Chapter II

REVIEW OF LITERATURE
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Review of literature

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BACKGROUND: In maternal medicine, research evidence is scattered making it difficult to access information for clinical decision making. Systematic reviews of good methodological quality are essential to provide valid inferences and to produce usable evidence summaries to guide management. This review assesses the methodological features of existing systematic reviews in maternal medicine, comparing Cochrane and non-Cochrane reviews in maternal medicine. METHODS: Medline, Embase, Database of Reviews of Effectiveness (DARE) and Cochrane Database of Systematic Reviews (CDSR) were searched for relevant reviews published between 2001 and 2006. We selected those reviews in which a minimum of two databases were searched and the primary outcome was related to the maternal condition. The selected reviews were assessed for information on framing of question, literature search and methods of review. RESULTS: Out of 2846 citations, 68 reviews were selected. Among these, 39 (57%) were Cochrane reviews. Most of the reviews (50/68, 74%) evaluated therapeutic interventions. Overall, 54/68 (79%) addressed a focussed question. Although 64/68 (94%) reviews had a detailed search description, only 17/68 (25%) searched without language restriction. 32/68 (47%) attempted to include unpublished data and 11/68 (16%) assessed for the risk of missing studies quantitatively. The reviews had deficiencies in the assessment of validity of studies and exploration for heterogeneity. When compared to Cochrane reviews,
other reviews were significantly inferior in specifying questions (OR 20.3, 95% CI 1.1-381.3, p = 0.04), framing focussed questions (OR 30.9, 95% CI 3.7-256.2, p = 0.001), use of unpublished data (OR 5.6, 95% CI 1.9-16.4, p = 0.002), assessment for heterogeneity (OR 38.1, 95% CI 2.1, 688.2, p = 0.01) and use of meta-analyses (OR 3.7, 95% CI 1.3-10.8, p = 0.02). CONCLUSION: This study identifies areas which have a strong influence on maternal morbidity and mortality but lack good quality systematic reviews. Overall quality of the existing systematic reviews was variable. Cochrane reviews were of better quality as compared to other reviews. There is a need for good quality systematic reviews to inform practice in maternal medicine.

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We set out to determine the quality of existing systematic reviews on multiple pregnancies. We conducted an electronic search in MEDLINE (1951 - 2005), EMBASE (1974 - 2005) and the Cochrane Database for Systematic reviews (2005:2) and a hand-search of reference lists without any language restrictions to identify relevant reviews. Two reviewers independently selected review articles in which a publicly available database was searched for studies concerning multiple pregnancies, and assessed them for quality of methods of review. Information was extracted on framing of question, literature search and data synthesis. Of 342 citations 14 (4%) eligible reviews were identified. Only 8/14 reviews specified the review question. Adequate literature search without language restriction and the use of a reference list was found in 7/14 reviews, but the risk of missing studies was assessed in only 1/14 reviews. Quality assessment of included studies was reported in 7/14 and
tabulation of their findings was reported in 8/14 reviews, but heterogeneity of results was evaluated in only 4/14 reviews. Meta-analysis was employed in 3/14 reviews. Systematic reviews of existing studies on multiple pregnancies are infrequent and it is difficult to generate robust inferences from them as they lack good methodology.

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BACKGROUND: Improving quality and effectiveness of health care is one of the priorities of health policies. Hospital or physician volume of activity may be a measurable variable with a relevant impact on effectiveness of health care. There are several studies and systematic reviews evaluating the association between volume and outcome of health care. The aim of this review is to identify: areas, clinical conditions or interventions (prevention, diagnostic, therapeutic, surgical or clinical) for which an association between volume and outcome has been investigated; those for which an association between volume and outcome has been proved.

METHODS: Overview of systematic reviews and Health Technology Assessment reports; search of MEDLINE, EMBASE, The Cochrane Library, Web sites of Health Technology Assessment, other HTA Agencies, National guideline Clearinghouse, National Health Care quality tools (1995-february 2005). For each studied area results are described separately for each review due to the heterogeneity of outcomes, volume thresholds and results reported. No metanalysis has been conducted. Completeness of reporting of the systematic reviews has been evaluated using the QUOROM statement. For each review we evaluated the number of studies included and the proportion of studies with statistically significant results (p < 0,05). As far as in-hospital mortality is concerned, the different areas have been
classified in the following groups: Strong evidence of positive association: areas with > or =10 studies included in the reviews, and high prevalence (> or =50%) of positive studies (p <0. 05) in the majority of reviews. Weak evidence of association: areas with 5 to 9 studies included in the reviews and high prevalence (> or =50%) of positive studies (p <0.05) in the majority of reviews. Weak evidence of lack of association: areas with 5 to 9 studies included in the reviews and high prevalence (>50%) of not statistically significant studies (p >0.05) in the majority of reviews. No sufficient evidence of association: areas with less than 5 studies included in the reviews. No evidence of association: areas with > or =10 studies included in the reviews, and high prevalence (>50%) of not statistically significant studies (p >0.05) in the majority of reviews. The same literature search was then applied to identify primary studies published in each considered area following the most recent systematic review published. RESULTS AND DISCUSSION: We identified 21 systematic reviews and included 11 of them analysing 46 different areas. The majority of studies evaluate the effect of specific surgical procedures; the main outcomes considered are hospital mortality and 5 year survival for cancers. Considering in-hospital mortality as outcome, in 11 areas there is strong evidence of association between volume of activity and outcome: abdominal aortic aneurysm (unruptured), percutaneous transluminal coronary angioplasty knee arthroplasty coronary artery bypass, surgery for oesophageal and pancreatic cancer, surgery for prostate cancer, colecistectomy, carotid endarterectomy, myocardial infarction, neonatal intensive care. It is never possible however to identify a unique volume threshold. For some of these areas, particularly coronary angioplasty and coronary artery bypass, there are many new studies published following the last systematic review; some specific aspects are being investigated such as the role of temporal changes in the association, the effect of
different risk adjustment procedures and the separate role of physician or hospital volume. In some cases, for example knee arthroplasty in-hospital mortality could be an inadequate outcome on which judging the strength of association, in fact, the few studies evaluating other outcomes such as complications provide inconsistent results. For a range of areas the evidence of association is weak: AIDS, appendicectomy, cardiac catheterization, surgery for breast, lung, stomach cancer, hernia repair, hip fracture, hysterectomy and injuries. As far as AIDS is concerned, the few number of studies found is probably due to the lack of studies published after the introduction of effective therapies. All the included studies show an evidence of association between volume and in-hospital mortality. In no case we found weak evidence of lack of association while we identified three conditions for which the number of studies included in the reviews together with the prevalence of non significant studies do suggest lack of association; these are abdominal aortic aneurysm (ruptured), hip arthroplasty and surgery for colorectal cancer. In the case of hip arthroplasty as well, inhospital mortality could be an inadequate outcome, but only one old study found a positive association with risk of complications. Eventually there is a group of areas (n=22) for which there is not enough evidence to draw conclusions about the association between volume and outcome due to a small number of studies. In some cases, such as transplants, this could be due to the low rate of events; in this case all the few published studies show positive results. There are some limitations which should be taken into account in the interpretation of these results: despite the overall good completeness of reporting of the included reviews, the majority of studies included in the reviews themselves are cross-sectional studies representing a very weak study design to evaluate causality of the investigated association. Moreover the methodology of risk adjustment applied is heterogenous among studies.
and it is difficult to know the extent to which this can affect the observed results. It is eventually necessary to consider the possible occurrence of publication bias which could lead to an overestimation of the positive effect of volume on health care outcomes attributable to the lack of publication of negative studies. CONCLUSIONS: In some areas the evidence seems strong enough to guide health care organizational choices, although it is not possible to identify well defined volume thresholds. In other areas, particularly for non surgical conditions, where there is not enough evidence, it seems necessary to conduct proper epidemiological studies. Also the evaluation of effectiveness of using volume as an instrument of health policy requires further research. Taking into account the rapid and continuing process of technology development, the definition of standard and prerequisite volumes of care should be specific of each temporal period and health care system. It is therefore a dynamic process requiring a continuous review of the available evidence. In the area of evidence based public health, the limited available evidence should not impair the choice of actions based on limited evidence, but rather it should lead to the application of the few available evidence on one side and to the planning of proper research in the areas of lack of evidence.

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OBJECTIVE: To independently appraise the methodological quality of a sample of reports of meta-analyses that address critical care topics in the Cochrane Database of Systematic Reviews compared with the quality of reports published in regular journals, using a validated assessment
instrument, the Overview Quality Assessment Questionnaire (OQAQ).

DATA SOURCE: Studies were selected from a search of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews from 1994 to 2003, using multiple search terms for critical care and sensitive filters to identify meta-analyses. STUDY SELECTION: Two authors independently selected meta-analyses that addressed topics pertinent to critical care medicine. DATA EXTRACTION: Two authors independently extracted the data. The proportion of reports that met each component of the OQAQ was determined, as was the overall quality score. Meta-analyses published in the Cochrane Database of Systematic Reviews were compared with those published in regular journals. DATA SYNTHESIS: There were 36 reports of meta-analyses in the Cochrane Database of Systematic Reviews and 103 reports of meta-analyses published in regular journals; 11 of these were reports of Cochrane reviews. The meta-analyses published in the Cochrane Database of Systematic Reviews were more likely to fulfill most components of the OQAQ. The median overall OQAQ scores indicated significant methodological problems in the reports regardless of the source of publication, although the reports in the Cochrane database scored higher than those in regular journals (five compared with two, p<.001). Major methodological flaws, notably failure to appropriately refer to the validity of included studies, were found in meta-analyses in both the Cochrane Database of Systematic Reviews and regular journals (44.4% and 79.3%, respectively). CONCLUSIONS: Although the quality of reports of meta-analyses published in the Cochrane Database of Systematic Reviews is superior to the quality of reports of meta-analyses published in regular journals, there is significant room for improvement. Clinicians should critically appraise all reports of meta-analyses before considering the results, regardless of the source of publication.
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BACKGROUND: Since the early 1970s, the efficacy of acupuncture for treating clinical conditions has been evaluated in several hundred randomized trials. Results from these trials have been synthesized in systematic reviews. A well-designed systematic review provides the highest level of evidence for establishing the efficacy of a clinical intervention. OBJECTIVES: The present study assesses the source of original literature contributing to Cochrane reviews on acupuncture. Databases searched to retrieve original studies are evaluated. The distribution of controlled trials in acupuncture across different topic areas and journals, the ability of the reviews to provide conclusive results, and the proportion of original studies indexed with MEDLINE are evaluated. METHODS: Systematic reviews on acupuncture were extracted from the Cochrane Database of Systematic Reviews. The key search term used was "acupuncture." When more than one systematic review was retrieved on the same topic, the most recent review was included. Indexing of individual clinical trials with MEDLINE was searched using the Single Citation Matcher in PubMed. RESULTS: A total of 94 papers were retrieved from the Cochrane database, of which 10 were included in the analysis. The most common subject areas were related to chronic pain. Considerable heterogeneity was observed in the number of databases searched (median 5, range 3-12). A total of 69% (74/108) papers were indexed with PubMed. Only 13% (14/108) of the papers were published in the primary acupuncture journals. Conclusive statements about the efficacy of acupuncture were made in only 2 of the 10 systematic reviews. CONCLUSIONS: Considerable methodological diversity exists
in the comprehensiveness of database searches for Cochrane systematic reviews on acupuncture. This diversity makes the reviews prone to bias and adds another layer of complexity in interpreting the acupuncture literature.

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CONTEXT: Review articles are important sources of information to help guide decisions by clinicians, patients, and other decision makers. Ideally, reviews should include strategies to minimize bias and to maximize precision and be reported so explicitly that any interested reader would be able to replicate them. OBJECTIVE: To compare the methodological and reporting aspects of systematic reviews and meta-analyses published by the Cochrane Collaboration with those published in paper-based journals indexed in MEDLINE. DATA SOURCES: The Cochrane Library, issue 2 of 1995, and a search of MEDLINE restricted to 1995. STUDY SELECTION: All 36 completed reviews published in the Cochrane Database of Systematic Reviews and a randomly selected sample of 39 meta-analyses or systematic reviews published in journals indexed by MEDLINE in 1995. DATA EXTRACTION: Number of authors, trials, and patients; trial sources; inclusion and exclusion criteria; language restrictions; primary outcome; trial quality assessment; heterogeneity testing; and effect estimates. Updating by 1997 was evaluated. RESULTS: Reviews found in MEDLINE included more authors (median, 3 vs 2; P<.001), more trials (median, 13.5 vs 5; P<.001), and more patients (median, 1280 vs 528; P<.001) than Cochrane reviews. More
Cochrane reviews, however, included a description of the inclusion and exclusion criteria (35/36 vs 18/39; P<.001) and assessed trial quality (36/36 vs 12/39; P<.001). No Cochrane reviews had language restrictions (0/36 vs 7/39; P<.01). There were no differences in sources of trials, heterogeneity testing, or description of effect estimates. By June 1997, 18 of 36 Cochrane reviews had been updated vs 1 of 39 reviews listed in MEDLINE. CONCLUSIONS: Cochrane reviews appear to have greater methodological rigor and are more frequently updated than systematic reviews or meta-analyses published in paper-based journals.

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BACKGROUND: In order to carry out a methodological research survey of systematic reviews of adverse effects we needed to retrieve a sample of systematic reviews in which the primary outcome is an adverse effect or effects. METHODS: We carried out searches of the Database of Abstracts of Reviews of Effects (DARE) and the Cochrane Database of Systematic Reviews (CDSR) for systematic reviews of adverse effects published between 1994 to 2005. The search strategies used a combination of text words in the title and abstract, Medical Subject Headings (MeSH) and subheadings/qualifiers. In addition, DARE records in progress were hand searched. No language restrictions were placed on any of the searches. The performance, in terms of sensitivity and precision, of the search strategies and their combinations were tested in DARE and CDSR. RESULTS: In total 3635 records were screened of which 257 met our inclusion criteria. The precision of the searches in CDSR was low (0% to 3%), and no one search strategy could retrieve all the relevant records in either DARE or CDSR. Hand searching the
records from DARE and CDSR not retrieved by our searches indicated that we had missed relevant systematic reviews in both DARE and CDSR. The sensitivities of many of the search combinations were comparable to those found when searching for primary studies in which adverse effects are secondary outcomes. CONCLUSION: Searching major databases of systematic reviews, for systematic reviews of adverse effects, proved more difficult than anticipated due to a lack of standard terminology used by the authors, inadequate indexing and the variations in the search interfaces of the databases. At present hand searching all records in DARE and CDSR seems to be the only way to ensure retrieval of all systematic reviews of adverse effects in these databases.

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BACKGROUND: Despite the growing reputation and subject coverage of the Cochrane Database of Systematic Reviews, many systematic reviews continue to be published solely in paper-based health care journals. This study was designed to determine why authors choose to publish their systematic reviews outside of the Cochrane Collaboration and if they might be interested in converting their reviews to Cochrane format for publication in the Cochrane Database of Systematic Reviews. METHODS: Cross-sectional survey of Australian primary authors of systematic reviews not published on the Cochrane Database of Systematic Reviews identified from the Database of Abstracts of Reviews of Effectiveness. RESULTS: We identified 88 systematic reviews from the Database of Abstracts of Reviews of Effectiveness with an Australian as the primary author. We surveyed 52 authors for whom valid contact
information was available. The response rate was 88 per cent (46/52). Ten authors replied without completing the survey, leaving 36 valid surveys for analysis. The most frequently cited reasons for not undertaking a Cochrane review were: lack of time (78%), the need to undergo specific Cochrane training (46%), unwillingness to update reviews (36%), difficulties with the Cochrane process (26%) and the review topic already registered with the Cochrane Collaboration (21%). (Percentages based on completed responses to individual questions.)

Nearly half the respondents would consider converting their review to Cochrane format. Dedicated time emerged as the most important factor in facilitating the potential conversion process. Other factors included navigating the Cochrane system, assistance with updating and financial support. Eighty-six per cent were willing to have their review converted to Cochrane format by another author. CONCLUSION: Time required to complete a Cochrane review and the need for specific training are the primary reasons why some authors publish systematic reviews outside of the Cochrane Collaboration. Encouragingly, almost half of the authors would consider converting their review to Cochrane format. Based on the current number of reviews in the Database of Abstracts of Reviews of Effectiveness, this could result in more than 700 additional Cochrane reviews. Ways of supporting these authors and how to provide dedicated time to convert systematic reviews needs further consideration.


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BACKGROUND: Provision of evidence on costs alongside evidence on
the effects of interventions can enhance the relevance of systematic reviews to decision-making. However, patterns of use of economics methods alongside systematic review remain unclear. Reviews of evidence on the effects of interventions are published by both the Cochrane and Campbell Collaborations. Although it is not a requirement that Cochrane or Campbell Reviews should consider economic aspects of interventions, many do. This study aims to explore and describe approaches to incorporating economics methods in a selection of Cochrane systematic reviews in the area of health promotion and public health, to help inform development of methodological guidance on economics for reviewers. METHODS: The Cochrane Database of Systematic Reviews was searched using a search strategy for potential economic evaluation studies. We included current Cochrane reviews and review protocols retrieved using the search that are also identified as relevant to health promotion or public health topics. A reviewer extracted data which describe the economics components of included reviews. Extracted data were summarised in tables and analysed qualitatively. RESULTS: Twenty-one completed Cochrane reviews and seven review protocols met inclusion criteria. None incorporate formal economic evaluation methods. Ten completed reviews explicitly aim to incorporate economics studies and data. There is a lack of transparent reporting of methods underpinning the incorporation of economics studies and data. Some reviews are likely to exclude useful economics studies and data due to a failure to incorporate search strategies tailored to the retrieval of such data or use of key specialist databases, and application of inclusion criteria designed for effectiveness studies. CONCLUSION: There is a need for consistency and transparency in the reporting and conduct of the economics components of Cochrane reviews, as well as regular dialogue between Cochrane reviewers and economists to develop increased
capacity for economic analyses alongside such reviews. Use of applicable economics methods in Cochrane reviews can help provide the international context within which economics data can be interpreted and assessed as a preliminary to full economic evaluation.

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**BACKGROUND:** Although the methods for conducting systematic reviews of efficacy are well established, there is much less guidance on how systematic reviews of adverse effects should be performed.

**METHODS:** In order to determine where methodological research is most needed to improve systematic reviews of adverse effects of health care interventions, we conducted a descriptive analysis of systematic reviews published between 1994 and 2005. We searched the Database of Abstracts of Reviews of Effects (DARE) and The Cochrane Database of Systematic Reviews (CDSR) to identify systematic reviews in which the primary outcome was an adverse effect or effects. We then extracted data on many of the elements of the systematic review process including: types of interventions studied, adverse effects of interest, resources searched, search strategies, data sources included in reviews, quality assessment of primary data, nature of the data analysis, and source of funding.

**RESULTS:** 256 reviews were included in our analysis, of which the majority evaluated drug interventions and pre-specified the adverse effect or effects of interest. A median of 3 resources were searched for each review and very few reviews (13/256) provided sufficient information to reproduce their search strategies. Although more than three quarters (185/243) of the reviews sought to include data from sources other than randomised controlled trials, fewer than half (106/256)
assessed the quality of the studies that were included. Data were pooled quantitatively in most of the reviews (165/256) but heterogeneity was not always considered. Less than half (123/256) of the reviews reported on the source of funding. CONCLUSION: There is an obvious need to improve the methodology and reporting of systematic reviews of adverse effects. The methodology around identification and quality assessment of primary data is the main concern.

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AIMS: To analyse the effect on systematic reviews in diabetes interventions of including only trials that are indexed in medline, and to assess the impact of adding trials from other databases and the grey literature. METHODS: All systematic reviews of diabetes interventions which included a meta-analysis of randomized controlled trials, and were published since 1996, were selected. The impact on the meta-analysis of including only those trials indexed in medline, and the effect of then adding trials from other sources, was assessed. Where possible this was measured quantitatively, by redoing the meta-analysis, otherwise a qualitative estimate was made. RESULTS: Forty-four systematic reviews met our inclusion criteria. There were 120 articles reporting trial data which were not indexed in medline. These came from 52% of the reviews. In 34% of the reviews, basing a meta-analysis on a search of only medline would miss trials that could affect the result. Sources of non-medline data which had the biggest effect on the meta-analyses were journal articles from central and embase (mainly in Diabetes, Nutrition and Metabolism) and unpublished data (mainly from industry). The exceptions were journal articles on herbal medicine, mostly indexed in
Chinese language databases. CONCLUSIONS: A search of only the medline database is insufficient for systematic reviews of diabetes, because in about 34% of reviews the missed trials could affect the results of the meta-analysis. It is recommended that central (on the Cochrane Library) also be searched. Scanning meeting abstracts, and seeking unpublished data are also recommended if the intervention has only recently been introduced.

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BACKGROUND: Systematic reviews can serve as a tool in translation of basic life sciences research from laboratory to human research and healthcare. The extent to which reviews of animal research are systematic and unbiased is not known. METHODS: We searched, without language restrictions, Medline, EMBASE, bibliographies of known reviews (1996-2004) and contacted experts to identify citations of reviews of basic science literature which, as a minimum, performed search of a publicly available resource. From these we identified reviews of animal studies where laboratory variables were measured or where treatments were administered to live animals to examine their effects, and compared them with reviews of bench studies in which human or animal tissues, cell systems or organ preparations were examined in laboratories to better understand mechanisms of diseases. RESULTS: Systematic reviews of animal studies often lacked methodological features such as specification of a testable hypothesis (9/30, 30%); literature search without language restriction (8/30, 26.6%); assessment of publication bias (5/30, 16.6%), study validity (15/30, 50%) and heterogeneity (10/30, 33.3%); and meta-analysis for quantitative synthesis (12/30, 40%). Compared to reviews of
bench studies, they were less prone to bias as they specified the question (96.6% vs. 80%, p = 0.04), searched multiple databases (60% vs. 26.6%, p = 0.01), assessed study quality (50% vs. 20%, p = 0.01), and explored heterogeneity (33.3% vs. 2.2%, p = 0.001) more often. CONCLUSION: There seems to be a gradient of frequency of methodological weaknesses among reviews: Attempted systematic reviews of whole animal research tend to be better than those of bench studies, though compared to systematic reviews of human clinical trials they are apparently poorer. There is a need for rigour when reviewing animal research.

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BACKGROUND: Failure to be comprehensive can distort the results of a systematic review. Conversely, extensive searches may yield unmanageable number of citations of which only few may be relevant. Knowledge of usefulness of each source of information may help to tailor search strategies in systematic reviews. METHODS: We conducted a systematic review of prevalence/incidence of maternal mortality and morbidities from 1997 to 2002. The search strategy included electronic databases, hand searching, screening of reference lists, congress abstract books, contacting experts active in the field and web sites from less developed countries. We evaluated the effectiveness of each source of data and discuss limitations and implications for future research on this topic. RESULTS: Electronic databases identified 64098 different citations of which 2093 were included. Additionally 487 citations were included from other sources. MEDLINE had the highest yield identifying
about 62% of the included citations. BIOSIS was the most precise with 13.2% of screened citations included. Considering electronic citations alone (2093), almost 20% were identified uniquely by MEDLINE (400), 7.4% uniquely by EMBASE (154), and 5.6% uniquely by LILACS (117). About 60% of the electronic citations included were identified by two or more databases. CONCLUSIONS: This analysis confirms the need for extending the search to other sources beyond well-known electronic databases in systematic reviews of maternal mortality and morbidity prevalence/incidence. These include regional databases such as LILACS and other topic specific sources such as hand searching of relevant journals not indexed in electronic databases. Guidelines for search strategies for prevalence/incidence studies need to be developed.

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BACKGROUND: Systematic reviewers seek to comprehensively search for relevant studies and summarize these to present the most valid estimate of intervention effectiveness. The more resources searched, the higher the yield, and thus time and costs required to conduct a systematic review. While there is an abundance of evidence to suggest how extensive a search for randomized controlled trials (RCTs) should be, it is neither conclusive nor consistent. This systematic review was conducted in order to assess the value of different resources to identify trials for inclusion in systematic reviews. METHODS: Seven electronic databases, four journals and Cochrane Colloquia were searched. Key authors were contacted and references of relevant articles screened. Included studies compared two or more sources to find RCTs or controlled clinical trials (CCTs). A checklist was developed and applied to assess quality of
reporting. Data were extracted by one reviewer and checked by a second. Medians and ranges for precision and recall were calculated; results were grouped by comparison. Meta-analysis was not performed due to large heterogeneity. Subgroup analyses were conducted for: search strategy (Cochrane, Simple, Complex, Index), expertise of the searcher (Cochrane, librarian, non-librarian), and study design (RCT and CCT).

RESULTS: Sixty-four studies representing 13 electronic databases met inclusion criteria. The most common comparisons were MEDLINE vs. handsearching (n = 23), MEDLINE vs. MEDLINE+handsearching (n = 13), and MEDLINE vs. reference standard (n = 13). Quality was low, particularly for the reporting of study selection methodology. Overall, recall and precision varied substantially by comparison and ranged from 0 to 100% and 0 to 99%, respectively. The trial registries performed the best with median recall of 89% (range 84, 95) and median precision of 96.5% (96, 97), although these results are based on a small number of studies. Inadequate or inappropriate indexing was the reason most cited for missing studies. Complex and Cochrane search strategies (SS) performed better than Simple SS.

CONCLUSION: Multiple-source comprehensive searches are necessary to identify all RCTs for a systematic review, although indexing needs to be improved. Although trial registries demonstrated the highest recall and precision, the Cochrane SS or a Complex SS in consultation with a librarian are recommended. Continued efforts to develop CENTRAL should be supported.