnaire onto a data collection template, designed a priori, using full text unblinded versions of the included studies. Data extracted included general characteristics as well as characteristics specific to systematic reviews and meta-analyses, which could not be abstracted from AMSTAR.

2.4. Assessment of Methodological Quality

Two authors (T. Muhammad and J. Yu) assessed the methodological quality of the included studies using AMSTAR, an empirically derived, reliable, validated 11-item critical appraisal tool (Appendix B) [15–17]. The AMSTAR tool has high construct and content validity as well as inter-rater reliability [18,19]. AMSTAR however only provides a qualitative evaluation and lacks the ability to appropriately quantify systematic review quality as well as adequately assess risk of bias [20,21]. Although new tools have been developed to assess these shortcomings (e.g., ROBIS, R-AMSTAR, etc.), the utility of these tools is still to be determined [22–24]. It should be noted that the developers of AMSTAR are currently updating their tool, which will address the limitations of the original tool and improve upon it [21,25]. AMSTAR currently remains the best available validated instrument to assess the methodological quality of systematic reviews of epidemiological studies.

The items were scored according to the following classification: "No", "Yes", "Can't Answer" and "Not Applicable", where "Yes" was scored if a study fulfilled all criteria proposed for each item. Additive scores for each evaluated systematic review were calculated with the lowest possible score being 0 and the highest being 11 for meta-analyses and 9 for systematic reviews (i.e., AMSTAR items #9 and #10 were not evaluated as they are not applicable to systematic reviews). We considered an AMSTAR score of 4 or less to be of less than fair quality, 5 to 7 and 5 to 8 to be of fair to good quality and 8 or greater and 9 or greater to be of good quality for systematic reviews and meta-analyses respectively [3].

2.5. Data Analysis

We assessed the agreement between reviewers for the assessment of methodological quality using κ statistics [26] via a random sample corresponding to 10% of the total studies included. As the assessment of methodological quality was not completed independently, the random sample consisted of a subset of studies completed by one reviewer for which the other reviewer independently repeated the assessment. A κ value > 0.6 was regarded as acceptable. The methodological quality of each item on AMSTAR (i.e., AMSTAR criterion satisfied) and study characteristics are reported for systematic reviews and meta-analyses separately due to the nature of specific AMSTAR criteria focusing specifically on meta-analyses [20].

A linear regression was performed to determine whether there was a relationship between frequency of systematic reviews published in the Radiation Oncology literature as well as quality of reporting and publication year. Multivariable logistic regression was used to estimate the association between AMSTAR score and factors that could impact a systematic review in having fair or higher methodological quality. Univariable analyses were conducted on each variable and variables that had a P-value < 0.1 in the univariable analysis were considered in the final multivariable model. Odds ratios with 95% confidence intervals were calculated. All statistical tests were two-sided and P-values < 0.05 were considered to be statistically significant. Statistical analyses were performed using Statistical Analysis Software (SAS) version 9.4 (SAS Institute, Inc., Cary, NC).

3. Results

3.1. Study Selection

Our search yielded 4281 records; of these, we removed 226 duplicates, 3452 records after screening titles and abstracts, and 90 items that were not available in full text. The remaining 513 records were retrieved in full text and were assessed, which resulted in the identification of 103 records that did not meet our eligibility criteria and were excluded. Hand-searching the reference lists of the included studies did not lead to the inclusion of additional studies. In total, 410 systematic reviews were included (Fig. 1 and Appendix C).