

BACKGROUND

ClinicalTrials.gov (CT) is an increasingly important resource for systematic reviewers attempting to identify published and unpublished clinical studies. In addition to clinical studies, however, some searches of the CT database also return systematic reviews (SRs) (Fig. 1). When I inquired about the SRs appearing in the results, the NLM Help Desk responded that “We do not recommend that systematic reviews be entered in ClinicalTrials.gov, since we only want the results of a clinical trial entered once. However, we will not refuse them if they are entered.” I wanted to find out how many SRs are included, describe their characteristics, and suggest search strategies for those wishing to exclude them.

| Descriptive Information | |
|---------------------------|---|
| Brief Title ICMJE | A Systematic Review of Studies of the Effect of Influenza Vaccine Against Mismatched Strains |
| Official Title ICMJE | Effect of Influenza Vaccine Against Mismatched Strains: Systematic Review |
| Brief Summary | The purpose of this study is to consolidate the cross-protection offered by influenza vaccines against circulating influenza A or B viruses that are not antigenically well-matched to vaccine strains and to determine the degree of cross-protection separately for influenza A and influenza B, through a systematic review of the literature. |
| Detailed Description | The research question of this project is: "What is the cross-protection afforded by vaccination (using an LAIV, TIV, or other type of vaccine) against influenza A or B and their subtypes and lineages?" The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement will be used to guide the reporting of this review. Studies reporting cross-protection data after vaccination with approved formulations of influenza vaccines with influenza A or B will be included. Inclusion will not be limited by publication status, or year of dissemination but will be limited to randomized clinical trials (RCTs) and quasi-RCTs comparing influenza vaccine(s) with placebo. Only RCTs written in English will be included. A meta-analysis will be conducted if there is sufficient data. |
| Study Type ICMJE | Observational |
| Study Design ICMJE | Not Provided |
| Target Follow-Up Duration | Not Provided |
| Biospecimen | Not Provided |
| Sampling Method | Non-Probability Sample |
| Study Population | Healthy subjects vaccinated with an influenza vaccine. |
| Condition ICMJE | Influenza |
| Intervention ICMJE | Biological: Vaccines Unadjuvanted, monovalent, and trivalent vaccines, and vaccines delivered intramuscularly, intradermally, or intranasally, depending on what is found in the included studies. |
| Study Group/Cohort (s) | Cross-Protection Studies Intervention: Biological: Vaccines |

Fig. 1. An example of a systematic review in ClinicalTrials.gov.

METHODS

Conduct a CT search for “systematic review” (see fig. 2) without limiting by field in case an SR was not explicitly titled as such. Screen the results for those records representing SRs as opposed to, e.g., mentioning one in the background to a clinical trial. Identify the total number of SRs. Test strategies for their ability to exclude them and calculate sensitivity, precision [1] and specificity [2].

Supplemental Data

The results coded with systematic review status are available as a supplemental file at <http://jdc.jefferson.edu/aisrpubs/45/>

Example: "Heart attack" AND "Los Angeles"

Search for studies: Search

Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

Home > Find Studies > Advanced Search Text Size

Advanced Search

Fill in any or all of the fields below. Click on the label to the left of each search field for more information or read the Help

Search Terms: Search Help

Recruitment: Exclude Unknown status

Study Type:

Study Results:

Eligibility Criteria:

Age: years or Group: Child (birth-17) Adult (18-65) Senior (66+)

Gender:

Accepts Healthy Volunteers: Healthy volunteers may participate in the study

Targeted Search:

Conditions:

Interventions:

Title Acronym/Titles:

Outcome Measures:

Sponsor/Collaborators:

Sponsor (Lead):

Study IDs:

Exact match Exact match

Fig. 2. The search was for the phrase “systematic review” in all fields.

RESULTS

I ran a search for “systematic review” (in quotes) in the advanced search > Search Terms (field) on July 14, 2016, and applying no other limits, downloaded 181 results for analysis from among the 220,113 total number of records in the CT database. Of the 181 records, 47 (26%) were systematic reviews (Fig. 3). All 47 were listed as Study Type: Observational. The remaining 134 records that were not SRs included a mix of Observational (21, 15.7%) and Interventional (113, 84.3%) study types.

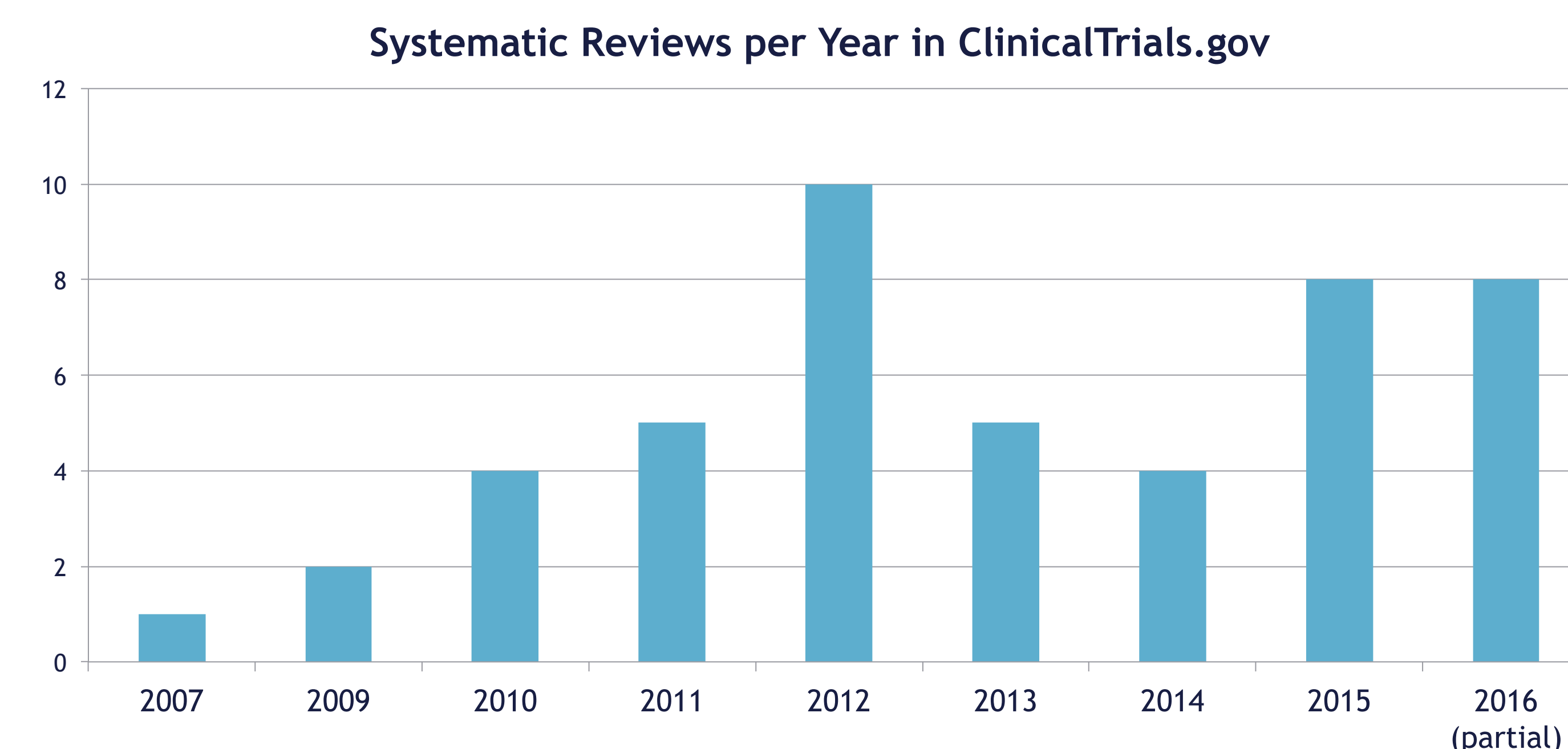


Fig. 3. The number of systematic reviews registered in ClinicalTrials.gov based on date “first received.”

FILTER

Title searching offers an effective way to avoid SRs: all but two true SRs had “systematic review” or “meta-analysis” in the Brief or Official Title. So in the expert search you could add the filter:

NOT ("systematic review" [TITLES] OR "metaanalysis" [TITLES]).

This filter has a sensitivity of 94.8%, precision of 96.9%, and specificity of 91.5%.

| Formulas for calculating sensitivity, specificity and precision | | | |
|---|--------------------|---------------------|----------------|
| Articles | Eligible articles | Ineligible articles | Total articles |
| Retrieved by search filter | 127 (a) | 4 (b) | 131 (a + b) |
| Not retrieved by search filter | 7 (c) | 43 (d) | 50 (c + d) |
| Total | 134 (a + c) | 47 (b + d) | 181 (N) |

Sensitivity = Number of eligible articles retrieved by the search filter / total number of eligible articles in the validation set = $a / (a + c) = 127 / 134 = 94.8\%$

Specificity = Number of ineligible articles not retrieved by the search filter / total number of ineligible articles = $d / (b + d) = 43 / 47 = 91.5\%$

Precision = Number of eligible articles retrieved by the search filter / total number of articles retrieved = $a / (a + b) = 127 / 131 = 96.9\%$

LIMITATIONS

This study didn’t search for records titled as meta analyses or other names such as “systematic overview” that would add to the number of records violating the intention of the database that the results of a clinical trial be entered once.

CONCLUSIONS

The number of systematic reviews registered in CT is small at this time. They can be accurately avoided if you are looking for interventional studies by using the Study Type field, but not if you are looking for observational studies. Using the proposed title searching filter offers an effective way to avoid them.

Librarians should advise their teams to register systematic reviews in appropriate sources such as PROSPERO (<http://www.crd.york.ac.uk/PROSPERO/>), but not ClinicalTrials.gov.

REFERENCES

- Lunny, C., McKenzie, J. E., & McDonald, S. (2016). Retrieval of overviews of systematic reviews in MEDLINE was improved by the development of an objectively derived and validated search strategy. *Journal of Clinical Epidemiology*, 74, 107-118. doi:10.1016/j.jclinepi.2015.12.002
- van de Glind, E. M., van Munster, B. C., Spijker, R., Scholten, R. J., & Hooft, L. (2012). Search filters to identify geriatric medicine in MEDLINE. *Journal of the American Medical Association: JAMA*, 19(3), 468-472. doi:10.1136/amiainl-2011-000319