Vaccine 32 (2014) 1678–1684

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Methodological quality of systematic reviews on influenza vaccination

Cornelius Remschmidt, Ole Wichmann, Thomas Harder*

Immunization Unit, Robert Koch Institute, Berlin, Germany

ARTICLE INFO

Article history:
Received 2 October 2013
Received in revised form
26 November 2013
Accepted 21 January 2014
Available online 7 February 2014

Keywords:
Influenza vaccination
Systematic review
Meta-analysis
Quality appraisal tool
AMSTAR
Methodological quality

ABSTRACT

Background: There is a growing body of evidence on the risks and benefits of influenza vaccination in various target groups. Systematic reviews are of particular importance for policy decisions. However, their methodological quality can vary considerably.
Objectives: To investigate the methodological quality of systematic reviews on influenza vaccination (efficacy, effectiveness, safety) and to identify influencing factors.
Methods: A systematic literature search on systematic reviews on influenza vaccination was performed, using MEDLINE, EMBASE and three additional databases (1990–2013). Review characteristics were extracted and the methodological quality of the reviews was evaluated using the assessment of multiple systematic reviews (AMSTAR) tool. *U*-test, Kruskal–Wallis test, chi-square test, and multivariable linear regression analysis were used to assess the influence of review characteristics on AMSTAR-score.
Results: Fourty-six systematic reviews fulfilled the inclusion criteria. Average methodological quality was high (median AMSTAR-score: 8), but variability was large (AMSTAR range: 0–11). Quality did not differ significantly according to vaccination target group. Cochrane reviews had higher methodological quality than non-Cochrane reviews ($p = 0.001$). Detailed analysis showed that this was due to better study selection and data extraction, inclusion of unpublished studies, and better reporting of study characteristics (all $p < 0.05$). In the adjusted analysis, no other factor, including industry sponsorship or journal impact factor had an influence on AMSTAR score.
Conclusions: Systematic reviews on influenza vaccination showed large differences regarding their methodological quality. Reviews conducted by the Cochrane collaboration were of higher quality than others. When using systematic reviews to guide the development of vaccination recommendations, the methodological quality of a review in addition to its content should be considered.

1. Introduction

When considering the best available evidence regarding vaccination, results of randomized controlled trials (RCTs), systematic reviews, and meta-analyses on vaccine efficacy and safety are commonly used to guide immunization policy decisions. For influenza vaccines, however, the unique epidemiological features of influenza viruses with seasonal variations potentially leading to a mismatch between vaccine and circulating strains complicate the interpretation of single studies reporting data from only one or two seasons and increase the importance of summarized evidence in terms of systematic reviews. In addition, since most influenza vaccines are licensed only based on RCTs demonstrating immunogenicity and not efficacy in preventing clinical outcomes, there is a need to consider high-quality observational studies assessing vaccine effectiveness [1,2]. Finally, the interpretation of efficacy and effectiveness studies is further complicated by the fact that there are obvious differences in influenza vaccine efficacy/effectiveness by vaccine type and age-group [3]. Therefore, systematic reviews of high quality that address the safety and protective effects of influenza vaccination in various vaccination target groups are of particular importance.

Systematic reviews and meta-analyses are used to synthesize results of primary investigations on a specific subject and have been advocated as a way to keep up to date with current medical literature [4]. Using a rigorous methodology with a clearly formulated research question and a comprehensive search strategy, systematic reviews should provide reproducible results and include all potentially relevant studies, thereby limiting bias and random errors [5,6]. When quantitative results are statistically summarized in meta-analyses they can provide more robust estimates than single studies [4,7]. However, systematic reviews and meta-analyses may differ considerably in their methodological quality [8,9]. Accordingly, systematic reviews with major methodological flaws might lead to false conclusions on the evidence, which might have a negative impact on decision-making processes [10].

Therefore, critical appraisal of the quality of systematic reviews is important. Several instruments have been developed that assess

* Corresponding author. Tel.: +49 30 18754 3565; fax: +49 30 18754 3341.
E-mail address: HarderT@rki.de (T. Harder).

0264-410X/$ – see front matter © 2014 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.vaccine.2014.01.060

the quality of systematic reviews and meta-analyses [11–13]. Based on the most commonly used instruments, Shea et al. developed a tool for the assessment of multiple systematic reviews (AMSTAR) to measure their methodological quality, comprising 11 domains [14]. AMSTAR can be used as a cumulative score where a higher number of fulfilled domains ("yes") corresponds to a higher methodological quality, which translates in a maximum (i.e., highest quality) score of 11 points [15,16].

The goal of this study was to systematically identify all systematic reviews on the efficacy, effectiveness and safety of vaccines used against seasonal influenza in various target groups and to assess their methodological quality using the AMSTAR tool. Furthermore, we investigated which characteristics had an impact on the quality of these reviews.

2. Methods

2.1. Literature search and study selection

To identify systematic reviews on influenza vaccination we performed a systematic literature search (date of search: 15 May 2013) using MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects and Health Technology Assessment Database (for search strategy, see Appendix A).

To be eligible, a systematic review had to fulfill the following inclusion criteria: (1) systematic review on the efficacy, effectiveness and/or safety of vaccines against seasonal influenza; (2) published after 1990; (3) written in English or German. Two reviewers (CR and TH) independently screened titles and abstracts of identified publications. Potentially eligible publications were reviewed as full text. Disagreements were resolved by discussions until consensus was achieved.

2.2. Data extraction and assessement of methodological quality

From each eligible systematic review, two independent reviewers (CR and TH) extracted study characteristics and assessed methodological quality. In the case of disagreements, a final decision was made by consensus.

The AMSTAR tool was used to determine the methodological quality of the included systematic reviews [14]. Investigators assessed each included review along the 11 domains of AMSTAR (Box 1). Each domain was answered with either "yes", "no", "not applicable (n/a)" or "can't answer". AMSTAR summary score was formed by summarizing the number of domains which were answered with "yes". A data base was constructed including the extracted review characteristics and the results of the quality assessment process for the AMSTAR summary score as well as for all 11 AMSTAR domains.

Box 1: Description of AMSTAR domains (according to Ref. [14]).

1. Was an 'a priori' design provided?
2. Was there duplicate study selection and data extraction?
3. Was a comprehensive literature search performed?
4. Was the status of publication (i.e., grey literature) used as an inclusion criterion?
5. Was a list of studies (included and excluded) provided?
6. Were the characteristics of the included studies provided?
7. Was the scientific quality of the included studies assessed and documented?
8. Was the scientific quality of the included studies used appropriately in formulating conclusion?
9. Were the methods used to combine the findings of the studies appropriate?
10. Was the likelihood of publication bias assessed?
11. Were potential conflicts of interest declared?

2.3. Definitions

2.3.1. Vaccination target groups

Each review was allocated independently by both reviewers (CR and TH) to one of the following groups according to the vaccination target groups defined in the respective review by in- and exclusion criteria: healthy children, healthy adults, elderly persons, health care personell, patients with lung diseases, patienties with malignancies, immunocompromised patients. Reviews covering healthy adults and healthy children without exclusion of special risk groups were defined as "general population". Reviews focusing on specific vaccines (e.g., only intradermal vaccines) or covering other (e.g., multiple sclerosis) or more than one of the above mentioned subgroups (e.g., healthy and chronically ill children and adults) were defined as miscellaneous. Again, any disagreement was resolved by discussion between the authors.

2.3.2. Specialized journal

A journal was defined as "specialized" if its aims and scopes focuses on vaccination or infectious diseases.

2.3.3. Impact factor

For the purpose of this study, the Thomson Reuters Impact factor was used as of May 2013 (http://wokinfo.com/essays/impact-factor/).

2.3.4. Journal article version of a Cochrane review

Systematic review that has been published–in addition to the Cochrane journal- as a shortened version in a non-Cochrane journal. In addition to the main analysis which included both versions of these reviews, a sensitivity analysis was performed by excluding the full Cochrane versions of the respective systematic reviews.

2.3.5. Publication bias

According to the recommended use of the AMSTAR-tool, systematic reviews with less than 10 studies were scored for domain 10 "yes" if the authors mentioned that publication bias could not be assessed because of fewer than 10 included studies.

2.4. Statistical analysis

Results of descriptive statistics were displayed as median and range or n (%), as appropriate. Differences in AMSTAR summary scores according to review characteristics were compared using Mann–Whitney U-test or Kruskal–Wallis test. Chi-squared test was used to compare single AMSTAR domains. Multivariable linear regression was applied to analyze the influence of review characteristics on AMSTAR summary score. Two-sided hypothesis tests were performed and a p-value of less than 0.05 was considered as statistically significant. All calculation were made using IBM SPSS Statistics 20.

3. Results

The systematic literature review led to the identification of 564 publications. After exclusion of irrelevant records or studies which did not fulfill the inclusion criteria (see Appendix B for the list of excluded studies), a total of 46 systematic reviews [17–62] were found to be eligible (Fig. 1). Review topics covered by the included systematic reviews are shown in Table 1. Two updates of systematic